FINAL REPORT

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Test Substance:
4-Nitro-3-(trifluoromethyl)phenol (TFM)

Sponsor:
U.S. Geological Survey (USGS)
2630 Fanta Reed Road
La Crosse, Wisconsin 54603

On behalf of:

U.S. Fish and Wildlife Service
Lake Champlain Fish and Wildlife Conservation Office
11 Lincoln Street
Essex Junction, Vermont 05452

Testing Facility:
Smithers Avanza Toxicology Services
11 Firstfield Road
Gaithersburg, Maryland 20878

Smithers Avanza Study Number:
2410-14374

Authors:
Caitlin Murphy, PhD, DABT
Stephanie Y. Goodnight, MS

Study Completion Date:
28 March 2019

TABLE OF CONTENTS

1.0 COMPLIANCE STATEMENT 6
2.0 QUALITY ASSURANCE STATEMENT 7
3.0 SIGNATURE PAGE 8
4.0 ABBREVIATIONS 9
5.0 NOTES TO THE DATA 10
6.0 EQUATIONS 11
7.0 STUDY PERSONNEL 12
8.0 TEST FACILITY 12
9.0 TEST SITES 12
10.0 ARCHIVES 13
11.0 PRINCIPAL INVESTIGATORS 13
12.0 CONTRIBUTING SCIENTISTS 13
13.0 STUDY TIMETABLE 14
14.0 SUMMARY 15
15.0 INTRODUCTION 16
16.0 METHODS AND MATERIALS 17
- 16.1 Test Substance and Vehicle/Control Substance 17
- 16.2 Test Animals and Husbandry 20
- 16.3 Experimental Design 21
- 16.4 Observations 22
- 16.5 Test Material Intake 26
- 16.6 Clinical Pathology 26
- 16.7 Termination, Necropsy, and Histopathology 29
- 16.8 Data Collection and Statistical Analyses 30
- 16.9 Record Retention 31

17.0 RESULTS 32
- 17.1 Stability Analysis 32
- 17.2 Dose Formulations 32
- 17.3 Stopper Analysis 32
- 17.4 Animal Disposition, Physical Examinations, Cageside Observations, and Veterinarian Examinations/Treatments 33
- 17.5 Body Weight and Body Weight Changes 33
- 17.6 Water Consumption 35
- 17.7 Food Consumption 37
- 17.8 Test Material Intake 39
- 17.9 Functional Observation Battery and Grip Strength 41
- 17.10 Locomotor Activity 42
- 17.11 Estrus Cyclicity 43
- 17.12 Ophthalmology 43
- 17.13 Clinical and Anatomic Pathology 43

18.0 CONCLUSION 47
19.0 REFERENCE 47

TABLE OF CONTENTS (CONTINUED)

LIST OF TEXT TABLES

Text Table 1: Neat Test Substance and Vehicle/Control Substance 17
Text Table 2: Formulated Dose Concentrations (mg/mL) 18
Text Table 3: Dosage Sampling 19
Text Table 4: Stability Parameters 20
Text Table 5: Animal Information 20
Text Table 6: Husbandry Information 21
Text Table 7: Study Design 22
Text Table 8: Animal Observations/Measurements 23
Text Table 9: Functional Observation Battery (FOB) Assessment 24
Text Table 10: Blood Sampling/Urine Collection Information for Clinical Pathology 26
Text Table 11: Clinical Chemistry Tests 26
Text Table 12: Hematology Tests 27
Text Table 13: Coagulation Tests 28
Text Table 14: Urinalysis Tests 29
Text Table 15: Summary of Test Material Intake 40
Text Table 16: Summary of Functional Observation Battery 41

LIST OF FIGURES

Figure 1: Mean Body Weights-Male 34
Figure 2: Mean Body Weights-Female 35
Figure 3: Mean Water Consumption - Male 36
Figure 4: Mean Water Consumption - Female 37
Figure 5: Mean Food Consumption - Male 38
Figure 6: Mean Food Consumption - Female 39
Figure 7: Mean Test Material Intake-Male 40
Figure 8: Mean Test Material Intake-Female 41
Figure 9: Locomotor Activity – Means 42

TABLE OF CONTENTS (CONTINUED)

LIST OF DATA TABLES

Table 1: Summary of Animal Disposition and Physical Examinations 48
Table 2: Summary of Cageside Observations 50
Table 3: Summary of Body Weights (g) 51
Table 4: Summary of Body Weight Changes (g) 56
Table 5: Summary of Water Consumption (g/animal/day) 61
Table 6: Summary of Food Consumption (g/animal/day) 66
Table 7: Summary of Test Material Intake 71
Table 8: Summary of Functional Observation Battery 73
Table 9: Summary of Locomotor Activity Data 83
Table 10: Summary of Estrus Cycling 85
Table 11: Summary of Clinical Chemistry Data 87
Table 12: Summary of Hematology Data 93
Table 13: Summary of Coagulation Data 99
Table 14: Summary of Urinalysis Data 101
Table 15: Summary of Gross Pathology Observations 103
Table 16: Summary of Organ Weight Data 121
Table 17: Summary of Histopathology Observations 131

TABLE OF CONTENTS (CONTINUED)

LIST OF APPENDICES

Appendix 1: Study Memos 141
Appendix 2: Certificates of Analysis 147
Appendix 3: Stability Report 157
Appendix 4: Dose Formulations Analysis Report 200
Appendix 5: Stopper Analysis Report 229
Appendix 6: Individual Animal Disposition and Physical Examinations 302
Appendix 7: Individual Cageside Observations 320
Appendix 8: Individual Veterinarian Examinations/Treatments 322
Appendix 9: Individual Body Weights 324
Appendix 10: Individual Body Weight Changes 337
Appendix 11: Individual Water Consumption 350
Appendix 12: Individual Food Consumption 359
Appendix 13: Individual Test Material Intake 368
Appendix 14: Individual Functional Observation Battery 375
Appendix 15: Individual Locomotor Activity Data 406
Appendix 16: Individual Vaginal Cytology 415
Appendix 17: Ophthalmology Report 425
Appendix 18: Clinical and Anatomic Pathology Report 428
Appendix 19: Histology Report 435
Appendix 20: Clinical Pathology Historical Control Data 439
Appendix 21: Individual Clinical Chemistry Data 442
Appendix 22: Individual Hematology Data 456
Appendix 23: Individual Coagulation Data 470
Appendix 24: Individual Urinalysis Data 475
Appendix 25: Individual Gross Pathology Observations 494
Appendix 26: Individual Organ Weight Data 503
Appendix 27: Individual Histopathology Observations 528
Appendix 28: Protocol, Amendments, and Deviations 575

1.0 COMPLIANCE STATEMENT

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

This study was conducted in compliance with current OECD Good Laboratory Practice Principles (GLP) (ENV/MC/CHEM(98)17) and Environmental Protection Agency TSCA Good Laboratory Practice Standards (40 CFR Part 792) with the following exceptions:

The stability information of the neat TFM under the conditions of storage and use were not provided.

The regulations/guidelines under which the TFM and deionized water were manufactured and characterized were not provided.

The water bottle stopper analyses presented in Appendix 5 were performed according to USGS approved SOPs.

There were no deviations from the aforementioned regulations that affected the quality or integrity of the study or the interpretations of the results in this report.

Study Director:

Caitlin Murphy, PhD, DABT — 28 Mar 2019
Date

Sponsor's Representative: — 3/28/2019

Stephen R. Lantz, PhD — Date

2.0 QUALITY ASSURANCE STATEMENT

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

This study was inspected/audited by Quality Assurance in accordance with current OECD Good Laboratory Practice Principles and Environmental Protection Agency TSCA Good Laboratory Practice Standards, the protocol, and Smithers Avanza Standard Operating Procedures. All findings were reported to the Study Director and Testing Facility Management as indicated below.

Type of Audit	Date(s) Audited	Date Reported to Study Director and Management
Protocol	23 April 2018	25 April 2018
Critical Phase (Water Consumption Procedure)	27 April 2018	11 May 2018
Raw Data Audit	7-9 May 2018	8 June 2018
Critical Phase (Necropsy Procedure)	25 July 2018	25 July 2018
Critical Phase (Necropsy Procedure)	26 July 2018	26 July 2018
Raw Data Audit, Protocol Amendment 1-6	10-16 August 2018	16 August 2018
Draft Report and Raw Data Audit	31 October – 15 November 2018	15 November 2018
Final Report Post Audit, Protocol Amendment 7	4-13 March 2019	13 March 2019

Histology processing evaluation was performed by Vet Path Services, Inc. (VPS) under the purview of their QAU. VPS' QA Statement is presented in Appendix 19. All audit findings have been adequately addressed. It is concluded that the final report accurately describes the methods and standard operating procedures and the reported results accurately reflect the raw data for this study.

Dana Coville

Dana Coville
Quality Assurance Auditor

3/28/19

Date

3.0 SIGNATURE PAGE

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Authors:

Caitlin Murphy, PhD, DABT
Study Director

28 Mar 2019
Date

Stephanie Goodnight

Stephanie Y. Goodnight, MS
Toxicology Associate

28 Mar 2019
Date

Peer Review:

C. Steven Godin, PhD, DABT

28 March 2019
Date

4.0 ABBREVIATIONS

Not all abbreviations listed are used in this report.

General:			
. /-/ NA	not applicable	**PM**	afternoon
~	approximately	**PVDF**	polyvinylidene fluoride
AM	morning	**QAU**	Quality Assurance Unit
Conc.	concentration	**R**	right
EOI	end of infusion/injection	**rcf**	relative centrifugal force
f	female	**rpm**	revolutions per minute
hr / HR / h	hour	**RSD**	relative standard deviation
i.d. / ID	intradermal	**RT**	room temperature
i.m. / IM	intramuscular	**s.c. / SC**	subcutaneous
i.p. / IP	intraperitoneal	**S.D.**	standard deviation
i.v. / IV	intravenous	**SD**	study day
L	left	**SE or S.E.**	standard error
m	male	**sec or s**	second
min	minute	**SOP**	Standard Operating Procedures
msec	millisecond	**UNS**	unscheduled
MTD	maximum tolerated dose	**wk**	week
		TFM	4-Nitro-3-(trifluoromethyl)phenol
N / No.	number	**TMI**	Test Material Intake
ND	not detected	**mg/kg/day**	mg of test substance per kg bodyweight per day
p.o. / PO	per os		

Clinical Pathology, General:			
DK	dark	**NS**	none seen
GrsHe	grossly hemolyzed	**NSS**	no sample submitted
HPF	high power field	**PClum**	platelets clumped
Inc	increased	**QNS**	quantity not sufficient for testing
K	thousand	**SC**	sample clotted
LPF	low power field	**SL**	slightly
M	million	**U**	units
NoClt	no clot		

5.0 NOTES TO THE DATA

For physical examinations, if an abnormality was noted at more than one site on the same day, it was presented as a single-day occurrence in the summary table.

Animals were fasted overnight for sample collection and/or prior to necropsy on the following days: SD 91, and 119.

Food consumption values resulting from wet feed, spilled feed, and/or technical error were excluded from totals, summary data, and statistical analyses. Total food consumption values were presented only when data was present for all measured intervals. Total food consumption = g/animal.

Water consumption and food consumption were measured by weighing feeders or bottles prior to being filled and after being filled. Provantis calculated daily water and food consumption (g/animal/day) using weekly totals (g), which were divided by the number of animals in the cage (g/animal) and days in the interval (/day).

Starting in Week 4, water bottles were emptied and refilled on the 4th day of the week.

The following organs were collected/weighed as follows: thyroid with parathyroids, testes with epididymides, and uterus with cervix.

Terminal body weights (TBW, g) and organ weights were presented together. Organ weights were presented as absolute weights (Abs, g), organ-to-body weight percentages (%TBW) and organ-to-brain weight ratios (/BR).

6.0 EQUATIONS

Test Material Intake (TMI):

$$TMI\left(\frac{mg}{kg\ day}\right) = \frac{\text{water consumption}\left(\frac{g}{day}\right) \times \text{CC}\left(\frac{mg}{g}\right)}{\frac{\left(\frac{\text{current BW (g)} + \text{previous BW (g)}}{2}\right)}{1000\left(\frac{g}{kg}\right)}}$$

Corrected Concentration (CC) for Weeks 1-3 was calculated using a linear equation describing average concentration reduction per week derived from formulation analysis data (see Appendix 4 and Section 17.2.3):

$$CC\left(\frac{mg}{g}\right) = Initial\ Concentration \times \left((Initial\ Concentration \times -0.1288) + 0.99546\right)$$

Corrected Concentration for Weeks 4 to 13 was calculated from modeled average weekly percent loss based on initial formulation concentration and formulation analysis data (see Appendix 1, Appendix 4, and Section 17.2.3) using an average of modeled daily concentrations:

$$CC\left(\frac{mg}{g}\right) = Initial\ Concentration - (Initial\ Concentration \times |Percent\ Loss|/100)$$

The weekly percent losses used for weeks 4 to 13 are:

Concentration Range (mg/mL)	Percent Loss
<0.0462	-6.79%
0.0462-0.164	-12.30%
0.165-0.603	-15.35%
>0.604	-18.88%

7.0 STUDY PERSONNEL

Study Director:	Caitlin Murphy, PhD, DABT C. Steven Godin, PhD, DABT (Effective 22 May 2018 to 28 May 2018)
Toxicology Associate:	Stephanie Y. Goodnight, MS
Director, Operations and Toxicology Support:	Michael Brunty, BS
Manager, Dose Formulations and Analysis:	James P. Hall, AAS, LATg
Technical Supervisor – In-Life:	Jefferson Hebler, BS
Technical Supervisor – Husbandry:	Eileen Howard-Lucas
Technical Supervisor – Necropsy:	Jennifer L. Duvall, BA
Attending Veterinarian:	Holly Atlee, DVM
Sponsor:	U.S. Geological Survey (USGS) 2630 Fanta Reed Road La Crosse, WI 54603 *On behalf of:* U.S. Fish and Wildlife Service Lake Champlain Fish and Wildlife Conservation Office 11 Lincoln St. Essex Junction, VT 05452
Sponsor's Representative:	Stephen R. Lantz, PhD

8.0 TEST FACILITY

Corporate Office and Clinical Pathology Laboratory:	Smithers Avanza Toxicology Services (Smithers Avanza) 11 Firstfield Road Gaithersburg, MD 20878
Vivarium and Dose Formulations Analysis:	Smithers Avanza 15 Firstfield Road Gaithersburg, MD 20878

9.0 TEST SITES

Histology and Clinical/Anatomic Pathology Evaluation:	Vet Path Services, Inc. (VPS) 6450 Castle Drive Mason, OH 45040

10.0 ARCHIVES

Paper Records:	Iron Mountain, Inc. 4451 Georgia Pacific Blvd., Suites L&M Frederick, MD 21704
Electronic Media:	Iron Mountain, Inc. 8928 McGaw Court Columbia, MD 21045
Preserved Specimens:	VPS Archives, LLC 6450 Castle Drive Mason, OH 45040
Chemicals:	Smithers Avanza 15 Firstfield Road Gaithersburg, MD 20878

11.0 PRINCIPAL INVESTIGATORS

Clinical and Anatomic Pathology Evaluation:	Roxanne Baumgartner, DVM, DACVP, DABT VPS
Histology:	Sheree K. Lovelace, LAT, HT (ASCP) VPS

12.0 CONTRIBUTING SCIENTISTS

Ocular Examinations:	Holly Atlee, DVM Smithers Avanza
Dose Formulations Analysis:	Surubhi Kalathur, MS Smithers Avanza

13.0 STUDY TIMETABLE

Study Initiation Date:	18 April, 2018
Experimental Start Date:	19 April 2018
Receipt of Animals:	19 April 2018
First Day of Dosing	
Males:	26 April 2018
Females:	27 April 2018
Last Day of Dosing	
Males:	24 July 2018
Females:	25 July 2018
Necropsy	
Main Study	
Males:	25 July 2018
Females:	26 July 2018
Recovery	
Males:	22 August 2018
Females:	23 August 2018
Experimental Completion Date:	13 September 2018
Study Completion Date:	28 March 2019

14.0 SUMMARY

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

The purpose of this study was to determine the potential toxicity of 4-nitro-3-(trifluoromethyl)phenol (TFM) when administered continuously for 90-days via drinking water to male and female Sprague Dawley rats and to determine the persistence or reversibility of any toxic effects over a 28-day recovery period.

One hundred and sixty (80/sex) Sprague Dawley rats were randomly assigned to 11 groups (20 animals/sex in Group 1, 10 males or females/group in Groups 2-5 and 7-10, respectively, and 20 males or females in Groups 6 and 11, respectively). Animals were administered control substance (deionized water, 0 mg/kg/day) or TFM-fortified deionized water at 1, 3, 10, 30, or 100 mg/kg/day via drinking water for at least 90 consecutive days. Animals were subjected to a full gross necropsy on Study Day (SD) 91 (terminal) or 119 (recovery).

Parameters evaluated during the study included mortality, physical examinations, cageside observations, body weights, body weight changes, food consumption, functional observation battery, locomotor activity, ophthalmic examination findings, clinical pathology (clinical chemistry, hematology, coagulation, and urinalysis), vaginal cytology, gross pathology findings, absolute and relative organ weights, and histopathology findings.

Dose levels of TFM at 0, 1, 3, 10, 30, or 100 mg/kg/day via drinking water were targeted and the concentration of the TFM-fortified water was adjusted weekly to maintain exposure levels. However, TFM interacted with and was absorbed into the water bottle stopper resulting in a reduction in test material concentration of the solution Thus, the mean calculated test material intakes were 0, 0.93, 2.82, 9.19, 26.13, 86.46 and 0, 0.96, 2.94, 9.83, 28.91, 77.20 mg/kg/day for males and females, respectively. Absorption of TFM by the neoprene stoppers was determined to be the primary factor accounting for the reduced TFM concentrations observed in the water bottles during the study.

Administration of TFM at doses up to 86.5 and 77.2 mg/kg/day in male and female rats, respectively had no effect on the parameters evaluated. These included mortality, physical examinations, cageside observations, body weights, body weight changes, food consumption, functional observation battery, locomotor activity, ophthalmic examination findings, clinical pathology (clinical chemistry, hematology, coagulation, and urinalysis), vaginal cytology, gross pathology findings, absolute and relative organ weights, or histopathology.

All animals survived to the scheduled necropsies. There were no test substance-related alterations in clinical pathology parameters, macroscopic observations, or organ weight changes at any time point, and there were no test substance-related microscopic findings at the terminal necropsy.

In summary, there was no toxicity observed after repeat dose administration via drinking water of TFM to male and female rats. The repeat dose no-observed-adverse-effect level (NOAEL) for male and female rats was considered to be the highest achieved dose levels, 86.5 and 77.2 mg/kg/day, respectively.

15.0 INTRODUCTION

The purpose of this study was to determine the potential toxicity of 4-nitro-3-(trifluoromethyl)phenol (TFM) when administered continuously for 90 days via drinking water to male and female Sprague Dawley rats, and to determine the persistence or reversibility of any toxic effects over a 28-day recovery period.

This study followed U.S. EPA Guideline OPPTS 870.3100: 90–Day Oral Toxicity in Rodents and OECD Guidelines for the Testing of Chemicals, Test No 408: Repeated Dose 90-Day Oral Toxicity Study in Rodents.

The rat was selected because it is a standard species for use in toxicology studies and are also being used as a rodent species per current EPA and OECD guidelines.

This study was designed to use the fewest number of animals possible, consistent with the objective of the study, the scientific needs of the Sponsor, contemporary scientific standards, and in consideration of applicable regulatory requirements.

The oral route via drinking water was selected because it is the anticipated route of potential human exposure.

The dose levels were selected based on subchronic studies in dogs, rats, and hamsters conducted in the early 1970s prior to the development of study guidelines and GLP standards. Test material used in previous studies likely contained toxicologically active impurities which could have influenced findings. Consistent findings of decreased body weight gain and inconsistent findings of decreased gonad weight, ovarian lesions, spleen congestion, increased leukocytes, and reduced hemoglobin were noted but not considered significant by study personnel. In a 1971 subchronic rat study (WARF Institute, Inc., Madison, Wisconsin, U.S. Department of the Interior, Bureau of Sport Fisheries & Wildlife, Contract No. 14-16-0008-620), rats were exposed to TFM through diet for 90 days, a trend of smaller than control gonads were observed in almost all treated female groups of rats; however, considered of no biological significance. Feeding rats with 500, 900, 1620, 2916, and 5248 ppm TFM-fortified diet (approximately 50, 90, 162, 292, and 525 mg/kg/day respectively) for 90 days resulted in no biologically significant difference among treated groups when compared with the control groups of animals regarding body weight, feed consumption or clinical pathology. Insignificant findings for increased leukocytes and decreased female gonad weight occurred as low as 50 mg/kg/day. Insignificant findings for decreased male gonad weight occurred as low as 90 mg/kg/day. Findings of decreased female and male body weight occurred as low as 292 and 525 mg/kg/day, respectively. The proposed dosage levels were expected to cause some organ weight alterations, but no adverse effect to animals when provided in drinking water.

The Institutional Animal Care and Use Committee (IACUC) of Smithers Avanza approved the study protocol and found it to be in accordance with provisions of the USDA Animal Welfare Act, the PHS Policy on Humane Care and Use of Laboratory Animals, and the US Interagency Research Animal Committee Principles for the Utilization and Care of Research Animals. The protocol, amendments, and deviations are presented in Appendix 28.

16.0 METHODS AND MATERIALS

16.1 Test Substance and Vehicle/Control Substance

16.1.1 Neat Materials

The neat test substance and vehicle/control substance used on this study are described in Text Table 1.

Text Table 1: Neat Test Substance and Vehicle/Control Substance

Name	Lot/Batch No.	Supplier	Purity
4-nitro-3-(trifluoromethyl)phenol (TFM)	LAM170517A- Extract	US Geological Survey La Crosse, WI	80.59%
Deionized (DI) Water	176155 180010 180885 181924 182557	ThermoFisher Scientific Fair Lawn, NJ	Assumed 100%

The test substance, TFM, was received at ambient temperature and stored protected from light at room temperature upon receipt. The control substance, DI water, was received at ambient temperature and stored at room temperature upon receipt. Certificates of Analysis are presented in Appendix 2.

Reserve samples (1 mL) of the neat test substance and control substance were taken and subsequently were archived under the same storage conditions as those of the neat materials.

All remaining test substance was returned to the Sponsor. All remaining control substance components were retained for use on subsequent studies. All empty containers were discarded after completion of the in-life phase of study.

16.1.2 Dose Formulations

The neat test substance was adjusted based on test substance purity (80.59%) and the vehicle/control substance was considered 100% pure for formulation purposes.

The vehicle/control substance, DI water, was used as received; no formulations were necessary.

Dose formulations were prepared weekly, Concentrations for Weeks 1 and 2 were based on bodyweight and water consumption data previously collected. After Week 2, concentrations were based on the bodyweight and water consumption data from the previous two weeks. Concentrations of formulations are presented in Text Table 2.

With the exception of Week 1, formulations for the highest doses for males and females were prepared separately by adding the appropriate amount of vehicle/control substance and test substance together and inverting approximately 30 times (Weeks 1-3), or mixing with a Max Sphere mixer for approximately 10 minutes (Weeks 4-13). The high dose formulations were then serially diluted with the appropriate amount of vehicle/control substance to achieve the concentrations listed in Text Table 2 and inverted approximately 30 times (Weeks 1-3), or mixed with a Max Sphere mixer for approximately 10 minutes. For Week 1, formulations for all groups were prepared in one mix, with the highest dose formulated first

via the same method as described above, then serially diluted with the appropriate amount of vehicle/control substance to achieve the desired concentration. Due to out of specification analytical results for Groups 7-10 during Week 2, the mixes were prepared again on SD 11. Formulations were stored at room temperature until used for dosing.

Text Table 2: Formulated Dose Concentrations (mg/mL)

	Week					
Group	**1 and 2**	**3**	**4**	**5**	**6**	**7**
1	0.0	0.0	0.0	0.0	0.0	0.0
2	0.00928	0.0087	0.00926	0.0103	0.0115	0.0119
3	0.0278	0.0268	0.0291	0.0316	0.0361	0.0341
4	0.0928	0.0917	0.099	0.109	0.113	0.125
5	0.278	0.312	0.348	0.382	0.407	0.431
6	0.93	1.16	1.24	1.50	1.65	1.87
7	0.0115	0.00917	0.0106	0.0114	0.0122	0.0125
8	0.0344	0.0288	0.0308	0.0334	0.0349	0.0373
9	0.115	0.0962	0.102	0.111	0.119	0.122
10	0.344	0.301	0.321	0.346	0.367	0.375
11	1.15	1.21	1.34	1.45	1.73	1.74
	Week					
Group	**8**	**9**	**10**	**11**	**12**	**13**
1	0.0	0.0	0.0	0.0	0.0	0.0
2	0.0139	0.0152	0.0154	0.0163	0.0173	0.0172
3	0.038	0.042	0.0403	0.0462	0.0467	0.0476
4	0.14	0.153	0.153	0.17	0.183	0.176
5	0.475	0.524	0.562	0.604	0.637	0.616
6	2.04	2.29	2.34	2.56	2.71	2.47
7	0.0126	0.0139	0.0139	0.0157	0.0151	0.0145
8	0.0383	0.0398	0.0392	0.0413	0.0409	0.0416
9	0.124	0.139	0.139	0.146	0.148	0.158
10	0.392	0.435	0.438	0.464	0.441	0.464
11	1.88	2.02	2.07	2.16	2.13	2.10

16.1.3 Dosage Sampling

The dose formulations were sampled and stored at room temperature as presented in Text Table 3.

Text Table 3: Dosage Sampling

Sample Type	Concentrations Sampled	Sample Volume (mL)	Number of Samples per Concentration			Intervals Sampled
			Collected	Analyzed	Backup	
Stability	3.5 mg/mL	3	2	1	1	Wk 7
Homogeneity	High (3.5 mg/mL) Top, Middle, and Bottom	3	2	1	1	Wk 7
Stability of Dosing Solutions stored in water bottles	Low and High	10	2	1	1	Wk 1[1, 2]
	Mid (Group 4) High (Group 11)	10	2	1	1	Wk 5[4]
	Groups 2-6	2	2	1	1	Wk 11[3]
Concentration Verification	All (includes vehicle/control)	10	2	1	1	Wk 1, 2, 8, 13
	Groups 7–11	10	2	1	1	Wk 3 (SD 8 and 11)

[1]Samples collected from similarly prepared water bottles to those administered to the animals were maintained at room temperature for at least 7 days.

[2]Samples collected and analyzed from the control and highest TFM solution (during the interval) from a single water bottle used for dosing of the animals for at least 7 days.

[3]Samples were collected from water bottles used for dosing animals and analyzed at Day 0, Day 1, Day 4 (prior to and after refilling dosing solutions), and day 7.

[4]Samples were collected from the formulation and similarly prepared water bottles and analyzed at 0, 1, 4, and 7 days.

Samples (10 mL) were collected prior to dose administration from formulations prepared for Week 4 dosing solutions (Groups 1, 7, 9, and 11). Additional samples (10 mL were collected from a representative bottle in each of the above groups after the Week 4 dosing solutions were in the water bottles for at least 4 days. Used stoppers (from a representative bottle in each of the above groups) and unused stoppers were collected. The samples and the stoppers were sent to the Sponsor for analysis of potential degradation of the test substance. The report is presented in Appendix 5.

All remaining samples not used for analysis will be disposed of in accordance with company SOPs, appropriate regulatory requirements, and/or information contained in the Safety Data Sheets after authorization from the Study Director prior to finalization of the report.

16.1.4 Dosage Analysis

Stability analysis of the dose formulations was performed under Smithers Avanza Study No. 2410-14256 as part of the method validation; the methodology is presented in Appendix 3.

Samples were analyzed for test substance concentration by Smithers Avanza using a validated method. The analytical methods are described in the Dose Formulation Analysis Report presented in Appendix 4.

At the end of Week 1, samples taken from the water bottles (lowest and highest doses) were analyzed and indicated a % change of <10% at the low concentration and <40% at the high concentration. Therefore, dosing solutions from water bottles at the middle and high doses were tested at Days 1, 4, and 7 and showed a similar trend of % change of 16% and 34%, respectively. Consequently, beginning on Week 4, the dosing solutions from the water bottles were emptied and refilled on the 4th day of the week to mitigate the reduction in concentration. Additional samples were collected at least on Day 0, Day 1, Day 4 (prior to and after refilling dosing solutions) and Day 7 from Group 2, 3, 4, 5, and 6 formulations

and of water bottles used for dosing from each group during Week 11 to determine the change in dosing solution concentrations.

During the course of the study, the concentration of the high dose surpassed the concentration analyzed for stability established in Study No. 2410-14256. Therefore, stability analysis was added at a concentration of 3.5 mg/mL (see Text Table 4) to cover the dosing solution.

Text Table 4: Stability Parameters

Sample Solution	Conditions	
High (3.5 mg/mL)	T_0	--
	Day 4	Room Temp at 21±5°C, protected from light
	Day 10	
	Day 28	
Water Bottle (3.5 mg/mL)	Day 1	Room Temp at 21±5°C, protected from light
	Day 4	
	Day 7	

16.2 Test Animals and Husbandry

16.2.1 Animals

Animal information is provided in Text Table 5.

Text Table 5: Animal Information

	Males	Females
Species and Strain	Sprague Dawley Rat	
Supplier	Charles River Breeding Labs; Raleigh, NC	
Method of Identification	Ear tag/Cage card	
Number of Animals Received	88	88
Number Used on Study	80	80
Age at First Dose	7-8 weeks	
Weight Range at First Dose	206.8-269.7 g	156.1-189.9 g
Disposition of Extra Animals	Euthanized	

Animals were acclimated to laboratory conditions for at least five days prior to the first dose and released from acclimation by a staff veterinarian. During that time, animals were identified by a temporary number that was recorded on each cage label.

16.2.2 Husbandry

Animal husbandry was provided as described in Text Table 6.

Text Table 6: Husbandry Information

Feed	Certified Global Teklad Laboratory Diet 2018 (pellets) was provided *ad libitum*, unless otherwise noted.
Water	Deionized water was provided *ad libitum* via water bottles
Bedding	Certified Sani Chips® hardwood bedding
Housing	Animals were housed in one room, paired, in polycarbonate cages suspended on stainless steel racks. Each cage was affixed with a cage card containing pertinent animal and study information.
Temperature Range	20-26°C
Humidity Range	30-70%
Light Cycle	12-hour light/12-hour dark, interrupted as necessary for study-related events. Animal room light was filtered to block certain UV light spectra to reduce potential photodegradation of the test substance.
Air Changes	Minimum of 10 air changes per hour

The feed was analyzed by the manufacturer for concentrations of specified heavy metals, aflatoxin, chlorinated hydrocarbons, and organophosphates. The water is routinely analyzed for contaminants and specific microbes. The bedding was analyzed by the manufacturer for acceptable levels of heavy metals, aflatoxins, bacteria, yeasts, molds, and organophosphates prior to certification. No contaminants were known to be present in the feed, water, or bedding at levels that might have interfered with achieving the objectives of the study.

Environmental controls were set to maintain animal room conditions as shown in Text Table 6. Actual temperature and relative humidity in the animal room were monitored continuously by a computerized system. All environmental parameters were maintained within the protocol requirements.

In addition to standard husbandry procedures, non-plastic environmental enrichment was provided.

16.3 Experimental Design

16.3.1 Group Assignment and Doses

Animals were initially accepted into the randomization pool based upon prestudy body weights, physical examinations, and ophthalmic examinations. They were assigned to study groups using computer-generated random numbers such that the mean body weight for each group was not statistically different ($p \leq 0.05$) from the control mean. Males and females were randomized separately. Following randomization each study animal was assigned a unique number.

The animals were assigned to groups as shown in Text Table 7.

Text Table 7: Study Design

Group	Treatment	Target Dose[a] (mg/kg/day)	Animal Numbers							
			Main Phase				Recovery Phase			
			N	Males	N	Females	N	Males	N	Females
1	Control	0	10	25234-25243	10	25254-25263	10	25244-25253	10	25264-25273
2	TFM	1	10	25274-25283	-	-	-	-	-	-
3	TFM	3	10	25284-25293	-	-	-	-	-	-
4	TFM	10	10	25294-25303	-	-	-	-	-	-
5	TFM	30	10	25304-25313	-	-	-	-	-	-
6	TFM	100	10	25314-25323	-	-	10	25324-25333	-	-
7	TFM	1	-	-	10	25334-25343	-	-	-	-
8	TFM	3	-	-	10	25344-25353	-	-	-	-
9	TFM	10	-	-	10	25354-25363	-	-	-	-
10	TFM	30	-	-	10	25364-25373	-	-	-	-
11	TFM	100	-	-	10	25374-25383	-	-	10	25384-25393

Control = DI water

[a]Target doses are presented, the calculated test material intake are summarized in the results section 0.

16.3.2 Dose Administration

The animals were dosed via test substance-fortified DI water provided *ad libitum* in clear glass water bottles with neoprene stoppers. Due to out of specification analytical results for Groups 7-10 during Week 2, formulations were freshly mixed, and dosing solutions for Groups 7-10 were changed on SD 11.

The neoprene water bottles, the stoppers and sippers were changed weekly throughout the study and were cleaned to limit the potential contamination via the process described in this memo (Appendix 1). The dosing solutions were changed weekly during Weeks 1-3 and twice weekly during Weeks 4-13. The first day of dosing was designated as SD 1 for each animal. Dosing solutions were noted to darken at the time of replacement of the solutions.

During the recovery phase, animals were provided non-fortified DI water *ad libitum* in clear glass water bottles with neoprene stoppers.

Excess formulations were disposed of in accordance with company SOPs, appropriate regulatory requirements, and/or information contained in the Safety Data Sheets.

16.4 Observations

Animals were observed as shown in Text Table 8.

Text Table 8: Animal Observations/Measurements

Procedure	Frequency of Testing
Physical Examinations	SD 1 (prior to initiation of dosing) Weekly thereafter Prior to necropsy
Cageside Observations	≥ 2 times daily
Body Weights	SD1 (prior to initiation of dosing) Weekly thereafter Day prior to necropsy (unfasted) Prior to necropsy (fasted)
Water Consumption	Weekly quantitative
Food Consumption	Weekly quantitative
Vaginal Cytology	Weeks 3 & 4 (daily) Weeks 11 & 12 (daily) Prior to necropsy (recovery animals only)
Ophthalmologic Examinations	Control and high dose groups only: SD 88/90 (f/m) SD 117/118 (f/m)
Functional Observation Battery (FOB) including Grip Strength	SD 84 ± 1
Locomotor Activity	SD 89

Cageside observations included observation for mortality, moribundity, general health, and signs of toxicity. Physical examinations included evaluation of skin and fur characteristics, eye and mucous membranes, respiratory, circulatory, autonomic, and central nervous systems, and somatomotor and behavior patterns.

Ophthalmologic observations were conducted using indirect ophthalmoscopy and slit-lamp biomicroscopy (as needed) following administration of 1% Tropicamide® mydriatic solution.

For neurotoxicity observations (FOB, grip strength, and locomotor activity), animals were transported to the testing room and acclimated to white noise for at least 10 minutes prior to testing. For locomotor activity, animals were placed into an activity chamber for 30 minutes. The Kinder Scientific Motor Monitor II recorded the total number of occurrences of basic movement, fine movement, and rearing during the 30-minute testing timeframe. Data was tabulated in 10-minute intervals. For the FOB, animals were transported to the testing room and acclimated to white noise for at least 10 minutes prior to testing. Animals were assessed and scored as described in Text Table 9. For all observations, a score of 0 indicated a normal finding.

Text Table 9: Functional Observation Battery (FOB) Assessment

Domain	Type of Observation	Parameter	Observation	Score
Activity Arousal	Hand Held	Handling Reactivity	None	2
			Low	1
			Moderate	0
			High	1
		Vocalization	None	0
			Upon Removal	1
			During Handling	2
			Continuous	3
	Home Cage	Posture	Typical	0
			Hunched	1
			Low	1
			Other	1
	Open Field	Posture	Typical	0
			Hunched	1
			Low	1
			Other	1
		Rearings	Quantitative	
Autonomic	Hand Held	Exopthalmus (each eye)	Absent	0
			Present	1
		Lacrimation	Absent	0
			Present	1
		Palpebral Closure	Wide Open	0
			Ptosis	1
			Closed	2
		Piloerection	Absent	0
			Present	1
		Pupillary Status	Miosis	1
			Normal	0
			Mydriasis	1
		Salivation	Absent	0
			Present	1
	Elicited Responses	Pupillary Response	Neither Constrict	2
			Left Constricts	1
			Right Constricts	1
			Both Constrict	0
	Open Field	Defecation	Quantitative	
		Urination	Quantitative	

Text Table 9 (continued): Functional Observation Battery (FOB) Assessment

Domain	Type of Observation	Parameter	Observation	Score
Neuromuscular	Hand Held	Fur Appearance	Groomed	0
			Stained	1
	Home Cage	Activity	None	2
			Low	1
			Moderate	0
			High	1
		Unusual Behavior	None	0
			Present	1
		Gait	Normal	0
			Ataxia	1
			Tiptoe	1
			Retropulsion	1
			Other	1
	Elicited Responses	Righting Reflex	Positive	0
			Negative	1
	Open Field	Activity	None	2
			Low	1
			Moderate	0
			High	1
		Gait	Normal	0
			Ataxia	1
			Tiptoe	1
			Retropulsion	1
			Other	1
		Unusual Behavior	None	0
			Present	1
		Grooms	Quantitative	
	Forelimb Grip Strength		Quantitative	
	Hindlimb Grip Strength		Quantitative	
	Hindlimb Splay		Quantitative	
Physiological	Hand Held	Respiration	Normal	0
			Rapid	1
			Labored	1
			Other	1
	Body Weight		Quantitative	
Sensory	Elicited Responses	Approach Response	Approaches	0
			No Reaction	1
			Avoidance	1
			Jumps	1
			Freezes	1
			Aggressive	1
		Click Response	None	1
			Responds	0
			Exaggerated	1
		Tail Pinch Response	None	1
			Responds	0
		Pinna Response	None	1
			Responds	0

16.5 Test Material Intake

Analytical data (2410-14256 and -14374) demonstrated that the concentration of each formulations solutions was decreased after contact with the water bottle stopper. This change in concentration was mitigated by refreshing dosing solution on a twice basis weekly. However this was not applied until after week 4 of the study.

To represent the changes in dosing solutions, analytical data were collected and corrections to the test material intake (TMI) for each animal and dosing solution were applied. For each concentration range of dosing solution, a percent loss was applied to determine the corrected TMI (see memo; Appendix 1).

16.6 Clinical Pathology

Blood samples and urine specimens were collected from all animals as shown in Text Table 10. Animals were fasted overnight (with water available) prior to sample collection.

Text Table 10: Blood Sampling/Urine Collection Information for Clinical Pathology

Parameter	Chemistry	Hematology	Coagulation	Urinalysis
Collection Day	Prior to scheduled termination (only animals scheduled for necropsy)			
Collection Method	Cardiac puncture under 70% CO_2/30% O_2 anesthesia			Metabolism cage
Volume Collected	At least 1 mL	At least 1.0 mL	At least 1.8 mL	Total volume recorded; up to 12 mL submitted
Tubes Used	serum separator	K_2 EDTA	sodium citrate	Urintek

Samples/specimens were transported to the Clinical Pathology Laboratory for analysis. All remaining samples were discarded prior to finalization of the report.

16.6.1 Serum Clinical Chemistry

The Siemens Dimension XPand chemistry analyzer was used to measure the serum concentrations of the clinical chemistry parameters listed in Text Table 11.

Text Table 11: Clinical Chemistry Tests

Parameter	Abbreviation	Units	Method
Albumin	ALB	g/dL	Bromcresol green (colorimetric)
Alkaline Phosphatase	ALPi	U/L	p-Nitrophenyl-phosphate (bichromatic rate)
Alanine Aminotransferase	ALTi	U/L	L-Alanine to Alpha Ketoglutarate (bichromatic rate)
Aspartate Aminotransferase	AST	U/L	L-Aspartate to Alpha Ketoglutarate (bichromatic rate)
Blood Urea Nitrogen	BUN	mg/dL	Urease (bichromatic rate)
Calcium	CA	mg/dL	o-cresolphthalein complexone (colorimetric)
Cholesterol	CHOL	mg/dL	Cholesterol Esters (colorimetric)
Creatine Kinase	CK	U/L	Creatine phosphate to Adenosine-Diphosphate (multiple point rate)
Chloride	CL	mmol/L	Ion-selective electrode (potentiometric)
Creatinine	CRE2	mg/dL	Creatinine + Picrate (bichromatic rate)
Gamma Glutamyltransferase	GGT	U/L	gamma-glutamyl-3-carboxy-4-nitroanilide to glycylglycine (bichromatic rate)
Glucose	GLU	mg/dL	Hexokinase-Glucose-6-Phosphate Dehydrogenase (colorimetric)

Parameter	Abbreviation	Units	Method
Potassium	K+	mmol/L	Ion-selective electrode (potentiometric)
Sodium	NA+	mmol/L	Ion-selective electrode (potentiometric)
Phosphorus	PHOS	mg/dL	Phosphomolybdate (colorimetric)
Total Bilirubin	TBILI	mg/dL	Diazo (colorimetric)
Total Protein	TPROT	g/dL	Biuret (colorimetric)
Triglycerides	TRIG	mg/dL	Glycerol-3-phosphate (colorimetric)

Commercially available controls were analyzed each day of testing.

Globulin (GLOB, g/dL) was calculated as the difference between total protein and albumin. The albumin to globulin ratio (A/G) was obtained by dividing the albumin value by the globulin value.

Values that were below the detection limit of the analyzer were reported as < the lowest limit of the measured parameter. For example, the lowest limit for triglyceride concentration determination was 15 mg/dL. A value that was observed to be less than this was reported as <15.

16.6.2 Hematology

The Siemens Advia 120 hematology analyzer was used to measure or calculate the hematology parameters listed in Text Table 12.

Text Table 12: Hematology Tests

Parameter	Abbreviation	Units	Method
Complete Blood Count			
White Blood Cells	WBC	K/µL	Flow cytometry by 2 angles of light scatter Low angle: number of nuclei present High angle: nuclear complexity
Red Blood Cells	RBC	M/µL	Flow cytometry by 2 angles of light scatter Low angle: size High angle: hemoglobin concentration
Hemoglobin	HGB	g/dL	Measured by cyanmethemoglobin
Hematocrit	HCT	%	Calculated: (RBC x MCV) ÷ 10
Mean Corpuscular Volume	MCV	fL	Mean of RBC volume histogram
Mean Corpuscular Hemoglobin	MCH	pg	Calculated: (HGB ÷ RBC) x 10
Mean Corpuscular Hemoglobin Concentration	MCHC	g/dL	Calculated: (HGB ÷ [RBC x MCV]) x 1000
Mean Platelet Volume	MPV	fL	Flow cytometry by low angle light scatter
Platelets	PLT	K/µL	Flow cytometry by 2 angles of light scatter Low angle: size High angle: refractive index
Red Cell Distribution Width	RDW	%	Calculated: 100 x (SD of RBC volume histogram ÷ MCV)

Parameter	Abbreviation	Units	Method
Leukocyte Differential Count			
Absolute Neutrophils	ABNEUT	K/µL	Individual cell types initially determined as % WBC. Absolute cell counts were calculated by multiplying the total white blood cell count by the decimal expression of the percentage of the individual cell population
Absolute Lymphocytes	ABLYMP	K/µL	
Absolute Monocytes	ABMONO	K/µL	
Absolute Eosinophils	ABSEOS	K/µL	
Absolute Basophils	ABBAS	K/µL	
Reticulocyte Count			
Absolute Reticulocytes	ABRETi	10^9/L	Calculated by multiplying the total red blood cell count by the decimal expression of the reticulocyte percent.
% Reticulocytes	RET	%	Same as RBC plus zero angle light scatter-light absorption (cells stained with oxazine 750 absorb more light than mature RBCs)

Commercially available controls were analyzed each day of testing.

When the white blood cell differential or reticulocyte count could not be calculated by the Advia 120 due to mechanical or sample limitations, a manual count was performed. If platelet clumps were observed on the hematology smear, the platelet count and mean platelet volume were reported as clumped.

Blood smears for cellular morphology were prepared for each animal and stained using a Modified Wright-Giemsa stain. The slide was evaluated when the data results from the automated hematology evaluation for that particular animal were outside the system standards. Morphology findings (if any) were categorized as follows: 1+ = minimal; 2+ = mild; 3+ = moderate; 4+ = marked.

16.6.3 Coagulation

The Instrumentation Laboratory ACL Elite Pro coagulation analyzer was used to measure the coagulation tests listed in Text Table 13.

Text Table 13: Coagulation Tests

Parameter	Abbreviation	Units	Method
Prothrombin Time	PT	seconds	Laser-nephelometric centrifugal analyzer
Activated Partial Thromboplastin Time	APTT	seconds	Laser-nephelometric centrifugal analyzer
Fibrinogen	FIB	mg/dL	Laser-nephelometric centrifugal analyzer based on the consumption of fibrinogen in the PT assay

Commercially available controls were analyzed each day of testing.

16.6.4 Urinalysis

Urine specimens were processed according to the procedures listed in Text Table 14. Reagent strips were run on a Siemens Clinitek Atlas analyzer or analyzed manually.

Text Table 14: Urinalysis Tests

Parameter	Abbreviation	Units	Method
Routine Urinalysis			
Volume	TUVol	mL	Direct measure (recorded in the animal laboratory)
Color			Observation or Siemens Reagent Strips
Clarity			Observation or measure of the transmission and scattering of light that passes through the specimen
Specific Gravity	SG		Refractometer or Refractive Index
Glucose	UGLU		Siemens Reagent Strips
Bilirubin	UBILI		Siemens Reagent Strips
Ketones	KET		Siemens Reagent Strips
Blood	BLO		Siemens Reagent Strips
pH	UpH		Siemens Reagent Strips
Protein	PRO		Siemens Reagent Strips
Urobilinogen	URO	U/dL	Siemens Reagent Strips
Nitrites	NIT		Siemens Reagent Strips
Leukocytes	LEU		Siemens Reagent Strips
Microscopic Examination of Sediment			
White Blood Cells	uWBC	/HPF	Observation
Red Blood Cells	uRBC	/HPF	Observation
Epithelial Cells	EPI	/HPF	Observation
Bacteria	Bacter	/HPF	Observation
Mucus		/HPF	Observation
Yeast		/HPF	Observation
Fecal		/HPF	Observation
Sperm		/HPF	Observation
Hyaline Cast	HYAL CA	/LPF	Observation
Granular Cast	GRAN CA	/LPF	Observation
Amorphous Crystals	Amorph	/HPF	Observation
Triple Phosphate Crystals	TP CRYS	/HPF	Observation
Calcium Oxalate Crystals	CAO CRYS	/HPF	Observation
Other Observations	Othr/Uri	/HPF	Observation

Commercially available controls were analyzed each day of testing. Qualitative measurements were made as follows: 1+ = 0-3, 2+ = 4-10, and 3+ = >10. Values for Specific Gravity that were above the detection limit of the analyzer were reported as >1.050, the highest limit of the measured parameter. Urine specimens with fecal contamination are designated as: 1+ = minimal, 2+ = moderate, and 3+ = heavy.

16.7 Termination, Necropsy, and Histopathology

16.7.1 Termination

On SD 91 for main phase animals and 119 for recovery animals, all surviving animals were euthanized by carbon dioxide inhalation followed by exsanguination prior to necropsy.

16.7.2 Necropsy

Animals were necropsied as soon as possible after the time of death. Animals were necropsied, bone marrow smears were prepared, required organs were weighed, and protocol-specified tissues were collected and preserved.

Gross necropsy included examination of the external surface of the body, all orifices, and the cranial, thoracic, and abdominal cavities and their contents. Organ weights were collected as soon as possible after dissection and paired organs were weighed together. Tissues were preserved in 10% neutral buffered formalin (NBF) with the exception of the eyes (and associated ocular tissue) and testes (with epididymides), which were preserved in modified Davidson's fixative and subsequently transferred to 10% NBF. Two bone marrow smears were prepared from the left femur and the slides were air-dried, fixed in methanol, and stored at room temperature for possible future evaluation. No analysis of the bone marrow smears was deemed necessary; therefore, the unstained slides were discarded prior to report finalization.

16.7.3 Histopathology

Preserved tissues were transferred to VPS where the protocol-required tissues were embedded in paraffin, sectioned, stained with hematoxylin and eosin, and examined by a board-certified veterinary pathologist. No target tissues were identified by the veterinary pathologist.

16.8 Data Collection and Statistical Analyses

Electronic data collection, including randomization, dose formulations and dispensing, dosing, animal husbandry, environmental enrichment, physical examinations, cageside observations, body weights, body weight changes, water and food consumption, clinical pathology, organ weights, gross pathology, microscopic pathology, and statistical analysis was performed using Provantis™ Version 8 (Instem LSS, Limited; Stone, UK). Environmental monitoring was performed using Rees Environmental Monitoring System (Rees Scientific Corporation; Trenton, NJ). Electronic data collection for dose analysis was performed using Empower 2 Build 2154 (Waters Corporation, Milford, MA).

Group mean, standard deviation, and sample size are reported for all quantitative measurement data. For calculated data and statistical analysis, minor differences in calculated values may occur due to differences in rounding procedures; these differences do not affect the integrity of the study or the interpretation of the results. Values presented as greater than or less than the measurable range for a given parameter are presented in the individual data, but are not included in means, standard deviations, or statistical analysis unless otherwise indicated. Qualitative gradings or observations are also not included in statistical analysis. Treatment groups with sample sizes of less than 3 were excluded from statistical analysis; if this occurred in the control group no analysis was conducted.

Quantitative data (body weights, body weight changes, water consumption, food consumption, clinical pathology, and organ weight data) from the treated groups were compared statistically to the data of the control group using one-way Analysis of Variance (ANOVA) techniques; sexes were analyzed separately. Prior to the ANOVA analysis, untransformed data were tested to determine if the data are normally distributed and have homogeneous variances among all groups. A Shapiro-Wilk test was used to test for normality, followed by the Levene's test to test the hypothesis of homogeneity of variances. If either the normality or homogeneity test failed (as indicated by a Shapiro-Wilk or Levene's test p-value ≤ 0.01), the data were transformed using log-transformed values and both the Shapiro-Wilk and Levene's tests were

repeated with the log-transformed values. If the results from either the Shapiro-Wilk or Levene's test on the log-transformed data failed, the analysis of the data continued using rank-transformed data using Kruskal-Wallis ANOVA. If both the Shapiro-Wilk or Levene's test were not statistically significant, the ANOVA was performed on the untransformed or log-transformed data, respectively. The Dunnett's t-test was used to determine which groups (if any) differed from the control group. Group comparisons were evaluated at the 0.05 (two-tailed) probability level. An arcsine square root transformation was used for some proportion/percentage data which do not meet the assumptions of parametric statistical tests in the attempt to normalize the data; this data was transformed prior to the ANOVA analysis. The term "significant" is used throughout the text of the report to indicate statistical significance at $p \leq 0.05$.

16.9 Record Retention

All study materials (including data and specimens generated by the test facility and VPS), professional reports, study protocol (including amendments), final report, and all communications concerning the conduct of the study will be retained in a Smithers Avanza-designated archive for a period of five years following issuance of the final report.

Following the five-year period (or before at Sponsor's request), the Sponsor will be contacted to determine the disposition of these materials. Smithers Avanza will maintain all electronic data and records regarding disposition of study materials at a designated archive facility.

Study data generated by the Sponsor or other subcontractors will be archived by the Sponsor or subcontractors, respectively.

17.0 RESULTS

17.1 Stability Analysis

Stability data are presented in Appendix 3.

Stability data demonstrates that the formulated test substance in the concentration range of 0.005-2.0 mg/mL is stable for up to 28 days after formulation when stored at room temperature and protected from light. The additional stability analysis conducted during this study demonstrates that the formulated test substance at 3.5 mg/mL is also stable up to 28 days when stored at room temperature and protected from light (see Appendix 4).

17.2 Dose Formulations

The Dose Formulations Analysis Report is presented in Appendix 4.

17.2.1 Concentration Verification

Dose concentration analysis showed that the test substance was properly formulated (90.1%-105.5% of the target concentrations). No test substance was detected in the control formulation.

17.2.2 Homogeneity

The 3.5 mg/mL formulation was considered homogeneous with a % RSD of 0.7.

17.2.3 Analysis of Formulations in Water Bottles

At the end of Week 1, water bottles prepared similarly to those used for dosing were analyzed at the lowest and highest concentration to determine if there was a change in concentration due to absorption from by the stoppers. The percent (%) change was less than 10% at the lowest concentration and less than 40% for the highest concentration. As a result, dosing solutions from water bottles at a middle dose and highest dose were tested for Day 1, Day 4 and Day 7 of Week 5, which showed a similar trend of overall % Change of 16% for the middle dose and overall % Change of 34% for the highest dose.

The 3.5 mg/mL formulation solution was also analyzed after being exposed to the water bottle for 4 days and refilled on Day 4 and tested on Day 7. This paradigm resulted in an overall % loss of 12.1%, which was less than if solutions were not emptied and refilled on Day 4. Subsequently, the dosing solutions were emptied from the water bottles and refilled on Day 4 to mitigate the loss in concentration. To confirm that this was similar in the water bottles provided to the animals, the dosing solutions during Week 11 of the study for Group 2 to 6, were tested and the % losses ranged from 10% to 18% on Day 7.

17.3 Stopper Analysis

The chemical analysis of the absorption of TFM into the neoprene rubber stoppers is presented in Appendix 5.

Absorption of TFM by the neoprene stoppers was determined to be the primary factor accounting for the reduced TFM concentrations observed in the water bottles during the study. Photodegradation was ruled out as a contributor as the concentrations of the degradation products were less than 1% in all samples analyzed.

With higher concentrations of TFM in the dosing solutions, more mass was extracted from the neoprene stopper. Due to the variation in the rat's drinking volumes, the total amount of TFM absorbed into the stoppers could not be determined and the total amount of TFM absorbed into the stoppers could not be verified. Although an exact amount of TFM absorbed into the stopper could not be calculated, the positive relationship between the concentration of TFM in the water bottles and the amount of TFM absorbed into the stopper supports the analytical results presented in Section 17.2.3.

17.4 Animal Disposition, Physical Examinations, Cageside Observations, and Veterinarian Examinations/Treatments

Data are summarized in Table 1 (animal disposition and physical examinations) and Table 2 (cageside observations). Individual data are presented in and Appendix 7, respectively. Some animals were evaluated/treated by the staff veterinarian, a summary of the evaluations and treatments are presented in Appendix 8. The full evaluation and treatment details are maintained with the study data.

Administration of TFM via drinking water did not result in mortality; all animals survived until the scheduled termination.

No abnormalities were noted during cageside observations and the observations listed below during physical examinations were considered incidental due to a lack of dose response, occurrence in a single animal, or the cause was determined to be unrelated to the test substance.

Several males exhibited rough haircoat on SD 29 (Group 5 [30 mg/kg/day]-two animals; Group 6 [100 mg/kg/day]-four animals). These animals had concurrent bodyweight loss and decreased food and water consumption and were examined by the veterinarian. It was noted that the water flow from the water bottles was inhibited, and the water bottles were subsequently replaced. The veterinarian treated these animals with subcutaneous fluids and nutritional support. All animals recovered and no other observations were noted, thus the observations were not related to administration of the test substance.

Several animals exhibited abrasions at one or two sites (face, nose, tail, gluteus, or inguinal) for various durations throughout the study: Group 1 [0 mg/kg/day]-one male, two females; Group 2 [1 mg/kg/day]-two males; Group 4 [10 mg/kg/day]–two males; Group 11 [100 mg/kg/day]-two females). Alopecia of the forepaws or shoulders was observed in Animals 25295 (4m) and 25381 (11f) during weekly examinations from SD 29-91 or SD 71-91, respectively. Female 25368 had a small movable tissue mass on the abdomen during weekly examinations from SD 43-91 and was examined by the veterinarian. The diagnosis was a ventral abdomen body wall reducible hernia, and no treatment was required. Female 25390 (11f) had brown discoloration of the face on SD 99.

17.5 Body Weight and Body Weight Changes

Data are summarized in Table 3 (body weights) and Table 4 (body weight changes). Individual data are presented in Appendix 9 and Appendix 10, respectively. Mean body weights are presented graphically in Figure 1 (males) and Figure 2 (females).

Administration with TFM had no effect on body weights or body weight changes. There were no significant differences in mean body weight throughout the study in males and females when compared to concurrent controls. Although not significant, there was a reduction in the mean body weight (610 and

548 grams, respectively) and absolute body weight change (373 and 320 grams, respectively) in Group 6 (100 mg/kg/day) males when compared to control. This was not adverse and was related to the reduction in water and food consumption (Cizek and Nocenti, 1965) as a result of palability of the test substance as discussed below. Mean body weight change for various intervals was significantly decreased for some groups during dosing or significantly increased (SD 64–71; Groups 5 [30 mg/kg/day] and 6 [100 mg/kg/day]) compared to the control. See summary tables for specific intervals. No significant differences in mean body weight change were observed during the recovery phase.

Figure 1: Mean Body Weights-Male

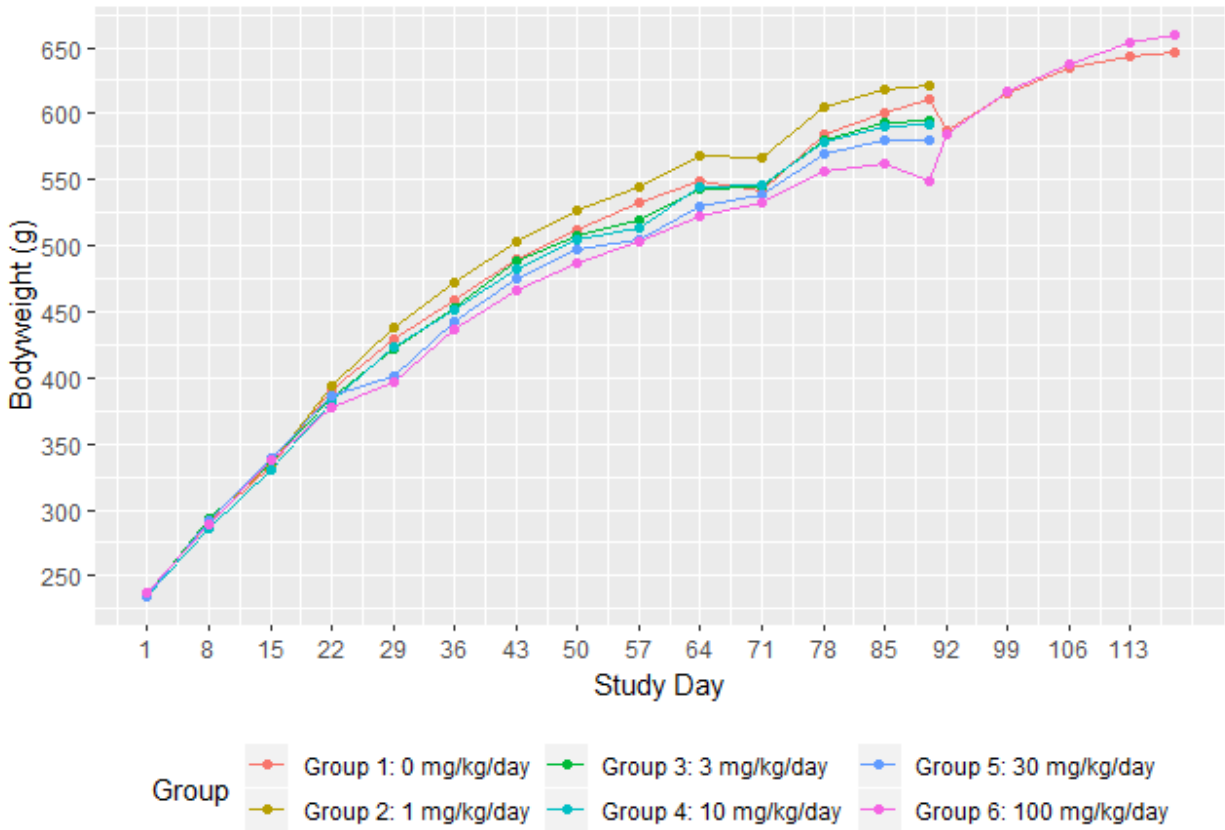
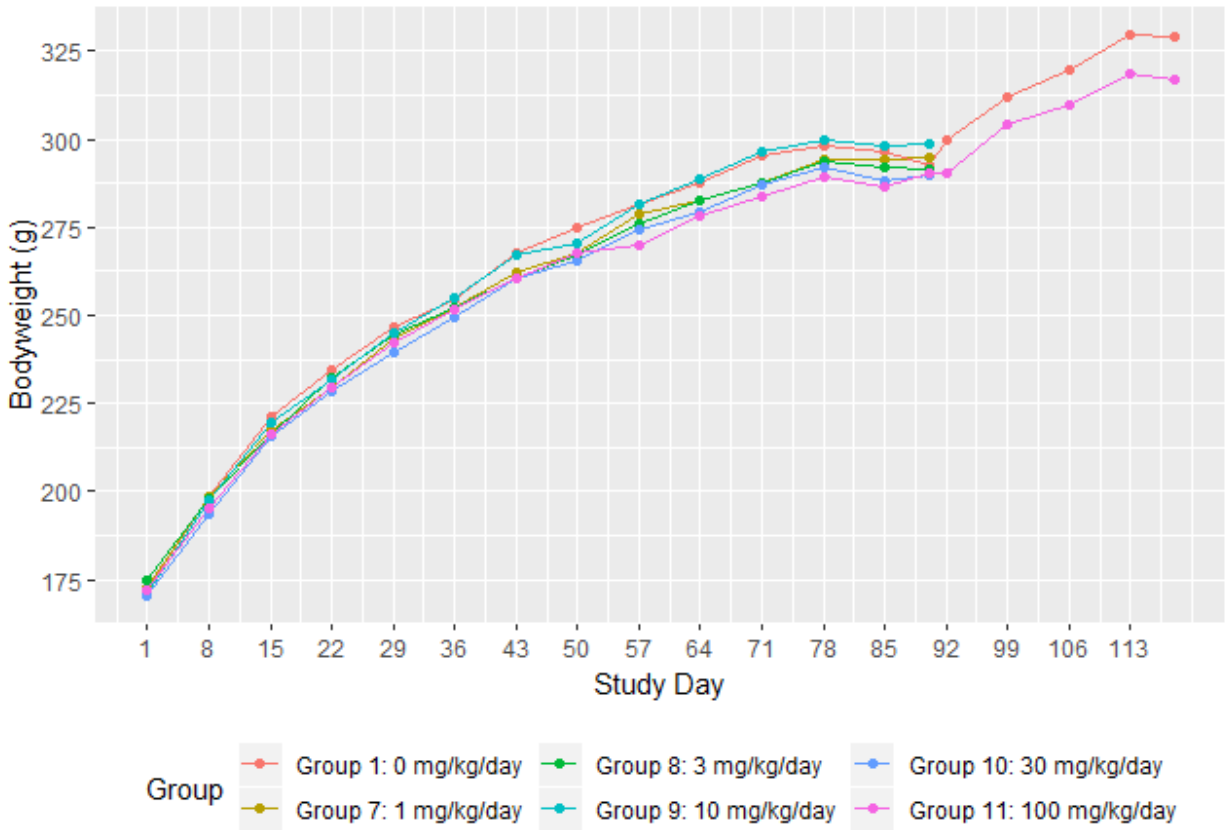


Figure 2: Mean Body Weights-Female



17.6 Water Consumption

Water consumption data are summarized in Table 5; individual data are presented in Appendix 11. Mean water consumption data are presented graphically in Figure 3 (males) and Figure 4 (females).

Administration of TFM via drinking water affected water consumption. Mean total water consumption (SD 1-90) was significantly decreased compared to the control in Group 7 (1 mg/kg/day), Groups 5 and 10 (30 mg/kg/day), 6 and 11 (100 mg/kg/day). The reduction in water consumption was related to palability of the test substance, as the mean water consumed decreased with increasing concentration of the dosing solutions. Mean total water consumption of recovery animals was significantly decreased compared to the control over the entire study period (SD 1–118), but comparable during the recovery phase (SD 92-118), due to the palability issues.

Figure 3: Mean Water Consumption - Male

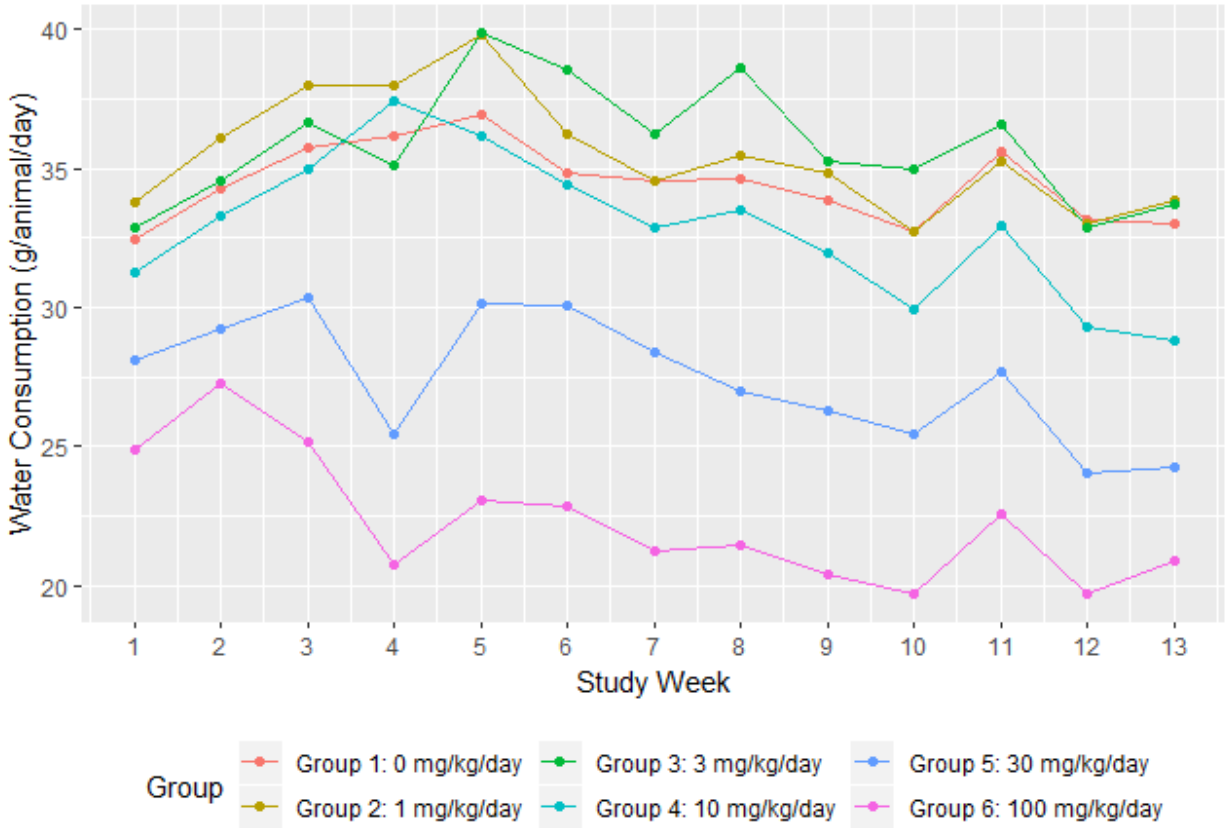
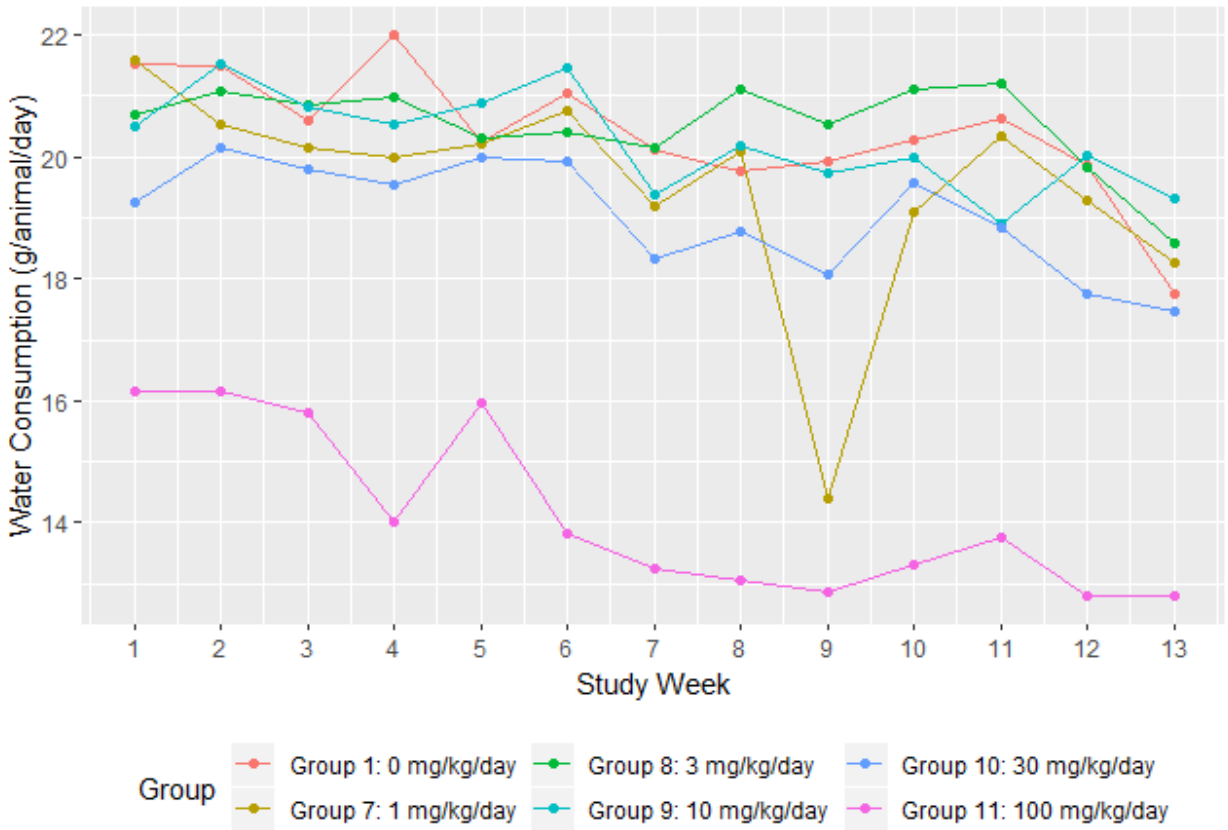


Figure 4: Mean Water Consumption - Female



17.7 Food Consumption

Food consumption data are summarized in Table 6; individual data are presented in Appendix 12. Mean food consumption data are presented graphically in Figure 5 (males) and Figure 6 (females).

Administration of TFM affected food consumption in male rats. There was a decrease in total food consumption from SD 1-90 in Groups 3 (3 mg/kg/day), 4 (10 mg/kg/day), 5 (30 mg/kg/day), and 6 (100 mg/kg/day) compared to the control, but only statistically significant for Group 6. Mean food consumption of males was significantly decreased in Groups 4 to 6 at various intervals throughout dosing. Mean food consumption of Group 6 was significantly higher than the control during the measured intervals from SD 99–118, and the mean total food consumption was significantly higher for the recovery period (SD 92–118). This corresponded to the reduction in water consumption during dosing that was a result of palability issues and was not considered to be test substance-related (Cizek and Nocenti, 1965).

Administration of TFM had no effect on food consumption in female rats. The only significant difference in mean food consumption of females was observed from SD 1–8, where Groups 7 (1 mg/kg/day), 10 (30 mg/kg/day), and 11 (100 mg/kg/day) had lower food consumption compared to the control. Mean total food consumptions of females from SD 1–90, 92–118, and 1–118 were comparable across groups.

Figure 5: Mean Food Consumption - Male

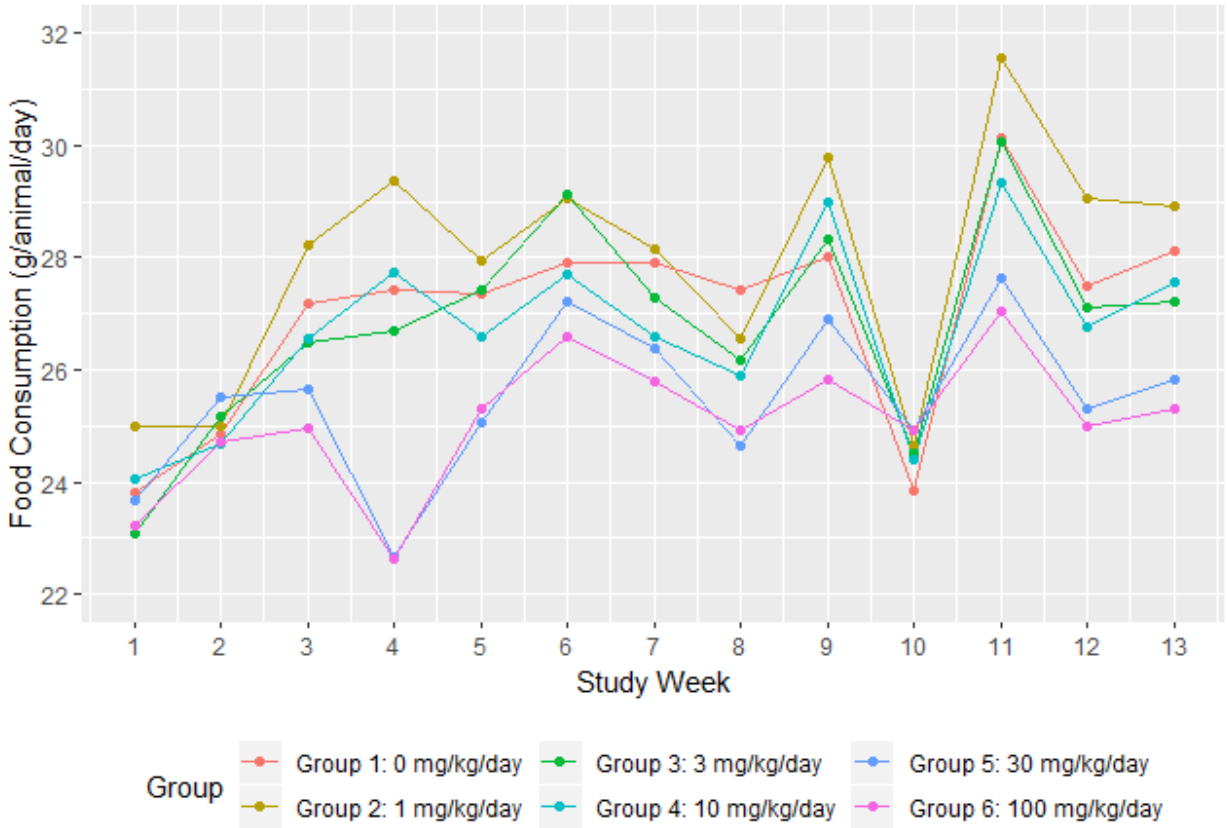
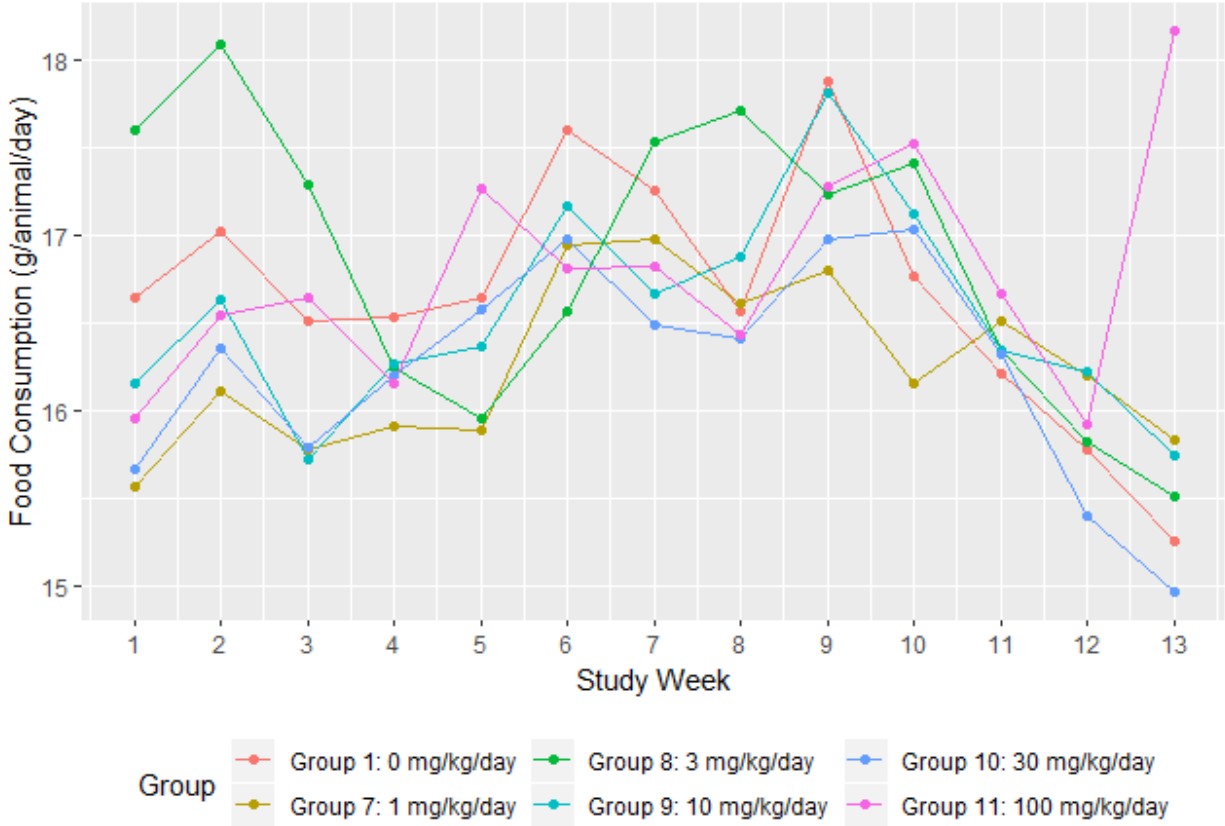


Figure 6: Mean Food Consumption - Female



17.8 Test Material Intake

Test Material Intake (TMI) data are summarized in Table 7; individual data are presented in Appendix 13. The mean achieved dose and mean percent of the target dose is presented in Text Table 15. Mean TMI data are presented graphically in Figure 7 (males) and Figure 8 (females).

Overall, achieved doses were lower than the target dose. The mean % of the target dose for the 13-week dosing period ranged from 86.46% to 93.91% for males and 77.20% to 98.25% for females. This was impacted by the test substance being absorbed into the water bottle stopper and reducing the concentration of the dosing solution.

Mean test material intake for Weeks 1 and 2 was higher than the target dose for Groups 2 and 7 (1 mg/kg/day), Groups 3 and 8 (3 mg/kg/day), Groups 4 (Wk 1 only) and 9 (10 mg/kg/day), and Group 10 (30 mg/kg/day). Doses during Weeks 1 and 2 that were higher than the target dose ranged from 101.03%-133.16% of the target dose. TMI was lower than the target dose for Groups 4 (Wk 2 only), 5 (30 mg/kg/day), 6 (100 mg/kg/day), and 11 (100 mg/kg/day) during Weeks 1 and 2. Mean TMI was higher than the target dose during Wk 11 for Groups 3 (3 mg/kg/day), 5 (30 mg/kg/day), 6 (100 mg/kg/day), 7 (1 mg/kg/day), 8 (3 mg/kg/day), and 10 (30 mg/kg/day). Additionally, mean TMI was higher than the target dose for Group 9 (10 mg/kg/day) during Weeks 12 and 13, and Group

10 (30 mg/kg/day) during Week 10. Mean TMI was below the target dose for all other time periods. The lowest mean TMI was during Week 4, with percents ranging from 64.68% (Group 6; 100 mg/kg/day)-92.19% (Group 8; 3 mg/kg/day).

Text Table 15: Summary of Test Material Intake

Group/Sex	Achieved Dose (mg/kg/day)	% of Target Dose
2m	0.93	93.44
3m	2.82	93.91
4m	9.19	91.91
5m	26.13	87.12
6m	86.46	86.46

Group/Sex	Achieved Dose (mg/kg/day)	% of Target Dose
7f	0.96	96.48
8f	2.94	98.07
9f	9.83	98.25
10f	28.91	96.36
11f	77.20	77.20

Figure 7: Mean Test Material Intake-Male

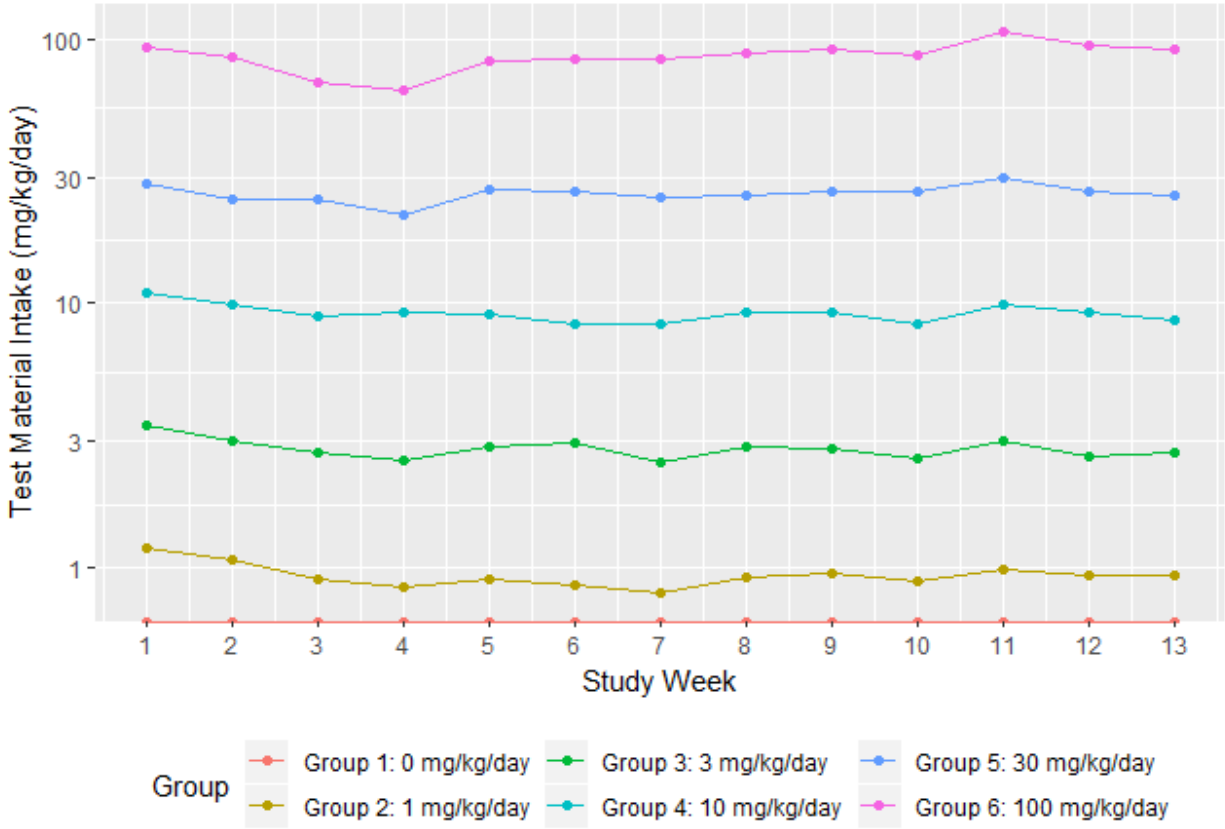
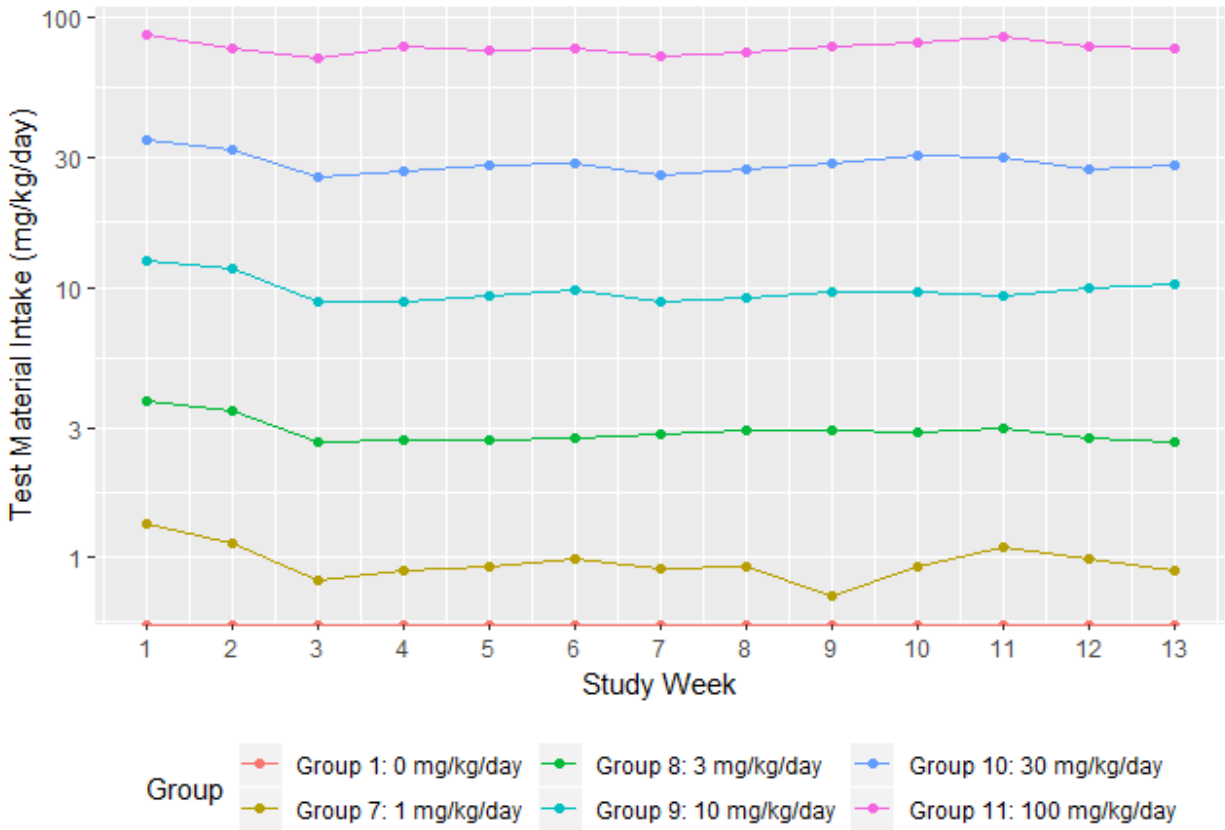


Figure 8: Mean Test Material Intake-Female



17.9 Functional Observation Battery and Grip Strength

Functional observation battery and grip strength data are summarized in Table 8; individual data are presented in Appendix 14. For functional observation battery parameters exopthalmus and palpebral closure, observations were recorded for each eye, but findings are presented for both eyes.

Several animals exhibited abnormalities when assessed and results are summarized in Text Table 16. Observations were not considered test substance-related as they occurred in only one animal of a group, two of the observations were in control animals, and there was no dose-response. Means of rearings, grooms, grip strength (forelimb and hindlimb), and hindlimb splay were comparable across groups.

Text Table 16: Summary of Functional Observation Battery

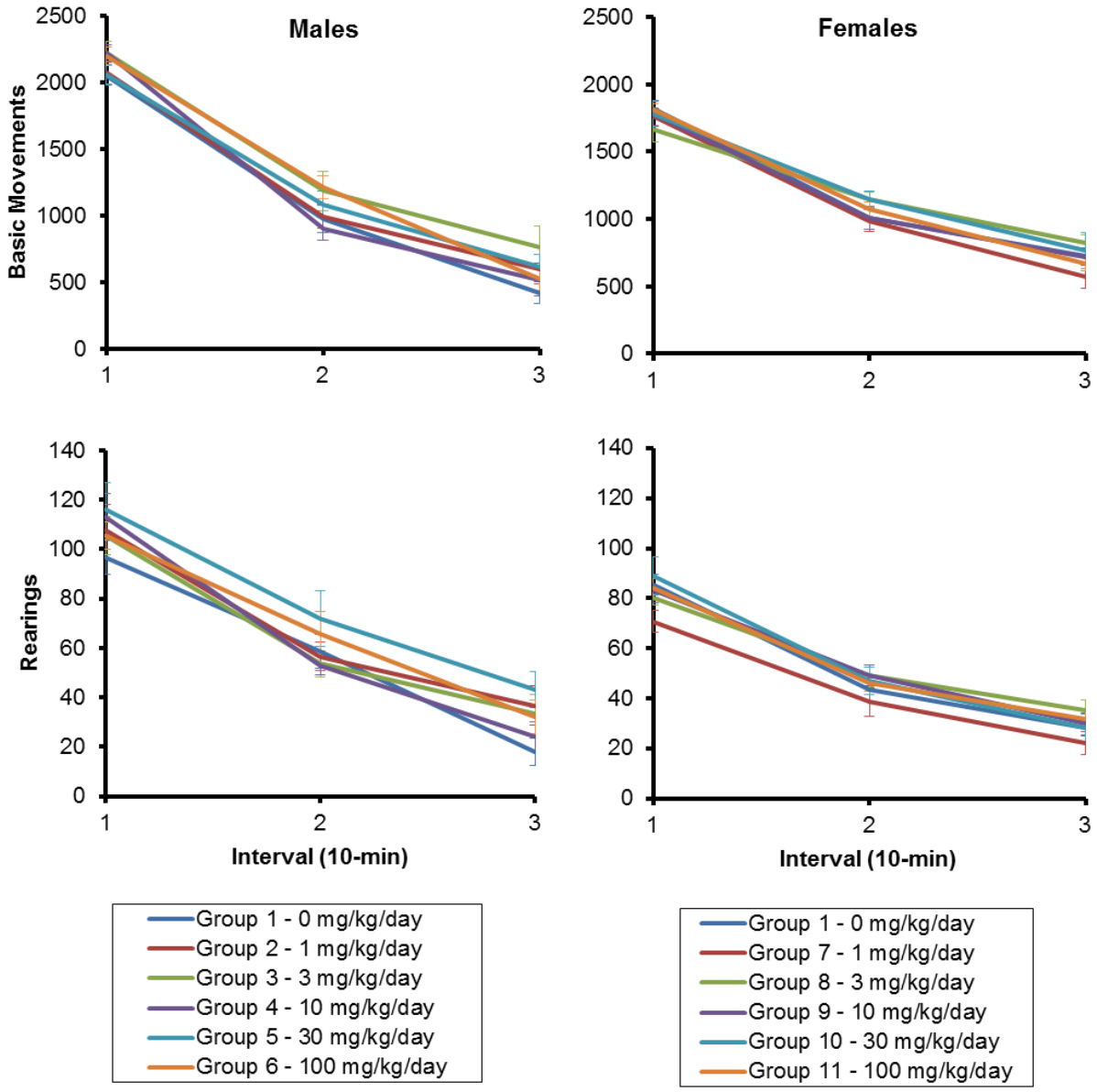
Group	Sex	Animal	FOB Test	Observation	Domain	Score
2	m	25279	Hand Held	Fur Appearance-Stained	Neuromuscular	1
5		25309	Hand Held	Vocalization-During Handling	Activity Arousal	2
1	f	25264	Home Cage	Unusual Behavior-Present	Neuromuscular	1
		25270	Hand Held	Fur Appearance-Stained	Neuromuscular	1
10		25373	Hand Held	Fur Appearance-Stained	Neuromuscular	1

17.10 Locomotor Activity

Locomotor activity data are summarized in Table 9; individual data are presented in Appendix 15. Mean basic movements and rearings are presented graphically with standard error bars in Figure 9.

Administration of TFM did not affect locomotor activity. Mean number of basic movements and rearings decreased over the three ten-minute intervals, showing normal habituation in all groups.

Figure 9: Locomotor Activity – Means



17.11 Estrus Cyclicity

Estrus cycling data are summarized in Table 10; individual vaginal cytology data are presented in Appendix 16.

There were no test substance-related changes in the number or length of the estrus cycle. During Weeks 3 and 4, 100% of rats were cycling, of which 80-100% were regularly cycling. During Weeks 11 and 12, there was an increase in the number of rats not cycling (5.0-11.1%) and the number cycling irregularly (10-40%). This change was consistent across all groups and correlated with an increase in age at the time of collection. Overall, prolonged estrus (greater than three estrus cycles in a row) was the reason for the irregular cycles in all groups. In Group 11 (highest dose), there was one female that had greater than 5 diestrus phases in a row. Typically, the percentage of rats exhibiting irregular estrous cycles increases beginning at 23 weeks of age and prolonged estrus is the most common irregularity noted. The rats were 18-19 weeks at the time of evaluation, however the change was similar across all groups, and there was no dose response, or correlating microscopic findings; therefore, this was not considered test substance-related.

17.12 Ophthalmology

The Ophthalmology Report is presented in Appendix 17.

Administration of TFM had no effect on ophthalmology; no ocular lesions were seen in any animals.

17.13 Clinical and Anatomic Pathology

The Clinical and Anatomic Pathology Report and Histology Report are presented in Appendix 18 and Appendix 19, respectively. Smithers Avanza clinical pathology historical control data are presented in Appendix 20.

17.13.1 Clinical Pathology

Summary data are presented in Table 11 (clinical chemistry), Table 12 (hematology), Table 13 (coagulation), and Table 14 (urinalysis). Individual data are presented in Appendix 21, Appendix 22, Appendix 23, and Appendix 24, respectively.

There were no test substance-related changes in clinical chemistry, hematology, coagulation, or urinalysis parameters at terminal or recovery necropsy.

All changes in mean clinical pathology test values at both timepoints, including those that were statistically significant in treated groups, were considered unrelated to TFM because they were negligible in magnitude, within normal biological variation, lacked a dose-response, were limited to a single sex and/or there were no correlating microscopic findings.

17.13.2 Clinical Chemistry

SD 91

There were no test substance-related changes in clinical chemistry parameters.

Increased mean creatine kinase (CK) in females given 100 mg/kg/day was not considered test article-related due to lack of dose-response, absence of similar changes in males, absence of correlating microscopic findings, and lack of statistical significance.

Decreased mean total protein (TPROT) in males given 100 mg/kg/day was not considered test article-related due to lack of dose-response, absence of similar changes in females, and absence of correlating microscopic findings.

Increased mean (ALTi) in females given 1 and 100 mg/kg/day was not considered test article-related due to lack of dose-response, absence of similar changes in males, and absence of correlating microscopic findings.

SD 119

There were no test substance-related changes in clinical chemistry parameters.

Increased mean calcium (CA) in males given 100 mg/kg/day was not considered test article-related due to the absence of a similar change in females, and because the mean value was within the range of historical control data.

Increased mean potassium (K+) in females given 100 mg/kg/day was not considered test article-related due to the absence of a similar change in males, and because the mean value was within the range of historical control data.

17.13.3 Hematology

SD 91

There were no test substance-related changes in hematology parameters.

Decreased mean absolute eosinophil count (ABSEOS) in males given 100 mg/kg/day was not considered test article-related due to the absence of a similar change in females, absence of dose-response, and because the mean value was within the range of historical control data.

SD 119

There were no test substance-related changes in hematology parameters.

Increased mean red blood cell count (RBC), hemoglobin (HGB), and hematocrit (HCT) in females given 100 mg/kg/day were not considered test article-related due to the absence of similar changes in males and because the mean values were within the range of historical control data.

Decreased mean platelet count (PLT) and increased mean platelet volume (MPV) in males given 100 mg/kg/day were not considered test article-related due to the absence of similar changes in females and because the mean values were within the range of historical control data.

17.13.4 Coagulation

SD 91

There were no test substance-related changes in coagulation parameters.

Decreased mean fibrinogen (FIB) in females given 100 mg/kg/day was not considered test article-related due to the lack of dose-response, absence of similar changes in males, absence of correlating microscopic findings, and because the mean values were within the range of historical control data.

SD 119

There were no test substance-related changes in coagulation parameters.

Increased mean activated partial thromboplastin time (APTT) in females given 100 mg/kg/day, and increased prothrombin time (PT) in males given 100 mg/kg/day were not considered test article-related due to the absence of similar changes in the opposite gender, and absence of correlating macroscopic or clinical observations.

17.13.5 Urinalysis

SD 91

There were no test substance-related changes in urinalysis parameters.

Decreased mean specific gravity (SG) in males given 100 mg/kg/day was not considered test article-related due to the absence of similar changes in females and because the mean value was within the range of historical control data. Increased mean urobilinogen (URO) in females given 100 mg/kg/day was not considered test article-related due to the absence of similar changes in males.

SD 119

There were no test substance-related changes in urinalysis parameters.

Increased mean total urinary volume (TUVOL) in males given 100 mg/kg/day/day was not considered test article-related due to the absence of similar changes in females and because the mean value was within the range of historical control data.

17.13.6 Macroscopic Findings

Gross pathology data are summarized in Table 15; individual data are presented in Appendix 25

Terminal Necropsy (SD 91)

There were no test substance-related macroscopic observations.

Bilateral, clear fluid-filled distention of the uterus was observed in two females administered 10 mg/kg/day and two females administered 30 mg/kg/day TFM, correlating microscopically with dilation of the uterine lumen. This finding of dilated uterine lumen was also observed microscopically in three control females and one females administered 100 mg/kg/day and was likely due to normal estrous cycle activity.

Recovery Necropsy (SD 119)

There were no test substance-related macroscopic observations.

Small testis correlating with severe hypospermatogenesis was observed in one male (25330) administered 100 mg/kg/day TFM. Hypospermatogenesis is a common incidental finding in Sprague Dawley rats, and was observed in two control and two high dose males at the terminal necropsy.

17.13.7 Organ Weights

Organ weight data are summarized in Table 16; individual data are presented in Appendix 26.

There were no test substance-related organ weight changes.

Significantly increased mean relative (to body weight) brain weight in males administered 100 mg/kg/day was due to decreased mean body weight in this group. Significantly increased mean relative (to brain weight) thymus weight in females administered 10 mg/kg/day was considered unrelated to TFM and due to individual variation (primarily attributed to an increase in two animals), as there was no dose response, and similar changes were not present in males.

17.13.8 Microscopic Findings

Histopathology data are summarized in Table 17; individual data are presented in Appendix 27.

There were no test substance-related microscopic findings.

All microscopic findings at the terminal necropsy are considered unrelated to TFM due to their low incidence rates and/or because they are common findings in Sprague Dawley rats of this age.

18.0 CONCLUSION

This study determined the potential toxicity of 4-nitro-3-(trifluoromethyl)phenol (TFM) when administered continuously for 90-days via drinking water to male and female Sprague Dawley rats, and the persistence or reversibility of any toxic effects over a 28-day recovery period.

There were no adverse findings during the in-life phase of study, and all animals survived to the scheduled necropsies. There were no test substance-related alterations in clinical pathology parameters, macroscopic observations, or organ weight changes at any time point, and there were no test substance-related microscopic findings at the terminal necropsy.

In conclusion, there was no toxicity observed after repeat dose administration of TFM to male and female rats. The repeat dose no-observed-adverse-effect level (NOAEL) for male and female rats was considered to be the highest achieved dose levels, 86.5 and 77.2 mg/kg/day, respectively.

19.0 REFERENCE

Cizek, LJ and Nocenti, MR (1965). Relationship Between Water and Food Ingestion in the Rat. American Journal of Physiology 208(4): 615-620.

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 1: Summary of Animal Disposition and Physical Examinations

Day Numbers Relative to Start Date

Animal Disposition

Males: Group:	1	2	3	4	5	6
Terminal Kill						
Number of Animals	20	10	10	10	10	20
Days from - to	91 119	91 91	91 91	91 91	91 91	91 119

Females: Group:	1	7	8	9	10	11
Terminal Kill						
Number of Animals	20	10	10	10	10	20
Days from - to	91 119	91 91	91 91	91 91	91 91	91 119

Physical Examinations:

Group:	1	2	3	4	5	6
Sex: Male						
Abrasion						
Number of Observations	10	9	.	10	.	.
Number of Animals	1	2	.	2	.	.
Days from - to	22 85	43 91	.	50 91	.	.
Alopecia						
Number of Observations	4	.	.	10	.	.
Number of Animals	1	.	.	1	.	.
Days from - to	99 119	.	.	29 91	.	.
Rough Haircoat						
Number of Observations	.	.	.	.	2	4
Number of Animals	.	.	.	.	2	4
Days from - to	.	.	.	.	29 29	29 29

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 1 (continued): Summary of Animal Disposition and Physical Examinations)

Day Numbers Relative to Start Date

Physical Examinations

Group:	1	7	8	9	10	11
Sex: Female						
Abrasion						
Number of Observations	16	.	.	.	.	5
Number of Animals	2	.	.	.	.	2
Days from - to	36 119	.	.	.	.	99 119
Alopecia						
Number of Observations	.	.	.	.	.	4
Number of Animals	.	.	.	.	.	1
Days from - to	.	.	.	.	.	71 91
Discoloration						
Number of Observations	.	.	.	.	.	1
Number of Animals	.	.	.	.	.	1
Days from - to	.	.	.	.	.	99 99
Small Movable Tissue Mass						
Number of Observations	.	.	.	.	8	.
Number of Animals	.	.	.	.	1	.
Days from - to	.	.	.	.	43 91	.

Target Dose: Group 1 - 0 mg/kg/day Groups 2 and 7 - 1 mg/kg/day Groups 3 and 8 - 3 mg/kg/day
Groups 4 and 9 - 10 mg/kg/day Groups 5 and 10 - 30 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 2: Summary of Cageside Observations

No abnormalities were observed throughout the study.

Target Dose:	Group 1 - 0 mg/kg/day	Groups 2 and 7 - 1 mg/kg/day	Groups 3 and 8 - 3 mg/kg/day
	Groups 4 and 9 - 10 mg/kg/day	Groups 5 and 10 - 30 mg/kg/day	Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 3: Summary of Body Weights (g)

			Day Numbers Relative to Start Date							
Group	Sex		1	8	15	22	29	36	43	50
1	m	Mean	236.09	289.96	333.87	390.70	429.88	459.16	489.85	512.67
		S.D.	17.57	19.14	24.30	31.05	38.42	43.11	48.27	51.36
		N	20	20	20	20	20	20	20	20
2	m	Mean	234.60	293.22	334.60	393.57	438.39	472.77	503.26	526.58
		S.D.	10.86	15.01	19.09	23.86	28.84	36.58	41.92	43.59
		N	10	10	10	10	10	10	10	10
3	m	Mean	234.00	294.02	335.85	385.22	421.89	453.30	487.62	507.93
		S.D.	9.12	12.99	14.57	24.38	37.00	38.29	42.94	47.64
		N	10	10	10	10	10	10	10	10
4	m	Mean	234.11	285.61	330.22	381.39	423.03	451.71	481.93	503.93
		S.D.	10.71	13.05	20.75	29.84	39.04	43.16	49.05	51.63
		N	10	10	10	10	10	10	10	10
5	m	Mean	234.09	292.12	339.23	386.83	401.87	441.89	475.26	496.85
		S.D.	8.40	8.41	12.47	16.62	58.83	29.38	30.04	30.25
		N	10	10	10	10	10	10	10	10
6	m	Mean	236.80	288.78	337.60	378.12	396.24	436.95	466.43	487.06
		S.D.	18.72	21.73	26.73	28.98	60.40	45.55	46.92	48.52
		N	20	20	20	20	20	20	20	20

Target Dose: Group 1 – 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 3 (continued): Summary of Body Weights (g)

			Day Numbers Relative to Start Date						
Group	Sex		57	64	71	78	85	90	91F
1	m	Mean	532.00	548.65	542.22	583.78	600.48	610.73	591.05
		S.D.	54.09	56.82	52.56	58.11	61.35	37.24	34.45
		N	20	20	20	20	20	10	10
2	m	Mean	544.67	568.07	565.92	604.74	617.94	620.56	603.94
		S.D.	50.77	54.83	51.58	59.32	67.60	71.34	68.58
		N	10	10	10	10	10	10	10
3	m	Mean	518.89	543.04	544.28	579.98	592.68	594.87	578.39
		S.D.	49.83	52.54	49.87	54.99	55.23	55.27	54.43
		N	10	10	10	10	10	10	10
4	m	Mean	514.17	544.04	546.47	578.95	590.29	592.34	574.39
		S.D.	60.02	60.83	49.53	63.03	66.71	67.29	66.21
		N	10	10	10	10	10	10	10
5	m	Mean	505.02	529.55	539.26	568.83	580.58	580.40	564.99
		S.D.	27.54	28.47	34.87	35.84	35.96	35.46	34.32
		N	10	10	10	10	10	10	10
6	m	Mean	503.03	522.91	533.04	556.63	562.56	548.64	536.76
		S.D.	49.00	52.50	53.93	58.38	61.24	75.78	73.84
		N	20	20	20	20	20	10	10

F = Fasted

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 3 (continued): Summary of Body Weights (g)

			Day Numbers Relative to Start Date							
Group	Sex		1	8	15	22	29	36	43	50
1	f	Mean	172.00	198.70	221.27	234.69	246.47	254.33	267.85	274.75
		S.D.	8.65	10.78	12.78	13.84	15.85	15.97	16.66	18.55
		N	20	20	20	20	20	20	20	20
7	f	Mean	172.31	198.35	217.18	229.31	243.17	252.08	261.91	267.69
		S.D.	5.81	7.14	12.21	13.07	15.76	17.79	21.12	21.27
		N	10	10	10	10	10	10	10	10
8	f	Mean	174.60	198.05	216.48	232.52	244.44	252.42	260.69	267.15
		S.D.	7.39	12.33	14.47	16.29	18.64	20.80	20.70	21.15
		N	10	10	10	10	10	10	10	10
9	f	Mean	170.70	197.18	219.43	231.81	245.15	254.99	267.11	270.27
		S.D.	7.39	9.21	10.26	13.39	14.81	15.41	16.65	15.39
		N	10	10	10	10	10	10	10	10
10	f	Mean	170.17	193.54	215.62	228.37	239.49	249.68	260.45	265.65
		S.D.	8.27	14.67	15.12	16.78	20.33	22.08	21.20	20.94
		N	10	10	10	10	10	10	10	10
11	f	Mean	171.98	195.46	216.33	229.70	242.24	251.66	260.40	267.41
		S.D.	10.46	13.29	16.75	18.68	22.43	24.13	24.97	26.62
		N	20	20	20	20	20	20	20	20

Target Dose: Group 1 – 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 3 (continued): Summary of Body Weights (g)

			Day Numbers Relative to Start Date						
Group	Sex		57	64	71	78	85	90	91F
1	f	Mean	281.68	287.80	295.39	298.28	296.54	292.82	280.44
		S.D.	21.25	22.52	24.69	25.86	26.77	34.33	34.47
		N	20	20	20	20	20	10	10
7	f	Mean	278.84	282.64	287.54	294.13	294.44	295.02	283.96
		S.D.	22.79	19.15	23.66	25.10	26.39	26.74	24.53
		N	10	10	10	10	10	10	10
8	f	Mean	275.82	282.83	287.66	293.44	291.88	291.68	283.43
		S.D.	24.03	26.64	25.96	25.99	28.18	25.25	25.66
		N	10	10	10	10	10	10	10
9	f	Mean	281.55	288.86	296.59	299.52	298.15	298.76	288.99
		S.D.	17.01	18.21	18.30	21.80	21.27	23.44	22.45
		N	10	10	10	10	10	10	10
10	f	Mean	274.45	279.50	287.23	291.91	288.20	289.88	278.59
		S.D.	24.51	28.43	26.99	27.21	27.09	25.37	25.82
		N	10	10	10	10	10	10	10
11	f	Mean	270.16	278.39	283.74	288.98	286.56	290.19	283.24
		S.D.	28.28	28.47	28.50	30.66	31.67	30.71	31.73
		N	20	20	20	20	20	10	10

F = Fasted

Target Dose: Group 1 – 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 3 (continued): Summary of Body Weights (g)

			Day Numbers Relative to Start Date						
Group	Sex		91	92	99	106	113	118	119F
1	m	Mean	591.05	586.59	615.99	633.83	643.81	646.83	630.08
		S.D.	34.45	78.25	87.59	91.72	93.39	94.30	90.72
		N	10	10	10	10	10	10	10
6	m	Mean	536.76	583.81	617.22	637.35	654.06	659.31	642.61
		S.D.	73.84	36.91	42.76	45.82	47.93	48.42	48.23
		N	10	10	10	10	10	10	10
1	f	Mean	280.44	299.80	312.11	319.61	329.52	328.91	316.20
		S.D.	34.47	18.94	20.49	22.64	27.66	30.89	29.72
		N	10	10	10	10	10	10	10
11	f	Mean	283.24	290.54	304.35	309.82	318.74	317.00	302.39
		S.D.	31.73	30.77	33.37	35.78	40.49	39.00	37.24
		N	10	10	10	10	10	10	10

F = Fasted

Target Dose: Group 1 – 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 4: Summary of Body Weight Changes (g)

Day Numbers Relative to Start Date

Group	Sex	From: / To:	1 / 8	8 / 15	15 / 22	22 / 29	29 / 36	36 / 43	43 / 50
1	m	Mean	53.87	43.91	56.83	39.19	29.28	30.69	22.82
		S.D.	9.66	10.18	15.97	10.28	7.23	6.92	4.88
		N	20	20	20	20	20	20	20
2	m	Mean	58.62	41.38	58.97	44.82	34.38	30.49	23.32
		S.D.	8.33	9.51	21.69	7.04	11.78	8.49	5.31
		N	10	10	10	10	10	10	10
3	m	Mean	60.02	41.83	49.37	36.67	31.41	34.32	20.31
		S.D.	7.40	7.88	16.04	16.16	11.17	12.56	7.23
		N	10	10	10	10	10	10	10
4	m	Mean	51.50	44.61	51.17	41.64	28.68	30.22	22.00
		S.D.	6.89	12.10	22.89	11.69	7.27	6.76	5.40
		N	10	10	10	10	10	10	10
5	m	Mean	58.03	47.11	47.60	15.04	40.02	33.37	21.59
		S.D.	6.04	7.79	10.44	50.30	32.74	8.25	5.28
		N	10	10	10	10	10	10	10
6	m	Mean	51.98	48.83	40.52*	18.13	40.71	29.48	20.63
		S.D.	8.62	11.10	12.08	49.39	28.36	7.30	5.41
		N	20	20	20	20	20	20	20

* - Significantly different from the control value, $p \leq 0.05$

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 4 (continued): Summary of Body Weight Changes (g)

Day Numbers Relative to Start Date

Group	Sex	From: To:	50 57	57 64	64 71	71 78	78 85	85 90	Absolute Change 1 90	Percent Change 1 90	90 91F
1	m	Mean	19.33	16.65	-6.44	41.57	16.69	0.41	373.21	158.08	-19.68
		S.D.	7.39	15.64	12.93	11.17	9.49	4.54	40.01	22.13	3.60
		N	20	20	20	20	20	10	10	10	10
2	m	Mean	18.09	23.40	-2.15	38.82	13.20	2.62	385.96	163.99	-16.62
		S.D.	8.67	9.78	9.09	14.27	9.00	5.39	62.62	21.14	5.74
		N	10	10	10	10	10	10	10	10	10
3	m	Mean	10.96*	24.15	1.24	35.70	12.70	2.19	360.87	154.24	-16.48
		S.D.	10.43	16.70	7.34	11.46	4.79	4.23	52.27	21.19	4.43
		N	10	10	10	10	10	10	10	10	10
4	m	Mean	10.24	29.87	2.43	32.48	11.34	2.05	358.23	152.90	-17.95
		S.D.	15.00	10.00	14.29	16.95	5.41	2.23	62.56	24.32	3.01
		N	10	10	10	10	10	10	10	10	10
5	m	Mean	8.17*	24.53	9.71*	29.57*	11.75	-0.18	346.31	148.40	-15.41
		S.D.	6.84	7.36	10.74	10.20	4.81	4.57	39.28	19.74	5.36
		N	10	10	10	10	10	10	10	10	10
6	m	Mean	15.98	19.88	10.13*	23.59*	5.94*	2.25	320.17	140.31	-11.88
		S.D.	8.43	13.13	5.98	8.50	7.51	4.11	68.84	29.53	4.20
		N	20	20	20	20	20	10	10	10	10

F = Fasted
* - Significantly different from the control value, $p \leq 0.05$

Target Dose: Group 1 – 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 4 (continued): Summary of Body Weight Changes (g)

			Day Numbers Relative to Start Date						
		From:	1	8	15	22	29	36	43
Group	Sex	To:	8	15	22	29	36	43	50
1	f	Mean	26.71	22.57	13.42	11.78	7.87	13.53	6.90
		S.D.	5.40	4.67	4.98	5.14	4.51	4.75	4.10
		N	20	20	20	20	20	20	20
7	f	Mean	26.04	18.83	12.13	13.86	8.91	9.83	5.78
		S.D.	4.44	7.16	4.98	5.11	4.96	4.68	4.49
		N	10	10	10	10	10	10	10
8	f	Mean	23.45	18.43	16.04	11.92	7.98	8.27*	6.46
		S.D.	7.88	5.64	8.36	6.64	4.23	3.09	4.41
		N	10	10	10	10	10	10	10
9	f	Mean	26.48	22.25	12.38	13.34	9.84	12.12	3.16
		S.D.	8.12	4.85	4.90	3.86	3.48	4.36	3.08
		N	10	10	10	10	10	10	10
10	f	Mean	23.37	22.08	12.75	11.12	10.19	10.77	5.20
		S.D.	8.96	4.88	5.99	4.64	4.46	4.06	4.41
		N	10	10	10	10	10	10	10
11	f	Mean	23.48	20.88	13.37	12.55	9.42	8.75*	7.01
		S.D.	6.60	5.55	4.64	5.66	5.19	4.21	4.28
		N	20	20	20	20	20	20	20

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 4 (continued): Summary of Body Weight Changes (g)

Day Numbers Relative to Start Date

Group	Sex	From: To:	50 57	57 64	64 71	71 78	78 85	85 90	Absolute Change 1 90	Percent Change 1 90	90 91F
1	f	Mean	6.93	6.12	7.60	2.89	-1.75	-0.24	122.90	72.12	-12.38
		S.D.	5.74	6.32	4.84	4.89	4.91	2.49	30.11	16.09	2.16
		N	20	20	20	20	20	10	10	10	10
7	f	Mean	11.15	3.80	4.90	6.59	0.31	0.58	122.71	71.30	-11.06
		S.D.	2.97	4.89	6.08	4.84	4.59	3.50	26.37	15.56	2.97
		N	10	10	10	10	10	10	10	10	10
8	f	Mean	8.67	7.01	4.83	5.78	-1.56	-0.20	117.08	67.00	-8.25
		S.D.	5.95	6.55	2.95	3.69	3.36	4.06	21.65	11.65	3.80
		N	10	10	10	10	10	10	10	10	10
9	f	Mean	11.28	7.31	7.73	2.93	-1.37	0.61	128.06	75.14	-9.77
		S.D.	4.25	3.86	4.35	5.50	5.57	3.62	22.31	13.01	5.40
		N	10	10	10	10	10	10	10	10	10
10	f	Mean	8.80	5.05	7.73	4.68	-3.71	1.68	119.71	70.23	-11.29
		S.D.	4.99	5.56	5.97	4.71	4.45	4.08	20.10	10.74	2.45
		N	10	10	10	10	10	10	10	10	10
11	f	Mean	2.76	8.23	5.35	5.24	-2.42	-0.83	117.74	68.18	-6.95
		S.D.	7.64	8.19	8.21	7.88	6.63	3.90	25.11	13.75	3.79
		N	20	20	20	20	20	10	10	10	10

F = Fasted

Target Dose: Group 1 – 0 mg/kg/day Groups 2 and 7 - 1 mg/kg/day Groups 3 and 8 - 3 mg/kg/day
Groups 4 and 9 - 10 mg/kg/day Groups 5 and 10 - 30 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 4 (continued): Summary of Body Weight Changes (g)

Day Numbers Relative to Start Date

Group	Sex	From: To:	85 92	92 99	99 106	106 113	113 118	Absolute Change 1 118	Percent Change 1 118	Absolute Change 92 118	Percent Change 92 118	118 119F
1	m	Mean	-4.04	29.40	17.84	9.98	3.02	412.17	175.74	60.24	10.12	-16.75
		S.D.	10.72	12.73	6.57	4.18	4.26	85.59	35.18	20.91	2.79	4.40
		N	10	10	10	10	10	10	10	10	10	10
6	m	Mean	5.08	33.41	20.13	16.71*	5.25	414.18	170.16	75.50	12.89	-16.70
		S.D.	9.41	10.01	6.91	5.40	4.71	53.15	28.87	19.28	3.04	3.33
		N	10	10	10	10	10	10	10	10	10	10
1	f	Mean	-0.21	12.31	7.50	9.91	-0.61	154.84	89.21	29.11	9.56	-12.71
		S.D.	6.17	5.23	4.07	7.81	6.86	29.67	17.60	14.82	4.42	2.91
		N	10	10	10	10	10	10	10	10	10	10
11	f	Mean	8.44*	13.81	5.47	8.92	-1.74	145.50	84.59	26.46	8.97	-14.61
		S.D.	7.29	5.30	6.02	10.20	3.63	31.98	15.81	10.34	2.68	2.58
		N	10	10	10	10	10	10	10	10	10	10

F = Fasted
* - Significantly different from the control value, $p \leq 0.05$

Target Dose: Group 1 – 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 5: Summary of Water Consumption (g/animal/day)

			Day Numbers Relative to Start Date						
		From:	1	8	15	22	29	36	43
Group	Sex	To:	8	15	22	29	36	43	50
1	m	Mean	32.42	34.27	35.71	36.19	36.96	34.82	34.57
		S.D.	5.00	6.21	7.30	7.89	7.69	8.23	7.23
		N	20	20	20	20	20	20	20
2	m	Mean	33.76	36.06	37.99	37.95	39.79	36.25	34.54
		S.D.	3.24	3.07	3.56	3.95	5.45	4.60	4.08
		N	10	10	10	10	10	10	10
3	m	Mean	32.84	34.57	36.66	35.09	39.86	38.51*	36.25
		S.D.	1.86	2.94	4.74	8.13	3.79	4.45	4.00
		N	10	10	10	10	10	10	10
4	m	Mean	31.23	33.28	34.97	37.39	36.13	34.40	32.89
		S.D.	2.30	3.05	4.77	5.24	5.01	3.72	3.28
		N	10	10	10	10	10	10	10
5	m	Mean	28.14*	29.21*	30.37*	25.42*	30.11*	30.05	28.40*
		S.D.	1.71	3.16	3.84	13.28	4.22	3.48	4.04
		N	10	10	10	10	10	10	10
6	m	Mean	24.88*	27.27*	25.13*	20.73*	23.09*	22.84*	21.27*
		S.D.	1.70	1.66	1.74	9.86	2.55	1.65	1.81
		N	20	20	20	20	20	20	20

* - Significantly different from the control value, $p \leq 0.05$

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 5 (continued): Summary of Water Consumption (g/animal/day)

Day Numbers Relative to Start Date

Group	Sex	From: / To:	50 / 57	57 / 64	64 / 71	71 / 78	78 / 85	85 / 90	Total 1 / 90
1	m	Mean	34.64	33.86	32.75	35.61	33.16	33.04	3069.81
		S.D.	7.61	7.55	6.99	5.32	6.37	7.06	605.20
		N	20	20	20	20	20	20	20
2	m	Mean	35.45	34.85	32.73	35.25	32.98	33.85	3162.44
		S.D.	4.07	4.93	4.28	4.25	3.56	4.96	351.93
		N	10	10	10	10	10	10	10
3	m	Mean	38.62*	35.23	34.96	36.56	32.84	33.68	3192.23
		S.D.	4.32	2.96	4.05	3.63	3.86	4.04	315.40
		N	10	10	10	10	10	10	10
4	m	Mean	33.50	31.94	29.90	32.92	29.29	28.84	2929.12
		S.D.	4.30	3.82	2.94	3.27	3.47	3.18	305.18
		N	10	10	10	10	10	10	10
5	m	Mean	26.96*	26.30*	25.41*	27.69*	24.01*	24.26*	2445.89*
		S.D.	2.46	2.62	2.79	2.76	2.48	2.26	317.41
		N	10	10	10	10	10	10	10
6	m	Mean	21.46*	20.37*	19.68*	22.57*	19.68*	20.92*	1987.40*
		S.D.	1.77	2.21	1.77	1.92	2.14	2.46	177.19
		N	20	20	20	20	20	20	20

* - Significantly different from the control value, $p \leq 0.05$

Target Dose: Group 1 – 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 5 (continued): Summary of Water Consumption (g/animal/day)

			Day Numbers Relative to Start Date						
		From:	1	8	15	22	29	36	43
Group	Sex	To:	8	15	22	29	36	43	50
1	f	Mean	21.53	21.49	20.59	22.00	20.25	21.06	20.13
		S.D.	1.55	1.31	1.94	3.12	1.24	1.31	1.31
		N	20	20	20	20	20	20	20
7	f	Mean	21.58	20.54	20.14	20.00	20.23	20.75	19.20
		S.D.	1.43	1.98	2.56	3.56	3.27	3.52	2.76
		N	10	10	10	10	10	10	10
8	f	Mean	20.68	21.08	20.86	20.99	20.32	20.40	20.14
		S.D.	4.71	3.30	3.64	4.04	3.10	3.33	2.71
		N	10	10	10	10	10	10	10
9	f	Mean	20.51	21.53	20.82	20.52	20.89	21.47	19.39
		S.D.	2.54	2.02	3.13	3.12	3.78	3.47	3.34
		N	10	10	10	10	10	10	10
10	f	Mean	19.27*	20.16	19.80	19.56	20.00	19.92	18.33
		S.D.	0.37	1.18	1.40	2.10	1.62	1.18	2.28
		N	10	10	10	10	10	10	10
11	f	Mean	16.14*	16.17*	15.80*	14.01*	15.97*	13.83*	13.24*
		S.D.	1.13	1.09	2.31	1.42	5.20	0.99	1.22
		N	20	20	20	20	20	20	20

* - Significantly different from the control value, $p \leq 0.05$

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 5 (continued): Summary of Water Consumption (g/animal/day)

Day Numbers Relative to Start Date

Group	Sex	From: / To:	50 / 57	57 / 64	64 / 71	71 / 78	78 / 85	85 / 90	Total 1 / 90
1	f	Mean	19.78	19.94	20.29	20.64	19.87	17.75	1821.81
		S.D.	1.94	1.55	1.20	1.63	1.89	3.44	120.22
		N	20	20	20	20	20	20	20
7	f	Mean	20.09	14.40*	19.10	20.33	19.29	18.28	1740.85*
		S.D.	2.89	7.93	3.41	3.15	3.17	2.93	254.47
		N	10	10	10	10	10	10	10
8	f	Mean	21.10	20.53	21.12	21.20	19.83	18.59	1830.71
		S.D.	3.61	3.31	3.25	2.50	2.67	3.01	287.61
		N	10	10	10	10	10	10	10
9	f	Mean	20.20	19.73	20.00	18.92	20.04	19.31	1804.71
		S.D.	4.01	3.90	3.55	2.50	3.97	2.99	277.59
		N	10	10	10	10	10	10	10
10	f	Mean	18.79	18.08*	19.57	18.85*	17.77	17.47	1698.00*
		S.D.	1.52	1.70	0.60	0.62	1.46	1.84	107.52
		N	10	10	10	10	10	10	10
11	f	Mean	13.04*	12.85*	13.32*	13.76*	12.79*	12.80*	1260.39*
		S.D.	3.08	1.43	1.04	1.42	1.12	1.04	95.47
		N	20	20	20	20	20	20	20

* - Significantly different from the control value, $p \leq 0.05$

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 5 (continued): Summary of Water Consumption (g/animal/day)

Day Numbers Relative to Start Date

Group	Sex	From: / To:	90 / 92	92 / 99	99 / 106	106 / 113	113 / 118	Total 92 / 118	Total 1 / 118
1	m	Mean	26.97	36.47	35.06	34.21	33.92	909.73	4244.39
		S.D.	7.06	9.83	10.18	9.09	9.96	252.50	1023.91
		N	10	10	10	10	10	10	10
6	m	Mean	36.43*	36.59	33.27	34.89	35.49	910.69	3035.32*
		S.D.	8.78	5.77	4.50	5.30	6.61	138.50	254.43
		N	10	10	10	10	10	10	10
1	f	Mean	19.53	19.57	20.90	21.31	21.75	541.28	2387.56
		S.D.	2.69	2.74	3.41	3.04	3.23	78.19	195.01
		N	10	10	10	10	10	10	10
11	f	Mean	25.24*	22.33*	21.55	22.04	22.11	572.00	1862.09*
		S.D.	3.58	2.76	2.87	3.97	3.09	80.90	166.46
		N	10	10	10	10	10	10	10

* - Significantly different from the control value, $p \leq 0.05$

Target Dose: Group 1 – 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 6: Summary of Food Consumption (g/animal/day)

			Day Numbers Relative to Start Date						
		From:	1	8	15	22	29	36	43
Group	Sex	To:	8	15	22	29	36	43	50
1	m	Mean	23.80	24.84	27.18	27.41	27.35	27.90	27.90
		S.D.	0.88	1.35	2.21	2.26	2.14	1.65	1.64
		N	20	20	20	20	20	20	20
2	m	Mean	24.98	24.99	28.24	29.36	27.95	29.07	28.14
		S.D.	1.15	0.88	3.01	3.38	2.22	2.47	1.93
		N	10	10	10	10	10	10	10
3	m	Mean	23.09	25.16	26.50	26.70	27.44	29.13	27.29
		S.D.	4.31	0.59	1.67	3.28	1.43	1.67	1.04
		N	10	10	10	10	10	10	10
4	m	Mean	24.07	24.68	26.55	27.74	26.60	27.69	26.60
		S.D.	0.60	1.06	3.44	4.04	2.74	3.23	1.80
		N	10	10	10	10	10	10	10
5	m	Mean	23.66	25.50	25.65	22.68	25.05*	27.21	26.37*
		S.D.	1.05	2.92	1.85	8.17	0.65	1.39	1.14
		N	10	10	10	10	10	10	10
6	m	Mean	23.22	24.70	24.96*	22.65	25.29*	26.60	25.79*
		S.D.	1.04	1.16	1.49	7.94	1.60	1.91	1.85
		N	20	20	20	20	20	20	20

* - Significantly different from the control value, $p \leq 0.05$

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 6 (continued): Summary of Food Consumption (g/animal/day)

Day Numbers Relative to Start Date

Group	Sex	From: / To:	50 / 57	57 / 64	64 / 71	71 / 78	78 / 85	85 / 90	Total 1 / 90
1	m	Mean	27.41	28.01	23.86	30.14	27.50	28.13	2442.23
		S.D.	1.52	2.58	1.26	1.26	1.45	0.90	56.74
		N	20	20	20	20	20	10	10
2	m	Mean	26.56	29.78	24.64	31.55	29.04	28.91	2484.64
		S.D.	2.28	3.32	0.85	4.10	4.27	3.43	189.66
		N	10	10	10	10	10	10	10
3	m	Mean	26.19	28.31	24.51	30.07	27.10	27.23	2386.49
		S.D.	1.99	2.23	1.91	1.50	1.42	0.71	99.23
		N	10	10	10	10	10	10	10
4	m	Mean	25.88*	28.99	24.40	29.33	26.76	27.58	2372.87
		S.D.	4.18	3.78	0.91	4.24	3.33	3.55	232.29
		N	10	10	10	10	10	10	10
5	m	Mean	24.64*	26.91	24.94	27.62*	25.30*	25.82	2267.80
		S.D.	1.05	2.12	1.53	1.16	1.16	0.98	140.73
		N	10	10	10	10	10	10	10
6	m	Mean	24.91*	25.83	24.92	27.06*	24.99*	25.32	2166.91*
		S.D.	1.24	2.06	1.23	2.30	2.15	2.93	161.06
		N	20	20	20	20	20	10	10

* - Significantly different from the control value, $p \leq 0.05$

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 6 (continued): Summary of Food Consumption (g/animal/day)

			Day Numbers Relative to Start Date						
		From:	1	8	15	22	29	36	43
Group	Sex	To:	8	15	22	29	36	43	50
1	f	Mean	16.65	17.02	16.51	16.53	16.65	17.60	17.26
		S.D.	0.60	0.85	1.12	1.06	0.95	0.95	1.18
		N	20	20	20	20	20	20	20
7	f	Mean	15.57*	16.11	15.78	15.91	15.89	16.95	16.98
		S.D.	0.37	0.98	0.90	0.72	1.61	1.56	1.46
		N	10	10	10	10	10	10	10
8	f	Mean	17.60	18.09	17.29	16.24	15.96	16.57	17.54
		S.D.	3.53	3.96	3.33	1.09	1.22	1.19	3.32
		N	10	10	10	10	10	10	10
9	f	Mean	16.15	16.63	15.72	16.27	16.37	17.17	16.67
		S.D.	0.78	0.57	0.60	0.71	0.34	0.59	0.36
		N	10	10	10	10	10	10	10
10	f	Mean	15.66*	16.36	15.79	16.20	16.58	16.98	16.49
		S.D.	1.09	0.94	1.02	1.30	0.90	0.75	0.69
		N	10	10	10	10	10	10	10
11	f	Mean	15.96*	16.55	16.65	16.16	17.27	16.81	16.82
		S.D.	1.24	1.69	2.21	1.38	2.60	1.61	1.40
		N	20	20	20	20	20	20	20

* - Significantly different from the control value, $p \leq 0.05$

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 6 (continued): Summary of Food Consumption (g/animal/day)

Day Numbers Relative to Start Date

Group	Sex	From: / To:	50 / 57	57 / 64	64 / 71	71 / 78	78 / 85	85 / 90	Total 1 / 90
1	f	Mean	16.57	17.88	16.77	16.21	15.78	15.25	1469.31
		S.D.	1.63	1.81	1.34	1.54	1.46	0.68	73.96
		N	20	20	20	20	20	10	10
7	f	Mean	16.61	16.80	16.16	16.51	16.20	15.83	1447.44
		S.D.	1.30	0.81	1.28	1.49	1.58	1.28	99.10
		N	10	10	10	10	10	10	10
8	f	Mean	17.72	17.24	17.41	16.35	15.82	15.51	1504.46
		S.D.	3.29	1.18	2.45	0.68	0.68	0.64	175.38
		N	10	10	10	10	10	10	10
9	f	Mean	16.88	17.82	17.13	16.34	16.22	15.74	1474.27
		S.D.	0.39	0.78	0.38	0.89	1.06	1.20	42.26
		N	10	10	10	10	10	10	10
10	f	Mean	16.41	16.98	17.04	16.32	15.40	14.96	1448.28
		S.D.	0.75	0.84	0.79	0.90	0.79	0.62	59.80
		N	10	10	10	10	10	10	10
11	f	Mean	16.43	17.28	17.53	16.67	15.92	18.17	1503.04
		S.D.	3.23	2.03	2.74	1.62	1.54	6.40	196.72
		N	20	20	20	20	20	10	10

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 6 (continued): Summary of Food Consumption (g/animal/day)

Day Numbers Relative to Start Date

Group	Sex	From: / To:	85 / 92	92 / 99	99 / 106	106 / 113	113 / 118	Total 92 / 118	Total 1 / 118
1	m	Mean	25.11	28.71	28.16	27.63	28.24	732.67	3132.88
		S.D.	0.88	1.74	1.95	1.37	1.66	40.70	180.16
		N	10	10	10	10	10	10	10
6	m	Mean	25.07	29.06	30.94*	29.78*	30.52*	781.06*	3128.94
		S.D.	0.94	1.12	1.79	1.57	1.53	35.82	88.13
		N	10	10	10	10	10	10	10
1	f	Mean	16.65	16.89	18.23	18.77	21.27	483.58	2026.94
		S.D.	4.19	1.35	1.89	2.10	5.66	56.83	165.46
		N	10	10	10	10	10	10	10
11	f	Mean	14.91	17.89	17.78	18.03	17.74	464.57	1957.27
		S.D.	0.68	1.26	0.94	1.56	1.85	34.59	136.76
		N	10	10	10	10	10	10	10

* - Significantly different from the control value, $p \leq 0.05$

Target Dose: Group 1 - 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 7: Summary of Test Material Intake

Day Numbers Relative to Start Date

Group/Sex		Wk1	Wk2	Wk3	Wk4	Wk5	Wk6	Wk7	Wk8	Wk9	Wk10	Wk11	Wk12	Wk13	Mean
1m	Mean	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	S.D.	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	N.	20	20	20	20	20	20	20	20	20	20	20	20	20	20
2m	Mean	1.18	1.06	0.90	0.85	0.90	0.85	0.80	0.92	0.95	0.89	0.98	0.93	0.94	0.93
	S.D.	0.10	0.09	0.08	0.08	0.10	0.08	0.08	0.09	0.10	0.10	0.09	0.06	0.07	0.10
	N.	10	10	10	10	10	10	10	10	10	10	10	10	10	10
3m	Mean	3.43	3.03	2.71	2.53	2.88	2.96	2.49	2.87	2.79	2.60	3.01	2.62	2.71	2.82
	S.D.	0.23	0.27	0.36	0.56	0.26	0.31	0.29	0.32	0.22	0.28	0.25	0.27	0.33	0.26
	N.	10	10	10	10	10	10	10	10	10	10	10	10	10	10
4m	Mean	10.99	9.89	8.89	9.22	9.02	8.34	8.38	9.26	9.29	8.42	9.95	9.20	8.63	9.19
	S.D.	1.00	1.00	1.27	1.39	1.26	0.86	0.95	1.23	1.20	0.91	0.84	1.05	1.11	0.75
	N.	10	10	10	10	10	10	10	10	10	10	10	10	10	10
5m	Mean	28.59	24.70	24.91	21.62	27.18	26.61	25.09	25.50	26.57	26.62	30.09	26.58	25.69	26.13
	S.D.	2.07	2.66	2.74	11.16	2.00	2.09	2.56	1.66	1.80	1.86	1.97	2.26	1.41	2.02
	N.	10	10	10	10	10	10	10	10	10	10	10	10	10	10
6m	Mean	92.60	85.16	69.26	64.68	83.33	83.85	83.71	88.71	91.12	87.62	106.45	95.64	91.83	86.46
	S.D.	6.64	6.92	6.69	30.28	6.55	7.97	7.43	7.55	9.48	8.17	9.61	9.66	9.56	10.70
	N.	20	20	20	20	20	20	20	20	20	20	20	20	20	20

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 7 (continued): Summary of Test Material Intake

Day Numbers Relative to Start Date

Group/Sex		Wk1	Wk2	Wk3	Wk4	Wk5	Wk6	Wk7	Wk8	Wk9	Wk10	Wk11	Wk12	Wk13	Mean
1f	Mean	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	S.D.	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	N.	20	20	20	20	20	20	20	20	20	20	20	20	20	20
7f	Mean	1.33	1.13	0.82	0.90	0.93	0.98	0.91	0.93	0.72	0.93	1.10	0.99	0.90	0.96
	S.D.	0.09	0.10	0.08	0.14	0.12	0.12	0.11	0.10	0.39	0.12	0.13	0.12	0.10	0.15
	N.	10	10	10	10	10	10	10	10	10	10	10	10	10	10
8f	Mean	3.79	3.47	2.65	2.71	2.73	2.77	2.85	2.97	2.93	2.91	3.02	2.78	2.66	2.94
	S.D.	0.87	0.53	0.44	0.48	0.41	0.42	0.37	0.44	0.43	0.42	0.33	0.36	0.42	0.33
	N.	10	10	10	10	10	10	10	10	10	10	10	10	10	10
9f	Mean	12.58	11.69	8.77	8.79	9.32	9.81	8.84	9.13	9.66	9.55	9.29	10.01	10.29	9.83
	S.D.	1.60	1.20	1.45	1.54	1.98	1.81	1.81	2.15	2.18	2.03	1.30	2.45	1.97	1.14
	N.	10	10	10	10	10	10	10	10	10	10	10	10	10	10
10f	Mean	34.79	32.42	25.79	26.93	28.44	28.78	26.21	27.41	28.60	30.52	30.41	27.22	28.25	28.91
	S.D.	2.02	3.31	2.43	3.50	3.02	2.67	3.54	3.34	3.94	3.20	2.99	3.48	4.05	2.56
	N.	10	10	10	10	10	10	10	10	10	10	10	10	10	10
11f	Mean	85.72	76.74	69.93	78.20	75.72	76.28	71.20	74.24	77.33	80.05	84.62	77.29	76.22	77.20
	S.D.	5.13	6.44	11.69	13.55	20.71	7.20	6.61	16.82	9.12	8.22	8.77	7.71	8.15	4.46
	N.	20	20	20	20	20	20	20	20	20	20	20	20	20	20

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 8: Summary of Functional Observation Battery

Days 83 or 84 Relative to Start Date

Activity Arousal:

Group	Sex		Handling Reactivity	Vocalization	Posture (Home Cage)	Posture (Open Field)	Rearings
1	m	Mean	0.0	0.0	0.0	0.0	12.0
		S.D.	0.0	0.0	0.0	0.0	5.4
		N	20	20	20	20	20
2	m	Mean	0.0	0.0	0.0	0.0	13.1
		S.D.	0.0	0.0	0.0	0.0	3.3
		N	10	10	10	10	10
3	m	Mean	0.0	0.0	0.0	0.0	9.6
		S.D.	0.0	0.0	0.0	0.0	3.6
		N	10	10	10	10	10
4	m	Mean	0.0	0.0	0.0	0.0	12.9
		S.D.	0.0	0.0	0.0	0.0	7.2
		N	10	10	10	10	10
5	m	Mean	0.0	0.2	0.0	0.0	13.1
		S.D.	0.0	0.6	0.0	0.0	4.6
		N	10	10	10	10	10
6	m	Mean	0.0	0.0	0.0	0.0	12.0
		S.D.	0.0	0.0	0.0	0.0	4.2
		N	20	20	20	20	20

Target Dose: Group 1 – 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 8 (continued): Summary of Functional Observation Battery

Days 83 or 84 Relative to Start Date

Autonomic:

Group Sex		Exopthalmus	Lacrimation	Palpebral Closure	Piloerection	Pupillary Status (Hand Held)	Salivation	Pupillary Response (Elicited)	No. Fecal Boli	No. Urine Pools
1m	Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.2	1.9
	S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.7	3.4
	N	20	20	20	20	20	20	20	20	20
2m	Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.3
	S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	2.6
	N	10	10	10	10	10	10	10	10	10
3m	Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	4.0
	S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.3	5.2
	N	10	10	10	10	10	10	10	10	10
4m	Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.3	0.7
	S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.9	1.6
	N	10	10	10	10	10	10	10	10	10
5m	Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.8
	S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.6
	N	10	10	10	10	10	10	10	10	10
6m	Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.5	0.7
	S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.4	1.6
	N	20	20	20	20	20	20	20	20	20

Target Dose: Group 1 - 0 mg/kg/day Groups 2 and 7 - 1 mg/kg/day Groups 3 and 8 - 3 mg/kg/day
Groups 4 and 9 - 10 mg/kg/day Groups 5 and 10 - 30 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 8 (continued): Summary of Functional Observation Battery

Days 83 or 84 Relative to Start Date

Neuromuscular:

Group	Sex		Activity (Home Cage)	Activity (Open Field)	Fur Appearance	Unusual Behavior (Home Cage)	Unusual Behavior (Open Field)
1	m	Mean	0.0	0.0	0.0	0.0	0.0
		S.D.	0.0	0.0	0.0	0.0	0.0
		N	20	20	20	20	20
2	m	Mean	0.0	0.0	0.1	0.0	0.0
		S.D.	0.0	0.0	0.3	0.0	0.0
		N	10	10	10	10	10
3	m	Mean	0.0	0.0	0.0	0.0	0.0
		S.D.	0.0	0.0	0.0	0.0	0.0
		N	10	10	10	10	10
4	m	Mean	0.0	0.0	0.0	0.0	0.0
		S.D.	0.0	0.0	0.0	0.0	0.0
		N	10	10	10	10	10
5	m	Mean	0.0	0.0	0.0	0.0	0.0
		S.D.	0.0	0.0	0.0	0.0	0.0
		N	10	10	10	10	10
6	m	Mean	0.0	0.0	0.0	0.0	0.0
		S.D.	0.0	0.0	0.0	0.0	0.0
		N	20	20	20	20	20

Target Dose: Group 1 – 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 8 (continued): Summary of Functional Observation Battery

Days 83 or 84 Relative to Start Date

Neuromuscular (continued):

Group	Sex		Gait (Home Cage)	Gait (Open Field)	Righting Response	Grooms	Forelimb Grip (kg)	Hindlimb Grip (kg)	Hindlimb Splay (mm)
1	m	Mean	0.0	0.0	0.0	0.4	1.7	0.8	81.8
		S.D.	0.0	0.0	0.0	0.9	0.2	0.1	9.5
		N	20	20	20	20	20	20	20
2	m	Mean	0.0	0.0	0.0	0.3	1.7	0.8	82.0
		S.D.	0.0	0.0	0.0	0.7	0.2	0.1	7.9
		N	10	10	10	10	10	10	10
3	m	Mean	0.0	0.0	0.0	0.3	1.7	0.8	84.5
		S.D.	0.0	0.0	0.0	0.5	0.1	0.1	8.6
		N	10	10	10	10	10	10	10
4	m	Mean	0.0	0.0	0.0	0.1	1.7	0.7	94.5
		S.D.	0.0	0.0	0.0	0.3	0.1	0.1	10.9
		N	10	10	10	10	10	10	10
5	m	Mean	0.0	0.0	0.0	0.5	1.7	0.8	84.0
		S.D.	0.0	0.0	0.0	0.8	0.1	0.1	10.2
		N	10	10	10	10	10	10	10
6	m	Mean	0.0	0.0	0.0	0.7	1.7	0.7	80.8
		S.D.	0.0	0.0	0.0	1.1	0.2	0.1	10.2
		N	20	20	20	20	20	20	20

Target Dose: Group 1 – 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 8 (continued): Summary of Functional Observation Battery

Days 83 or 84 Relative to Start Date

Physiological:					Sensory Motor:			
Group	Sex		Respiration	SD 85 Body Weight(g)	Approach Response	Auditory Response	Tail Pinch	Pinna Response
1	m	Mean	0.0	600.5	0.0	0.0	0.0	0.0
		S.D.	0.0	61.4	0.0	0.0	0.0	0.0
		N	20	20	20	20	20	20
2	m	Mean	0.0	617.9	0.0	0.0	0.0	0.0
		S.D.	0.0	67.6	0.0	0.0	0.0	0.0
		N	10	10	10	10	10	10
3	m	Mean	0.0	592.7	0.0	0.0	0.0	0.0
		S.D.	0.0	55.2	0.0	0.0	0.0	0.0
		N	10	10	10	10	10	10
4	m	Mean	0.0	590.3	0.0	0.0	0.0	0.0
		S.D.	0.0	66.7	0.0	0.0	0.0	0.0
		N	10	10	10	10	10	10
5	m	Mean	0.0	580.6	0.0	0.0	0.0	0.0
		S.D.	0.0	36.0	0.0	0.0	0.0	0.0
		N	10	10	10	10	10	10
6	m	Mean	0.0	562.6	0.0	0.0	0.0	0.0
		S.D.	0.0	61.2	0.0	0.0	0.0	0.0
		N	20	20	20	20	20	20

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 8 (continued): Summary of Functional Observation Battery

Days 84 to 85 Relative to Start Date

Activity Arousal:

Group	Sex		Handling Reactivity	Vocalization	Posture (Home Cage)	Posture (Open Field)	Rearings
1	f	Mean	0.0	0.0	0.0	0.0	14.1
		S.D.	0.0	0.0	0.0	0.0	5.9
		N	20	20	20	20	20
7	f	Mean	0.0	0.0	0.0	0.0	12.7
		S.D.	0.0	0.0	0.0	0.0	2.6
		N	10	10	10	10	10
8	f	Mean	0.0	0.0	0.0	0.0	12.9
		S.D.	0.0	0.0	0.0	0.0	2.9
		N	10	10	10	10	10
9	f	Mean	0.0	0.0	0.0	0.0	12.7
		S.D.	0.0	0.0	0.0	0.0	6.2
		N	10	10	10	10	10
10	f	Mean	0.0	0.0	0.0	0.0	14.0
		S.D.	0.0	0.0	0.0	0.0	4.8
		N	10	10	10	10	10
11	f	Mean	0.0	0.0	0.0	0.0	14.5
		S.D.	0.0	0.0	0.0	0.0	5.4
		N	20	20	20	20	20

Target Dose: Group 1 – 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 8 (continued): Summary of Functional Observation Battery

Days 84 to 85 Relative to Start Date

Autonomic:

Group Sex		Exopthalmus	Lacrimation	Palpebral Closure	Piloerection	Pupillary Status (Hand Held)	Salivation	Pupillary Response (Elicited)	No. Fecal Boli	No. Urine Pools
1f	Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.1
	S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	2.8
	N	20	20	20	20	20	20	20	20	20
7f	Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.3
	S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.5
	N	10	10	10	10	10	10	10	10	10
8f	Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.7
	S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.3
	N	10	10	10	10	10	10	10	10	10
9f	Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.3
	S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.7
	N	10	10	10	10	10	10	10	10	10
10f	Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.5
	S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.3
	N	10	10	10	10	10	10	10	10	10
11f	Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.8
	S.D.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.2	1.3
	N	20	20	20	20	20	20	20	20	20

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 8 (continued): Summary of Functional Observation Battery

Days 84 to 85 Relative to Start Date

Neuromuscular:

Group	Sex		Activity (Home Cage)	Activity (Open Field)	Fur Appearance	Unusual Behavior (Home Cage)	Unusual Behavior (Open Field)
1	f	Mean	0.0	0.0	0.1	0.0	0.0
		S.D.	0.0	0.0	0.2	0.0	0.0
		N	20	20	20	20	20
7	f	Mean	0.0	0.0	0.0	0.0	0.0
		S.D.	0.0	0.0	0.0	0.0	0.0
		N	10	10	10	10	10
8	f	Mean	0.0	0.0	0.0	0.0	0.0
		S.D.	0.0	0.0	0.0	0.0	0.0
		N	10	10	10	10	10
9	f	Mean	0.0	0.0	0.0	0.0	0.0
		S.D.	0.0	0.0	0.0	0.0	0.0
		N	10	10	10	10	10
10	f	Mean	0.0	0.0	0.1	0.0	0.0
		S.D.	0.0	0.0	0.3	0.0	0.0
		N	10	10	10	10	10
11	f	Mean	0.0	0.0	0.0	0.0	0.0
		S.D.	0.0	0.0	0.0	0.0	0.0
		N	20	20	20	20	20

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 8 (continued): Summary of Functional Observation Battery

Days 84 to 85 Relative to Start Date

Neuromuscular (continued):

Group	Sex		Gait (Home Cage)	Gait (Open Field)	Righting Response	Grooms	Forelimb Grip (kg)	Hindlimb Grip (kg)	Hindlimb Splay (mm)
1	f	Mean	0.0	0.0	0.0	0.6	1.4	0.6	78.0
		S.D.	0.0	0.0	0.0	1.3	0.1	0.1	13.5
		N	20	20	20	20	20	20	20
7	f	Mean	0.0	0.0	0.0	0.7	1.4	0.6	79.5
		S.D.	0.0	0.0	0.0	1.3	0.1	0.1	16.4
		N	10	10	10	10	10	10	10
8	f	Mean	0.0	0.0	0.0	0.2	1.5	0.7	84.0
		S.D.	0.0	0.0	0.0	0.4	0.1	0.1	13.9
		N	10	10	10	10	10	10	10
9	f	Mean	0.0	0.0	0.0	0.1	1.4	0.6	84.0
		S.D.	0.0	0.0	0.0	0.3	0.2	0.1	21.4
		N	10	10	10	10	10	10	10
10	f	Mean	0.0	0.0	0.0	0.8	1.4	0.6	90.5
		S.D.	0.0	0.0	0.0	0.9	0.1	0.1	12.3
		N	10	10	10	10	10	10	10
11	f	Mean	0.0	0.0	0.0	0.2	1.5	0.6	81.5
		S.D.	0.0	0.0	0.0	0.5	0.1	0.1	16.0
		N	20	20	20	20	20	20	20

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 8 (continued): Summary of Functional Observation Battery

Days 84 to 85 Relative to Start Date

Physiological:					Sensory Motor:			
Group	Sex		Respiration	SD 85 Body Weight(g)	Approach Response	Auditory Response	Tail Pinch	Pinna Response
1	f	Mean	0.0	296.5	0.0	0.0	0.0	0.0
		S.D.	0.0	26.8	0.0	0.0	0.0	0.0
		N	20	20	20	20	20	20
7	f	Mean	0.0	294.4	0.0	0.0	0.0	0.0
		S.D.	0.0	26.4	0.0	0.0	0.0	0.0
		N	10	10	10	10	10	10
8	f	Mean	0.0	291.9	0.0	0.0	0.0	0.0
		S.D.	0.0	28.2	0.0	0.0	0.0	0.0
		N	10	10	10	10	10	10
9	f	Mean	0.0	298.2	0.0	0.0	0.0	0.0
		S.D.	0.0	21.3	0.0	0.0	0.0	0.0
		N	10	10	10	10	10	10
10	f	Mean	0.0	288.2	0.0	0.0	0.0	0.0
		S.D.	0.0	27.1	0.0	0.0	0.0	0.0
		N	10	10	10	10	10	10
11	f	Mean	0.0	286.6	0.0	0.0	0.0	0.0
		S.D.	0.0	31.7	0.0	0.0	0.0	0.0
		N	20	20	20	20	20	20

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 9: Summary of Locomotor Activity Data

Day 89 Relative to Start Date

			Basic Movements			Fine Movements			Rearing		
Group	Sex	Interval:	1	2	3	1	2	3	1	2	3
1	m	Mean	2051.10	973.30	418.85	1089.35	594.80	277.60	96.75	58.60	17.95
		SE	73.44	100.26	81.63	50.42	57.16	52.90	7.02	7.00	5.50
		N	20	20	20	20	20	20	20	20	20
2	m	Mean	2073.50	992.70	594.90	1140.30	631.80	390.90	107.80	56.50	36.60
		SE	82.43	90.33	110.98	44.63	49.52	70.38	10.07	5.82	8.02
		N	10	10	10	10	10	10	10	10	10
3	m	Mean	2219.80	1184.40	765.30	1169.60	703.30	483.20	105.50	53.60	33.30
		SE	92.83	148.00	152.29	69.13	83.16	94.03	7.91	5.45	8.08
		N	10	10	10	10	10	10	10	10	10
4	m	Mean	2222.60	903.50	517.30	1205.90	563.80	339.90	113.00	52.80	24.10
		SE	65.02	87.74	123.57	49.08	45.66	80.35	9.57	3.81	6.06
		N	10	10	10	10	10	10	10	10	10
5	m	Mean	2062.60	1084.80	615.60	1058.60	669.20	408.70	116.20	71.90	43.00
		SE	74.42	97.32	90.13	59.92	66.64	60.37	10.54	11.08	7.26
		N	10	10	10	10	10	10	10	10	10
6	m	Mean	2200.45	1215.80	524.95	1163.35	736.60	341.10	105.50	65.70	32.05
		SE	70.41	85.59	84.13	39.52	45.00	49.73	5.54	8.84	6.70
		N	20	20	20	20	20	20	20	20	20

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 9(continued): Summary of Locomotor Activity Data

Day 89 Relative to Start Date

			Basic Movements			Fine Movements			Rearing		
Group	Sex	Interval:	1	2	3	1	2	3	1	2	3
1	f	Mean	1820.90	1004.80	728.00	669.45	420.90	343.35	85.60	43.70	28.15
		SE	58.10	77.81	60.27	34.67	28.57	25.13	4.03	4.57	3.35
		N	20	20	20	20	20	20	20	20	20
7	f	Mean	1759.80	986.60	568.00	649.80	449.90	276.50	70.70	38.60	22.20
		SE	63.50	80.51	85.71	40.16	35.07	34.29	4.34	5.70	4.70
		N	10	10	10	10	10	10	10	10	10
8	f	Mean	1662.30	1145.00	826.10	575.40	462.70	362.10	80.20	49.10	35.10
		SE	91.15	56.57	59.78	60.01	35.69	30.76	3.04	4.36	4.14
		N	10	10	10	10	10	10	10	10	10
9	f	Mean	1780.60	1008.60	716.30	653.60	436.70	343.00	83.40	49.20	29.80
		SE	31.71	82.62	100.79	19.13	31.31	41.95	5.02	3.96	4.47
		N	10	10	10	10	10	10	10	10	10
10	f	Mean	1778.30	1143.90	766.40	661.60	507.30	373.60	88.90	47.00	28.30
		SE	90.78	63.10	134.17	38.41	37.82	66.91	7.73	5.63	5.59
		N	10	10	10	10	10	10	10	10	10
11	f	Mean	1813.30	1072.65	665.85	662.20	458.70	324.35	84.10	46.30	31.85
		SE	40.93	57.03	49.49	19.97	23.14	23.22	3.63	3.32	2.96
		N	20	20	20	20	20	20	20	20	20

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 10: Summary of Estrus Cycling

Weeks 3 and 4 Relative to Start Date

Group	Sex	% Cycling	% Regular		Number of Cycles	Cycle Length
1	f	100	100	Mean	2.80	4.03
				SD	0.41	0.11
				N	20	20
7	f	100	100	Mean	2.40	4.15
				SD	0.70	0.34
				N	10	10
8	f	100	90	Mean	2.40	4.12
				SD	0.52	0.36
				N	10	10
9	f	100	80	Mean	2.60	4.10
				SD	0.52	0.47
				N	10	10
10	f	100	100	Mean	2.80	4.00
				SD	0.42	0.00
				N	10	10
11	f	100	100	Mean	2.55	4.15
				SD	0.51	0.36
				N	20	20

Target Dose: Group 1 – 0 mg/kg/day Group 7 - 1 mg/kg/day Group 8 - 3 mg/kg/day Group 9 - 10 mg/kg/day Group 10 - 30 mg/kg/day Group 11 - 100 mg/kg

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 10 (continued): Summary of Estrus Cycling

Weeks 11 and 12 Relative to Start Date

Group	Sex	% Cycling	% Regular		Number of Cycles	Cycle Length
1	f	90	80	Mean	2.61	4.24
				SD	0.70	0.79
				N	18	18
7	f	90	90	Mean	2.44	4.22
				SD	0.53	0.44
				N	9	9
8	f	100	100	Mean	2.60	4.00
				SD	0.52	0.14
				N	10	10
9*	f	88.9	66.7	Mean	2.25	4.13
				SD	0.46	0.35
				N	8	8
10	f	100	60	Mean	2.80	4.26
				SD	0.63	0.71
				N	10	10
11	f	95	80	Mean	2.39	4.28
				SD	0.61	0.66
				N	18	18

*Per SOP, Animal 25357 (9f) was excluded from summary calculations due to a cycle length of 12.0 days.

Target Dose: Group 1 - 0 mg/kg/day Group 7 - 1 mg/kg/day Group 8 - 3 mg/kg/day Group 9 - 10 mg/kg/day Group 10 - 30 mg/kg/day Group 11 - 100 mg/kg

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 11: Summary of Clinical Chemistry Data

Day 91 Relative to Start Date

Group	Sex		GLU mg/dL	BUN mg/dL	CRE2 mg/dL	NA+ mmol/L	K+ mmol/L	CL mmol/L	CA mg/dL	PHOS mg/dL	CHOL mg/dL	TRIG mg/dL
1	m	Mean	127.5	12.5	0.37	148.4	6.04	103.8	11.58	8.50	90.9	86.1
		S.D.	7.1	2.1	0.08	0.7	0.34	1.0	0.27	0.70	13.6	21.0
		N	10	10	10	10	10	10	10	10	10	10
2	m	Mean	136.6	14.1	0.39	148.4	6.28	104.3	10.86*	8.73	82.5	93.9
		S.D.	17.3	1.4	0.06	1.2	0.43	0.5	0.25	0.50	21.4	53.7
		N	10	10	10	10	10	10	10	10	10	10
3	m	Mean	124.5	12.4	0.39	148.5	6.22	103.8	10.70*	8.60	78.9	72.3
		S.D.	12.7	1.6	0.07	1.2	0.30	0.6	0.41	0.65	13.4	24.0
		N	10	10	10	10	10	10	10	10	10	10
4	m	Mean	128.3	12.4	0.41	149.3	6.13	104.2	10.52*	8.46	87.5	85.4
		S.D.	14.0	1.4	0.14	1.6	0.49	1.1	0.63	0.56	27.8	51.8
		N	10	10	10	10	10	10	10	10	10	10
5	m	Mean	130.5	11.4	0.38	148.1	5.91	104.1	11.17	8.65	83.7	80.8
		S.D.	14.9	1.1	0.10	1.0	0.37	1.1	0.32	0.68	10.6	23.7
		N	10	10	10	10	10	10	10	10	10	10
6	m	Mean	130.9	11.0	0.41	148.1	6.08	104.5	11.24	8.74	92.3	72.0
		S.D.	13.0	1.4	0.06	1.5	0.43	1.5	0.30	0.88	22.9	17.0
		N	10	10	10	10	10	10	10	10	10	10

* - Significantly different from the control value, $p \leq 0.05$

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 11 (continued): Summary of Clinical Chemistry Data

Day 91 Relative to Start Date

Group	Sex		TPROT g/dL	ALB g/dL	GLOB g/dL	A/G ratio	AST U/L	ALTi U/L	ALPi U/L	TBILI mg/dL	GGT U/L	CK U/L
1	m	Mean	7.07	3.28	3.79	0.88	115.4	46.2	85.9	0.18	4.6	416.8
		S.D.	0.28	0.14	0.16	0.04	29.5	8.1	19.0	0.04	0.8	228.3
		N	10	10	10	10	10	10	10	10	10	10
2	m	Mean	7.06	3.13	3.93	0.78*	117.3	44.9	84.2	0.20	4.6	298.7
		S.D.	0.30	0.16	0.22	0.04	49.1	23.6	21.9	0.05	0.7	115.3
		N	10	10	10	10	10	10	10	8	10	10
3	m	Mean	7.10	3.27	3.83	0.83	119.8	40.0	86.7	0.19	4.2	406.0
		S.D.	0.09	0.09	0.14	0.05	33.4	7.7	15.2	0.03	0.4	244.1
		N	10	10	10	10	10	10	10	10	10	10
4	m	Mean	7.14	3.26	3.88	0.83	126.5	39.8	78.2	0.20	4.1	442.9
		S.D.	0.33	0.18	0.19	0.05	87.2	8.6	10.0	0.05	0.3	567.8
		N	10	10	10	10	10	10	10	8	10	10
5	m	Mean	7.09	3.20	3.89	0.83	119.9	41.6	82.4	0.21	4.9	414.8
		S.D.	0.37	0.12	0.28	0.05	36.1	6.1	9.7	0.04	0.3	236.3
		N	10	10	10	10	10	10	10	8	10	10
6	m	Mean	6.75*	3.16	3.59	0.86	119.7	42.7	87.7	0.18	5.0	311.5
		S.D.	0.18	0.08	0.16	0.05	26.9	11.3	17.3	0.04	0.7	194.3
		N	10	10	10	10	10	10	10	10	10	10

* - Significantly different from the control value, $p \leq 0.05$

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 11 (continued): Summary of Clinical Chemistry Data

Day 91 Relative to Start Date

Group	Sex		GLU mg/dL	BUN mg/dL	CRE2 mg/dL	NA+ mmol/L	K+ mmol/L	CL mmol/L	CA mg/dL	PHOS mg/dL	CHOL mg/dL	TRIG mg/dL
1	f	Mean	114.0	13.8	0.56	147.6	5.52	103.4	11.57	7.45	102.4	48.0
		S.D.	12.2	2.1	0.05	1.2	0.28	1.3	0.62	0.81	17.4	11.0
		N	10	10	10	10	10	10	10	10	10	10
7	f	Mean	113.2	13.7	0.57	147.0	5.60	102.2	11.26	7.31	111.5	48.4
		S.D.	10.1	1.8	0.08	1.6	0.49	1.8	0.44	0.65	31.0	22.2
		N	10	10	10	10	10	10	10	10	10	10
8	f	Mean	108.0	14.2	0.52	147.0	5.83	103.3	11.49	7.80	97.2	35.0*
		S.D.	11.0	2.0	0.06	0.8	0.51	0.9	0.65	1.34	18.9	7.7
		N	10	10	10	10	10	10	10	10	10	10
9	f	Mean	112.7	13.7	0.51	146.9	5.47	102.3	11.60	7.72	108.7	40.4
		S.D.	14.1	1.9	0.11	1.4	0.54	1.2	0.54	0.90	27.6	16.9
		N	10	10	10	10	10	10	10	10	10	10
10	f	Mean	116.9	13.2	0.52	147.4	5.94	103.0	11.66	7.95	111.3	45.0
		S.D.	12.6	1.4	0.10	1.3	0.53	1.5	0.61	0.62	20.0	9.5
		N	10	10	10	10	10	10	10	10	10	10
11	f	Mean	114.5	13.3	0.52	146.2	5.82	102.3	11.69	8.07	110.1	37.9
		S.D.	11.3	3.0	0.13	1.0	0.46	1.3	0.38	0.96	17.9	10.3
		N	10	10	9	10	10	10	10	10	10	10

* - Significantly different from the control value, $p \leq 0.05$

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 11 (continued): Summary of Clinical Chemistry Data

Day 91 Relative to Start Date

Group	Sex		TPROT g/dL	ALB g/dL	GLOB g/dL	A/G ratio	AST U/L	ALTi U/L	ALPi U/L	TBILI mg/dL	GGT U/L	CK U/L
1	f	Mean	8.18	4.12	4.06	1.02	108.3	34.5	48.6	0.21	4.5	206.4
		S.D.	0.43	0.33	0.20	0.08	37.5	14.3	11.4	0.06	0.5	136.5
		N	10	10	10	10	10	10	10	10	10	10
7	f	Mean	8.21	4.14	4.07	1.04	186.6	94.4*	43.3	0.26	4.8	247.3
		S.D.	0.52	0.27	0.30	0.07	111.5	100.5	14.3	0.16	0.4	148.5
		N	10	10	10	10	10	10	10	10	10	10
8	f	Mean	7.97	3.99	3.98	1.03	110.9	38.0	40.0	0.14*	3.5*	230.6
		S.D.	0.33	0.28	0.20	0.09	51.8	10.9	13.4	0.05	0.5	198.7
		N	10	10	10	10	10	10	10	10	10	10
9	f	Mean	8.23	4.14	4.09	1.00	199.1	84.9	41.6	0.21	4.0	187.3
		S.D.	0.64	0.42	0.26	0.08	197.1	94.2	10.4	0.03	0.7	72.2
		N	10	10	10	10	10	10	10	10	10	10
10	f	Mean	8.47	4.23	4.24	0.99	203.1	71.6	39.5	0.21	4.1	364.4
		S.D.	0.62	0.40	0.26	0.06	145.7	85.2	10.2	0.06	0.6	399.4
		N	10	10	10	10	10	10	10	10	10	10
11	f	Mean	8.06	4.10	3.96	1.03	201.8	68.3*	45.0	0.20	4.8	815.3
		S.D.	0.54	0.42	0.20	0.09	151.8	44.3	14.6	0.05	1.0	1585.4
		N	10	10	10	10	10	10	10	9	10	10

* - Significantly different from the control value, $p \leq 0.05$

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 11 (continued): Summary of Clinical Chemistry Data

Day 119 Relative to Start Date

Group	Sex		GLU mg/dL	BUN mg/dL	CRE2 mg/dL	NA mmol/L	K mmol/L	CL mmol/L	CA mg/dL	PHOS mg/dL	CHOL mg/dL	TRIG mg/dL
1	m	Mean	111.7	12.7	0.48	147.5	6.10	103.7	10.90	8.34	99.0	122.3
		S.D.	8.0	1.4	0.06	1.3	0.48	1.3	0.19	0.29	19.2	99.7
		N	10	10	10	10	10	10	10	10	10	10
6	m	Mean	111.2	11.7	0.51	148.1	6.21	104.0	11.17*	8.53	96.9	94.2
		S.D.	9.6	1.2	0.06	0.7	0.52	0.8	0.29	0.96	12.3	27.6
		N	10	10	10	10	10	10	10	10	10	10
1	f	Mean	105.4	15.3	0.59	144.6	5.87	102.5	11.61	7.43	122.9	56.0
		S.D.	12.3	1.8	0.16	2.1	0.59	1.3	0.40	0.83	37.9	11.4
		N	10	10	10	10	10	10	10	10	10	10
11	f	Mean	105.2	13.9	0.51	144.4	6.52*	103.0	11.63	8.35	118.7	64.3
		S.D.	15.0	2.0	0.17	0.7	0.57	0.7	0.47	1.23	22.3	20.8
		N	10	10	10	10	10	10	10	10	10	10

* - Significantly different from the control value, $p \leq 0.05$

Target Dose: Group 1 – 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 11 (continued): Summary of Clinical Chemistry Data

Day 119 Relative to Start Date

Group	Sex		TPROT g/dL	ALB g/dL	GLOB g/dL	A/G ratio	AST U/L	ALTi U/L	ALPi U/L	TBILI mg/dL	GGT U/L	CK U/L
1	m	Mean	6.91	3.14	3.77	0.82	94.2	41.0	90.0	0.17	4.0	196.3
		S.D.	0.33	0.14	0.24	0.06	14.8	11.7	27.5	0.05	0.7	53.1
		N	10	10	10	10	10	10	10	7	10	10
6	m	Mean	6.89	3.09	3.80	0.83	114.0	37.4	88.1	0.20	4.0	319.1
		S.D.	0.25	0.10	0.19	0.05	29.6	4.6	20.4	0.06	0.5	210.1
		N	10	10	10	10	10	10	10	7	10	10
1	f	Mean	8.40	4.31	4.09	1.06	335.2	135.4	49.4	0.20	3.5	437.9
		S.D.	0.60	0.29	0.40	0.11	237.1	116.8	7.4	0.07	0.7	426.7
		N	10	10	10	10	10	10	10	9	10	10
11	f	Mean	8.11	4.08	4.03	1.01	289.2	102.2	45.7	0.20	3.9	710.6
		S.D.	0.57	0.41	0.17	0.07	116.2	74.5	8.0	0.05	0.6	525.6
		N	10	10	10	10	10	10	10	10	10	10

Target Dose: Group 1 – 0 mg/kg/day Groups 6 and 11 – 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 12: Summary of Hematology Data

Day 91 Relative to Start Date

Group	Sex		RBC M/µL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RDW %	RET %	ABRETi 10^9/L
1	m	Mean	8.987	15.07	48.41	53.88	16.76	31.11	14.70	2.38	211.93
		S.D.	0.380	0.63	2.19	1.75	0.56	0.43	1.37	0.53	39.51
		N	10	10	10	10	10	10	10	10	10
2	m	Mean	9.057	14.92	48.55	53.71	16.51	30.75	13.97	2.22	200.47
		S.D.	0.631	0.61	2.41	2.50	0.88	0.51	0.81	0.48	40.50
		N	10	10	10	10	10	10	10	10	10
3	m	Mean	9.021	15.26	48.81	54.09	16.91	31.25	14.14	1.99	178.75
		S.D.	0.397	0.68	2.61	1.37	0.46	0.53	0.79	0.35	29.59
		N	10	10	10	10	10	10	10	10	10
4	m	Mean	8.943	15.12	48.62	54.41	16.93	31.11	14.20	2.17	193.30
		S.D.	0.428	0.49	1.87	1.31	0.52	0.33	1.08	0.28	28.22
		N	9	9	9	9	9	9	9	9	9
5	m	Mean	8.777	14.66	47.03	53.63	16.71	31.16	14.04	2.16	187.78
		S.D.	0.311	0.66	1.99	1.98	0.62	0.31	1.11	0.25	18.71
		N	9	9	9	9	9	9	9	9	9
6	m	Mean	8.646	14.70	47.61	55.07	17.01	30.88	13.89	2.20	190.25
		S.D.	0.365	0.66	2.06	1.70	0.45	0.30	0.90	0.55	44.26
		N	10	10	10	10	10	10	10	10	10

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 12 (continued): Summary of Hematology Data

Day 91 Relative to Start Date

Group	Sex		PLT K/µL	MPV fL	WBC K/µL	ABNEUT K/µL	ABLYMP K/µL	ABMONO K/µL	ABSEOS K/µL	ABBAS K/µL
1	m	Mean	648.3	7.74	12.739	2.928	8.999	0.517	0.132	0.074
		S.D.	187.1	0.87	1.995	0.984	1.820	0.248	0.032	0.037
		N	9	9	10	10	10	10	10	10
2	m	Mean	818.7	7.78	13.079	2.141	10.336	0.354	0.100	0.068
		S.D.	109.3	0.23	1.387	0.485	1.310	0.123	0.033	0.015
		N	10	10	10	10	10	10	10	10
3	m	Mean	803.4	7.76	11.970	2.245	9.135	0.333	0.124	0.059
		S.D.	155.7	0.54	1.715	0.738	1.747	0.169	0.037	0.017
		N	10	10	10	10	10	10	10	10
4	m	Mean	728.0	8.11	12.028	2.304	9.124	0.374	0.099	0.058
		S.D.	133.5	0.52	2.386	0.614	1.788	0.146	0.031	0.024
		N	9	9	9	9	9	9	9	9
5	m	Mean	760.6	8.03	13.334	3.173	9.410	0.462	0.128	0.069
		S.D.	188.0	0.36	4.222	1.973	2.550	0.243	0.060	0.045
		N	9	9	9	9	9	9	9	9
6	m	Mean	827.8	7.91	13.109	3.059	9.431	0.390	0.092*	0.057
		S.D.	120.3	0.18	2.527	0.900	2.940	0.052	0.036	0.025
		N	10	10	10	10	10	10	10	10

* - Significantly different from the control value, $p \leq 0.05$

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 12 (continued): Summary of Hematology Data

Day 91 Relative to Start Date

Group	Sex		RBC M/µL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RDW %	RET %	ABRETi 10^9/L
1	f	Mean	8.077	14.47	45.88	56.81	17.95	31.58	11.97	2.12	170.15
		S.D.	0.428	0.55	2.00	1.22	0.53	0.40	0.50	0.59	47.84
		N	10	10	10	10	10	10	10	10	10
7	f	Mean	8.215	14.84	46.65	56.82	18.08	31.83	11.98	1.96	159.44
		S.D.	0.412	0.51	1.87	1.37	0.44	0.45	0.32	0.44	34.41
		N	10	10	10	10	10	10	10	10	10
8	f	Mean	8.118	14.59	45.89	56.55	17.97	31.78	11.80	1.71	138.56
		S.D.	0.459	0.73	2.75	1.97	0.66	0.34	0.37	0.41	31.77
		N	10	10	10	10	10	10	10	10	10
9	f	Mean	8.189	14.49	45.86	56.04	17.72	31.59	11.84	1.81	148.38
		S.D.	0.419	0.52	1.86	1.56	0.54	0.36	0.39	0.25	23.41
		N	10	10	10	10	10	10	10	10	10
10	f	Mean	8.296	14.72	46.86	56.53	17.75	31.40	11.92	2.08	172.01
		S.D.	0.477	0.64	2.06	1.49	0.59	0.31	0.46	0.75	59.91
		N	10	10	10	10	10	10	10	10	10
11	f	Mean	7.786	14.08	44.03	56.52	18.08	32.01	11.76	1.91	147.95
		S.D.	0.441	0.84	2.92	1.60	0.49	0.38	0.36	0.43	31.81
		N	10	10	10	10	10	10	10	10	10

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 12 (continued): Summary of Hematology Data

Day 91 Relative to Start Date

Group	Sex		PLT K/µL	MPV fL	WBC K/µL	ABNEUT K/µL	ABLYMP K/µL	ABMONO K/µL	ABSEOS K/µL	ABBAS K/µL
1	f	Mean	732.2	7.13	8.045	1.062	6.588	0.255	0.042	0.038
		S.D.	177.5	0.55	1.517	0.442	1.378	0.137	0.019	0.011
		N	10	10	10	10	10	10	10	10
7	f	Mean	694.6	7.08	9.668	1.321	7.885	0.295	0.050	0.041
		S.D.	96.9	0.34	1.800	0.549	1.580	0.097	0.011	0.013
		N	10	10	10	10	10	10	10	10
8	f	Mean	770.9	7.04	8.771	1.158	7.184	0.255	0.068	0.033
		S.D.	132.3	0.47	1.811	0.388	1.661	0.080	0.034	0.013
		N	10	10	10	10	10	10	10	10
9	f	Mean	755.4	7.03	8.884	1.436	6.986	0.286	0.056	0.043
		S.D.	128.2	0.71	3.303	0.523	2.949	0.154	0.038	0.031
		N	10	10	10	10	10	10	10	10
10	f	Mean	786.9	7.10	9.849	1.414	7.929	0.311	0.074	0.046
		S.D.	117.0	0.39	2.687	0.378	2.436	0.103	0.032	0.025
		N	10	10	10	10	10	10	10	10
11	f	Mean	671.6	7.21	8.675	0.930	7.334	0.250	0.057	0.043
		S.D.	137.9	0.59	2.483	0.349	2.176	0.129	0.037	0.019
		N	9	9	10	10	10	10	10	10

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 12 (continued): Summary of Hematology Data

Day 119 Relative to Start Date

Group	Sex		RBC M/µL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RDW %	RET %	ABRETi 10^9/L
1	m	Mean	8.414	14.48	45.96	54.66	17.24	31.54	15.06	2.56	214.63
		S.D.	0.421	0.61	2.02	1.98	0.63	0.50	1.19	0.42	28.10
		N	10	10	10	10	10	10	10	10	10
6	m	Mean	8.517	14.68	46.73	54.86	17.25	31.41	14.59	2.34	198.91
		S.D.	0.246	0.72	1.87	1.31	0.62	0.53	0.68	0.28	19.86
		N	10	10	10	10	10	10	10	10	10
1	f	Mean	7.552	14.10	43.48	57.58	18.69	32.43	12.27	2.17	162.97
		S.D.	0.348	0.63	2.16	1.84	0.72	0.57	0.41	0.47	28.45
		N	10	10	10	10	10	10	10	10	10
11	f	Mean	8.013*	14.76*	45.34*	56.66	18.44	32.56	12.07	2.07	163.35
		S.D.	0.377	0.51	1.60	1.98	0.58	0.45	0.22	0.55	41.84
		N	10	10	10	10	10	10	10	10	10

* - Significantly different from the control value, $p \leq 0.05$

Target Dose: Group 1 – 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 12 (continued): Summary of Hematology Data

Day 119 Relative to Start Date

Group	Sex		PLT K/µL	MPV fL	WBC K/µL	ABNEUT K/µL	ABLYMP K/µL	ABMONO K/µL	ABSEOS K/µL	ABBAS K/µL
1	m	Mean	841.2	7.50	10.984	2.070	8.286	0.389	0.106	0.041
		S.D.	139.1	0.27	1.754	0.616	1.351	0.145	0.036	0.013
		N	10	10	10	10	10	10	10	10
6	m	Mean	653.4*	7.94*	11.934	2.230	9.109	0.378	0.097	0.044
		S.D.	99.6	0.30	2.571	0.935	2.347	0.104	0.042	0.020
		N	10	10	10	10	10	10	10	10
1	f	Mean	643.3	7.78	5.775	1.162	4.232	0.250	0.060	0.017
		S.D.	205.8	1.14	1.759	0.440	1.357	0.112	0.024	0.009
		N	10	10	10	10	10	10	10	10
11	f	Mean	676.2	7.38	7.042	1.189	5.422	0.292	0.063	0.024
		S.D.	128.8	0.30	1.693	0.468	1.424	0.132	0.026	0.013
		N	9	9	10	10	10	10	10	10

* - Significantly different from the control value, $p \leq 0.05$

Target Dose: Group 1 - 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 13: Summary of Coagulation Data

Day 91 Relative to Start Date

Group	Sex		PT sec	APTT sec	FIB mg/dL	Group	Sex		PT sec	APTT sec	FIB mg/dL
1	m	Mean	15.84	22.98	329.4	1	f	Mean	14.95	24.27	229.6
		S.D.	0.52	6.47	82.1			S.D.	0.54	8.19	43.2
		N	10	10	10			N	10	10	10
2	m	Mean	16.18	20.56	350.3	7	f	Mean	14.74	26.38	214.4
		S.D.	0.55	6.34	60.5			S.D.	0.69	6.28	27.3
		N	10	10	10			N	10	10	10
3	m	Mean	16.04	18.84	310.6	8	f	Mean	14.99	23.25	203.6
		S.D.	0.56	3.24	39.0			S.D.	0.55	7.31	17.8
		N	9	9	9			N	10	10	10
4	m	Mean	15.96	21.18	319.0	9	f	Mean	15.12	23.65	216.2
		S.D.	0.51	6.27	59.8			S.D.	1.08	7.63	18.1
		N	9	9	9			N	10	10	10
5	m	Mean	16.57	25.77	332.8	10	f	Mean	15.21	22.36	231.7
		S.D.	0.75	7.70	91.1			S.D.	0.71	7.72	32.3
		N	9	9	9			N	10	10	10
6	m	Mean	16.14	17.73	342.6	11	f	Mean	15.38	22.67	192.7*
		S.D.	0.76	5.00	42.1			S.D.	0.93	8.90	21.7
		N	10	10	10			N	9	9	9

* - Significantly different from the control value, $p \leq 0.05$

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 13 (continued): Summary of Coagulation Data

Day 119 Relative to Start Date

Group	Sex		PT sec	APTT sec	FIB mg/dL
1	m	Mean	15.97	24.60	328.9
		S.D.	0.50	3.49	28.2
		N	10	10	10
6	m	Mean	16.72*	26.30	312.9
		S.D.	0.60	7.12	81.1
		N	9	9	9
1	f	Mean	14.23	22.19	202.0
		S.D.	0.86	5.37	21.0
		N	9	9	9
11	f	Mean	15.09	28.67*	208.4
		S.D.	1.50	6.77	56.0
		N	9	9	9

* - Significantly different from the control value, $p \leq 0.05$

Target Dose: Group 1 – 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 14: Summary of Urinalysis Data

Day 91 Relative to Start Date

Group	Sex		SG	UpH	URO U/dL	TUVol mL	Group	Sex		SG	UpH	URO U/dL	TUVol mL
1	m	Mean	1.0263	7.45	0.20	7.75	1	f	Mean	1.0333	6.65	0.20	4.90
		S.D.	0.0105	0.44	0.00	4.32			S.D.	0.0082	0.34	0.00	2.18
		N	9	10	10	10			N	9	10	10	10
2	m	Mean	1.0289	7.30	0.20	7.75	7	f	Mean	1.0296	7.00	0.20	5.30
		S.D.	0.0067	0.79	0.00	4.10			S.D.	0.0106	0.53	0.00	3.53
		N	8	10	10	10			N	9	10	10	10
3	m	Mean	1.0227	7.45	0.20	10.50	8	f	Mean	1.0250	6.70	0.20	6.50
		S.D.	0.0106	0.55	0.00	2.64			S.D.	0.0093	0.42	0.00	3.24
		N	10	10	10	10			N	10	10	10	10
4	m	Mean	1.0265	7.25	0.28	9.15	9	f	Mean	1.0259	6.50	0.20	7.30
		S.D.	0.0166	0.59	0.25	4.31			S.D.	0.0142	0.53	0.00	3.47
		N	10	10	10	10			N	10	10	10	10
5	m	Mean	1.0209	7.50	0.20	10.50	10	f	Mean	1.0237	6.80	0.20	7.40
		S.D.	0.0074	0.47	0.00	2.32			S.D.	0.0082	0.42	0.00	3.20
		N	10	10	10	10			N	10	10	10	10
6	m	Mean	1.0146*	6.90	0.20	11.40	11	f	Mean	1.0220	6.35	0.36*	6.10
		S.D.	0.0062	0.39	0.00	1.26			S.D.	0.0110	0.41	0.34	3.60
		N	10	10	10	10			N	8	10	10	10

* - Significantly different from the control value, $p \leq 0.05$

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 14 (continued): Summary of Urinalysis Data

Day 119 Relative to Start Date

Group	Sex		SG	UpH	URO U/dL	TUVol mL
1	m	Mean	1.0238	7.15	0.20	8.90
		S.D.	0.0121	0.34	0.00	3.00
		N	10	10	10	10
6	m	Mean	1.0203	7.45	0.20	11.30*
		S.D.	0.0076	0.55	0.00	1.64
		N	10	10	10	10
1	f	Mean	1.0236	6.72	0.20	8.00
		S.D.	0.0116	0.71	0.00	3.57
		N	9	9	9	9
11	f	Mean	1.0151	6.95	0.20	9.50
		S.D.	0.0053	0.55	0.00	3.14
		N	10	10	10	10

* - Significantly different from the control value, $p \leq 0.05$

Target Dose: Group 1 – 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 15: Summary of Gross Pathology Observations

Terminal Necropsy: SD 91	MALES					
Group:	1	2	3	4	5	6
Number of Animals:	(10)	(10)	(10)	(10)	(10)	(10)
adrenal gland;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
aorta;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
brain;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
bone with marrow - femur;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
bone with marrow - sternum;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
cecum;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
cervix;						
Submitted	(-)	(-)	(-)	(-)	(-)	(-)
No Visible Lesions	-	-	-	-	-	-
colon;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 15 (continued): Summary of Gross Pathology Observations

Terminal Necropsy: SD 91	MALES					
Group:	1	2	3	4	5	6
Number of Animals:	(10)	(10)	(10)	(10)	(10)	(10)
duodenum;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
epididymis;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
esophagus;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
eye;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
harderian gland;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
heart;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
ileum;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
jejunum;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 15 (continued): Summary of Gross Pathology Observations

Terminal Necropsy: SD 91	MALES					
Group:	1	2	3	4	5	6
Number of Animals:	(10)	(10)	(10)	(10)	(10)	(10)
kidney;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
lacrimal gland;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
liver;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
lung;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
lymph node - mandibular;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
lymph node - mesenteric;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
mandibular salivary gland;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
nerve - optic;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 15 (continued): Summary of Gross Pathology Observations

Terminal Necropsy: SD 91	MALES					
Group:	1	2	3	4	5	6
Number of Animals:	(10)	(10)	(10)	(10)	(10)	(10)
nerve - sciatic;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
pancreas;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
parathyroid gland;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
pituitary;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
prostate;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
rectum;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
seminal vesicle;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
skeletal muscle;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 15 (continued): Summary of Gross Pathology Observations

Terminal Necropsy: SD 91	MALES					
Group:	1	2	3	4	5	6
Number of Animals:	(10)	(10)	(10)	(10)	(10)	(10)
skin;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	9	10	7	10	10
no correlate with clinical observation	0	1	0	3	0	0
spinal cord - cervical;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
spinal cord - thoracic;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
spinal cord - lumbar;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
spleen;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
stomach;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
testis;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 15 (continued): Summary of Gross Pathology Observations

Terminal Necropsy: SD 91	MALES					
Group:	1	2	3	4	5	6
Number of Animals:	(10)	(10)	(10)	(10)	(10)	(10)
thymus;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
thyroid gland;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
tongue;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
trachea;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
urinary bladder;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 15 (continued): Summary of Gross Pathology Observations

Terminal Necropsy: SD 91	FEMALES					
Group:	1	7	8	9	10	11
Number of Animals:	(10)	(10)	(10)	(10)	(10)	(10)
adrenal gland;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
aorta;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
brain;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
bone with marrow - femur;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
bone with marrow - sternum;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
cecum;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
cervix;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
colon;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 15 (continued): Summary of Gross Pathology Observations

Terminal Necropsy: SD 91	FEMALES					
Group:	1	7	8	9	10	11
Number of Animals:	(10)	(10)	(10)	(10)	(10)	(10)
duodenum;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
esophagus;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
eye;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
harderian gland;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
heart;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
ileum;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
jejunum;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
kidney;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10

Target Dose: Group 1 – 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 15 (continued): Summary of Gross Pathology Observations

Terminal Necropsy: SD 91	FEMALES					
Group:	1	7	8	9	10	11
Number of Animals:	(10)	(10)	(10)	(10)	(10)	(10)
lacrimal gland;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
liver;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
lung;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
lymph node - mandibular;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
lymph node - mesenteric;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
mammary gland;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
mandibular salivary gland;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
nerve - optic;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 15 (continued): Summary of Gross Pathology Observations

Terminal Necropsy: SD 91	FEMALES					
Group:	1	7	8	9	10	11
Number of Animals:	(10)	(10)	(10)	(10)	(10)	(10)
nerve - sciatic;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
ovary;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
pancreas;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
parathyroid gland;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
pituitary;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
rectum;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
skeletal muscle;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
skin;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	9	10	10	10	9	9
no correlate with clinical observation	1	0	0	0	1	1

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 15 (continued): Summary of Gross Pathology Observations

Terminal Necropsy: SD 91	FEMALES					
Group:	1	7	8	9	10	11
Number of Animals:	(10)	(10)	(10)	(10)	(10)	(10)
spinal cord - cervical;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
spinal cord - thoracic;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
spinal cord - lumbar;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
spleen;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
stomach;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
thymus;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
thyroid gland;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
tongue;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 15 (continued): Summary of Gross Pathology Observations

Terminal Necropsy: SD 91	FEMALES					
Group:	1	7	8	9	10	11
Number of Animals:	(10)	(10)	(10)	(10)	(10)	(10)
trachea;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
urinary bladder;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10
uterus;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	8	8	10
distention; fluid-filled; bilateral	0	0	0	2	2	0
vagina;						
Submitted	(10)	(10)	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10	10	10

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 15 (continued): Summary of Gross Pathology Observations

Recovery Necropsy: SD 119	---- MALES ---		--- FEMALES ---	
Group:	1	6	1	11
Number of Animals:	(10)	(10)	(10)	(10)
adrenal gland;				
Submitted	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10
aorta;				
Submitted	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10
brain;				
Submitted	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10
bone with marrow - femur;				
Submitted	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10
bone with marrow - sternum;				
Submitted	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10
cecum;				
Submitted	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10
cervix;				
Submitted	(-)	(-)	(10)	(10)
No Visible Lesions	-	-	10	10
colon;				
Submitted	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10

Target Dose: Group 1 - 0 mg/kg/day Groups 6 and 11 - 100 mg/kg

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 15 (continued): Summary of Gross Pathology Observations

Recovery Necropsy: SD 119	---- MALES ---		--- FEMALES ---	
Group:	1	6	1	11
Number of Animals:	(10)	(10)	(10)	(10)
duodenum;				
Submitted	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10
epididymis;				
Submitted	(10)	(10)	(-)	(-)
No Visible Lesions	10	10	-	-
esophagus;				
Submitted	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10
eye;				
Submitted	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10
harderian gland;				
Submitted	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10
heart;				
Submitted	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10
ileum;				
Submitted	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10
jejunum;				
Submitted	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10

Target Dose: Group 1 - 0 mg/kg/day Groups 6 and 11 - 100 mg/kg

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 15 (continued): Summary of Gross Pathology Observations

Recovery Necropsy: SD 119	---- MALES ---		--- FEMALES ---	
Group:	1	6	1	11
Number of Animals:	(10)	(10)	(10)	(10)
kidney;				
Submitted	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10
lacrimal gland;				
Submitted	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10
liver;				
Submitted	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10
lung;				
Submitted	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10
lymph node - mandibular;				
Submitted	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10
lymph node - mesenteric;				
Submitted	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10
mammary gland;				
Submitted	(-)	(-)	(10)	(10)
No Visible Lesions	-	-	10	10
mandibular salivary gland;				
Submitted	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10

Target Dose: Group 1 - 0 mg/kg/day Groups 6 and 11 - 100 mg/kg

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 15 (continued): Summary of Gross Pathology Observations

Recovery Necropsy: SD 119	---- MALES ---		--- FEMALES ---	
Group:	1	6	1	11
Number of Animals:	(10)	(10)	(10)	(10)
nerve - optic;				
Submitted	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10
nerve - sciatic;				
Submitted	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10
ovary;				
Submitted	(-)	(-)	(10)	(10)
No Visible Lesions	-	-	10	10
pancreas;				
Submitted	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10
parathyroid gland;				
Submitted	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10
pituitary;				
Submitted	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10
prostate;				
Submitted	(10)	(10)	(-)	(-)
No Visible Lesions	10	10	-	-
rectum;				
Submitted	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10

Target Dose: Group 1 - 0 mg/kg/day Groups 6 and 11 - 100 mg/kg

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 15 (continued): Summary of Gross Pathology Observations

Recovery Necropsy: SD 119	---- MALES ---		--- FEMALES ---	
Group:	1	6	1	11
Number of Animals:	(10)	(10)	(10)	(10)
seminal vesicle;				
Submitted	(10)	(10)	(-)	(-)
No Visible Lesions	10	10	-	-
skeletal muscle;				
Submitted	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10
skin;				
Submitted	(10)	(10)	(10)	(10)
No Visible Lesions	9	10	9	9
no correlate with clinical observation	1	0	1	1
spinal cord - cervical;				
Submitted	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10
spinal cord - thoracic;				
Submitted	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10
spinal cord - lumbar;				
Submitted	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10
spleen;				
Submitted	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10
stomach;				
Submitted	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10

Target Dose: Group 1 - 0 mg/kg/day Groups 6 and 11 - 100 mg/kg

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 15 (continued): Summary of Gross Pathology Observations

Recovery Necropsy: SD 119	---- MALES ---		--- FEMALES ---	
Group:	1	6	1	11
Number of Animals:	(10)	(10)	(10)	(10)
testis;				
Submitted	(10)	(10)	(-)	(-)
No Visible Lesions	10	9	-	-
small; right	0	1	-	-
thymus;				
Submitted	(10)	(9)	(10)	(10)
No Visible Lesions	10	9	10	10
thyroid gland;				
Submitted	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10
tongue;				
Submitted	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10
trachea;				
Submitted	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10
urinary bladder;				
Submitted	(10)	(10)	(10)	(10)
No Visible Lesions	10	10	10	10
uterus;				
Submitted	(-)	(-)	(10)	(10)
No Visible Lesions	-	-	10	10
vagina;				
Submitted	(-)	(-)	(10)	(10)
No Visible Lesions	-	-	10	10

Target Dose: Group 1 - 0 mg/kg/day Groups 6 and 11 - 100 mg/kg

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 16: Summary of Organ Weight Data

Day 91 Relative to Start Date

Group	Sex		TBW g	--- Brain ---- Abs	%TBW	---- Adrenal Gland ----- Abs	%TBW	/BR	------- Heart --------- Abs	%TBW	/BR
1	m	Mean	591.05	2.1982	0.37368	0.05605	0.00948	0.02568	1.6831	0.28520	0.76841
		S.D.	34.45	0.1210	0.03749	0.00728	0.00106	0.00433	0.1221	0.02110	0.07536
		N	10	10	10	10	10	10	10	10	10
2	m	Mean	603.94	2.2947	0.38342	0.05219	0.00867	0.02282	1.7651	0.29326	0.77041
		S.D.	68.58	0.1381	0.04116	0.01002	0.00161	0.00474	0.2303	0.03222	0.10058
		N	10	10	10	10	10	10	10	10	10
3	m	Mean	578.39	2.2893	0.39915	0.04914	0.00852	0.02148	1.7596	0.30453	0.76968
		S.D.	54.43	0.0665	0.04125	0.00805	0.00125	0.00362	0.1955	0.02334	0.09331
		N	10	10	10	10	10	10	10	10	10
4	m	Mean	574.39	2.2183	0.38962	0.05555	0.00972	0.02498	1.7902	0.31222	0.80623
		S.D.	66.21	0.0887	0.03570	0.01075	0.00190	0.00436	0.2086	0.02008	0.07829
		N	10	10	10	10	10	10	10	10	10
5	m	Mean	564.99	2.2648	0.40172	0.05507	0.00978	0.02435	1.7382	0.30777	0.76731
		S.D.	34.32	0.0953	0.02125	0.01063	0.00183	0.00473	0.1692	0.02496	0.06633
		N	10	10	10	10	10	10	10	10	10
6	m	Mean	536.76	2.2492	0.42549*	0.05110	0.00961	0.02279	1.5762	0.29543	0.70153
		S.D.	73.84	0.1480	0.05585	0.00944	0.00184	0.00430	0.1926	0.02930	0.08195
		N	10	10	10	10	10	10	10	10	10

* - Significantly different from the control value, $p \leq 0.05$
Organ weight data are presented as terminal body weights (TBW, g), absolute weights (Abs, g), organ-to-body weight percentages (%TBW) and organ-to-brain weight ratios (/BR).

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 16 (continued): Summary of Organ Weight Data

Day 91 Relative to Start Date

Group	Sex		Kidneys Abs	Kidneys %TBW	Kidneys /BR	Liver Abs	Liver %TBW	Liver /BR	Spleen Abs	Spleen %TBW	Spleen /BR
1	m	Mean	3.1864	0.53851	1.45708	14.4818	2.44902	6.62883	0.9347	0.15832	0.42697
		S.D.	0.3839	0.04815	0.22395	1.3074	0.14878	0.93144	0.1780	0.02913	0.08710
		N	10	10	10	10	10	10	10	10	10
2	m	Mean	3.2419	0.54071	1.41583	15.2823	2.53277	6.66715	1.0527	0.17461	0.45637
		S.D.	0.3425	0.06384	0.15829	2.4906	0.33722	1.05007	0.2227	0.03261	0.07555
		N	10	10	10	10	10	10	10	10	10
3	m	Mean	3.2302	0.56111	1.41388	13.9681	2.41032	6.10916	0.9433	0.16402	0.41240
		S.D.	0.2988	0.05678	0.15880	1.8510	0.16879	0.86083	0.1005	0.01990	0.04595
		N	10	10	10	10	10	10	10	10	10
4	m	Mean	3.2582	0.57017	1.47069	14.1521	2.45297	6.35906	0.9913	0.17386	0.44681
		S.D.	0.2735	0.04263	0.13636	2.4244	0.14901	0.86498	0.1210	0.02391	0.05069
		N	10	10	10	10	10	10	10	10	10
5	m	Mean	3.1234	0.55265	1.37649	13.5045	2.38817	5.95554	0.9547	0.16866	0.42071
		S.D.	0.4132	0.06419	0.14906	1.4513	0.19498	0.52235	0.1530	0.02275	0.05835
		N	10	10	10	10	10	10	10	10	10
6	m	Mean	2.9903	0.55801	1.33041	12.4654	2.30506	5.55756	0.8653	0.16000	0.38740
		S.D.	0.4113	0.03577	0.17699	2.5619	0.18130	1.23476	0.2213	0.02625	0.11505
		N	10	10	10	10	10	10	10	10	10

Organ weight data are presented as terminal body weights (TBW, g), absolute weights (Abs, g), organ-to-body weight percentages (%TBW) and organ-to-brain weight ratios (/BR).

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 16 (continued): Summary of Organ Weight Data

Day 91 Relative to Start Date

			Thymus			Thyroid			Testes		
Group	Sex		Abs	%TBW	/BR	Abs	%TBW	/BR	Abs	%TBW	/BR
1	m	Mean	0.4585	0.07702	0.21073	0.03161	0.00532	0.01447	5.2590	0.89134	2.39794
		S.D.	0.1440	0.02095	0.07187	0.00963	0.00155	0.00458	0.3279	0.05980	0.18368
		N	10	10	10	10	10	10	10	10	10
2	m	Mean	0.4584	0.07488	0.19991	0.03272	0.00546	0.01421	5.3617	0.89627	2.33987
		S.D.	0.1343	0.01548	0.05678	0.00859	0.00144	0.00342	0.5713	0.12806	0.24869
		N	10	10	10	10	10	10	10	10	10
3	m	Mean	0.3839	0.06681	0.16722	0.02931	0.00508	0.01274	5.2198	0.90669	2.28321
		S.D.	0.1001	0.01788	0.04082	0.00874	0.00151	0.00335	0.3895	0.07668	0.20394
		N	10	10	10	10	10	10	10	10	10
4	m	Mean	0.3605	0.06235	0.16239	0.02810	0.00489	0.01267	4.9732	0.87375	2.24693
		S.D.	0.1125	0.01679	0.04951	0.00768	0.00128	0.00339	0.6687	0.14164	0.32908
		N	10	10	10	10	10	10	10	10	10
5	m	Mean	0.4079	0.07194	0.17930	0.02573	0.00456	0.01138	5.3921	0.95475	2.38060
		S.D.	0.0992	0.01577	0.03924	0.00441	0.00084	0.00210	0.4537	0.06257	0.17220
		N	10	10	10	10	10	10	10	10	10
6	m	Mean	0.3849	0.07150	0.17157	0.03384	0.00622	0.01495	4.7891	0.89945	2.13708
		S.D.	0.0964	0.01355	0.04438	0.01325	0.00194	0.00541	0.6911	0.11983	0.34104
		N	10	10	10	10	10	10	10	10	10

Organ weight data are presented as terminal body weights (TBW, g), absolute weights (Abs, g), organ-to-body weight percentages (%TBW) and organ-to-brain weight ratios (/BR).

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 16 (continued): Summary of Organ Weight Data

Day 91 Relative to Start Date

Group	Sex		TBW g	--- Brain ---- Abs	%TBW	---- Adrenal Gland ----- Abs	%TBW	/BR	------- Heart --------- Abs	%TBW	/BR
1	f	Mean	280.44	2.0335	0.73209	0.05836	0.02085	0.02871	1.0237	0.37089	0.50587
		S.D.	34.47	0.1277	0.07226	0.01012	0.00294	0.00472	0.1486	0.07330	0.08174
		N	10	10	10	10	10	10	10	10	10
7	f	Mean	283.96	2.0200	0.71688	0.05608	0.01980	0.02776	0.9757	0.34309	0.48380
		S.D.	24.53	0.0665	0.07571	0.00805	0.00267	0.00394	0.1196	0.02466	0.06278
		N	10	10	10	10	10	10	10	10	10
8	f	Mean	283.43	2.0005	0.70864	0.05342	0.01890	0.02680	0.9800	0.34714	0.49117
		S.D.	25.66	0.1545	0.05932	0.00901	0.00307	0.00458	0.0704	0.02499	0.03329
		N	10	10	10	10	10	10	10	10	10
9	f	Mean	288.99	1.9877	0.68961	0.05930	0.02059	0.02991	0.9527	0.33044	0.47905
		S.D.	22.45	0.1076	0.03774	0.00442	0.00197	0.00285	0.1344	0.04565	0.05830
		N	10	10	10	10	10	10	10	10	10
10	f	Mean	278.59	2.0102	0.72726	0.05771	0.02092	0.02867	0.9683	0.34906	0.48198
		S.D.	25.82	0.0732	0.07467	0.00934	0.00431	0.00416	0.1181	0.04263	0.05814
		N	10	10	10	10	10	10	10	10	10
11	f	Mean	283.24	1.9997	0.71509	0.05683	0.02009	0.02856	1.0613	0.37490	0.53115
		S.D.	31.73	0.0648	0.09395	0.01401	0.00446	0.00752	0.1448	0.02988	0.07370
		N	10	10	10	10	10	10	10	10	10

Organ weight data are presented as terminal body weights (TBW, g), absolute weights (Abs, g), organ-to-body weight percentages (%TBW) and organ-to-brain weight ratios (/BR).

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 16 (continued): Summary of Organ Weight Data

Day 91 Relative to Start Date

			Kidneys			Liver			Spleen		
Group	Sex		Abs	%TBW	/BR	Abs	%TBW	/BR	Abs	%TBW	/BR
1	f	Mean	1.7468	0.63000	0.86231	7.2408	2.59434	3.56302	0.5773	0.20641	0.28449
		S.D.	0.1151	0.07777	0.08084	0.6709	0.17819	0.28557	0.0832	0.02098	0.04254
		N	10	10	10	10	10	10	10	10	10
7	f	Mean	1.6653	0.58918	0.82476	7.0666	2.49037	3.49830	0.5408	0.19063	0.26843
		S.D.	0.1118	0.04954	0.05436	0.8260	0.20237	0.37306	0.0698	0.02031	0.03894
		N	10	10	10	10	10	10	10	10	10
8	f	Mean	1.6957	0.60155	0.85096	7.0430	2.48698	3.52941	0.5559	0.19741	0.27818
		S.D.	0.0949	0.05156	0.06512	0.7027	0.14340	0.33677	0.0582	0.02524	0.02298
		N	10	10	10	10	10	10	10	10	10
9	f	Mean	1.7264	0.59778	0.86916	7.4480	2.57003	3.74407	0.5802	0.20137	0.29260
		S.D.	0.1791	0.04388	0.08038	1.2853	0.31053	0.57105	0.0641	0.02298	0.03567
		N	10	10	10	10	10	10	10	10	10
10	f	Mean	1.7833	0.64327	0.88720	7.3883	2.65521	3.67445	0.5277	0.18932	0.26259
		S.D.	0.1332	0.05608	0.05838	0.9497	0.26733	0.43324	0.0732	0.01869	0.03589
		N	10	10	10	10	10	10	10	10	10
11	f	Mean	1.9009	0.67243	0.95054	7.3415	2.58451	3.67705	0.5825	0.20772	0.29134
		S.D.	0.3131	0.09151	0.15569	1.2146	0.23295	0.62766	0.0711	0.03054	0.03461
		N	10	10	10	10	10	10	10	10	10

Organ weight data are presented as terminal body weights (TBW, g), absolute weights (Abs, g), organ-to-body weight percentages (%TBW) and organ-to-brain weight ratios (/BR).

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 16 (continued): Summary of Organ Weight Data

Day 91 Relative to Start Date

Group	Sex		Thymus Abs	Thymus %TBW	Thymus /BR	Thyroid Abs	Thyroid %TBW	Thyroid /BR
1	f	Mean	0.2813	0.10026	0.13786	0.05209	0.01796	0.02531
		S.D.	0.0487	0.01325	0.01968	0.10054	0.03411	0.04855
		N	10	10	10	10	10	10
7	f	Mean	0.3402	0.12087	0.16844	0.02248	0.00811	0.01108
		S.D.	0.0361	0.01789	0.01735	0.00668	0.00319	0.00302
		N	10	10	10	10	10	10
8	f	Mean	0.2882	0.10225	0.14390	0.01658	0.00586	0.00829
		S.D.	0.0636	0.02409	0.03096	0.00347	0.00112	0.00154
		N	10	10	10	10	10	10
9	f	Mean	0.3475	0.12034	0.17415*	0.01975	0.00682	0.00993
		S.D.	0.0730	0.02431	0.03212	0.00567	0.00183	0.00261
		N	10	10	10	10	10	10
10	f	Mean	0.3350	0.12012	0.16684	0.02149	0.00781	0.01071
		S.D.	0.0718	0.02124	0.03558	0.00669	0.00254	0.00330
		N	10	10	10	10	10	10
11	f	Mean	0.3031	0.10719	0.15168	0.01717	0.00614	0.00859
		S.D.	0.0597	0.01942	0.03038	0.00465	0.00176	0.00245
		N	10	10	10	10	10	10

* - Significantly different from the control value, $p \leq 0.05$
Organ weight data are presented as terminal body weights (TBW, g), absolute weights (Abs, g), organ-to-body weight percentages (%TBW) and organ-to-brain weight ratios (/BR).

Target Dose: Group 1 – 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 16 (continued): Summary of Organ Weight Data

Day 91 Relative to Start Date

			Ovaries			Uterus			Mammary		
Group	Sex		Abs	%TBW	/BR	Abs	%TBW	/BR	Abs	%TBW	/BR
1	f	Mean	0.10535	0.03714	0.05160	0.7204	0.26013	0.35741	0.61552	0.20980	0.30024
		S.D.	0.03651	0.01061	0.01698	0.1190	0.05231	0.07450	0.47766	0.14757	0.23780
		N	10	10	10	10	10	10	10	10	10
7	f	Mean	0.11782	0.04178	0.05862	0.5881	0.20737	0.29097	1.49330	0.49559	0.71576
		S.D.	0.03382	0.01215	0.01756	0.1100	0.03394	0.05261	2.89916	0.90989	1.35372
		N	10	10	10	10	10	10	10	10	10
8	f	Mean	0.10845	0.03820	0.05450	0.6830	0.24599	0.34483	1.27933	0.43978	0.63382
		S.D.	0.02566	0.00781	0.01340	0.1784	0.08286	0.09965	2.16949	0.74268	1.06330
		N	10	10	10	10	10	10	10	10	10
9	f	Mean	0.11238	0.03908	0.05669	0.7053	0.24481	0.35509	0.80207	0.28059	0.40557
		S.D.	0.02284	0.00827	0.01172	0.1170	0.04185	0.05949	0.34120	0.12203	0.17793
		N	10	10	10	10	10	10	10	10	10
10	f	Mean	0.08651	0.03106	0.04288	0.7161	0.26264	0.35749	0.53633	0.18914	0.26500
		S.D.	0.02825	0.00993	0.01368	0.1811	0.08945	0.09528	0.35513	0.11581	0.16948
		N	10	10	10	10	10	10	10	10	10
11	f	Mean	0.09558	0.03344	0.04809	0.6197	0.21973	0.31047	0.39627	0.13801	0.19993
		S.D.	0.03179	0.01019	0.01671	0.1131	0.04095	0.05917	0.15946	0.05066	0.08445
		N	10	10	10	10	10	10	10	10	10

Organ weight data are presented as terminal body weights (TBW, g), absolute weights (Abs, g), organ-to-body weight percentages (%TBW) and organ-to-brain weight ratios (/BR).

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 16 (continued): Summary of Organ Weight Data

Day 119 Relative to Start Date

Group	Sex		TBW g	--- Brain ---- Abs	%TBW	---- Adrenal Gland ----- Abs	%TBW	/BR	------- Heart --------- Abs	%TBW	/BR
1	m	Mean	630.08	2.2356	0.36051	0.05219	0.00827	0.02326	1.7856	0.28413	0.79887
		S.D.	90.72	0.1103	0.04680	0.01028	0.00099	0.00393	0.2808	0.02736	0.11798
		N	10	10	10	10	10	10	10	10	10
6	m	Mean	642.61	2.2533	0.35172	0.05631	0.00877	0.02497	1.9024	0.29677	0.84502
		S.D.	48.23	0.0890	0.01733	0.00705	0.00103	0.00271	0.1335	0.02035	0.06060
		N	10	10	10	10	10	10	10	10	10
1	f	Mean	316.20	2.1029	0.66854	0.05890	0.01855	0.02797	1.1844	0.37636	0.56606
		S.D.	29.72	0.1297	0.05368	0.01032	0.00237	0.00446	0.1059	0.03798	0.07176
		N	10	10	10	10	10	10	10	10	10
11	f	Mean	302.39	2.0230	0.67745	0.05543	0.01869	0.02745	1.1136	0.37093	0.55123
		S.D.	37.24	0.0925	0.08275	0.00653	0.00357	0.00336	0.1230	0.04405	0.06205
		N	10	10	10	10	10	10	10	10	10

Organ weight data are presented as terminal body weights (TBW, g), absolute weights (Abs, g), organ-to-body weight percentages (%TBW) and organ-to-brain weight ratios (/BR).

Target Dose: Group 1 - 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 16 (continued): Summary of Organ Weight Data

Day 119 Relative to Start Date

			Kidneys			Liver			Spleen		
Group	Sex		Abs	%TBW	/BR	Abs	%TBW	/BR	Abs	%TBW	/BR
1	m	Mean	3.2155	0.50949	1.43508	15.1506	2.39461	6.75889	1.0625	0.17051	0.47545
		S.D.	0.6053	0.05391	0.24247	2.7124	0.13680	1.06292	0.1936	0.03239	0.08217
		N	10	10	10	10	10	10	10	10	10
6	m	Mean	3.3127	0.51616	1.47032	15.1220	2.35422	6.70980	1.0757	0.16758	0.47784
		S.D.	0.2816	0.03172	0.11119	1.3457	0.12521	0.51717	0.1315	0.01770	0.05805
		N	10	10	10	10	10	10	10	10	10
1	f	Mean	1.8622	0.59176	0.88782	8.3242	2.63629	3.96707	0.6050	0.19154	0.28771
		S.D.	0.1316	0.04958	0.07488	0.9396	0.22340	0.46479	0.0882	0.02403	0.03891
		N	10	10	10	10	10	10	10	10	10
11	f	Mean	1.8923	0.62970	0.93890	7.8594	2.60031	3.88783	0.6225	0.20852	0.30899
		S.D.	0.2216	0.07282	0.13227	1.0289	0.15245	0.50462	0.0668	0.03176	0.04349
		N	10	10	10	10	10	10	10	10	10

Organ weight data are presented as terminal body weights (TBW, g), absolute weights (Abs, g), organ-to-body weight percentages (%TBW) and organ-to-brain weight ratios (/BR).

Target Dose: Group 1 - 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 16 (continued): Summary of Organ Weight Data

Day 119 Relative to Start Date

Group	Sex		Thymus Abs	Thymus %TBW	Thymus /BR	Thyroid Abs	Thyroid %TBW	Thyroid /BR	Testes Abs	Testes %TBW	Testes /BR
1	m	Mean	0.3668	0.05886	0.16382	0.02846	0.00456	0.01275	5.2066	0.83437	2.32926
		S.D.	0.0738	0.01238	0.03011	0.00352	0.00058	0.00156	0.6748	0.11208	0.27857
		N	10	10	10	10	10	10	10	10	10
6	m	Mean	0.3735	0.05800	0.16556	0.02981	0.00465	0.01322	5.1794	0.80746	2.29617
		S.D.	0.1103	0.01631	0.04758	0.00488	0.00074	0.00200	0.5800	0.08537	0.21707
		N	10	10	10	10	10	10	10	10	10

Group	Sex		Thymus Abs	Thymus %TBW	Thymus /BR	Thyroid Abs	Thyroid %TBW	Thyroid /BR
1	f	Mean	0.2767	0.08703	0.13213	0.02122	0.00677	0.01019
		S.D.	0.0580	0.01253	0.02929	0.00557	0.00190	0.00295
		N	10	10	10	10	10	10
11	f	Mean	0.2900	0.09606	0.14418	0.02022	0.00675	0.01000
		S.D.	0.0649	0.01724	0.03573	0.00338	0.00123	0.00165
		N	10	10	10	10	10	10

Group	Sex		Ovaries Abs	Ovaries %TBW	Ovaries /BR	Uterus Abs	Uterus %TBW	Uterus /BR	Mammary Gland Abs	Mammary Gland %TBW	Mammary Gland /BR
1	f	Mean	0.08767	0.02760	0.04172	0.8141	0.25931	0.38821	0.54240	0.16353	0.25443
		S.D.	0.03335	0.01014	0.01575	0.1461	0.05170	0.07280	0.52811	0.14396	0.24458
		N	10	10	10	10	10	10	10	10	10
11	f	Mean	0.14261	0.04979	0.07093	0.6951	0.23075	0.34255	0.57490	0.18862	0.28293
		S.D.	0.11561	0.04724	0.05750	0.1467	0.04683	0.06481	0.40280	0.12827	0.19374
		N	10	10	10	10	10	10	10	10	10

Organ weight data are presented as terminal body weights (TBW, g), absolute weights (Abs, g), organ-to-body weight percentages (%TBW) and organ-to-brain weight ratios (/BR).

Target Dose: Group 1 - 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 17: Summary of Histopathology Observations

Terminal Necropsy: SD 91	--- MALES ---		-- FEMALES --	
Group:	1	6	1	11
Number of Animals:	(10)	(10)	(10)	(10)
adrenal gland;				
Examined	(10)	(10)	(10)	(10)
Within Normal Limits	10	10	10	10
aorta;				
Examined	(10)	(10)	(10)	(10)
Within Normal Limits	10	10	10	10
bone with marrow - femur;				
Examined	(10)	(9)	(10)	(10)
Within Normal Limits	10	9	10	10
Not Examined: NOT PRESENT	0	1	0	0
bone with marrow - sternum;				
Examined	(10)	(10)	(10)	(10)
Within Normal Limits	10	10	10	10
brain;				
Examined	(10)	(10)	(10)	(10)
Within Normal Limits	10	10	10	10
cecum;				
Examined	(10)	(10)	(10)	(10)
Within Normal Limits	10	10	10	10
cervix;				
Examined	(-)	(-)	(10)	(10)
Within Normal Limits	-	-	10	10
colon;				
Examined	(10)	(10)	(10)	(10)
Within Normal Limits	10	10	10	10

Target Dose: Group 1 - 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 17 (continued): Summary of Histopathology Observations

Terminal Necropsy: SD 91	--- MALES ---		-- FEMALES --	
Group:	1	6	1	11
Number of Animals:	(10)	(10)	(10)	(10)
duodenum;				
Examined	(10)	(10)	(10)	(10)
Within Normal Limits	10	10	10	10
epididymis;				
Examined	(10)	(10)	(-)	(-)
Within Normal Limits	6	5	-	-
vacuolation; epithelial	(0)	(1)	(-)	(-)
minimal	0	1	-	-
infiltrate, mononuclear cell	(4)	(4)	(-)	(-)
minimal	4	4	-	-
esophagus;				
Examined	(10)	(10)	(10)	(10)
Within Normal Limits	10	10	10	10
eye;				
Examined	(10)	(10)	(10)	(10)
Within Normal Limits	10	9	10	10
dysplasia; retina	(0)	(1)	(0)	(0)
minimal	0	1	0	0
harderian gland;				
Examined	(10)	(10)	(10)	(10)
Within Normal Limits	9	10	6	9
infiltrate, mononuclear cell	(1)	(0)	(4)	(1)
minimal	1	0	4	1

Target Dose: Group 1 - 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 17 (continued): Summary of Histopathology Observations

Terminal Necropsy: SD 91	--- MALES ---		-- FEMALES --	
Group:	1	6	1	11
Number of Animals:	(10)	(10)	(10)	(10)
heart;				
Examined	(10)	(10)	(10)	(10)
Within Normal Limits	7	7	10	8
degeneration / necrosis; myocardium	(3)	(1)	(0)	(0)
minimal	3	1	0	0
infiltrate, mononuclear cell; myocardium	(3)	(3)	(0)	(2)
minimal	3	3	0	2
ileum;				
Examined	(10)	(10)	(10)	(10)
Within Normal Limits	10	10	10	10
jejunum;				
Examined	(10)	(10)	(10)	(10)
Within Normal Limits	10	10	10	10
kidney;				
Examined	(10)	(10)	(10)	(10)
Within Normal Limits	4	8	9	8
chronic progressive nephropathy	(4)	(0)	(0)	(1)
minimal	4	0	0	1
inflammation; chronic active; focal	(0)	(1)	(0)	(0)
mild	0	1	0	0
mineralization; tubular; corticomedullary junction	(0)	(0)	(1)	(1)
minimal	0	0	1	1
cyst; medulla	(0)	(1)	(0)	(0)
present, no grade assigned	0	1	0	0
infiltrate, mononuclear cell	(2)	(0)	(0)	(1)
minimal	2	0	0	1

Target Dose: Group 1 - 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 17 (continued): Summary of Histopathology Observations

Terminal Necropsy: SD 91	--- MALES ---		-- FEMALES --	
Group:	1	6	1	11
Number of Animals:	(10)	(10)	(10)	(10)
lacrimal gland;				
Examined	(10)	(10)	(10)	(10)
Within Normal Limits	8	10	8	8
infiltrate, mononuclear cell	(1)	(0)	(2)	(2)
minimal	1	0	2	2
alteration; harderian gland	(1)	(0)	(0)	(0)
mild	1	0	0	0
liver;				
Examined	(10)	(10)	(10)	(10)
Within Normal Limits	8	8	6	3
necrosis; hepatocellular	(0)	(0)	(2)	(1)
minimal	0	0	2	1
vacuolation; hepatocellular	(0)	(1)	(1)	(2)
minimal	0	0	0	1
mild	0	1	1	1
infiltrate, mononuclear cell	(2)	(1)	(3)	(4)
minimal	2	1	3	3
mild	0	0	0	1
lung;				
Examined	(10)	(10)	(10)	(10)
Within Normal Limits	8	9	7	9
metaplasia; osseus	(0)	(1)	(0)	(0)
minimal	0	1	0	0
alveolar macrophages	(1)	(0)	(1)	(1)
minimal	1	0	1	1
infiltrate, mononuclear cell; interstitial	(0)	(1)	(2)	(0)
minimal	0	1	2	0
infiltrate, mononuclear cell; perivascular	(1)	(0)	(0)	(0)
minimal	1	0	0	0

Target Dose: Group 1 - 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 17 (continued): Summary of Histopathology Observations

Terminal Necropsy: SD 91	--- MALES ---		-- FEMALES --	
Group:	1	6	1	11
Number of Animals:	(10)	(10)	(10)	(10)
lymph node - mandibular;				
Examined	(10)	(10)	(10)	(10)
Within Normal Limits	9	9	10	10
sinus erythrocytosis	(1)	(1)	(0)	(0)
minimal	1	0	0	0
mild	0	1	0	0
lymph node - mesenteric;				
Examined	(10)	(10)	(10)	(10)
Within Normal Limits	10	10	10	10
mammary gland;				
Examined	(-)	(-)	(10)	(10)
Within Normal Limits	-	-	10	10
mandibular salivary gland;				
Examined	(10)	(10)	(10)	(10)
Within Normal Limits	10	10	10	9
hyperplasia; lymphoid	(0)	(0)	(0)	(1)
moderate	0	0	0	1
nerve - sciatic;				
Examined	(10)	(10)	(10)	(10)
Within Normal Limits	10	10	10	10
nerve - optic;				
Examined	(10)	(10)	(9)	(10)
Within Normal Limits	10	10	9	10
Not Examined: NOT PRESENT	0	0	1	0

Target Dose: Group 1 - 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 17 (continued): Summary of Histopathology Observations

Terminal Necropsy: SD 91	--- MALES ---		-- FEMALES --	
Group:	1	6	1	11
Number of Animals:	(10)	(10)	(10)	(10)
ovary;				
Examined	(-)	(-)	(10)	(10)
Within Normal Limits	-	-	9	9
cyst(s), follicular	(-)	(-)	(1)	(1)
present, no grade assigned	-	-	1	1
pancreas;				
Examined	(10)	(10)	(10)	(10)
Within Normal Limits	7	7	9	8
inflammation; chronic	(1)	(1)	(0)	(0)
minimal	1	0	0	0
mild	0	1	0	0
atrophy; acinar cell; focal	(0)	(1)	(0)	(0)
minimal	0	1	0	0
infiltrate, mononuclear cell	(2)	(1)	(1)	(2)
minimal	2	1	1	2
parathyroid gland;				
Examined	(9)	(10)	(9)	(9)
Within Normal Limits	9	10	9	9
Not Examined: NOT PRESENT	1	0	1	1
pituitary;				
Examined	(10)	(10)	(10)	(10)
Within Normal Limits	10	10	10	9
infiltrate; lymphocyte; pars distalis; focal	(0)	(0)	(0)	(1)
minimal	0	0	0	1

Target Dose: Group 1 - 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 17 (continued): Summary of Histopathology Observations

Terminal Necropsy: SD 91

	--- MALES ---		-- FEMALES --	
Group:	1	6	1	11
Number of Animals:	(10)	(10)	(10)	(10)
prostate;				
Examined	(10)	(10)	(-)	(-)
Within Normal Limits	3	6	-	-
infiltrate, mononuclear cell	(6)	(4)	(-)	(-)
minimal	6	4	-	-
exudate; luminal	(2)	(1)	(-)	(-)
minimal	2	1	-	-
rectum;				
Examined	(10)	(10)	(10)	(10)
Within Normal Limits	10	10	10	10
seminal vesicle;				
Examined	(10)	(10)	(-)	(-)
Within Normal Limits	10	10	-	-
skeletal muscle;				
Examined	(10)	(10)	(10)	(10)
Within Normal Limits	9	10	10	10
infiltrate, mononuclear cell	(1)	(0)	(0)	(0)
minimal	1	0	0	0
skin;				
Examined	(10)	(10)	(10)	(10)
Within Normal Limits	10	10	10	10
spinal cord - cervical;				
Examined	(9)	(10)	(10)	(10)
Within Normal Limits	9	10	10	10
Not Examined: NOT PRESENT	1	0	0	0

Target Dose: Group 1 - 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 17 (continued): Summary of Histopathology Observations

Terminal Necropsy: SD 91	--- MALES ---		-- FEMALES --	
Group:	1	6	1	11
Number of Animals:	(10)	(10)	(10)	(10)
spinal cord - thoracic;				
Examined	(9)	(10)	(10)	(10)
Within Normal Limits	9	10	10	10
Not Examined: NOT PRESENT	1	0	0	0
spinal cord - lumbar;				
Examined	(9)	(10)	(10)	(10)
Within Normal Limits	9	10	10	10
Not Examined: NOT PRESENT	1	0	0	0
spleen;				
Examined	(10)	(10)	(10)	(10)
Within Normal Limits	10	10	10	10
stomach;				
Examined	(10)	(10)	(10)	(10)
Within Normal Limits	6	7	8	9
ectasia; glandular; glandular stomach	(4)	(3)	(1)	(1)
minimal	3	3	1	1
mild	1	0	0	0
infiltrate, mononuclear cell; glandular stomach; submuc	(0)	(0)	(1)	(0)
minimal	0	0	1	0
testis;				
Examined	(10)	(10)	(-)	(-)
Within Normal Limits	8	8	-	-
hypospermatogenesis	(2)	(2)	(-)	(-)
minimal	2	1	-	-
moderate	0	1	-	-
thymus;				
Examined	(10)	(10)	(10)	(10)
Within Normal Limits	10	10	10	10

Target Dose: Group 1 - 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 17 (continued): Summary of Histopathology Observations

Terminal Necropsy: SD 91

	--- MALES ---		--------- FEMALES ----------			
Group:	1	6	1	9	10	11
Number of Animals:	(10)	(10)	(10)	(10)	(10)	(10)
thyroid gland;						
Examined	(10)	(10)	(10)	(0)	(0)	(10)
Within Normal Limits	10	10	10	0	0	10
tongue;						
Examined	(10)	(10)	(10)	(0)	(0)	(10)
Within Normal Limits	10	10	10	0	0	10
trachea;						
Examined	(10)	(10)	(10)	(0)	(0)	(10)
Within Normal Limits	10	10	10	0	0	10
urinary bladder;						
Examined	(10)	(10)	(10)	(0)	(0)	(10)
Within Normal Limits	10	10	10	0	0	10
uterus;						
Examined	(-)	(-)	(10)	(2)	(2)	(10)
Within Normal Limits	-	-	7	0	0	9
dilation; lumen	(-)	(-)	(3)	(2)	(2)	(1)
mild	-	-	2	1	0	0
moderate	-	-	1	0	1	1
marked	-	-	0	1	0	0
severe	-	-	0	0	1	0
vagina;						
Examined	(-)	(-)	(10)	(0)	(0)	(10)
Within Normal Limits	-	-	10	0	0	9
mucification; epithelial	(-)	(-)	(0)	(0)	(0)	(1)
mild	-	-	0	0	0	1

Target Dose: Group 1 - 0 mg/kg/day Group 9 - 10 mg/kg/day Group 10 - 30 mg/kg/day Groups 6 and 11 - 100 mg/kg

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Table 17 (continued): Summary of Histopathology Observations

Recovery Necropsy: SD 119	- MALES -
Group:	6
Number of Animals:	(10)
testis;	
Examined	(1)
hypospermatogenesis	(1)
severe	1

Target Dose: Group 6 - 100 mg/kg

APPENDIX 1: STUDY MEMOS

SMITHERS AVANZA

SAS
4/16/18

TO: Study # 2410-14213
Study # 2410-14285
Study # 2410-14256
Study # 2410-14374

FROM: Shakil Saghir (Study Director)

DATE: April 16, 2018

SUBJECT: **SUMMARY OF EXPERIMENTS CONDUCTED TO UNDERSTAND BINDING OF TFM TO STOPPERS OF WATER BOTTLES**

Discolored water was noted in several of the bottles which were attached to the cages of animals during the acclimation period for Study 2410-14213. Binding of the test article, TFM, with the Silicone-rubber stoppers of the water bottles was suspected because the stoppers were used in the recently conducted palatability study (SAV Study No 2410-14285). A series of experiments were conducted in order to determine binding, method(s) to remove the bound TFM from the Silicone-rubber stoppers and use of an alternate material:

1. The first experiment was to confirm that the discolored water contained TFM.
   a. Presence of TFM in the discolored water was confirmed and further confirmed by exposing Silicone-rubber stoppers to TFM-fortified water.
2. The second experiment was to explore methods for the removal of Silicone-rubber-bound TFM.
   a. The Silicone-rubber-bound TFM could not be removed completely.
3. The third experiment was to determine if an alternative to Silicone-rubber can be used by determining binding of TFM to Neoprene stoppers and extent of removal of the bound TFM.
   a. Binding of TFM to Neoprene was less than to Silicone-rubber; however, the bound TFM could not be completely removed.
   b. Decision was made to use Neoprene in the subsequent experiments and in the definitive study (SAV Study No 2410-14374).
4. The fourth experiment was conducted to determine the extent of binding of TFM to Neoprene stoppers by determining loss of TFM from the dose solution (drinking water) due to binding. A one-week experiment was conducted using the lowest concentration specified for Study 2410-14213 (0.01195 mg/mL in water). The dose, formulated in water, was poured into five water bottles connected with individual Neoprene stoppers and sipper tubes. Each water bottle was placed on the top of an empty rat cage to simulate experimental conditions. Samples (1 mL) of water from each bottle and from the container in which the dose formulation was prepared were taken and analyzed on Day 0, Day 1, Day 4 and Day 7 to evaluate the % change in the concentration of TFM.
   a. In seven days, the maximum loss of TFM through binding to the stoppers was approximately 1-3%.

Based on the results of the binding of the TFM to stoppers, new stoppers will be used at every exchange of TFM-fortified water (once every week) in the planned 90-day study (SAV Study No 2410-14374). The study protocol will also address the issue of test-article binding.

All data for the various discovery experiments will be archived with the method validation study, SAV Study No 2410-14256. This memo will be included in all studies utilizing TFM administered in the water.

SMITHERS AVANZA

TO: Study # 2410-14374

FROM: Jim Hall (Manager Dose Formulations and Analysis) 27-APR-2018

CC: Caitlin Murphy (Study Director) CM 27 Apr 2018

DATE: April 27, 2018

SUBJECT: **SPECIAL PROCEDURES FOR WATER BOTTLES AND COMPONENTS**

In order to ensure adequate decontamination of water bottles and associated components the following special procedures will be implemented for study 2410-14374.

1. Decontaminated water bottles and sippers will be washed in cage wash per standard procedures
   a. New unused neoprene stoppers will be installed for each week of use
   b. Document installation and cleaning of new stoppers (1)
2. Clean bin with water bottles/stoppers and assembled sippers will be placed in the animal room
3. Fortified test substance water will be changed weekly as follows
   a. Disassemble stopper / sipper on old water bottle
   b. Dispose of used stoppers in red-bag waste and discard residual solutions
   c. Place dirty water bottle / sippers in designated 'dirty' feed bin to be transferred to Achem
   d. Document accountability for old and new water bottles
4. Analytical chemistry / DFA will process glassware and sippers in under counter dishwasher
   a. Install sippers with the 'rat side' inserted partially into the manifold and process using appropriate dishwashing cleaner
   b. Orient used bottles over cleaning jets
   c. Document cleaning procedure performed in Achem
   d. Clean water bottles and sippers will be transported to 'dirty side' cagewash where the process begins once again at step 1 above

(1) Stoppers were cleaned upon arrival and will not be documented CM 30 Apr 18

SMITHERS
AVANZA

CM 08 June 2018

TO: Caitlin Murphy, Mark Kelley, Renee Keys, Terry Gordon, Daniel Jack
FROM: Jennifer Duvall
DATE: 6/8/18

SUBJECT: 2410-14374 Mammary Gland Collection Procedure

The morphological characteristics of the rat mammary gland are both site and age-specific. Therefore, it is important to use sexually mature rats and to collect the same mammary pair for all animals.

Locate the caudal-most pair of inguinal mammary glands. With forceps, grasp the mammary gland at the base. Using a scalpel blade, excise the mammary gland by cutting directly below the forceps. The overlying skin should be collected with the mammary gland. Place the tissue into a labeled cassette. Repeat the procedure for the remaining mammary gland from the pair. The mammary glands should be collected and weighed together as a paired tissue.

After a weight has been collected, the mammary glands should be placed back into the labeled cassette and preserved in 10% neutral buffered formalin for histological processing, as required.

SMITHERS AVANZA

TO: Study # 2410-14374

FROM: Caitlin Murphy (Study Director) CM 23 Oct 2018

CC: Stephanie Goodnight (Toxicology Associate)
Surubhi Kalathur (Chemist)
Jim Hall (Formulations Manager)

DATE: October 23, 2018

SUBJECT: **TEST MATERIAL INTAKE CALCULATIONS**

It was determined that the test substance, TFM, interacts with the water bottle stopper. Analytical data (2410-14256 and -14374) demonstrated that the concentration of each formulations solutions was decreased after exposure to the water bottle stopper. This change in concentration was mitigated by refreshing the dosing solution on a twice basis weekly. However this was not applied until week 4 of the study.

To represent the changes in dosing solutions, analytical data was collected and corrections to the test material intake (TMI) for each animal and dosing solution were applied. For each concentration range of dosing solution a percent loss was applied to determine the corrected TMI.

During study weeks 1-3, a linear correction was applied for the loss based on the low and high concentrations of 0.0093 and 1.147 mg/mL, respectively.

During study weeks 4-13, the following corrections were observed analytical to have an overall loss over 7 days.

- Concentrations between 0.00928 to 0.0416 mg/mL: -7.53%
- Concentrations between 0.0462 to 0.158 mg/mL: -13.29%
- Concentrations between 0.17 to 0.562 mg/mL: -16.92%
- Concentrations between 0.604 to 2.47 mg/mL: -20.04%

This summary loss (%) is applied in weekly increments to give the average TMI intake over the same period (see data and equations) since both the water consumption data and body weight data are also summarized weekly.

SMITHERS AVANZA

TO: Study # 2410-14374

FROM: Caitlin Murphy (Study Director) CM 28 Feb 19

CC: Stephanie Goodnight (Toxicology Associate) SYG 28Feb19

DATE: 28 Feb 2019

SUBJECT: **CORRECTED TEST MATERIAL INTAKE CALCULATIONS**

In the memo titled "Test material intake calculations", there was an error in the correction values for study weeks 4-13. Below is the corrected concentration corrections used to calculate the test material intake for weeks 4-13.

During study weeks 4-13, the following corrections were observed analytical to have an overall loss over 7 days.

- Concentrations less than 0.0462 mg/mL: -6.79%
- Concentrations between 0.0462 to 0.164 mg/mL: -12.30%
- Concentrations between 0.165 to 0.603 mg/mL: -15.35%
- Concentrations greater than 0.604 mg/mL: -18.88%

The summary loss (%) is applied in weekly increments based on the concentration of the dose solution (mg/mL). The average TMI intake is then determined based on the corrected dosing solution concentration and is applied over weekly increment for the same period (see data and equations).

APPENDIX 2: CERTIFICATES OF ANALYSIS

United States Department of the Interior

U.S. GEOLOGICAL SURVEY
Upper Midwest Environmental Sciences Center
2630 Fanta Reed Road
La Crosse, Wisconsin 54603

Certificate of Analysis

Product name: TFM HP Sea Lamprey Larvicide-Extract

Batch or lot number(s) received and analyzed: LAM170517A
Expiration Date: 05-18-2019

Manufacturer:

Iofina
1025 Mary Laidley Drive
Covington, KY 41017

Kurt Jones (Vice President Sales and Business Development)
Phone: (859)-356-8000 Ext. 11

Mean percent active ingredient found (TFM): 80.59 (Std. Dev. 3.57)

Extracting/ Performing laboratory:

USGS Upper Midwest Environmental Sciences Center
2630 Fanta Reed Road
La Crosse, Wisconsin 54603
Phone: (608)783-6451
Fax: (608)783-6066

Date of analysis: 15 December 2017
LC-MS analyst: J. Schueller
Instrument of analysis: Agilent 1290-6530 LC-MS Q-TOF (SN: SG11342307)

Quality Control Review Acceptance Date: 18 Dec 17

Kim Fredricks, QAO

Kim Fredricks, Quality Assurance Officer

2017 TFM HP Sea Lamprey Larvicide Extract - QA Procedure

LC-MS Analysis by: J. Schueller
Date of Analysis: 15 December 2017
Batche Analyzed: LAM170517A

Created by: J. Schueller 12-18-17
Proofed by Jeff Bernardy (Chemist) 12-18-17
Reviewed by Steve Lantz (Chemist) 12/18/17
Verified by Kim Fredricks (QA Officer) 12/18/17

Calculations:
Percent TFM = HPLC TFM conc. (ng/ml)/sample weight (g)/dilution factor*100
Percent TFM sodium Salt = Percent TFM * Conversion Factor (1.106)

Standard curve linearity (R^2) = 0.99991945

Results Coating Place Sample Identification	HPLC NIC Conc. (ng/mL)	Sample Weight (g)	Percent TFM	Triplicate Mean (%)	Std. Dev.	% RSD
LAM170517A-Extract 1	815.4680	0.09650	84.50	80.59	3.57	4.44
LAM170517A-Extract 2	777.1821	0.10028	77.50			
LAM170517A-Extract 3	764.9114	0.09590	79.76			

Procedure:
A five-point standard curve was prepared from TFM technical (Lot #MKBT9428V Sigma) by weighing 0.00997 g and diluting with 100 mL methanol (Standard Stock A, 100mg/L).
Further dilutions of Standard Stock A - .1:100, 0.3:100, 0.5:100, 0.7:100, and 1.0:100 with methanol solution resulted in working standards of: 100, 300, 500, 700, 1000 ng/mL
Standards were injected in on Agilent 1290-6530 Series LC-MS QTOF for analysis
Subsamples of the Iofina TFM HP Sea Lamprey Larvicide were weighed (Aproximately 0.10 g) into 100 ml volumetric flasks, then bringing to volume in methanol. Futher dilutions were made by delivering 0.1 ml of each stock sample into a 100 ml volumetric flask, bringing to volume with an methanol solution. (Dilution Factor 10000)

LC-MS conditions:
1) Agilent 1290 Series LC-MS QTOF
2) Column: Kinetex EVO-C18, 1.7 um, 100 A, 2.1x100 mm
3) Mobile Phases: A: water (900 mL) methanol (100 mL) ammonium acetate (385 mg) B: methanol (1000 mL) ammonium acetate (385 mg)
4) Column temperature: 50°C
5) Flow Rate: 0.3 mL/min., Injection volume: 2 μL, TFM peak retention time about 3.0 min., sample run time: 9.0 min.
6) Detector m/z 206.0068 in Negative Mode

United States Department of the Interior

U.S. GEOLOGICAL SURVEY
Upper Midwest Environmental Sciences Center
2630 Fanta Reed Road
La Crosse, Wisconsin 54603

Certificate of Analysis

Product name: TFM HP Sea Lamprey Larvicide

Batch or lot number(s) received and analyzed: LAM170517A
Expiration Date: 05-18-2019

Manufacturer:

Iofina
1025 Mary Laidley Drive
Covington, KY 41017

Kurt Jones (Vice President Sales and Business Development)
Phone: (859)-356-8000 Ext. 11

Mean percent active ingredient found (TFM): 32.69 (Std. Dev. 0.95)

Certified Limits = 32% - 34% as TFM

Performing laboratory:

USGS Upper Midwest Environmental Sciences Center
2630 Fanta Reed Road
La Crosse, Wisconsin 54603
Phone: (608)783-6451
Fax: (608)783-6066

Date of analysis: 15 December 2017
LC-MS analyst: J. Schueller
Instrument of analysis: Agilent 1290-6530 LC-MS Q-TOF (SN: SG11342307)

Quality Control Review Acceptance Date: 18 Dec 17

Kim Fredricks, QAO

Kim Fredricks, Quality Assurance Officer

2017 TFM HP Sea Lamprey Larvicide 33% - QA Procedure

LC-MS Analysis by: J. Schueller
te of Analysis: 15 December 2017
.che Analyzed: LAM170517A

Created by: J. Schueller 12-18-17
Proofed by Jeff Bernardy (Chemist) 12-18-17
Reviewed by Steve Lantz (Chemist) 12/18/17
Verified by Kim Fredricks (QA Officer) 12/18/17

Calculations:
Percent TFM = HPLC TFM conc. (ng/ml)/sample weight (g)/dilution factor*100

Standard curve linearity (R^2) = 0.99991945 TFM acceptable range = 32% - 34%

Results Coating Place

Sample Identification	HPLC NIC Conc. (ng/mL)	Sample Weight (g)	Percent TFM	Triplicate Mean (%)	Std. Dev.	% RSD
LAM170517A-Liquid 1	895.7840	0.28280	31.68	32.69	0.95	2.92
LAM170517A-Liquid 2	946.0161	0.28835	32.81			
LAM170517A-Liquid 3	948.2485	0.28244	33.57			

Procedure:
A five-point standard curve was prepared from TFM technical (Lot #MKBT9428V Sigma) by weighing 0.00997 g and diluting with 100 mL methanol (Standard Stock A, 100mg/L).
Further dilutions of Standard Stock A - .1:100, 0.3:100, 0.5:100, 0.7:100, and 1.0:100 with methanol solution resulted in working standards of: 100, 300, 500, 700, 1000 ng/mL
Standards were injected in on Agilent 1290-6530 Series LC-MS QTOF for analysis
Subsamples of the Iofina TFM HP Sea Lamprey Larvicide were weighed (Aproximately 0.30 g) into 100 ml volumetric flasks, then bringing to volume in methanol. Futher dilutions were made by delivering 0.1 ml of each stock sample into a 100 ml volumetric flask, ·n bringing to volume with an methanol solution. (Dilution Factor 10000)

MS conditions:
1) Agilent 1290 Series LC-MS QTOF
2) Column: Kinetex EVO-C18, 1.7 um, 100 A, 2.1x100 mm
3) Mobile Phases: A: water (900 mL) methanol (100 mL) ammonium acetate (385 mg) B: methanol (1000 mL) ammonium acetate (385 mg)
4) Column temperature: 50°C
5) Flow Rate: 0.3 mL/min., Injection volume: 2 μL, TFM peak retention time about 3.0 min., sample run time: 9.0 min.
6) Detector m/z 206.0068 in Negative Mode

Certificate of Analysis **Page 1 of 1**

ThermoFisher SCIENTIFIC

1 Reagent Lane
Fair Lawn, NJ 07410
201.796.7100 tel
201.796.1329 fax

Certificate of Analysis

Thermo Fisher Scientific's Quality System has been found to conform to Quality Management System Standard ISO9001:2008 standard by SAI Global Certificate Number CERT - 0090918

This is to certify that units of the lot number below were tested and found to comply with the specifications of the grade listed. Certain data have been supplied by third parties. Thermo Fisher Scientific expressly disclaims all warranties, expressed or implied, including the implied warranties of merchantability and fitness for a particular purpose. Certain products (USP/FCC/NF/EP/BP/JP grades) are sold for use in food, drug, or medical device manufacturing. Fisher does not claim regulatory coverage under 21 CFR nor maintain DMF's with the FDA. The following are the actual analytical results obtained:

Catalog Number	**W2**	**Quality Test / Release Date**	**10/16/2017**
Lot Number	**176155**		
Description	**WATER, DIUF**		
Country of Origin	**United States**	*** Suggested Retest Date**	**Oct-2022**
Chemical Origin	**Inorganic-non animal**		
BSE/TSE Comment	No animal products are used as starting raw material ingredients, or used in processing, including lubricants, processing aids, or any other material that might migrate to the finished product.		

Result name	Units	Specifications	Test Value
APPEARANCE		REPORT	CLEAR,COLORLESS LIQUID
COLOR	APHA	<= 5	<5
IDENTIFICATION	PASS/FAIL	= PASS TEST	PASS TEST
PH AT 25 DEGREES C		Inclusive Between 5.4 - 7.0	5.9
SPECIFIC CONDUCTANCE	MICROMHO/CM	<= 2.0	0.8

Jerusa Bailey-Wyche

Quality Assurance Specialist - Certificate of Analysis Fair Lawn

Note: The data listed is valid for all package sizes of this lot of this product, expressed as a extension of this catalog number listed above. If there are any questions with this certificate, please call Chemical Services at (800) 227-6701.
*Based on suggested storage condition.

Certificate of Analysis Page 1 of 1

ThermoFisher SCIENTIFIC

1 Reagent Lane
Fair Lawn, NJ 07410
201.796.7100 tel
201.796.1329 fax

Certificate of Analysis

Thermo Fisher Scientific's Quality System has been found to conform to Quality Management System Standard ISO9001:2008 standard by SAI Global Certificate Number CERT - 0090918

This is to certify that units of the lot number below were tested and found to comply with the specifications of the grade listed. Certain data have been supplied by third parties. Thermo Fisher Scientific expressly disclaims all warranties, expressed or implied, including the implied warranties of merchantability and fitness for a particular purpose. Certain products (USP/FCC/NF/EP/BP/JP grades) are sold for use in food, drug, or medical device manufacturing. Fisher does not maintain DMF's with the FDA. The following are the actual analytical results obtained:

Catalog Number	**W2**	**Quality Test / Release Date**	**1/31/2018**
Lot Number	**180010**		
Description	**WATER, DIUF**		
Country of Origin	**United States**	*** Suggested Retest Date**	**Jan-2023**
Chemical Origin	**Inorganic-non animal**		
BSE/TSE Comment	No animal products are used as starting raw material ingredients, or used in processing, including lubricants, processing aids, or any other material that might migrate to the finished product.		

Result name	Units	Specifications	Test Value
APPEARANCE		REPORT	Clear, colorless liquid
COLOR	APHA	<= 5	<5
IDENTIFICATION	PASS/FAIL	= PASS TEST	PASS TEST
PH AT 25 DEGREES C		Inclusive Between 5.4 - 7.0	5.7
SPECIFIC CONDUCTANCE	MICROMHO/CM	<= 2.0	1.8

Teresa Bailey-Wyche

Quality Assurance Specialist - Certificate of Analysis Fair Lawn

Note: The data listed is valid for all package sizes of this lot of this product, expressed as an extension of this catalog number listed above. If there are any questions with this certificate, please call (800) 227-6701.
*Based on suggested storage condition.

Certificate of Analysis

Page 1 of 1

ThermoFisher SCIENTIFIC

Certificate of Analysis

1 Reagent Lane
Fair Lawn, NJ 07410
201.796.7100 tel
201.796.1329 fax

ThermoFisher Scientific's Quality System has been found to conform to Quality Management System Standard ISO9001:2008 standard by SAI Global Certificate Number CERT - 0090918

This is to certify that units of the lot number below were tested and found to comply with the specifications of the grade listed. Certain data have been supplied by third parties. ThermoFisher Scientific expressly disclaims all warranties, expressed or implied, including the implied warranties of merchantability and fitness for a particular purpose. Certain products (USP/FCC/NF/EP/BP/JP grades) are sold for use in food, drug, or medical device manufacturing.ThermoFisher does not maintain DMF's with the FDA. The following are the actual analytical results obtained:

Catalog Number	W2	Quality Test / Release Date	03/15/2018
Lot Number	180885		
Description	WATER, DIUF		
Country of Origin	United States	Suggested Retest Date	Mar/2023
Chemical Origin	Inorganic-non animal		
BSE/TSE Comment	No animal products are used as starting raw material ingredients, or used in processing, including lubricants, processing aids, or any other material that might migrate to the finished product.		
Chemical Comment			

Result Name	Units	Specifications	Test Value
APPEARANCE		REPORT	Clear, colorless liquid
COLOR	APHA	<= 5	<5
SPECIFIC CONDUCTANCE	MICROMHO/CM	<= 2.0	1.2
PH AT 25 DEGREES C		Inclusive Between 5.4 - 7.0	5.8
IDENTIFICATION	PASS/FAIL	= PASS TEST	PASS TEST

Teresa Bailey-Wyche

Quality Assurance Specialist - Certificate of Analysis Fair Lawn

Note: The data listed is valid for all package sizes of this lot of this product, expressed as an extension of this catalog number listed above.
If there are any questions with this certificate, please call at (800) 227-6701.
*Based on suggested storage condition.

Certificate of Analysis

Page 1 of 1

ThermoFisher SCIENTIFIC

Certificate of Analysis

1 Reagent Lane
Fair Lawn, NJ 07410
201.796.7100 tel
201.796.1329 fax

ThermoFisher Scientific's Quality System has been found to conform to Quality Management System Standard ISO9001:2008 standard by SAI Global Certificate Number CERT - 0090918

This is to certify that units of the lot number below were tested and found to comply with the specifications of the grade listed. Certain data have been supplied by third parties. ThermoFisher Scientific expressly disclaims all warranties, expressed or implied, including the implied warranties of merchantability and fitness for a particular purpose. Certain products (USP/FCC/NF/EP/BP/JP grades) are sold for use in food, drug, or medical device manufacturing.ThermoFisher does not maintain DMF's with the FDA. The following are the actual analytical results obtained:

Catalog Number	W2	Quality Test / Release Date	04/27/2018
Lot Number	181924		
Description	WATER, DIUF		
Country of Origin	United States	Suggested Retest Date	Apr/2023
Chemical Origin	Inorganic-non animal		
BSE/TSE Comment	No animal products are used as starting raw material ingredients, or used in processing, including lubricants, processing aids, or any other material that might migrate to the finished product.		
Chemical Comment			

Result Name	Units	Specifications	Test Value
APPEARANCE		REPORT	clear, colorless liquid
COLOR	APHA	<= 5	<5
SPECIFIC CONDUCTANCE	MICROMHO/CM	<= 2.0	1.4
PH AT 25 DEGREES C		Inclusive Between 5.4 - 7.0	6.0
IDENTIFICATION	PASS/FAIL	= PASS TEST	PASS TEST

Teresa Bailey-Wyche

Quality Assurance Specialist - Certificate of Analysis Fair Lawn

Note: The data listed is valid for all package sizes of this lot of this product, expressed as an extension of this catalog number listed above.
If there are any questions with this certificate, please call at (800) 227-6701.
*Based on suggested storage condition.

Certificate of Analysis

Page 1 of 1

ThermoFisher SCIENTIFIC

Certificate of Analysis

1 Reagent Lane
Fair Lawn, NJ 07410
201.796.7100 tel
201.796.1329 fax

ThermoFisher Scientific's Quality System has been found to conform to Quality Management System Standard ISO9001:2008 standard by SAI Global Certificate Number CERT - 0090918

This is to certify that units of the lot number below were tested and found to comply with the specifications of the grade listed. Certain data have been supplied by third parties. ThermoFisher Scientific expressly disclaims all warranties, expressed or implied, including the implied warranties of merchantability and fitness for a particular purpose. Certain products (USP/FCC/NF/EP/BP/JP grades) are sold for use in food, drug, or medical device manufacturing.ThermoFisher does not maintain DMF's with the FDA. The following are the actual analytical results obtained:

Catalog Number	W2	Quality Test / Release Date	06/13/2018
Lot Number	182557		
Description	WATER, DIUF		
Country of Origin	United States	Suggested Retest Date	Jun/2023
Chemical Origin	Inorganic-non animal		
BSE/TSE Comment	No animal products are used as starting raw material ingredients, or used in processing, including lubricants, processing aids, or any other material that might migrate to the finished product.		
Chemical Comment			

Result Name	Units	Specifications	Test Value
APPEARANCE		REPORT	Clear, colorless liquid
COLOR	APHA	<= 5	<5
SPECIFIC CONDUCTANCE	MICROMHO/CM	<= 2.0	1.61
PH AT 25 DEGREES C		Inclusive Between 5.4 - 7.0	5.8
IDENTIFICATION	PASS/FAIL	= PASS TEST	PASS TEST

Teresa Bailey-Wyche

Quality Assurance Specialist - Certificate of Analysis Fair Lawn

Note: The data listed is valid for all package sizes of this lot of this product, expressed as an extension of this catalog number listed above.
If there are any questions with this certificate, please call at (800) 227-6701.
*Based on suggested storage condition.

APPENDIX 3: STABILITY REPORT

ANALYTICAL REPORT

4-Nitro-3-(trifluoromethyl)phenol (TFM): Validation of a High-Performance Liquid Chromatography (HPLC) Method and Assessment of Formulation Stability

Test Article:
4-Nitro-3-(trifluoromethyl)phenol (TFM)

Sponsor:
U.S. Geological Survey (USGS)
2630 Fanta Reed Road,
La Crosse, Wisconsin 54603

On behalf of:

U.S. Fish and Wildlife Service
Lake Champlain Fish and Wildlife Conservation Office
11 Lincoln Street
Essex Junction, Vermont 05452

Analytical Testing Facility:
Smithers Avanza Toxicology Services
15 Firstfield Road
Gaithersburg, Maryland 20878

Smithers Avanza Study Number:
2410-14256

Author:
Surubhi Kalathur, MS

Study Completion Date:
January 9, 2019

TABLE OF CONTENTS

1.0 COMPLIANCE STATEMENT 4
2.0 QUALITY ASSURANCE STATEMENT 5
3.0 SIGNATURE PAGE 6
4.0 STUDY PERSONNEL 7
5.0 STUDY INFORMATION 7
6.0 STUDY TIMETABLE 7
7.0 ABBREVIATIONS 8
8.0 DEVIATIONS 8
9.0 SUMMARY 9
10.0 MATERIALS 10
10.1 Test Article, Reference Standard and Vehicle 10
10.2 Dose Formulation 10
10.3 Method Validation 10
10.4 Formulation Stability 11
11.0 DATA COLLECTION AND STATISTICAL ANALYSES 11
12.0 RECORD RETENTION 11
13.0 RESULTS AND DISCUSSION 11
13.1 Acceptance Criteria 11
13.2 Method Validation 12
13.3 Formulation Stability 17
14.0 CONCLUSION 19

LIST OF TEXT TABLES

Text Table 1: Test Article/Reference Standard and Vehicle 10
Text Table 2: List of Parameters and Criteria 12
Text Table 3: System Suitability Results 12
Text Table 4: Method Validation Calibration Curve Results 13
Text Table 5: Standard Curve Results 14
Text Table 6: Standard Agreement 14
Text Table 7: Accuracy and Precision Results –0.005 mg/mL Formulation 14
Text Table 8: Accuracy and Precision Results – 2 mg/mL Formulation 15
Text Table 9: Homogeneity Results – 0.005 mg/mL MV Formulation 15
Text Table 10: Homogeneity Results – 2 mg/mL MV Formulation 16
Text Table 11: Stability Sample Appearance 18
Text Table 12: Formulation Stability Recovery Results 18

TABLE OF CONTENTS (CONTINUED)

LIST OF FIGURES

Figure 1: Calibration Curve 13
Figure 2: Chromatogram of Vehicle 17
Figure 3: Chromatogram of Sample Diluent 17

LIST OF APPENDICES

Appendix 1: Analytical Method Validation Protocol 20
Appendix 2: Analytical Chemistry Method No. 0296 29
Appendix 3: Certificates of Analysis 38

1.0 COMPLIANCE STATEMENT

4-Nitro-3-(trifluoromethyl)phenol (TFM): Validation of a High-Performance Liquid Chromatography (HPLC) Method and Assessment of Formulation Stability

This study, as performed by Smithers Avanza, was conducted in compliance with the current OECD Good Laboratory Practice Principles (GLP) (ENV/MV/CHEM(98)17), and the Environmental Protection Agency TSCA Good Laboratory Practice Standards (40 CFR Part 792) following exceptions:

The regulations under which the test and reference materials were manufactured and characterized were not provided.

The regulations under which the vehicle (DI Water) manufactured and characterized were not provided.

The stability of neat reference material was not provided.

There were no deviations from the aforementioned regulations that affected the quality or integrity of the study or the interpretations of the results in this report.

Study Director:

K.V. Surubhi — 09 Jan 2019

Surubhi Kalathur, MS — Date

Sponsor Representative:

1/8/2019

Stephen R. Lantz, PhD — Date

2.0 QUALITY ASSURANCE STATEMENT

4-Nitro-3-(trifluoromethyl)phenol (TFM): Validation of a High-Performance Liquid Chromatography (HPLC) Method and Assessment of Formulation Stability

This study was inspected/audited by Quality Assurance in accordance with OECD Good Laboratory Practice regulations and Environmental Protection Agency TSCA Good Laboratory Practice Standards (40 CFR Part 792), the protocol, and Smithers Avanza Standard Operating Procedures. All findings were reported to the Study Director (SD) and Testing Facility Management as indicated below.

Type of Audit	Date(s) Audited	Date Reported to SD, and Test Facility Management
Protocol	February 01, 2018	February 01, 2018
Day 4 Stability Analysis	February 09, 2018	February 14, 2018
Draft Report and Raw Data Audit	April 26, 2018	April 26, 2018
Final Report Post Audit	January 08, 2019	January 08, 2019

All audit findings have been adequately addressed. It is concluded that the final report accurately describes the methods and standard operating procedures and the reported results accurately reflect the raw data for this study.

Kibru Lakew, RQAP-GLP
Sr. Quality Assurance

08 January 2019
Date

3.0 SIGNATURE PAGE

4-Nitro-3-(trifluoromethyl)phenol (TFM): Validation of a High-Performance Liquid Chromatography (HPLC) Method and Assessment of Formulation Stability

Author:

K. V. Surubhi

Surubhi Kalathur, MS

09 Jan 2019

Date

4.0 STUDY PERSONNEL

Study Director/ Analytical Chemist:	Surubhi Kalathur, MS

5.0 STUDY INFORMATION

Smithers Avanza Study Number:	2410-14256
Test Article (TA):	4-Nitro-3-(trifluromethyl)phenol (TFM)
Sponsor:	U.S.Geological Survey (USGS) 2630 Fanta Reed Road La Crosse, WI 54603
Sponsor's Representative:	Stephen R. Lantz, PhD
Testing Facility:	Smithers Avanza 15 Firstfield Road Gaithersburg, MD 20878
Archive Location (s)	
Paper Records:	Iron Mountain, Inc. 4451 Georgia Pacific Blvd., Suites L & M Frederick, MD 21704
Electronic Media:	Iron Mountain, Inc. 8928 McGaw Court Columbia, MD 21045

6.0 STUDY TIMETABLE

Study Initiation:	February 1, 2018
Analytical Initiation:	February 5, 2018
Analytical Completion:	March 5, 2018
Study Completion:	January 9, 2019

7.0 ABBREVIATIONS

°C	Centigrade degrees	**R or r**	correlation coefficient
%	percent	**R^2 or r^2**	square of r
<	less than	**slope**	slope of standard curve
>	greater than	**y-int**	y intercept of standard curve
sec	second	**SD**	standard deviation
min	minute	**RSD**	relative standard deviation
hr	hour	**LOQ**	limit of quantitation
mol (M)	mole	**LOD**	limit of detection
mM	millimole	**Conc.**	concentration
N	normal	**ND**	not detected
µg	microgram	**NA**	not applicable
mg	milligram	**T_0**	Stability time zero
g	gram	**MP**	mobile phase
µL	microliter	**HPLC**	High performance liquid chromatography
mL	milliliter	**UV**	ultraviolet
L	liter	**CV**	concentration verification
µm	micron	**PFL**	protect from light
nm	nanometer	**RT**	Room temperature
QAU	Quality Assurance Unit	**STD C**	Standard C, a midpoint standard of standard curve
SOP	Standard Operating Procedures	**inj**	injection
C of A	certificate of analysis	**v/v**	Volume/volume

8.0 DEVIATIONS

No deviations occurred during dose formulation or dose analysis.

9.0 SUMMARY

The purpose of this project was to validate a HPLC method for the analysis of TFM in dose formulations prepared in deionized drinking water and to assess formulation stability.

This study was conducted according to the analytical study protocol, "4-Nitro-3-(trifluromethyl)phenol (TFM): Validation of a High-Performance Liquid Chromatograpy (HPLC) Method and Assessment of Formulation Stability" (see Appendix 1).

Smithers Avanza Analytical Chemistry Method No. 0296 (see Appendix 2) is a reverse phase HPLC UV method using a Zorbax XDB C18, 4.6x 250 mm, 5µm column with UV detection at 290 nm and mobile phase consisting of 0.1 % formic acid in water and 0.1 % formic acid in acetonitrile, was validated based on acceptable accuracy and precision results. The stability of formulations containing TFM was assessed under room temperature storage conditions (21 ± 5 ºC) with formulation stability established for up to 28 days.

10.0 MATERIALS

10.1 Test Article, Reference Standard and Vehicle

The test article, reference standard, and vehicle used on this study are described in Text Table 1.

Text Table 1: Test Article/Reference Standard and Vehicle

Name	Lot/Batch No.	Supplier	Purity
4-Nitro-3-(trifluromethyl)phenol (TFM)	LAM170517A-Extract	U.S.Geological Survey La Crosse, WI	80.59 %[a]
Reference Standard	MKBX5239V	Sigma-Aldrich Milwaukee, WI	99.90 % [a]
Deionized (DI) Water	174802	ThermoFisher Scientific Fair Lawn, NJ	Assumed 100 %

a - Data from Certificate of Analysis

The test article and reference standard were stored at room temperature and protected from light. The vehicle was stored at room temperature. No reserve samples were collected.

The Certificates of Analysis of TFM and DI water are presented in Appendix 3.

Any remaining test article was retained for use in future toxicological studies.

10.2 Dose Formulation

A 2.0 mg/mL dose formulation (Group High) was prepared by dissolving an appropriate amount of the test substance, TFM in DI water followed by mixing until visually uniform. The formulation was corrected for purity of the test substance. The 2.0 mg/mL high dose formulation was used to prepare a Premix formulation at a concentration of 0.10 mg/mL and then further diluted with the vehicle DI water to a formulation at 0.005 mg/mL (Group Low). Both the Group High formulation and Group Low formulation were observed to be visually clear formulations with a pale yellow color.

The residual formulations not used for analyses were discarded after acceptable analytical results were obtained.

10.3 Method Validation

Analytical method 0296 was based on protocol-specified method conditions and was followed during method validation analysis. Duplicate replicate 1 mL sample aliquots were collected from the top, middle and bottom of the 0.005 mg/mL and directly analyzed on the HPLC column. Duplicate replicate 1 mL sample aliquots were collected from the top, middle, and bottom of the 2.0 mg/mL dose formulation. Each aliquot from the 2.0 mg/mL formulation was diluted in the sample diluent, DI water, to the middle range of the standard curve and analyzed for test article concentration. A single 1.0 mL of DI water was analyzed similarly to Group Low formulation.

Method validation samples were quantified using a six-point standard curve with concentrations ranging from 0.00122 mg/mL to 0.0153 mg/mL. The standards were corrected for purity during preparation.

10.4 Formulation Stability

Following collection of method validation samples, six sets of 3 mL and three sets of 5 mL stability sample aliquots were collected from the middle of Group High and six sets of 1 mL and three sets of 5 mL stability sample aliquots were collected from the middle of Group Low dose formulations. All sets (in amber glass vials) were stored at room temperature (RT) at 21 ± 5 ºC. A pair of 3 mL of Group High formulation and a pair of 1 mL Group Low formulations were analyzed at each stability point.

Prior to stability sample analysis, the appearance of formulation samples was observed for color and clarity with findings recorded in study data. The backup samples not used for analyses were discarded at study finalization.

11.0 DATA COLLECTION AND STATISTICAL ANALYSES

Electronic data collection for dose formulations was performed using Provantis™ Version 8 (Instem LSS, Limited; Stone, UK). Electronic data collection for dose analysis was performed using Empower 2 Build 2154 (Waters Corporation, Milford, MA).

Environmental monitoring was performed using Rees Environmental Monitoring System (Rees Scientific Corporation; Trenton, NJ).

Descriptive statistics (mean, standard deviation, relative standard deviation [RSD], coefficient of determination [r^2], slope, intercept) from Empower 2 software were used for quantitative measurement data, as appropriate.

12.0 RECORD RETENTION

All raw data, protocol and amendments, documentation, records, and the final report generated as a result of this study will be archived in the storage facilities designated by Smithers Avanza for a period of five years following submission of the final report to the Sponsor. Five years after submission of the final report, the Sponsor will be contacted and given the option of taking custody of the materials, having Smithers Avanza dispose of them, or extending the period of storage.

13.0 RESULTS AND DISCUSSION

13.1 Acceptance Criteria

Acceptance criteria for method validation and stability determination are listed in Text Table 2.

Text Table 2: List of Parameters and Criteria

Parameters	Acceptance Criteria
System Suitability	The % RSD for the retention time and peak area of test article will be ≤ 2 % for the five consecutive system suitability injections and ≤ 5 % for overall system suitability injections.
Standard Curve	The linearity of the standard curve (r^2 value) will be ≥ 0.99 and % error for each standard point should be ± 10 %.
Standard Agreement	The % Target of the QC will be within ±5 %
Accuracy & Precision	The mean % Target of the six replicates at each concentration level will be 80–120 % and % RSD ≤ 5 %.
Homogeneity	The % RSD (n=3) of the homogeneity samples (top, middle and bottom) ≤ 10 %.
Specificity	There will be no interference from the vehicle or the sample diluent at the retention time of the test article. Any detection of artifact within the retention window of the test article should have peak area no more than 2 % of the peak area of the lowest standard.
Stability	The formulations are considered chemically stable if the % Change of the calculated mean concentration is within ±10 % of the Time Zero (T_0) value.

13.2 Method Validation

13.2.1 System Suitability

System suitability was evaluated by using five consecutive injections of a mid-point standard (STD C) of the standard curve at the beginning of sample set and bracket injection of the same standard after injections of no more than six sample injections throughout the sample set. The resulting % RSD for retention time and peak area are presented in Text Table 3. All % RSD values were less than 5 % for the five consecutive injections of STD C at the beginning of the sample set and for overall system suitability (five consecutive injections plus all bracket injections).

Text Table 3: System Suitability Results

Sample Set Name	System Suitability	% RSD (Retention Time)	% RSD (Peak Area)
Method Validation	n = 5 consecutive inj of STD C	0.087	0.27
	All injections of STD C	0.086	0.21
4 Days RT Stability	n = 5 consecutive inj of STD C	0.022	0.64
	All injections of STD C	0.071	0.88
10 Days RT Stability	n = 5 consecutive inj of STD C	0.053	0.80
	All injections of STD C	0.049	0.92
28 Days RT Stability	n = 5 consecutive inj of STD C	0.026	0.27
	All injections of STD C	0.055	0.52

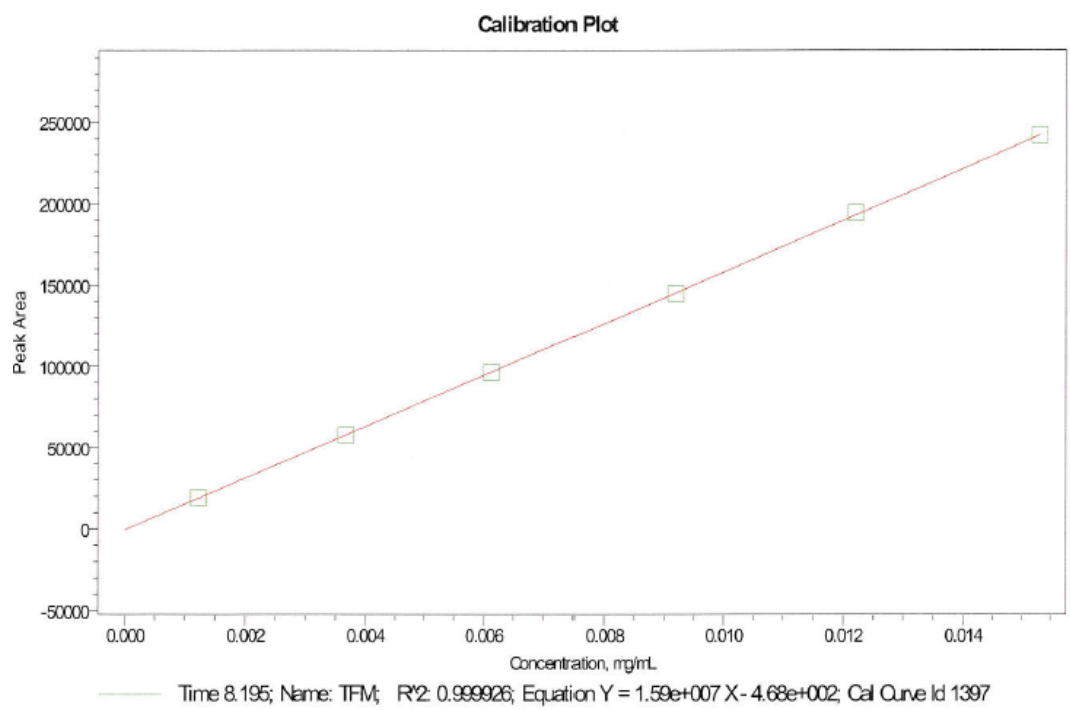
13.2.2 Standard Curve Linearity and Standard Point Accuracy

A six-point standard curve, prepared at TFM concentrations of 0.0153, 0.0122, 0.00918, 0.00612, 0.00367, and 0.00122 mg/mL was analyzed during method validation. A linear regression equation relating the peak areas (Y) to the TFM concentration (X) injected was determined. The linearity, expressed as square of correlation coefficient (R^2), was higher than 0.99. The accuracy, % error (or % Deviation), for each standard injected [((observed - expected) / expected) x 100 %] was within ± 5 % of expected concentration. The linearity parameters for the method validation analysis are presented in Text Table 4 and Calibration Curve is shown in Figure 1. The linearity parameters for the remaining stability timepoints are presented in Text Table 5.

Text Table 4: Method Validation Calibration Curve Results

Standard ID	Peak Area	Percent Deviation
A (0.0153 mg/mL)	241854	-0.162
B (0.0122 mg/mL)	194317	0.644
C (0.00918 mg/mL)	144470	-0.474
D (0.00612 mg/mL)	96083	-0.552
E (0.00367 mg/mL)	57739	-0.022
F (0.00122 mg/mL)	19271	1.992
	Weighting	None
	Y-Intercept	-4.68e+002
	Slope	1.59e+007
	R^2	0.999926

Figure 1: Calibration Curve



Text Table 5: Standard Curve Results

Sample Set Name	% Deviation Range	R^2
4 Days RT Stability	-2.672 to 6.579	0.999355
10 Days RT Stability	-1.694 to 1.499	0.999666
28 Days RT Stability	-2.565 to 3.320	0.999482

13.2.3 Standard Agreement

The accuracy of the prepared stock standards was demonstrated by standard agreement of similarly prepared standard solutions (i.e. STD C and Quality Control (QC)). The % Target of the QC was calculated from the curve and the % Target of the QC should be within ±5 %. Based on the results presented in Text Table 6, the agreement met criteria for all the sampling sets.

Text Table 6: Standard Agreement

Sample Set Name	% Target of QC
Method Validation	101.8
4 Days RT Stability	102.8
10 Days RT Stability	104.1
28 Days RT Stability	101.2

13.2.4 Accuracy and Precision

The accuracy for both formulations met the accuracy criteria with mean recoveries within 80–120 % of target. The precision for the six sample aliquots analyzed at each dose concentration was excellent with % RSD of less than 5 %. The accuracy and precision results are listed in Text Table 7 and Text Table 8 for Group Low (0.005 mg/mL) and Group High (2 mg/mL) formulations respectively.

Text Table 7: Accuracy and Precision Results –0.005 mg/mL Formulation

Sample Number	Dilution Factor	Calculated Concentration mg/mL	% Nominal Target
1	1	0.00487	97.4
2	1	0.00487	97.3
3	1	0.00488	97.5
4	1	0.00486	97.2
5	1	0.00487	97.4
6	1	0.00489	97.7
	Mean		97.4
	STDEV		0.18
	% RSD		0.2

Text Table 8: Accuracy and Precision Results – 2 mg/mL Formulation

Sample Number	Dilution Factor	Calculated Concentration mg/mL	% Nominal Target
1	200	2.02	101.1
2	200	2.09	104.3
3	200	1.94	97.1
4	200	2.05	102.6
5	200	1.98	99.1
6	200	2.02	100.8
	Mean		100.8
	STDEV		2.54
	% RSD		2.5

13.2.5 Homogeneity

The formulations were stirred during the collection of aliquots from the top, middle and bottom of the MV formulation for Group Low (0.005mg/mL) and for the Group High (2 mg/mL). The % RSD (n=3) of the homogeneity samples met the acceptance criteria ≤10 %. The data are presented in Text Table 9 and Text Table 10. Due to increase in concentration from 2 mg/mL to 3.5 mg/mL additional testing was performed in study 2410-14374. The data is presented in Text Table 11.

Text Table 9: Homogeneity Results – 0.005 mg/mL MV Formulation

Sample Location	Dilution Factor	Calculated Concentration mg/mL	% Nominal Target	Mean % Nominal Target
Top	1	0.00487	97.4	97.4
	1	0.00487	97.3	
Middle	1	0.00488	97.5	97.4
	1	0.00486	97.2	
Bottom	1	0.00487	97.4	97.6
	1	0.00489	97.7	
	Mean			97.5
	STDEV			0.12
	% RSD			0.1

Text Table 10: Homogeneity Results – 2 mg/mL MV Formulation

Sample Location	Dilution Factor	Calculated Concentration mg/mL	% Nominal Target	Mean % Nominal Target
Top	200	2.02	101.1	102.7
	200	2.09	104.3	
Middle	200	1.94	97.1	99.7
	200	2.05	102.6	
Bottom	200	1.98	99.1	100.0
	200	2.02	100.8	
	Mean			100.9
	STDEV			1.59
	% RSD			1.6

Text Table 11: Homogeneity Results – 3.50 mg/mL Formulation[a]

Sample Location	Dilution Factor	Calculated Concentration mg/mL	% Nominal Target	Mean
Top	500	3.514	100.4	100.4
	500	3.514	100.4	
Middle	500	3.502	100.0	100.1
	500	3.504	100.1	
Bottom	500	3.474	99.3	99.1
	500	3.463	98.9	
	Mean			99.9
	STDEV			0.68
	% RSD			0.7

a – Data from study 2410-14374.

13.2.6 Specificity

There was no interference from the vehicle or the sample diluent at the retention time of ~8.2 min, which corresponded to that of the test substance. Representative chromatograms for the vehicle and sample diluent are shown in Figure 2 and Figure 3, respectively.

A single vehicle sample was analyzed similarly as low dose concentration samples. There was no detection of test article in the vehicle sample analyzed.

Figure 2: Chromatogram of Vehicle

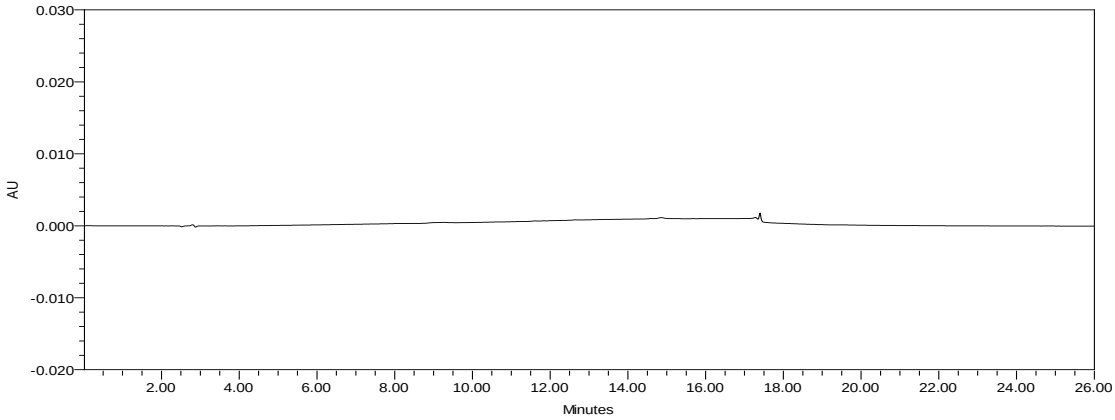
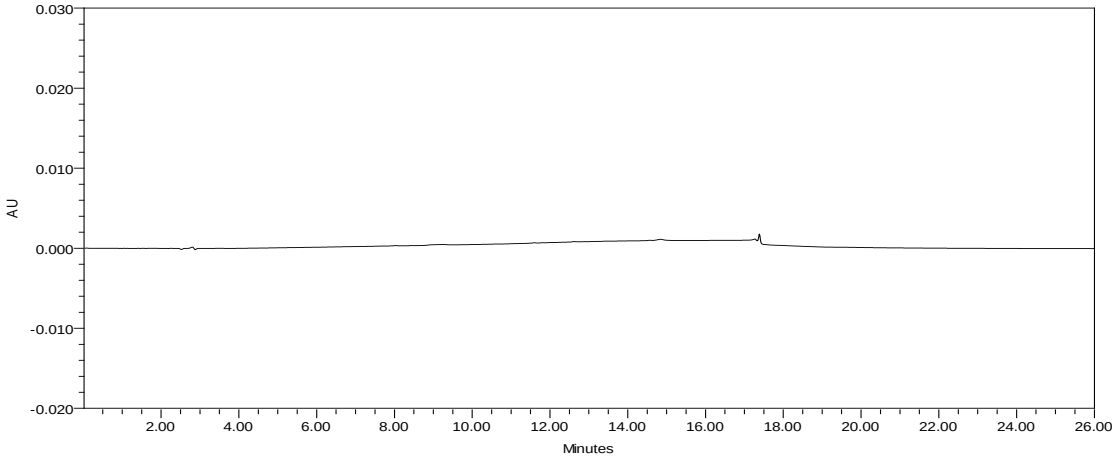


Figure 3: Chromatogram of Sample Diluent



13.3 Formulation Stability

The mean calculated concentration value from accuracy and precision samples from method validation analysis served as Stability Time Zero (T_0) value. The formulation stability was assessed after room temperature storage protected from light for 4 days, 10 days and 28 days. Prior to initiation of stability analysis, each stability sample was inspected visually for change in appearance, with results summarized in Text Table 12. The % recovery results of the stability samples are presented in Text Table 13.

There was no obvious change in appearance in any stability samples under the storage conditions tested. All stability samples met the recovery criteria with % change within ± 10 % of T_0 values.

Text Table 12: Stability Sample Appearance

Sample Solution	Condition	Appearance
Low (0.005 mg/mL)	T_0	Pale yellow or light yellow, clear
	Day 4, RT	Pale yellow, clear
	Day 10, RT	Pale yellow, clear
	Day 28 RT	Pale yellow, clear
High (2 mg/mL)	T_0	Pale yellow or light yellow, clear
	Day 4, RT	Pale yellow, clear
	Day 10, RT	Pale yellow, clear
	Day 28 RT	Pale yellow, clear

Text Table 13: Formulation Stability Recovery Results

Sample Solution	Conditions		Dilution Factor	Mean Calculated Concentration	% Recovery relative to T_0	% Change from T_0
Low (0.005 mg/mL)	T_0	--	1	0.00487	100	---
	Day 4	RT, PFL	1	0.00503	103	3.29
	Day 10	RT, PFL	1	0.00512	105	5.13
	Day 28	RT, PFL	1	0.00498	102	2.26
High (2 mg/mL)	T_0	--	200	2.00	100	---
	Day 4	RT, PFL	200	2.02	101	1.00
	Day 10	RT, PFL	200	2.04	102	2.00
	Day 28	RT, PFL	200	1.98	99.0	-1.00

Note: PFL – protected from light

Due to increase in concentration from 2 mg/mL to 3.5 mg/mL additional stability testing was performed in study 2410-14374. The data is presented in Text Table 14.

Text Table 14: Recovery Results of 3.50 mg/mL

Sample Solution	Conditions		Dilution Factor	Mean Calculated Concentration	% Recovery relative to T_0	% Change from T_0
High (3.50 mg/mL)	T_0	--	500	3.495	100	---
	Day 10	RT	500	3.532	101	1.06
	Day 28	RT	500	3.617	103	3.49

14.0 CONCLUSION

Smithers Avanza Analytical Method 0296 for the determination of TFM in formulations prepared in DI Water has been validated for the concentration range of 0.005–2.0 mg/mL. % RSD values for system suitability injections were well below criteria of 5 %. The linear range of the standard curve was determined to be from 0.00122 to 0.0153 mg/mL. Formulation preparations were verified to have been prepared accurately. The method is specific for HPLC-UV measurement of TFM prepared in water.

The formulations in the concentration range of 0.005–2.0 mg/mL are stable for up to 28 Days at room temperature storage conditions, protected from light. In study 2410-14374, it was determined that a concentration of 3.5 mg/mL TFM in water is stable up to 28 Days at room temperature storage conditions, protected from light.

APPENDIX 1: ANALYTICAL METHOD VALIDATION PROTOCOL

SMITHERS AVANZA

Smithers Avanza's contract research laboratories support the pharmaceutical, agrochemical, and chemical industries

STUDY PROTOCOL

4-Nitro-3-(trifluoromethyl)phenol (TFM): Validation of a High-Performance Liquid Chromatography (HPLC) Method and Assessment of Formulation Stability

Smithers Avanza Study No. 2410-14256

APPROVALS:

K.V. Surubhi — 2/1/18
Surubhi Kalathur, MS — Date
Study Director
Smithers Avanza Toxicology Services, LLC

Michael A. Dorato — 2 Feb 2018
Michael A. Dorato, PhD, DABT, Fellow ATS — Date
Test Facility Management
Smithers Avanza Toxicology Services, LLC

STEPHEN LANTZ Digitally signed by STEPHEN LANTZ Date: 2018.01.31 17:10:41 -06'00' — 1/31/2018
Stephen R. Lantz, PhD — Date
Sponsor Representative
U.S. Geological Survey

www.smithersavanza.com
info@smithrsavanza.com

Smithers Avanza
Toxicology Services
11-B Firstfield Road
Gaithersburg, MD 20878
Tel: 1.240.364.6360
Fax: 1.240.787.3020

U.S.Geological Survey Smithers Avanza Study No. 2410-14256

PROTOCOL

1.0 STUDY TITLE

4-Nitro-3-(trifluoromethyl)phenol (TFM): Validation of a High-Performance Liquid Chromatography (HPLC) Method and Assessment of Formulation Stability.

2.0 PURPOSE

The purpose of this project is to validate a HPLC method for the analysis of TFM in dose formulations prepared in deionized drinking water and to assess formulation stability.

3.0 SPONSOR INFORMATION

3.1 Name and Address

U.S. Geological Survey (USGS)
2630 Fanta Reed Road
La Crosse, WI 54603

3.2 Study Monitor for the Sponsor

Stephen R. Lantz, PhD
Chemist
U.S. Geological Survey (USGS)
2630 Fanta Reed Road
La Crosse, WI 54603
P: (608) 781-6326
slantz@usgs.gov

3.3 Alternate Sponsor Contact

Kim Fredricks, PhD
Biologist, Quality Assurance Officer
U.S. Geological Survey (USGS)
2630 Fanta Reed Road
La Crosse, WI 54603
P: (608) 781-6287
kfredricks@usgs.gov

4.0 SMITHERS AVANZA STUDY DIRECTOR

4.1 Study Director

Surubhi Kalathur, MS
15 Firstfield Road
Gaithersburg, MD 20878-1704
Phone: (240) 364-6304
FAX: (240) 787-3020
Email: surubhi.kalathur@smithers.com

5.0 TEST FACILITY

5.1 Corporate Office

Smithers Avanza
11 Firstfield Road
Gaithersburg, MD 20878

U.S.Geological Survey Smithers Avanza Study No. 2410-14256

5.2	**Formulation Analysis**	Smithers Avanza 15 Firstfield Road Gaithersburg, MD 20878

6.0 ARCHIVE FACILITIES

6.1	**Paper Records**	Iron Mountain, Inc. 4451 Georgia Pacific Blvd. Suites L&M Frederick, MD 21704
6.2	**Electronic Media**	Iron Mountain, Inc. 8928 McGaw Ct. Columbia, MD 21045

7.0 REGULATORY INFORMATION

7.1 Compliance

This study will be conducted according to the protocol, Smithers Avanza's Standard Operating Procedures (SOPs), and in compliance with the current OECD Good Laboratory Practice Principles (GLP) (ENV/MC/CHEM(98)17), and the Environmental Protection Agency TSCA Good Laboratory Practice Standards (40 CFR Part 792).

7.2 Quality Assurance

The Quality Assurance Unit (QAU) of Smithers Avanza will audit this study in accordance with the protocol, amendment(s), SOPs and referenced GLP(s).

7.3 Data Collection System

Electronic data for dose analysis will be collected using Empower 2 Build 2154 (Waters Corporation, Milford, MA). Electronic data for test substance formulations and usage will be collected using Provantis™ 8 (Instem LSS, Limited; Stone, UK). Environmental monitoring data will be collected using Rees Environmental Monitoring System (Rees Scientific Corporation, Trenton, NJ).

7.4 Record Retention

All study data and communications concerning the conduct of the study will be retained in the designated archives for a period of 5 years following issuance of the final report.

Following the 5-year contract, the Sponsor will be contacted to determine disposition of study materials; additional charges will be applied for disposition of these materials. All electronic data and records regarding disposition of study materials will be maintained by Smithers Avanza.

U.S.Geological Survey Smithers Avanza Study No. 2410-14256

8.0 PROPOSED STUDY TIMETABLE

8.1	**Study Initiation Date**	Date Study Director signs protocol
8.2	**Experimental Start Date**	Date analytical testing is initiated
8.3	**Experimental Completion Date**	Date of final formulation stability analysis
8.4	**Submission of Unaudited Draft Report**	March 19, 2018
8.5	**Study Completion Date**	Date Study Director signs final report

9.0 TEST SUBSTANCE AND VEHICLE

9.1 Identification and Supplier

9.1.1. Test substance

The test substance, 4-Nitro-3-(trifluoromethyl)phenol (TFM) (CAS #88-30-2), will be supplied by the Sponsor or Sponsor's designee. The test substance purity is 80.59% according to the Certificate of Analysis (CoA) provided for the test substance (Lot Number LAM170517A-Extract).

The reference substance, 4-Nitro-3-(trifluoromethyl)phenol (TFM) (CAS #88-30-2), will be supplied by Sigma-Aldrich (catalog reference N27802). The reference material purity is 99% according to the CoA provided by the vendor/supplier (Lot Number MKBX5239V).

9.1.2. Vehicle

The vehicle will be deionized water. A CoA for each lot or batch of the vehicle will be provided by the vendor/supplier.

9.1.3. Diluent

The diluent, water (HPLC Grade, Fisher W5) will be provided by a vendor/supplier. A CoA for each lot or batch of the diluent will be retained in the study data.

9.2 Purity and Stability

9.2.1. Test substance/Reference Standard

The purity and/or other characteristics that appropriately define the test substance, and stability information for the test substance, are the responsibility of the Sponsor or the Sponsor's designee. The information will be provided to Smithers Avanza.

The purity and/or other characteristics that appropriately define the reference substance, and stability information for the reference substance, are the responsibility of the vendor/supplier. The information will be provided to Smithers Avanza.

Dosing solutions as well as analytical standards will be prepared with correction for purity.

U.S.Geological Survey Smithers Avanza Study No. 2410-14256

9.2.2. Vehicle and Diluent

The purity and/or other characteristics that appropriately define the vehicle, and diluent, as well as stability information for each component, will be provided by the vendor/supplier.

9.3 Storage Conditions

9.3.1. Test substance

The test substance will be stored at 21±5°C, protected from light (wrapped in foil) unless stated otherwise in receipt paperwork.

9.3.2. Vehicle and Diluent

The vehicle and diluent will be stored at 21±5°C, unless otherwise stated in receipt paperwork.

9.4 Reserve Samples and Disposition

9.4.1. Reserve samples

Not applicable.

9.4.2. Test substance and Reference Substance Disposition

Any remaining test substance and reference substance will be retained for use on subsequent studies.

9.4.3. Vehicle and Diluent Disposition

All remaining vehicle and components of the diluent will be returned to Smithers Avanza stock and/or discarded at the discretion of Smithers Avanza.

10.0 EXPERIMENTAL PROCEDURES

10.1 Formulation Preparation

10.1.1. Vehicle Preparation

The vehicle will be used as supplied.

10.1.2. Test substance Preparation

The test substance will be a solution of TFM in water and prepared according to a procedure approved by the Study Director. The formulations will be stored at room temperature at 21±5°C protected from exposure to light (amber glass and/or aluminum foil) following preparation. The formulation concentration will be as follows:

High (2 mg/mL) Low (0.005 mg/mL)

The solution concentrations may be adjusted as required to encompass projected dosing solution concentrations on subsequent studies.

U.S.Geological Survey Smithers Avanza Study No. 2410-14256

10.2 Formulation Analysis

10.2.1. Analytical Standards

A stock standard will be prepared by dissolving an appropriate amount of test substance in diluent. A standard curve of at least five working standards will be prepared and assessed during method validation. A working standard will be prepared and used as system suitability and bracket standard. A QC standard will be prepared and diluted to a single point within the standard curve established.

Samples will be quantified based on a method confirmed during method validation (Method No. 0296).

10.2.2. Method Conditions

HPLC Column: Zorbax XDB C18, 4.6 x 250 mm, 5 µm
Column Temperature: Ambient
Sample Temperature: Ambient
Mobile Phase A: 0.1% Formic Acid in Water
Mobile Phase B: 0.1% Formic Acid in Acetonitrile
Autosampler Flush: 50:50 water/acetonitrile
Flow Rate: 1.0 mL/minute
Injection Volume: 10 µL
UV Detection: 290 nm
Run Time: 26 min
Gradient Pump Program:

Step	Step Time (minutes)	Elapsed Time (minutes)	% A (Aqueous)	% B (Organic)	Curve
0	0.0	0.0	75	25	6
1	10	10	0	100	6
2	4	14	0	100	6
3	2	16	75	25	6
4	10	26	75	25	6

Note: modifications may be made to the method at the discretion of the contributing scientist and/or Study Director prior to method validation.

11.0 METHOD VALIDATION

The following analytical performance characteristics will be assessed during method validation. In the event that a sample falls outside the acceptance criteria, re-analysis may be performed at the discretion of the Study Director.

11.1 System Suitability

At least five (5) consecutive system suitability injections (typically the mid-point working standard) will be performed at the start of a sample set to assess the suitability of the instrument for use. Additional injections of system suitability (as bracket standards) will be performed after every six or less samples to assess overall system suitability.

U.S.Geological Survey Smithers Avanza Study No. 2410-14256

Acceptance criteria: The % RSD (Relative Standard Deviation) for the retention time and peak area of test substance in the system suitability standard should be ≤ 2% for the five consecutive system suitability injections and ≤ 5% for overall system suitability injections (i.e., five consecutive system suitability injections plus bracketing injections).

11.2 Standard Curve

At least a five point standard curve at appropriate concentrations will be prepared. A linear regression equation relating the peak area to the concentrations of each test substance standard injection will be determined, and the percent recovery for each standard will be calculated.

Acceptance criteria: The linearity of the standard curve (r^2 value) should be ≥ 0.99 and % error for each standard point should be within ± 10%.

11.3 Standard Agreement

The accuracy of prepared stock standards must be demonstrated by standard agreement of similarly prepared standard solutions (STD C and QC). The % Target will be calculated from the curve.

Acceptance criteria: The % Target of the QC should be within ± 5%.

11.4 Accuracy and Precision

Upon completion of the preparation each solution will stand without agitation for ≥30 minutes prior to sampling for accuracy and precision.

Six replicate sample aliquots, with two samples each collected from the top (T), middle (M) and bottom (B) locations of each formulation batch will be collected and diluted to within the linearity range and analyzed.

Acceptance criteria: The mean % Target of the six replicates at each concentration level = 80 - 120% and % RSD ≤ 5%.

11.5 Homogeneity

The accuracy and precision sample aliquots will also serve to confirm homogeneity of the dose formulations.

Acceptance criteria: The % RSD (n = 3) of the homogeneity samples (top, middle and bottom) ≤ 10%.

11.6 Specificity

Chromatographic injections of vehicle and diluent will be determined to assess the specificity of the analytical method.

Acceptance criteria: There should be no interference from the vehicle or the sample diluent at the retention time of the test article. Any detection of artifact within the retention window of the test article should have peak area no more than 2 % of the peak area of the lowest standard.

U.S.Geological Survey Smithers Avanza Study No. 2410-14256

12.0 FORMULATION STABILITY

Stability of the each test substance formulation will be assessed following storage conditions as described in the following table:

Storage Condition	Stability Time Point
Room Temp at 21±5°C	At least 4 days, protected from light
Room Temp at 21±5°C	At least 10 days protected from light
Room Temp at 21±5°C	At least 28 days protected from light

The stability time points may be modified based upon the results and/or at the discretion of the Study Director.

If method validation formulations are used for stability determination, the mean calculated concentration from the mid layer strata samples of the accuracy and precision samples will be used as the Time Zero (T_0) value. If separate stability formulations are prepared, the mean calculated concentration from duplicate samples collected from the mid layer strata will be analyzed on the day of preparation will be used as the Time Zero (T_0) value.

At each stability time point, the appearance of the sample will be observed and documented.

Acceptance criteria: The formulations are considered chemically stable if the % Change of the calculated mean concentration is within ±10% of the Time Zero (T_0) value.

13.0 PROPOSED STATISTICAL ANALYSES

Descriptive statistics (mean, standard deviations, % RSDs as applicable) will be presented for all measurement data.

14.0 FINAL REPORT

A report will be prepared which accurately describes the methods used in the generation and analysis of the data and meets the regulatory requirements previously noted. The audited draft report will be provided to the Study Monitor for the Sponsor for review and comment. The Study Director may finalize the report 60 days after submission of the audited draft report if no comments are received.

At finalization, an electronic copy of the final report will be submitted to the Study Monitor for the Sponsor.

APPENDIX 2: ANALYTICAL CHEMISTRY METHOD NO. 0296

ANALYTICAL CHEMISTRY METHOD

METHOD No. 0296R3

Effective Date: 20NOV2018
Approved By: 20NOV2018
Jim Hall, Manager, DFA

TITLE: Determination of 4-Nitro-3-(trifluoromethyl)phenol(TFM) in Water

DEVELOPED BY: U.S.Geological Survey adapted for use by Smithers Avanza

1. SCOPE:

This is a High Performance Liquid Chromatography (HPLC-UV) method for the analysis of 4-Nitro-3-(trifluoromethyl)phenol (TFM) in Water in the concentration range of 0.005 mg/mL to **3.5** mg/mL.

2. PRINCIPLE:

4-Nitro-3-(trifluoromethyl)phenol dosing formulation in water is diluted with diluent water to fall into the concentration range of the standard curve. The API 4-Nitro-3-(trifluoromethyl)phenol is quantified by reverse phase HPLC with UV detection at 290 nm. The quantitation is accomplished using external standard curve.

3. EQUIPMENT:

3.1 HPLC: Waters Alliance HPLC system with Waters Empower2 Data Collection system; Waters 2690 Separations Module; Waters 2487 Dual Wavelength Absorbance Detector (detection at 290 nm), or equivalent equipment.

3.2 Column: Zorbax XDB C18 5µm, 4.6 x 250 mm column or equivalent

3.3 Pipette: Air displacement or positive displacement pipette, or equivalent.

3.4 General laboratory equipment and glassware.

4. REAGENTS:

METHOD No. 0296R3

4.1 Water (H_2O): Fisher (W5) or equivalent

4.2 Mobile Phase A (MPA): (MPA) (Water with 0.1% Formic Acid): Fisher (LS118) used as supplied or equivalent

4.3 Mobile Phase **B** (MPB): (MPB) (0.1% Formic Acid in Acetonitrile (V/V)): Fisher (HB9823) used as supplied or equivalent

4.4 Diluent: Water. Use as supplied.

5. STANDARD PREPARATIONS:

5.1 Preparation of Stock Standard Solution (Stock) (target 1.00 mg/mL):
Accurately weigh appropriate amount of reference standard TFM into a 25 mL volumetric flask. Dilute to a final volume of 25 mL with water. Briefly sonicate to dissolve the chemical. *Standard concentrations are corrected for purity.*

5.2 Preparation of QC Stock Solution (QC Stock) (target 1.00 mg/mL):
Accurately weigh appropriate amount of reference standard TFM into a 25 mL volumetric flask. Dilute to a final volume of 25 mL with water. Briefly sonicate to dissolve the chemical. *Standard concentrations are corrected for purity.*

5.3 Preparation of Standard Curve:
At least five standard points are prepared in the diluent according to the following scheme. Dilution scheme may vary as needed.

Standard (STD) ID	Aliquot Taken (mL)	Taken From	Final Volume (mL)	Target Concentration (mg/mL)
A	1.5	STOCK	100	0.0150
B	20.0	A	25	0.0120
C	6.0	A	10	0.00900
D	10.0	A	25	0.00600
E	6.0	A	25	0.00360
F	2.0	A	25	0.00120
QC	0.9	QC STOCK	100	0.00900

6. SAMPLE PREPARATION:

Samples are collected while formulation is sitting without stirring.

METHOD No. 0296R3

Prepare duplicate dilutions for each dose concentration sample by diluting appropriate sample aliquot with sample diluent to fall within the standard curve range. Vehicle is diluted similarly as the lowest Test Substance concentration sample analyzed and is prepared singly.

Example of dosing formulation dilution scheme

Formulation Conc. (mg/mL)	Aliquot Taken (mL)	First Dilution Volume (mL)	Aliquot Taken (mL)	Final Dilution Volume (mL)	Final Concentration (ppm)
0	NA	NA	NA	NA	NA
0.005	NA	NA	NA	NA	NA
2	1.00	10.0	0.50	10.0	0.0100

7. INSTRUMENT PARAMETERS

HPLC Column: Zorbax XDB C18, 4.6 x 250 mm, 5 µm

Mobile Phase A (MPA): 0.1% Formic Acid in Water

Mobile Phase B (MPB): 0.1% Formic Acid in Acetonitrile

Autosample Flush: Water: Acetonitrile (50:50,v/v)

Diluent: Water

Gradient:

Step	Step Time (minutes)	Elapsed Time (minutes)	% A (Aqueous)	% B (Organic)	Curve
0	0.0	0.0	75	25	6
1	10	10	0	100	6
2	4	14	0	100	6
3	2	16	75	25	6
4	10	26	75	25	6

Flow Rate : 1.0 mL/min

UV Detector : 290 nm

METHOD No. 0296R3

Injection Volume	:	10 µL
Sample Temperature	:	Ambient
Column Temperature	:	Ambient
Integration	:	Peak Area
Retention Time	:	Approx. 8.2 minutes
Run Time	:	26 minutes

Note: instrument parameter may be modified to optimize retention time and/or chromatography

8. CALCULATIONS

8.1 Compute the linear regression relating the peak area of the standards to the mg/mL of TFM injected for each standard.

8.2 Using the peak area of the sample and the linear regression equation determine the mg/mL detected of TFM for each sample. The linear regression equation is y = mx + b, where m = slope and b = intercept, y = peak area, and x = mg/mL of TFM.

8.3 Calculated Concentration (mg/mL) = mg/mL Detected x Dilution Factor

where Dilution Factor = $\frac{A}{B} \times \frac{C}{D}$

A = Final volume of first dilution, mL.
B = Aliquot taken for the first dilution, mL.
C = Final volume of the final dilution, mL, if applicable.
D = Aliquot taken for the final dilution, mL, if applicable.

8.4 % Target = mg/mL Calculated Concentration/Target in mg/mL x 100

9. NOTES:

9.1 Significant Figures:

METHOD No. 0296R3

All concentrations - recorded to at least three significant figures.

% Target – recorded to at least three significant figures.

9.2 System Suitability:

The %RSD of peak areas and retention times of TFM should be equal or less than 2% for five replicate system suitability injections, and equal or less than 5% for overall system suitability injection including bracket standard injections.

9.3 Standard Curve Linearity

The coefficient of determination, R^2, of the standard curve should be $\geq$ 0.99 and the percent recovery for each standard concentration should be within 100±10%.

9.4 Formulation Stability

Formulation stability in water at Room Temperature for at least 28 days was determined at the high and low concentrations when **stored in amber glass containers with PTFE lined screw capped closures. The concentration of TFM in Deionized water is negatively impacted when stored in contact with rubber, or neoprene closure.**

10. LIST OF FIGURES:

Figure 1 Representative Chromatogram, Standard

Figure 2 Standard Curve

Figure 3 Representative Chromatogram, QC Standard

Figure 4 Representative Chromatogram, Control Article

METHOD No. 0296R3

Figure 1 Representative Chromatogram, Standard

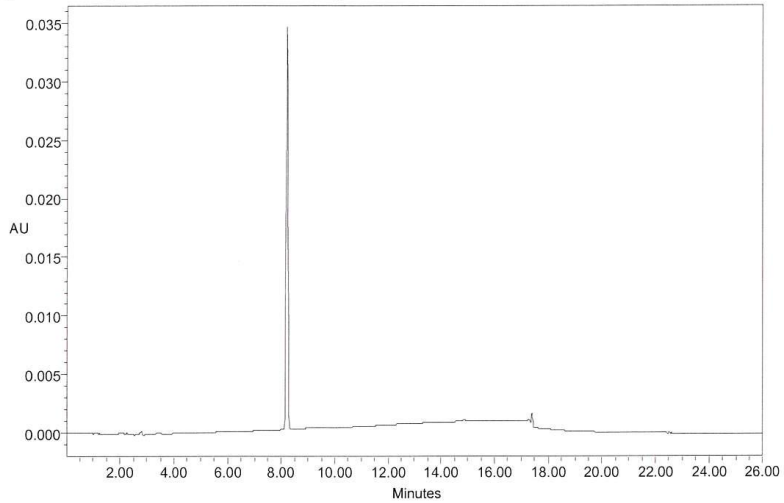
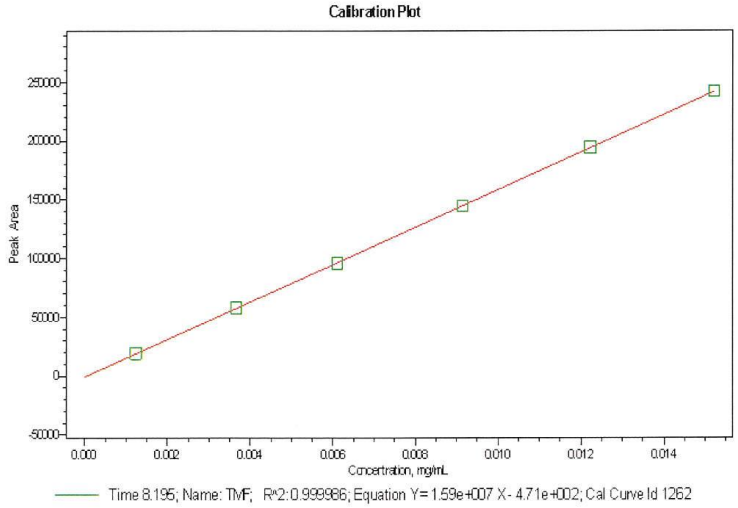


Figure 2 Standard Curve



Page 6 of 8

METHOD No. 0296R3

Figure 3 Representative Chromatogram, Sample

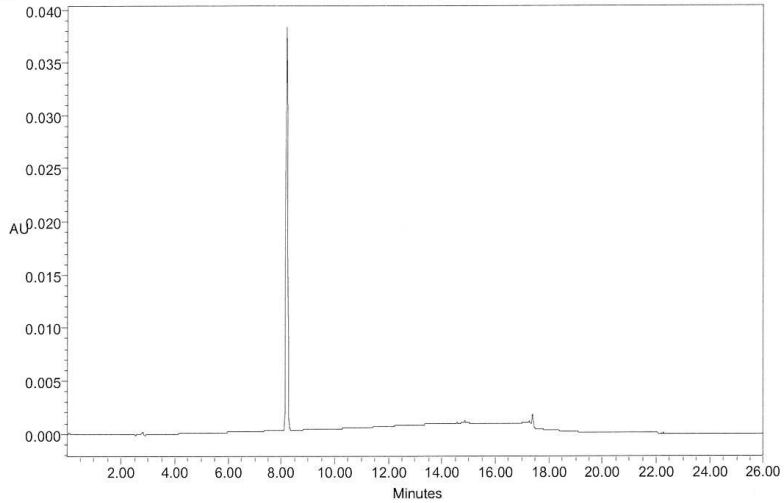
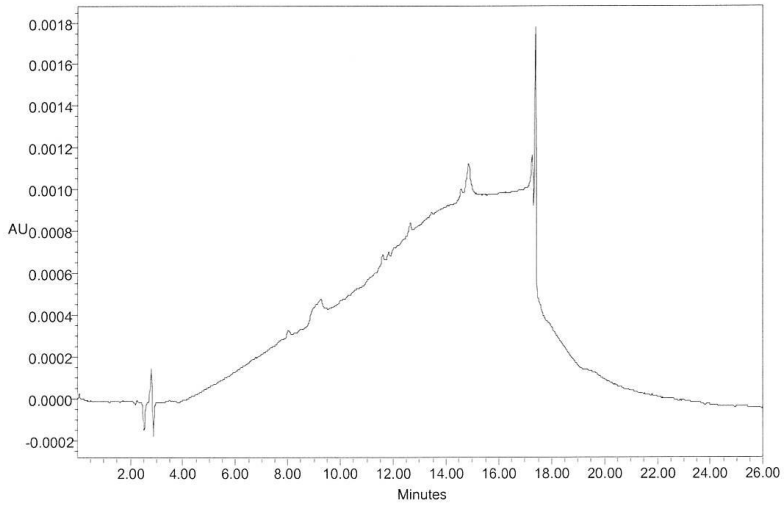


Figure 4 Representative Chromatogram, Vehicle



Page 7 of 8

METHOD No. 0296R3

REVISION HISTORY

Version	Date	Description of Revision	Reason
Original	06Feb2018	•	•
0296R1	09Feb2018	• Minor formatting • Figure 2 on page 6 replaced	• The Curve concentration changed the R^2, slope and intercept of the curve
0296R2	15Mar2018	• Update % A and % B • Update Figure 1 and Figure 3 to include X axis	• Typographical error
0296R3	20Nov2018	• Updated Scope from 2 mg/mL to 3.5 mg/mL • Updated Mobile Phase B • Updated Section 9.4 to include storage.	• Additional testing performed • Typographical error • Additional testing performed

APPENDIX 3: CERTIFICATES OF ANALYSIS

United States Department of the Interior

U.S. GEOLOGICAL SURVEY
Upper Midwest Environmental Sciences Center
2630 Fanta Reed Road
La Crosse, Wisconsin 54603

Certificate of Analysis

Product name: TFM HP Sea Lamprey Larvicide-Extract

Batch or lot number(s) received and analyzed: LAM170517A
Expiration Date: 05-18-2019

Manufacturer:

Iofina
1025 Mary Laidley Drive
Covington, KY 41017

Kurt Jones (Vice President Sales and Business Development)
Phone: (859)-356-8000 Ext. 11

Mean percent active ingredient found (TFM): 80.59 (Std. Dev. 3.57)

Extracting/ Performing laboratory:

USGS Upper Midwest Environmental Sciences Center
2630 Fanta Reed Road
La Crosse, Wisconsin 54603
Phone: (608)783-6451
Fax: (608)783-6066

Date of analysis: 15 December 2017
LC-MS analyst: J. Schueller
Instrument of analysis: Agilent 1290-6530 LC-MS Q-TOF (SN: SG11342307)

Quality Control Review Acceptance Date: 18 Dec 17

Kim Fredricks, QAO

Kim Fredricks, Quality Assurance Officer

2017 TFM HP Sea Lamprey Larvicide Extract - QA Procedure

LC-MS Analysis by: J. Schueller
Date of Analysis: 15 December 2017
Batche Analyzed: LAM170517A

Created by: J. Schueller 12-18-17
Proofed by Jeff Bernardy (Chemist) 12-19-17
Reviewed by Steve Lantz (Chemist) 12/18/17
Verified by Kim Fredricks (QA Officer) 12/18/17

Calculations:
Percent TFM = HPLC TFM conc. (ng/ml)/sample weight (g)/dilution factor*100
Percent TFM sodium Salt = Percent TFM * Conversion Factor (1.106)

Standard curve linearity (R^2) = 0.99991945

Results Coating Place

Sample Identification	HPLC NIC Conc. (ng/mL)	Sample Weight (g)	Percent TFM	Triplicate Mean (%)	Std. Dev.	% RSD
LAM170517A-Extract 1	815.4680	0.09650	84.50	80.59	3.57	4.44
LAM170517A-Extract 2	777.1821	0.10028	77.50			
LAM170517A-Extract 3	764.9114	0.09590	79.76			

Procedure:
A five-point standard curve was prepared from TFM technical (Lot #MKBT9428V Sigma) by weighing 0.00997 g and diluting with 100 mL methanol (Standard Stock A, 100mg/L).
Further dilutions of Standard Stock A - .1:100, 0.3:100, 0.5:100, 0.7:100, and 1.0:100 with methanol solution resulted in working standards of: 100, 300, 500, 700, 1000 ng/mL
Standards were injected in on Agilent 1290-6530 Series LC-MS QTOF for analysis
Subsamples of the Iofina TFM HP Sea Lamprey Larvicide were weighed (Aproximately 0.10 g) into 100 ml volumetric flasks, then bringing to volume in methanol. Futher dilutions were made by delivering 0.1 ml of each stock sample into a 100 ml volumetric flask, bringing to volume with an methanol solution. (Dilution Factor 10000)

LC-MS conditions:
1) Agilent 1290 Series LC-MS QTOF
2) Column: Kinetex EVO-C18, 1.7 um, 100 A, 2.1x100 mm
3) Mobile Phases: A: water (900 mL) methanol (100 mL) ammonium acetate (385 mg) B: methanol (1000 mL) ammonium acetate (385 mg)
4) Column temperature: 50°C
5) Flow Rate: 0.3 mL/min., Injection volume: 2 μL, TFM peak retention time about 3.0 min., sample run time: 9.0 min.
6) Detector m/z 206.0068 in Negative Mode

SIGMA-ALDRICH®

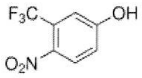
sigma-aldrich.com

3050 Spruce Street, Saint Louis, MO 63103, USA
Website: www.sigmaaldrich.com
Email USA: techserv@sial.com
Outside USA: eurtechserv@sial.com

Certificate of Analysis

Product Name:
4-Nitro-3-(trifluoromethyl)phenol - 99% (GC)

Product Number:	**N27802**
Batch Number:	**MKBX5239V**
Brand:	ALDRICH
CAS Number:	88-30-2
MDL Number:	MFCD00014714
Formula:	C7H4F3NO3
Formula Weight:	207.11 g/mol
Quality Release Date:	29 JAN 2016



Test	Specification	Result
Appearance (Color)	Yellow to Tan	Faint Tan
Appearance (Form) Powder or Crystals and/or Chunks	Conforms to Requirements	Crystalline Powder
Infrared Spectrum	Conforms to Structure	Conforms
Carbon	39.9 - 41.2 %	40.7 %
Purity (GC)	≥ 98.5 %	99.9 %

Michael Grady, Manager
Quality Control
Milwaukee, WI US

Sigma-Aldrich warrants, that at the time of the quality release or subsequent retest date this product conformed to the information contained in this publication. The current Specification sheet may be available at Sigma-Aldrich.com. For further inquiries, please contact Technical Service. Purchaser must determine the suitability of the product for its particular use. See reverse side of invoice or packing slip for additional terms and conditions of sale.

Version Number: 1 Page 1 of 1

Certificate of Analysis Page 1 of 1

Fisher Scientific

1 Reagent Lane
Fair Lawn, NJ 07410
201.796.7100 tel
201.796.1329 fax

Certificate of Analysis

Fisher Scientific's Quality System has been found to conform to Quality Management System Standard ISO9001:2008 standard by SAI Global Certificate Number CERT - 0090918

This is to certify that units of the lot number below were tested and found to comply with the specifications of the grade listed. Certain data have been supplied by third parties. Fisher Scientific expressly disclaims all warranties, expressed or implied, including the implied warranties of merchantability and fitness for a particular purpose. Certain products (USP/FCC/NF/EP/BP/JP grades) are sold for use in food, drug, or medical device manufacturing. Fisher does not claim regulatory coverage under 21 CFR nor maintain DMF's with the FDA. The following are the actual analytical results obtained:

Catalog Number	W2	Quality Test / Release Date 8/7/2017	
Lot Number	174802		
Description	WATER, DIUF		
Country of Origin	United States	* Suggested Retest Date	Aug-2022
Chemical Origin	Inorganic-non animal		
BSE/TSE Comment	No animal products are used as starting raw material ingredients, or used in processing, including lubricants, processing aids, or any other material that might migrate to the finished product.		

Result name	Units	Specifications	Test Value
APPEARANCE		REPORT	CLEAR,COLORLESS LIQUID
COLOR	APHA	<= 5	<5
IDENTIFICATION	PASS/FAIL	= PASS TEST	PASS TEST
PH AT 25 DEGREES C		Inclusive Between 5.4 - 7.0	6.0
SPECIFIC CONDUCTANCE	MICROMHO/CM	<= 2.0	0.8

CERTIFIED BY

Teresa Bailey-Wyche

Quality Assurance Specialist - Certificate of Analysis Fair Lawn

APPENDIX 4: DOSE FORMULATIONS ANALYSIS REPORT

CONTRIBUTING SCIENTIST REPORT
DOSE FORMULATION ANALYSIS

4-Nitro-3-(trifluromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Sponsor:
U.S.Geological Survey (USGS)
2630 Fanta Reed Road
La Crosse, WI 54603

On behalf of:

U.S. Fish and Wildlife Service
Lake Champlain Fish and Wildlife Conservation Office
11 Lincoln Street
Essex Junction, Vermont 05452

Testing Facility:
Smithers Avanza Toxicology Services
15 Firstfield Road
Gaithersburg, MD 20878

Smithers Avanza Study Number:
2410-14374

Author:
Surubhi Kalathur, MS

Dose Formulation and Analysis Study Completion Date:
March 26, 2019

TABLE OF CONTENTS

1.0 SIGNATURE PAGE 3
2.0 STUDY TIMETABLE 4
3.0 DEVIATIONS 4
4.0 MATERIALS 4
4.1 Test Substance/Reference Standard and Vehicle/Control Substance 4
4.2 Samples 4
5.0 RESULTS AND DISCUSSION 5
5.1 Acceptance Criteria 5
5.2 System Suitability 5
5.3 Standard Curve 6
5.4 Standard Agreement 7
5.5 Concentration Analyses 8
5.6 Homogeneity 11
5.7 Stability Analysis of 3.5 mg/mL TFM Solution 12
5.8 Analysis of TFM Dosing Solutions in Water Bottles 12
5.9 Analysis of TFM Dosing Solutions in Water Bottles with/without Acid 12
5.10 Analysis of TFM Dosing Solutions in Water Bottles 13
5.11 Analysis of TFM Dosing Solutions in Water Bottle 13
6.0 CONCLUSION 15

LIST OF TABLES

Text Table 1: Test Substance/Reference Standard and Vehicle 4
Text Table 2: System Suitability Results 6
Text Table 3: Standard Curve Results 7
Text Table 4: Standard Agreement Results (QC and STD C) 7
Text Table 5: Concentration Verification Results (Week 1) 8
Text Table 6: Concentration Verification Results (Week 2) 9
Text Table 7: Concentration Verification Results (Week 2 and Week 3) 9
Text Table 8: Concentration Verification Results (Week 8) 10
Text Table 9: Concentration Verification Results (Week 8 Contd.) 10
Text Table 10: Concentration Verification Results (Week 13) 11
Text Table 11: Homogeneity Results – 3.50 mg/mL Formulation 11
Text Table 12: Recovery Results of 3.50 mg/mL 12
Text Table 13: Recovery Results (Low and High) 12
Text Table 14: Recovery Results with/without Acid (High) 13
Text Table 15: Recovery Results (Mid and High) 13
Text Table 16: Recovery Results of Dosing Solutions in the Water Bottle 14

APPENDICES

Appendix 1: Certificate of Analysis 16
Appendix 2: Analytical Chemistry Method No. 0296R3 20

1.0 SIGNATURE PAGE

4-Nitro-3-(trifluoromethyl)phenyl (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Author:

K. V. Surubhi

Surubhi Kalathur
Contributing Scientist (Dose Formulation Analysis)

26 Mar 2019
Date

2.0 STUDY TIMETABLE

Study Initiation Date:	18 April 2018
Analysis Initiation Date:	25 April 2018
Analysis Completion Date:	July 19, 2018
Analysis Study Completion Date:	March 26, 2019

3.0 DEVIATIONS

One deviation occurred during the analysis of Day 4 samples of the 3.5 mg/mL solution. Although the results were not reported additional time points provided the necessary data for the study. Therefore this had a minor impact on the study.

4.0 MATERIALS

4.1 Test Substance/Reference Standard and Vehicle/Control Substance

The test substance, 4-Nitro-3(trifluoromethyl) phenyl (TFM), MKBX5239V was corrected for purity of 99.9% for the preparation of all analytical chemistry standards. The test substance was at room temperature, protected light.

The information for test substance used in this study, and the formulation vehicle used for preparation of formulation, are described in Text Table 1.

Text Table 1: Test Substance/Reference Standard and Vehicle

Name	Lot/Batch No.	Supplier	Purity	Expiration Date
TFM	MKBX5239V	Sigma Aldrich	99.9%[a]	26 Dec 2022
Water	173848	Fischer Scientific	Not Applicable	30 Jun 22

a Data from Certificate of Analysis

The Certificate of Analysis for TFM and water is presented in Appendix 1.

4.2 Samples

The dose verification samples (10 mL from each group) from formulations prepared for Study Week 1, Week 2, Week 3 (Study Day 11 for Group 7-11), Week 8, and Week 13 were received on April 24, 2018, May 3, 2018, May 7, 2018, June 13, 2018 and June 18, 2018 analyzed for concentration within the confirmed formulation stability.

From Week 1 and Week 2, duplicate sample aliquots (1 mL each) were collected from Group 1, Group 2 and Group 7 and directly assayed. Duplicate sample aliquots (0.5-3.0 mL each) were collected from Group 3-Group 6, Group 8 - Group 11 dosing formulations and were diluted with water to within the standard curve range. As the concentrations of the dosing solutions increased, all group dosing solutions from were diluted with water to within the standard curve range. All samples were analyzed using a validated analytical method (Smithers Avanza Method 0296R3), presented in Appendix 2. The method was previously validated under Smithers Avanza Study 2410-14256. The formulations (0.005-2.0 mg/mL) are stable up to 28 days at room temperature storage conditions.

Formulations in study 2410-14374 exceeded those previously determined for stability (study 2410-14256) therefore additional testing to encompass the stability data were collected at a concentration of 3.5 mg/mL

and assessed for 28 Days at room temperature. The samples were taken from the stock and water bottle exposed to neoprene stopper to determine the percentage change in concentration due to potential of the test substance binding to the neoprene stoppers. The data are presented in Text Table 11 and Text Table 12.

Duplicate samples of 10 mL each were received from stability formulation prepared during Week 1 at the Low concentration (0.0093 mg/mL) and High concentration (1.147 mg/mL) that were stored in the animal watering bottle configuration during week 1. These samples were diluted with water to fall within the standard curve range and analyzed on May 2, 2018. The samples were analyzed to show binding to the neoprene stoppers. The data are presented in Text Table 13.

During week 3 analysis, four replicate samples of 0.5 mL from the water bottle from Group 11 (1.15 mg/mL) from week 2 was prepared. Two samples were diluted with water and two samples were diluted with 0.1% formic acid in water to fall within the standard curve range and analyzed on May 7, 2018. The samples were analyzed to show the effects of pH on dosing solutions. The data are presented in Text Table 14.

Duplicate samples of 10 mL each were received from stability formulation at the Mid concentration (0.109 mg/mL) and High concentration (1.450 mg/mL) that were stored in the animal watering bottle configuration during week 5. Samples were collected at least on Day 1, Day 4 and Day 7, These samples were diluted with water to within the standard curve range and analyzed on June 11, 2018. The samples were analyzed to show binding to the neoprene stoppers. The data are presented in Text Table 15.

Duplicate samples of 2 mL each were received from Group 2, 3, 4, 5, and 6 formulation and similarly prepared water bottles from each group during week 11. Samples were collected at least on Day 0, Day 1, Day 4 (prior to and after refilling dosing solutions) and Day 7. These samples were diluted with water to within the standard curve range and analyzed on July 6, 2018, July 9, 2018 and July 12, 2018. The samples were analyzed to determine the potential changes in concentrations of the solutions after exposure to the neoprene stoppers at different concentrations. The data are presented in Text Table 16.

5.0 RESULTS AND DISCUSSION

5.1 Acceptance Criteria

The acceptance criteria for dose verification samples are 90 - 110% of the nominal concentration. However, the acceptance criteria was not used if the analysis was not a dosing formulation.

5.2 System Suitability

System suitability was evaluated by using five consecutive injections of a mid-point standard (STD C) of the standard curve at the beginning of sample set and bracket injection of the same standard after injections of no more than six sample injections throughout the sample set. The resulting % RSD for retention time and peak area are presented in Text Table 2. All % RSD values were less than 5% for the five consecutive injections of STD C at the beginning of the sample set and for overall system suitability (five consecutive injections plus all bracket injections).

Text Table 2: System Suitability Results

Sample Set Name	System Suitability	%RSD (Retention Time)	%RSD (Peak Area)
Week 1	n = 5 consecutive inj of STD C	0.027	0.23
	All injections of STD C	0.056	0.17
Stability Week 1	n = 5 consecutive inj of STD C	0.075	0.21
	All injections of STD C	0.112	0.26
Week 2	n = 5 consecutive inj of STD C	0.024	0.20
	All injections of STD C	0.189	0.18
Week 2 repeat (week 3)	n = 5 consecutive inj of STD C	0.083	0.12
	All injections of STD C	0.093	0.30
Group 4_Group 11_ High Day 0_3.5mg/mL	n = 5 consecutive inj of STD C	0.047	0.12
	All injections of STD C	0.074	0.26
High Day 1_3.5mg/mL (bottle) & Week 8 (Group 1 – Group 6)	n = 5 consecutive inj of STD C	0.045	1.39
	All injections of STD C	0.089	1.19
Week 8 (Group 7 –Group 11)	n = 5 consecutive inj of STD C	0.070	0.15
	All injections of STD C	0.071	0.36
High Day 7_3.5mg/mL (bottle)	n = 5 consecutive inj of STD C	0.013	0.43
	All injections of STD C	0.044	0.67
High Day 10_3.5mg/mL	n = 5 consecutive inj of STD C	0.022	0.07
	All injections of STD C	0.049	0.20
Mix 11	n = 5 consecutive inj of STD C	0.025	0.06
	All injections of STD C	0.074	0.18
Mix 11_Day4 (before and after refill)_ High Day 28_3.5mg/mL	n = 5 consecutive inj of STD C	0.062	0.24
	All injections of STD C	0.082	0.37
Mix 11_Day7	n = 5 consecutive inj of STD C	0.023	0.09
	All injections of STD C	0.029	0.17
Week 13	n = 5 consecutive inj of STD C	0.067	0.61
	All injections of STD C	0.094	0.59
Week 13 Backup	n = 5 consecutive inj of STD C	0.048	0.15
	All injections of STD C	0.057	0.25

5.3 Standard Curve

A linear regression equation relating the peak areas (Y) to the TFM concentration (X) injected was determined. The linearity, expressed as square of correlation coefficient (R^2), was higher than 0.99. The accuracy, % error (or % Deviation), for each standard injected [((observed - expected) / expected) x 100 %] was within ± 10% of expected concentration. The resulting standard curve results are presented in Text Table 3.

Text Table 3: Standard Curve Results

Sample Set Name	%Deviation Range	R^2
Week 1	-2.651 to 2.365	0.999461
Stability Week 1	-1.395 to 1.508	0.999850
Week 2	-3.184 to 0.796	0.999920
Week 2 repeat (week 3)	-0.789 tp 0.239	0.999993
Group 4_Group 11_High Day 0_3.5mg/mL	-1.021 to 1.406	0.999924
High Day 1_3.5mg/mL (bottle) & Week 8 (Group 1 – Group 6)	-3.810 to 2.182	0.999066
Week 8 (Group 7 –Group 11)	-4.040 to 3.739	0.999648
High Day 7_3.5mg/mL (bottle)	-5.060 to 1.568	0.999583
High Day 10_3.5mg/mL	-1.529 to 0.916	0.999935
Mix 11	-0.597 to 0.643	0.999896
Mix 11_Day4 (before and after refill)_ High Day 28_3.5mg/mL	-0.597 to 0.878	0.999942
Mix 11_Day 7	-0.584 to 0.595	0.999956
Week 13	-5.216 to 1.801	0.999728
Week 13 Backup	-0.548 to 0.617	0.999936

5.4 Standard Agreement

The accuracy of the prepared stock standards was demonstrated by standard agreement of similarly prepared standard solutions (i.e. STD C and QC) with detector response of the two standard solutions within 5% of each other. The % Target of the QC should be within ±5%. The agreement met criteria for all the sampling sets. The resulting standard agreement results are presented in Text Table 4.

Text Table 4: Standard Agreement Results (QC and STD C)

Sample Set Name	% Target of QC
Week 1	99.2
Stability Week 1	99.6
Week 2	100.8
Week 2 repeat (week 3)	103.4
Group 4_Group 11_High Day 0_3.5mg/mL	95.9
High Day 1_3.5mg/mL (bottle) & Week 8 (Group 1 – Group 6)	99.7
Week 8 (Group 7 –Group 11)	97.7
High Day 7_3.5mg/mL (bottle)	102.2
High Day 10_3.5mg/mL	100.8
Mix 11	98.8
Mix 11_Day4 (before and after refill)_ High Day 28_3.5mg/mL	99.2
Mix 11_Day 7	103.9
Week 13	98.2
Week 13 Backup	98.9

5.5 Concentration Analyses

The method specified criteria for system suitability and standard curve linearity were met during the analysis. Results of the Concentration analysis are presented in Text Table 5, Text Table 6, Text Table 7, Text Table 8, Text Table 9, and Text Table 10.

Text Table 5: Concentration Verification Results (Week 1)

Analysis Interval	Target Dose Level mg/kg/day	Dose Concentration mg/mL	Calculated Concentration mg/mL	Mean Calculated Concentration mg/mL	% Target	Mean % Target
Week 1 (Group 1 – Group 6)	0	0	None Detected	NA	NA	NA
	1	0.00930	0.00897	0.00897	96.5	96.5
			0.00897		96.4	
	3	0.0278	0.0263	0.0263	94.7	94.7
			0.0263		94.7	
	10	0.0930	0.0894	0.0895	96.1	96.2
			0.0895		96.3	
	30	0.278	0.272	0.271	97.7	97.6
			0.271		97.4	
	100	0.930	0.917	0.917	98.6	98.6
			0.916		98.5	
Week 1 (Group 7- Group 11)	1	0.01147	0.01107	0.01108	96.5	96.6
			0.01109		96.7	
	3	0.0344	0.0330	0.0329	95.8	95.8
			0.0329		95.7	
	10	0.1147	0.1104	0.1103	96.3	96.1
			0.1101		96.0	
	30	0.344	0.316	0.317	92.0	92.0
			0.317		92.1	
	100	1.147	1.127	1.126	98.3	98.1
			1.124		98.0	

Text Table 6: Concentration Verification Results (Week 2)

Analysis Interval	Target Dose Level mg/kg/day	Dose Concentration mg/mL	Calculated Concentration mg/mL	Mean Calculated Concentration mg/mL	% Target	Mean % Target
Week 2 (Group 1 – Group 6)	0	0	None Detected	NA	NA	NA
	1	0.00928	0.00880	0.00879	94.9	94.8
			0.00879		94.7	
	3	0.0278	0.0263	0.0263	94.5	94.5
			0.0263		94.5	
	10	0.0928	0.0870	0.0871	93.8	93.8
			0.0871		93.9	
	30	0.278	0.260	0.260	93.5	93.6
			0.260		93.6	
	100	0.928	0.898	0.899	96.8	96.8
			0.899		96.9	

Text Table 7: Concentration Verification Results (Week 2 and Week 3)

Analysis Interval	Target Dose Level mg/kg/day	Dose Concentration mg/mL	Calculated Concentration mg/mL	Mean Calculated Concentration mg/mL	% Target	Mean % Target
Week 2 (Group 7-Group 11)	1	0.0115 (repeat)[a]	0.00945	0.00948	82.2	82.4
			0.00951		82.7	
	3	0.0344 (repeat)[a]	0.0276	0.0276	80.1	80.1
			0.0276		80.1	
	10	0.115 (repeat)[a]	0.0936	0.0936	81.5	81.4
			0.0936		84.4	
	30	0.344 (repeat)[a]	0.281	0.282	81.7	82.0
			0.283		82.2	
	100	1.15	1.154	1.155	100.3	100.4
			1.156		100.5	
Week 3 (Group 7-Group 11)	1	0.0115	0.0113	0.0113	97.9	97.9
			0.0113		98.0	
	3	0.0344	0.0335	0.0335	97.3	97.4
			0.0335		97.5	
	10	0.115	0.109	0.109	95.0	94.8
			0.109		94.8	
	30	0.344	0.330	0.330	95.9	95.8
			0.329		95.8	

a-Due to the low results from week 2, samples were prepared on week 3 and analyzed.

Text Table 8: Concentration Verification Results (Week 8)

Analysis Interval	Target Dose Level mg/kg/day	Dose Concentration mg/mL	Calculated Concentration mg/mL	Mean Calculated Concentration mg/mL	% Target	Mean % Target
Week 8 (Group 1 – Group 6)	0	0	None Detected	NA	NA	NA
	1	0.0139	0.0136	0.0136	97.5	97.6
			0.0136		97.7	
	3	0.0380	0.0368	0.369	96.9	97.0
			0.0369		97.1	
	10	0.140	0.132	0.133	93.9	94.7
			0134		95.5	
	30	0.475	0.448	0.452	94.3	95.1
			0.456		96.0	
	100	2.04	2.016	2.021	98.8	99.1
			2.026		99.3	

Text Table 9: Concentration Verification Results (Week 8 Contd.)

Analysis Interval	Target Dose Level mg/kg/day	Dose Concentration mg/mL	Calculated Concentration mg/mL	Mean Calculated Concentration mg/mL	% Target	Mean % Target
Week 8 (Group 7 – Group 11)	1	0.0126	0.0119	0.0119	94.7	94.7
			0.0119		94.8	
	3	0.0383	0.0349	0.0349	91.1	91.2
			0.0350		91.3	
	10	0.124	0.113	0.113	91.3	91.2
			0.113		91.1	
	30	0.392	0.363	0.363	92.7	92.6
			0.362		92.4	
	100	1.88	1.793	1.793	95.4	95.4
			1.793		95.3	

Text Table 10: Concentration Verification Results (Week 13)

Analysis Interval	Target Dose Level mg/kg/day	Dose Concentration mg/mL	Calculated Concentration mg/mL	Mean Calculated Concentration mg/mL	% Target	Mean % Target
Week 13	0	0	None Detected	NA	NA	NA
	1	0.0172	0.0166	0.0164	96.4	95.8
			0.0165		95.1	
	3	0.0476	0.0461	0.0461	96.9	96.8
			0.0460		96.7	
	10 (Backup)	0.176	0.186	0.186	105.7	105.5
			0.185		105.3	
	30	0.616	0.554	0.555	90.0	90.1
			0.556		90.2	
	100	2.47	2.257	2.248	91.4	91.0
			2.240		90.7	
	1	0.0145	0.0133	0.0132	91.8	91.2
			0.0131		90.6	
	3 (Backup)	0.0416	0.0397	0.0400	95.4	96.1
			0.0403		96.8	
	10 (Backup)	0.158	0.155	0.154	98.0	97.6
			0.154		97.2	
	30 (Backup)	0.464	0.445	0.445	96.0	96.0
			0.446		96.0	
	100 (Backup)	2.10	2.089	2.089	99.5	99.5
			2.088		99.4	

5.6 Homogeneity

Aliquots from top, middle and bottom of 3.5 mg/mL formulation were analyzed as a new Group High to cover the dose range in this study. The data are presented in Text Table 11.

Text Table 11: Homogeneity Results – 3.50 mg/mL Formulation

Sample Location	Dilution Factor	Calculated Concentration mg/mL	% Nominal Target	Mean
Top	500	3.514	100.4	100.4
	500	3.514	100.4	
Middle	500	3.502	100.0	100.1
	500	3.504	100.1	
Bottom	500	3.474	99.3	99.1
	500	3.463	98.9	
	Mean			99.9
	STDEV			0.68
	% RSD			0.7

5.7 Stability Analysis of 3.5 mg/mL TFM Solution

The method specified criteria for system suitability and standard curve linearity were met during the analysis on Day 0, Day 1 Day 7 and Day 28 but did not meet acceptance criteria on Day 4. Results of the stability analysis of 3.50 mg/mL TFM stock solution and water bottle exposed solutions (replaced and refilled on day 4) for all except from Day 4 are presented in Text Table 12.

Text Table 12: Recovery Results of 3.50 mg/mL

Sample Solution	Conditions		Dilution Factor	Mean Calculated Concentration	% Recovery relative to T_0	% Change from T_0
High (3.50 mg/mL)	T_0	--	500	3.495	100	---
	Day 10	RT	500	3.532	101	1.06
	Day 28	RT	500	3.617	103	3.49
Water Bottle (3.50 mg/mL)	Day 1	--	500	2.998	85.8	-14.2
	Day 7	RT	500	3.072	87.9	-12.1

a-The % Recovery and % Change for Day 1 and 7 is calculated based on T_0.

5.8 Analysis of TFM Dosing Solutions in Water Bottles

The method specified criteria for system suitability and standard curve linearity were met during the Week 1 analysis. Results of the analysis of lowest (0.00930 mg/mL) and highest (1.147 mg/mL) TFM stock solutions stored in/not in water bottles are presented in Text Table 13:

Text Table 13: Recovery Results (Low and High)

Sample Solution	Conditions		Dilution Factor	Mean Calculated Concentration	% Recovery relative to T_0	% Change from T_0
Low (0.00930 mg/mL)	T_0	--	1	0.00897	100	---
	Day 7	RT	1	0.00888	99.0	-1.00
Bottle (0.00930 mg/mL)	Day 7	RT	1	0.00814	90.7	-9.25
High (1.147 mg/mL)	Day 1	--	100	1.126	100	---
	Day 7	RT	100	1.032	91.7	-8.35
Bottle (1.147 mg/mL)	Day 7	RT	100	0.697	61.9	-38.10

5.9 Analysis of TFM Dosing Solutions in Water Bottles with/without Acid

The method specified criteria for system suitability and standard curve linearity were met during the Week 2 analysis. Results of the analysis of highest (1.150 mg/mL) TFM stock solutions stored in/not in water bottles and the solutions prepared with water or 0.1% Formic Acid in water are presented in Text Table 14. The appearance of the solution diluted with water was pale yellow in color while the appearance of the solution diluted with 0.1% Formic acid was clear.

Text Table 14: Recovery Results with/without Acid (High)

Sample Solution	Conditions		Dilution Factor	Mean Calculated Concentration	% Recovery relative to T_0	% Change from T_0
High (1.150 mg/mL)	Day 1	--	100	1.155	100	---
Bottle[a] (1.150 mg/mL)	Day 13	RT	100	0.873	75.6	-24.4
Bottle[b] (1.150 mg/mL)	Day 13	RT	100	0.868	75.2	-24.8

a- the solution is diluted with water. b- the solution is diluted with 0.1% Formic Acid in water.

5.10 Analysis of TFM Dosing Solutions in Water Bottles

The method specified criteria for system suitability and standard curve linearity were met during the following Week 5 analysis. Results of the analysis of middle concentration (0.109 mg/mL) and highest (1.450 mg/mL) TFM stock solutions (T_0) and from solutions stored water bottles (Day 1, 4, and 7) are presented in Text Table 15.

Text Table 15: Recovery Results (Mid and High)

Sample Solution	Conditions		Dilution Factor	Mean Calculated Concentration	% Recovery relative to T_0	% Change from T_0
Mid (0.109 mg/mL)	T_0	--	10	0.104	100	--
	Day 1	RT	10	0.0948	91.2	-8.85
	Day 4	RT	10	0.0875	84.1	-15.87
	Day 7	RT	10	0.0866	83.3	-16.73
High (1.450 mg/mL)	T_0	--	200	1.411	100	--
	Day 1	RT	200	1.198	84.9	-15.10
	Day 4	RT	200	1.056	74.8	-25.16
	Day 7	RT	200	0.931	66.0	-34.02

The data in the table above was used to calculate the linear equation describing the average concentration reduction per week for weeks 1-3, in which water bottles were not refilled. The test material intake was corrected for as noted in the equations section of the study report based on the model for weeks 1-3.

5.11 Analysis of TFM Dosing Solutions in Water Bottle

The method specified criteria for system suitability and standard curve linearity were met during the analysis. Results of the stability analysis of Group 2, Group 3, Group 4, Group 5 and Group 6 TFM stock solution (T_0) from Week 11 and water bottle exposure (Day 1- Day 7) are presented in Text Table 16.

Text Table 16: Recovery Results of Dosing Solutions in the Water Bottle

Sample Solution	Conditions		Dilution Factor	Mean Calculated Concentration	% Recovery relative to T_0	% Change from T_0
Group 2 (0.0163 mg/mL) and Group 2 Water Bottle Cage # 21	T_0	--	2.00	0.0154	100	---
	Day 1	RT	2.00	0.0142	92.2	-7.79
	Day 4	RT	2.00	0.0142	92.2	-7.79
	Day 4 Fresh	RT	2.00	0.0162	105.2	5.19
	Day 7[a]	RT	2.00	0.0145	89.5	-10.5
Group 3 (0.0462 mg/mL) and Group 3 Water Bottle Cage # 26	T_0	--	5.00	0.0445	100	---
	Day 1	RT	5.00	0.0427	96.0	-4.04
	Day 4	RT	5.00	0.0386	86.7	-13.26
	Day 4 Fresh	RT	5.00	0.0442	99.3	-0.67
	Day 7[a]	RT	5.00	0.0384	86.9	-13.1
Group 4 (0.170 mg/ml)and Group 4 Water Bottle Cage # 31	T_0	--	20.0	0.164	100	---
	Day 1	RT	20.0	0.148	90.2	-9.76
	Day 4	RT	20.0	0.127	77.4	-22.56
	Day 4 Fresh	RT	20.0	0.163	99.4	-0.61
	Day 7[a]	RT	20.0	0.133	81.6	-18.4
Group 5 (0.604 mg/mL) and Group 5 Water Bottle Cage # 36	T_0	--	100	0.569	100	---
	Day 1	RT	100	0.486	85.4	-14.59
	Day 4	RT	100	0.389	68.4	-31.63
	Day 4 Fresh	RT	100	0.598	105.1	5.10
	Day 7[a]	RT	100	0.486	81.3	-18.7
Group 6 (2.56 mg/mL) and Group 6 Water Bottle Cage # 41	T_0	--	250	2.482	100	---
	Day 1	RT	250	2.003	80.7	-19.30
	Day 4	RT	250	1.529	61.6	-38.40
	Day 4 Fresh	RT	250	2.501	100.8	0.77
	Day 7[a]	RT	250	2.070	82.8	-17.2

a-The % Recovery and % Change for Day 7 is calculated based on Day 4 Fresh.

The data in the above table was used to model the average reduction in concentration for each solution over a week. The refill of the water bottles on Day 4 was accounted for by averaging the loss per week and was applied to weeks 4-13 in which the dosing solutions were refilled. The test material intake was corrected for as noted in the equations section of the study report based on the model for weeks 4-13.

6.0 CONCLUSION

All concentration verification results met acceptance criteria with the mean % target results ranging from 90.1% to 105.5%. There was no detection of test substance in the Control samples analyzed. All % RSD of system suitability were less than 5%. During the course of the study, the concentration of the High dose was reaching the concentration beyond the stability established in study 2410-14256. As a result, stability was added at a concentration of 3.5 mg/mL to cover the potential highest dosing solution that would be used on this study. The 3.5 mg/mL solution is stable at room temperature for at least 28 days.

At the end of week 1, water bottles were analyzed at the lowest and highest concentration the percent (%) change was less than 10% at the low concentration and less than 40% for the High concentration. As a result, dosing solutions from water bottles at a Middle dose and High dose were tested for Day 1, Day 4 and Day 7 of Week 5, which showed a similar trend of overall % Change of 17% for Middle dose and overall % Change of 34% for the High dose.

During week 3, with the addition of analyzing dosing solutions, Group 11 dosing solution from week 2 water bottle was diluted with water and with 0.1% Formic acid in water which showed that there was no effect of pH on the % change from time zero.

The 3.5 mg/mL formulation solution was also analyzed after being exposed to water bottle for 4 days and refiled on Day 4 and tested on Day 7. This paradigm resulted in an overall % loss of 12.1%, which was less than if solutions were not emptied and refilled on Day 4. Subsequently, the dosing solutions were emptied from the water bottles and refilled on Day 4 to mitigate the loss in concentration. To confirm this was similar in the water bottles provided to the animals, the dosing solutions during Week 11 of the study for Group 2 to 6, were tested and the % loss ranges were from 10% to 19% on Day 7.

APPENDIX 1: CERTIFICATE OF ANALYSIS

SIGMA-ALDRICH

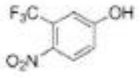
sigma-aldrich.com

3050 Spruce Street, Saint Louis, MO 63103, USA
Website: www.sigmaaldrich.com
Email USA: techserv@sial.com
Outside USA: eurtechserv@sial.com

Certificate of Analysis

Product Name:
4-Nitro-3-(trifluoromethyl)phenol - 99% (GC)

Product Number:	**N27802**
Batch Number:	**MKBX5239V**
Brand:	ALDRICH
CAS Number:	88-30-2
MDL Number:	MFCD00014714
Formula:	C7H4F3NO3
Formula Weight:	207.11 g/mol
Quality Release Date:	29 JAN 2016



Test	Specification	Result
Appearance (Color)	Yellow to Tan	Faint Tan
Appearance (Form) Powder or Crystals and/or Chunks	Conforms to Requirements	Crystalline Powder
Infrared Spectrum	Conforms to Structure	Conforms
Carbon	39.9 - 41.2 %	40.7 %
Purity (GC)	≥ 98.5 %	99.9 %

Michael Grady, Manager
Quality Control
Milwaukee, WI US

Sigma-Aldrich warrants, that at the time of the quality release or subsequent retest date this product conformed to the information contained in this publication. The current Specification sheet may be available at Sigma-Aldrich.com. For further inquiries, please contact Technical Service. Purchaser must determine the suitability of the product for its particular use. See reverse side of invoice or packing slip for additional terms and conditions of sale.

Version Number: 1

Page 1 of 1

Certificate of Analysis Page 1 of 1

Fisher Scientific

1 Reagent Lane
Fair Lawn, NJ 07410
201.796.7100 tel
201.796.1329 fax

Certificate of Analysis

Fisher Scientific's Quality System has been found to conform to Quality Management System Standard ISO9001:2008 standard by SAI Global Certificate Number CERT - 0090918

This is to certify that units of the lot number below were tested and found to comply with the specifications of the grade listed. Certain data have been supplied by third parties. Fisher Scientific expressly disclaims all warranties, expressed or implied, including the implied warranties of merchantability and fitness for a particular purpose. Certain products (USP/FCC/NF/EP/BP/JP grades) are sold for use in food, drug, or medical device manufacturing. Fisher does not claim regulatory coverage under 21 CFR nor maintain DMF's with the FDA. The following are the actual analytical results obtained:

Catalog Number	W2	Quality Test / Release Date 8/7/2017	
Lot Number	174802		
Description	WATER, DIUF		
Country of Origin	United States	* Suggested Retest Date	Aug-2022
Chemical Origin	Inorganic-non animal		
BSE/TSE Comment	No animal products are used as starting raw material ingredients, or used in processing, including lubricants, processing aids, or any other material that might migrate to the finished product.		

Result name	Units	Specifications	Test Value
APPEARANCE		REPORT	CLEAR,COLORLESS LIQUID
COLOR	APHA	<= 5	<5
IDENTIFICATION	PASS/FAIL	= PASS TEST	PASS TEST
PH AT 25 DEGREES C		Inclusive Between 5.4 - 7.0	6.0
SPECIFIC CONDUCTANCE	MICROMHO/CM	<= 2.0	0.8

CERTIFIED BY

Teresa Bailey-Wyche

Quality Assurance Specialist - Certificate of Analysis Fair Lawn

Certificate of Analysis Page 1 of 1

ThermoFisher SCIENTIFIC

1 Reagent Lane
Fair Lawn, NJ 07410
201.796.7100 tel
201.796.1329 fax

Certificate of Analysis

Thermo Fisher Scientific's Quality System has been found to conform to Quality Management System Standard ISO9001:2008 standard by SAI Global Certificate Number CERT - 0090918

This is to certify that units of the lot number below were tested and found to comply with the specifications of the grade listed. Certain data have been supplied by third parties. Thermo Fisher Scientific expressly disclaims all warranties, expressed or implied, including the implied warranties of merchantability and fitness for a particular purpose. Certain products (USP/FCC/NF/EP/BP/JP grades) are sold for use in food, drug, or medical device manufacturing. Fisher does not maintain DMF's with the FDA. The following are the actual analytical results obtained:

Catalog Number	W5	Quality Test / Release Date 2/6/2018	
Lot Number	179141		
Description	WATER, HPLC GRADE		
Country of Origin	United States	* Suggested Retest Date	Feb-2023
Chemical Origin	Inorganic-non animal		
BSE/TSE Comment	No animal products are used as starting raw material ingredients, or used in processing, including lubricants, processing aids, or any other material that might migrate to the finished product.		

Result name	Units	Specifications	Test Value
APPEARANCE		REPORT	CLEAR COLORLESS LIQUID
COLOR	APHA	<= 5	5
EVAPORATION RESIDUE	ppm	<= 1	<0.1
LC GRADIENT AT 254 NM	PASS/FAIL	= PASS TEST	PASS TEST

Teresa Bailey-Wyche

Quality Assurance Specialist - Certificate of Analysis BPF

Note: The data listed is valid for all package sizes of this lot of this product, expressed as an extension of this catalog number listed above. If there are any questions with this certificate, please call (800) 227-6701.
*Based on suggested storage condition.

APPENDIX 2: ANALYTICAL CHEMISTRY METHOD NO. 0296R3

ANALYTICAL CHEMISTRY METHOD

METHOD No. 0296R3

Effective Date: 20NOV2018
Approved By: 20NOV2018
Jim Hall, Manager, DFA

TITLE: Determination of 4-Nitro-3-(trifluoromethyl)phenol(TFM) in Water

DEVELOPED BY: U.S.Geological Survey adapted for use by Smithers Avanza

1. SCOPE:

This is a High Performance Liquid Chromatography (HPLC-UV) method for the analysis of 4-Nitro-3-(trifluoromethyl)phenol (TFM) in Water in the concentration range of 0.005 mg/mL to **3.5** mg/mL.

2. PRINCIPLE:

4-Nitro-3-(trifluoromethyl)phenol dosing formulation in water is diluted with diluent water to fall into the concentration range of the standard curve. The API 4-Nitro-3-(trifluoromethyl)phenol is quantified by reverse phase HPLC with UV detection at 290 nm. The quantitation is accomplished using external standard curve.

3. EQUIPMENT:

3.1 HPLC: Waters Alliance HPLC system with Waters Empower2 Data Collection system; Waters 2690 Separations Module; Waters 2487 Dual Wavelength Absorbance Detector (detection at 290 nm), or equivalent equipment.

3.2 Column: Zorbax XDB C18 5µm, 4.6 x 250 mm column or equivalent

3.3 Pipette: Air displacement or positive displacement pipette, or equivalent.

3.4 General laboratory equipment and glassware.

4. REAGENTS:

METHOD No. 0296R3

4.1 Water (H_2O): Fisher (W5) or equivalent

4.2 Mobile Phase A (MPA): (MPA) (Water with 0.1% Formic Acid): Fisher (LS118) used as supplied or equivalent

4.3 Mobile Phase **B** (MPB): (MPB) (0.1% Formic Acid in Acetonitrile (V/V)): Fisher (HB9823) used as supplied or equivalent

4.4 Diluent: Water. Use as supplied.

5. STANDARD PREPARATIONS:

5.1 Preparation of Stock Standard Solution (Stock) (target 1.00 mg/mL):
Accurately weigh appropriate amount of reference standard TFM into a 25 mL volumetric flask. Dilute to a final volume of 25 mL with water. Briefly sonicate to dissolve the chemical. *Standard concentrations are corrected for purity.*

5.2 Preparation of QC Stock Solution (QC Stock) (target 1.00 mg/mL):
Accurately weigh appropriate amount of reference standard TFM into a 25 mL volumetric flask. Dilute to a final volume of 25 mL with water. Briefly sonicate to dissolve the chemical. *Standard concentrations are corrected for purity.*

5.3 Preparation of Standard Curve:
At least five standard points are prepared in the diluent according to the following scheme. Dilution scheme may vary as needed.

Standard (STD) ID	Aliquot Taken (mL)	Taken From	Final Volume (mL)	Target Concentration (mg/mL)
A	1.5	STOCK	100	0.0150
B	20.0	A	25	0.0120
C	6.0	A	10	0.00900
D	10.0	A	25	0.00600
E	6.0	A	25	0.00360
F	2.0	A	25	0.00120
QC	0.9	QC STOCK	100	0.00900

6. SAMPLE PREPARATION:

Samples are collected while formulation is sitting without stirring.

METHOD No. 0296R3

Prepare duplicate dilutions for each dose concentration sample by diluting appropriate sample aliquot with sample diluent to fall within the standard curve range. Vehicle is diluted similarly as the lowest Test Substance concentration sample analyzed and is prepared singly.

Example of dosing formulation dilution scheme

Formulation Conc. (mg/mL)	Aliquot Taken (mL)	First Dilution Volume (mL)	Aliquot Taken (mL)	Final Dilution Volume (mL)	Final Concentration (ppm)
0	NA	NA	NA	NA	NA
0.005	NA	NA	NA	NA	NA
2	1.00	10.0	0.50	10.0	0.0100

7. INSTRUMENT PARAMETERS

HPLC Column: Zorbax XDB C18, 4.6 x 250 mm, 5 µm

Mobile Phase A (MPA): 0.1% Formic Acid in Water

Mobile Phase B (MPB): 0.1% Formic Acid in Acetonitrile

Autosample Flush: Water: Acetonitrile (50:50,v/v)

Diluent: Water

Gradient:

Step	Step Time (minutes)	Elapsed Time (minutes)	% A (Aqueous)	% B (Organic)	Curve
0	0.0	0.0	75	25	6
1	10	10	0	100	6
2	4	14	0	100	6
3	2	16	75	25	6
4	10	26	75	25	6

Flow Rate : 1.0 mL/min

UV Detector : 290 nm

METHOD No. 0296R3

Injection Volume	:	10 µL
Sample Temperature	:	Ambient
Column Temperature	:	Ambient
Integration	:	Peak Area
Retention Time	:	Approx. 8.2 minutes
Run Time	:	26 minutes

Note: instrument parameter may be modified to optimize retention time and/or chromatography

8. CALCULATIONS

8.1 Compute the linear regression relating the peak area of the standards to the mg/mL of TFM injected for each standard.

8.2 Using the peak area of the sample and the linear regression equation determine the mg/mL detected of TFM for each sample. The linear regression equation is y = mx + b, where m = slope and b = intercept, y = peak area, and x = mg/mL of TFM.

8.3 Calculated Concentration (mg/mL) = mg/mL Detected x Dilution Factor

where Dilution Factor = $\frac{A}{B} \times \frac{C}{D}$

A = Final volume of first dilution, mL.
B = Aliquot taken for the first dilution, mL.
C = Final volume of the final dilution, mL, if applicable.
D = Aliquot taken for the final dilution, mL, if applicable.

8.4 % Target = mg/mL Calculated Concentration/Target in mg/mL x 100

9. NOTES:

9.1 Significant Figures:

METHOD No. 0296R3

All concentrations - recorded to at least three significant figures.

% Target – recorded to at least three significant figures.

9.2 System Suitability:

The %RSD of peak areas and retention times of TFM should be equal or less than 2% for five replicate system suitability injections, and equal or less than 5% for overall system suitability injection including bracket standard injections.

9.3 Standard Curve Linearity

The coefficient of determination, R^2, of the standard curve should be $\geq$ 0.99 and the percent recovery for each standard concentration should be within 100±10%.

9.4 Formulation Stability

Formulation stability in water at Room Temperature for at least 28 days was determined at the high and low concentrations when **stored in amber glass containers with PTFE lined screw capped closures. The concentration of TFM in Deionized water is negatively impacted when stored in contact with rubber, or neoprene closure.**

10. LIST OF FIGURES:

Figure 1 Representative Chromatogram, Standard

Figure 2 Standard Curve

Figure 3 Representative Chromatogram, QC Standard

Figure 4 Representative Chromatogram, Control Article

METHOD No. 0296R3

Figure 1 Representative Chromatogram, Standard

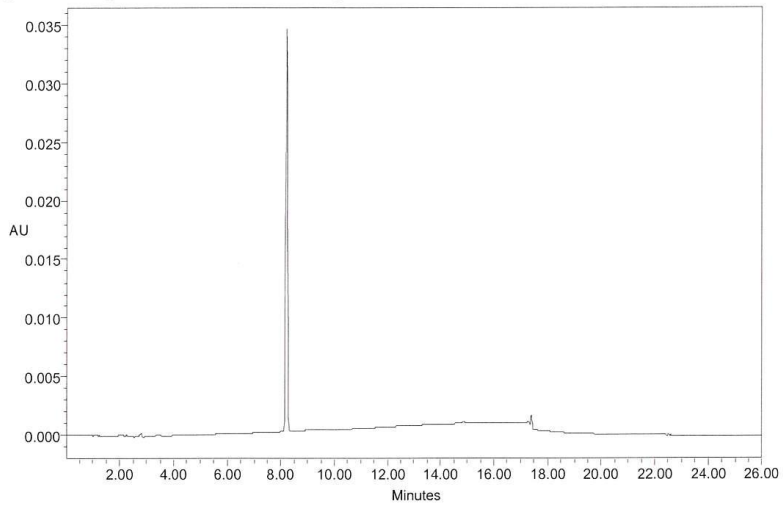
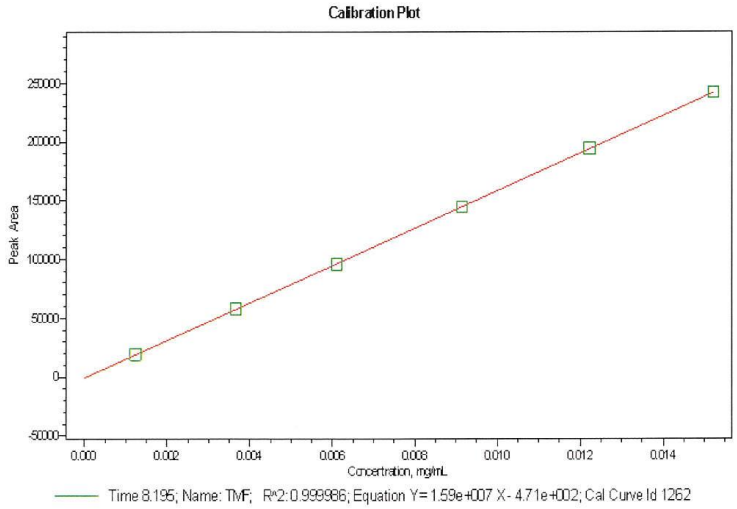


Figure 2 Standard Curve



Page 6 of 8

METHOD No. 0296R3

Figure 3 Representative Chromatogram, Sample

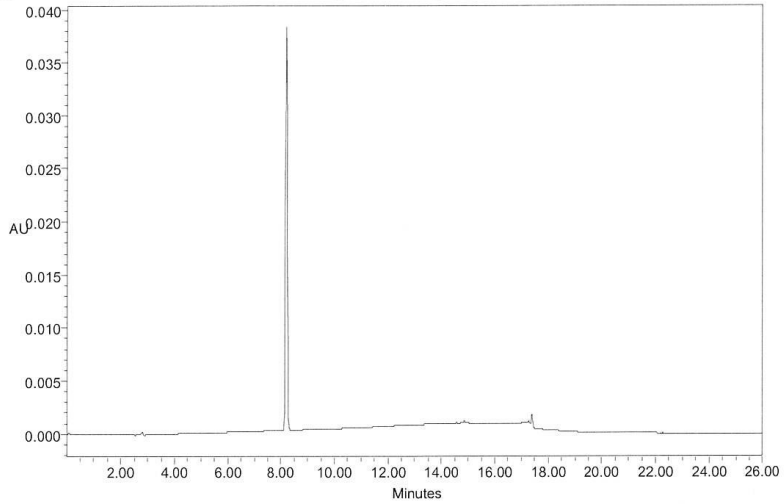
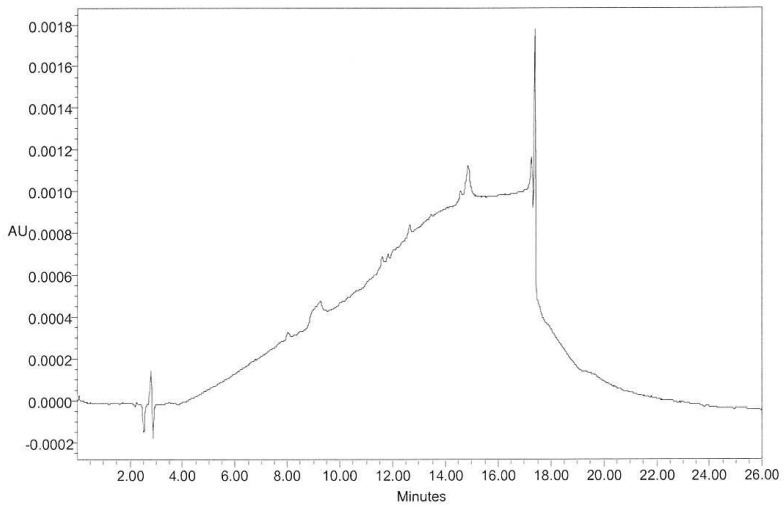


Figure 4 Representative Chromatogram, Vehicle



Page 7 of 8

METHOD No. 0296R3

REVISION HISTORY

Version	Date	Description of Revision	Reason
Original	06Feb2018	•	•
0296R1	09Feb2018	• Minor formatting • Figure 2 on page 6 replaced	• The Curve concentration changed the R^2, slope and intercept of the curve
0296R2	15Mar2018	• Update % A and % B • Update Figure 1 and Figure 3 to include X axis	• Typographical error
0296R3	20Nov2018	• Updated Scope from 2 mg/mL to 3.5 mg/mL • Updated Mobile Phase B • Updated Section 9.4 to include storage.	• Additional testing performed • Typographical error • Additional testing performed

APPENDIX 5: STOPPER ANALYSIS REPORT

United States Department of the Interior
U.S. GEOLOGICAL SURVEY
Upper Midwest Environmental Sciences Center
2630 Fanta Reed Road
La Crosse, WI 54603

Executive Summary

Chemical Analysis to Describe the Absorption of 4-Nitro-3-(trifluoromethyl) phenol (TFM) into Neoprene Rubber Stoppers

Introduction

The study "*4-Nitro-3-(trifluoromethyl) phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period*" (Smithers Avanza Study Number 2410-14374) was conducted to improve the mammalian toxicology database for the sea lamprey (*Petromyzon marinus*) piscicide, TFM. In the study, inverted glass bottles administered test solutions to male and female rats via a stainless-steel drinking tube inserted into a neoprene rubber stopper. The testing facility filtered light in the room that housed the animals to prevent photodegradation of the test solutions. Bottles and stoppers were replaced weekly and formulations adjusted as needed based on target dose, rate of consumption, and body weight. TFM concentration verification conducted at the end of the week indicated that TFM concentration decreased. Visual inspection indicated that TFM was absorbed into the stopper. Stoppers were sent to the Upper Midwest Environmental Sciences Center (UMESC) for analysis to determine if the TFM concentration reduction was due to photodegradation or absorption into the stopper. A liquid chromatography-triple quadrupole mass spectrometry (LC-QQQ) method was developed to identify TFM and three known[1] TFM degradation products: 2,5-dihydroxybenzoic acid (gentisic acid; GA), maleic acid (MA), and 1,2,4-benzenetriol (Triol) in the matrix of the stopper and in water samples. Two preliminary tests determined an efficient way to extract TFM from the stoppers prior to analyzing the water and stopper samples from the study.

Materials

Reference technical standard information for TFM, GA, MA (Sigma Aldrich, Milwaukee, Wisconsin) and Triol (Santa Cruz Biotechnology, Inc, Dallas, Texas) are found in Supplemental Table 1 (all Supplemental Tables are in Attachment 1). Reference technical standards were stored in a desiccator at ambient temperature in the dark. An 80.12% TFM concentrate (Batch #: LAM170517A-LE180625, Attachment 2) was used in the preliminary tests. Study stoppers were transferred from Smithers Avanza Study Number 2410-14374 (Attachment 3). Ultra-pure (E-pure) water (18 MΩ-cm, Barnstead Model 7119 E-pure purifier; S/N: 277265-131), formic acid (Lot #K44451164; EMD Millipore Corporation), and liquid chromatography-mass spectrometry grade methanol (MeOH) (Lot #17K304014; VWR BDH Chemicals) were used for mobile phases. High-performance liquid chromatography grade MeOH (Lot #18A084019; VWR BDH Chemicals) was used for the TFM stopper extractions. VWR neoprene size 2 stoppers (Catalog Number: 59589-154) were used for the preliminary work. Instruments used in the extraction process include: Sartorius model 200D (S/N: 20903620) and Sartorius model MSU225S-100-DI (S/N: 29505562) balances, 2010 Geno/Grinder (S/N: 10161), VWR Standard Shaker Model 3500 (S/N: 170124003), and a Beckman Avanti 30 microfuge (S/N: NGE96H30). An Agilent 1290 LC (Supplemental Table 2) with an Agilent 6460A triple quadrupole mass spectrometer (QQQ) with a ESI source was used to identify TFM and TFM degradates. MassHunter Workstation LC/MS Data Acquisition for 6400 Series Triple Quadrupole (Version B.08.00; Build 8.0.8023.0), MassHunter Workstation Qualitative Analysis (Version B.07.00; Build 7.0.7024.29), and MassHunter Workstation Quantitative Analysis (Version B.07.01 SPI; Build 7.1.524.1) were used for data acquisition and analysis.

Calculations and statistics (single factor ANOVA) were run on Microsoft Office 365 ProPlus Excel (Version 1803; Build 9126.2295).

Methods

Part A: TFM Photodegradation Preliminary Tests

Part A1: Preliminary Test 1 - TFM Absorption Depth

A seven-point set of TFM standards was made in MeOH. The stock solution contained 0.00991 g of TFM in 100 mL of MeOH (99,100 ng/mL). The stock was volumetrically diluted 100-fold in MeOH to 991 ng/mL. Further MeOH dilutions yielded standard concentrations shown in Supplemental Table 3. To perform a check for photodegradation products in the water samples, previously prepared and processed GA, MA, and Triol standards were used.

To replicate the highest TFM concentration stopper conditions from Smithers Avanza Study Number 2410-14374, 3.5 mg/mL TFM solution was made using an 80.12% TFM concentrate in E-pure water. Six 20-mL scintillation vials containing 10 mL of the TFM solution were stoppered with VWR neoprene stoppers, inverted, and placed in the dark at ambient temperature. Two scintillation vials containing 10 mL of TFM solution were capped normally. One was placed upright in a -4°C freezer. The second was placed upright with the other vials in the dark at ambient temperature. All vials were stored for one week. Once a day, the stoppered solutions were up-righted, and the stopper removed for a few seconds to simulate air flow the water bottles received daily from the rats drinking. The vials were re-stoppered, inverted, and stored as described above.

After the one-week storage period, three vials were taken out of storage. Triplicates of the liquid from the capped vial from the freezer, the capped vial stored ambiently, and the first stoppered solution (Stopper 1) were diluted 10,000-fold to fit the range of the TFM standard curve. The samples were put in LC vials and injected on the LC-QQQ (LC-QQQ parameters in Supplemental Tables 4, 5, and 6), and analyzed for TFM. Although all three solutions were stored in the dark and photodegradation was not expected, a check for photodegradation products was made.

The stopper from the first stoppered sample was cut into six different layers, named A through F; Layer A was in contact with the TFM solution. Thickness and mass of each slice was recorded (Supplemental Table 7). Each slice was cut into 3x3 mm pieces and placed in separate 15 mL centrifuge tubes. Ten mL of MeOH was added to each tube. The tubes were placed in the Geno/Grinder for 15 minutes at 1,200 strokes/minute. The liquid was removed from each tube and transferred into individual 15 mL centrifuge tubes. The extraction steps were repeated for a total of four extractions. MeOH was added to each extracted solution tube as needed to yield 10 mL samples. The solutions were vortexed for 5 seconds. One mL of each sample was transferred into a 2 mL centrifuge tube and centrifuged for 10 minutes at 12,000xg. A 0.5 mL aliquot of the supernatant was pipetted into a LC vial and the samples were injected on the LC-QQQ. The LC-QQQ parameters and method are shown in Supplemental Tables 4, 5, and 6. The injection volume of the four extraction solutions from layer A was adjusted to 1 µL instead of 10 µL injection to obtain a concentration within the standard curve.

Part A2: Preliminary Test 2 - Stopper Extraction Time

A seven-point set of TFM standards was made in MeOH. The stock solution contained 0.01031 g of TFM in 100 mL of MeOH (103,100 ng/mL). The stock was volumetrically diluted 100-fold with MeOH to 1,031 ng/mL. Further dilutions yielded standard concentrations shown in Supplemental Table 3. To perform a check for photodegradation products in the water samples, previously prepared and processed GA, MA and Triol standards were used.

Two weeks after the solution in the first preliminary test was prepared, triplicates of the liquid from the capped vial stored in the freezer, the capped vial stored ambiently, and three stoppered solutions (Stopper

solution 2, 3, and 4) were diluted 10,000-fold to fit the range of the TFM standard curve. The samples were put in LC vials and injected on the LC-QQQ. The samples were analyzed for TFM. Although all three solutions were stored in the dark and photodegradation was not expected, a check for photodegradation products was made.

TFM was extracted from the stoppers used for three ambient solutions (Stopper 2, 3, and 4). The 3 mm of stopper in closest contact with the TFM solution was removed from the three stoppers and the mass recorded (Supplemental Table 8). Each slice was cut into 3x3 mm pieces and placed into individual 15 mL centrifuge tubes. Ten mL of MeOH was added to each tube. The tubes were placed in the Geno/Grinder at 1,200 strokes/minute for differing amounts of time (Supplemental Table 8). After the given time interval, the liquid was removed from each tube and transferred into individual 15 mL centrifuge tubes. After each stopper underwent 240 minutes on the Geno/Grinder, MeOH was added to each extracted solution as needed to yield 10 mL samples. The samples were vortexed for 5 minutes. One mL of each sample was transferred into a 2 mL centrifuge tube and centrifuged for 10 minutes at 12,000xg. A 0.5 mL aliquot of the supernatant was pipetted into a LC vial and the samples were injected on the LC-QQQ. The injection volume of the first two extractions of Stopper 4 was adjusted to 1 µL instead of 10 µL to obtain a concentration within the standard curve. Samples that had a higher concentration than the highest standard were injected on the LC-QQQ at the 1 µL injection volume. Data was analyzed to determine the time interval that would be the most efficient to extract TFM from the stoppers. Assuming the total reduction of TFM in the water samples was caused by absorption into the stoppers, the data was extrapolated to determine the length of time a stopper sample would need to be on the Geno/Grinder to obtain the total mass of TFM.

Part B: TFM Analysis of Water Samples and Stoppers from Smithers Avanza Study Number 2410-14374

Part B1: Analysis of Water Samples for TFM and Photodegradation Products

Standards were made the same day as the water analysis. Stock solutions of 101,500 ng/mL MA in E-pure water, 98,000 ng/mL Triol in E-pure water, and 101,600 ng/mL of GA in MeOH were made. Two stock solutions of 102,200 ng/mL and 102,700 ng/mL of TFM in MeOH were made for two separate sets of standards. The GA, MA, and 102,200 ng/mL TFM stock solution were volumetrically diluted 100-fold in E-pure water. The Triol and the 102,700 ng/mL TFM stock solution were volumetrically diluted 100-fold in E-pure water. These solutions were E-pure water diluted by weight to make the sets of standards shown in Supplemental Table 9. Some samples were required to be re-analyzed and new standards were made from 96,800 ng/mL MA in E-pure, 99,800 ng/mL GA in MeOH, and 102,700 ng/mL TFM in MeOH stock solutions. The standards were made the same way as the original standards were made in Part B1 (Supplemental Table 9). Triol was omitted due to insignificance in the analysis as determined in Part A (see Results).

The study water samples are described in Supplemental Table 10. Samples were taken prior to stopper exposure (pre-stopper) and four days later (post-stopper) when the drinking water solution was changed and shipped to UMESC. The samples were removed from the shipping package. Several samples had leaked, most prominently were samples G1, G7, and G9. The pre- and post-stopper samples from G7, G9, and G11 were diluted volumetrically in triplicate until the expected concentration of TFM was at the upper limit of TFM standards (High TFM Conc. in Supplemental Table 10). The exception was G7, which did not have enough sample for triplicate analysis. To determine if photodegradation products were present, the standards and one of the three replicates from G7 and G9 (pre- and post-stopper) were injected at the high injection volume (10 µL). More accurate TFM concentration determination was completed at the low injection volume (1 µL) for each replicate (Low TFM Conc. in Supplemental Table 10). Group G11 had the highest intended TFM dosing concentration for the drinking water and was most likely to have quantifiable photodegradation products, if present. All three replicates of the pre- and post-stopper samples for G11 were injected at the high injection volume to analyze for the photodegradation products and the low injection volume to have an accurate TFM concentration determination. The pre-

and post-stopper drinking water samples from G1 were put into LC vials and injected into the LC-QQQ at the normal injection volume.

Part B2: TFM Extraction from Neoprene Stoppers
Two sets of TFM standards were made. The stock solutions were 101,300 ng/mL and 102,300 ng/mL TFM in MeOH. Both were volumetrically diluted 100-fold in MeOH before being diluted further by weight (Supplemental Table 11). Due to instrument failure, the samples had to be re-run approximately two weeks later. Two new TFM standard curves were created (Supplemental Table 11) with the original stock solutions being 99,800 ng/mL and 99,600 ng/mL TFM in MeOH.

Five stoppers from different dose groups of Smithers Avanza Study Number 2410-14374 were analyzed (Supplemental Table 12). A 3–6 mm layer of stopper in contact with TFM was removed from the stopper and the mass of each slice recorded (Supplemental Table 12). Because the study stoppers were larger than the preliminary stoppers used, to obtain a similar size and mass as the preliminary tests, the layer was cut into fourths. Each fourth was cut into 3x3 mm pieces placed in a 15 mL centrifuge tube for the entire extraction process. To extract the TFM and potential degradates, 10 mL of MeOH was added to each tube and were placed in the Geno/Grinder at 1,200 strokes/minute for 30 minutes. The liquid was removed from each centrifuge tube and was transferred into separate 250 mL volumetric flasks. Extraction continued with an additional 10 mL of MeOH added to each 15 mL centrifuge tube. These extraction steps were repeated for a total of ten 30-minute extractions. The liquid from each fourth was pooled into separate 250 mL volumetric flasks. After the ten 30-minute extractions, 10 mL of MeOH was added to the 15 mL centrifuge tubes and tubes were shaken on a shaker plate for 4.5 hours at 300 rpm. The liquid was pooled into the 250 mL volumetric flasks. One 30-minute round on the Geno/Grinder was done before 10 mL of MeOH was added to the tubes and they were shaken on the shaker plate for 11 hours. The solution was pooled in the 250 mL flasks. One more 30-minute and three 60-minute rounds on the Geno/Grinder were completed. In total, each quarter of a stopper underwent 9 hours on the Geno/Grinder and 15.5 hours on the VWR shaker plate.

The 250 mL flasks were brought to volume with MeOH. One mL aliquots from each 250 mL volumetric flask were transferred to 2 mL centrifuge tubes. Triplicate 1 mL aliquots were taken from one of the 250 mL volumetric flask from each sample group. The aliquots from samples in group G11 were diluted 100-fold prior to placement in the 2 mL centrifuge tubes. The 2 mL tubes were centrifuged for 10 minutes at 12,000xg. The samples were diluted as shown in Supplemental Table 12, placed in LC vials and injected on the LC-QQQ system.

A prediction range was calculated for the total mass of TFM in each stopper. The Smithers Avanza Study Number 2410-14374 stoppers underwent an equivalent to 18 extractions at a 30-minute interval on the Geno/Grinder. Time on the shaker plate was assumed to be equal to time on the Geno/Grinder. The 15.5 hours on the shaker plate simulate 30 extractions in 30-minute intervals on the Geno/Grinder. Using the trendline from Figure 2 (Equation 1), the fact that the Stopper 3 solution had a 10.59 mg reduction of TFM, and achieving 18–49 similar extractions to the 30-minute extractions in the second preliminary test, a predicted percent recovery range was calculated. The percent recoveries were used to calculate the predicted range of total mass of TFM in each stopper.

$$Total\ TFM\ Mass\ Extracted\ (mg) = 1.7094 \ln(Extraction\ Number) + 2.5406 \quad (1)$$

Results
<u>Part A: TFM Photodegradation Preliminary Tests</u>
Part A1: Preliminary Test 1 - TFM Absorption Depth
MassHunter Workstation Quantitative Analysis and Qualitative Analysis software were used to analyze the water samples for GA, MA, and Triol. The samples were diluted 10,000-fold when injected on LC-

QQQ. The method of analysis had a 1 ng/mL detection limit and after dilution correction the detection limit in the samples was 0.01 mg/mL. None of the degradation products were detected. The original solution was 3.5 mg/mL TFM. If degradants were present at concentrations less than the detection limit, they would have made up less than 0.1% of the original TFM when combined. The final mass of TFM in the water samples in each scintillation vial are shown in Table 1. There was no statistically significant difference (α =0.05, p=0.392) between the mass of TFM in the scintillation vial stored ambiently in the dark compared to the frozen scintillation vial. Comparatively, mass of TFM in the stoppered scintillation vial decreased by 7.13 mg, 21.9% (α =0.05, p=5.67×10^{-6}).

Table 1. Total mass of TFM from each solution from the first preliminary test.

Liquid	Final TFM Mass (mg)
Capped, Freezer	34.3
Capped, Ambient	34.0
Stopper, Ambient	26.8

Individual TFM amounts from each extraction layer are shown in Table 2. The total mass of TFM recovered was 3.13 mg, a 43.9% recovery. Most of the TFM was recovered from layer A. Less than 1% of total TFM was recovered from the rest of the layers combined.

Table 2. Mass of recovered TFM from each extraction and the total mass from individual layers from second preliminary test.

Layer	Extraction Number	Mass Recovered per Extraction (mg)	Total Mass Extracted[a] (mg)
A	1	1.72	1.72
	2	0.55	2.27
	3	0.426	2.70
	4	0.422	3.12
B	1	4.83×10^{-3}	4.83×10^{-3}
	2	6.02×10^{-4}	5.43×10^{-3}
	3	3.63×10^{-4}	5.79×10^{-3}
	4	3.44×10^{-4}	6.13×10^{-3}
C	1	3.21×10^{-3}	3.21×10^{-3}
	2	4.76×10^{-4}	3.69×10^{-3}
	3	3.03×10^{-4}	4.00×10^{-3}
	4	2.96×10^{-4}	4.29×10^{-3}
D	1	3.04×10^{-4}	3.04×10^{-4}
	2	3.79×10^{-5}	3.42×10^{-4}
	3	2.05×10^{-5}	3.63×10^{-4}
	4	1.99×10^{-5}	3.83×10^{-4}
E	1	1.54×10^{-4}	1.54×10^{-4}
	2	1.49×10^{-5}	1.69×10^{-4}
	3	7.79×10^{-6}	1.77×10^{-4}
	4	5.08×10^{-6}	1.82×10^{-4}
F	1	2.20×10^{-4}	2.20×10^{-4}
	2	2.77×10^{-5}	2.48×10^{-4}
	3	1.38×10^{-5}	2.62×10^{-4}
	4	1.38×10^{-5}	2.76×10^{-4}

[a] Cumulative mass of TFM recovered after each extraction by layer

Part A2: Preliminary Test 2 - Stopper Extraction Time

The water samples did not contain detectable amounts of GA, MA or Triol (detection limit = 0.01 mg/mL in samples). The amount of TFM in the water samples is shown in Table 3. There was no statistically significant difference (α=0.05, p=0.175) between the mass of TFM in the scintillation vial stored ambiently in the dark compared to the frozen scintillation vial. Comparatively, the mass of TFM in Stopper 2 (α=0.05, p=1.67×10^{-7}), 3 (α=0.05, p=4.71×10^{-8}), and 4 (α=0.05, p=4.79×10^{-8}) solutions were significantly different than the solution from the capped vial stored upright in the freezer. A decrease of 26.8–30.1% TFM in stopper vials was observed compared to solution stored in the freezer.

Table 3. Second preliminary test stopper sample TFM recovery information.

Liquid	Final Mass in Solution (mg)	Total Mass Loss Compared to Freezer (mg)	% TFM Present Compared to Freezer (%)	Mass of TFM Recovered from Stopper (mg)	Total Mass of TFM Recovered (%)
Capped, Freezer	33.72	NA	NA	NA	NA
Capped, Ambient	34.18	NA	101.3	NA	NA
Stopper 2	24.69	9.482	73.23	5.432	57.3
Stopper 3	23.59	10.59	69.94	5.521	52.1
Stopper 4	24.37	9.805	72.29	5.614	57.2

NA=Not Applicable

The amount of TFM recovered from each extraction of Stopper 2, 3, and 4 is in Tables 4, 5, and 6. The total amount of TFM recovered is shown in Table 3. A graph was made to compare the amount of TFM extracted over time (Figure 1). There was no substantial difference between extraction time interval and the amount of TFM extracted. Assuming the total reduction of TFM in the water samples was caused by absorption into the stoppers, using data extrapolation, it would take 43.5–55.5 hours on the Geno/Grinder to recover the total mass of TFM that was absorbed by the stopper. Due to practical limitations, the 30-minute interval was determined to have the best efficiency for the stoppers in the study. Because stopper 3 had a 30-minute time interval on the Geno/Grinder, the extrapolation for that stopper helped determine the percent of TFM extracted and predict the total amount of TFM in the study stoppers (Figure 2).

Table 4. Stopper 2 extraction data from the second preliminary test.

Extraction Number	Time (min)	Mass Recovered Per Extraction (mg)	Total Mass Extracted (mg)
1	15	1.055	1.055
2	30	0.6947	1.749
3	45	0.5348	2.284
4	60	0.4411	2.725
5	75	0.3997	3.125
6	90	0.3500	3.475
7	105	0.2989	3.774
8	120	0.2726	4.046
9	135	0.2300	4.276
10	150	0.1846	4.461
11	165	0.1797	4.641
12	180	0.1666	4.807
13	195	0.1571	4.964
14	210	0.1407	5.105
15	225	0.0621	5.167
16	240	0.2648	5.432

Table 5. Stopper 3 extraction data from the second preliminary test.

Extraction Number	Time (min)	Mass Recovered Per Extraction (mg)	Total Mass Extracted (mg)
1	30	2.604	2.604
2	60	1.016	3.620
3	90	0.7593	4.379
4	120	0.5578	4.937
5	150	0.3858	5.323
6	180	0.3193	5.642
7	210	0.2785	5.921
8	240	0.1042	6.025

Table 6. Stopper 4 extraction data from the second preliminary test.

Extraction Number	Time (min)	Mass Recovered Per Extraction (mg)	Total Mass Extracted (mg)
1	60	3.207	3.207
2	120	1.306	4.513
3	180	0.6457	5.159
4	240	0.4546	5.613

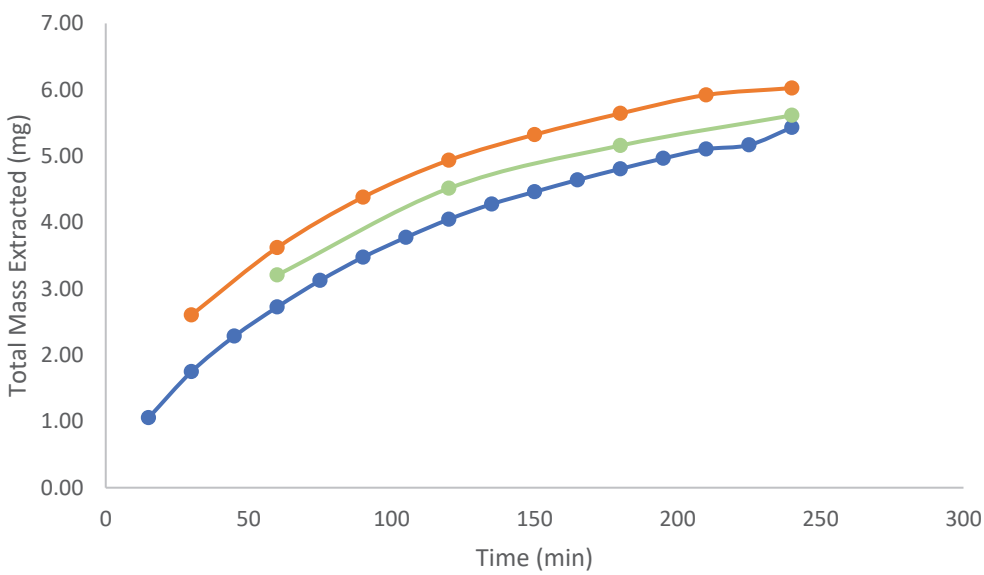


Figure 1. Logarithmic curves of the three interval extractions done in the second preliminary test. Blue represents the 15-minute interval data, orange is the 30-minute data and green is the 60-minute data.

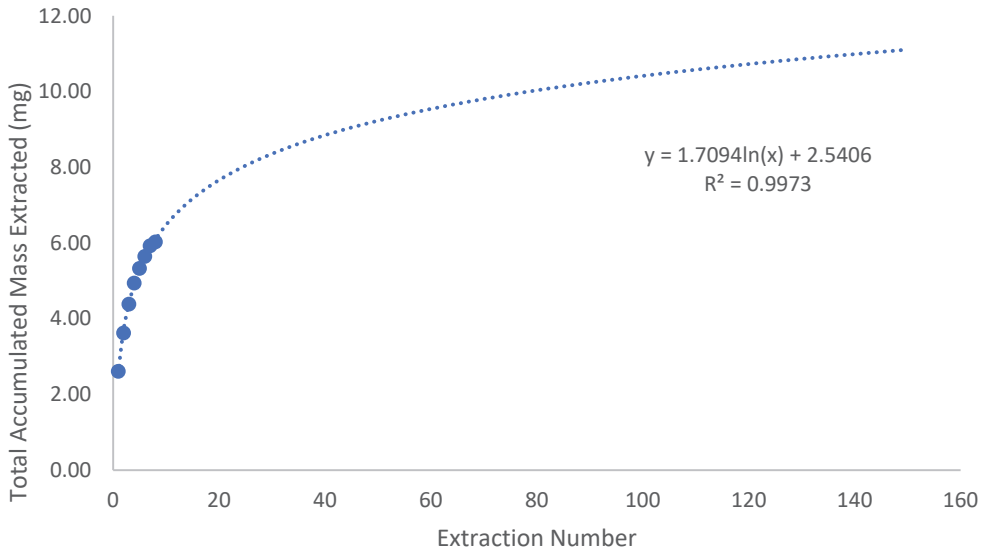


Figure 2. TFM extraction data using stopper 3 30-minute intervals on the Geno/Grinder. To obtain 10.59 g of TFM from the stopper, a total of 111 extractions 55.5 hours would be required. Extrapolation to 10.59 mg, the total mass of TFM lost from the solution.

Part B: TFM Analysis of Water Samples and Stoppers from Smithers Avanza Study Number 2410-14374

Part B1: Analysis of Water Samples for TFM and Photodegradation Products

The photodegradates GA, MA, and Triol were not detected in any of the diluted water samples. If the degradation products were present, their concentrations were below the quantitation limit after diluting TFM. The final TFM concentrations in water samples are shown in Table 7. ANOVA tests were run comparing the pre- and post-stopper solutions of sample groups G7 (α=0.05, p=1.21x10^{-2}), G9 (α=0.05, p=3.98x10^{-3}), and G11 (α=0.05, p=1.75x10^{-5}) which determined that there was a significant decrease of TFM concentration in the water samples. The aliquots for each sample group taken before stopper exposure were, on average, 11% lower in TFM concentration than expected. There was reduced TFM concentration in the water samples after one week in the water bottles and the magnitude of the concentration reduction was greater at higher initial TFM concentrations (Table 7).

Table 7. TFM analysis on water samples from Smithers Avanza Study Number 2410-14374 including comparisons to the intended concentrations as well as pre- and post-stopper samples.

Sample Group	Intended Concentration (mg/mL)	Pre/Post-Stopper	Average Final Concentration (SD) (mg/mL)	% of Intended Concentration (%)	% TFM Present Post-Stopper (%)
G1	0	Pre	ND	NA	NA
		Post	ND	NA	NA
G7	0.0106	Pre	9.65x10^{-3} (6x10^{-5})	91.1	NA
		Post	8.99x10^{-3}	NA	93.1
G9	0.102	Pre	8.79x10^{-2} (4.0x10^{-3})	86.2	NA
		Post	7.35x10^{-2} (1.1x10^{-3})	NA	83.6
G11	1.34	Pre	1.19 (1x10^{-2})	88.6	NA
		Post	0.911 (1.0x10^{-2})	NA	76.7

NA=Not Applicable
ND=Not Detected

Part B2: TFM Extraction from Neoprene Stoppers

The total mass of TFM that was extracted from each stopper is shown in Table 8. The unused stopper and the control group (G1) showed possible small amounts of TFM, but both stoppers were statistically equal which indicates that the quantified amount may be a MeOH leachable compound in the stopper material. The concentration of the leached stopper compound was less than 1/50 the concentration of TFM in low concentration stopper (G7, Table 8) solution and did not interfere with the TFM quantification. An ANOVA test was done between all the TFM masses extracted from the stoppers (α=0.05, p=9.92x10^{-13}) and showed they were statistically different. ANOVA tests were done comparing the mass of TFM extracted from the unused stopper to the sample group G1 (α=0.05, p=0.341), G7 (α=0.05, p=5.73x10^{-6}), G9 (α=0.05, p=3.16x10^{-6}), and G11 (α=0.05, p=7.66x10^{-6}). Compared to the unused stopper, sample groups G7, G9, and G11 were statistically different but the control sample group G1 was not. Based on the number of extractions, the time on the shaker plate, and the stopper 3 data from the preliminary analysis, it was predicted that 70.6-86.8% of the total TFM in the stopper was extracted. After accounting for predicted extraction efficiency, the total amount of TFM in each stopper is predicted in Table 8.

Table 8. Analysis on the TFM extracted from the stoppers from Smithers Avanza Study Number 2410-14374 including the total predicted TFM mass that was in each stopper using extrapolated data in the second preliminary test.

Sample Group	Cage	Quarter	TFM Mass in Quarter (SD) (mg)	Total TFM Mass Recovered in Stopper (mg)	Predicted Total TFM Mass in Stopper (mg)
--	Unused	A	2.31x10^{-4} (4x10^{-6})	2.31x10^{-4}	2.67x10^{-4} to 3.28x10^{-4}
		B	<LOQ		
		C	<LOQ		
		D	<LOQ		
G1	17	A	2.12x10^{-3}	4.44x10^{-3}	5.12x10^{-3} to 6.29x10^{-3}
		B	9.52x10^{-4} (1.3x10^{-5})		
		C	5.41x10^{-4}		
		D	8.27x10^{-4}		
G7	54	A	0.152	0.592	0.682 to 0.838
		B	0.123		
		C	0.145 (2x10^{-3})		
		D	0.171		
G9	61	A	2.51	9.17	10.6 to 13.0
		B	2.18		
		C	1.95		
		D	2.54 (0.11)		
G11	71	A	30.3 (0.6)	142	163 to 201
		B	33.4		
		C	36.0		
		D	42.1		

<LOQ = Below limit of quantification (0.5 ng/mL in extraction samples)

Discussion

Results from the preliminary tests provided useful information to develop the method used with the study materials. TFM could be extracted from the stopper and 99% of the TFM did not travel past the first 3 mm of the stopper. Because the first preliminary test had a low recovery of TFM from the stopper with just 60 minutes on the Geno/Grinder, an efficient way to extract the TFM needed to be developed. The three tested extraction intervals in preliminary test two allowed for determination of the most efficient extraction period to obtain the best recovery. Short extractions required relatively large amounts of time removing and reloading solvent, allowing less time on the Geno/Grinder and low recovery. Long

extractions allowed for the potential of TFM saturated MeOH, inhibiting extraction efficiency. Extrapolation of recovered TFM per extraction round predicted total extraction time to be approximately 2 days which was not feasible to accomplish on the Geno/Grinder system. With this information, and the goal of a high TFM recovery, a 30-minute time interval on the Geno/Grinder was selected for most of the extractions as well as a shaker plate used as a surrogate to the Geno/Grinder overnight.

The decrease in TFM concentration in the stoppered water samples in the preliminary tests could be from temperature, light, and absorption into the stopper. The ANOVA test in the first preliminary trial determined there was no significant difference between the samples stored at ambient temperature and in the freezer, suggesting temperature was not the cause of the decrease. Photodegradation was another possible factor for a reduction in TFM concentration. GA primarily degrades to Triol and Triol degrades to MA.[1] The degradation products were separated in standards to avoid complicating the analysis and avoid altered concentrations of the multiple analytes in a given set of standards. The separation allowed for efficient tracking of standard concentration changes over time. GA, MA, and Triol were not detected in any of the preliminary water samples. Accounting for the dilution in sample prep, less than 10,000 ng/mL of GA, MA, and Triol could have been present initially, which is less than 0.5% of the original TFM concentration, suggesting photodegradation was not the major reason for the TFM concentration reduction. TFM solutions stored in contact with neoprene stoppers were the only samples from the preliminary experiments with a significant reduction in TFM concentration. Absorption of TFM to the neoprene stoppers was determined to be the primary factor accounting for reduced TFM concentrations.

There was a statistically significant TFM concentration reduction between the pre- and post-stopper water samples for each sample group from Smither Avanza Study Number 2410-14374. The samples could have decreased from the same factors as the preliminary water samples as well as time. The study samples were made on May 16th, 2018 and were not analyzed until August 7th, 2018. The lampricide and degradation products could have degraded during this time. Consistent with preliminary tests, GA, MA, and Triol were not detected (maximum possible concentrations less than 1%) ruling out photodegradation as a contributor to reduced TFM concentrations.

The statistical decrease of TFM concentration between the pre- and post-stopper water samples and the lack of photodegradation products indicates that TFM absorption into the neoprene stoppers was the cause of the concentration reduction in the water. Due to the variation in the rats' drinking volumes in Smithers Avanza Study Number 2410-14374, the total amount of TFM absorbed into the stoppers from each water sample cannot be determined and the percent TFM recovered from the stoppers cannot be verified. The amount of TFM recovered from the stopper of each sample group was statistically different from each other. When comparing the water samples and the amount of TFM extracted from the stopper of each sample group, as the concentration in the water samples increase, the mass extracted from the stopper increases. Although an exact amount of TFM absorbed into the stoppers cannot be calculated, this positive relationship shows that as the TFM concentration rises, the amount of TFM absorbed into the neoprene stopper rises and supports the visual stopper observations and analytical results in Smithers Avanza Study Number 2410-14374.

Reference

1. McConville, M.B., Hubert, T.D., Remucal, C.K. Direct Photolysis and Transformation Pathways of the Lampricides TFM and Niclosamide in Simulated Sunlight. Environ. Sci. Technol. 2016, 50, 9998-10006.

Signatures

Analyst:

COURTNEY KIRKEENG Digitally signed by COURTNEY KIRKEENG Date: 2018.11.30 08:47:26 -06'00'

Courtney A. Kirkeeng, B.S.

Technical Reviewer:

STEPHEN LANTZ Digitally signed by STEPHEN LANTZ Date: 2018.11.30 09:40:55 -06'00'

Stephen R. Lantz, Ph.D.

Attachment 1: Supplemental Tables

Supplemental Table 1. TFM and the photodegradation product reference standard information.

Compound	Manufacturer	Lot Number	Manufacture Date	Expiration Date
TFM	Sigma Aldrich	MKBX5239V	29 January 2016	09 April 2023
GA	Sigma Aldrich	WXBC5091V	05 May 2017	11 June 2023
MA	Sigma Aldrich	SLBV4466	18 December 2017	18 December 2023
Triol	Santa Cruz Biotech.	F0518	Not Provided	11 June 2023

Supplemental Table 2. Model and serial numbers for each of the Agilent 1290 LC-QQQ components.

Component	Model	S/N
Column Compartment	G7116B 1290 MCT	DEBA401314
Autosampler	G7167B 1290 Multisampler	DEBA500738
Quaternary Pump	G7104A 1290 Flexible Pump	DEBA300323
VWD	G1314E 1290 VWD	DEBAH00211
QQQ	6460 Triple Quad Tandem Mass Spec	SG10427005
ESI Source	G1958-65138 ESI Source	US1043901F7

Supplemental Table 3. Standard TFM concentrations used in the two preliminary experiments.

Standard Level	Conc. for Prelim. 1 (ng/mL)	Conc. for Prelim. 2 (ng/mL)
1	0.991	1.031
2	4.95	5.155
3	9.91	10.31
4	49.5	51.55
5	99.1	103.1
6	495	515.5
7	991	1,031

Supplemental Table 4. LC method parameters.

Parameter Name	Setting
Injection Volume	10.00 µL
Column Temperature	50.0°C
Binary Pump Flow Rate	0.325 mL/min
Mobile Phase A	E-pure (1000 mL), 0.2% Formic Acid
Mobile Phase B	LC-MS MeOH (1000 mL)

Supplemental Table 5. The quaternary pump gradient time table.

Time Segment	Time (min)	A (%)	B (%)	Flow (mL/min)
1	0.00	60.00	40.00	0.300
2	7.00	0.00	100.00	0.300
3	7.50	0.00	100.00	0.300
4	8.00	60.00	40.00	0.300

Supplemental Table 6. QQQ method parameters.

Parameter Name	Setting	Parameter Name	Setting
Ion Polarity	Negative	Sheath Gas Flow	11 L/min
m/z range	100-1100 m/z	Collision Energy	0
Scan Rate	3.00 spectra/sec	Vcap	3000
Gas Temperature	325°C	Nozzle Voltage	1000 V
Gas Flow	9 L/min	Fragmenter	115
Nebulizer	35 psig	Skimmer1	65
Sheath Gas Temperature	350°C	Octopole RF Peak	750

Supplemental Table 7. Layer thickness and mass of stopper 1 used in preliminary test 1.

Layer	Thickness (mm)	Mass (g)
A	3–4	0.8947
B	3	0.9082
C	3	1.1942
D	5	1.4279
E	4-7	1.5120
F	7-9	2.9715

Supplemental Table 8. Layer thickness, mass, and separate extraction time interval on the Geno/Grinder for stoppers 2, 3, and 4 used in preliminary test 2.

Stopper	Layer Thickness (mm)	Mass (g)	Extraction Time Interval (min)
2	4	0.8204	15
3	3	0.9561	30
4	2.5	0.8419	60

Supplemental Table 9. Analyte concentrations for the standard sets used to analyze the drinking water samples from Smithers Avanza Study Number 2410-14374. The 180806 standards were for the original analysis and the 180808 standards were used for any re-ran water samples.

Standard Set 1[a]	Analyte	Concentration (ng/mL)	Standard Set 2[b]	Analyte	Concentration (ng/mL)	Standard 3[a]	Analyte	Concentration (ng/mL)
180806 TGM CC1	TFM	0.5071	180806 TT CC1	TFM	0.5097	180808 TGM CC1	TFM	0.5032
	GA	0.5041		Triol	0.486		GA	0.489
	MA	0.5036					MA	0.474
180806 TGM CC2	TFM	1.014	180806 TT CC2	TFM	1.019	180808 TGM CC2	TFM	1.007
	GA	1.008		Triol	0.972		GA	0.978
	MA	1.007					MA	0.949
180806 TGM CC3	TFM	5.073	180806 TT CC3	TFM	5.103	180808 TGM CC3	TFM	5.045
	GA	5.043		Triol	4.87		GA	4.90
	MA	5.038					MA	4.76
180806 TGM CC4	TFM	10.14	180806 TT CC4	TFM	10.20	180808 TGM CC4	TFM	10.09
	GA	10.08		Triol	9.74		GA	9.81
	MA	10.07					MA	9.51
180806 TGM CC5	TFM	50.75	180806 TT CC5	TFM	51.00	180808 TGM CC5	TFM	50.85
	GA	50.45		Triol	48.7		GA	49.4
	MA	50.40					MA	47.9
180806 TGM CC6	TFM	101.5	180806 TT CC6	TFM	102.1	180808 TGM CC6	TFM	101.8
	GA	100.9		Triol	97.4		GA	98.9
	MA	100.8					MA	95.9
180806 TGM CC7	TFM	509.0	180806 TT CC7	TFM	513.2	180808 TGM CC7	TFM	513.2
	GA	506.1		Triol	490		GA	499
	MA	505.6					MA	484
180806 TGM CC8	TFM	1022	180806 TT CC8	TFM	1027	180808 TGM CC8	TFM	1027
	GA	1016		Triol	980		GA	998
	MA	1015					MA	968

[a] Standard Set 1 and 3 Nomenclature: Number=date YYMMDD, TGM=TFM, GA, and MA, CCX=Chemical Concentration where X=standard number (1=lowest concentration)

[b] Standard Set 2 Nomenclature: Number= date YYMMDD, TT=TFM and Triol, CCX= Chemical Concentration where X=standard number (1=lowest concentration)

Supplemental Table 10. Water sample group numbers from Smithers Avanza Study Number 2410-14374 with corresponding exposure concentrations and dilutions used in analysis. The "High TFM Conc." refers to the samples at the upper limit of the TFM standards to look for photodegradation products and "Low TFM Conc." refers to samples injected at a lower volume to obtain a more accurate TFM concentration.

Group Number	Intended Concentration (mg/mL)	Dose Level (mg/kg)	Pre/Post Stopper	High/Low TFM Conc.	UMESC Lab Dilution	Injection Volume (µL)	Total Dilution Factor
G1	--	0	Pre	NA	0	10	1
			Post	NA		10	1
G7	0.0106	1	Pre	Low	10	1	100
			Pre	High		10	10
			Post	Low		1	100
			Post	High		10	10
G9	0.102	10	Pre	Low	100	1	1000
			Pre	High		10	100
			Post	Low		1	1000
			Post	High		10	100
G11	1.34	100	Pre	Low	1000	1	10000
			Pre	High		10	1000
			Post	Low		1	10000
			Post	High		10	1000

NA=Not Applicable

Supplemental Table 11. TFM concentrations for the standard sets used to analyze Smithers Avanza Study Number 2410-14374 water bottle stopper samples. Standard set 1 and 2 were used in the initial stopper analysis. Standard set 3 and 4 were used to analyze re-ran stopper samples.

Standard Set 1[a]	Concentration (ng/mL)	Standard Set 2[b]	Concentration (ng/mL)	Standard Set 3[a]	Concentration (ng/mL)	Standard Set 4[b]	Concentration (ng/mL)
180718 TA CC1	0.4800	180718 TB CC1	0.4841	180730 TA CC1	0.501	180730 TB CC1	0.474
180718 TA CC2	0.9633	180718 TB CC2	0.9715	180730 TA CC2	1.00	180730 TB CC2	0.950
180718 TA CC3	4.903	180718 TB CC3	4.962	180730 TA CC3	4.95	180730 TB CC3	4.90
180718 TA CC4	9.829	180718 TB CC4	9.939	180730 TA CC4	9.92	180730 TB CC4	9.84
180718 TA CC5	49.87	180718 TB CC5	50.50	180730 TA CC5	49.6	180730 TB CC5	50.8
180718 TA CC6	99.75	180718 TB CC6	101.3	180730 TA CC6	99.2	180730 TB CC6	102
180718 TA CC7	507.6	180718 TB CC7	511.2	180730 TA CC7	498	180730 TB CC7	498
180718 TA CC8	1013	180718 TB CC8	1023	180730 TA CC8	998	180730 TB CC8	996

[a] Standard Set 1 and 3 Nomenclature: Number=date YYMMDD, TA=TFM curve A used for calibration, CCX=Chemical Concentration where X=standard number (1=lowest concentration)

[b] Standard Set 2 and 4 Nomenclature: Number=date YYMMDD, TB=TFM curve B used to verify calibration curve A, CCX=Chemical Concentration where X=standard number (1=lowest concentration)

Supplemental Table 12. Smithers Avanza Study Number 2410-14374 stopper group numbers with dose levels, intended TFM concentration in the drinking water, masses of the stopper quarters and the final dilution factor used to get the final concentration within the TFM standard curve.

Group Number	Cage Number	Rat Dose Level (mg/kg)	Intended Concentration (mg/mL)	Quarter	Mass (g)	UMESC Dilution Factor
Unused	--	N/A	N/A	A	1.092	1
				B	0.9692	
				C	1.0797	
				D	1.1388	
G1	17	0	N/A	A	1.2520	1
				B	1.0513	
				C	1.5660	
				D	1.4215	
G7	54	1	0.0106	A	1.3748	2
				B	1.3456	
				C	1.5018	
				D	1.2412	
G9	61	10	0.102	A	1.7519	100
				B	1.4569	
				C	1.2847	
				D	1.5445	
G11	71	100	1.34	A	2.3367	200
				B	2.2280	
				C	2.0411	
				D	2.0782	

Attachment 2: Certificate of Analysis for 80.12% TFM Concentrate Batch #: LAM170517A-LE180625

United States Department of the Interior
U.S. GEOLOGICAL SURVEY
Upper Midwest Environmental Sciences Center
2630 Fanta Reed Road
La Crosse, WI 54603

Certificate of Analysis

UMESC name: TFM HP-Liquid Extract

Batch or lot number(s) analyzed: LAM170517A-LE20180625
Expiration Date: 25 June 2020

Source material batch or lot number(s): LAM170517A
Manufacturer of source material:
Iofina Chemical
1025 Mary Laidley Drive
Covington, KY 41017
Phone: 859-356-8000

Extracting/Performing laboratory:
USGS Upper Midwest Environmental Sciences Center
2630 Fanta Reed Road
La Crosse, Wisconsin 54603
Phone: (608)783-6451
Fax: (608)783-6066

Date of analysis: 25 June 2018
HPLC analyst: J. Schueller (Chemist)
Method of analysis: High Performance Liquid Chromatography
Instrument of analysis: Agilent 1260 Series HPLC

Individual batch results:
LAM170517A-LE20180625 Percent TFM found (standard deviation) 80.12% (0.28)

Kim Fredricks, Quality Assurance Officer: KIM FREDRICKS Digitally signed by KIM FREDRICKS Date: 2018.06.26 12:42:00 -05'00'

TFM Active Ingredient Analytical Procedure

HPLC Analysis by: J. Schueller
Date of Analysis: 25 June 2018
Batch Analyzed: LAM170517A-LE20180625

HPLC Analysis by: Justin R. Schueller (Chemist) JUSTIN SCHUELLER Digitally signed by JUSTIN SCHUELLER Date: 2018.06.26 12:41:03 -05'00'

QA Review by Kim T. Fredricks (QA Officer) KIM FREDRICKS Digitally signed by KIM FREDRICKS Date: 2018.06.26 12:42:15 -05'00'

Procedural Review by Stephen R. Lantz (Supervisory Chemist) STEPHEN LANTZ Digitally signed by STEPHEN LANTZ Date: 2018.06.26 12:52:36 -05'00'

Calculations:
Percent TFM = HPLC TFM conc. (ppm)/sample weight (g)/dilution factor*100

Standard curve linearity (R^2) = 1.00000

Results Table

Sample Identification	HPLC TFM Conc. (mg/L)	Sample Weight (g)	TFM (%)	Triplicate Mean (%)	Std. Dev.	RSD (%)
20180625-LE (A)	8.06021	0.10030	80.36			
20180625-LE (B)	7.93133	0.09938	79.81	80.12	0.28	0.35
20180625-LE (C)	8.09665	0.10098	80.18			

Procedure based on SOP AEH409.4
Standard Preparation:
A five-point standard curve was prepared from TFM technical (Lot # MKBX52939V; Sigma) by weighing 0.01001 g and diluting with 100 mL methanol (Standard Stock A, 100 mg/L). (Lot # 17J194007; VWR)
Further dilutions of Standard Stock A - 1:100, 4:100, 7:100, 10:100, & 15:100 with E-pure water solution resulted in working standards of: 1, 4, 7, 10, 15 mg/L.
Sample Preparation:
Subsamples of the liquid extract of Iofina TFM HP Sea Lamprey Larvicide were weighed (Approximately 0.10 g) into 100 mL volumetric flasks, then brought to volume in methanol. Futher dilutions were made by delivering 1 mL of each stock sample into a 100 mL volumetric flask, then brought to volume with an E-Pure water solution. (Dilution Factor 100)
HPLC analysis conditions:
1) Agilent 1260 Series HPLC
2) Column: Kinetex EVO-C18, 2.6 µm, 100 Å, 3.0x50 mm (SN: 570343-34)
3) Mobile Phases: A: water (750 mL) MeOH (250 mL) ammonium acetate (770 mg) acetic acid (3 mL)
B: MeOH (1000 mL) ammonium acetate (770 mg) acetic acid (3 mL)
Mobile phase: Acetic Acid (Lot # BO527756; Acros) MeOH (Lot # DS582-US; Honeywell), Amonnium Acetate (Lot # 1497C298; VWR)
4) Column temperature: 50°C
5) Flow Rate: 1.25 mL/min, injection volume: 25 µL, TFM peak retention time about 1.0 min, sample run time: 1.5 min
6) Diode Array Detector: 295 nm with 10 nm bandwidth
Analytical Balance Sartorius Model MSU225S-100-DI, S/N 29505562

Procedure for preparation of TFM HP-Liquid Extract

June 25, 2018

One liter of TFM HP Sea Lamprey Larvicide (Lot: LAM170517A, Iofina Chemical) was placed in a 2-liter separatory funnel. One liter of ACS Grade Hydrochloric Acid 36.5-38% (Lot: 2017092837, VWR) was added to the funnel. The separatory funnel was agitated for five minutes, and its contents were allowed to separate for twenty minutes. The lower layer was transferred to a 1-liter Erlenmeyer flask. The upper layer was discarded and the separatory funnel was washed three times in de-ionized water.

The lower layer was added back into the separatory funnel. One liter of de-ionized water was added. The separatory funnel was agitated for five minutes, and its contents we allowed to separate for twenty minutes. The lower layer was transferred to another 1-liter Erlenmeyer flask. The upper layer was discarded and the separatory funnel was washed three times in de-ionized water.

The above steps were repeated once, and the contents from both extractions were combined in an Erlenmeyer flask. Material was assigned lot number LAM170517A-LE20180625 and analyzed by HPLC as described in the Certificate of Analysis date June 25, 2018.

After analysis the extract was divided into three aliquots.
Aliquot 1: 324.2 grams of extract was placed in a 500 mL bottle. The bottle was capped and wrapped with parafilm. Labeled as LAM170517A-LE20180625 Bottle 1.
Aliquot 2: 535.7 grams of extract was placed in a 500 mL bottle. The bottle was capped and wrapped with parafilm. Labeled as LAM170517A-LE20180625 Bottle 2.
Aliquot 3: 19.11 grams of extract was placed in a 20 mL vial. The bottle was capped, wrapped with parafilm, and archived. Labeled as LAM170517A-LE20180625 Bottle 3.

Batch Report: C:\CHEM32\1\DATA\2018FIELDSTANDARDS\20180625LE-TFM 2018-06-25 10-43-43\20180625LE-TFM.

Batch Review Method: C:\Chem32\1\Data\2018FieldStandards\20180625LE-TFM 2018-06-25 10-43-43\TFM-SOP-409-4-A.M,.M

['#' ==> Run has not been reprocessed with Batch Review Method
'*' ==> Run has been saved with batch file]

#*	Sample	Location	Inj	SampleType	Run	TFM Area	TFM RT	TFM Amount
#	Blank	9	1	Blank	1	0.00000	0.000	0.00000
#	Blank	10	1	Blank	2	0.00000	0.000	0.00000
#*	1.001 ppm STD	1	1	Calibration	3	18.16127	1.051	1.02335
#*	4.004 ppm STD	2	1	Calibration	4	70.98321	1.051	4.02363
#*	7.007 ppm STD	3	1	Calibration	5	123.16059	1.052	6.98731
#*	10.01 ppm STD	4	1	Calibration	6	175.96591	1.049	9.98664
#*	15.015 ppm STD	5	1	Calibration	7	264.38544	1.050	15.00887
#	Blank	9	1	Blank	8	0.00000	0.000	0.00000
#	Blank	10	1	Blank	9	0.00000	0.000	0.00000
#	20180625-LEA	11	1	Sample	10	142.04970	1.054	8.06021
#	20180625-LE3B	12	1	Sample	11	139.78078	1.054	7.93133
#	20180625-LE3C	13	1	Sample	12	142.69135	1.060	8.09665
#	Blank	9	1	Blank	13	0.00000	0.000	0.00000
#	Blank	10	1	Blank	14	0.00000	0.000	0.00000
#	1.001 ppm STD	1	1	Calibration	15	17.83201	1.058	1.00465
#	4.004 ppm STD	2	1	Calibration	16	70.46019	1.052	3.99393
#	7.007 ppm STD	3	1	Calibration	17	123.66747	1.055	7.01610
#	10.01 ppm STD	4	1	Calibration	18	176.30200	1.053	10.00573
#	15.015 ppm STD	5	1	Calibration	19	264.93726	1.051	15.04021
#	Blank	9	1	Blank	20	0.00000	0.000	0.00000
#	Blank	10	1	Blank	21	0.00000	0.000	0.00000

*** End of Report ***

Method C:\Chem32\1\Data\2018FieldStandards\20180625LE-TFM 2018-06-25 10-43-43\TFM-SOP-409-4-A.M,.M

```
==================================================================
                          Calibration Table
==================================================================


------------------------------------------------------------------
                     General Calibration Setting
------------------------------------------------------------------

Calib. Data Modified  :      Monday, June 25, 2018 12:25:37 PM
Signals calculated separately :      No


Rel. Reference Window :      5.000 %
Abs. Reference Window :      0.000 min
Rel. Non-ref. Window  :      5.000 %
Abs. Non-ref. Window  :      0.000 min
Uncalibrated Peaks    :      not reported
Partial Calibration   :      Yes, identified peaks are recalibrated
Correct All Ret. Times:      No, only for identified peaks

Curve Type            :      Linear
Origin                :      Included
Weight                :      Equal

Recalibration Settings:
Average Response      :      Average all calibrations
Average Retention Time:      Floating Average New 75%

Calibration Report Options :
    Printout of recalibrations within a sequence:
        Calibration Table after Recalibration
        Normal Report after Recalibration
    If the sequence is done with bracketing:
        Results of first cycle (ending previous bracket)

------------------------------------------------------------------


------------------------------------------------------------------
                           Signal Details
------------------------------------------------------------------

Signal 1: DAD1 A, Sig=295,10 Ref=350,80

------------------------------------------------------------------


------------------------------------------------------------------
                           Overview Table
------------------------------------------------------------------

   RT Sig Lvl  Amount      Area   Rsp.Factor Ref ISTD #   Compound
               [ng/ul]
-------|-|--|----------|----------|----------|---|---|-|-------------------
  1.052 1  1    1.00100   17.99664 5.56215e-2  No  No   TFM
           2    4.00400   70.72170 5.66163e-2
           3    7.00700  123.41403 5.67764e-2
```

1260 HPLC 6/25/2018 12:29:09 PM Justin Schueller Page 1 of 2

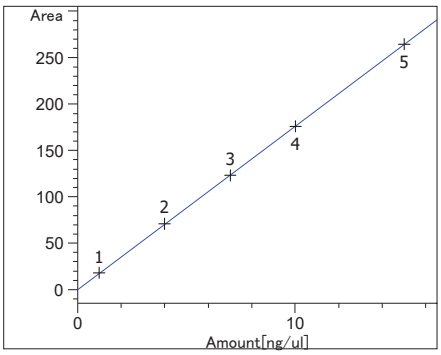
Method C:\Chem32\1\Data\2018FieldStandards\20180625LE-TFM 2018-06-25 10-43-43\TFM-SOP-409-4-A.M,.M

RT	Sig	Lvl	Amount [ng/ul]	Area	Rsp.Factor	Ref	ISTD #	Compound
		4	10.01000	176.13396	5.68317e-2			
		5	15.01500	264.66135	5.67329e-2			

Peak Sum Table

No Entries in table

Calibration Curves



TFM at exp. RT: 1.052
DAD1 A, Sig=295,10 Ref=350,80
Correlation: 1.00000
Residual Std. Dev.: 0.20999
Formula: y = mx + b
m: 17.60565
b: 1.44512e-1
x: Amount[ng/ul]
y: Area

TFM (3-trifluoromethyl-4-nitrophenol) Chemical Standard Weigh Sheet

Chemical Name: TFM Stock Solution, 100 mg/L

Lot or batch number: MKBX5239V Manufacturer: Sigma

Date: 6-21-18

Initials: US

Amount Chemical weighed: 0.01001

Balance ID: MSU225S-100-DI
Serial Number: 29505562

Chemical Weight Sheet

Chemical: Liquid TFM Extract

Date: 06-25-18

Lot or batch number: LAM170517A-LE20180625

Initials: JJ

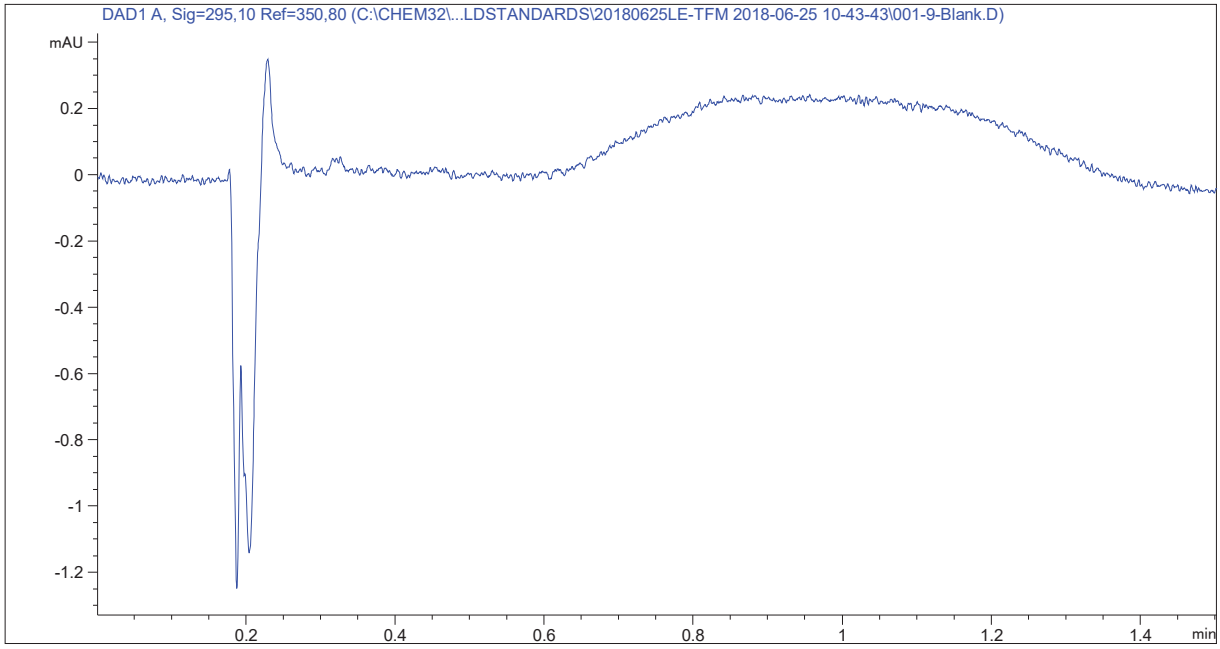
Source: Iofina Chemical

Sample Name	Weight (g)
20180625-LE (A)	0.10030
20180625-LE (B)	0.09938
20180625-LE (C)	0.10098
Not used	
6-25-18 JS	

Balance ID: MSU225S-100-DI Serial Number: 29505562

Batch Run # 1 of 21
Data File C:\CHEM32\...2018FIELDSTANDARDS\20180625LE-TFM 2018-06-25 10-43-43\001-9-Blank.D
Sample Name: Blank

```
==================================================================
Acq. Operator   : Justin Schueller              Seq. Line :   1
Acq. Instrument : 1260 HPLC                      Location :   9
Injection Date  : 6/25/2018 10:44:42 AM               Inj :   1
                                               Inj Volume : 25.000 µl
Acq. Method     : C:\Chem32\1\Data\2018FieldStandards\20180625LE-TFM 2018-06-25 10-43-43\TFM-
                  SOP-409-4-A.M,.M
Last changed    : 6/25/2018 10:43:43 AM by Justin Schueller
Analysis Method : C:\Chem32\1\Data\2018FieldStandards\20180625LE-TFM 2018-06-25 10-43-43\TFM-
                  SOP-409-4-A.M,.M (Sequence Method)
Last changed    : 6/25/2018 12:25:38 PM by Justin Schueller
                  (modified after loading)
```

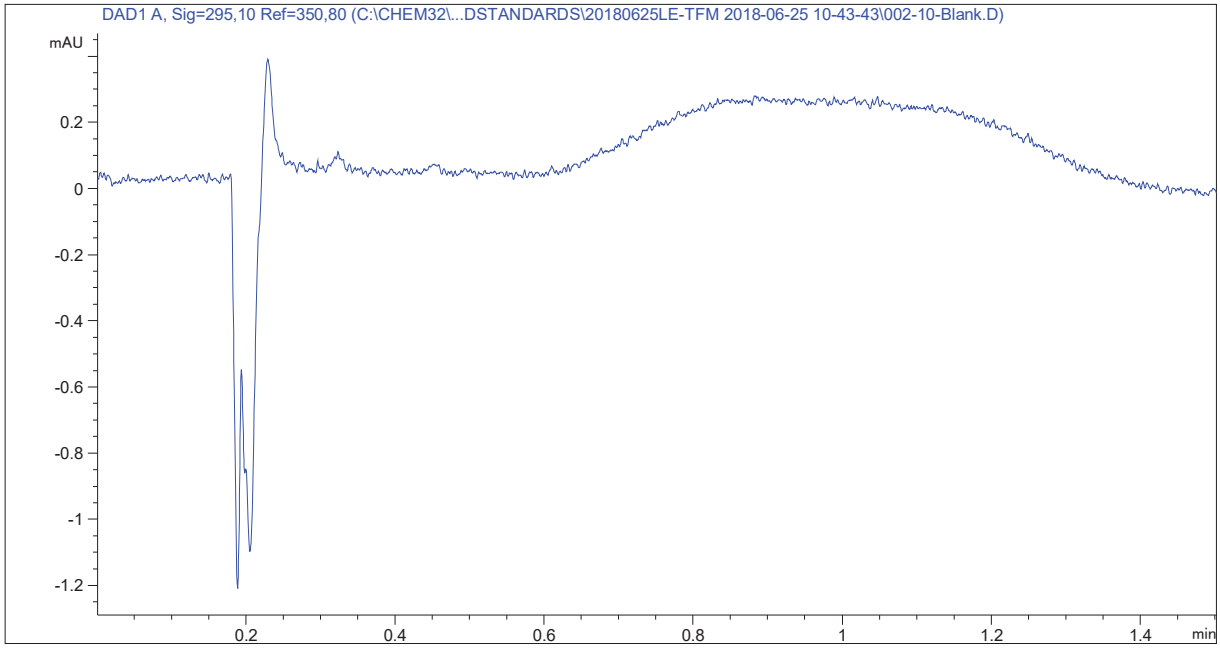



```
==================================================================
                          Area Percent Report
==================================================================

Sorted By             :      Signal
Calib. Data Modified  :      Monday, June 25, 2018 12:25:37 PM
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=295,10 Ref=350,80

Peak RetTime  Type   Width     Area      Area    Name
  #   [min]          [min]   [mAU*s]       %
----|-------|------|-------|----------|--------|---------------------
   1   1.052         0.0000    0.00000   0.0000 TFM

Totals :                       0.00000
```

1260 HPLC 6/25/2018 12:28:01 PM Justin Schueller Page 1 of 2

```
Batch Run # 1 of 21
Data File C:\CHEM32\...2018FIELDSTANDARDS\20180625LE-TFM 2018-06-25 10-43-43\001-9-Blank.D
Sample Name: Blank

    1 Warnings or Errors :

    Warning : Calibrated compound(s) not found

    ======================================================================
                            *** End of Report ***
```

```
Batch Run # 2 of 21
Data File C:\CHEM32\...018FIELDSTANDARDS\20180625LE-TFM 2018-06-25 10-43-43\002-10-Blank.D
Sample Name: Blank

    ==================================================================
    Acq. Operator   : Justin Schueller              Seq. Line :   2
    Acq. Instrument : 1260 HPLC                      Location :   10
    Injection Date  : 6/25/2018 10:47:11 AM               Inj :   1
                                                   Inj Volume : 25.000 µl
    Acq. Method     : C:\Chem32\1\Data\2018FieldStandards\20180625LE-TFM 2018-06-25 10-43-43\TFM-
                      SOP-409-4-A.M,.M
    Last changed    : 6/25/2018 10:43:43 AM by Justin Schueller
    Analysis Method : C:\Chem32\1\Data\2018FieldStandards\20180625LE-TFM 2018-06-25 10-43-43\TFM-
                      SOP-409-4-A.M,.M (Sequence Method)
    Last changed    : 6/25/2018 12:25:38 PM by Justin Schueller
                      (modified after loading)
```

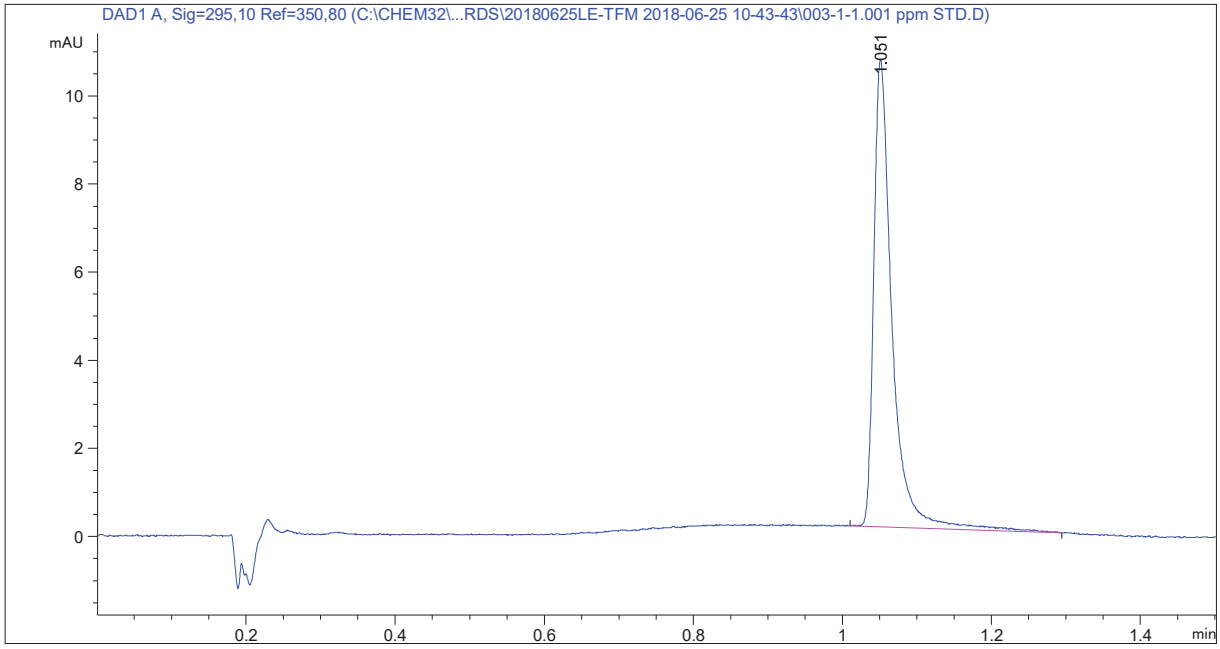



```
    ==================================================================
                              Area Percent Report
    ==================================================================

    Sorted By             :      Signal
    Calib. Data Modified  :      Monday, June 25, 2018 12:25:37 PM
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 A, Sig=295,10 Ref=350,80

    Peak RetTime  Type   Width     Area      Area    Name
      #   [min]          [min]   [mAU*s]       %
    ----|-------|------|-------|----------|--------|---------------------
       1   1.052         0.0000    0.00000   0.0000 TFM

    Totals :                       0.00000


1260 HPLC 6/25/2018 12:28:04 PM Justin Schueller                    Page   1 of 2
```

```
Batch Run # 2 of 21
Data File C:\CHEM32\...018FIELDSTANDARDS\20180625LE-TFM 2018-06-25 10-43-43\002-10-Blank.D
Sample Name: Blank

    1 Warnings or Errors :

    Warning : Calibrated compound(s) not found

    ======================================================================
                            *** End of Report ***
```

Batch Run # 3 of 21
Data File C:\CHEM32\...DSTANDARDS\20180625LE-TFM 2018-06-25 10-43-43\003-1-1.001 ppm STD.D
Sample Name: 1.001 ppm STD

```
==================================================================
Acq. Operator   : Justin Schueller              Seq. Line :   3
Acq. Instrument : 1260 HPLC                      Location :   1
Injection Date  : 6/25/2018 10:49:41 AM               Inj :   1
                                               Inj Volume : 25.000 µl
Acq. Method     : C:\Chem32\1\Data\2018FieldStandards\20180625LE-TFM 2018-06-25 10-43-43\TFM-
                  SOP-409-4-A.M,.M
Last changed    : 6/25/2018 10:43:43 AM by Justin Schueller
Analysis Method : C:\Chem32\1\Data\2018FieldStandards\20180625LE-TFM 2018-06-25 10-43-43\TFM-
                  SOP-409-4-A.M,.M (Sequence Method)
Last changed    : 6/25/2018 12:25:38 PM by Justin Schueller
                  (modified after loading)  (Results are from a previously saved Batch)
```

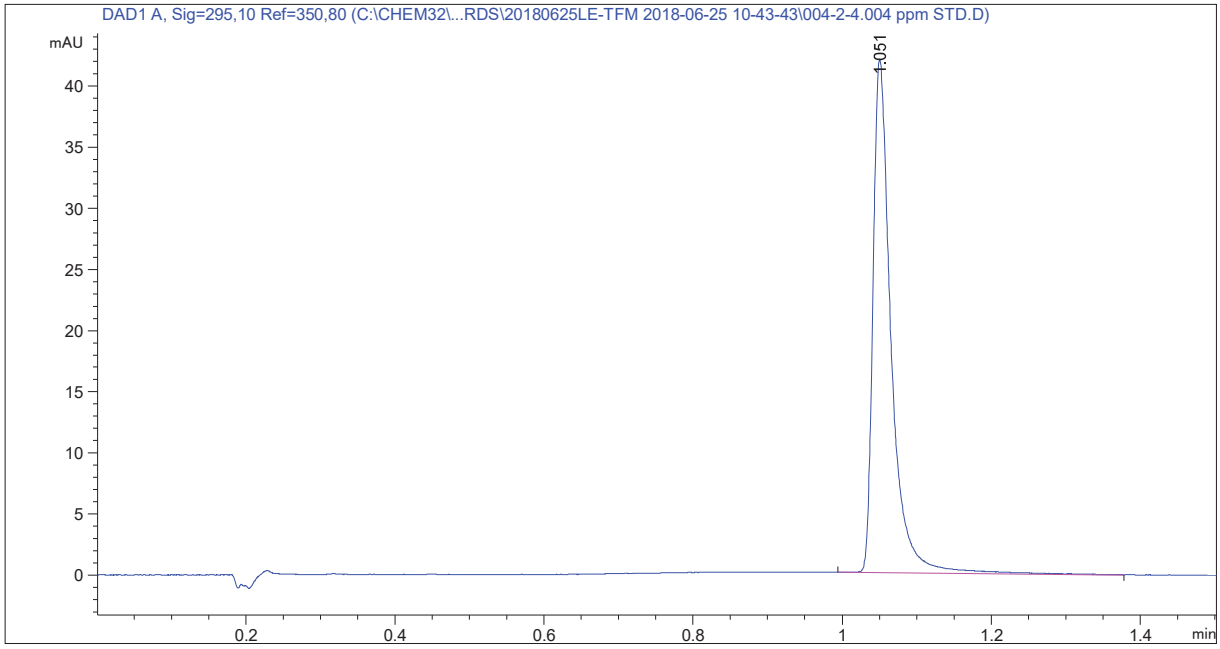



```
==================================================================
                          Area Percent Report
==================================================================

Sorted By             :      Signal
Calib. Data Modified  :      Monday, June 25, 2018 12:25:37 PM
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=295,10 Ref=350,80

Peak RetTime  Type   Width     Area      Area    Name
  #   [min]          [min]   [mAU*s]       %
----|-------|------|-------|----------|--------|---------------------
   1   1.051 BB      0.0255   18.16127 100.0000 TFM

Totals :                      18.16127
```

```
Batch Run # 3 of 21
Data File C:\CHEM32\...DSTANDARDS\20180625LE-TFM 2018-06-25 10-43-43\003-1-1.001 ppm STD.D
Sample Name: 1.001 ppm STD

    ======================================================================
                            *** End of Report ***
```

Batch Run # 4 of 21
Data File C:\CHEM32\...DSTANDARDS\20180625LE-TFM 2018-06-25 10-43-43\004-2-4.004 ppm STD.D
Sample Name: 4.004 ppm STD

```
==================================================================
Acq. Operator   : Justin Schueller              Seq. Line :   4
Acq. Instrument : 1260 HPLC                      Location :   2
Injection Date  : 6/25/2018 10:52:08 AM               Inj :   1
                                               Inj Volume : 25.000 µl
Acq. Method     : C:\Chem32\1\Data\2018FieldStandards\20180625LE-TFM 2018-06-25 10-43-43\TFM-
                  SOP-409-4-A.M,.M
Last changed    : 6/25/2018 10:43:43 AM by Justin Schueller
Analysis Method : C:\Chem32\1\Data\2018FieldStandards\20180625LE-TFM 2018-06-25 10-43-43\TFM-
                  SOP-409-4-A.M,.M (Sequence Method)
Last changed    : 6/25/2018 12:25:38 PM by Justin Schueller
                  (modified after loading)  (Results are from a previously saved Batch)
```

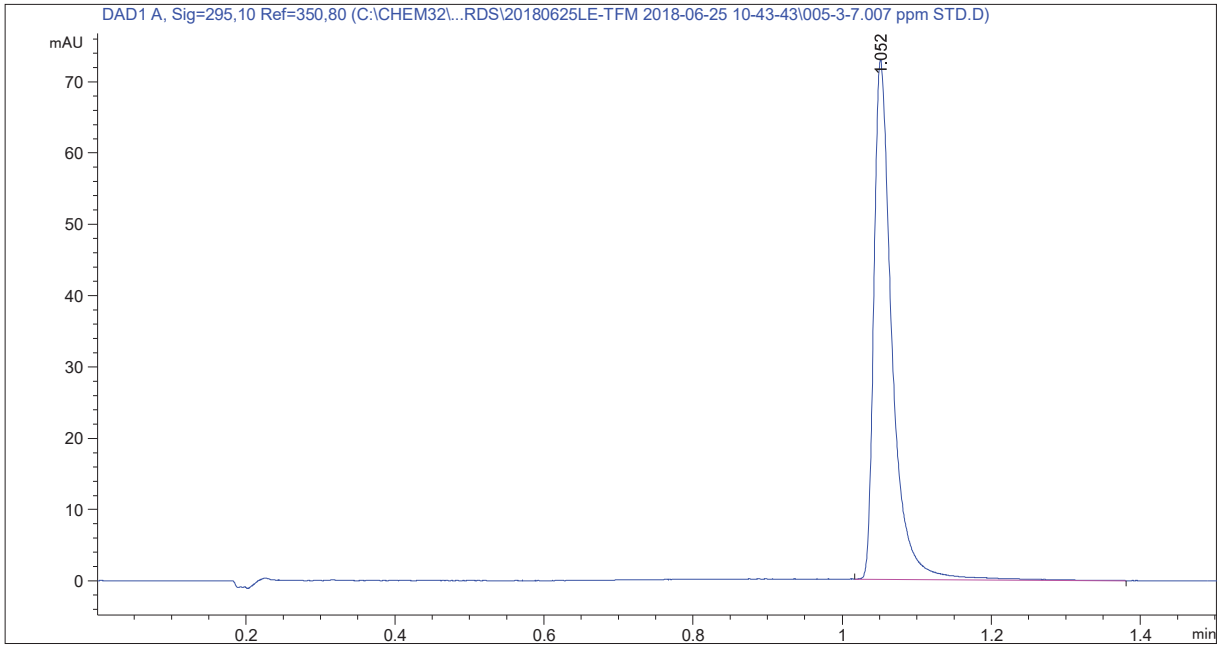



```
==================================================================
                          Area Percent Report
==================================================================

Sorted By             :      Signal
Calib. Data Modified  :      Monday, June 25, 2018 12:25:37 PM
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=295,10 Ref=350,80

Peak RetTime  Type   Width     Area      Area    Name
  #   [min]          [min]   [mAU*s]       %
----|-------|------|-------|----------|--------|---------------------
   1   1.051 BB      0.0253   70.98321 100.0000 TFM

Totals :                      70.98321
```

```
Batch Run # 4 of 21
Data File C:\CHEM32\...DSTANDARDS\20180625LE-TFM 2018-06-25 10-43-43\004-2-4.004 ppm STD.D
Sample Name: 4.004 ppm STD

    ======================================================================
                            *** End of Report ***
```

Batch Run # 5 of 21
Data File C:\CHEM32\...DSTANDARDS\20180625LE-TFM 2018-06-25 10-43-43\005-3-7.007 ppm STD.D
Sample Name: 7.007 ppm STD

```
==================================================================
Acq. Operator   : Justin Schueller              Seq. Line :   5
Acq. Instrument : 1260 HPLC                      Location :   3
Injection Date  : 6/25/2018 10:54:36 AM               Inj :   1
                                               Inj Volume : 25.000 µl
Acq. Method     : C:\Chem32\1\Data\2018FieldStandards\20180625LE-TFM 2018-06-25 10-43-43\TFM-
                  SOP-409-4-A.M,.M
Last changed    : 6/25/2018 10:43:43 AM by Justin Schueller
Analysis Method : C:\Chem32\1\Data\2018FieldStandards\20180625LE-TFM 2018-06-25 10-43-43\TFM-
                  SOP-409-4-A.M,.M (Sequence Method)
Last changed    : 6/25/2018 12:25:38 PM by Justin Schueller
                  (modified after loading)  (Results are from a previously saved Batch)
```




```
==================================================================
                          Area Percent Report
==================================================================

Sorted By             :      Signal
Calib. Data Modified  :      Monday, June 25, 2018 12:25:37 PM
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=295,10 Ref=350,80

Peak RetTime  Type   Width     Area      Area    Name
  #   [min]          [min]   [mAU*s]       %
----|-------|------|-------|----------|--------|---------------------
   1   1.052 BB      0.0257  123.16059 100.0000 TFM

Totals :                     123.16059
```

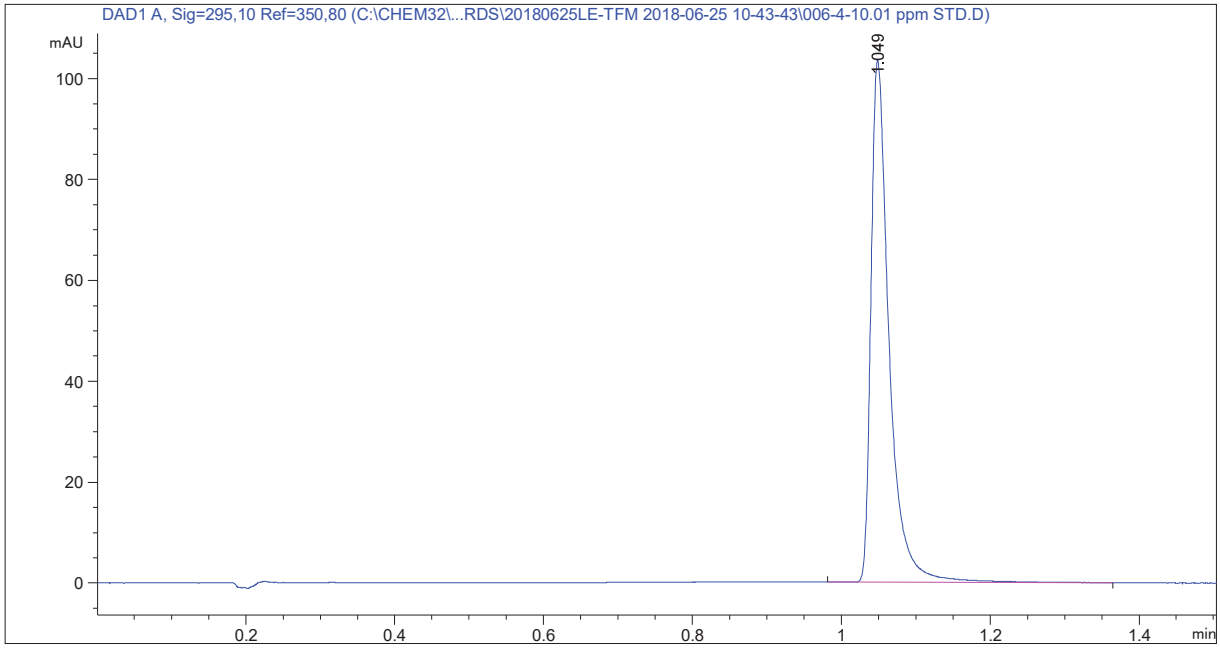
Batch Run # 5 of 21
Data File C:\CHEM32\...DSTANDARDS\20180625LE-TFM 2018-06-25 10-43-43\005-3-7.007 ppm STD.D
Sample Name: 7.007 ppm STD

==========

*** End of Report ***

Batch Run # 6 of 21
Data File C:\CHEM32\...DSTANDARDS\20180625LE-TFM 2018-06-25 10-43-43\006-4-10.01 ppm STD.D
Sample Name: 10.01 ppm STD

```
==================================================================
Acq. Operator   : Justin Schueller              Seq. Line :   6
Acq. Instrument : 1260 HPLC                      Location :   4
Injection Date  : 6/25/2018 10:57:05 AM               Inj :   1
                                               Inj Volume : 25.000 µl
Acq. Method     : C:\Chem32\1\Data\2018FieldStandards\20180625LE-TFM 2018-06-25 10-43-43\TFM-
                  SOP-409-4-A.M,.M
Last changed    : 6/25/2018 10:43:43 AM by Justin Schueller
Analysis Method : C:\Chem32\1\Data\2018FieldStandards\20180625LE-TFM 2018-06-25 10-43-43\TFM-
                  SOP-409-4-A.M,.M (Sequence Method)
Last changed    : 6/25/2018 12:25:38 PM by Justin Schueller
                  (modified after loading)  (Results are from a previously saved Batch)
```




```
==================================================================
                          Area Percent Report
==================================================================

Sorted By             :      Signal
Calib. Data Modified  :      Monday, June 25, 2018 12:25:37 PM
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=295,10 Ref=350,80

Peak RetTime  Type   Width     Area      Area    Name
  #   [min]          [min]   [mAU*s]       %
----|-------|------|-------|----------|--------|---------------------
   1   1.049 BB      0.0254  175.96591 100.0000 TFM

Totals :                     175.96591
```

1260 HPLC 6/25/2018 12:28:15 PM Justin Schueller Page 1 of 2

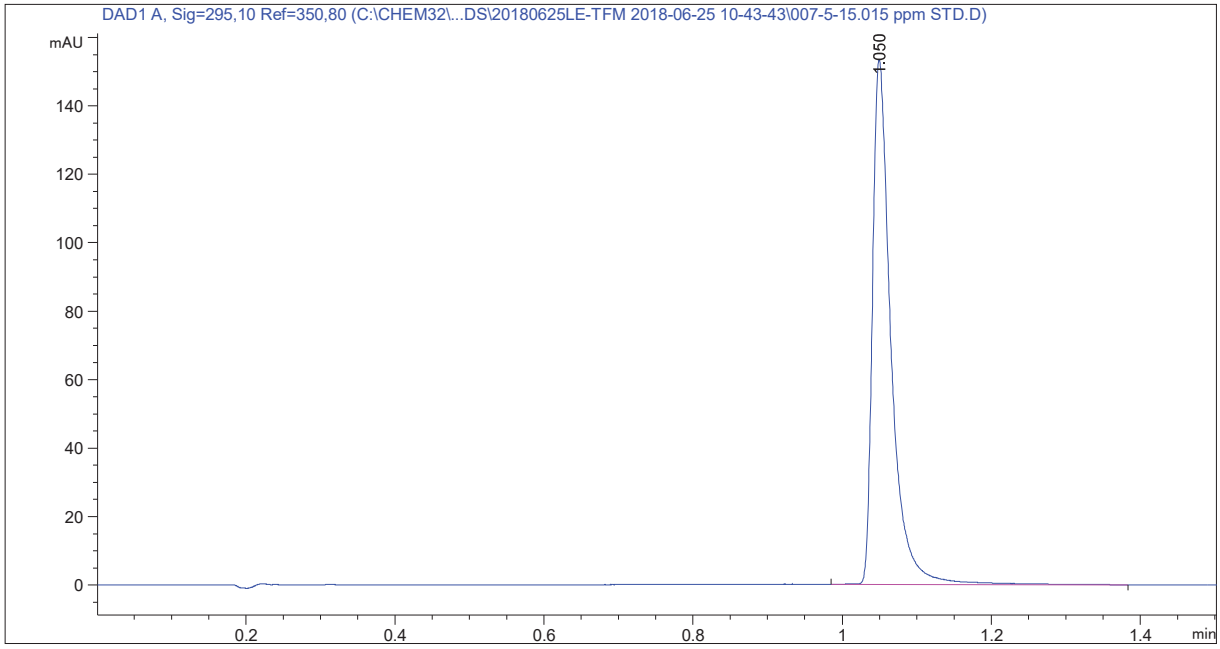
Batch Run # 6 of 21
Data File C:\CHEM32\...DSTANDARDS\20180625LE-TFM 2018-06-25 10-43-43\006-4-10.01 ppm STD.D
Sample Name: 10.01 ppm STD

==========

*** End of Report ***

Batch Run # 7 of 21
Data File C:\CHEM32\...STANDARDS\20180625LE-TFM 2018-06-25 10-43-43\007-5-15.015 ppm STD.D
Sample Name: 15.015 ppm STD

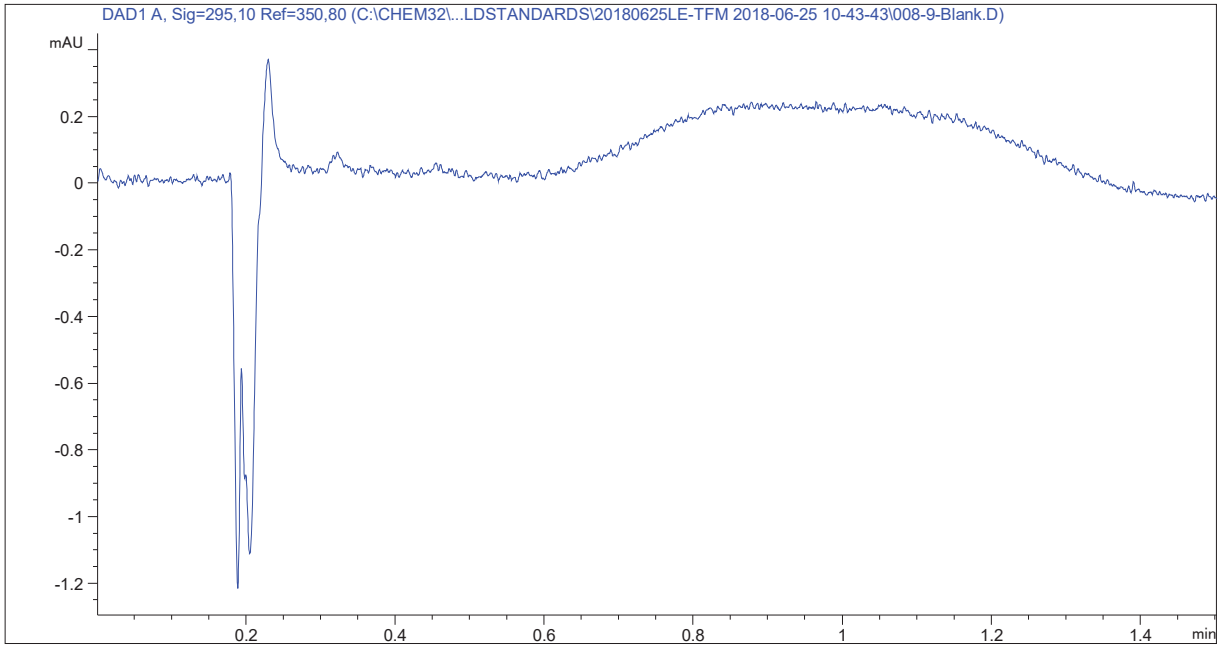
```
==================================================================
Acq. Operator   : Justin Schueller              Seq. Line :   7
Acq. Instrument : 1260 HPLC                      Location :   5
Injection Date  : 6/25/2018 10:59:32 AM               Inj :   1
                                               Inj Volume : 25.000 µl
Acq. Method     : C:\Chem32\1\Data\2018FieldStandards\20180625LE-TFM 2018-06-25 10-43-43\TFM-
                  SOP-409-4-A.M,.M
Last changed    : 6/25/2018 10:43:43 AM by Justin Schueller
Analysis Method : C:\Chem32\1\Data\2018FieldStandards\20180625LE-TFM 2018-06-25 10-43-43\TFM-
                  SOP-409-4-A.M,.M (Sequence Method)
Last changed    : 6/25/2018 12:25:38 PM by Justin Schueller
                  (modified after loading)  (Results are from a previously saved Batch)
```




```
==================================================================
                          Area Percent Report
==================================================================

Sorted By             :      Signal
Calib. Data Modified  :      Monday, June 25, 2018 12:25:37 PM
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=295,10 Ref=350,80

Peak RetTime  Type   Width     Area      Area    Name
  #   [min]          [min]   [mAU*s]       %
----|-------|------|-------|----------|--------|---------------------
   1   1.050 BB      0.0261  264.38544 100.0000 TFM

Totals :                     264.38544
```

```
Batch Run # 7 of 21
Data File C:\CHEM32\...STANDARDS\20180625LE-TFM 2018-06-25 10-43-43\007-5-15.015 ppm STD.D
Sample Name: 15.015 ppm STD

    ==================================================================
                            *** End of Report ***
```

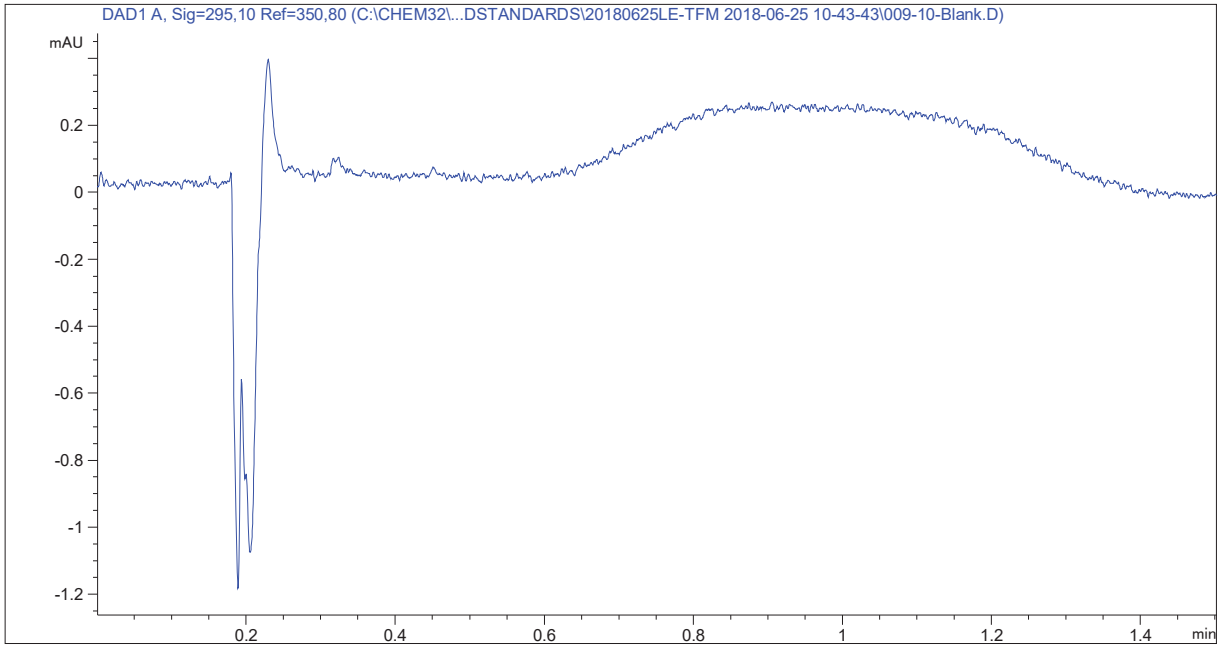
```
Batch Run # 8 of 21
Data File C:\CHEM32\...2018FIELDSTANDARDS\20180625LE-TFM 2018-06-25 10-43-43\008-9-Blank.D
Sample Name: Blank

    ==================================================================
    Acq. Operator   : Justin Schueller              Seq. Line :   8
    Acq. Instrument : 1260 HPLC                      Location :   9
    Injection Date  : 6/25/2018 11:02:02 AM               Inj :   1
                                                   Inj Volume : 25.000 µl
    Acq. Method     : C:\Chem32\1\Data\2018FieldStandards\20180625LE-TFM 2018-06-25 10-43-43\TFM-
                      SOP-409-4-A.M,.M
    Last changed    : 6/25/2018 10:43:43 AM by Justin Schueller
    Analysis Method : C:\Chem32\1\Data\2018FieldStandards\20180625LE-TFM 2018-06-25 10-43-43\TFM-
                      SOP-409-4-A.M,.M (Sequence Method)
    Last changed    : 6/25/2018 12:25:38 PM by Justin Schueller
                      (modified after loading)
```




```
    ==================================================================
                            Area Percent Report
    ==================================================================

    Sorted By             :      Signal
    Calib. Data Modified  :      Monday, June 25, 2018 12:25:37 PM
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 A, Sig=295,10 Ref=350,80

    Peak RetTime  Type   Width     Area      Area    Name
      #   [min]          [min]   [mAU*s]       %
    ----|-------|------|-------|----------|--------|---------------------
       1   1.052         0.0000    0.00000   0.0000 TFM

    Totals :                       0.00000


1260 HPLC 6/25/2018 12:28:20 PM Justin Schueller                    Page   1 of 2
```

```
Batch Run # 8 of 21
Data File C:\CHEM32\...2018FIELDSTANDARDS\20180625LE-TFM 2018-06-25 10-43-43\008-9-Blank.D
Sample Name: Blank

    1 Warnings or Errors :

    Warning : Calibrated compound(s) not found

    ======================================================================
                            *** End of Report ***
```

```
Batch Run # 9 of 21
Data File C:\CHEM32\...018FIELDSTANDARDS\20180625LE-TFM 2018-06-25 10-43-43\009-10-Blank.D
Sample Name: Blank

    ==================================================================
    Acq. Operator   : Justin Schueller              Seq. Line :   9
    Acq. Instrument : 1260 HPLC                      Location :   10
    Injection Date  : 6/25/2018 11:04:34 AM               Inj :   1
                                                   Inj Volume : 25.000 µl
    Acq. Method     : C:\Chem32\1\Data\2018FieldStandards\20180625LE-TFM 2018-06-25 10-43-43\TFM-
                      SOP-409-4-A.M,.M
    Last changed    : 6/25/2018 10:43:43 AM by Justin Schueller
    Analysis Method : C:\Chem32\1\Data\2018FieldStandards\20180625LE-TFM 2018-06-25 10-43-43\TFM-
                      SOP-409-4-A.M,.M (Sequence Method)
    Last changed    : 6/25/2018 12:25:38 PM by Justin Schueller
                      (modified after loading)
```

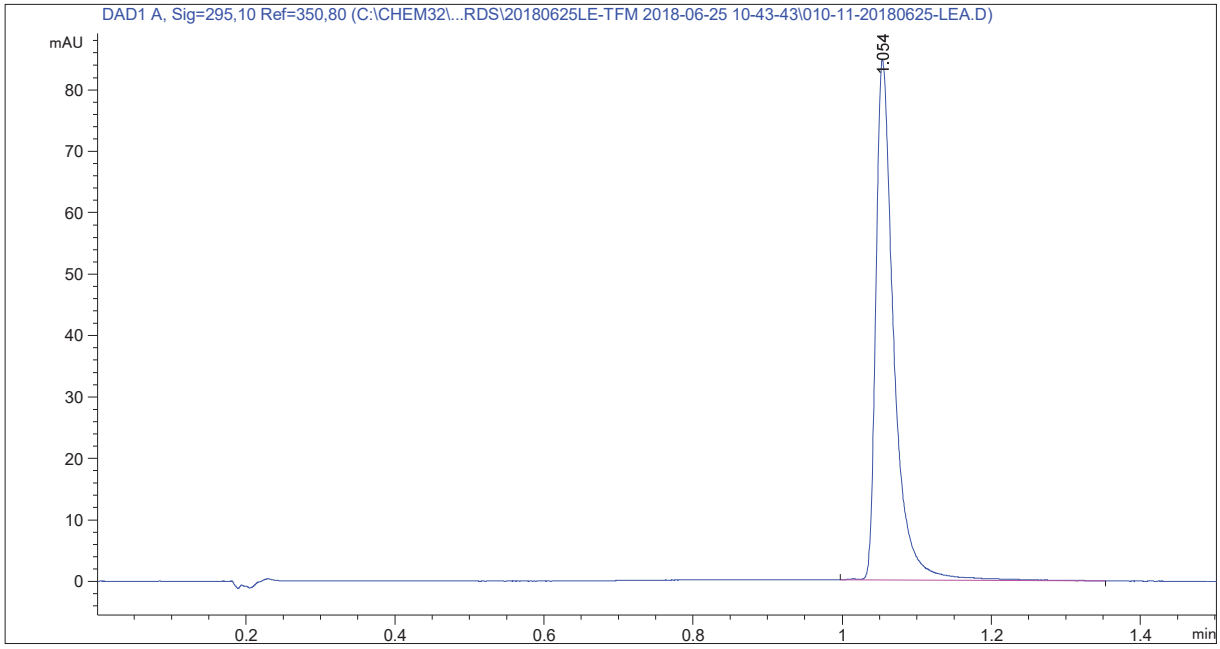



```
    ==================================================================
                              Area Percent Report
    ==================================================================

    Sorted By             :      Signal
    Calib. Data Modified  :      Monday, June 25, 2018 12:25:37 PM
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 A, Sig=295,10 Ref=350,80

    Peak RetTime  Type   Width     Area      Area    Name
      #   [min]          [min]   [mAU*s]       %
    ----|-------|------|-------|----------|--------|---------------------
       1   1.052         0.0000    0.00000   0.0000 TFM

    Totals :                       0.00000


1260 HPLC 6/25/2018 12:28:23 PM Justin Schueller                    Page   1 of 2
```

```
Batch Run # 9 of 21
Data File C:\CHEM32\...018FIELDSTANDARDS\20180625LE-TFM 2018-06-25 10-43-43\009-10-Blank.D
Sample Name: Blank

    1 Warnings or Errors :

    Warning : Calibrated compound(s) not found

    ======================================================================
                            *** End of Report ***
```

Batch Run # 10 of 21
Data File C:\CHEM32\...DSTANDARDS\20180625LE-TFM 2018-06-25 10-43-43\010-11-20180625-LEA.D
Sample Name: 20180625-LEA

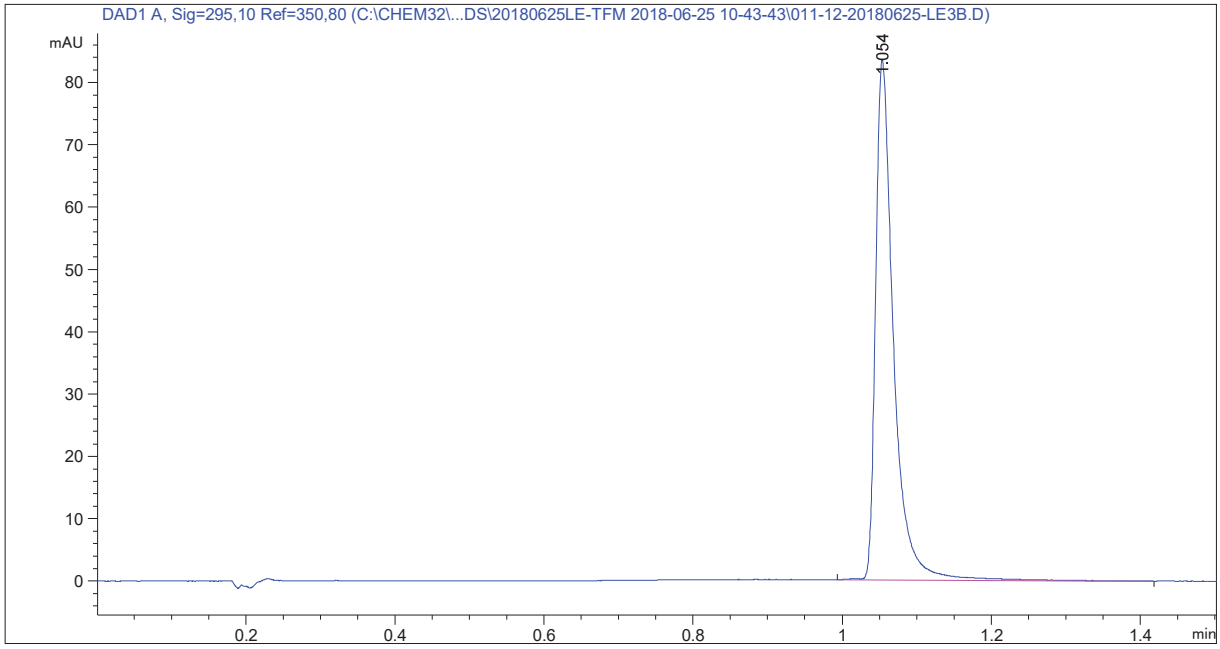
```
==================================================================
Acq. Operator   : Justin Schueller              Seq. Line :  10
Acq. Instrument : 1260 HPLC                      Location :   11
Injection Date  : 6/25/2018 11:07:03 AM               Inj :   1
                                               Inj Volume : 25.000 µl
Acq. Method     : C:\Chem32\1\Data\2018FieldStandards\20180625LE-TFM 2018-06-25 10-43-43\TFM-
                  SOP-409-4-A.M,.M
Last changed    : 6/25/2018 10:43:43 AM by Justin Schueller
Analysis Method : C:\Chem32\1\Data\2018FieldStandards\20180625LE-TFM 2018-06-25 10-43-43\TFM-
                  SOP-409-4-A.M,.M (Sequence Method)
Last changed    : 6/25/2018 12:25:38 PM by Justin Schueller
                  (modified after loading)
```




```
==================================================================
                          Area Percent Report
==================================================================

Sorted By             :      Signal
Calib. Data Modified  :      Monday, June 25, 2018 12:25:37 PM
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=295,10 Ref=350,80

Peak RetTime  Type   Width     Area      Area    Name
  #   [min]          [min]   [mAU*s]       %
----|-------|------|-------|----------|--------|---------------------
   1   1.054 BB      0.0251  142.04970 100.0000 TFM

Totals :                     142.04970
```

```
Batch Run # 10 of 21
Data File C:\CHEM32\...DSTANDARDS\20180625LE-TFM 2018-06-25 10-43-43\010-11-20180625-LEA.D
Sample Name: 20180625-LEA

    ======================================================================
                            *** End of Report ***
```

```
Batch Run # 11 of 21
Data File C:\CHEM32\...STANDARDS\20180625LE-TFM 2018-06-25 10-43-43\011-12-20180625-LE3B.D
Sample Name: 20180625-LE3B

    ==================================================================
    Acq. Operator   : Justin Schueller              Seq. Line :  11
    Acq. Instrument : 1260 HPLC                      Location :   12
    Injection Date  : 6/25/2018 11:09:29 AM               Inj :   1
                                                   Inj Volume : 25.000 µl
    Acq. Method     : C:\Chem32\1\Data\2018FieldStandards\20180625LE-TFM 2018-06-25 10-43-43\TFM-
                      SOP-409-4-A.M,.M
    Last changed    : 6/25/2018 10:43:43 AM by Justin Schueller
    Analysis Method : C:\Chem32\1\Data\2018FieldStandards\20180625LE-TFM 2018-06-25 10-43-43\TFM-
                      SOP-409-4-A.M,.M (Sequence Method)
    Last changed    : 6/25/2018 12:25:38 PM by Justin Schueller
                      (modified after loading)
```



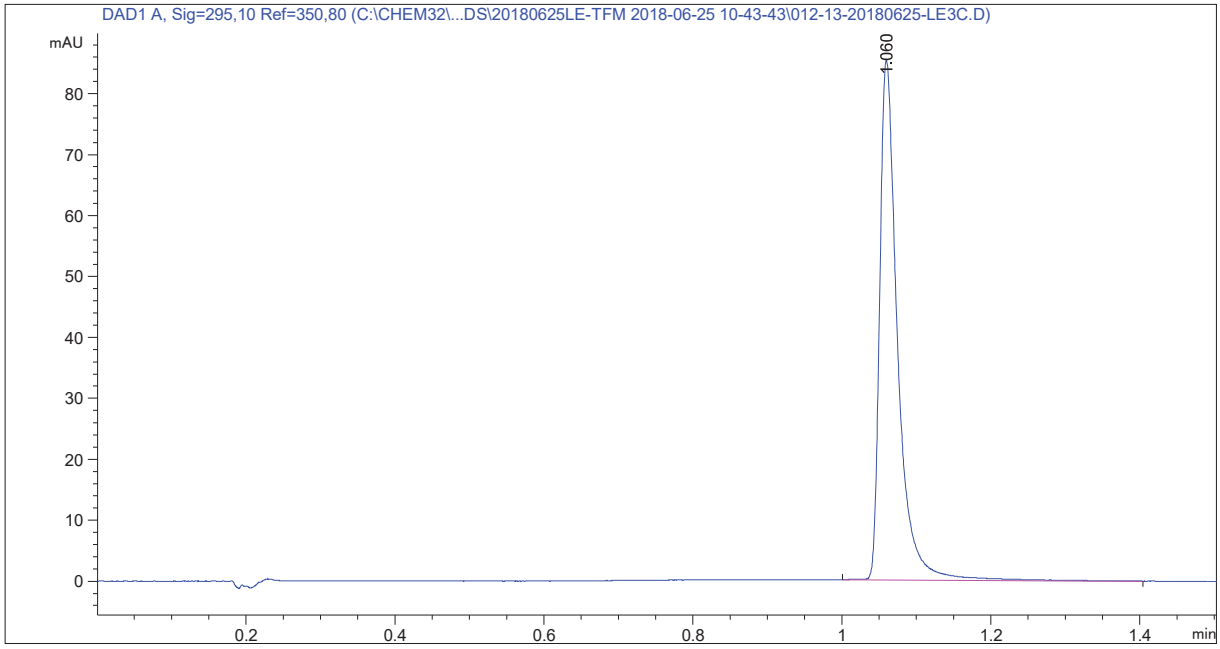

```
    ==================================================================
                            Area Percent Report
    ==================================================================

    Sorted By             :      Signal
    Calib. Data Modified  :      Monday, June 25, 2018 12:25:37 PM
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 A, Sig=295,10 Ref=350,80

    Peak RetTime  Type   Width     Area      Area    Name
      #   [min]          [min]   [mAU*s]       %
    ----|-------|------|-------|----------|--------|---------------------
       1   1.054 BB      0.0251  139.78078 100.0000 TFM

    Totals :                     139.78078


1260 HPLC 6/25/2018 12:28:28 PM Justin Schueller                    Page   1 of 2
```

Batch Run # 11 of 21
Data File C:\CHEM32\...STANDARDS\20180625LE-TFM 2018-06-25 10-43-43\011-12-20180625-LE3B.D
Sample Name: 20180625-LE3B

==========

*** End of Report ***

```
Batch Run # 12 of 21
Data File C:\CHEM32\...STANDARDS\20180625LE-TFM 2018-06-25 10-43-43\012-13-20180625-LE3C.D
Sample Name: 20180625-LE3C

    ======================================================================
    Acq. Operator   : Justin Schueller              Seq. Line :  12
    Acq. Instrument : 1260 HPLC                      Location :   13
    Injection Date  : 6/25/2018 11:11:56 AM               Inj :   1
                                                   Inj Volume : 25.000 µl
    Acq. Method     : C:\Chem32\1\Data\2018FieldStandards\20180625LE-TFM 2018-06-25 10-43-43\TFM-
                      SOP-409-4-A.M,.M
    Last changed    : 6/25/2018 10:43:43 AM by Justin Schueller
    Analysis Method : C:\Chem32\1\Data\2018FieldStandards\20180625LE-TFM 2018-06-25 10-43-43\TFM-
                      SOP-409-4-A.M,.M (Sequence Method)
    Last changed    : 6/25/2018 12:25:38 PM by Justin Schueller
                      (modified after loading)
```



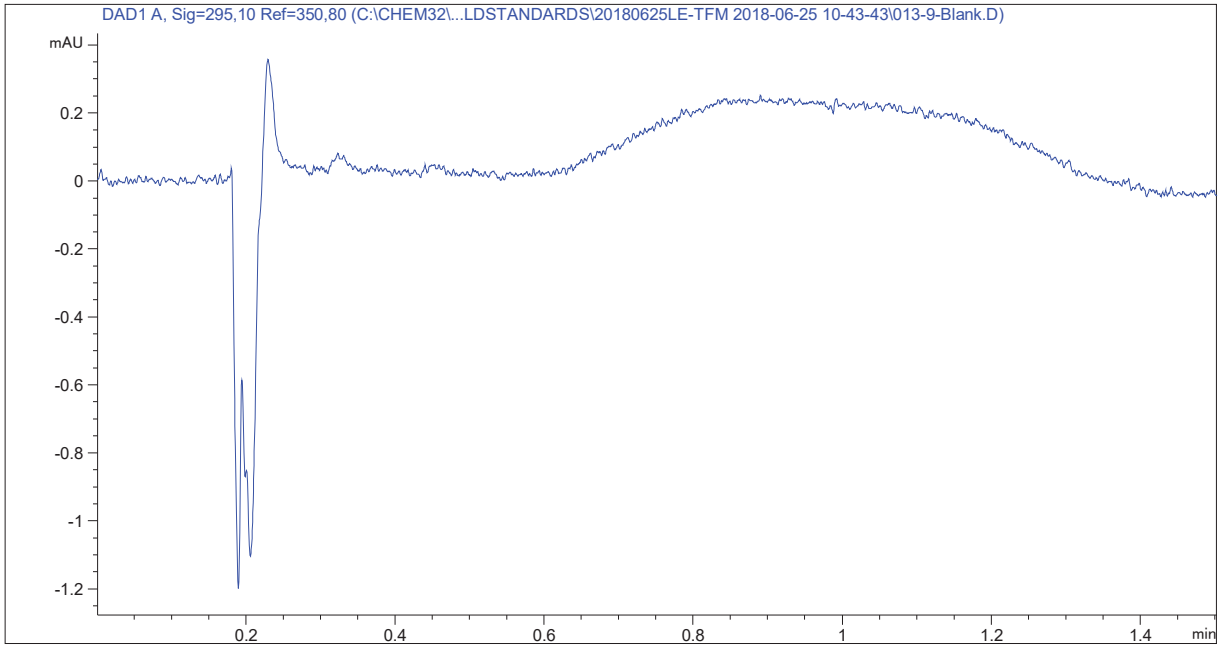

```
    ======================================================================
                              Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Calib. Data Modified  :      Monday, June 25, 2018 12:25:37 PM
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 A, Sig=295,10 Ref=350,80

    Peak RetTime  Type   Width     Area      Area    Name
      #   [min]          [min]   [mAU*s]       %
    ----|-------|------|-------|----------|--------|---------------------
       1   1.060 BB      0.0250  142.69135 100.0000 TFM

    Totals :                     142.69135
```

Batch Run # 12 of 21
Data File C:\CHEM32\...STANDARDS\20180625LE-TFM 2018-06-25 10-43-43\012-13-20180625-LE3C.D
Sample Name: 20180625-LE3C

==========

*** End of Report ***

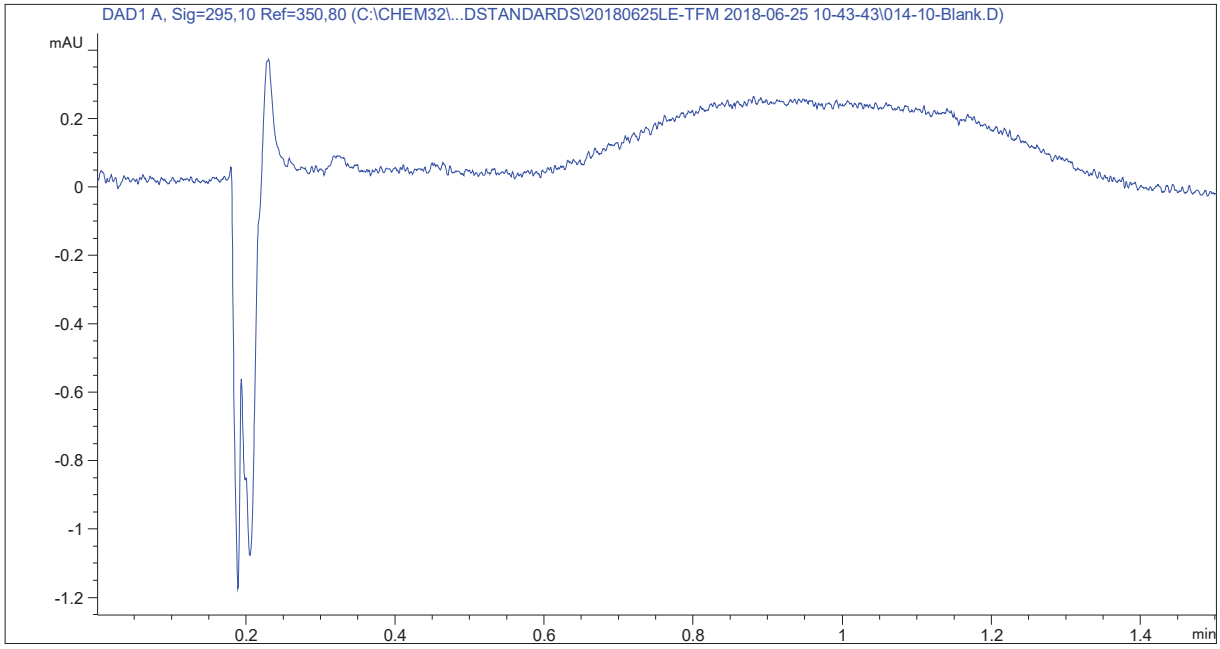
```
Batch Run # 13 of 21
Data File C:\CHEM32\...2018FIELDSTANDARDS\20180625LE-TFM 2018-06-25 10-43-43\013-9-Blank.D
Sample Name: Blank

    ======================================================================
    Acq. Operator   : Justin Schueller               Seq. Line :  13
    Acq. Instrument : 1260 HPLC                       Location :   9
    Injection Date  : 6/25/2018 11:14:25 AM                Inj :   1
                                                   Inj Volume : 25.000 µl
    Acq. Method     : C:\Chem32\1\Data\2018FieldStandards\20180625LE-TFM 2018-06-25 10-43-43\TFM-
                      SOP-409-4-A.M,.M
    Last changed    : 6/25/2018 10:43:43 AM by Justin Schueller
    Analysis Method : C:\Chem32\1\Data\2018FieldStandards\20180625LE-TFM 2018-06-25 10-43-43\TFM-
                      SOP-409-4-A.M,.M (Sequence Method)
    Last changed    : 6/25/2018 12:25:38 PM by Justin Schueller
                      (modified after loading)
```




```
    ======================================================================
                              Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Calib. Data Modified  :      Monday, June 25, 2018 12:25:37 PM
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 A, Sig=295,10 Ref=350,80

    Peak RetTime  Type   Width     Area      Area    Name
      #   [min]          [min]   [mAU*s]       %
    ----|-------|------|-------|----------|--------|---------------------
       1   1.052         0.0000    0.00000   0.0000 TFM

    Totals :                       0.00000


1260 HPLC 6/25/2018 12:28:34 PM Justin Schueller                    Page   1 of 2
```

```
Batch Run # 13 of 21
Data File C:\CHEM32\...2018FIELDSTANDARDS\20180625LE-TFM 2018-06-25 10-43-43\013-9-Blank.D
Sample Name: Blank

    1 Warnings or Errors :

    Warning : Calibrated compound(s) not found

    ======================================================================
                            *** End of Report ***
```

```
Batch Run # 14 of 21
Data File C:\CHEM32\...018FIELDSTANDARDS\20180625LE-TFM 2018-06-25 10-43-43\014-10-Blank.D
Sample Name: Blank

    ==================================================================
    Acq. Operator   : Justin Schueller              Seq. Line :  14
    Acq. Instrument : 1260 HPLC                      Location :   10
    Injection Date  : 6/25/2018 11:16:55 AM               Inj :   1
                                                   Inj Volume : 25.000 µl
    Acq. Method     : C:\Chem32\1\Data\2018FieldStandards\20180625LE-TFM 2018-06-25 10-43-43\TFM-
                      SOP-409-4-A.M,.M
    Last changed    : 6/25/2018 10:43:43 AM by Justin Schueller
    Analysis Method : C:\Chem32\1\Data\2018FieldStandards\20180625LE-TFM 2018-06-25 10-43-43\TFM-
                      SOP-409-4-A.M,.M (Sequence Method)
    Last changed    : 6/25/2018 12:25:38 PM by Justin Schueller
                      (modified after loading)
```

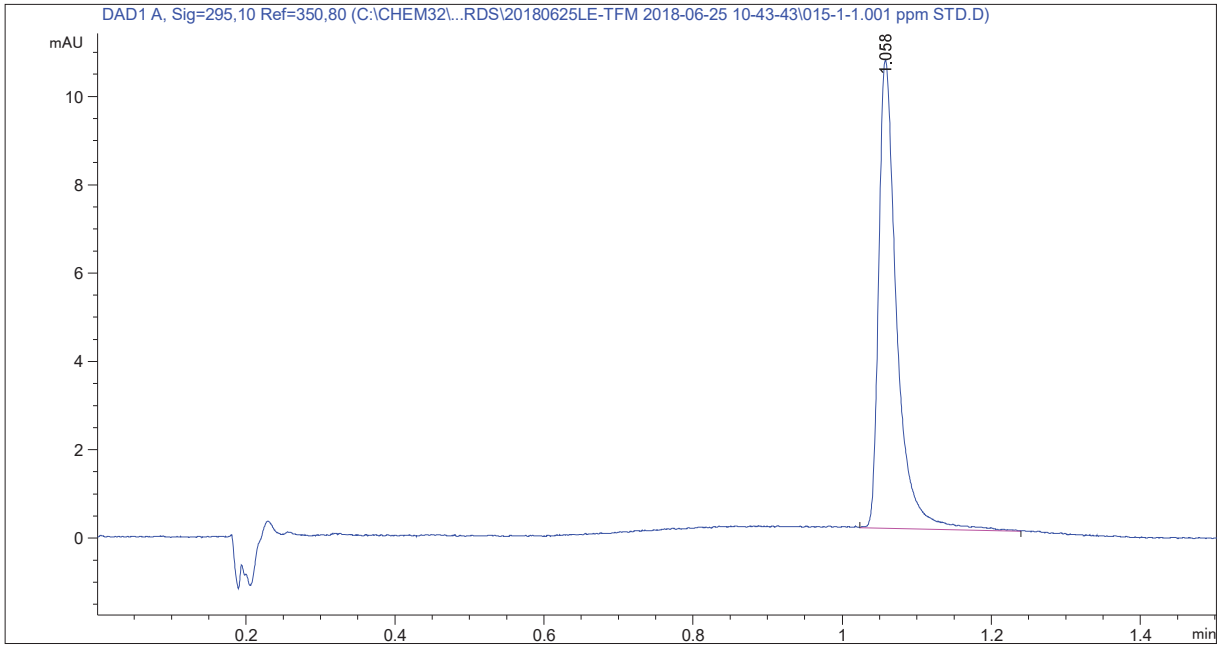



```
    ==================================================================
                              Area Percent Report
    ==================================================================

    Sorted By             :      Signal
    Calib. Data Modified  :      Monday, June 25, 2018 12:25:37 PM
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 A, Sig=295,10 Ref=350,80

    Peak RetTime  Type   Width     Area      Area    Name
      #   [min]          [min]   [mAU*s]       %
    ----|-------|------|-------|----------|--------|---------------------
       1   1.052         0.0000    0.00000   0.0000 TFM

    Totals :                       0.00000


1260 HPLC 6/25/2018 12:28:37 PM Justin Schueller                    Page   1 of 2
```

```
Batch Run # 14 of 21
Data File C:\CHEM32\...018FIELDSTANDARDS\20180625LE-TFM 2018-06-25 10-43-43\014-10-Blank.D
Sample Name: Blank

    1 Warnings or Errors :

    Warning : Calibrated compound(s) not found

    ======================================================================
                            *** End of Report ***
```

Batch Run # 15 of 21
Data File C:\CHEM32\...DSTANDARDS\20180625LE-TFM 2018-06-25 10-43-43\015-1-1.001 ppm STD.D
Sample Name: 1.001 ppm STD

```
==================================================================
Acq. Operator   : Justin Schueller              Seq. Line :  15
Acq. Instrument : 1260 HPLC                      Location :   1
Injection Date  : 6/25/2018 11:19:26 AM               Inj :   1
                                               Inj Volume : 25.000 µl
Acq. Method     : C:\Chem32\1\Data\2018FieldStandards\20180625LE-TFM 2018-06-25 10-43-43\TFM-
                  SOP-409-4-A.M,.M
Last changed    : 6/25/2018 10:43:43 AM by Justin Schueller
Analysis Method : C:\Chem32\1\Data\2018FieldStandards\20180625LE-TFM 2018-06-25 10-43-43\TFM-
                  SOP-409-4-A.M,.M (Sequence Method)
Last changed    : 6/25/2018 12:25:38 PM by Justin Schueller
                  (modified after loading)
```




```
==================================================================
                          Area Percent Report
==================================================================

Sorted By             :      Signal
Calib. Data Modified  :      Monday, June 25, 2018 12:25:37 PM
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=295,10 Ref=350,80

Peak RetTime  Type   Width     Area      Area    Name
  #   [min]          [min]   [mAU*s]       %
----|-------|------|-------|----------|--------|---------------------
   1   1.058 BB      0.0251   17.83201 100.0000 TFM

Totals :                      17.83201
```

1260 HPLC 6/25/2018 12:28:39 PM Justin Schueller Page 1 of 2

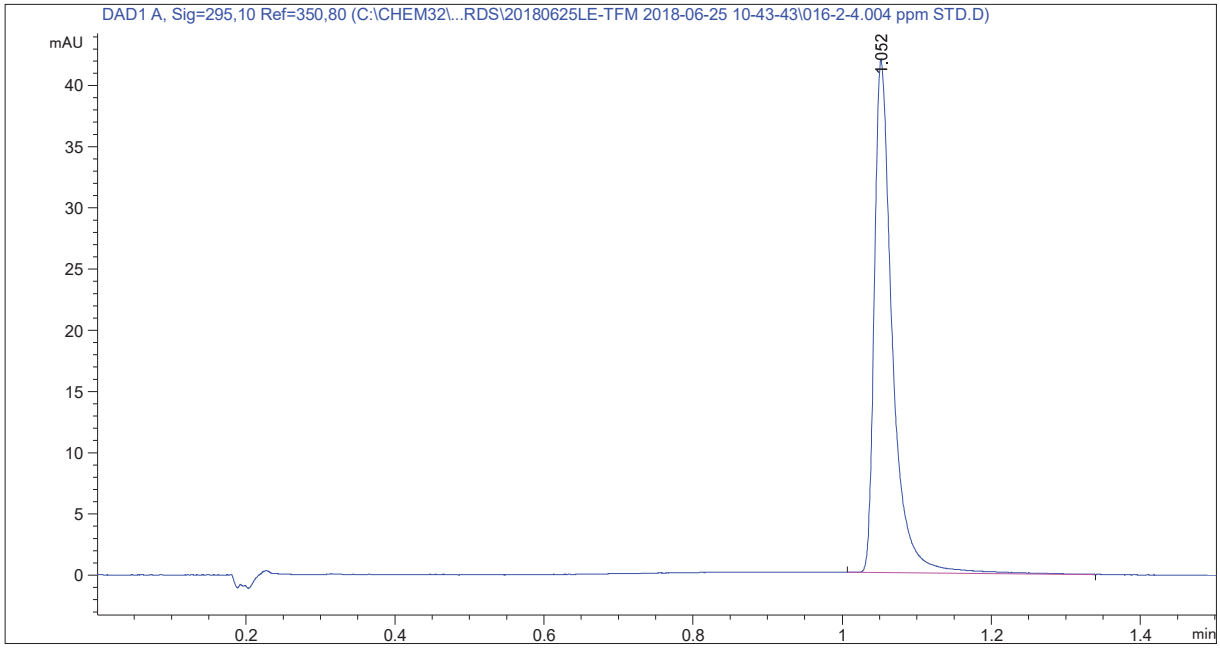
Batch Run # 15 of 21
Data File C:\CHEM32\...DSTANDARDS\20180625LE-TFM 2018-06-25 10-43-43\015-1-1.001 ppm STD.D
Sample Name: 1.001 ppm STD

==========

*** End of Report ***

Batch Run # 16 of 21
Data File C:\CHEM32\...DSTANDARDS\20180625LE-TFM 2018-06-25 10-43-43\016-2-4.004 ppm STD.D
Sample Name: 4.004 ppm STD

```
==================================================================
Acq. Operator   : Justin Schueller              Seq. Line :  16
Acq. Instrument : 1260 HPLC                      Location :   2
Injection Date  : 6/25/2018 11:21:52 AM               Inj :   1
                                               Inj Volume : 25.000 µl
Acq. Method     : C:\Chem32\1\Data\2018FieldStandards\20180625LE-TFM 2018-06-25 10-43-43\TFM-
                  SOP-409-4-A.M,.M
Last changed    : 6/25/2018 10:43:43 AM by Justin Schueller
Analysis Method : C:\Chem32\1\Data\2018FieldStandards\20180625LE-TFM 2018-06-25 10-43-43\TFM-
                  SOP-409-4-A.M,.M (Sequence Method)
Last changed    : 6/25/2018 12:25:38 PM by Justin Schueller
                  (modified after loading)
```




```
==================================================================
                          Area Percent Report
==================================================================

Sorted By             :      Signal
Calib. Data Modified  :      Monday, June 25, 2018 12:25:37 PM
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=295,10 Ref=350,80

Peak RetTime  Type   Width     Area      Area    Name
  #   [min]          [min]   [mAU*s]       %
----|-------|------|-------|----------|--------|---------------------
   1   1.052 BB      0.0251   70.46019 100.0000 TFM

Totals :                      70.46019
```

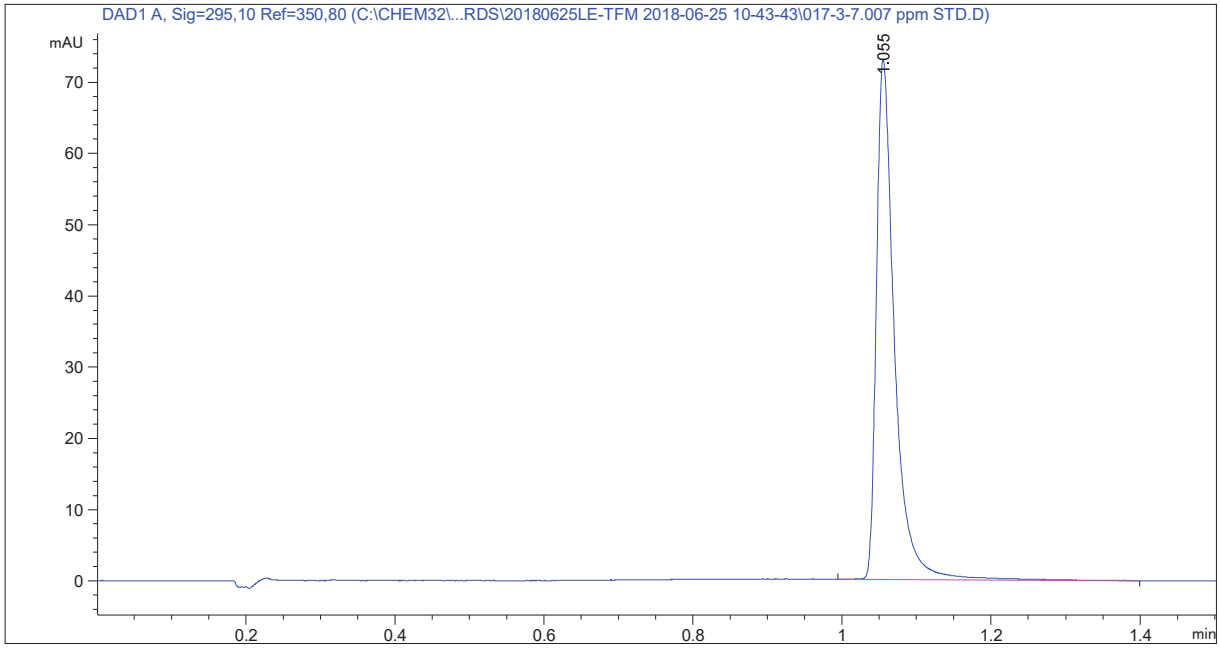
Batch Run # 16 of 21
Data File C:\CHEM32\...DSTANDARDS\20180625LE-TFM 2018-06-25 10-43-43\016-2-4.004 ppm STD.D
Sample Name: 4.004 ppm STD

==========

*** End of Report ***

Batch Run # 17 of 21
Data File C:\CHEM32\...DSTANDARDS\20180625LE-TFM 2018-06-25 10-43-43\017-3-7.007 ppm STD.D
Sample Name: 7.007 ppm STD

```
==================================================================
Acq. Operator   : Justin Schueller              Seq. Line :  17
Acq. Instrument : 1260 HPLC                      Location :   3
Injection Date  : 6/25/2018 11:24:20 AM               Inj :   1
                                               Inj Volume : 25.000 µl
Acq. Method     : C:\Chem32\1\Data\2018FieldStandards\20180625LE-TFM 2018-06-25 10-43-43\TFM-
                  SOP-409-4-A.M,.M
Last changed    : 6/25/2018 10:43:43 AM by Justin Schueller
Analysis Method : C:\Chem32\1\Data\2018FieldStandards\20180625LE-TFM 2018-06-25 10-43-43\TFM-
                  SOP-409-4-A.M,.M (Sequence Method)
Last changed    : 6/25/2018 12:25:38 PM by Justin Schueller
                  (modified after loading)
```




```
==================================================================
                          Area Percent Report
==================================================================

Sorted By             :      Signal
Calib. Data Modified  :      Monday, June 25, 2018 12:25:37 PM
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=295,10 Ref=350,80

Peak RetTime  Type   Width     Area      Area    Name
  #   [min]          [min]   [mAU*s]       %
----|-------|------|-------|----------|--------|---------------------
   1   1.055 BB      0.0253  123.66747 100.0000 TFM

Totals :                     123.66747
```

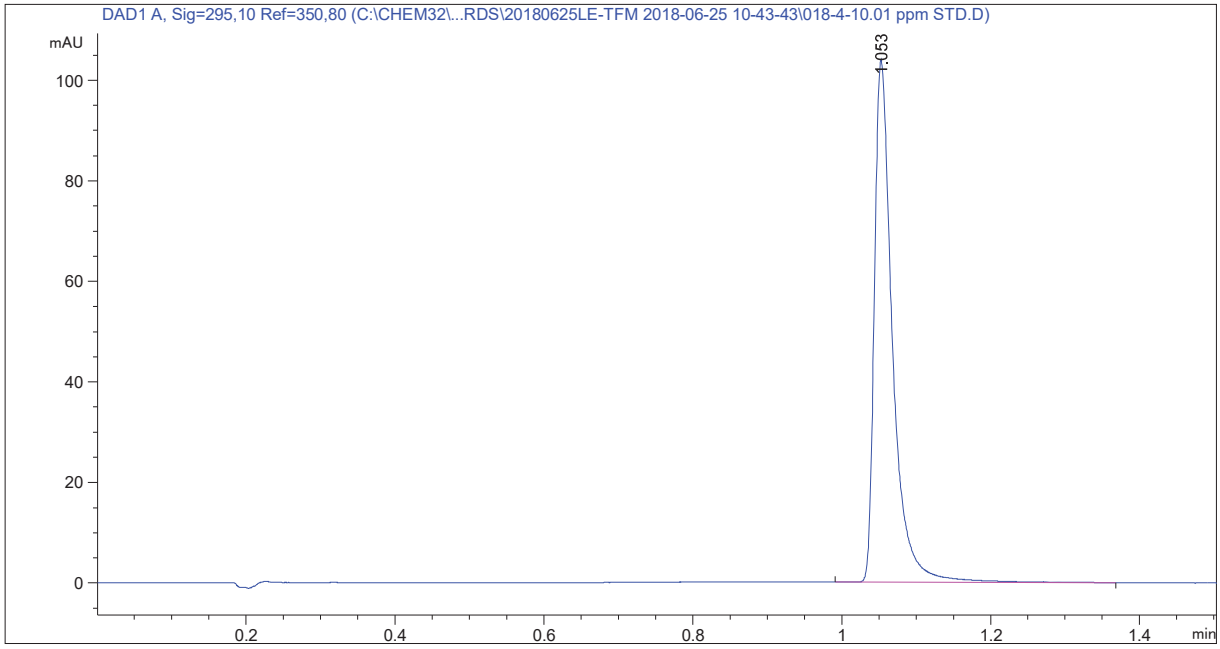
Batch Run # 17 of 21
Data File C:\CHEM32\...DSTANDARDS\20180625LE-TFM 2018-06-25 10-43-43\017-3-7.007 ppm STD.D
Sample Name: 7.007 ppm STD

==========

*** End of Report ***

Batch Run # 18 of 21
Data File C:\CHEM32\...DSTANDARDS\20180625LE-TFM 2018-06-25 10-43-43\018-4-10.01 ppm STD.D
Sample Name: 10.01 ppm STD

```
==================================================================
Acq. Operator   : Justin Schueller              Seq. Line :  18
Acq. Instrument : 1260 HPLC                      Location :   4
Injection Date  : 6/25/2018 11:26:49 AM               Inj :   1
                                               Inj Volume : 25.000 µl
Acq. Method     : C:\Chem32\1\Data\2018FieldStandards\20180625LE-TFM 2018-06-25 10-43-43\TFM-
                  SOP-409-4-A.M,.M
Last changed    : 6/25/2018 10:43:43 AM by Justin Schueller
Analysis Method : C:\Chem32\1\Data\2018FieldStandards\20180625LE-TFM 2018-06-25 10-43-43\TFM-
                  SOP-409-4-A.M,.M (Sequence Method)
Last changed    : 6/25/2018 12:25:38 PM by Justin Schueller
                  (modified after loading)
```



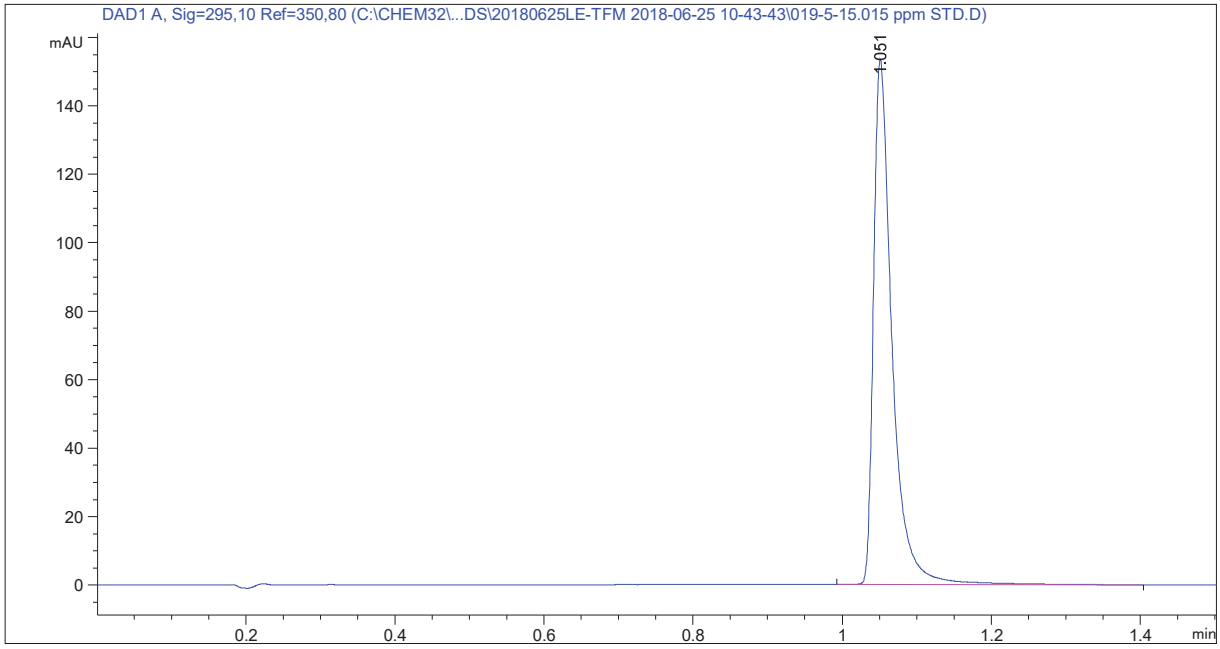

```
==================================================================
                          Area Percent Report
==================================================================

Sorted By             :      Signal
Calib. Data Modified  :      Monday, June 25, 2018 12:25:37 PM
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=295,10 Ref=350,80

Peak RetTime  Type   Width     Area      Area    Name
  #   [min]          [min]   [mAU*s]       %
----|-------|------|-------|----------|--------|---------------------
   1   1.053 BB      0.0258  176.30200 100.0000 TFM

Totals :                     176.30200
```

Batch Run # 18 of 21
Data File C:\CHEM32\...DSTANDARDS\20180625LE-TFM 2018-06-25 10-43-43\018-4-10.01 ppm STD.D
Sample Name: 10.01 ppm STD

==========

*** End of Report ***

```
Batch Run # 19 of 21
Data File C:\CHEM32\...STANDARDS\20180625LE-TFM 2018-06-25 10-43-43\019-5-15.015 ppm STD.D
Sample Name: 15.015 ppm STD

    ======================================================================
    Acq. Operator   : Justin Schueller               Seq. Line :  19
    Acq. Instrument : 1260 HPLC                       Location :   5
    Injection Date  : 6/25/2018 11:29:16 AM                Inj :   1
                                                   Inj Volume : 25.000 µl
    Acq. Method     : C:\Chem32\1\Data\2018FieldStandards\20180625LE-TFM 2018-06-25 10-43-43\TFM-
                      SOP-409-4-A.M,.M
    Last changed    : 6/25/2018 10:43:43 AM by Justin Schueller
    Analysis Method : C:\Chem32\1\Data\2018FieldStandards\20180625LE-TFM 2018-06-25 10-43-43\TFM-
                      SOP-409-4-A.M,.M (Sequence Method)
    Last changed    : 6/25/2018 12:25:38 PM by Justin Schueller
                      (modified after loading)
```




```
    ======================================================================
                              Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Calib. Data Modified  :      Monday, June 25, 2018 12:25:37 PM
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 A, Sig=295,10 Ref=350,80

    Peak RetTime  Type   Width     Area      Area    Name
      #   [min]          [min]   [mAU*s]       %
    ----|-------|------|-------|----------|--------|---------------------
       1   1.051 BB      0.0262  264.93726 100.0000 TFM

    Totals :                     264.93726

1260 HPLC 6/25/2018 12:28:51 PM Justin Schueller                    Page   1 of 2
```

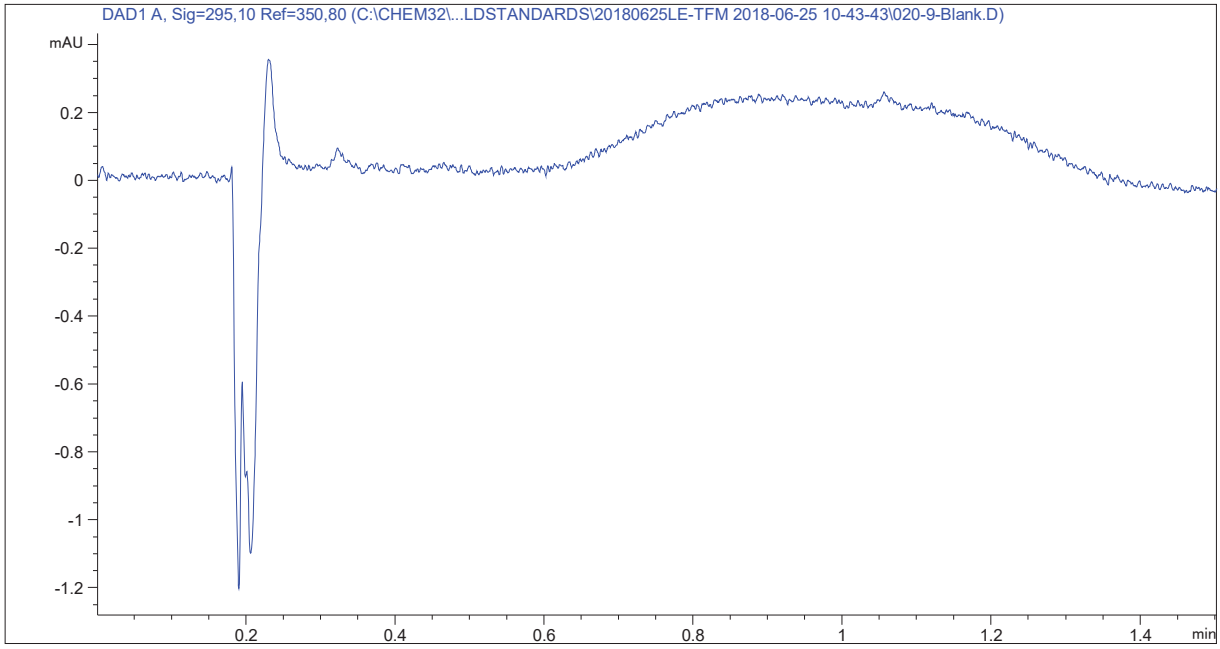
Batch Run # 19 of 21
Data File C:\CHEM32\...STANDARDS\20180625LE-TFM 2018-06-25 10-43-43\019-5-15.015 ppm STD.D
Sample Name: 15.015 ppm STD

==========

*** End of Report ***

Batch Run # 20 of 21
Data File C:\CHEM32\...2018FIELDSTANDARDS\20180625LE-TFM 2018-06-25 10-43-43\020-9-Blank.D
Sample Name: Blank

```
==================================================================
Acq. Operator   : Justin Schueller              Seq. Line :  20
Acq. Instrument : 1260 HPLC                      Location :   9
Injection Date  : 6/25/2018 11:31:45 AM               Inj :   1
                                               Inj Volume : 25.000 µl
Acq. Method     : C:\Chem32\1\Data\2018FieldStandards\20180625LE-TFM 2018-06-25 10-43-43\TFM-
                  SOP-409-4-A.M,.M
Last changed    : 6/25/2018 10:43:43 AM by Justin Schueller
Analysis Method : C:\Chem32\1\Data\2018FieldStandards\20180625LE-TFM 2018-06-25 10-43-43\TFM-
                  SOP-409-4-A.M,.M (Sequence Method)
Last changed    : 6/25/2018 12:25:38 PM by Justin Schueller
                  (modified after loading)
```

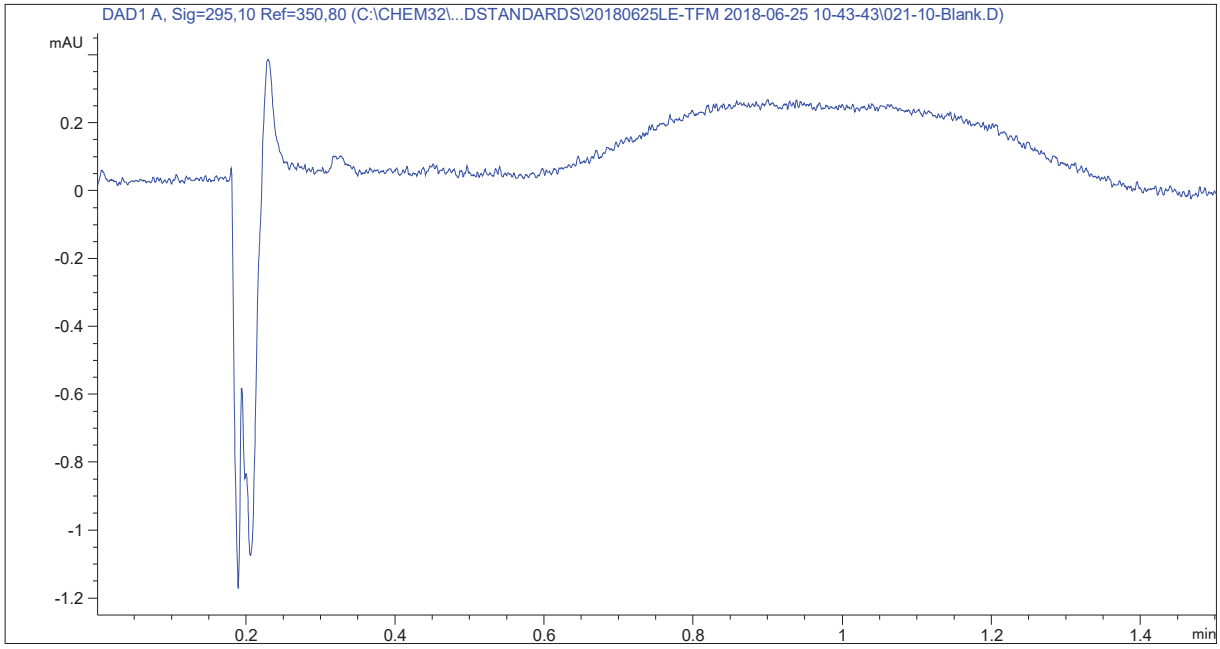



```
==================================================================
                          Area Percent Report
==================================================================

Sorted By             :      Signal
Calib. Data Modified  :      Monday, June 25, 2018 12:25:37 PM
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=295,10 Ref=350,80

Peak RetTime  Type   Width     Area      Area    Name
  #   [min]          [min]   [mAU*s]       %
----|-------|------|-------|----------|--------|---------------------
   1   1.052         0.0000    0.00000   0.0000 TFM

Totals :                       0.00000
```

1260 HPLC 6/25/2018 12:28:54 PM Justin Schueller Page 1 of 2

```
Batch Run # 20 of 21
Data File C:\CHEM32\...2018FIELDSTANDARDS\20180625LE-TFM 2018-06-25 10-43-43\020-9-Blank.D
Sample Name: Blank

    1 Warnings or Errors :

    Warning : Calibrated compound(s) not found

    ======================================================================
                            *** End of Report ***
```

```
Batch Run # 21 of 21
Data File C:\CHEM32\...018FIELDSTANDARDS\20180625LE-TFM 2018-06-25 10-43-43\021-10-Blank.D
Sample Name: Blank

    ==================================================================
    Acq. Operator   : Justin Schueller              Seq. Line :  21
    Acq. Instrument : 1260 HPLC                      Location :   10
    Injection Date  : 6/25/2018 11:34:16 AM               Inj :   1
                                                   Inj Volume : 25.000 µl
    Acq. Method     : C:\Chem32\1\Data\2018FieldStandards\20180625LE-TFM 2018-06-25 10-43-43\TFM-
                      SOP-409-4-A.M,.M
    Last changed    : 6/25/2018 10:43:43 AM by Justin Schueller
    Analysis Method : C:\Chem32\1\Data\2018FieldStandards\20180625LE-TFM 2018-06-25 10-43-43\TFM-
                      SOP-409-4-A.M,.M (Sequence Method)
    Last changed    : 6/25/2018 12:25:38 PM by Justin Schueller
                      (modified after loading)
```




```
    ==================================================================
                            Area Percent Report
    ==================================================================

    Sorted By             :      Signal
    Calib. Data Modified  :      Monday, June 25, 2018 12:25:37 PM
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 A, Sig=295,10 Ref=350,80

    Peak RetTime  Type   Width     Area      Area    Name
      #   [min]          [min]   [mAU*s]       %
    ----|-------|------|-------|----------|--------|---------------------
       1   1.052         0.0000    0.00000   0.0000 TFM

    Totals :                      0.00000


1260 HPLC 6/25/2018 12:28:57 PM Justin Schueller                    Page   1 of 2
```

```
Batch Run # 21 of 21
Data File C:\CHEM32\...018FIELDSTANDARDS\20180625LE-TFM 2018-06-25 10-43-43\021-10-Blank.D
Sample Name: Blank

    1 Warnings or Errors :

    Warning : Calibrated compound(s) not found

    ======================================================================
                            *** End of Report ***
```

Attachment 3: Transfer Documentation for Drinking Water and Stopper Samples from Smithers Avanza Study Number 2410-14374

SMITHERS AVANZA	Sample Submittal / Acknowledgement of Receipt	Doc. Number	FORM0501
		Version	2
		Effective Date	03/21/11
		Replaces	12/28/09
		Replaces FORM	FORM0501v1

Ship To: U.S.Geological Survey
Attention: Steve Lanz, PhD, Chemist
Address: 2630 Fanta Reed Road, La Crosse WI 54603
Phone Number: 608-781-6326

Study Number: 2410-14374
Study Interval: Week 4
Test Article : TFM
Vehicle: Water
Lot/Batch Number: Not Provided
ID Number: 1701B8

Sample Identification *Bulk TA Formulations–Group#; Mix # Vehicle (Circle)*	Dose Level (mg/kg)	Intended Concentration (mg/mL)	Sample Size (stoppers)	Number of samples	Mix Date
G1 – Cage 17	0	NA	1	1	16 May 2018
G7 – Cage 54	1	0.0106	1	1	16 May 2018
G9 – Cage 61	10	0.102	1	1	16 May 2018
G11 – Cage 71	100	1.34	1	1	16 May 2018
Unused	0	NA	1	1	NA

Type of Container:	Amber Glass		**Date of Shipment:**	30-MAR-18
Shipping Conditions:	**Dry Ice** ☐	**Cool Packs** ☐	**Ambient** ☒	**Ice Packs** ☐ **Other** ☐
Method of Recipient Notification (Circle) (Phone/Email/Fax/Other_____)		**Shipped by/Date:**	30 MAY 18	

Prepared By: (Initials/Date)	SVC 5/30/18	Received By: (Sign/Date)	5/31/18
Approved By: (Initials/Date)	30 MAY 2018	Conditions Upon Receipt:	good

****PLEASE SIGN AND RETURN TO: Smithers Avanza, via mail or fax to 240-787-3020****

Smithers Avanza
11 Firstfield Road
Gaithersburg, MD 20878

NOTE: If discrepancies involving the enclosed inventory and package are apparent, please respond formally within three days of receipt.

Reviewed By: KIM FREDRICKS Digitally signed by KIM FREDRICKS Date: 2018.11.26 14:54:14 -06'00' Date: _____

Printed On: 05/30/18 ***CONFIDENTIAL*** Page 1 of 1 Printed On: 05/30/18

SMITHERS AVANZA	Sample Submittal / Acknowledgement of Receipt	Doc. Number	FORM0501
		Version	2
		Effective Date	03/21/11
		Replaces	12/28/09
		Replaces FORM	FORM0501v1

Ship To: U.S.Geological Survey
Attention: Steve Lanz, PhD, Chemist
Address: 2630 Fanta Reed Road, La Crosse WI 54603
Phone Number: 608-781-6326

Study Number: 2410-14374
Study Interval: Week 4
Test Article : TFM
Vehicle: Water
Lot/Batch Number: Not Provided
ID Number: 1701B8

Sample Identification Bulk TA Formulations–Group#; Mix # Vehicle (Circle)	Dose Level (mg/kg)	Intended Concentration (mg/mL)	Sample Size (mL/vial)	Number of samples	Mix Date	Sample leaked when received
G1 - Pre (Predose) Post (Post-Stopper Exposure)	0	NA	10	2	16 May 2018	1 of 2
G7 Pre (Predose) Post (Post-Stopper Exposure)	1	0.0106	10	2	16 May 2018	1 of 2
G9 Pre (Predose) Post (Post-Stopper Exposure)	10	0.102	10	2	16 May 2018	1 of 2
G11 Pre (Predose) Post (Post-Stopper Exposure)	100	1.34	10	2	16 May 2018	0 of 2

Type of Container:	Amber Glass	**Date of Shipment:**	30-MAR-18

Shipping Conditions:	Dry Ice	Cool Packs	Ambient	Ice Packs	Other
	☐	☐	☒	☐	☐

Method of Recipient Notification (Circle) (Phone/Email/Fax/Other_____)		**Shipped by/Date:**	30MAY18

Prepared By: (Initials/Date)	SVC 5/30/18	Received By: (Sign/Date)	5/31/18
Approved By: (Initials/Date)	30MAY2018	Conditions Upon Receipt:	Some vials leaked (see above)

****PLEASE SIGN AND RETURN TO: Smithers Avanza, via mail or fax to 240-787-3020****

Smithers Avanza
11 Firstfield Road
Gaithersburg, MD 20878

NOTE: If discrepancies involving the enclosed inventory and package are apparent, please respond formally within three days of receipt.

Reviewed By: KIM FREDRICKS Digitally signed by KIM FREDRICKS Date: 2018.11.26 14:55:02 -06'00' Date: _____

Printed On: 05/30/18 ***CONFIDENTIAL*** Page 1 of 1 Printed On: 05/30/18

APPENDIX 6: INDIVIDUAL ANIMAL DISPOSITION AND PHYSICAL EXAMINATIONS

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 6: Individual Animal Disposition and Physical Examinations

Day Numbers Relative to Start Date

Group	Sex	Animal	Clinical Sign	Site	1	8	15	22	29	36	43	50	57	64	71	78	85	91
1	m	25234	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25235	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25236	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25237	No Abnormalities Detected		X	X	X	.	.	.	.	.	.	.	.	.	.	X
			Abrasion	Face: Right Side	.	.	.	.	.	.	X	X	X	X	X	X	X	.
			Abrasion	Tail: sacral	.	.	.	X	X	X	X	X	X	.	.	.	.	.
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25238	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25239	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25240	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25241	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25242	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25243	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25244	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	.
		25245	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	.
		25246	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	.
		25247	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	.
		25248	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	.
		25249	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	.
		25250	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	.
		25251	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	.
		25252	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	.
		25253	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	.

Target Dose: Group 1 - 0 mg/kg/day Groups 2 and 7 - 1 mg/kg/day Groups 3 and 8 - 3 mg/kg/day
Groups 4 and 9 - 10 mg/kg/day Groups 5 and 10 - 30 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 6 (continued): Individual Animal Disposition and Physical Examinations

Day Numbers Relative to Start Date

Group	Sex	Animal	Clinical Sign	Site	1	8	15	22	29	36	43	50	57	64	71	78	85	91
2	m	25274	No Abnormalities Detected		X	X	X	X	X	X	.	.	.	.	.	.	.	.
			Abrasion	Face: Left Side	.	.	.	.	.	.	X	X	X	X	X	X	X	X
			Abrasion	Face: Right Side	.	.	.	.	.	.	X	X	X	X	X	.	.	.
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25275	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25276	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25277	No Abnormalities Detected		X	X	X	X	X	X	.	X	X	X	X	X	X	X
			Abrasion	Nose	.	.	.	.	.	.	X	.	.	.	.	.	.	.
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25278	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25279	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25280	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25281	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25282	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25283	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X

Target Dose: Group 1 - 0 mg/kg/day Groups 2 and 7 - 1 mg/kg/day Groups 3 and 8 - 3 mg/kg/day
Groups 4 and 9 - 10 mg/kg/day Groups 5 and 10 - 30 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 6 (continued): Individual Animal Disposition and Physical Examinations

Day Numbers Relative to Start Date

Group	Sex	Animal	Clinical Sign	1	8	15	22	29	36	43	50	57	64	71	78	85	91
3	m	25284	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25285	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25286	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25287	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25288	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25289	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25290	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25291	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25292	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25293	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 6 (continued): Individual Animal Disposition and Physical Examinations

Day Numbers Relative to Start Date

Group	Sex	Animal	Clinical Sign	Site	1	8	15	22	29	36	43	50	57	64	71	78	85	91
4	m	25294	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25295	No Abnormalities Detected		X	X	X	X	.	.	.	.	.	.	.	.	.	.
			Alopecia	Forepaw/hand: Left	.	.	.	.	X	X	X	X	X	X	X	X	X	X
			Alopecia	Forepaw/hand: Right	.	.	.	.	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25296	No Abnormalities Detected		X	X	X	X	X	X	X	.	.	.	.	.	.	.
			Abrasion	Face: Left Side	.	.	.	.	.	.	.	X	X	X	X	X	X	X
			Abrasion	Face: Right Side	.	.	.	.	.	.	.	X	.	.	.	.	.	.
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25297	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25298	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	.	.	.
			Abrasion	Face: Left Side	.	.	.	.	.	.	.	.	.	.	.	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25299	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25300	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25301	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25302	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25303	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 6 (continued): Individual Animal Disposition and Physical Examinations

Day Numbers Relative to Start Date

Group	Sex	Animal	Clinical Sign	1	8	15	22	29	36	43	50	57	64	71	78	85	91
5	m	25304	No Abnormalities Detected	X	X	X	X	.	X	X	X	X	X	X	X	X	X
			Rough Haircoat	.	.	.	.	X	.	.	.	.	.	.	.	.	.
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25305	No Abnormalities Detected	X	X	X	X	.	X	X	X	X	X	X	X	X	X
			Rough Haircoat	.	.	.	.	X	.	.	.	.	.	.	.	.	.
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25306	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25307	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25308	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25309	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25310	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25311	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25312	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25313	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X

Target Dose: Group 1 – 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 6 (continued): Individual Animal Disposition and Physical Examinations

Day Numbers Relative to Start Date

Group	Sex	Animal	Clinical Sign	1	8	15	22	29	36	43	50	57	64	71	78	85	91
6	m	25314	No Abnormalities Detected	X	X	X	X	.	X	X	X	X	X	X	X	X	X
			Rough Haircoat	.	.	.	.	X	.	.	.	.	.	.	.	.	.
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25315	No Abnormalities Detected	X	X	X	X	.	X	X	X	X	X	X	X	X	X
			Rough Haircoat	.	.	.	.	X	.	.	.	.	.	.	.	.	.
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25316	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25317	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25318	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25319	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25320	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25321	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25322	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25323	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X

Target Dose: Group 1 – 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 6 (continued): Individual Animal Disposition and Physical Examinations

Day Numbers Relative to Start Date

Group	Sex	Animal	Clinical Sign	1	8	15	22	29	36	43	50	57	64	71	78	85
6	m	25324	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X
		25325	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X
		25326	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X
		25327	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X
		25328	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X
		25329	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X
		25330	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X
		25331	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X
		25332	No Abnormalities Detected	X	X	X	X	.	X	X	X	X	X	X	X	X
			Rough Haircoat	.	.	.	.	X	.	.	.	.	.	.	.	.
		25333	No Abnormalities Detected	X	X	X	X	.	X	X	X	X	X	X	X	X
			Rough Haircoat	.	.	.	.	X	.	.	.	.	.	.	.	.

Target Dose: Group 1 - 0 mg/kg/day Groups 2 and 7 - 1 mg/kg/day Groups 3 and 8 - 3 mg/kg/day
Groups 4 and 9 - 10 mg/kg/day Groups 5 and 10 - 30 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 6 (continued): Individual Animal Disposition and Physical Examinations

Day Numbers Relative to Start Date

Group	Sex	Animal	Clinical Sign	Site	92	99	106	113	119
1	m	25244	No Abnormalities Detected		X	X	X	X	X
			Terminal Kill		.	.	.	.	X
		25245	No Abnormalities Detected		X	X	X	X	X
			Terminal Kill		.	.	.	.	X
		25246	No Abnormalities Detected		X	X	X	X	X
			Terminal Kill		.	.	.	.	X
		25247	No Abnormalities Detected		X	X	X	X	X
			Terminal Kill		.	.	.	.	X
		25248	No Abnormalities Detected		X	X	X	X	X
			Terminal Kill		.	.	.	.	X
		25249	No Abnormalities Detected		X	X	X	X	X
			Terminal Kill		.	.	.	.	X
		25250	No Abnormalities Detected		X	X	X	X	X
			Terminal Kill		.	.	.	.	X
		25251	No Abnormalities Detected		X	X	X	X	X
			Terminal Kill		.	.	.	.	X
		25252	No Abnormalities Detected		X	X	X	X	X
			Terminal Kill		.	.	.	.	X
		25253	No Abnormalities Detected		X	.	.	.	.
			Alopecia	Inguinal, Left	.	X	X	X	X
			Terminal Kill		.	.	.	.	X

Target Dose: Group 1 - 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 6 (continued): Individual Animal Disposition and Physical Examinations

Day Numbers Relative to Start Date

Group	Sex	Animal	Clinical Sign	92	99	106	113	119
6	m	25324	No Abnormalities Detected	X	X	X	X	X
			Terminal Kill	.	.	.	.	X
		25325	No Abnormalities Detected	X	X	X	X	X
			Terminal Kill	.	.	.	.	X
		25326	No Abnormalities Detected	X	X	X	X	X
			Terminal Kill	.	.	.	.	X
		25327	No Abnormalities Detected	X	X	X	X	X
			Terminal Kill	.	.	.	.	X
		25328	No Abnormalities Detected	X	X	X	X	X
			Terminal Kill	.	.	.	.	X
		25329	No Abnormalities Detected	X	X	X	X	X
			Terminal Kill	.	.	.	.	X
		25330	No Abnormalities Detected	X	X	X	X	X
			Terminal Kill	.	.	.	.	X
		25331	No Abnormalities Detected	X	X	X	X	X
			Terminal Kill	.	.	.	.	X
		25332	No Abnormalities Detected	X	X	X	X	X
			Terminal Kill	.	.	.	.	X
		25333	No Abnormalities Detected	X	X	X	X	X
			Terminal Kill	.	.	.	.	X

Target Dose: Group 1 - 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 6 (continued): Individual Animal Disposition and Physical Examinations

Day Numbers Relative to Start Date

Group	Sex	Animal	Clinical Sign	Site	1	8	15	22	29	36	43	50	57	64	71	78	85	91
1	f	25254	No Abnormalities Detected		X	X	X	X	X	X	.	.	.	.	.	.	.	.
			Abrasion	Face: Right Side	.	.	.	.	.	.	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25255	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25256	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25257	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25258	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25259	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25260	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25261	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25262	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25263	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25264	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	.
		25265	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	.
		25266	No Abnormalities Detected		X	X	X	X	X	.	.	.	.	.	.	X	X	.
			Abrasion	Face: Left Side	.	.	.	.	.	X	X	X	X	X	X	.	.	.
			Abrasion	Face: Right Side	.	.	.	.	.	X	X	X	X	X	X	.	.	.
		25267	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	.
		25268	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	.
		25269	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	.
		25270	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	.
		25271	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	.
		25272	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	.
		25273	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	.

Target Dose: Group 1 - 0 mg/kg/day Groups 2 and 7 - 1 mg/kg/day Groups 3 and 8 - 3 mg/kg/day
Groups 4 and 9 - 10 mg/kg/day Groups 5 and 10 - 30 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 6 (continued): Individual Animal Disposition and Physical Examinations

Day Numbers Relative to Start Date

Group	Sex	Animal	Clinical Sign	1	8	15	22	29	36	43	50	57	64	71	78	85	91
7	f	25334	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25335	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25336	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25337	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25338	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25339	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25340	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25341	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25342	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25343	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X

Target Dose: Group 1 - 0 mg/kg/day Groups 2 and 7 - 1 mg/kg/day Groups 3 and 8 - 3 mg/kg/day
Groups 4 and 9 - 10 mg/kg/day Groups 5 and 10 - 30 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 6 (continued): Individual Animal Disposition and Physical Examinations

Day Numbers Relative to Start Date

Group	Sex	Animal	Clinical Sign	1	8	15	22	29	36	43	50	57	64	71	78	85	91
8	f	25344	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25345	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25346	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25347	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25348	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25349	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25350	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25351	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25352	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25353	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 6 (continued): Individual Animal Disposition and Physical Examinations

Day Numbers Relative to Start Date

Group	Sex	Animal	Clinical Sign	1	8	15	22	29	36	43	50	57	64	71	78	85	91
9	f	25354	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25355	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25356	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25357	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25358	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25359	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25360	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25361	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25362	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25363	No Abnormalities Detected	X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill	.	.	.	.	.	.	.	.	.	.	.	.	.	X

Target Dose: Group 1 - 0 mg/kg/day Groups 2 and 7 - 1 mg/kg/day Groups 3 and 8 - 3 mg/kg/day
Groups 4 and 9 - 10 mg/kg/day Groups 5 and 10 - 30 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 6 (continued): Individual Animal Disposition and Physical Examinations

Day Numbers Relative to Start Date

Group	Sex	Animal	Clinical Sign		1	8	15	22	29	36	43	50	57	64	71	78	85	91
10	f	25364	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25365	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25366	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25367	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25368	No Abnormalities Detected		X	X	X	X	X	X	.	.	.	.	.	.	.	.
			Small Movable Tissue Mass	Abdomen	.	.	.	.	.	.	2	2	2	2	2	2	1	2
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25369	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25370	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25371	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25372	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25373	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X

1 = 0.2 cm or less 2 = 0.3 to 1.0 cm

Target Dose: Group 1 - 0 mg/kg/day Groups 2 and 7 - 1 mg/kg/day Groups 3 and 8 - 3 mg/kg/day
Groups 4 and 9 - 10 mg/kg/day Groups 5 and 10 - 30 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 6 (continued): Individual Animal Disposition and Physical Examinations

Day Numbers Relative to Start Date

Group	Sex	Animal	Clinical Sign	Site	1	8	15	22	29	36	43	50	57	64	71	78	85	91
11	f	25374	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25375	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25376	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25377	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25378	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25379	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25380	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25381	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	.	.	.	.
			Alopecia	Shoulder: Left	.	.	.	.	.	.	.	.	.	.	.	.	X	X
			Alopecia	Shoulder: Right	.	.	.	.	.	.	.	.	.	.	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25382	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25383	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	X
			Terminal Kill		.	.	.	.	.	.	.	.	.	.	.	.	.	X
		25384	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	.
		25385	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	.
		25386	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	.
		25387	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	.
		25388	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	.
		25389	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	.
		25390	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	.
		25391	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	.
		25392	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	.
		25393	No Abnormalities Detected		X	X	X	X	X	X	X	X	X	X	X	X	X	.

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 6 (continued): Individual Animal Disposition and Physical Examinations

Day Numbers Relative to Start Date

Group	Sex	Animal	Clinical Sign	Site	92	99	106	113	119
1	f	25264	No Abnormalities Detected		X	X	X	X	X
			Terminal Kill		.	.	.	.	X
		25265	No Abnormalities Detected		X	X	X	X	X
			Terminal Kill		.	.	.	.	X
		25266	No Abnormalities Detected		X	X	X	.	.
			Abrasion	Face: Left Side	.	.	.	X	X
			Abrasion	Face: Right Side	.	.	.	X	X
			Terminal Kill		.	.	.	.	X
		25267	No Abnormalities Detected		X	X	X	X	X
			Terminal Kill		.	.	.	.	X
		25268	No Abnormalities Detected		X	X	X	X	X
			Terminal Kill		.	.	.	.	X
		25269	No Abnormalities Detected		X	X	X	X	X
			Terminal Kill		.	.	.	.	X
		25270	No Abnormalities Detected		X	X	X	X	X
			Terminal Kill		.	.	.	.	X
		25271	No Abnormalities Detected		X	X	X	X	X
			Terminal Kill		.	.	.	.	X
		25272	No Abnormalities Detected		X	X	X	X	X
			Terminal Kill		.	.	.	.	X
		25273	No Abnormalities Detected		X	X	X	X	X
			Terminal Kill		.	.	.	.	X

Target Dose: Group 1 - 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 6 (continued): Individual Animal Disposition and Physical Examinations

Day Numbers Relative to Start Date

Group	Sex	Animal	Clinical Sign	Site	92	99	106	113	119
11	f	25384	No Abnormalities Detected		X	X	X	X	X
			Terminal Kill		.	.	.	.	X
		25385	No Abnormalities Detected		X	X	X	X	X
			Terminal Kill		.	.	.	.	X
		25386	No Abnormalities Detected		X	X	X	X	X
			Terminal Kill		.	.	.	.	X
		25387	No Abnormalities Detected		X	X	X	X	X
			Terminal Kill		.	.	.	.	X
		25388	No Abnormalities Detected		X	X	X	X	X
			Terminal Kill		.	.	.	.	X
		25389	No Abnormalities Detected		X	.	.	.	.
			Abrasion	Gluteus: Dorsal lumbar	.	X	X	X	X
			Terminal Kill		.	.	.	.	X
		25390	No Abnormalities Detected		X	.	X	X	X
			Discoloration	Face: Left Side	.	R	.	.	.
			Terminal Kill		.	.	.	.	X
		25391	No Abnormalities Detected		X	X	X	X	X
			Terminal Kill		.	.	.	.	X
		25392	No Abnormalities Detected		X	X	X	X	X
			Terminal Kill		.	.	.	.	X
		25393	No Abnormalities Detected		X	.	X	X	X
			Abrasion	Face: Left Side	.	X	.	.	.
			Abrasion	Face: Right Side	.	X	.	.	.
			Terminal Kill		.	.	.	.	X

R = Brown

Target Dose: Group 1 - 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

APPENDIX 7: INDIVIDUAL CAGESIDE OBSERVATIONS

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 7: Individual Cageside Observations

No abnormalities were observed in any animal.

Target Dose:	Group 1 - 0 mg/kg/day	Groups 2 and 7 - 1 mg/kg/day	Groups 3 and 8 - 3 mg/kg/day
	Groups 4 and 9 - 10 mg/kg/day	Groups 5 and 10 - 30 mg/kg/day	Groups 6 and 11 - 100 mg/kg/day

APPENDIX 8: INDIVIDUAL VETERINARIAN EXAMINATIONS/TREATMENTS

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 8: Individual Veterinarian Examinations/Treatments

Day Numbers Relative to Start Date

Group	Sex	Animal	Veterinarian Examination Summary	Treatments	Treatment Study Days
5	m	25304 25305	Rough haircoat, bodyweight loss, decreased food and water consumption	LRS	29
6	m	25314 25315			
		25332 25333		Diet Gel Recovery Pack	29-31
10	f	25368	Small movable tissue mass Dx: Ventral abdomen body wall reducible hernia	-	-

Veterinarian exam day = first treatment day unless otherwise noted
Note: All conditions/observations were resolved or resolving by the end of the specified treatment period unless noted otherwise.

Dx – Diagnosis
LRS – Lactated ringer solution

APPENDIX 9: INDIVIDUAL BODY WEIGHTS

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 9: Individual Body Weights (g)

			Day Numbers Relative to Start Date										
Group	Sex	Animal	1	8	15	22	29	36	43	50	57	64	71
1	m	25234	223.0	280.4	320.7	388.7	432.5	464.8	493.8	514.8	526.2	547.0	535.3
		25235	256.0	322.3	360.9	446.4	488.6	526.9	561.0	578.8	605.1	626.0	611.8
		25236	238.5	297.4	333.0	391.2	424.2	452.6	481.8	504.0	534.7	518.4	513.1
		25237	233.8	290.9	336.2	398.2	441.7	474.4	508.5	533.1	562.2	557.3	555.2
		25238	250.8	297.0	337.9	375.0	411.1	443.3	466.6	483.5	495.4	499.5	484.6
		25239	235.7	301.1	355.3	402.5	464.1	501.1	530.5	559.4	583.8	602.2	580.5
		25240	264.9	304.0	349.7	406.5	442.2	466.7	494.1	512.5	543.7	565.8	575.4
		25241	222.8	262.8	309.0	371.6	407.0	432.1	459.2	487.4	509.7	530.8	538.4
		25242	217.0	279.9	311.4	378.8	424.7	459.1	494.9	520.6	536.9	570.1	567.4
		25243	232.7	293.2	316.8	386.1	423.4	455.0	481.7	502.8	519.6	539.8	533.1
		25244	206.8	256.2	293.7	325.2	346.9	370.1	391.4	408.1	428.7	444.2	451.5
		25245	256.2	311.6	359.6	398.3	422.9	446.3	472.5	496.4	517.4	552.5	559.2
		25246	264.7	320.6	367.8	431.1	472.8	504.3	544.1	572.5	586.1	621.1	592.7
		25247	230.4	288.8	340.3	413.7	457.7	486.3	521.9	545.3	561.1	597.8	561.5
		25248	259.8	302.4	354.9	396.0	435.0	457.7	502.8	524.2	532.9	568.3	555.3
		25249	237.5	279.5	326.7	365.0	393.8	401.4	430.5	452.2	459.1	489.5	484.2
		25250	209.8	258.4	293.1	323.7	344.9	369.3	386.3	398.5	414.4	414.4	421.7
		25251	232.9	303.6	376.9	437.0	491.4	529.0	571.7	603.0	632.8	633.7	644.2
		25252	227.8	268.3	309.5	380.7	426.9	462.9	492.5	520.7	536.2	537.6	534.3
		25253	220.7	280.8	323.9	398.2	445.9	479.9	511.2	535.6	554.0	557.0	544.9
2	m	25274	231.5	271.5	298.9	382.9	432.2	489.5	527.0	558.1	580.2	612.4	604.3
		25275	256.0	313.1	356.2	445.0	502.8	552.2	594.6	612.9	650.5	676.9	680.2
		25276	236.0	298.3	326.1	396.1	436.6	471.8	497.4	525.7	538.2	579.4	569.2
		25277	249.8	316.8	351.4	418.9	458.5	496.1	518.4	546.3	562.6	596.5	581.3
		25278	227.8	287.7	328.2	400.3	451.1	474.7	516.9	544.4	565.9	586.7	582.9
		25279	226.1	274.3	312.1	378.5	419.2	439.5	475.0	499.2	522.6	537.5	527.6
		25280	236.7	300.2	351.4	387.5	437.5	472.5	498.9	518.4	533.6	545.0	547.8
		25281	234.7	298.7	353.4	391.8	437.7	472.8	503.4	526.5	538.5	552.0	549.2
		25282	224.3	284.9	333.7	363.6	401.3	426.0	444.5	461.3	467.3	487.7	499.1
		25283	223.1	286.7	334.6	371.1	407.0	432.6	456.5	473.0	487.3	506.6	517.6

Target Dose: Group 1 - 0 mg/kg/day Groups 2 and 7 - 1 mg/kg/day Groups 3 and 8 - 3 mg/kg/day
Groups 4 and 9 - 10 mg/kg/day Groups 5 and 10 - 30 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 9 (continued): Individual Body Weights (g)

			Day Numbers Relative to Start Date										
Group	Sex	Animal	1	8	15	22	29	36	43	50	57	64	71
3	m	25284	227.6	284.2	330.4	374.3	413.0	443.6	467.9	480.9	495.7	520.9	528.5
		25285	236.6	282.5	317.2	345.0	367.5	390.1	415.0	435.3	438.8	461.1	466.1
		25286	245.9	314.6	354.8	423.9	473.6	524.6	557.5	590.1	584.1	645.2	642.2
		25287	234.3	300.1	332.6	385.6	422.1	454.2	477.2	484.9	490.1	519.6	519.8
		25288	245.8	300.7	340.8	382.9	421.6	457.9	479.9	500.9	503.0	525.7	528.7
		25289	220.2	276.0	318.6	362.5	359.6	409.2	443.0	459.2	469.6	492.1	496.6
		25290	236.1	302.4	357.9	392.7	445.3	471.0	514.6	543.8	555.9	582.3	593.4
		25291	220.7	282.7	336.2	373.0	414.9	434.4	470.6	490.3	504.4	533.9	537.8
		25292	232.1	288.0	321.7	390.1	435.2	457.7	520.9	540.8	568.6	567.1	561.8
		25293	240.7	309.0	348.3	422.2	466.1	490.3	529.6	553.1	578.7	582.5	567.9
4	m	25294	226.5	280.4	330.1	363.7	403.4	428.3	459.0	482.3	487.3	511.3	526.3
		25295	226.6	280.5	348.2	385.0	436.6	458.0	494.5	521.9	527.4	557.2	565.1
		25296	230.9	278.1	312.0	344.9	373.5	391.5	410.8	428.2	437.6	461.4	474.6
		25297	236.2	295.8	345.2	378.9	409.6	432.2	458.1	484.8	493.2	520.9	538.4
		25298	252.3	302.1	353.0	388.7	422.6	452.8	479.6	492.6	501.8	529.6	540.4
		25299	226.4	278.6	326.5	366.0	395.6	426.3	448.7	464.8	487.4	502.9	514.4
		25300	246.4	292.5	336.2	431.2	494.3	536.5	577.0	606.4	641.0	671.5	648.9
		25301	238.0	279.6	321.1	402.0	456.1	488.9	522.7	546.7	575.2	601.1	584.3
		25302	216.8	262.9	284.3	337.3	377.1	412.9	442.5	466.4	451.6	501.7	498.1
		25303	241.0	305.6	345.6	416.2	461.5	489.7	526.4	545.2	539.2	582.8	574.2
5	m	25304	245.7	294.7	336.4	366.1	285.0	387.7	419.0	439.3	452.4	474.3	478.3
		25305	240.4	297.0	343.4	383.6	305.1	405.7	444.8	472.9	492.0	519.4	518.8
		25306	224.9	277.9	321.5	363.1	398.8	428.2	455.5	476.5	480.0	505.8	508.2
		25307	240.5	290.4	338.3	377.3	407.2	429.6	454.8	470.7	480.0	506.8	508.6
		25308	234.8	294.6	329.7	391.6	432.8	462.3	492.2	520.7	536.3	553.6	566.6
		25309	227.1	294.1	333.4	396.3	435.4	465.2	486.8	507.6	518.9	529.8	528.9
		25310	227.9	288.5	348.5	395.1	446.3	470.2	503.0	529.1	526.8	561.1	570.6
		25311	243.0	303.8	358.3	409.0	445.8	468.9	505.0	527.8	527.6	563.2	577.2
		25312	235.4	300.9	356.8	411.0	445.1	467.0	508.1	519.5	526.4	547.9	570.0
		25313	221.2	279.3	326.0	375.2	417.2	434.1	483.4	504.4	509.8	533.6	565.4

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 9 (continued): Individual Body Weights (g)

Day Numbers Relative to Start Date

Group	Sex	Animal	1	8	15	22	29	36	43	50	57	64	71
6	m	25314	248.8	287.6	327.6	366.4	286.5	378.7	416.1	435.9	475.6	479.1	487.6
		25315	228.2	286.1	331.1	372.5	306.1	381.7	419.3	443.3	456.1	492.0	505.6
		25316	216.5	269.6	315.9	351.9	403.7	435.6	461.1	480.8	487.2	518.0	515.4
		25317	230.2	293.5	362.0	402.1	453.7	493.7	530.5	561.8	579.8	621.8	632.3
		25318	210.9	258.6	307.4	337.2	369.2	396.3	414.9	428.9	443.3	470.2	476.4
		25319	217.6	271.8	326.2	368.7	401.5	429.3	450.3	475.4	488.2	513.8	524.5
		25320	269.7	332.9	385.3	430.6	464.2	492.4	515.9	535.2	562.5	573.3	595.1
		25321	228.6	277.0	330.5	369.1	404.1	434.8	462.4	477.0	492.9	500.8	516.1
		25322	224.4	283.1	342.3	377.6	418.6	438.9	465.5	485.6	504.2	518.1	527.0
		25323	209.8	239.3	275.4	297.2	318.1	327.7	349.5	362.7	379.2	385.1	393.4
		25324	216.5	270.8	319.2	360.4	410.2	433.3	465.4	492.4	498.5	524.6	531.6
		25325	238.2	302.8	354.9	396.5	451.4	492.2	525.9	546.5	563.1	594.2	599.2
		25326	230.8	287.5	349.1	400.5	436.1	475.6	511.2	534.5	536.5	571.5	590.3
		25327	264.1	312.6	359.9	401.0	436.3	454.9	487.9	501.8	512.1	540.1	554.4
		25328	260.4	312.9	364.6	390.4	442.2	470.4	495.9	516.1	528.0	546.3	552.3
		25329	242.3	299.7	363.1	395.6	458.0	482.5	519.8	533.8	558.8	562.2	571.4
		25330	256.6	302.2	348.4	388.3	426.5	451.5	470.7	486.6	508.8	507.2	508.2
		25331	263.7	317.3	366.7	398.6	438.3	467.3	489.8	512.3	528.0	530.3	538.1
		25332	240.9	284.3	304.0	359.9	290.3	376.2	406.5	429.8	437.9	460.1	473.8
		25333	237.8	285.9	318.4	397.8	309.8	426.0	470.0	500.7	519.9	549.4	568.0

Target Dose: Group 1 - 0 mg/kg/day Groups 2 and 7 - 1 mg/kg/day Groups 3 and 8 - 3 mg/kg/day
Groups 4 and 9 - 10 mg/kg/day Groups 5 and 10 - 30 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 9 (continued): Individual Body Weights (g)

			Day Numbers Relative to Start Date									
Group	Sex	Animal	78	85	90	91F	92	99	106	113	118	119F
1	m	25234	584.5	608.1	610.2	589.6	.	.	.	.	.	.
		25235	661.1	678.1	682.1	658.0	.	.	.	.	.	.
		25236	568.6	581.4	576.7	558.5	.	.	.	.	.	.
		25237	610.9	631.4	638.6	618.6	.	.	.	.	.	.
		25238	530.2	551.2	546.9	532.3	.	.	.	.	.	.
		25239	629.7	640.0	638.0	611.7	.	.	.	.	.	.
		25240	607.0	606.2	601.0	584.9	.	.	.	.	.	.
		25241	573.3	587.4	593.9	577.5	.	.	.	.	.	.
		25242	602.9	621.8	621.3	601.4	.	.	.	.	.	.
		25243	577.8	597.6	598.6	578.0	.	.	.	.	.	.
		25244	466.9	473.9	.	.	468.6	484.9	499.7	508.9	509.7	497.5
		25245	597.2	602.2	.	.	597.1	614.8	636.1	650.7	647.5	635.5
		25246	616.1	655.7	.	.	638.0	675.5	701.1	709.3	718.2	697.8
		25247	600.3	634.5	.	.	610.7	653.3	673.6	683.1	679.9	662.8
		25248	600.3	615.0	.	.	618.7	636.3	648.6	654.1	657.5	644.5
		25249	518.3	530.7	.	.	539.4	566.2	581.7	589.8	593.0	577.1
		25250	452.9	462.6	.	.	468.9	482.5	488.5	492.4	498.5	486.0
		25251	703.3	723.3	.	.	729.7	774.7	794.5	806.7	813.6	788.9
		25252	583.3	607.5	.	.	601.0	646.8	675.1	685.6	692.5	671.6
		25253	591.0	600.9	.	.	593.8	624.9	639.4	657.5	657.9	639.1
2	m	25274	641.1	662.0	670.1	649.2	.	.	.	.	.	.
		25275	729.4	761.6	770.9	749.9	.	.	.	.	.	.
		25276	621.0	633.0	643.0	624.0	.	.	.	.	.	.
		25277	618.9	640.4	643.1	619.2	.	.	.	.	.	.
		25278	613.1	622.2	624.6	603.5	.	.	.	.	.	.
		25279	559.3	568.9	574.0	557.3	.	.	.	.	.	.
		25280	605.2	615.2	611.5	599.2	.	.	.	.	.	.
		25281	604.9	614.4	612.4	607.5	.	.	.	.	.	.
		25282	517.3	520.7	516.3	503.9	.	.	.	.	.	.
		25283	537.2	541.0	539.7	525.7	.	.	.	.	.	.

F = Fasted

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 9 (continued): Individual Body Weights (g)

			Day Numbers Relative to Start Date			
Group	Sex	Animal	78	85	90	91F
3	m	25284	554.0	574.4	586.5	573.3
		25285	488.2	498.6	498.1	485.2
		25286	687.3	701.8	702.8	685.8
		25287	546.2	553.0	551.0	535.3
		25288	569.2	580.7	584.9	565.8
		25289	545.7	562.5	563.1	550.3
		25290	620.4	624.4	621.7	597.6
		25291	562.5	576.2	580.9	558.4
		25292	609.5	625.2	627.2	616.8
		25293	616.8	630.0	632.5	615.4
4	m	25294	550.0	556.0	558.7	538.6
		25295	594.3	607.1	610.2	593.8
		25296	487.3	490.3	495.2	476.6
		25297	558.5	564.3	563.6	549.5
		25298	559.3	576.1	575.2	552.8
		25299	534.2	550.3	552.6	536.6
		25300	713.4	732.6	738.0	715.1
		25301	635.2	647.0	650.1	632.3
		25302	545.2	553.2	553.8	538.5
		25303	612.1	626.0	626.0	610.1
5	m	25304	499.2	509.3	506.1	496.9
		25305	545.7	558.7	559.4	541.5
		25306	545.9	564.0	565.7	544.0
		25307	542.3	556.1	561.0	545.1
		25308	617.6	637.3	632.5	610.9
		25309	565.3	575.6	572.2	560.3
		25310	597.2	607.9	608.7	595.2
		25311	602.2	610.5	605.0	588.2
		25312	589.6	592.4	601.4	595.8
		25313	583.3	594.0	592.0	572.0

F = Fasted

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 9 (continued): Individual Body Weights (g)

Day Numbers Relative to Start Date

Group	Sex	Animal	78	85	90	91F	92	99	106	113	118	119F
6	m	25314	507.1	509.7	511.6	497.2	.	.	.	.	.	.
		25315	521.0	534.0	534.9	524.8	.	.	.	.	.	.
		25316	541.8	550.7	551.0	540.9	.	.	.	.	.	.
		25317	665.5	692.0	692.1	681.1	.	.	.	.	.	.
		25318	497.1	505.5	517.1	504.4	.	.	.	.	.	.
		25319	543.7	553.6	557.7	541.0	.	.	.	.	.	.
		25320	624.0	628.2	629.6	616.8	.	.	.	.	.	.
		25321	541.2	541.3	546.8	533.1	.	.	.	.	.	.
		25322	547.9	544.4	544.9	529.3	.	.	.	.	.	.
		25323	406.2	404.5	400.7	399.0	.	.	.	.	.	.
		25324	558.9	552.5	.	.	553.3	594.4	615.8	634.4	644.1	629.9
		25325	633.3	628.9	.	.	622.2	663.6	680.9	694.5	697.3	681.0
		25326	616.1	629.7	.	.	632.2	679.1	708.8	736.4	743.9	725.9
		25327	572.1	583.7	.	.	579.9	612.2	630.4	644.2	652.7	636.9
		25328	568.5	572.2	.	.	579.1	615.5	624.4	648.1	645.9	623.4
		25329	597.1	600.6	.	.	613.5	640.9	660.7	671.3	675.1	658.2
		25330	548.7	553.8	.	.	559.0	591.6	616.6	634.8	632.5	621.3
		25331	576.6	585.2	.	.	580.2	620.3	651.1	664.5	676.1	655.4
		25332	484.2	491.5	.	.	510.5	524.8	537.6	549.7	555.9	538.1
		25333	581.5	589.2	.	.	608.2	629.8	647.2	662.7	669.6	656.0

F = Fasted

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 9 (continued): Individual Body Weights (g)

			Day Numbers Relative to Start Date										
Group	Sex	Animal	1	8	15	22	29	36	43	50	57	64	71
1	f	25254	167.5	200.5	229.1	241.7	254.9	262.9	275.8	283.9	295.8	295.6	310.4
		25255	164.3	185.9	207.8	219.6	229.7	229.9	250.5	251.3	256.6	261.0	271.1
		25256	173.1	197.9	219.8	227.2	239.5	245.6	255.5	265.5	252.6	250.1	251.5
		25257	171.1	193.4	211.5	219.3	223.4	234.2	250.5	252.5	256.8	269.2	275.9
		25258	176.3	206.5	234.7	249.8	268.4	277.7	289.4	301.2	313.3	328.8	335.2
		25259	156.3	175.4	199.6	209.6	218.5	224.5	232.6	239.0	243.5	244.9	251.1
		25260	170.2	190.9	208.8	226.0	240.8	254.0	260.8	268.1	276.0	284.6	289.7
		25261	181.5	211.4	241.2	254.6	267.4	279.0	301.5	312.3	321.6	330.8	344.4
		25262	163.0	186.6	208.0	226.9	247.9	250.5	259.6	269.5	278.8	283.4	283.5
		25263	175.9	212.9	229.5	246.9	262.7	267.7	274.8	286.2	292.4	297.1	299.5
		25264	163.0	186.9	204.2	212.7	220.3	232.5	242.3	246.9	254.4	266.1	268.3
		25265	175.6	201.7	223.2	227.9	230.1	244.5	265.3	269.0	273.0	288.0	295.1
		25266	163.4	198.2	212.0	229.1	245.6	251.0	266.2	265.9	279.1	276.9	286.1
		25267	187.6	214.5	237.6	254.6	265.3	271.1	285.1	294.0	305.7	305.3	318.1
		25268	189.5	207.6	233.3	240.5	254.5	259.9	274.5	275.7	281.9	284.1	285.9
		25269	178.3	210.8	236.9	247.0	249.7	268.5	280.4	283.7	286.1	303.0	311.6
		25270	163.5	186.4	212.2	227.4	240.2	244.5	264.4	278.0	287.1	288.8	302.7
		25271	168.5	197.8	218.0	242.8	260.9	266.3	276.7	287.5	301.7	305.0	309.2
		25272	172.8	204.8	234.8	250.3	260.8	264.8	281.8	289.6	296.8	298.4	307.7
		25273	178.5	203.9	223.1	239.9	248.7	257.5	269.4	275.2	280.3	294.8	310.8
7	f	25334	172.9	192.5	202.9	205.9	221.4	226.2	232.1	232.8	243.7	250.6	251.8
		25335	182.0	207.1	225.3	232.0	247.4	251.3	258.8	257.2	266.2	277.2	279.0
		25336	171.7	199.2	215.9	231.8	245.9	261.7	273.8	284.8	298.3	296.3	310.3
		25337	172.8	199.4	232.5	247.6	268.0	277.9	291.9	296.1	306.4	303.6	315.7
		25338	172.6	194.1	217.3	228.6	239.6	242.8	259.0	270.3	280.4	282.8	292.5
		25339	169.9	200.1	218.1	227.7	248.2	260.2	273.8	276.3	292.4	295.8	295.8
		25340	164.0	184.5	191.2	209.9	216.6	221.0	221.1	232.1	239.9	248.2	242.5
		25341	163.0	194.8	217.1	228.2	235.3	251.5	262.1	267.5	274.5	283.9	291.0
		25342	176.2	207.8	228.2	240.0	249.6	261.8	272.2	279.6	294.5	293.8	300.4
		25343	178.0	204.0	223.3	241.4	259.7	266.4	274.3	280.2	292.1	294.2	296.4

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 9 (continued): Individual Body Weights (g)

			Day Numbers Relative to Start Date										
Group	Sex	Animal	1	8	15	22	29	36	43	50	57	64	71
8	f	25344	183.1	217.9	241.5	260.4	276.1	287.0	293.6	295.7	309.4	313.6	321.4
		25345	168.3	189.1	211.5	222.2	230.8	233.1	243.1	251.1	263.7	264.8	270.2
		25346	178.5	203.0	213.3	221.2	227.0	238.7	241.1	246.4	255.4	253.8	257.8
		25347	179.8	211.0	230.6	248.6	259.5	268.0	274.0	288.4	299.3	305.1	308.1
		25348	167.5	198.0	225.5	239.2	245.6	255.8	266.9	276.1	287.0	295.4	304.0
		25349	182.8	205.2	217.8	227.0	239.6	244.8	249.7	261.3	275.4	278.5	279.6
		25350	171.7	200.6	221.5	231.8	233.9	247.4	256.5	256.3	250.5	265.8	271.6
		25351	165.4	179.3	191.0	202.1	217.7	217.8	229.2	233.3	236.8	238.9	247.9
		25352	166.5	181.2	201.1	229.7	246.2	254.8	265.4	269.5	279.3	294.2	295.5
		25353	182.4	195.2	211.0	243.0	268.0	276.8	287.4	293.4	301.4	318.2	320.5
9	f	25354	177.7	216.4	242.5	262.2	275.4	289.6	300.4	301.4	318.9	329.2	336.2
		25355	171.5	198.6	217.4	224.5	243.1	250.9	263.6	265.2	281.0	292.9	299.2
		25356	182.0	208.0	224.0	233.1	243.7	254.6	259.0	258.6	274.7	282.2	283.9
		25357	160.9	186.0	202.2	212.1	219.2	232.0	241.7	245.9	253.7	262.8	273.1
		25358	164.1	199.5	220.4	228.0	244.7	250.5	266.1	272.4	283.6	287.0	291.8
		25359	163.8	197.0	217.2	233.3	241.9	258.0	272.1	278.0	282.1	295.3	305.3
		25360	172.3	192.9	223.9	240.6	256.7	263.6	284.8	283.3	292.6	298.8	312.3
		25361	163.2	192.4	219.2	235.9	252.6	260.5	271.6	273.2	284.1	287.5	288.2
		25362	172.8	187.9	212.6	227.3	242.1	250.8	261.1	266.7	278.9	285.5	296.9
		25363	178.7	193.1	214.9	221.1	232.1	239.4	250.7	258.0	265.9	267.4	279.0
10	f	25364	171.6	192.8	212.4	220.1	233.0	240.0	250.3	257.3	262.5	263.4	273.0
		25365	179.9	211.7	231.0	246.3	260.2	275.4	280.1	292.8	305.4	317.6	319.2
		25366	162.1	175.4	194.5	204.4	212.1	214.9	225.7	229.6	233.3	232.0	238.2
		25367	160.8	192.2	208.9	226.5	238.0	249.5	259.2	269.3	280.4	286.0	294.8
		25368	171.4	199.0	222.0	236.2	246.2	257.9	269.0	274.2	278.6	284.7	296.1
		25369	178.2	215.9	239.1	247.9	267.2	279.7	284.8	285.7	301.5	303.3	312.8
		25370	167.5	181.8	207.1	225.3	237.9	241.9	258.2	262.8	265.2	263.1	279.2
		25371	172.9	184.5	218.4	242.1	256.4	264.6	282.2	279.0	294.9	309.3	304.3
		25372	156.8	175.0	193.9	198.9	202.2	216.2	226.7	232.4	239.2	242.9	249.2
		25373	180.5	207.1	228.9	236.0	241.7	256.7	268.3	273.4	283.5	292.7	305.5

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 9 (continued): Individual Body Weights (g)

			Day Numbers Relative to Start Date										
Group	Sex	Animal	1	8	15	22	29	36	43	50	57	64	71
11	f	25374	189.9	227.3	256.1	276.0	292.7	305.0	313.2	317.9	330.3	327.5	340.1
		25375	189.1	213.7	234.3	244.6	259.5	274.7	279.1	280.5	293.9	298.6	303.5
		25376	162.8	182.3	204.0	218.4	221.3	232.5	234.8	245.9	249.2	246.0	259.0
		25377	160.1	177.3	191.8	202.8	207.9	210.8	220.4	222.0	227.2	233.4	239.1
		25378	173.2	199.8	221.1	226.6	235.4	247.7	256.9	262.3	265.0	274.5	280.6
		25379	171.7	203.1	225.2	236.9	253.1	261.6	272.3	283.7	289.8	298.5	301.0
		25380	167.6	202.7	233.3	250.1	270.9	283.9	288.6	300.9	291.9	317.6	300.6
		25381	176.9	206.0	228.8	243.3	261.6	270.8	281.3	293.4	281.5	303.0	292.2
		25382	170.1	182.4	193.3	211.7	219.7	226.9	231.1	242.0	247.6	250.9	254.7
		25383	163.1	189.2	207.2	218.3	233.4	243.0	251.9	253.1	266.1	271.8	280.4
		25384	184.6	202.1	219.0	238.7	257.8	275.1	284.3	298.5	309.5	317.1	322.5
		25385	180.9	202.9	231.9	250.1	261.6	272.7	289.0	298.6	308.4	315.3	334.8
		25386	185.4	202.0	222.4	231.3	244.6	245.5	259.4	265.3	255.6	269.2	279.9
		25387	161.5	179.1	207.5	216.8	231.3	229.7	243.6	243.8	239.2	262.0	258.6
		25388	175.5	197.7	220.7	238.1	253.4	258.7	269.4	274.3	278.8	276.7	286.7
		25389	162.0	185.0	197.6	210.1	230.2	237.3	238.0	245.8	250.8	254.1	262.7
		25390	177.3	193.7	217.1	224.3	235.9	240.0	253.9	258.8	262.2	261.3	270.0
		25391	156.1	177.9	192.1	203.8	205.0	218.3	222.3	227.5	224.6	236.9	238.2
		25392	173.5	202.5	220.2	241.0	252.1	263.8	273.2	284.1	279.7	289.4	296.7
		25393	158.2	182.4	203.0	211.0	217.4	235.1	245.3	249.7	251.9	264.0	273.5

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 9 (continued): Individual Body Weights (g)

			Day Numbers Relative to Start Date									
Group	Sex	Animal	78	85	90	91F	92	99	106	113	118	119F
1	f	25254	308.3	309.5	309.6	293.7	.	.	.	.	.	.
		25255	270.5	270.8	268.1	254.5	.	.	.	.	.	.
		25256	246.5	238.8	241.2	230.8	.	.	.	.	.	.
		25257	275.8	275.8	278.9	268.8	.	.	.	.	.	.
		25258	340.1	344.8	342.9	331.8	.	.	.	.	.	.
		25259	256.2	254.6	254.0	238.5	.	.	.	.	.	.
		25260	297.4	297.1	295.7	283.9	.	.	.	.	.	.
		25261	346.5	340.7	344.4	332.5	.	.	.	.	.	.
		25262	287.6	290.1	288.3	278.3	.	.	.	.	.	.
		25263	308.2	308.4	305.1	291.6	.	.	.	.	.	.
		25264	269.2	269.5	.	.	271.5	278.0	278.8	282.8	281.0	270.2
		25265	292.2	291.8	.	.	301.9	309.1	316.6	325.7	317.6	306.0
		25266	289.6	280.0	.	.	279.3	288.8	295.8	297.6	302.4	288.3
		25267	316.3	316.6	.	.	315.3	328.9	337.7	347.2	344.0	333.7
		25268	294.7	294.5	.	.	286.2	297.4	300.6	312.7	307.9	293.5
		25269	308.1	296.8	.	.	287.4	309.3	320.5	329.3	321.9	311.3
		25270	305.7	299.2	.	.	294.9	310.2	322.4	326.2	329.4	314.4
		25271	316.3	311.8	.	.	317.1	335.6	349.2	356.8	357.0	344.0
		25272	321.7	316.2	.	.	315.2	321.5	327.8	340.5	336.6	327.9
		25273	314.7	323.7	.	.	329.2	342.3	346.7	376.4	391.3	372.7
7	f	25334	252.7	246.0	248.4	240.7	.	.	.	.	.	.
		25335	282.2	283.7	279.6	273.2	.	.	.	.	.	.
		25336	319.7	326.1	331.9	316.2	.	.	.	.	.	.
		25337	322.0	322.1	322.2	307.2	.	.	.	.	.	.
		25338	294.3	292.6	295.0	283.6	.	.	.	.	.	.
		25339	308.4	309.4	308.1	295.4	.	.	.	.	.	.
		25340	252.1	258.4	257.3	247.1	.	.	.	.	.	.
		25341	293.7	287.0	292.8	281.8	.	.	.	.	.	.
		25342	304.8	308.5	304.6	295.8	.	.	.	.	.	.
		25343	311.4	310.6	310.3	298.6	.	.	.	.	.	.

F = Fasted

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 9 (continued): Individual Body Weights (g)

			Day Numbers Relative to Start Date			
Group	Sex	Animal	78	85	90	91F
8	f	25344	323.0	327.6	325.4	316.7
		25345	274.0	268.4	267.8	256.4
		25346	262.9	260.2	265.7	258.1
		25347	321.1	318.2	317.0	303.5
		25348	303.9	302.5	302.2	293.9
		25349	288.1	291.1	290.4	278.3
		25350	277.8	274.3	274.3	269.2
		25351	254.9	249.4	257.0	247.1
		25352	300.4	298.4	292.2	291.3
		25353	328.3	328.7	324.8	319.8
9	f	25354	347.7	346.0	350.2	343.8
		25355	303.9	301.5	304.6	287.9
		25356	280.6	284.8	281.6	274.9
		25357	268.7	271.5	267.5	264.3
		25358	298.5	288.7	291.0	279.1
		25359	305.3	296.3	303.0	295.0
		25360	310.8	317.4	316.8	302.3
		25361	296.4	290.1	286.7	284.3
		25362	304.6	304.7	306.9	289.0
		25363	278.7	280.5	279.3	269.3
10	f	25364	279.3	277.7	277.5	264.6
		25365	320.4	316.4	323.1	308.8
		25366	239.9	233.3	238.8	227.1
		25367	298.7	301.3	297.1	287.4
		25368	299.1	291.4	292.4	279.7
		25369	317.1	318.6	314.1	304.5
		25370	279.4	275.8	281.0	267.1
		25371	319.8	311.2	310.1	299.2
		25372	258.7	259.5	263.9	252.7
		25373	306.7	296.8	300.8	294.8

F = Fasted

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 9 (continued): Individual Body Weights (g)

Day Numbers Relative to Start Date

Group	Sex	Animal	78	85	90	91F	92	99	106	113	118	119F
11	f	25374	337.2	337.9	339.7	328.2	.	.	.	.	.	.
		25375	304.3	305.5	298.7	296.4	.	.	.	.	.	.
		25376	267.4	266.7	266.5	254.2	.	.	.	.	.	.
		25377	234.8	235.9	234.8	226.0	.	.	.	.	.	.
		25378	278.2	280.8	276.6	271.9	.	.	.	.	.	.
		25379	304.5	296.3	300.7	296.6	.	.	.	.	.	.
		25380	326.9	324.1	322.7	315.8	.	.	.	.	.	.
		25381	312.2	312.4	308.1	304.7	.	.	.	.	.	.
		25382	264.9	258.9	264.5	253.0	.	.	.	.	.	.
		25383	288.2	291.7	289.6	285.6	.	.	.	.	.	.
		25384	333.4	337.9	.	.	344.0	363.6	367.5	396.1	394.6	375.5
		25385	338.5	337.3	.	.	334.9	357.7	373.5	376.2	371.4	355.1
		25386	283.5	278.8	.	.	289.0	299.1	311.6	312.0	311.8	298.2
		25387	268.4	260.0	.	.	270.0	284.4	280.8	295.2	294.6	280.7
		25388	286.1	293.5	.	.	294.2	304.2	307.2	326.6	321.6	305.6
		25389	260.4	264.3	.	.	269.9	275.0	282.5	283.6	284.5	270.6
		25390	278.6	269.7	.	.	276.0	288.4	296.3	297.4	298.9	281.4
		25391	236.6	233.1	.	.	240.7	259.0	261.3	264.5	264.8	253.8
		25392	302.2	279.9	.	.	301.1	311.6	309.6	327.2	317.6	306.2
		25393	273.2	266.5	.	.	285.6	300.5	307.9	308.6	310.2	296.8

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

APPENDIX 10: INDIVIDUAL BODY WEIGHT CHANGES

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 10: Individual Body Weight Changes (g)

Day Numbers Relative to Start Date

Group	Sex	Animal	From: 1 To: 8	8 15	15 22	22 29	29 36	36 43	43 50	50 57	57 64	64 71	71 78	78 85
1	m	25234	57.4	40.3	68.0	43.8	32.3	29.0	21.0	11.4	20.8	-11.7	49.2	23.6
		25235	66.3	38.6	85.5	42.2	38.3	34.1	17.8	26.3	20.9	-14.2	49.3	17.0
		25236	58.9	35.6	58.2	33.0	28.4	29.2	22.2	30.7	-16.3	-5.3	55.5	12.8
		25237	57.1	45.3	62.0	43.5	32.7	34.1	24.6	29.1	-4.9	-2.1	55.7	20.5
		25238	46.2	40.9	37.1	36.1	32.2	23.3	16.9	11.9	4.1	-14.9	45.6	21.0
		25239	65.4	54.2	47.2	61.6	37.0	29.4	28.9	24.4	18.4	-21.7	49.2	10.3
		25240	39.1	45.7	56.8	35.7	24.5	27.4	18.4	31.2	22.1	9.6	31.6	-0.8
		25241	40.0	46.2	62.6	35.4	25.1	27.1	28.2	22.3	21.1	7.6	34.9	14.1
		25242	62.9	31.5	67.4	45.9	34.4	35.8	25.7	16.3	33.2	-2.7	35.5	18.9
		25243	60.5	23.6	69.3	37.3	31.6	26.7	21.1	16.8	20.2	-6.7	44.7	19.8
		25244	49.4	37.5	31.5	21.7	23.2	21.3	16.7	20.6	15.5	7.3	15.4	7.0
		25245	55.4	48.0	38.7	24.6	23.4	26.2	23.9	21.0	35.1	6.7	38.0	5.0
		25246	55.9	47.2	63.3	41.7	31.5	39.8	28.4	13.6	35.0	-28.4	23.4	39.6
		25247	58.4	51.5	73.4	44.0	28.6	35.6	23.4	15.8	36.7	-36.3	38.8	34.2
		25248	42.6	52.5	41.1	39.0	22.7	45.1	21.4	8.7	35.4	-13.0	45.0	14.7
		25249	42.0	47.2	38.3	28.8	7.6	29.1	21.7	6.9	30.4	-5.3	34.1	12.4
		25250	48.6	34.7	30.6	21.2	24.4	17.0	12.2	15.9	0.0	7.3	31.2	9.7
		25251	70.7	73.3	60.1	54.4	37.6	42.7	31.3	29.8	0.9	10.5	59.1	20.0
		25252	40.5	41.2	71.2	46.2	36.0	29.6	28.2	15.5	1.4	-3.3	49.0	24.2
		25253	60.1	43.1	74.3	47.7	34.0	31.3	24.4	18.4	3.0	-12.1	46.1	9.9
2	m	25274	40.0	27.4	84.0	49.3	57.3	37.5	31.1	22.1	32.2	-8.1	36.8	20.9
		25275	57.1	43.1	88.8	57.8	49.4	42.4	18.3	37.6	26.4	3.3	49.2	32.2
		25276	62.3	27.8	70.0	40.5	35.2	25.6	28.3	12.5	41.2	-10.2	51.8	12.0
		25277	67.0	34.6	67.5	39.6	37.6	22.3	27.9	16.3	33.9	-15.2	37.6	21.5
		25278	59.9	40.5	72.1	50.8	23.6	42.2	27.5	21.5	20.8	-3.8	30.2	9.1
		25279	48.2	37.8	66.4	40.7	20.3	35.5	24.2	23.4	14.9	-9.9	31.7	9.6
		25280	63.5	51.2	36.1	50.0	35.0	26.4	19.5	15.2	11.4	2.8	57.4	10.0
		25281	64.0	54.7	38.4	45.9	35.1	30.6	23.1	12.0	13.5	-2.8	55.7	9.5
		25282	60.6	48.8	29.9	37.7	24.7	18.5	16.8	6.0	20.4	11.4	18.2	3.4
		25283	63.6	47.9	36.5	35.9	25.6	23.9	16.5	14.3	19.3	11.0	19.6	3.8

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 10 (continued): Individual Body Weight Changes (g)

Day Numbers Relative to Start Date

Group	Sex	Animal	From: 1 To: 8	8 15	15 22	22 29	29 36	36 43	43 50	50 57	57 64	64 71	71 78	78 85
3	m	25284	56.6	46.2	43.9	38.7	30.6	24.3	13.0	14.8	25.2	7.6	25.5	20.4
		25285	45.9	34.7	27.8	22.5	22.6	24.9	20.3	3.5	22.3	5.0	22.1	10.4
		25286	68.7	40.2	69.1	49.7	51.0	32.9	32.6	-6.0	61.1	-3.0	45.1	14.5
		25287	65.8	32.5	53.0	36.5	32.1	23.0	7.7	5.2	29.5	0.2	26.4	6.8
		25288	54.9	40.1	42.1	38.7	36.3	22.0	21.0	2.1	22.7	3.0	40.5	11.5
		25289	55.8	42.6	43.9	-2.9	49.6	33.8	16.2	10.4	22.5	4.5	49.1	16.8
		25290	66.3	55.5	34.8	52.6	25.7	43.6	29.2	12.1	26.4	11.1	27.0	4.0
		25291	62.0	53.5	36.8	41.9	19.5	36.2	19.7	14.1	29.5	3.9	24.7	13.7
		25292	55.9	33.7	68.4	45.1	22.5	63.2	19.9	27.8	-1.5	-5.3	47.7	15.7
		25293	68.3	39.3	73.9	43.9	24.2	39.3	23.5	25.6	3.8	-14.6	48.9	13.2
4	m	25294	53.9	49.7	33.6	39.7	24.9	30.7	23.3	5.0	24.0	15.0	23.7	6.0
		25295	53.9	67.7	36.8	51.6	21.4	36.5	27.4	5.5	29.8	7.9	29.2	12.8
		25296	47.2	33.9	32.9	28.6	18.0	19.3	17.4	9.4	23.8	13.2	12.7	3.0
		25297	59.6	49.4	33.7	30.7	22.6	25.9	26.7	8.4	27.7	17.5	20.1	5.8
		25298	49.8	50.9	35.7	33.9	30.2	26.8	13.0	9.2	27.8	10.8	18.9	16.8
		25299	52.2	47.9	39.5	29.6	30.7	22.4	16.1	22.6	15.5	11.5	19.8	16.1
		25300	46.1	43.7	95.0	63.1	42.2	40.5	29.4	34.6	30.5	-22.6	64.5	19.2
		25301	41.6	41.5	80.9	54.1	32.8	33.8	24.0	28.5	25.9	-16.8	50.9	11.8
		25302	46.1	21.4	53.0	39.8	35.8	29.6	23.9	-14.8	50.1	-3.6	47.1	8.0
		25303	64.6	40.0	70.6	45.3	28.2	36.7	18.8	-6.0	43.6	-8.6	37.9	13.9
5	m	25304	49.0	41.7	29.7	-81.1	102.7	31.3	20.3	13.1	21.9	4.0	20.9	10.1
		25305	56.6	46.4	40.2	-78.5	100.6	39.1	28.1	19.1	27.4	-0.6	26.9	13.0
		25306	53.0	43.6	41.6	35.7	29.4	27.3	21.0	3.5	25.8	2.4	37.7	18.1
		25307	49.9	47.9	39.0	29.9	22.4	25.2	15.9	9.3	26.8	1.8	33.7	13.8
		25308	59.8	35.1	61.9	41.2	29.5	29.9	28.5	15.6	17.3	13.0	51.0	19.7
		25309	67.0	39.3	62.9	39.1	29.8	21.6	20.8	11.3	10.9	-0.9	36.4	10.3
		25310	60.6	60.0	46.6	51.2	23.9	32.8	26.1	-2.3	34.3	9.5	26.6	10.7
		25311	60.8	54.5	50.7	36.8	23.1	36.1	22.8	-0.2	35.6	14.0	25.0	8.3
		25312	65.5	55.9	54.2	34.1	21.9	41.1	11.4	6.9	21.5	22.1	19.6	2.8
		25313	58.1	46.7	49.2	42.0	16.9	49.3	21.0	5.4	23.8	31.8	17.9	10.7

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 10 (continued): Individual Body Weight Changes (g)

Day Numbers Relative to Start Date

Group	Sex	Animal	From: 1 To: 8	8 15	15 22	22 29	29 36	36 43	43 50	50 57	57 64	64 71	71 78	78 85
6	m	25314	38.8	40.0	38.8	-79.9	92.2	37.4	19.8	39.7	3.5	8.5	19.5	2.6
		25315	57.9	45.0	41.4	-66.4	75.6	37.6	24.0	12.8	35.9	13.6	15.4	13.0
		25316	53.1	46.3	36.0	51.8	31.9	25.5	19.7	6.4	30.8	-2.6	26.4	8.9
		25317	63.3	68.5	40.1	51.6	40.0	36.8	31.3	18.0	42.0	10.5	33.2	26.5
		25318	47.7	48.8	29.8	32.0	27.1	18.6	14.0	14.4	26.9	6.2	20.7	8.4
		25319	54.2	54.4	42.5	32.8	27.8	21.0	25.1	12.8	25.6	10.7	19.2	9.9
		25320	63.2	52.4	45.3	33.6	28.2	23.5	19.3	27.3	10.8	21.8	28.9	4.2
		25321	48.4	53.5	38.6	35.0	30.7	27.6	14.6	15.9	7.9	15.3	25.1	0.1
		25322	58.7	59.2	35.3	41.0	20.3	26.6	20.1	18.6	13.9	8.9	20.9	-3.5
		25323	29.5	36.1	21.8	20.9	9.6	21.8	13.2	16.5	5.9	8.3	12.8	-1.7
		25324	54.3	48.4	41.2	49.8	23.1	32.1	27.0	6.1	26.1	7.0	27.3	-6.4
		25325	64.6	52.1	41.6	54.9	40.8	33.7	20.6	16.6	31.1	5.0	34.1	-4.4
		25326	56.7	61.6	51.4	35.6	39.5	35.6	23.3	2.0	35.0	18.8	25.8	13.6
		25327	48.5	47.3	41.1	35.3	18.6	33.0	13.9	10.3	28.0	14.3	17.7	11.6
		25328	52.5	51.7	25.8	51.8	28.2	25.5	20.2	11.9	18.3	6.0	16.2	3.7
		25329	57.4	63.4	32.5	62.4	24.5	37.3	14.0	25.0	3.4	9.2	25.7	3.5
		25330	45.6	46.2	39.9	38.2	25.0	19.2	15.9	22.2	-1.6	1.0	40.5	5.1
		25331	53.6	49.4	31.9	39.7	29.0	22.5	22.5	15.7	2.3	7.8	38.5	8.6
		25332	43.4	19.7	55.9	-69.6	85.9	30.3	23.3	8.1	22.2	13.7	10.4	7.3
		25333	48.1	32.5	79.4	-88.0	116.2	44.0	30.7	19.2	29.5	18.6	13.5	7.7

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 10 (continued): Individual Body Weight Changes (g)

Day Numbers Relative to Start Date

Group	Sex	Animal	From: 85 To: 90	Absolute Change 1 90	Percent Change 1 90	90 91F	Group	Sex	Animal	From: 85 To: 90	Absolute Change 1 90	Percent Change 1 90	90 91F
1	m	25234	2.1	387.2	173.63	-20.6	3	m	25284	12.1	358.9	157.69	-13.2
		25235	4.0	426.1	166.45	-24.1			25285	-0.5	261.5	110.52	-12.9
		25236	-4.7	338.2	141.80	-18.2			25286	1.0	456.9	185.81	-17.0
		25237	7.2	404.8	173.14	-20.0			25287	-2.0	316.7	135.17	-15.7
		25238	-4.3	296.1	118.06	-14.6			25288	4.2	339.1	137.96	-19.1
		25239	-2.0	402.3	170.68	-26.3			25289	0.6	342.9	155.72	-12.8
		25240	-5.2	336.1	126.88	-16.1			25290	-2.7	385.6	163.32	-24.1
		25241	6.5	371.1	166.56	-16.4			25291	4.7	360.2	163.21	-22.5
		25242	-0.5	404.3	186.31	-19.9			25292	2.0	395.1	170.23	-10.4
		25243	1.0	365.9	157.24	-20.6			25293	2.5	391.8	162.78	-17.1
2	m	25274	8.1	438.6	189.46	-20.9	4	m	25294	2.7	332.2	146.67	-20.1
		25275	9.3	514.9	201.13	-21.0			25295	3.1	383.6	169.29	-16.4
		25276	10.0	407.0	172.46	-19.0			25296	4.9	264.3	114.47	-18.6
		25277	2.7	393.3	157.45	-23.9			25297	-0.7	327.4	138.61	-14.1
		25278	2.4	396.8	174.19	-21.1			25298	-0.9	322.9	127.98	-22.4
		25279	5.1	347.9	153.87	-16.7			25299	2.3	326.2	144.08	-16.0
		25280	-3.7	374.8	158.34	-12.3			25300	5.4	491.6	199.51	-22.9
		25281	-2.0	377.7	160.93	-4.9			25301	3.1	412.1	173.15	-17.8
		25282	-4.4	292.0	130.18	-12.4			25302	0.6	337.0	155.44	-15.3
		25283	-1.3	316.6	141.91	-14.0			25303	0.0	385.0	159.75	-15.9

F = Fasted

Target Dose: Group 1 - 0 mg/kg/day Groups 2 and 7 - 1 mg/kg/day Groups 3 and 8 - 3 mg/kg/day
Groups 4 and 9 - 10 mg/kg/day Groups 5 and 10 - 30 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 10 (continued): Individual Body Weight Changes (g)

Day Numbers Relative to Start Date

Group	Sex	Animal	From: 85 To: 90	Absolute Change 1 90	Percent Change 1 90	90 91F
5	m	25304	-3.2	260.4	105.98	-9.2
		25305	0.7	319.0	132.70	-17.9
		25306	1.7	340.8	151.53	-21.7
		25307	4.9	320.5	133.26	-15.9
		25308	-4.8	397.7	169.38	-21.6
		25309	-3.4	345.1	151.96	-11.9
		25310	0.8	380.8	167.09	-13.5
		25311	-5.5	362.0	148.97	-16.8
		25312	9.0	366.0	155.48	-5.6
		25313	-2.0	370.8	167.63	-20.0
6	m	25314	1.9	262.8	105.63	-14.4
		25315	0.9	306.7	134.40	-10.1
		25316	0.3	334.5	154.50	-10.1
		25317	0.1	461.9	200.65	-11.0
		25318	11.6	306.2	145.19	-12.7
		25319	4.1	340.1	156.30	-16.7
		25320	1.4	359.9	133.44	-12.8
		25321	5.5	318.2	139.20	-13.7
		25322	0.5	320.5	142.83	-15.6
		25323	-3.8	190.9	90.99	-1.7

F = Fasted

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 10 (continued): Individual Body Weight Changes (g)

Day Numbers Relative to Start Date

Group	Sex	Animal	From: 85 To: 92	92 99	99 106	106 113	113 118	Absolute Change 1 118	Percent Change 1 118	Absolute Change 92 118	Percent Change 92 118	118 119F
1	m	25244	-5.3	16.3	14.8	9.2	0.8	302.9	146.47	41.1	8.77	-12.2
		25245	-5.1	17.7	21.3	14.6	-3.2	391.3	152.73	50.4	8.44	-12.0
		25246	-17.7	37.5	25.6	8.2	8.9	453.5	171.33	80.2	12.57	-20.4
		25247	-23.8	42.6	20.3	9.5	-3.2	449.5	195.10	69.2	11.33	-17.1
		25248	3.7	17.6	12.3	5.5	3.4	397.7	153.08	38.8	6.27	-13.0
		25249	8.7	26.8	15.5	8.1	3.2	355.5	149.68	53.6	9.94	-15.9
		25250	6.3	13.6	6.0	3.9	6.1	288.7	137.61	29.6	6.31	-12.5
		25251	6.4	45.0	19.8	12.2	6.9	580.7	249.33	83.9	11.50	-24.7
		25252	-6.5	45.8	28.3	10.5	6.9	464.7	203.99	91.5	15.22	-20.9
		25253	-7.1	31.1	14.5	18.1	0.4	437.2	198.10	64.1	10.79	-18.8
6	m	25324	0.8	41.1	21.4	18.6	9.7	427.6	197.51	90.8	16.41	-14.2
		25325	-6.7	41.4	17.3	13.6	2.8	459.1	192.74	75.1	12.07	-16.3
		25326	2.5	46.9	29.7	27.6	7.5	513.1	222.31	111.7	17.67	-18.0
		25327	-3.8	32.3	18.2	13.8	8.5	388.6	147.14	72.8	12.55	-15.8
		25328	6.9	36.4	8.9	23.7	-2.2	385.5	148.04	66.8	11.54	-22.5
		25329	12.9	27.4	19.8	10.6	3.8	432.8	178.62	61.6	10.04	-16.9
		25330	5.2	32.6	25.0	18.2	-2.3	375.9	146.49	73.5	13.15	-11.2
		25331	-5.0	40.1	30.8	13.4	11.6	412.4	156.39	95.9	16.53	-20.7
		25332	19.0	14.3	12.8	12.1	6.2	315.0	130.76	45.4	8.89	-17.8
		25333	19.0	21.6	17.4	15.5	6.9	431.8	181.58	61.4	10.10	-13.6

F = Fasted

Target Dose: Group 1 - 0 mg/kg/day Group 6 - 100 mg/kg

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 10 (continued): Individual Body Weight Changes (g)

Day Numbers Relative to Start Date

Group	Sex	Animal	From: 1 To: 8	8 15	15 22	22 29	29 36	36 43	43 50	50 57	57 64	64 71	71 78	78 85
1	f	25254	33.0	28.6	12.6	13.2	8.0	12.9	8.1	11.9	-0.2	14.8	-2.1	1.2
		25255	21.6	21.9	11.8	10.1	0.2	20.6	0.8	5.3	4.4	10.1	-0.6	0.3
		25256	24.8	21.9	7.4	12.3	6.1	9.9	10.0	-12.9	-2.5	1.4	-5.0	-7.7
		25257	22.3	18.1	7.8	4.1	10.8	16.3	2.0	4.3	12.4	6.7	-0.1	0.0
		25258	30.2	28.2	15.1	18.6	9.3	11.7	11.8	12.1	15.5	6.4	4.9	4.7
		25259	19.1	24.2	10.0	8.9	6.0	8.1	6.4	4.5	1.4	6.2	5.1	-1.6
		25260	20.7	17.9	17.2	14.8	13.2	6.8	7.3	7.9	8.6	5.1	7.7	-0.3
		25261	29.9	29.8	13.4	12.8	11.6	22.5	10.8	9.3	9.2	13.6	2.1	-5.8
		25262	23.6	21.4	18.9	21.0	2.6	9.1	9.9	9.3	4.6	0.1	4.1	2.5
		25263	37.0	16.6	17.4	15.8	5.0	7.1	11.4	6.2	4.7	2.4	8.7	0.2
		25264	23.9	17.3	8.5	7.6	12.2	9.8	4.6	7.5	11.7	2.2	0.9	0.3
		25265	26.1	21.5	4.7	2.2	14.4	20.8	3.7	4.0	15.0	7.1	-2.9	-0.4
		25266	34.8	13.8	17.1	16.5	5.4	15.2	-0.3	13.2	-2.2	9.2	3.5	-9.6
		25267	26.9	23.1	17.0	10.7	5.8	14.0	8.9	11.7	-0.4	12.8	-1.8	0.3
		25268	18.1	25.7	7.2	14.0	5.4	14.6	1.2	6.2	2.2	1.8	8.8	-0.2
		25269	32.5	26.1	10.1	2.7	18.8	11.9	3.3	2.4	16.9	8.6	-3.5	-11.3
		25270	22.9	25.8	15.2	12.8	4.3	19.9	13.6	9.1	1.7	13.9	3.0	-6.5
		25271	29.3	20.2	24.8	18.1	5.4	10.4	10.8	14.2	3.3	4.2	7.1	-4.5
		25272	32.0	30.0	15.5	10.5	4.0	17.0	7.8	7.2	1.6	9.3	14.0	-5.5
		25273	25.4	19.2	16.8	8.8	8.8	11.9	5.8	5.1	14.5	16.0	3.9	9.0
7	f	25334	19.6	10.4	3.0	15.5	4.8	5.9	0.7	10.9	6.9	1.2	0.9	-6.7
		25335	25.1	18.2	6.7	15.4	3.9	7.5	-1.6	9.0	11.0	1.8	3.2	1.5
		25336	27.5	16.7	15.9	14.1	15.8	12.1	11.0	13.5	-2.0	14.0	9.4	6.4
		25337	26.6	33.1	15.1	20.4	9.9	14.0	4.2	10.3	-2.8	12.1	6.3	0.1
		25338	21.5	23.2	11.3	11.0	3.2	16.2	11.3	10.1	2.4	9.7	1.8	-1.7
		25339	30.2	18.0	9.6	20.5	12.0	13.6	2.5	16.1	3.4	0.0	12.6	1.0
		25340	20.5	6.7	18.7	6.7	4.4	0.1	11.0	7.8	8.3	-5.7	9.6	6.3
		25341	31.8	22.3	11.1	7.1	16.2	10.6	5.4	7.0	9.4	7.1	2.7	-6.7
		25342	31.6	20.4	11.8	9.6	12.2	10.4	7.4	14.9	-0.7	6.6	4.4	3.7
		25343	26.0	19.3	18.1	18.3	6.7	7.9	5.9	11.9	2.1	2.2	15.0	-0.8

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 10 (continued): Individual Body Weight Changes (g)

Day Numbers Relative to Start Date

Group	Sex	Animal	From: 1 To: 8	8 15	15 22	22 29	29 36	36 43	43 50	50 57	57 64	64 71	71 78	78 85
8	f	25344	34.8	23.6	18.9	15.7	10.9	6.6	2.1	13.7	4.2	7.8	1.6	4.6
		25345	20.8	22.4	10.7	8.6	2.3	10.0	8.0	12.6	1.1	5.4	3.8	-5.6
		25346	24.5	10.3	7.9	5.8	11.7	2.4	5.3	9.0	-1.6	4.0	5.1	-2.7
		25347	31.2	19.6	18.0	10.9	8.5	6.0	14.4	10.9	5.8	3.0	13.0	-2.9
		25348	30.5	27.5	13.7	6.4	10.2	11.1	9.2	10.9	8.4	8.6	-0.1	-1.4
		25349	22.4	12.6	9.2	12.6	5.2	4.9	11.6	14.1	3.1	1.1	8.5	3.0
		25350	28.9	20.9	10.3	2.1	13.5	9.1	-0.2	-5.8	15.3	5.8	6.2	-3.5
		25351	13.9	11.7	11.1	15.6	0.1	11.4	4.1	3.5	2.1	9.0	7.0	-5.5
		25352	14.7	19.9	28.6	16.5	8.6	10.6	4.1	9.8	14.9	1.3	4.9	-2.0
		25353	12.8	15.8	32.0	25.0	8.8	10.6	6.0	8.0	16.8	2.3	7.8	0.4
9	f	25354	38.7	26.1	19.7	13.2	14.2	10.8	1.0	17.5	10.3	7.0	11.5	-1.7
		25355	27.1	18.8	7.1	18.6	7.8	12.7	1.6	15.8	11.9	6.3	4.7	-2.4
		25356	26.0	16.0	9.1	10.6	10.9	4.4	-0.4	16.1	7.5	1.7	-3.3	4.2
		25357	25.1	16.2	9.9	7.1	12.8	9.7	4.2	7.8	9.1	10.3	-4.4	2.8
		25358	35.4	20.9	7.6	16.7	5.8	15.6	6.3	11.2	3.4	4.8	6.7	-9.8
		25359	33.2	20.2	16.1	8.6	16.1	14.1	5.9	4.1	13.2	10.0	0.0	-9.0
		25360	20.6	31.0	16.7	16.1	6.9	21.2	-1.5	9.3	6.2	13.5	-1.5	6.6
		25361	29.2	26.8	16.7	16.7	7.9	11.1	1.6	10.9	3.4	0.7	8.2	-6.3
		25362	15.1	24.7	14.7	14.8	8.7	10.3	5.6	12.2	6.6	11.4	7.7	0.1
		25363	14.4	21.8	6.2	11.0	7.3	11.3	7.3	7.9	1.5	11.6	-0.3	1.8
10	f	25364	21.2	19.6	7.7	12.9	7.0	10.3	7.0	5.2	0.9	9.6	6.3	-1.6
		25365	31.8	19.3	15.3	13.9	15.2	4.7	12.7	12.6	12.2	1.6	1.2	-4.0
		25366	13.3	19.1	9.9	7.7	2.8	10.8	3.9	3.7	-1.3	6.2	1.7	-6.6
		25367	31.4	16.7	17.6	11.5	11.5	9.7	10.1	11.1	5.6	8.8	3.9	2.6
		25368	27.6	23.0	14.2	10.0	11.7	11.1	5.2	4.4	6.1	11.4	3.0	-7.7
		25369	37.7	23.2	8.8	19.3	12.5	5.1	0.9	15.8	1.8	9.5	4.3	1.5
		25370	14.3	25.3	18.2	12.6	4.0	16.3	4.6	2.4	-2.1	16.1	0.2	-3.6
		25371	11.6	33.9	23.7	14.3	8.2	17.6	-3.2	15.9	14.4	-5.0	15.5	-8.6
		25372	18.2	18.9	5.0	3.3	14.0	10.5	5.7	6.8	3.7	6.3	9.5	0.8
		25373	26.6	21.8	7.1	5.7	15.0	11.6	5.1	10.1	9.2	12.8	1.2	-9.9

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 10 (continued): Individual Body Weight Changes (g)

Day Numbers Relative to Start Date

Group	Sex	Animal	From: 1 To: 8	8 15	15 22	22 29	29 36	36 43	43 50	50 57	57 64	64 71	71 78	78 85
11	f	25374	37.4	28.8	19.9	16.7	12.3	8.2	4.7	12.4	-2.8	12.6	-2.9	0.7
		25375	24.6	20.6	10.3	14.9	15.2	4.4	1.4	13.4	4.7	4.9	0.8	1.2
		25376	19.5	21.7	14.4	2.9	11.2	2.3	11.1	3.3	-3.2	13.0	8.4	-0.7
		25377	17.2	14.5	11.0	5.1	2.9	9.6	1.6	5.2	6.2	5.7	-4.3	1.1
		25378	26.6	21.3	5.5	8.8	12.3	9.2	5.4	2.7	9.5	6.1	-2.4	2.6
		25379	31.4	22.1	11.7	16.2	8.5	10.7	11.4	6.1	8.7	2.5	3.5	-8.2
		25380	35.1	30.6	16.8	20.8	13.0	4.7	12.3	-9.0	25.7	-17.0	26.3	-2.8
		25381	29.1	22.8	14.5	18.3	9.2	10.5	12.1	-11.9	21.5	-10.8	20.0	0.2
		25382	12.3	10.9	18.4	8.0	7.2	4.2	10.9	5.6	3.3	3.8	10.2	-6.0
		25383	26.1	18.0	11.1	15.1	9.6	8.9	1.2	13.0	5.7	8.6	7.8	3.5
		25384	17.5	16.9	19.7	19.1	17.3	9.2	14.2	11.0	7.6	5.4	10.9	4.5
		25385	22.0	29.0	18.2	11.5	11.1	16.3	9.6	9.8	6.9	19.5	3.7	-1.2
		25386	16.6	20.4	8.9	13.3	0.9	13.9	5.9	-9.7	13.6	10.7	3.6	-4.7
		25387	17.6	28.4	9.3	14.5	-1.6	13.9	0.2	-4.6	22.8	-3.4	9.8	-8.4
		25388	22.2	23.0	17.4	15.3	5.3	10.7	4.9	4.5	-2.1	10.0	-0.6	7.4
		25389	23.0	12.6	12.5	20.1	7.1	0.7	7.8	5.0	3.3	8.6	-2.3	3.9
		25390	16.4	23.4	7.2	11.6	4.1	13.9	4.9	3.4	-0.9	8.7	8.6	-8.9
		25391	21.8	14.2	11.7	1.2	13.3	4.0	5.2	-2.9	12.3	1.3	-1.6	-3.5
		25392	29.0	17.7	20.8	11.1	11.7	9.4	10.9	-4.4	9.7	7.3	5.5	-22.3
		25393	24.2	20.6	8.0	6.4	17.7	10.2	4.4	2.2	12.1	9.5	-0.3	-6.7

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 10 (continued): Individual Body Weight Changes (g)

Day Numbers Relative to Start Date

Group	Sex	Animal	From: 85 To: 90	Absolute Change 1 90	Percent Change 1 90	90 91F	Group	Sex	Animal	From: 85 To: 90	Absolute Change 1 90	Percent Change 1 90	90 91F
1	f	25254	0.1	142.1	84.84	-15.9	8	f	25344	-2.2	142.3	77.72	-8.7
		25255	-2.7	103.8	63.18	-13.6			25345	-0.6	99.5	59.12	-11.4
		25256	2.4	68.1	39.34	-10.4			25346	5.5	87.2	48.85	-7.6
		25257	3.1	107.8	63.00	-10.1			25347	-1.2	137.2	76.31	-13.5
		25258	-1.9	166.6	94.50	-11.1			25348	-0.3	134.7	80.42	-8.3
		25259	-0.6	97.7	62.51	-15.5			25349	-0.7	107.6	58.86	-12.1
		25260	-1.4	125.5	73.74	-11.8			25350	0.0	102.6	59.76	-5.1
		25261	3.7	162.9	89.75	-11.9			25351	7.6	91.6	55.38	-9.9
		25262	-1.8	125.3	76.87	-10.0			25352	-6.2	125.7	75.50	-0.9
		25263	-3.3	129.2	73.45	-13.5			25353	-3.9	142.4	78.07	-5.0
7	f	25334	2.4	75.5	43.67	-7.7	9	f	25354	4.2	172.5	97.07	-6.4
		25335	-4.1	97.6	53.63	-6.4			25355	3.1	133.1	77.61	-16.7
		25336	5.8	160.2	93.30	-15.7			25356	-3.2	99.6	54.73	-6.7
		25337	0.1	149.4	86.46	-15.0			25357	-4.0	106.6	66.25	-3.2
		25338	2.4	122.4	70.92	-11.4			25358	2.3	126.9	77.33	-11.9
		25339	-1.3	138.2	81.34	-12.7			25359	6.7	139.2	84.98	-8.0
		25340	-1.1	93.3	56.89	-10.2			25360	-0.6	144.5	83.87	-14.5
		25341	5.8	129.8	79.63	-11.0			25361	-3.4	123.5	75.67	-2.4
		25342	-3.9	128.4	72.87	-8.8			25362	2.2	134.1	77.60	-17.9
		25343	-0.3	132.3	74.33	-11.7			25363	-1.2	100.6	56.30	-10.0

F = Fasted

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 10 (continued): Individual Body Weight Changes (g)

Day Numbers Relative to Start Date

Group	Sex	Animal	From: 85 To: 90	Absolute Change 1 90	Percent Change 1 90	90 91F
10	f	25364	-0.2	105.9	61.71	-12.9
		25365	6.7	143.2	79.60	-14.3
		25366	5.5	76.7	47.32	-11.7
		25367	-4.2	136.3	84.76	-9.7
		25368	1.0	121.0	70.60	-12.7
		25369	-4.5	135.9	76.26	-9.6
		25370	5.2	113.5	67.76	-13.9
		25371	-1.1	137.2	79.35	-10.9
		25372	4.4	107.1	68.30	-11.2
		25373	4.0	120.3	66.65	-6.0
11	f	25374	1.8	149.8	78.88	-11.5
		25375	-6.8	109.6	57.96	-2.3
		25376	-0.2	103.7	63.70	-12.3
		25377	-1.1	74.7	46.66	-8.8
		25378	-4.2	103.4	59.70	-4.7
		25379	4.4	129.0	75.13	-4.1
		25380	-1.4	155.1	92.54	-6.9
		25381	-4.3	131.2	74.17	-3.4
		25382	5.6	94.4	55.50	-11.5
		25383	-2.1	126.5	77.56	-4.0

F = Fasted

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 10 (continued): Individual Body Weight Changes (g)

Day Numbers Relative to Start Date

Group	Sex	Animal	From: 85 To: 92	92 99	99 106	106 113	113 118	Absolute Change 1 118	Percent Change 1 118	Absolute Change 92 118	Percent Change 92 118	118 119F
1	f	25264	2.0	6.5	0.8	4.0	-1.8	118.0	72.39	9.5	3.50	-10.8
		25265	10.1	7.2	7.5	9.1	-8.1	142.0	80.87	15.7	5.20	-11.6
		25266	-0.7	9.5	7.0	1.8	4.8	139.0	85.07	23.1	8.27	-14.1
		25267	-1.3	13.6	8.8	9.5	-3.2	156.4	83.37	28.7	9.10	-10.3
		25268	-8.3	11.2	3.2	12.1	-4.8	118.4	62.48	21.7	7.58	-14.4
		25269	-9.4	21.9	11.2	8.8	-7.4	143.6	80.54	34.5	12.00	-10.6
		25270	-4.3	15.3	12.2	3.8	3.2	165.9	101.47	34.5	11.70	-15.0
		25271	5.3	18.5	13.6	7.6	0.2	188.5	111.87	39.9	12.58	-13.0
		25272	-1.0	6.3	6.3	12.7	-3.9	163.8	94.79	21.4	6.79	-8.7
		25273	5.5	13.1	4.4	29.7	14.9	212.8	119.22	62.1	18.86	-18.6
11	f	25384	6.1	19.6	3.9	28.6	-1.5	210.0	113.76	50.6	14.71	-19.1
		25385	-2.4	22.8	15.8	2.7	-4.8	190.5	105.31	36.5	10.90	-16.3
		25386	10.2	10.1	12.5	0.4	-0.2	126.4	68.18	22.8	7.89	-13.6
		25387	10.0	14.4	-3.6	14.4	-0.6	133.1	82.41	24.6	9.11	-13.9
		25388	0.7	10.0	3.0	19.4	-5.0	146.1	83.25	27.4	9.31	-16.0
		25389	5.6	5.1	7.5	1.1	0.9	122.5	75.62	14.6	5.41	-13.9
		25390	6.3	12.4	7.9	1.1	1.5	121.6	68.58	22.9	8.30	-17.5
		25391	7.6	18.3	2.3	3.2	0.3	108.7	69.63	24.1	10.01	-11.0
		25392	21.2	10.5	-2.0	17.6	-9.6	144.1	83.05	16.5	5.48	-11.4
		25393	19.1	14.9	7.4	0.7	1.6	152.0	96.08	24.6	8.61	-13.4

F = Fasted

Nominal Dose: Group 1 - 0 mg/kg/day Group 11 - 100 mg/kg/day

APPENDIX 11: INDIVIDUAL WATER CONSUMPTION

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 11: Individual Water Consumption (g/animal/day)

Day Numbers Relative to Start Date

Group	Sex	Animal	From: 1 To: 8	8 15	15 22	22 29	29 36	36 43	43 50	50 57	57 64	64 71	71 78	78 85	85 90	Total 1 90
1	m	25234	31.9	33.2	37.2	35.5	38.0	33.8	38.5	36.1	34.1	34.9	37.1	34.9	36.5	3158.9
		25235	31.9	33.2	37.2	35.5	38.0	33.8	38.5	36.1	34.1	34.9	37.1	34.9	36.5	3158.9
		25236	33.5	33.6	35.5	37.5	37.8	36.8	34.9	37.4	34.5	36.6	39.0	36.3	36.6	3217.2
		25237	33.5	33.6	35.5	37.5	37.8	36.8	34.9	37.4	34.5	36.6	39.0	36.3	36.6	3217.2
		25238	29.1	29.1	28.8	30.1	30.6	27.3	28.0	26.8	26.9	24.3	29.9	27.6	25.6	2497.9
		25239	29.1	29.1	28.8	30.1	30.6	27.3	28.0	26.8	26.9	24.3	29.9	27.6	25.6	2497.9
		25240	28.6	29.8	30.1	29.8	30.3	28.7	27.2	28.8	27.5	27.1	29.9	26.8	27.5	2549.6
		25241	28.6	29.8	30.1	29.8	30.3	28.7	27.2	28.8	27.5	27.1	29.9	26.8	27.5	2549.6
		25242	31.6	31.4	33.5	33.8	34.4	33.6	33.3	31.8	31.1	30.2	34.7	30.5	28.4	2871.1
		25243	31.6	31.4	33.5	33.8	34.4	33.6	33.3	31.8	31.1	30.2	34.7	30.5	28.4	2871.1
		25244	28.8	29.0	28.7	28.9	28.5	26.2	27.2	28.6	29.4	28.4	29.9	27.2	26.3	2516.8
		25245	28.8	29.0	28.7	28.9	28.5	26.2	27.2	28.6	29.4	28.4	29.9	27.2	26.3	2516.8
		25246	44.8	50.1	54.4	56.0	55.2	55.0	48.9	53.9	52.6	47.9	43.6	47.5	48.2	4510.0
		25247	44.8	50.1	54.4	56.0	55.2	55.0	48.9	53.9	52.6	47.9	43.6	47.5	48.2	4510.0
		25248	36.8	39.8	40.0	42.5	44.1	41.1	44.5	37.8	38.9	38.0	42.4	37.7	38.5	3577.8
		25249	36.8	39.8	40.0	42.5	44.1	41.1	44.5	37.8	38.9	38.0	42.4	37.7	38.5	3577.8
		25250	31.3	33.9	35.4	36.1	37.4	35.4	33.5	34.9	36.2	34.5	39.5	35.3	35.4	3141.1
		25251	31.3	33.9	35.4	36.1	37.4	35.4	33.5	34.9	36.2	34.5	39.5	35.3	35.4	3141.1
		25252	27.7	32.9	33.7	31.7	33.2	30.3	29.7	30.2	27.3	25.4	30.2	27.8	27.4	2658.1
		25253	27.7	32.9	33.7	31.7	33.2	30.3	29.7	30.2	27.3	25.4	30.2	27.8	27.4	2658.1
2	m	25274	32.3	37.9	40.0	38.8	42.8	39.2	35.7	37.2	37.6	35.0	37.4	36.1	39.9	3349.4
		25275	32.3	37.9	40.0	38.8	42.8	39.2	35.7	37.2	37.6	35.0	37.4	36.1	39.9	3349.4
		25276	35.5	37.3	41.1	39.3	44.2	39.2	38.3	39.5	39.5	36.5	39.6	36.3	38.7	3456.5
		25277	35.5	37.3	41.1	39.3	44.2	39.2	38.3	39.5	39.5	36.5	39.6	36.3	38.7	3456.5
		25278	33.5	34.0	35.6	35.9	35.2	32.5	31.4	32.3	31.6	29.1	32.9	31.9	30.7	2924.4
		25279	33.5	34.0	35.6	35.9	35.2	32.5	31.4	32.3	31.6	29.1	32.9	31.9	30.7	2924.4
		25280	38.3	39.6	40.7	43.6	44.7	40.8	38.5	38.7	38.3	36.4	37.8	33.6	32.5	3459.2
		25281	38.3	39.6	40.7	43.6	44.7	40.8	38.5	38.7	38.3	36.4	37.8	33.6	32.5	3459.2
		25282	29.2	31.5	32.5	32.3	32.0	29.7	28.7	29.5	27.3	26.7	28.5	27.1	27.6	2622.8
		25283	29.2	31.5	32.5	32.3	32.0	29.7	28.7	29.5	27.3	26.7	28.5	27.1	27.6	2622.8

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 11 (continued): Individual Water Consumption (g/animal/day)

Day Numbers Relative to Start Date

Group	Sex	Animal	From: 1 To: 8	8 15	15 22	22 29	29 36	36 43	43 50	50 57	57 64	64 71	71 78	78 85	85 90	Total 1 90
3	m	25284	34.9	36.1	40.3	39.1	40.2	38.2	36.6	37.9	33.9	34.3	32.7	29.2	30.3	3185.4
		25285	34.9	36.1	40.3	39.1	40.2	38.2	36.6	37.9	33.9	34.3	32.7	29.2	30.3	3185.4
		25286	33.5	35.2	39.3	40.2	43.9	44.4	42.1	44.6	37.1	36.0	38.3	33.8	35.9	3458.4
		25287	33.5	35.2	39.3	40.2	43.9	44.4	42.1	44.6	37.1	36.0	38.3	33.8	35.9	3458.4
		25288	29.7	29.4	29.6	20.1	33.3	31.6	30.2	32.0	30.7	27.9	32.2	28.0	29.2	2627.8
		25289	29.7	29.4	29.6	20.1	33.3	31.6	30.2	32.0	30.7	27.9	32.2	28.0	29.2	2627.8
		25290	32.6	34.6	33.2	35.5	39.7	37.5	36.3	38.3	35.5	37.6	40.6	37.3	39.8	3268.9
		25291	32.6	34.6	33.2	35.5	39.7	37.5	36.3	38.3	35.5	37.6	40.6	37.3	39.8	3268.9
		25292	33.5	37.6	41.0	40.6	42.1	40.9	36.0	40.3	38.9	39.0	39.0	35.9	33.2	3420.9
		25293	33.5	37.6	41.0	40.6	42.1	40.9	36.0	40.3	38.9	39.0	39.0	35.9	33.2	3420.9
4	m	25294	33.4	36.5	35.3	40.4	43.4	38.2	36.8	39.2	35.8	33.9	35.0	31.3	26.6	3206.3
		25295	33.4	36.5	35.3	40.4	43.4	38.2	36.8	39.2	35.8	33.9	35.0	31.3	26.6	3206.3
		25296	27.2	28.1	26.5	28.1	28.6	27.8	27.3	26.8	25.2	25.4	27.1	22.8	24.8	2369.6
		25297	27.2	28.1	26.5	28.1	28.6	27.8	27.3	26.8	25.2	25.4	27.1	22.8	24.8	2369.6
		25298	32.7	34.3	35.5	38.0	34.8	34.6	34.4	32.0	32.0	30.3	33.0	31.1	33.5	2986.8
		25299	32.7	34.3	35.5	38.0	34.8	34.6	34.4	32.0	32.0	30.3	33.0	31.1	33.5	2986.8
		25300	30.8	35.0	38.9	37.7	37.5	36.5	33.4	34.4	32.9	30.9	36.0	31.2	30.4	3058.5
		25301	30.8	35.0	38.9	37.7	37.5	36.5	33.4	34.4	32.9	30.9	36.0	31.2	30.4	3058.5
		25302	32.0	32.6	38.7	42.6	36.3	34.9	32.6	35.2	33.9	29.0	33.4	30.1	28.9	3024.6
		25303	32.0	32.6	38.7	42.6	36.3	34.9	32.6	35.2	33.9	29.0	33.4	30.1	28.9	3024.5
5	m	25304	25.7	24.0	24.4	0.7	24.3	26.9	24.4	23.4	22.4	20.7	22.7	20.7	20.5	1923.8
		25305	25.7	24.0	24.4	0.7	24.3	26.9	24.4	23.4	22.4	20.7	22.7	20.7	20.5	1923.8
		25306	26.7	28.9	28.6	29.5	28.3	27.4	26.9	27.0	25.9	24.5	27.5	24.8	23.4	2399.8
		25307	26.7	28.9	28.6	29.5	28.3	27.4	26.9	27.0	25.9	24.5	27.5	24.8	23.4	2399.8
		25308	29.3	28.9	31.5	29.0	29.3	28.5	27.6	26.0	26.2	26.1	29.2	22.2	25.5	2464.7
		25309	29.3	28.9	31.5	29.0	29.3	28.5	27.6	26.0	26.2	26.1	29.2	22.2	25.5	2464.7
		25310	29.6	32.7	35.1	36.1	36.2	35.8	35.7	30.5	30.2	28.0	29.1	27.4	26.6	2837.4
		25311	29.6	32.7	35.1	36.1	36.2	35.8	35.7	30.5	30.2	28.0	29.1	27.4	26.6	2837.4
		25312	29.5	31.6	32.3	31.9	32.4	31.7	27.4	27.8	26.8	27.7	29.9	25.0	25.4	2603.9
		25313	29.5	31.6	32.3	31.9	32.4	31.7	27.4	27.8	26.8	27.7	29.9	25.0	25.4	2603.9

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 11 (continued): Individual Water Consumption (g/animal/day)

Day Numbers Relative to Start Date

Group	Sex	Animal	From: 1 To: 8	8 15	15 22	22 29	29 36	36 43	43 50	50 57	57 64	64 71	71 78	78 85	85 90	Total 1 90
6	m	25314	23.1	23.7	22.6	2.5	18.4	20.3	19.2	19.8	19.0	18.2	20.1	17.7	18.0	1661.4
		25315	23.1	23.7	22.6	2.5	18.4	20.3	19.2	19.8	19.0	18.2	20.1	17.7	18.0	1661.4
		25316	22.0	28.2	26.0	27.2	26.4	25.1	23.9	24.0	24.1	21.5	26.1	23.9	23.0	2204.4
		25317	22.0	28.2	26.0	27.2	26.4	25.1	23.9	24.0	24.1	21.5	26.1	23.9	23.0	2204.4
		25318	23.7	27.7	24.6	23.9	24.1	22.3	21.0	21.7	21.1	18.4	22.5	20.3	22.4	2010.9
		25319	23.7	27.7	24.6	23.9	24.1	22.3	21.0	21.7	21.1	18.4	22.5	20.3	22.4	2010.9
		25320	27.0	27.5	23.5	25.1	23.4	22.7	20.4	21.3	18.7	20.8	21.6	18.3	20.6	1995.4
		25321	27.0	27.5	23.5	25.1	23.4	22.7	20.4	21.3	18.7	20.8	21.6	18.3	20.6	1995.4
		25322	23.2	25.6	22.8	22.2	19.9	20.5	18.0	17.8	16.3	16.7	19.5	15.8	15.3	1743.1
		25323	23.2	25.6	22.8	22.2	19.9	20.5	18.0	17.8	16.3	16.7	19.5	15.8	15.3	1743.1
		25324	26.4	29.0	26.9	27.8	24.7	23.5	23.3	22.5	21.5	21.3	24.3	19.8	21.7	2145.1
		25325	26.4	29.0	26.9	27.8	24.7	23.5	23.3	22.5	21.5	21.3	24.3	19.8	21.7	2145.1
		25326	25.7	27.4	25.1	24.4	23.9	23.6	21.5	21.2	21.4	18.0	23.3	21.2	21.4	2044.0
		25327	25.7	27.4	25.1	24.4	23.9	23.6	21.5	21.2	21.4	18.0	23.3	21.2	21.4	2044.0
		25328	26.5	29.6	25.7	27.8	25.7	24.6	22.9	23.8	22.4	22.3	23.6	20.9	23.5	2187.4
		25329	26.5	29.6	25.7	27.8	25.7	24.6	22.9	23.8	22.4	22.3	23.6	20.9	23.5	2187.4
		25330	25.5	27.6	25.9	25.3	23.8	21.4	20.4	21.1	18.5	19.7	23.3	19.9	22.5	2019.6
		25331	25.5	27.6	25.9	25.3	23.8	21.4	20.4	21.1	18.5	19.7	23.3	19.9	22.5	2019.6
		25332	25.9	26.3	28.2	1.2	20.5	24.4	22.1	21.4	20.6	20.1	21.4	19.1	21.0	1862.9
		25333	25.9	26.3	28.2	1.2	20.5	24.4	22.1	21.4	20.6	20.1	21.4	19.1	21.0	1862.9

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 11 (continued): Individual Water Consumption (g/animal/day)

Day Numbers Relative to Start Date

Group	Sex	Animal	From: 90 To: 92	92 99	99 106	106 113	113 118	Total 1 118	Total 92 118
1	m	25244	21.5	28.2	27.2	26.8	23.8	3254.1	694.3
		25245	21.5	28.2	27.2	26.8	23.8	3254.1	694.3
		25246	37.3	53.1	52.5	50.0	49.3	5920.6	1336.0
		25247	37.3	53.1	52.5	50.0	49.3	5920.6	1336.0
		25248	31.1	39.2	37.8	35.3	38.7	4619.6	979.6
		25249	31.1	39.2	37.8	35.3	38.7	4619.6	979.6
		25250	26.4	34.2	31.6	32.8	32.9	4048.3	854.6
		25251	26.4	34.2	31.6	32.8	32.9	4048.3	854.6
		25252	18.6	27.7	26.1	26.2	24.8	3379.4	684.2
		25253	18.6	27.7	26.1	26.2	24.8	3379.4	684.2
6	m	25324	26.6	37.9	37.3	39.8	39.8	3202.1	1004.0
		25325	26.6	37.9	37.3	39.8	39.8	3202.1	1004.0
		25326	27.6	31.7	30.4	31.9	30.0	2907.2	808.1
		25327	27.6	31.7	30.4	31.9	30.0	2907.2	808.1
		25328	48.7	44.8	38.4	39.7	41.5	3352.7	1067.9
		25329	48.7	44.8	38.4	39.7	41.5	3352.7	1067.9
		25330	39.7	39.1	33.4	36.4	40.1	3061.1	962.2
		25331	39.7	39.1	33.4	36.4	40.1	3061.1	962.2
		25332	39.7	29.5	26.9	26.6	26.0	2653.6	711.4
		25333	39.7	29.5	26.9	26.6	26.0	2653.6	711.4

Target Dose: Group 1 – 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 11 (continued): Individual Water Consumption (g/animal/day)

Day Numbers Relative to Start Date

Group	Sex	Animal	From: 1 To: 8	8 15	15 22	22 29	29 36	36 43	43 50	50 57	57 64	64 71	71 78	78 85	85 90	Total 1 90
1	f	25254	20.3	20.3	19.6	19.7	19.1	20.7	20.2	20.3	18.5	20.3	19.6	19.8	18.8	1761.8
		25255	20.3	20.3	19.6	19.7	19.1	20.7	20.2	20.3	18.5	20.3	19.6	19.8	18.8	1761.8
		25256	23.3	22.2	19.6	20.5	19.7	21.1	19.8	18.2	21.9	20.7	20.5	19.5	19.6	1827.2
		25257	23.3	22.2	19.6	20.5	19.7	21.1	19.8	18.2	21.9	20.7	20.5	19.5	19.6	1827.2
		25258	23.4	23.9	24.1	23.5	22.6	22.8	21.9	21.5	21.1	21.6	22.8	21.2	20.6	1996.2
		25259	23.4	23.9	24.1	23.5	22.6	22.8	21.9	21.5	21.1	21.6	22.8	21.2	20.6	1996.2
		25260	19.4	20.0	19.3	19.7	19.2	20.2	18.8	18.2	18.8	19.4	18.8	17.2	17.4	1690.6
		25261	19.4	20.0	19.3	19.7	19.2	20.2	18.8	18.2	18.8	19.4	18.8	17.2	17.4	1690.6
		25262	22.6	22.1	22.7	23.4	20.3	22.8	21.5	22.4	21.9	20.8	22.0	22.9	9.7	1906.3
		25263	22.6	22.1	22.7	23.4	20.3	22.8	21.5	22.4	21.9	20.8	22.0	22.9	9.7	1906.3
		25264	20.6	19.6	17.7	19.8	18.6	19.0	18.3	16.7	17.7	18.4	18.5	17.4	16.1	1636.4
		25265	20.6	19.6	17.7	19.8	18.6	19.0	18.3	16.7	17.7	18.4	18.5	17.4	16.1	1636.4
		25266	23.3	22.7	22.4	29.9	21.2	22.0	20.7	21.4	19.4	21.5	20.8	19.8	21.3	1961.3
		25267	23.3	22.7	22.4	29.9	21.2	22.0	20.7	21.4	19.4	21.5	20.8	19.8	21.3	1961.3
		25268	22.4	22.1	19.5	22.0	20.5	19.7	19.2	17.6	18.6	18.3	18.8	18.6	15.4	1737.7
		25269	22.4	22.1	19.5	22.0	20.5	19.7	19.2	17.6	18.6	18.3	18.8	18.6	15.4	1737.7
		25270	20.3	21.1	21.6	22.3	21.7	22.2	22.0	21.9	21.8	21.5	22.7	22.7	21.4	1940.9
		25271	20.3	21.1	21.6	22.3	21.7	22.2	22.0	21.9	21.8	21.5	22.7	22.7	21.4	1940.9
		25272	19.9	20.9	19.4	19.2	19.7	20.0	18.9	19.6	19.8	20.4	21.9	19.5	17.2	1759.9
		25273	19.9	20.9	19.4	19.2	19.7	20.0	18.9	19.6	19.8	20.4	21.9	19.5	17.2	1759.9
7	f	25334	23.2	17.9	17.4	17.4	15.7	16.4	15.1	16.6	14.9	15.0	15.7	15.3	14.8	1477.6
		25335	23.2	17.9	17.4	17.4	15.7	16.4	15.1	16.6	14.9	15.0	15.7	15.3	14.8	1477.6
		25336	23.1	23.7	23.5	25.1	25.3	25.8	23.1	24.7	21.7	24.3	24.2	23.6	22.4	2128.9
		25337	23.1	23.7	23.5	25.1	25.3	25.8	23.1	24.7	21.7	24.3	24.2	23.6	22.4	2128.9
		25338	19.7	20.0	20.0	15.8	19.6	19.2	18.0	18.3	0.0	18.9	18.7	17.0	16.0	1516.7
		25339	19.7	20.0	20.0	15.8	19.6	19.2	18.0	18.3	0.0	18.9	18.7	17.0	16.0	1516.7
		25340	20.9	20.0	17.6	19.4	19.6	19.1	19.8	20.2	17.8	16.6	20.4	18.9	17.8	1700.4
		25341	20.9	20.0	17.6	19.4	19.6	19.1	19.8	20.2	17.8	16.6	20.4	18.9	17.8	1700.4
		25342	21.0	21.1	22.2	22.3	21.0	23.2	20.0	20.7	17.6	20.6	22.7	21.6	20.4	1880.8
		25343	21.0	21.1	22.2	22.3	21.0	23.2	20.0	20.7	17.6	20.6	22.7	21.6	20.4	1880.8

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 11 (continued): Individual Water Consumption (g/animal/day)

Day Numbers Relative to Start Date

Group	Sex	Animal	From: 1 To: 8	8 15	15 22	22 29	29 36	36 43	43 50	50 57	57 64	64 71	71 78	78 85	85 90	Total 1 90
8	f	25344	27.1	24.3	23.6	24.2	22.0	23.3	22.2	23.4	22.0	23.0	22.5	21.8	21.3	2062.1
		25345	27.1	24.3	23.6	24.2	22.0	23.3	22.2	23.4	22.0	23.0	22.5	21.8	21.3	2062.1
		25346	14.5	18.8	17.4	16.9	16.7	17.1	17.2	16.9	16.6	17.1	18.3	16.5	15.6	1506.4
		25347	14.5	18.8	17.4	16.9	16.7	17.1	17.2	16.9	16.6	17.1	18.3	16.5	15.6	1506.4
		25348	23.2	24.0	25.0	24.7	24.4	23.0	23.2	24.7	25.2	25.6	24.1	23.0	22.5	2143.2
		25349	23.2	24.0	25.0	24.7	24.4	23.0	23.2	24.7	25.2	25.6	24.1	23.0	22.5	2143.2
		25350	17.0	16.2	16.2	15.8	17.2	16.0	17.0	17.0	17.6	18.4	18.4	17.3	15.6	1506.7
		25351	17.0	16.2	16.2	15.8	17.2	16.0	17.0	17.0	17.6	18.4	18.4	17.3	15.6	1506.7
		25352	21.6	22.2	22.0	23.4	21.2	22.6	21.0	23.5	21.4	21.5	22.7	20.5	17.9	1935.2
		25353	21.6	22.2	22.0	23.4	21.2	22.6	21.0	23.5	21.4	21.5	22.7	20.5	17.9	1935.2
9	f	25354	21.1	21.6	21.6	20.9	20.5	21.9	19.5	20.2	20.5	19.2	19.9	20.1	18.7	1821.6
		25355	21.1	21.6	21.6	20.9	20.5	21.9	19.5	20.2	20.5	19.2	19.9	20.1	18.7	1821.6
		25356	24.6	24.6	25.7	25.4	27.3	26.6	24.7	27.1	26.0	26.1	20.0	26.9	23.3	2251.2
		25357	24.6	24.6	25.7	25.4	27.3	26.6	24.7	27.1	26.0	26.1	20.0	26.9	23.3	2251.2
		25358	19.0	21.5	19.4	19.5	21.3	21.7	19.4	20.0	19.7	20.6	21.8	20.1	19.7	1805.8
		25359	19.0	21.5	19.4	19.5	21.3	21.7	19.4	20.0	19.7	20.6	21.8	20.1	19.7	1805.8
		25360	20.4	21.6	21.0	20.5	18.9	20.8	18.7	17.8	17.6	17.7	18.3	16.9	20.3	1712.9
		25361	20.4	21.6	21.0	20.5	18.9	20.8	18.7	17.8	17.6	17.7	18.3	16.9	20.3	1712.9
		25362	17.4	18.5	16.6	16.2	16.5	16.3	14.7	15.9	14.9	16.4	14.7	16.2	14.6	1432.3
		25363	17.4	18.5	16.6	16.2	16.5	16.3	14.7	15.9	14.9	16.4	14.7	16.2	14.6	1432.3
10	f	25364	19.8	20.8	21.7	22.6	22.9	21.8	21.9	21.0	20.9	20.5	19.1	20.2	19.8	1872.0
		25365	19.8	20.8	21.7	22.6	22.9	21.8	21.9	21.0	20.9	20.5	19.1	20.2	19.8	1872.0
		25366	19.0	19.9	19.0	18.7	18.5	18.7	15.5	18.5	17.7	19.1	18.3	17.4	17.2	1628.6
		25367	19.0	19.9	19.0	18.7	18.5	18.7	15.5	18.5	17.7	19.1	18.3	17.4	17.2	1628.6
		25368	19.1	18.8	18.3	16.7	19.2	19.0	17.0	16.5	16.1	19.3	18.3	15.9	14.5	1571.2
		25369	19.1	18.8	18.3	16.7	19.2	19.0	17.0	16.5	16.1	19.3	18.3	15.9	14.5	1571.2
		25370	18.9	22.0	21.1	20.7	19.6	20.5	18.2	18.9	17.2	19.1	19.9	17.7	18.4	1726.4
		25371	18.9	22.0	21.1	20.7	19.6	20.5	18.2	18.9	17.2	19.1	19.9	17.7	18.4	1726.4
		25372	19.6	19.3	18.9	19.0	19.9	19.6	19.1	19.0	18.5	20.0	18.7	17.7	17.5	1691.9
		25373	19.6	19.3	18.9	19.0	19.9	19.6	19.1	19.0	18.5	20.0	18.7	17.7	17.5	1691.9

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 11 (continued): Individual Water Consumption (g/animal/day)

Day Numbers Relative to Start Date

Group	Sex	Animal	From: To:	1 8	8 15	15 22	22 29	29 36	36 43	43 50	50 57	57 64	64 71	71 78	78 85	85 90	Total 1 90
11	f	25374		18.6	16.8	16.1	15.6	15.3	13.5	13.1	13.0	12.0	13.5	14.1	13.2	13.6	1292.7
		25375		18.6	16.8	16.1	15.6	15.3	13.5	13.1	13.0	12.0	13.5	14.1	13.2	13.6	1292.7
		25376		16.4	17.5	16.0	14.9	14.9	13.7	13.7	12.9	11.8	13.9	14.2	13.6	13.3	1281.2
		25377		16.4	17.5	16.0	14.9	14.9	13.7	13.7	12.9	11.8	13.9	14.2	13.6	13.3	1281.2
		25378		15.5	15.6	13.7	13.9	13.5	13.6	12.9	20.9	12.6	12.8	12.9	12.3	12.6	1253.4
		25379		15.5	15.6	13.7	13.9	13.5	13.6	12.9	20.9	12.6	12.8	12.9	12.3	12.6	1253.4
		25380		17.0	16.9	15.9	12.6	30.7	14.9	15.2	13.0	15.1	12.8	16.8	14.4	14.4	1438.8
		25381		17.0	16.9	15.9	12.6	30.7	14.9	15.2	13.0	15.1	12.8	16.8	14.4	14.4	1438.8
		25382		14.9	14.4	14.0	12.7	12.7	12.8	12.5	12.2	11.5	12.2	12.7	12.1	11.3	1139.8
		25383		14.9	14.4	14.0	12.7	12.7	12.8	12.5	12.2	11.5	12.2	12.7	12.1	11.3	1139.8
		25384		16.6	17.2	17.0	16.3	16.6	15.8	15.3	13.9	14.3	15.3	15.1	14.5	12.6	1378.3
		25385		16.6	17.2	17.0	16.3	16.6	15.8	15.3	13.9	14.3	15.3	15.1	14.5	12.6	1378.3
		25386		15.4	16.8	15.2	13.7	12.9	13.5	11.9	8.3	15.1	14.3	14.3	11.9	12.9	1206.8
		25387		15.4	16.8	15.2	13.7	12.9	13.5	11.9	8.3	15.1	14.3	14.3	11.9	12.9	1206.8
		25388		15.5	15.3	21.6	12.0	13.6	12.2	12.2	12.5	11.6	12.8	12.4	13.1	12.5	1215.5
		25389		15.5	15.3	21.6	12.0	13.6	12.2	12.2	12.5	11.6	12.8	12.4	13.1	12.5	1215.5
		25390		14.8	14.5	13.0	13.0	13.5	14.2	11.9	11.0	11.5	11.6	11.9	11.5	11.0	1120.3
		25391		14.8	14.5	13.0	13.0	13.5	14.2	11.9	11.0	11.5	11.6	11.9	11.5	11.0	1120.3
		25392		16.7	16.6	15.6	15.4	16.0	14.1	13.8	12.8	13.2	13.9	13.2	11.3	13.9	1277.3
		25393		16.7	16.6	15.6	15.4	16.0	14.1	13.8	12.8	13.2	13.9	13.2	11.3	13.9	1277.3

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 11 (continued): Individual Water Consumption (g/animal/day)

Day Numbers Relative to Start Date

Group	Sex	Animal	From: 90 To: 92	92 99	99 106	106 113	113 118	Total 1 118	Total 92 118
1	f	25264	17.5	16.4	17.9	18.3	18.5	2131.7	460.4
		25265	17.5	16.4	17.9	18.3	18.5	2131.7	460.4
		25266	21.6	18.9	20.0	19.5	19.5	2511.0	506.6
		25267	21.6	18.9	20.0	19.5	19.5	2511.0	506.6
		25268	17.2	19.3	19.7	20.0	20.1	2285.6	513.5
		25269	17.2	19.3	19.7	20.0	20.1	2285.6	513.5
		25270	23.5	24.3	27.2	26.4	26.7	2666.9	679.0
		25271	23.5	24.3	27.2	26.4	26.7	2666.9	679.0
		25272	17.9	19.0	19.7	22.4	23.9	2342.7	547.1
		25273	17.9	19.0	19.7	22.4	23.9	2342.7	547.1
11	f	25384	28.8	26.7	25.8	28.3	27.1	2137.1	701.3
		25385	28.8	26.7	25.8	28.3	27.1	2137.1	701.3
		25386	22.5	22.4	22.6	23.4	23.3	1846.8	595.1
		25387	22.5	22.4	22.6	23.4	23.3	1846.8	595.1
		25388	20.4	18.6	17.9	18.4	18.5	1732.4	476.2
		25389	20.4	18.6	17.9	18.4	18.5	1732.4	476.2
		25390	25.6	21.4	19.5	18.0	21.0	1688.6	517.0
		25391	25.6	21.4	19.5	18.0	21.0	1688.6	517.0
		25392	29.0	22.6	22.0	22.2	20.7	1905.7	570.6
		25393	29.0	22.6	22.0	22.2	20.7	1905.7	570.6

Target Dose: Group 1 – 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

APPENDIX 12: INDIVIDUAL FOOD CONSUMPTION

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 12: Individual Food Consumption (g/animal/day)

Day Numbers Relative to Start Date

Group	Sex	Animal	From: 1 To: 8	8 15	15 22	22 29	29 36	36 43	43 50	50 57	57 64	64 71	71 78	78 85	85 90	Total 1 90
1	m	25234	24.9	25.5	30.2	30.3	30.2	27.5	28.7	28.6	30.6	24.9	31.3	29.0	29.6	2538.8
		25235	24.9	25.5	30.2	30.3	30.2	27.5	28.7	28.6	30.6	24.9	31.3	29.0	29.6	2538.8
		25236	24.4	24.5	28.0	27.9	28.2	28.7	29.3	30.0	25.9	21.9	31.3	29.0	28.3	2444.5
		25237	24.4	24.5	28.0	27.9	28.2	28.7	29.3	30.0	25.9	21.9	31.3	29.0	28.3	2444.5
		25238	24.3	25.3	25.9	28.8	28.6	28.1	28.0	27.7	27.1	22.6	29.4	28.8	27.3	2408.9
		25239	24.3	25.3	25.9	28.8	28.6	28.1	28.0	27.7	27.1	22.6	29.4	28.8	27.3	2408.9
		25240	23.1	25.8	27.6	26.1	25.5	26.3	27.5	27.7	28.4	25.8	29.9	26.6	27.3	2378.7
		25241	23.1	25.8	27.6	26.1	25.5	26.3	27.5	27.7	28.4	25.8	29.9	26.6	27.3	2378.7
		25242	24.5	22.7	28.5	27.7	28.0	29.1	28.3	27.1	29.8	24.8	30.4	27.7	28.1	2440.3
		25243	24.5	22.7	28.5	27.7	28.0	29.1	28.3	27.1	29.8	24.8	30.4	27.7	28.1	2440.3
		25244	22.2	22.7	23.0	22.7	23.7	24.2	24.6	24.6	25.9	24.3	27.3	24.3	.	.
		25245	22.2	22.7	23.0	22.7	23.7	24.2	24.6	24.6	25.9	24.3	27.3	24.3	.	.
		25246	24.7	27.2	29.8	29.2	29.0	30.0	30.6	28.2	33.1	22.7	32.0	28.6	.	.
		25247	24.7	27.2	29.8	29.2	29.0	30.0	30.6	28.2	33.1	22.7	32.0	28.6	.	.
		25248	22.8	25.7	25.2	25.9	24.9	28.9	27.4	25.2	29.0	23.7	30.3	26.5	.	.
		25249	22.8	25.7	25.2	25.9	24.9	28.9	27.4	25.2	29.0	23.7	30.3	26.5	.	.
		25250	23.7	24.7	25.3	25.8	25.9	27.1	26.0	27.1	24.5	25.0	29.5	26.7	.	.
		25251	23.7	24.7	25.3	25.8	25.9	27.1	26.0	27.1	24.5	25.0	29.5	26.7	.	.
		25252	23.5	24.4	28.4	29.8	29.5	29.1	28.6	27.8	26.0	22.9	30.0	27.6	.	.
		25253	23.5	24.4	28.4	29.8	29.5	29.1	28.6	27.8	26.0	22.9	30.0	27.6	.	.
2	m	25274	24.5	25.0	31.3	34.3	30.9	32.4	27.8	27.6	34.3	24.5	36.6	34.8	32.1	2708.6
		25275	24.5	25.0	31.3	34.3	30.9	32.4	27.8	27.6	34.3	24.5	36.6	34.8	32.1	2708.6
		25276	26.9	25.3	29.9	31.0	28.1	27.8	29.6	23.9	32.2	25.7	33.8	31.5	32.4	2582.6
		25277	26.9	25.3	29.9	31.0	28.1	27.8	29.6	23.9	32.2	25.7	33.8	31.5	32.4	2582.6
		25278	24.1	23.7	30.3	28.8	27.2	30.5	29.6	28.7	28.9	24.7	29.7	27.3	28.5	2476.2
		25279	24.1	23.7	30.3	28.8	27.2	30.5	29.6	28.7	28.9	24.7	29.7	27.3	28.5	2476.2
		25280	25.4	26.2	25.8	28.1	29.0	29.2	29.0	28.6	28.0	25.0	32.5	28.9	28.2	2490.6
		25281	25.4	26.2	25.8	28.1	29.0	29.2	29.0	28.6	28.0	25.0	32.5	28.9	28.2	2490.6
		25282	24.0	24.8	23.9	24.6	24.5	25.5	24.7	24.0	25.4	23.2	25.2	22.7	23.4	2165.3
		25283	24.0	24.8	23.9	24.6	24.5	25.5	24.7	24.0	25.4	23.2	25.2	22.7	23.4	2165.3

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 12 (continued): Individual Food Consumption (g/animal/day)

Day Numbers Relative to Start Date

Group	Sex	Animal	From: 1 To: 8	8 15	15 22	22 29	29 36	36 43	43 50	50 57	57 64	64 71	71 78	78 85	85 90	Total 1 90
3	m	25284	23.0	25.1	24.6	25.3	26.2	26.4	27.6	24.5	26.1	22.7	27.9	24.9	26.2	2260.5
		25285	23.0	25.1	24.6	25.3	26.2	26.4	27.6	24.5	26.1	22.7	27.9	24.9	26.2	2260.5
		25286	27.0	25.0	27.9	29.8	29.8	29.9	27.8	24.5	31.8	27.0	31.9	27.5	27.9	2517.1
		25287	27.0	25.0	27.9	29.8	29.8	29.9	27.8	24.5	31.8	27.0	31.9	27.5	27.9	2517.1
		25288	25.1	24.6	25.6	21.5	28.1	28.4	25.4	25.2	28.1	24.4	29.7	26.6	26.8	2322.8
		25289	25.1	24.6	25.6	21.5	28.1	28.4	25.4	25.2	28.1	24.4	29.7	26.6	26.8	2322.8
		25290	15.3	26.2	25.6	27.2	26.2	30.0	27.4	27.8	29.2	26.1	29.5	27.5	27.4	2363.3
		25291	15.3	26.2	25.6	27.2	26.2	30.0	27.4	27.8	29.2	26.1	29.5	27.5	27.4	2363.3
		25292	25.0	24.9	28.8	29.8	27.0	31.0	28.3	29.0	26.2	22.4	31.4	29.0	28.0	2468.9
		25293	25.0	24.9	28.8	29.8	27.0	31.0	28.3	29.0	26.2	22.4	31.4	29.0	28.0	2468.9
4	m	25294	23.6	25.9	24.7	27.2	25.4	27.1	26.8	24.2	27.0	23.5	28.1	26.1	26.8	2300.8
		25295	23.6	25.9	24.7	27.2	25.4	27.1	26.8	24.2	27.0	23.5	28.1	26.1	26.8	2300.8
		25296	23.5	23.4	23.2	23.9	24.1	24.5	24.9	23.4	26.3	24.9	25.4	23.1	25.4	2160.9
		25297	23.5	23.4	23.2	23.9	24.1	24.5	24.9	23.4	26.3	24.9	25.4	23.1	25.4	2160.9
		25298	24.2	24.8	24.0	23.9	24.6	24.9	24.5	24.3	25.1	24.0	26.0	25.2	24.7	2192.7
		25299	24.2	24.8	24.0	23.9	24.6	24.9	24.5	24.3	25.1	24.0	26.0	25.2	24.7	2192.7
		25300	24.0	25.7	31.6	34.0	31.2	32.9	29.1	33.8	33.9	25.8	36.5	32.6	34.1	2766.9
		25301	24.0	25.7	31.6	34.0	31.2	32.9	29.1	33.8	33.9	25.8	36.5	32.6	34.1	2766.9
		25302	25.1	23.7	29.2	29.7	27.7	29.0	27.7	23.7	32.7	23.8	30.7	26.8	26.9	2443.2
		25303	25.1	23.7	29.2	29.7	27.7	29.0	27.7	23.7	32.7	23.8	30.7	26.8	26.9	2443.2
5	m	25304	22.3	23.1	23.2	7.2	24.5	26.2	24.4	24.0	24.9	23.3	25.6	23.3	24.0	2025.2
		25305	22.3	23.1	23.2	7.2	24.5	26.2	24.4	24.0	24.9	23.3	25.6	23.3	24.0	2025.2
		25306	22.7	23.8	24.3	25.2	24.4	26.3	26.0	24.1	25.8	24.3	28.0	25.3	26.0	2231.6
		25307	22.7	23.8	24.3	25.2	24.4	26.3	26.0	24.1	25.8	24.3	28.0	25.3	26.0	2231.6
		25308	24.6	23.4	27.5	26.5	26.0	26.7	27.2	25.6	25.6	24.6	29.0	26.6	26.2	2324.8
		25309	24.6	23.4	27.5	26.5	26.0	26.7	27.2	25.6	25.6	24.6	29.0	26.6	26.2	2324.8
		25310	24.0	30.3	25.4	27.0	24.8	27.1	27.2	23.4	30.4	24.8	27.9	25.3	26.2	2355.2
		25311	24.0	30.3	25.4	27.0	24.8	27.1	27.2	23.4	30.4	24.8	27.9	25.3	26.2	2355.2
		25312	24.7	26.9	27.8	27.4	25.5	29.8	27.0	26.0	27.8	27.6	27.6	25.9	26.7	2402.2
		25313	24.7	26.9	27.8	27.4	25.5	29.8	27.0	26.0	27.8	27.6	27.6	25.9	26.7	2402.2

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 12 (continued): Individual Food Consumption (g/animal/day)

Day Numbers Relative to Start Date

Group	Sex	Animal	From: 1 To: 8	8 15	15 22	22 29	29 36	36 43	43 50	50 57	57 64	64 71	71 78	78 85	85 90	Total 1 90
6	m	25314	23.4	23.8	23.8	6.8	23.7	25.2	23.5	24.0	24.0	24.8	25.3	23.1	24.5	2022.4
		25315	23.4	23.8	23.8	6.8	23.7	25.2	23.5	24.0	24.0	24.8	25.3	23.1	24.5	2022.4
		25316	22.8	26.1	24.1	28.5	27.3	27.7	27.9	25.8	29.1	25.7	29.7	29.1	29.1	2413.4
		25317	22.8	26.1	24.1	28.5	27.3	27.7	27.9	25.8	29.1	25.7	29.7	29.1	29.1	2413.4
		25318	22.0	24.0	24.1	23.8	24.0	23.8	23.2	23.7	25.2	24.0	25.6	24.3	26.1	2144.6
		25319	22.0	24.0	24.1	23.8	24.0	23.8	23.2	23.7	25.2	24.0	25.6	24.3	26.1	2144.6
		25320	23.2	24.9	24.8	25.4	25.2	26.2	25.5	24.9	24.9	26.0	27.2	24.9	26.2	2252.5
		25321	23.2	24.9	24.8	25.4	25.2	26.2	25.5	24.9	24.9	26.0	27.2	24.9	26.2	2252.5
		25322	21.1	25.0	22.7	23.6	22.1	23.3	22.9	22.7	22.4	22.6	22.1	20.8	20.6	2001.8
		25323	21.1	25.0	22.7	23.6	22.1	23.3	22.9	22.7	22.4	22.6	22.1	20.8	20.6	2001.8
		25324	23.5	25.8	26.0	28.3	27.0	28.5	26.9	25.9	28.3	25.6	28.7	24.2	.	.
		25325	23.5	25.8	26.0	28.3	27.0	28.5	26.9	25.9	28.3	25.6	28.7	24.2	.	.
		25326	23.2	24.3	25.5	25.3	25.5	27.2	26.6	24.0	26.7	25.9	29.8	26.5	.	.
		25327	23.2	24.3	25.5	25.3	25.5	27.2	26.6	24.0	26.7	25.9	29.8	26.5	.	.
		25328	24.7	25.9	24.7	29.4	26.8	28.0	27.6	26.5	26.4	25.5	27.8	25.3	.	.
		25329	24.7	25.9	24.7	29.4	26.8	28.0	27.6	26.5	26.4	25.5	27.8	25.3	.	.
		25330	24.4	25.1	25.6	26.8	26.0	26.8	26.3	26.4	23.9	23.1	28.5	26.5	.	.
		25331	24.4	25.1	25.6	26.8	26.0	26.8	26.3	26.4	23.9	23.1	28.5	26.5	.	.
		25332	23.9	22.2	28.3	8.5	25.3	29.2	27.4	25.2	27.3	26.0	26.0	25.3	.	.
		25333	23.9	22.2	28.3	8.5	25.3	29.2	27.4	25.2	27.3	26.0	26.0	25.3	.	.

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 12 (continued): Individual Food Consumption (g/animal/day)

Day Numbers Relative to Start Date

Group	Sex	Animal	From: To:	85 92	92 99	99 106	106 113	113 118	Total 1 118	Total 92 118
1	m	25244		23.6	27.3	26.1	26.0	25.8	2876.5	684.7
		25245		23.6	27.3	26.1	26.0	25.8	2876.5	684.7
		25246		25.7	31.9	30.9	29.1	30.4	3390.8	795.2
		25247		25.7	31.9	30.9	29.1	30.4	3390.8	795.2
		25248		25.8	28.1	26.6	26.8	27.6	3095.6	708.2
		25249		25.8	28.1	26.6	26.8	27.6	3095.6	708.2
		25250		24.9	28.5	27.5	26.9	28.0	3074.0	720.4
		25251		24.9	28.5	27.5	26.9	28.0	3074.0	720.4
		25252		25.6	27.8	29.7	29.2	29.5	3227.6	755.0
		25253		25.6	27.8	29.7	29.2	29.5	3227.6	755.0
6	m	25324		23.9	29.9	31.0	30.2	30.4	3188.6	790.0
		25325		23.9	29.9	31.0	30.2	30.4	3188.6	790.0
		25326		24.9	30.0	31.7	31.4	31.3	3155.5	808.4
		25327		24.9	30.0	31.7	31.4	31.3	3155.5	808.4
		25328		25.7	29.6	30.7	29.1	30.6	3187.5	778.4
		25329		25.7	29.6	30.7	29.1	30.6	3187.5	778.4
		25330		24.5	28.5	33.3	31.0	32.4	3148.3	811.1
		25331		24.5	28.5	33.3	31.0	32.4	3148.3	811.1
		25332		26.5	27.2	28.1	27.2	28.0	2965.0	717.5
		25333		26.5	27.2	28.1	27.2	28.0	2965.0	717.5

Target Dose: Group 1 – 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 12 (continued): Individual Food Consumption (g/animal/day)

Day Numbers Relative to Start Date

Group	Sex	Animal	From: 1 To: 8	8 15	15 22	22 29	29 36	36 43	43 50	50 57	57 64	64 71	71 78	78 85	85 90	Total 1 90
1	f	25254	15.9	16.7	16.0	15.9	15.9	18.6	16.2	16.2	16.6	16.7	15.3	14.9	14.7	1437.6
		25255	15.9	16.7	16.0	15.9	15.9	18.6	16.2	16.2	16.6	16.7	15.3	14.9	14.7	1437.6
		25256	16.5	16.6	15.1	15.5	15.5	16.7	16.0	13.3	14.9	14.0	14.2	13.6	14.7	1347.2
		25257	16.5	16.6	15.1	15.5	15.5	16.7	16.0	13.3	14.9	14.0	14.2	13.6	14.7	1347.2
		25258	17.1	17.6	16.7	16.8	16.7	16.9	17.0	16.8	17.6	17.4	16.4	15.6	16.4	1498.0
		25259	17.1	17.6	16.7	16.8	16.7	16.9	17.0	16.8	17.6	17.4	16.4	15.6	16.4	1498.0
		25260	17.0	17.1	16.8	17.0	17.2	18.2	18.0	17.4	18.4	18.1	16.8	15.2	15.5	1527.8
		25261	17.0	17.1	16.8	17.0	17.2	18.2	18.0	17.4	18.4	18.1	16.8	15.2	15.5	1527.8
		25262	17.4	17.5	17.8	17.7	16.9	18.1	18.2	17.2	17.7	17.0	16.9	16.4	15.1	1536.1
		25263	17.4	17.5	17.8	17.7	16.9	18.1	18.2	17.2	17.7	17.0	16.9	16.4	15.1	1536.1
		25264	15.6	15.1	14.4	14.2	14.7	15.9	15.7	14.1	15.9	15.3	14.3	14.4	.	.
		25265	15.6	15.1	14.4	14.2	14.7	15.9	15.7	14.1	15.9	15.3	14.3	14.4	.	.
		25266	16.9	16.5	16.9	17.1	17.1	17.7	17.0	17.3	17.5	17.3	16.4	15.7	.	.
		25267	16.9	16.5	16.9	17.1	17.1	17.7	17.0	17.3	17.5	17.3	16.4	15.7	.	.
		25268	16.9	17.4	16.3	16.2	17.4	17.0	16.4	16.9	21.0	15.6	15.5	16.1	.	.
		25269	16.9	17.4	16.3	16.2	17.4	17.0	16.4	16.9	21.0	15.6	15.5	16.1	.	.
		25270	16.1	17.4	17.1	17.2	17.6	19.2	19.0	18.6	19.9	18.5	16.7	17.0	.	.
		25271	16.1	17.4	17.1	17.2	17.6	19.2	19.0	18.6	19.9	18.5	16.7	17.0	.	.
		25272	17.3	18.4	18.2	17.7	17.6	17.9	18.9	18.1	19.3	17.7	19.7	19.0	.	.
		25273	17.3	18.4	18.2	17.7	17.6	17.9	18.9	18.1	19.3	17.7	19.7	19.0	.	.
7	f	25334	15.2	14.5	14.3	14.8	13.3	14.8	14.7	14.8	15.5	14.4	14.5	14.5	13.8	1294.6
		25335	15.2	14.5	14.3	14.8	13.3	14.8	14.7	14.8	15.5	14.4	14.5	14.5	13.8	1294.6
		25336	15.5	16.8	16.1	16.6	17.2	18.3	18.8	17.7	17.4	17.3	18.1	18.0	17.5	1542.1
		25337	15.5	16.8	16.1	16.6	17.2	18.3	18.8	17.7	17.4	17.3	18.1	18.0	17.5	1542.1
		25338	16.0	16.7	15.9	16.0	16.9	17.4	17.1	17.2	17.7	16.4	15.9	15.2	15.7	1465.5
		25339	16.0	16.7	15.9	16.0	16.9	17.4	17.1	17.2	17.7	16.4	15.9	15.2	15.7	1465.5
		25340	15.2	15.6	15.7	15.7	15.0	15.6	16.5	15.6	16.7	15.1	16.0	15.4	15.6	1394.2
		25341	15.2	15.6	15.7	15.7	15.0	15.6	16.5	15.6	16.7	15.1	16.0	15.4	15.6	1394.2
		25342	16.0	17.0	16.9	16.6	17.1	18.6	17.9	17.9	16.8	17.5	18.1	18.0	16.5	1540.9
		25343	16.0	17.0	16.9	16.6	17.1	18.6	17.9	17.9	16.8	17.5	18.1	18.0	16.5	1540.9

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 12 (continued): Individual Food Consumption (g/animal/day)

Day Numbers Relative to Start Date

Group	Sex	Animal	From: 1 To: 8	8 15	15 22	22 29	29 36	36 43	43 50	50 57	57 64	64 71	71 78	78 85	85 90	Total 1 90
8	f	25344	16.3	16.7	16.6	16.3	15.1	16.2	16.1	16.7	16.6	16.5	16.1	15.4	15.3	1437.1
		25345	16.3	16.7	16.6	16.3	15.1	16.2	16.1	16.7	16.6	16.5	16.1	15.4	15.3	1437.1
		25346	16.0	15.8	15.3	15.1	14.5	15.3	15.8	15.1	15.8	15.1	15.9	15.0	15.1	1366.7
		25347	16.0	15.8	15.3	15.1	14.5	15.3	15.8	15.1	15.8	15.1	15.9	15.0	15.1	1366.7
		25348	16.0	16.9	15.9	15.5	16.3	16.5	16.5	17.2	17.8	17.2	16.1	15.9	16.0	1464.5
		25349	16.0	16.9	15.9	15.5	16.3	16.5	16.5	17.2	17.8	17.2	16.1	15.9	16.0	1464.5
		25350	15.5	15.5	15.2	16.2	16.1	16.3	15.5	15.8	17.0	16.4	16.1	16.0	16.4	1423.0
		25351	15.5	15.5	15.2	16.2	16.1	16.3	15.5	15.8	17.0	16.4	16.1	16.0	16.4	1423.0
		25352	24.3	25.5	23.5	18.1	17.9	18.7	23.8	23.8	19.1	21.9	17.6	16.9	14.8	1831.1
		25353	24.3	25.5	23.5	18.1	17.9	18.7	23.8	23.8	19.1	21.9	17.6	16.9	14.8	1831.1
9	f	25354	17.2	17.2	16.2	17.3	16.6	17.0	17.1	17.5	19.3	17.7	18.0	17.3	17.2	1544.2
		25355	17.2	17.2	16.2	17.3	16.6	17.0	17.1	17.5	19.3	17.7	18.0	17.3	17.2	1544.2
		25356	16.3	16.2	15.1	15.8	15.9	16.3	16.3	17.0	17.6	17.4	15.6	17.3	16.5	1459.5
		25357	16.3	16.2	15.1	15.8	15.9	16.3	16.3	17.0	17.6	17.4	15.6	17.3	16.5	1459.5
		25358	16.6	16.7	15.8	16.0	16.9	17.4	16.6	17.0	17.4	16.7	16.0	14.6	15.8	1461.6
		25359	16.6	16.7	15.8	16.0	16.9	17.4	16.6	17.0	17.4	16.7	16.0	14.6	15.8	1461.6
		25360	15.6	17.2	16.5	16.8	16.3	18.1	17.0	16.6	17.5	17.0	16.3	16.2	15.5	1483.6
		25361	15.6	17.2	16.5	16.8	16.3	18.1	17.0	16.6	17.5	17.0	16.3	16.2	15.5	1483.6
		25362	15.1	15.9	15.0	15.5	16.2	17.1	16.3	16.4	17.3	16.9	15.9	15.8	13.8	1422.5
		25363	15.1	15.9	15.0	15.5	16.2	17.1	16.3	16.4	17.3	16.9	15.9	15.8	13.8	1422.5
10	f	25364	15.2	15.9	15.3	15.7	16.4	16.7	16.9	15.9	17.5	16.5	15.8	15.2	15.8	1429.6
		25365	15.2	15.9	15.3	15.7	16.4	16.7	16.9	15.9	17.5	16.5	15.8	15.2	15.8	1429.6
		25366	15.0	15.4	15.1	14.9	15.2	16.3	15.2	15.3	15.5	15.8	15.0	14.2	14.3	1351.3
		25367	15.0	15.4	15.1	14.9	15.2	16.3	15.2	15.3	15.5	15.8	15.0	14.2	14.3	1351.3
		25368	17.6	17.9	17.1	17.7	17.4	17.5	16.9	16.9	17.0	17.6	16.6	15.2	14.5	1509.6
		25369	17.6	17.9	17.1	17.7	17.4	17.5	16.9	16.9	17.0	17.6	16.6	15.2	14.5	1509.6
		25370	14.8	16.7	16.8	17.6	17.6	18.1	16.6	16.9	17.3	17.5	17.5	16.3	14.7	1498.9
		25371	14.8	16.7	16.8	17.6	17.6	18.1	16.6	16.9	17.3	17.5	17.5	16.3	14.7	1498.9
		25372	15.7	15.8	14.7	15.0	16.3	16.3	16.9	17.1	17.7	17.8	16.8	16.1	15.6	1452.2
		25373	15.7	15.8	14.7	15.0	16.3	16.3	16.9	17.1	17.7	17.8	16.8	16.1	15.6	1452.2

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 12 (continued): Individual Food Consumption (g/animal/day)

Day Numbers Relative to Start Date

Group	Sex	Animal	From: 1 To: 8	8 15	15 22	22 29	29 36	36 43	43 50	50 57	57 64	64 71	71 78	78 85	85 90	Total 1 90
11	f	25374	18.5	18.0	18.2	17.5	18.4	17.9	17.7	17.8	17.4	17.4	17.0	16.4	16.2	1567.1
		25375	18.5	18.0	18.2	17.5	18.4	17.9	17.7	17.8	17.4	17.4	17.0	16.4	16.2	1567.1
		25376	14.2	14.3	14.1	14.0	14.3	14.0	15.1	13.9	14.4	15.0	14.7	14.6	13.7	1276.4
		25377	14.2	14.3	14.1	14.0	14.3	14.0	15.1	13.9	14.4	15.0	14.7	14.6	13.7	1276.4
		25378	15.8	16.0	15.5	15.7	16.0	16.6	16.4	16.8	17.2	16.4	16.3	16.1	15.8	1443.4
		25379	15.8	16.0	15.5	15.7	16.0	16.6	16.4	16.8	17.2	16.4	16.3	16.1	15.8	1443.4
		25380	17.2	18.2	17.8	18.4	19.2	18.9	19.6	23.4	21.8	24.9	20.8	19.0	30.2	1826.8
		25381	17.2	18.2	17.8	18.4	19.2	18.9	19.6	23.4	21.8	24.9	20.8	19.0	30.2	1826.8
		25382	15.2	14.8	15.4	15.3	15.5	16.2	16.5	16.0	16.0	16.7	16.6	15.3	14.9	1401.6
		25383	15.2	14.8	15.4	15.3	15.5	16.2	16.5	16.0	16.0	16.7	16.6	15.3	14.9	1401.6
		25384	16.0	17.1	17.0	17.1	18.4	19.6	18.2	17.9	18.6	18.7	17.5	16.9	.	.
		25385	16.0	17.1	17.0	17.1	18.4	19.6	18.2	17.9	18.6	18.7	17.5	16.9	.	.
		25386	15.1	15.8	15.2	15.1	15.3	16.1	15.5	10.5	18.7	16.7	16.0	15.3	.	.
		25387	15.1	15.8	15.2	15.1	15.3	16.1	15.5	10.5	18.7	16.7	16.0	15.3	.	.
		25388	16.9	19.8	21.9	17.0	23.3	16.4	16.7	17.0	16.4	17.3	16.2	17.4	.	.
		25389	16.9	19.8	21.9	17.0	23.3	16.4	16.7	17.0	16.4	17.3	16.2	17.4	.	.
		25390	14.9	15.0	14.9	14.6	15.1	15.5	15.1	14.5	15.3	15.1	15.3	14.3	.	.
		25391	14.9	15.0	14.9	14.6	15.1	15.5	15.1	14.5	15.3	15.1	15.3	14.3	.	.
		25392	15.7	16.4	16.4	16.9	17.3	16.8	17.4	16.5	17.0	17.0	16.4	13.9	.	.
		25393	15.7	16.4	16.4	16.9	17.3	16.8	17.4	16.5	17.0	17.0	16.4	13.9	.	.

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 12 (continued): Individual Food Consumption (g/animal/day)

Day Numbers Relative to Start Date

Group	Sex	Animal	From: To:	85 92	92 99	99 106	106 113	113 118	Total 1 118	Total 92 118
1	f	25264		13.3	14.7	15.2	15.8	14.8	1743.0	393.9
		25265		13.3	14.7	15.2	15.8	14.8	1743.0	393.9
		25266		14.5	16.5	17.8	17.4	17.9	1975.1	450.9
		25267		14.5	16.5	17.8	17.4	17.9	1975.1	450.9
		25268		24.4	17.0	18.3	19.5	30.4	2125.4	535.6
		25269		24.4	17.0	18.3	19.5	30.4	2125.4	535.6
		25270		15.3	18.3	20.6	19.6	19.7	2114.1	508.0
		25271		15.3	18.3	20.6	19.6	19.7	2114.1	508.0
		25272		15.8	18.0	19.3	21.5	23.5	2177.3	529.6
		25273		15.8	18.0	19.3	21.5	23.5	2177.3	529.6
11	f	25384		15.2	20.0	19.1	20.6	21.2	2122.4	524.0
		25385		15.2	20.0	19.1	20.6	21.2	2122.4	524.0
		25386		14.5	17.9	17.3	17.2	16.7	1847.8	450.4
		25387		14.5	17.9	17.3	17.2	16.7	1847.8	450.4
		25388		15.4	17.1	17.6	17.6	17.3	2073.0	452.1
		25389		15.4	17.1	17.6	17.6	17.3	2073.0	452.1
		25390		13.8	16.5	16.5	16.3	16.3	1779.9	426.3
		25391		13.8	16.5	16.5	16.3	16.3	1779.9	426.3
		25392		15.6	18.0	18.4	18.6	17.2	1963.4	470.3
		25393		15.6	18.0	18.4	18.6	17.2	1963.4	470.3

Target Dose: Group 1 – 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

APPENDIX 13: INDIVIDUAL TEST MATERIAL INTAKE

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 13: Individual Test Material Intake (mg/kg/day)

Day Numbers Relative to Start Date

Group/Sex	Animal	Wk1	Wk2	Wk3	Wk4	Wk5	Wk6	Wk7	Wk8	Wk9	Wk10	Wk11	Wk12	Wk13	Mean
1m	25234	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	25235	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	25236	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	25237	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	25238	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	25239	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	25240	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	25241	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	25242	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	25243	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	25244	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	25245	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	25246	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	25247	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	25248	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	25249	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	25250	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	25251	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	25252	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	25253	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2m	25274	1.18	1.23	1.02	0.88	0.96	0.89	0.78	0.91	0.96	0.89	0.98	0.96	1.03	0.97
	25275	1.05	1.04	0.86	0.76	0.84	0.79	0.70	0.82	0.86	0.79	0.86	0.84	0.90	0.85
	25276	1.23	1.10	0.98	0.87	1.00	0.93	0.89	1.03	1.07	0.98	1.08	1.00	1.04	1.02
	25277	1.16	1.03	0.92	0.83	0.95	0.89	0.86	0.99	1.04	0.95	1.07	1.00	1.04	0.98
	25278	1.20	1.02	0.85	0.78	0.78	0.75	0.70	0.81	0.83	0.77	0.90	0.89	0.85	0.86
	25279	1.24	1.07	0.89	0.83	0.84	0.82	0.77	0.88	0.91	0.84	0.99	0.98	0.92	0.92
	25280	1.32	1.12	0.94	0.98	1.01	0.97	0.90	1.02	1.08	1.03	1.07	0.95	0.91	1.02
	25281	1.33	1.12	0.93	0.97	1.01	0.96	0.89	1.01	1.07	1.02	1.07	0.95	0.91	1.02
	25282	1.06	0.94	0.79	0.78	0.80	0.78	0.75	0.88	0.87	0.83	0.91	0.90	0.91	0.86
	25283	1.06	0.94	0.78	0.77	0.78	0.77	0.73	0.85	0.83	0.80	0.88	0.87	0.88	0.84

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 13 (continued): Individual Test Material Intake (mg/kg/day)

Day Numbers Relative to Start Date

Group/Sex	Animal	Wk1	Wk2	Wk3	Wk4	Wk5	Wk6	Wk7	Wk8	Wk9	Wk10	Wk11	Wk12	Wk13	Mean
3m	25284	3.76	3.24	3.04	2.89	2.96	3.02	2.63	2.95	2.80	2.63	2.79	2.41	2.48	2.89
	25285	3.71	3.32	3.24	3.19	3.35	3.42	2.93	3.29	3.16	2.98	3.16	2.76	2.89	3.19
	25286	3.30	2.90	2.68	2.61	2.78	2.96	2.50	2.88	2.53	2.25	2.66	2.27	2.43	2.67
	25287	3.46	3.07	2.91	2.89	3.16	3.44	2.98	3.47	3.08	2.79	3.32	2.87	3.09	3.12
	25288	3.00	2.53	2.17	1.45	2.39	2.43	2.10	2.42	2.51	2.13	2.71	2.27	2.38	2.35
	25289	3.30	2.73	2.31	1.62	2.74	2.68	2.28	2.62	2.68	2.27	2.85	2.36	2.47	2.53
	25290	3.34	2.89	2.35	2.46	2.74	2.75	2.34	2.65	2.62	2.58	3.09	2.80	3.04	2.74
	25291	3.57	3.08	2.49	2.62	2.95	2.99	2.57	2.92	2.87	2.83	3.41	3.06	3.27	2.97
	25292	3.55	3.40	3.06	2.86	2.98	3.02	2.31	2.76	2.88	2.78	3.07	2.71	2.52	2.92
	25293	3.36	3.15	2.83	2.66	2.78	2.89	2.27	2.70	2.81	2.73	3.04	2.69	2.50	2.80
4m	25294	12.03	10.91	9.18	10.42	11.36	9.72	9.76	11.31	10.96	9.99	11.04	10.34	8.39	10.41
	25295	12.02	10.60	8.69	9.72	10.56	9.05	9.04	10.45	10.09	9.23	10.25	9.52	7.68	9.76
	25296	9.75	8.69	7.28	7.74	8.14	7.82	8.12	8.66	8.57	8.29	9.56	8.52	8.84	8.46
	25297	9.33	8.00	6.60	7.05	7.40	7.05	7.23	7.66	7.59	7.33	8.39	7.42	7.73	7.60
	25298	10.77	9.56	8.63	9.26	8.66	8.38	8.84	9.00	9.48	8.65	10.19	10.01	10.23	9.36
	25299	11.82	10.35	9.25	9.87	9.22	8.93	9.40	9.40	9.88	9.10	10.68	10.48	10.68	9.93
	25300	10.43	10.16	9.14	8.06	7.92	7.40	7.05	7.71	7.66	7.15	8.97	7.88	7.27	8.22
	25301	10.86	10.64	9.70	8.69	8.64	8.14	7.80	8.57	8.55	7.97	10.02	8.89	8.24	8.98
	25302	12.18	10.87	11.23	11.79	10.00	9.21	8.96	10.72	10.87	8.86	10.87	10.01	9.18	10.37
	25303	10.69	9.14	9.16	9.60	8.31	7.75	7.60	9.08	9.23	7.66	9.56	8.88	8.11	8.83
5m	25304	25.38	20.29	20.70	0.75	27.56	27.10	24.47	24.89	25.29	24.39	28.00	26.10	24.83	23.06
	25305	25.52	20.00	20.01	0.71	26.08	25.71	22.88	23.00	23.17	22.38	25.71	23.83	22.55	21.66
	25306	28.33	25.73	24.90	26.91	26.10	25.20	24.84	26.78	27.49	27.12	31.46	28.41	25.47	26.83
	25307	26.83	24.53	23.82	26.13	25.80	25.18	25.02	26.94	27.46	27.08	31.55	28.71	25.76	26.52
	25308	29.53	24.70	26.03	24.45	24.97	24.27	23.45	23.33	25.15	26.15	29.73	22.50	24.69	25.30
	25309	30.00	24.57	25.73	24.23	24.82	24.33	23.89	24.03	26.14	27.67	32.18	24.74	27.32	26.13
	25310	30.58	27.39	28.14	29.82	30.13	29.90	29.77	27.40	29.05	27.77	30.04	28.91	26.89	28.91
	25311	28.88	26.35	27.27	29.35	30.19	29.88	29.75	27.41	28.97	27.55	29.75	28.73	26.91	28.54
	25312	29.35	25.64	25.08	25.89	27.10	26.42	22.95	25.21	26.10	27.81	31.09	26.89	26.16	26.59
	25313	31.45	27.86	27.46	27.98	29.03	28.08	23.87	26.00	26.88	28.29	31.38	27.00	26.34	27.82

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 13 (continued): Individual Test Material Intake (mg/kg/day)

Day Numbers Relative to Start Date

Group/ Sex	Animal	Wk1	Wk2	Wk3	Wk4	Wk5	Wk6	Wk7	Wk8	Wk9	Wk10	Wk11	Wk12	Wk13	Mean
6m	25314	83.93	75.08	63.92	9.48	82.83	84.13	84.12	88.46	90.98	87.94	103.27	94.17	86.90	79.63
	25315	87.53	74.84	63.05	9.12	80.10	83.48	83.09	89.65	91.61	85.22	100.06	90.76	83.03	78.58
	25316	88.20	93.87	76.42	89.11	94.19	92.20	94.72	100.97	109.60	97.18	126.16	118.35	102.94	98.76
	25317	81.87	83.84	66.79	78.67	83.44	80.72	81.68	85.61	91.69	80.08	102.77	95.24	81.93	84.18
	25318	98.38	95.38	74.91	83.75	94.27	90.55	92.90	101.32	105.59	90.80	118.11	109.53	108.01	97.19
	25319	94.38	90.27	69.49	76.81	86.86	83.51	84.68	91.71	96.26	82.78	107.64	100.08	99.39	89.53
	25320	87.32	74.62	56.53	69.44	73.25	74.15	72.45	79.02	75.26	83.16	90.54	79.06	80.75	76.58
	25321	104.07	88.22	65.93	80.35	83.52	83.34	81.06	89.43	86.03	95.55	104.40	91.45	93.35	88.21
	25322	89.09	79.78	62.17	69.02	69.49	74.66	70.65	73.23	72.89	74.64	92.71	78.25	69.25	75.06
	25323	100.68	96.93	78.16	89.31	92.27	99.71	94.35	97.70	97.49	100.20	124.63	105.43	93.69	97.73
	25324	105.58	95.79	77.69	89.30	87.68	86.13	90.81	92.47	96.06	94.20	113.88	96.38	96.76	94.06
	25325	95.10	85.93	70.27	81.16	78.38	76.03	81.11	82.58	84.93	83.37	100.76	84.86	85.52	83.85
	25326	96.64	83.88	65.72	72.19	78.50	78.77	76.75	80.61	88.29	72.37	98.70	92.06	83.62	82.16
	25327	86.85	79.40	64.75	72.13	80.30	82.45	81.09	85.15	92.97	76.82	105.70	99.23	90.68	84.43
	25328	90.08	85.15	66.81	82.65	84.32	83.85	84.47	92.83	95.32	94.82	107.61	99.12	100.64	89.82
	25329	95.29	87.04	66.49	80.62	81.82	80.84	81.14	88.71	91.35	91.89	103.21	94.40	95.44	87.56
	25330	88.93	82.68	69.01	76.86	81.17	76.43	79.55	86.32	83.24	90.63	112.66	97.65	99.69	86.52
	25331	85.54	78.64	66.43	74.83	78.69	73.65	75.99	82.60	79.91	86.13	106.82	92.66	95.19	82.85
	25332	96.11	87.12	83.37	4.57	92.10	102.68	98.65	100.43	104.87	100.54	114.16	105.90	103.34	91.83
	25333	96.38	84.82	77.29	4.20	83.42	89.70	84.99	85.39	88.07	84.03	95.14	88.26	86.47	80.63

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 13 (continued): Individual Test Material Intake (mg/kg/day)

Day Numbers Relative to Start Date

Group/Sex	Animal	Wk1	Wk2	Wk3	Wk4	Wk5	Wk6	Wk7	Wk8	Wk9	Wk10	Wk11	Wk12	Wk13	Mean
1f	25254	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	25255	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	25256	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	25257	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	25258	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	25259	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	25260	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	25261	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	25262	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	25263	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	25264	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	25265	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	25266	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	25267	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	25268	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	25269	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	25270	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	25271	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	25272	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	25273	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
7f	25334	1.45	1.03	0.78	0.86	0.80	0.87	0.81	0.88	0.84	0.83	0.98	0.93	0.87	0.92
	25335	1.36	0.95	0.69	0.77	0.72	0.78	0.73	0.80	0.76	0.75	0.88	0.82	0.76	0.83
	25336	1.42	1.31	0.96	1.11	1.14	1.17	1.03	1.07	1.01	1.11	1.21	1.10	0.99	1.13
	25337	1.42	1.25	0.89	1.03	1.06	1.10	0.98	1.03	0.99	1.09	1.19	1.11	1.01	1.09
	25338	1.23	1.11	0.82	0.71	0.93	0.93	0.85	0.84	0.00	0.91	1.00	0.87	0.79	0.85
	25339	1.22	1.09	0.82	0.70	0.88	0.88	0.82	0.81	0.00	0.89	0.97	0.83	0.75	0.82
	25340	1.37	1.22	0.80	0.96	1.02	1.05	1.09	1.08	1.01	0.94	1.29	1.12	1.00	1.07
	25341	1.34	1.11	0.72	0.89	0.92	0.91	0.93	0.94	0.89	0.80	1.09	0.98	0.89	0.95
	25342	1.25	1.11	0.86	0.96	0.94	1.06	0.91	0.91	0.83	0.96	1.18	1.06	0.96	1.00
	25343	1.26	1.13	0.87	0.94	0.91	1.05	0.90	0.91	0.83	0.97	1.17	1.05	0.95	1.00

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 13 (continued): Individual Test Material Intake (mg/kg/day)

Day Numbers Relative to Start Date

Group/Sex	Animal	Wk1	Wk2	Wk3	Wk4	Wk5	Wk6	Wk7	Wk8	Wk9	Wk10	Wk11	Wk12	Wk13	Mean
8f	25344	4.61	3.61	2.69	2.78	2.61	2.80	2.81	2.96	2.81	2.84	2.88	2.74	2.71	2.99
	25345	5.17	4.14	3.11	3.29	3.17	3.41	3.35	3.48	3.31	3.37	3.41	3.29	3.30	3.52
	25346	2.59	3.08	2.29	2.32	2.39	2.49	2.63	2.58	2.59	2.62	2.90	2.58	2.47	2.58
	25347	2.53	2.90	2.07	2.05	2.11	2.20	2.28	2.20	2.18	2.18	2.40	2.11	2.04	2.25
	25348	4.33	3.86	3.07	3.14	3.25	3.07	3.19	3.36	3.44	3.35	3.27	3.10	3.09	3.35
	25349	4.08	3.87	3.21	3.26	3.36	3.24	3.38	3.52	3.62	3.59	3.50	3.25	3.22	3.47
	25350	3.11	2.62	2.04	2.09	2.39	2.21	2.47	2.57	2.71	2.68	2.76	2.56	2.36	2.51
	25351	3.36	2.98	2.35	2.32	2.64	2.50	2.74	2.77	2.94	2.96	3.02	2.80	2.56	2.77
	25352	4.24	3.96	2.92	3.03	2.82	3.03	2.93	3.28	2.97	2.86	3.14	2.80	2.52	3.11
	25353	3.90	3.73	2.77	2.82	2.60	2.79	2.70	3.02	2.75	2.64	2.89	2.55	2.28	2.88
9f	25354	12.08	10.62	8.09	7.92	8.04	8.82	7.90	8.07	8.78	8.01	8.49	8.57	8.48	8.76
	25355	12.86	11.71	9.25	9.11	9.20	10.12	8.99	9.16	9.92	9.00	9.62	9.82	9.74	9.88
	25356	14.23	12.84	10.63	10.85	12.15	12.31	11.63	12.59	12.96	12.80	10.33	14.07	12.98	12.34
	25357	15.99	14.29	11.73	12.00	13.42	13.35	12.34	13.44	13.98	13.52	10.77	14.72	13.64	13.32
	25358	11.79	11.55	8.18	8.41	9.54	9.98	8.78	8.91	9.59	9.88	10.77	10.12	10.73	9.86
	25359	11.88	11.71	8.15	8.36	9.45	9.73	8.59	8.84	9.47	9.52	10.41	9.88	10.37	9.72
	25360	12.60	11.69	8.55	8.40	8.05	9.02	8.02	7.66	8.26	8.04	8.57	7.95	10.10	8.99
	25361	12.94	11.84	8.73	8.55	8.17	9.29	8.36	7.91	8.55	8.54	9.13	8.52	11.11	9.36
	25362	10.88	10.42	7.14	7.03	7.42	7.57	6.79	7.22	7.33	7.82	7.13	7.86	7.53	7.86
	25363	10.56	10.23	7.20	7.28	7.76	7.91	7.04	7.52	7.76	8.33	7.69	8.56	8.23	8.16
10f	25364	35.56	33.59	28.90	31.97	33.45	32.59	32.31	31.63	34.52	33.43	32.04	31.94	33.04	32.69
	25365	33.09	30.75	26.18	28.60	29.54	28.76	28.63	27.48	29.14	28.16	27.67	27.94	28.69	28.82
	25366	36.84	35.21	27.43	28.78	29.94	31.10	25.49	31.28	33.04	35.53	35.47	32.38	33.76	32.02
	25367	35.22	32.47	25.13	25.81	26.22	26.94	21.96	26.34	27.15	28.76	28.57	25.54	26.63	27.44
	25368	33.74	29.22	23.00	22.19	26.32	26.43	23.44	23.36	24.83	29.06	28.49	23.71	23.01	25.91
	25369	31.72	27.04	21.64	20.78	24.26	24.67	22.31	22.00	23.12	27.40	26.92	22.03	21.23	24.24
	25370	35.41	37.02	28.10	28.65	28.23	30.04	26.16	28.02	28.28	30.81	33.01	28.08	30.62	30.19
	25371	34.61	35.73	26.39	26.62	25.99	27.48	24.29	25.78	24.73	27.23	29.54	24.70	27.44	27.73
	25372	38.66	34.24	27.71	30.36	32.86	32.43	31.15	31.54	33.33	35.55	34.11	30.08	30.98	32.54
	25373	33.09	28.97	23.41	25.50	27.59	27.36	26.40	26.71	27.89	29.24	28.30	25.83	27.13	27.49

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 13 (continued): Individual Test Material Intake (mg/kg/day)

Day Numbers Relative to Start Date

Group/Sex	Animal	Wk1	Wk2	Wk3	Wk4	Wk5	Wk6	Wk7	Wk8	Wk9	Wk10	Wk11	Wk12	Wk13	Mean
11f	25374	86.89	67.73	61.48	73.38	60.22	61.29	58.60	61.17	59.79	67.91	72.95	67.57	68.38	66.72
	25375	89.99	73.08	68.31	82.78	67.38	68.42	66.08	69.03	66.37	75.30	81.30	74.80	76.69	73.81
	25376	92.62	88.29	76.96	90.65	77.24	82.29	80.46	79.47	78.09	92.44	94.53	87.99	84.98	85.08
	25377	94.73	92.40	82.39	97.05	83.72	89.18	87.42	87.59	83.96	98.80	105.01	99.85	96.27	92.18
	25378	80.99	72.23	62.18	80.48	65.74	75.65	70.14	120.89	76.54	77.44	80.90	76.04	77.02	78.17
	25379	80.60	70.98	60.24	75.88	61.70	71.50	65.50	111.15	70.19	71.70	74.66	70.75	71.91	73.60
	25380	89.47	75.54	66.83	64.69	130.18	73.05	72.79	66.89	81.19	69.54	93.82	76.44	75.85	79.71
	25381	86.53	75.75	68.43	66.75	135.65	75.75	74.66	68.97	84.66	72.22	97.41	79.67	79.07	81.96
	25382	82.38	74.70	70.24	78.75	66.90	78.44	74.59	76.00	75.60	81.04	85.65	79.83	73.56	76.74
	25383	82.43	70.80	66.85	75.21	62.71	72.59	69.88	71.67	70.07	74.20	78.27	72.11	66.23	71.77
	25384	83.66	79.60	75.47	87.82	73.28	79.28	74.11	69.73	74.79	80.34	80.68	74.64	62.95	76.64
	25385	84.29	77.09	71.66	85.21	73.09	78.95	73.50	69.85	75.14	79.04	78.59	74.15	63.86	75.73
	25386	77.47	77.15	68.07	77.01	61.92	75.05	64.02	48.60	94.30	87.46	88.95	73.13	77.41	74.66
	25387	88.12	84.69	72.79	81.78	65.83	80.06	68.92	52.41	98.74	92.25	95.09	77.83	82.93	80.11
	25388	80.94	71.27	47.17	33.33	62.48	64.84	63.34	68.93	68.44	76.30	75.86	78.11	72.47	66.42
	25389	87.05	77.93	107.65	72.90	68.44	72.04	71.19	76.77	75.29	83.18	83.07	86.28	79.72	80.12
	25390	77.75	68.79	59.84	75.56	66.73	80.70	65.52	64.40	71.99	73.32	76.02	72.48	68.68	70.91
	25391	86.36	76.38	66.72	85.06	75.03	90.46	74.69	74.21	81.66	82.00	87.83	84.61	79.10	80.32
	25392	86.56	76.54	68.73	83.54	72.96	73.70	69.90	69.25	76.01	79.65	77.24	67.08	81.51	75.59
	25393	95.56	83.94	76.56	96.16	83.18	82.38	78.70	77.83	83.85	86.85	84.61	72.35	85.78	83.67

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

APPENDIX 14: INDIVIDUAL FUNCTIONAL OBSERVATION BATTERY

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 14: Individual Functional Observation Battery

Day 83 or 84 Relative to Start Date

Activity Arousal:

Group	Sex	Animal	Handling Reactivity	Vocalization	Posture (Home Cage)	Posture (Open Field)	Rearings
1	m	25234	0	0	0	0	16
		25235	0	0	0	0	21
		25236	0	0	0	0	13
		25237	0	0	0	0	11
		25238	0	0	0	0	7
		25239	0	0	0	0	12
		25240	0	0	0	0	5
		25241	0	0	0	0	10
		25242	0	0	0	0	10
		25243	0	0	0	0	9
		25244	0	0	0	0	9
		25245	0	0	0	0	8
		25246	0	0	0	0	8
		25247	0	0	0	0	27
		25248	0	0	0	0	11
		25249	0	0	0	0	17
		25250	0	0	0	0	9
		25251	0	0	0	0	15
		25252	0	0	0	0	6
		25253	0	0	0	0	15
2	m	25274	0	0	0	0	18
		25275	0	0	0	0	18
		25276	0	0	0	0	12
		25277	0	0	0	0	9
		25278	0	0	0	0	13
		25279	0	0	0	0	13
		25280	0	0	0	0	8
		25281	0	0	0	0	13
		25282	0	0	0	0	15
		25283	0	0	0	0	12

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 14 (continued): Individual Functional Observation Battery

Day 83 or 84 Relative to Start Date

Activity Arousal:

Group	Sex	Animal	Handling Reactivity	Vocalization	Posture (Home Cage)	Posture (Open Field)	Rearings
3	m	25284	0	0	0	0	8
		25285	0	0	0	0	7
		25286	0	0	0	0	16
		25287	0	0	0	0	8
		25288	0	0	0	0	8
		25289	0	0	0	0	7
		25290	0	0	0	0	6
		25291	0	0	0	0	10
		25292	0	0	0	0	10
		25293	0	0	0	0	16
4	m	25294	0	0	0	0	18
		25295	0	0	0	0	14
		25296	0	0	0	0	25
		25297	0	0	0	0	11
		25298	0	0	0	0	4
		25299	0	0	0	0	23
		25300	0	0	0	0	12
		25301	0	0	0	0	6
		25302	0	0	0	0	6
		25303	0	0	0	0	10
5	m	25304	0	0	0	0	14
		25305	0	0	0	0	16
		25306	0	0	0	0	9
		25307	0	0	0	0	12
		25308	0	0	0	0	5
		25309	0	2	0	0	9
		25310	0	0	0	0	17
		25311	0	0	0	0	14
		25312	0	0	0	0	21
		25313	0	0	0	0	14

Target Dose: Group 1 - 0 mg/kg/day Groups 2 and 7 - 1 mg/kg/day Groups 3 and 8 - 3 mg/kg/day
Groups 4 and 9 - 10 mg/kg/day Groups 5 and 10 - 30 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 14 (continued): Individual Functional Observation Battery

Day 83 or 84 Relative to Start Date

Activity Arousal:

Group	Sex	Animal	Handling Reactivity	Vocalization	Posture (Home Cage)	Posture (Open Field)	Rearings
6	m	25314	0	0	0	0	18
		25315	0	0	0	0	16
		25316	0	0	0	0	6
		25317	0	0	0	0	15
		25318	0	0	0	0	10
		25319	0	0	0	0	13
		25320	0	0	0	0	2
		25321	0	0	0	0	14
		25322	0	0	0	0	9
		25323	0	0	0	0	11
		25324	0	0	0	0	9
		25325	0	0	0	0	17
		25326	0	0	0	0	14
		25327	0	0	0	0	17
		25328	0	0	0	0	10
		25329	0	0	0	0	14
		25330	0	0	0	0	12
		25331	0	0	0	0	7
		25332	0	0	0	0	16
		25333	0	0	0	0	9

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 14 (continued): Individual Functional Observation Battery

Day 83 or 84 Relative to Start Date

Autonomic:

Group Sex	Animal	Exopthalmus	Lacrimation	Palpebral Closure	Piloerection	Pupillary Status (Hand Held)	Salivation	Pupillary Response (Elicited)	No. Fecal Boli	No. Urine Pools
1m	25234	0	0	0	0	0	0	0	3	2
	25235	0	0	0	0	0	0	0	0	1
	25236	0	0	0	0	0	0	0	0	0
	25237	0	0	0	0	0	0	0	0	0
	25238	0	0	0	0	0	0	0	0	1
	25239	0	0	0	0	0	0	0	0	0
	25240	0	0	0	0	0	0	0	0	0
	25241	0	0	0	0	0	0	0	0	9
	25242	0	0	0	0	0	0	0	0	8
	25243	0	0	0	0	0	0	0	0	11
	25244	0	0	0	0	0	0	0	0	0
	25245	0	0	0	0	0	0	0	0	3
	25246	0	0	0	0	0	0	0	1	3
	25247	0	0	0	0	0	0	0	0	0
	25248	0	0	0	0	0	0	0	0	0
	25249	0	0	0	0	0	0	0	0	0
	25250	0	0	0	0	0	0	0	0	0
	25251	0	0	0	0	0	0	0	0	0
	25252	0	0	0	0	0	0	0	0	0
	25253	0	0	0	0	0	0	0	0	0
2m	25274	0	0	0	0	0	0	0	0	0
	25275	0	0	0	0	0	0	0	0	0
	25276	0	0	0	0	0	0	0	0	0
	25277	0	0	0	0	0	0	0	0	3
	25278	0	0	0	0	0	0	0	0	0
	25279	0	0	0	0	0	0	0	0	0
	25280	0	0	0	0	0	0	0	0	2
	25281	0	0	0	0	0	0	0	0	0
	25282	0	0	0	0	0	0	0	0	8
	25283	0	0	0	0	0	0	0	0	0

Target Dose: Group 1 - 0 mg/kg/day Groups 2 and 7 - 1 mg/kg/day Groups 3 and 8 - 3 mg/kg/day
Groups 4 and 9 - 10 mg/kg/day Groups 5 and 10 - 30 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 14 (continued): Individual Functional Observation Battery

Day 83 or 84 Relative to Start Date

Autonomic:

Group Sex	Animal	Exopthalmus	Lacrimation	Palpebral Closure	Piloerection	Pupillary Status (Hand Held)	Salivation	Pupillary Response (Elicited)	No. Fecal Boli	No. Urine Pools
3m	25284	0	0	0	0	0	0	0	0	2
	25285	0	0	0	0	0	0	0	0	11
	25286	0	0	0	0	0	0	0	0	2
	25287	0	0	0	0	0	0	0	0	2
	25288	0	0	0	0	0	0	0	0	10
	25289	0	0	0	0	0	0	0	0	13
	25290	0	0	0	0	0	0	0	0	0
	25291	0	0	0	0	0	0	0	0	0
	25292	0	0	0	0	0	0	0	1	0
	25293	0	0	0	0	0	0	0	0	0
4m	25294	0	0	0	0	0	0	0	3	0
	25295	0	0	0	0	0	0	0	0	0
	25296	0	0	0	0	0	0	0	0	0
	25297	0	0	0	0	0	0	0	0	0
	25298	0	0	0	0	0	0	0	0	5
	25299	0	0	0	0	0	0	0	0	0
	25300	0	0	0	0	0	0	0	0	0
	25301	0	0	0	0	0	0	0	0	0
	25302	0	0	0	0	0	0	0	0	0
	25303	0	0	0	0	0	0	0	0	2

Target Dose: Group 1 - 0 mg/kg/day Groups 2 and 7 - 1 mg/kg/day Groups 3 and 8 - 3 mg/kg/day
Groups 4 and 9 - 10 mg/kg/day Groups 5 and 10 - 30 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 14 (continued): Individual Functional Observation Battery

Day 83 or 84 Relative to Start Date

Autonomic:

Group Sex	Animal	Exopthalmus	Lacrimation	Palpebral Closure	Piloerection	Pupillary Status (Hand Held)	Salivation	Pupillary Response (Elicited)	No. Fecal Boli	No. Urine Pools
5m	25304	0	0	0	0	0	0	0	0	0
	25305	0	0	0	0	0	0	0	0	0
	25306	0	0	0	0	0	0	0	0	0
	25307	0	0	0	0	0	0	0	0	0
	25308	0	0	0	0	0	0	0	0	0
	25309	0	0	0	0	0	0	0	0	2
	25310	0	0	0	0	0	0	0	0	1
	25311	0	0	0	0	0	0	0	0	5
	25312	0	0	0	0	0	0	0	0	0
	25313	0	0	0	0	0	0	0	0	0
6m	25314	0	0	0	0	0	0	0	0	0
	25315	0	0	0	0	0	0	0	0	0
	25316	0	0	0	0	0	0	0	0	1
	25317	0	0	0	0	0	0	0	0	0
	25318	0	0	0	0	0	0	0	0	0
	25319	0	0	0	0	0	0	0	0	0
	25320	0	0	0	0	0	0	0	5	5
	25321	0	0	0	0	0	0	0	0	0
	25322	0	0	0	0	0	0	0	0	0
	25323	0	0	0	0	0	0	0	0	0
	25324	0	0	0	0	0	0	0	4	2
	25325	0	0	0	0	0	0	0	0	5
	25326	0	0	0	0	0	0	0	0	0
	25327	0	0	0	0	0	0	0	0	0
	25328	0	0	0	0	0	0	0	0	0
	25329	0	0	0	0	0	0	0	0	0
	25330	0	0	0	0	0	0	0	0	0
	25331	0	0	0	0	0	0	0	0	0
	25332	0	0	0	0	0	0	0	0	0
	25333	0	0	0	0	0	0	0	0	0

Target Dose: Group 1 - 0 mg/kg/day Groups 2 and 7 - 1 mg/kg/day Groups 3 and 8 - 3 mg/kg/day
Groups 4 and 9 - 10 mg/kg/day Groups 5 and 10 - 30 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 14 (continued): Individual Functional Observation Battery

Day 83 or 84 Relative to Start Date

Neuromuscular:

Group Sex	Animal	Activity (Home Cage)	Activity (Open Field)	Fur Appearance	Unusual Behavior (Home Cage)	Unusual Behavior (Open Field)
1m	25234	0	0	0	0	0
	25235	0	0	0	0	0
	25236	0	0	0	0	0
	25237	0	0	0	0	0
	25238	0	0	0	0	0
	25239	0	0	0	0	0
	25240	0	0	0	0	0
	25241	0	0	0	0	0
	25242	0	0	0	0	0
	25243	0	0	0	0	0
	25244	0	0	0	0	0
	25245	0	0	0	0	0
	25246	0	0	0	0	0
	25247	0	0	0	0	0
	25248	0	0	0	0	0
	25249	0	0	0	0	0
	25250	0	0	0	0	0
	25251	0	0	0	0	0
	25252	0	0	0	0	0
	25253	0	0	0	0	0
2m	25274	0	0	0	0	0
	25275	0	0	0	0	0
	25276	0	0	0	0	0
	25277	0	0	0	0	0
	25278	0	0	0	0	0
	25279	0	0	1	0	0
	25280	0	0	0	0	0
	25281	0	0	0	0	0
	25282	0	0	0	0	0
	25283	0	0	0	0	0

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 14 (continued): Individual Functional Observation Battery

Day 83 or 84 Relative to Start Date

Neuromuscular:

Group Sex	Animal	Activity (Home Cage)	Activity (Open Field)	Fur Appearance	Unusual Behavior (Home Cage)	Unusual Behavior (Open Field)
3m	25284	0	0	0	0	0
	25285	0	0	0	0	0
	25286	0	0	0	0	0
	25287	0	0	0	0	0
	25288	0	0	0	0	0
	25289	0	0	0	0	0
	25290	0	0	0	0	0
	25291	0	0	0	0	0
	25292	0	0	0	0	0
	25293	0	0	0	0	0
4m	25294	0	0	0	0	0
	25295	0	0	0	0	0
	25296	0	0	0	0	0
	25297	0	0	0	0	0
	25298	0	0	0	0	0
	25299	0	0	0	0	0
	25300	0	0	0	0	0
	25301	0	0	0	0	0
	25302	0	0	0	0	0
	25303	0	0	0	0	0
5m	25304	0	0	0	0	0
	25305	0	0	0	0	0
	25306	0	0	0	0	0
	25307	0	0	0	0	0
	25308	0	0	0	0	0
	25309	0	0	0	0	0
	25310	0	0	0	0	0
	25311	0	0	0	0	0
	25312	0	0	0	0	0
	25313	0	0	0	0	0

Target Dose: Group 1 - 0 mg/kg/day Groups 2 and 7 - 1 mg/kg/day Groups 3 and 8 - 3 mg/kg/day
Groups 4 and 9 - 10 mg/kg/day Groups 5 and 10 - 30 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 14 (continued): Individual Functional Observation Battery

Day 83 or 84 Relative to Start Date

Neuromuscular:

Group Sex	Animal	Activity (Home Cage)	Activity (Open Field)	Fur Appearance	Unusual Behavior (Home Cage)	Unusual Behavior (Open Field)
6m	25314	0	0	0	0	0
	25315	0	0	0	0	0
	25316	0	0	0	0	0
	25317	0	0	0	0	0
	25318	0	0	0	0	0
	25319	0	0	0	0	0
	25320	0	0	0	0	0
	25321	0	0	0	0	0
	25322	0	0	0	0	0
	25323	0	0	0	0	0
	25324	0	0	0	0	0
	25325	0	0	0	0	0
	25326	0	0	0	0	0
	25327	0	0	0	0	0
	25328	0	0	0	0	0
	25329	0	0	0	0	0
	25330	0	0	0	0	0
	25331	0	0	0	0	0
	25332	0	0	0	0	0
	25333	0	0	0	0	0

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 14 (continued): Individual Functional Observation Battery

Day 83 or 84 Relative to Start Date

Neuromuscular (continued):

Group	Sex	Animal	Gait (Home Cage)	Gait (Open Field)	Righting Response	Grooms	Forelimb Grip (kg)	Hindlimb Grip (kg)	Hindlimb Splay (mm)
1	m	25234	0	0	0	2	1.543	0.828	95
		25235	0	0	0	1	1.983	0.995	95
		25236	0	0	0	0	1.415	0.843	90
		25237	0	0	0	0	1.563	0.880	75
		25238	0	0	0	0	1.558	0.958	80
		25239	0	0	0	0	1.805	0.685	75
		25240	0	0	0	0	1.610	0.823	85
		25241	0	0	0	0	1.388	0.725	90
		25242	0	0	0	0	1.850	0.840	105
		25243	0	0	0	0	1.888	0.873	75
		25244	0	0	0	0	1.476	0.610	85
		25245	0	0	0	0	1.740	0.640	80
		25246	0	0	0	0	1.650	0.823	80
		25247	0	0	0	2	1.810	0.780	80
		25248	0	0	0	0	1.940	0.723	65
		25249	0	0	0	0	1.558	0.553	75
		25250	0	0	0	0	1.643	0.548	75
		25251	0	0	0	0	1.563	0.803	80
		25252	0	0	0	3	1.645	0.703	80
		25253	0	0	0	0	1.710	0.905	70
2	m	25274	0	0	0	0	1.845	0.725	85
		25275	0	0	0	0	1.935	0.960	90
		25276	0	0	0	0	1.755	0.690	70
		25277	0	0	0	0	1.565	0.805	80
		25278	0	0	0	0	1.500	0.780	85
		25279	0	0	0	2	1.620	0.663	95
		25280	0	0	0	0	1.535	0.873	70
		25281	0	0	0	1	1.720	0.633	85
		25282	0	0	0	0	1.815	0.890	80
		25283	0	0	0	0	1.533	0.775	80

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 14 (continued): Individual Functional Observation Battery

Day 83 or 84 Relative to Start Date

Neuromuscular (continued):

Group	Sex	Animal	Gait (Home Cage)	Gait (Open Field)	Righting Response	Grooms	Forelimb Grip (kg)	Hindlimb Grip (kg)	Hindlimb Splay (mm)
3	m	25284	0	0	0	0	1.835	0.730	90
		25285	0	0	0	0	1.835	0.908	90
		25286	0	0	0	0	1.890	0.758	80
		25287	0	0	0	0	1.590	1.095	85
		25288	0	0	0	0	1.555	0.770	95
		25289	0	0	0	1	1.670	0.695	90
		25290	0	0	0	0	1.688	0.843	90
		25291	0	0	0	0	1.470	0.663	65
		25292	0	0	0	1	1.623	0.800	80
		25293	0	0	0	1	1.843	0.740	80
4	m	25294	0	0	0	1	1.795	0.735	95
		25295	0	0	0	0	1.690	0.625	85
		25296	0	0	0	0	1.405	0.833	120
		25297	0	0	0	0	1.678	0.730	85
		25298	0	0	0	0	1.753	0.625	85
		25299	0	0	0	0	1.650	0.700	95
		25300	0	0	0	0	1.640	0.675	105
		25301	0	0	0	0	1.945	0.783	95
		25302	0	0	0	0	1.780	0.685	90
		25303	0	0	0	0	1.825	0.950	90
5	m	25304	0	0	0	0	1.850	0.723	80
		25305	0	0	0	0	1.713	0.680	80
		25306	0	0	0	0	1.540	0.788	75
		25307	0	0	0	0	1.693	0.828	95
		25308	0	0	0	2	1.843	0.840	85
		25309	0	0	0	0	1.720	1.090	90
		25310	0	0	0	2	1.820	0.760	105
		25311	0	0	0	0	1.638	0.773	80
		25312	0	0	0	1	1.768	0.788	70
		25313	0	0	0	0	1.740	0.743	80

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 14 (continued): Individual Functional Observation Battery

Day 83 or 84 Relative to Start Date

Neuromuscular (continued):

Group	Sex	Animal	Gait (Home Cage)	Gait (Open Field)	Righting Response	Grooms	Forelimb Grip (kg)	Hindlimb Grip (kg)	Hindlimb Splay (mm)
6	m	25314	0	0	0	0	1.878	0.828	95
		25315	0	0	0	2	1.925	0.765	75
		25316	0	0	0	0	1.613	0.708	85
		25317	0	0	0	3	1.800	0.858	90
		25318	0	0	0	0	1.823	0.775	80
		25319	0	0	0	0	1.575	0.615	85
		25320	0	0	0	0	1.463	0.690	70
		25321	0	0	0	0	1.668	0.645	75
		25322	0	0	0	3	1.585	0.888	95
		25323	0	0	0	0	1.603	0.740	100
		25324	0	0	0	0	1.858	0.830	80
		25325	0	0	0	0	1.690	0.678	75
		25326	0	0	0	0	1.783	0.658	85
		25327	0	0	0	1	1.835	0.748	85
		25328	0	0	0	0	1.820	0.898	65
		25329	0	0	0	1	1.978	0.798	80
		25330	0	0	0	0	1.445	0.485	70
		25331	0	0	0	3	1.283	0.798	85
		25332	0	0	0	0	1.620	0.563	60
		25333	0	0	0	0	1.690	0.658	80

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 14 (continued): Individual Functional Observation Battery

Day 83 or 84 Relative to Start Date

Physiological:					Sensory Motor:			
Group	Sex	Animal	Respiration	SD 85 Body Weight (g)	Approach Response	Auditory Response	Tail Pinch	Pinna Response
1	m	25234	0	608.1	0	0	0	0
		25235	0	678.1	0	0	0	0
		25236	0	581.4	0	0	0	0
		25237	0	631.4	0	0	0	0
		25238	0	551.2	0	0	0	0
		25239	0	640.0	0	0	0	0
		25240	0	606.2	0	0	0	0
		25241	0	587.4	0	0	0	0
		25242	0	621.8	0	0	0	0
		25243	0	597.6	0	0	0	0
		25244	0	473.9	0	0	0	0
		25245	0	602.2	0	0	0	0
		25246	0	655.7	0	0	0	0
		25247	0	634.5	0	0	0	0
		25248	0	615.0	0	0	0	0
		25249	0	530.7	0	0	0	0
		25250	0	462.6	0	0	0	0
		25251	0	723.3	0	0	0	0
		25252	0	607.5	0	0	0	0
		25253	0	600.9	0	0	0	0
2	m	25274	0	662.0	0	0	0	0
		25275	0	761.6	0	0	0	0
		25276	0	633.0	0	0	0	0
		25277	0	640.4	0	0	0	0
		25278	0	622.2	0	0	0	0
		25279	0	568.9	0	0	0	0
		25280	0	615.2	0	0	0	0
		25281	0	614.4	0	0	0	0
		25282	0	520.7	0	0	0	0
		25283	0	541.0	0	0	0	0

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 14 (continued): Individual Functional Observation Battery

Day 83 or 84 Relative to Start Date

Physiological:					Sensory Motor:			
Group	Sex	Animal	Respiration	SD 85 Body Weight (g)	Approach Response	Auditory Response	Tail Pinch	Pinna Response
3	m	25284	0	574.4	0	0	0	0
		25285	0	498.6	0	0	0	0
		25286	0	701.8	0	0	0	0
		25287	0	553.0	0	0	0	0
		25288	0	580.7	0	0	0	0
		25289	0	562.5	0	0	0	0
		25290	0	624.4	0	0	0	0
		25291	0	576.2	0	0	0	0
		25292	0	625.2	0	0	0	0
		25293	0	630.0	0	0	0	0
4	m	25294	0	556.0	0	0	0	0
		25295	0	607.1	0	0	0	0
		25296	0	490.3	0	0	0	0
		25297	0	564.3	0	0	0	0
		25298	0	576.1	0	0	0	0
		25299	0	550.3	0	0	0	0
		25300	0	732.6	0	0	0	0
		25301	0	647.0	0	0	0	0
		25302	0	553.2	0	0	0	0
		25303	0	626.0	0	0	0	0
5	m	25304	0	509.3	0	0	0	0
		25305	0	558.7	0	0	0	0
		25306	0	564.0	0	0	0	0
		25307	0	556.1	0	0	0	0
		25308	0	637.3	0	0	0	0
		25309	0	575.6	0	0	0	0
		25310	0	607.9	0	0	0	0
		25311	0	610.5	0	0	0	0
		25312	0	592.4	0	0	0	0
		25313	0	594.0	0	0	0	0

Target Dose: Group 1 - 0 mg/kg/day Groups 2 and 7 - 1 mg/kg/day Groups 3 and 8 - 3 mg/kg/day
Groups 4 and 9 - 10 mg/kg/day Groups 5 and 10 - 30 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 14 (continued): Individual Functional Observation Battery

Day 83 or 84 Relative to Start Date

Physiological:					Sensory Motor:			
Group	Sex	Animal	Respiration	SD 85 Body Weight (g)	Approach Response	Auditory Response	Tail Pinch	Pinna Response
6	m	25314	0	509.7	0	0	0	0
		25315	0	534.0	0	0	0	0
		25316	0	550.7	0	0	0	0
		25317	0	692.0	0	0	0	0
		25318	0	505.5	0	0	0	0
		25319	0	553.6	0	0	0	0
		25320	0	628.2	0	0	0	0
		25321	0	541.3	0	0	0	0
		25322	0	544.4	0	0	0	0
		25323	0	404.5	0	0	0	0
		25324	0	552.5	0	0	0	0
		25325	0	628.9	0	0	0	0
		25326	0	629.7	0	0	0	0
		25327	0	583.7	0	0	0	0
		25328	0	572.2	0	0	0	0
		25329	0	600.6	0	0	0	0
		25330	0	553.8	0	0	0	0
		25331	0	585.2	0	0	0	0
		25332	0	491.5	0	0	0	0
		25333	0	589.2	0	0	0	0

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 14 (continued): Individual Functional Observation Battery

Day 84 or 85 Relative to Start Date

Activity Arousal:

Group	Sex	Animal	Handling Reactivity	Vocalization	Posture (Home Cage)	Posture (Open Field)	Rearings
1	f	25254	0	0	0	0	11
		25255	0	0	0	0	15
		25256	0	0	0	0	9
		25257	0	0	0	0	18
		25258	0	0	0	0	9
		25259	0	0	0	0	14
		25260	0	0	0	0	6
		25261	0	0	0	0	12
		25262	0	0	0	0	15
		25263	0	0	0	0	14
		25264	0	0	0	0	15
		25265	0	0	0	0	8
		25266	0	0	0	0	14
		25267	0	0	0	0	21
		25268	0	0	0	0	28
		25269	0	0	0	0	10
		25270	0	0	0	0	13
		25271	0	0	0	0	13
		25272	0	0	0	0	9
		25273	0	0	0	0	28
7	f	25334	0	0	0	0	17
		25335	0	0	0	0	15
		25336	0	0	0	0	10
		25337	0	0	0	0	12
		25338	0	0	0	0	11
		25339	0	0	0	0	13
		25340	0	0	0	0	8
		25341	0	0	0	0	13
		25342	0	0	0	0	14
		25343	0	0	0	0	14

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 14 (continued): Individual Functional Observation Battery

Day 84 or 85 Relative to Start Date

Activity Arousal:

Group	Sex	Animal	Handling Reactivity	Vocalization	Posture (Home Cage)	Posture (Open Field)	Rearings
8	f	25344	0	0	0	0	12
		25345	0	0	0	0	15
		25346	0	0	0	0	9
		25347	0	0	0	0	12
		25348	0	0	0	0	15
		25349	0	0	0	0	10
		25350	0	0	0	0	11
		25351	0	0	0	0	14
		25352	0	0	0	0	12
		25353	0	0	0	0	19
9	f	25354	0	0	0	0	21
		25355	0	0	0	0	10
		25356	0	0	0	0	11
		25357	0	0	0	0	9
		25358	0	0	0	0	11
		25359	0	0	0	0	9
		25360	0	0	0	0	10
		25361	0	0	0	0	10
		25362	0	0	0	0	27
		25363	0	0	0	0	9
10	f	25364	0	0	0	0	19
		25365	0	0	0	0	21
		25366	0	0	0	0	10
		25367	0	0	0	0	10
		25368	0	0	0	0	10
		25369	0	0	0	0	9
		25370	0	0	0	0	20
		25371	0	0	0	0	15
		25372	0	0	0	0	16
		25373	0	0	0	0	10

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 14 (continued): Individual Functional Observation Battery

Day 84 or 85 Relative to Start Date

Activity Arousal:

Group	Sex	Animal	Handling Reactivity	Vocalization	Posture (Home Cage)	Posture (Open Field)	Rearings
11	f	25374	0	0	0	0	18
		25375	0	0	0	0	8
		25376	0	0	0	0	12
		25377	0	0	0	0	20
		25378	0	0	0	0	14
		25379	0	0	0	0	8
		25380	0	0	0	0	22
		25381	0	0	0	0	8
		25382	0	0	0	0	12
		25383	0	0	0	0	16
		25384	0	0	0	0	13
		25385	0	0	0	0	19
		25386	0	0	0	0	20
		25387	0	0	0	0	16
		25388	0	0	0	0	23
		25389	0	0	0	0	16
		25390	0	0	0	0	6
		25391	0	0	0	0	15
		25392	0	0	0	0	5
		25393	0	0	0	0	18

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 14 (continued): Individual Functional Observation Battery

Day 84 or 85 Relative to Start Date

Autonomic:

Group Sex	Animal	Exopthalmus	Lacrimation	Palpebral Closure	Piloerection	Pupillary Status (Hand Held)	Salivation	Pupillary Response (Elicited)	No. Fecal Boli	No. Urine Pools
1f	25254	0	0	0	0	0	0	0	0	0
	25255	0	0	0	0	0	0	0	0	0
	25256	0	0	0	0	0	0	0	0	0
	25257	0	0	0	0	0	0	0	0	7
	25258	0	0	0	0	0	0	0	0	0
	25259	0	0	0	0	0	0	0	0	0
	25260	0	0	0	0	0	0	0	0	0
	25261	0	0	0	0	0	0	0	0	11
	25262	0	0	0	0	0	0	0	0	0
	25263	0	0	0	0	0	0	0	0	0
	25264	0	0	0	0	0	0	0	0	0
	25265	0	0	0	0	0	0	0	0	0
	25266	0	0	0	0	0	0	0	0	1
	25267	0	0	0	0	0	0	0	0	0
	25268	0	0	0	0	0	0	0	0	2
	25269	0	0	0	0	0	0	0	0	0
	25270	0	0	0	0	0	0	0	0	0
	25271	0	0	0	0	0	0	0	0	0
	25272	0	0	0	0	0	0	0	0	0
	25273	0	0	0	0	0	0	0	0	0
7f	25334	0	0	0	0	0	0	0	0	1
	25335	0	0	0	0	0	0	0	0	0
	25336	0	0	0	0	0	0	0	0	0
	25337	0	0	0	0	0	0	0	0	1
	25338	0	0	0	0	0	0	0	0	0
	25339	0	0	0	0	0	0	0	0	0
	25340	0	0	0	0	0	0	0	0	0
	25341	0	0	0	0	0	0	0	0	0
	25342	0	0	0	0	0	0	0	0	1
	25343	0	0	0	0	0	0	0	0	0

Target Dose: Group 1 - 0 mg/kg/day Groups 2 and 7 - 1 mg/kg/day Groups 3 and 8 - 3 mg/kg/day
Groups 4 and 9 - 10 mg/kg/day Groups 5 and 10 - 30 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 14 (continued): Individual Functional Observation Battery

Day 84 or 85 Relative to Start Date

Autonomic:

Group Sex	Animal	Exopthalmus	Lacrimation	Palpebral Closure	Piloerection	Pupillary Status (Hand Held)	Salivation	Pupillary Response (Elicited)	No. Fecal Boli	No. Urine Pools
8f	25344	0	0	0	0	0	0	0	0	0
	25345	0	0	0	0	0	0	0	0	0
	25346	0	0	0	0	0	0	0	0	0
	25347	0	0	0	0	0	0	0	0	0
	25348	0	0	0	0	0	0	0	0	0
	25349	0	0	0	0	0	0	0	0	0
	25350	0	0	0	0	0	0	0	0	1
	25351	0	0	0	0	0	0	0	0	4
	25352	0	0	0	0	0	0	0	0	0
	25353	0	0	0	0	0	0	0	0	2
9f	25354	0	0	0	0	0	0	0	0	0
	25355	0	0	0	0	0	0	0	0	0
	25356	0	0	0	0	0	0	0	0	0
	25357	0	0	0	0	0	0	0	0	0
	25358	0	0	0	0	0	0	0	0	0
	25359	0	0	0	0	0	0	0	0	0
	25360	0	0	0	0	0	0	0	0	0
	25361	0	0	0	0	0	0	0	0	1
	25362	0	0	0	0	0	0	0	0	2
	25363	0	0	0	0	0	0	0	0	0

Target Dose: Group 1 - 0 mg/kg/day Groups 2 and 7 - 1 mg/kg/day Groups 3 and 8 - 3 mg/kg/day
Groups 4 and 9 - 10 mg/kg/day Groups 5 and 10 - 30 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 14 (continued): Individual Functional Observation Battery

Day 84 or 85 Relative to Start Date

Autonomic:

Group Sex	Animal	Exopthalmus	Lacrimation	Palpebral Closure	Piloerection	Pupillary Status (Hand Held)	Salivation	Pupillary Response (Elicited)	No. Fecal Boli	No. Urine Pools
10f	25364	0	0	0	0	0	0	0	0	0
	25365	0	0	0	0	0	0	0	0	4
	25366	0	0	0	0	0	0	0	0	0
	25367	0	0	0	0	0	0	0	0	0
	25368	0	0	0	0	0	0	0	0	0
	25369	0	0	0	0	0	0	0	0	0
	25370	0	0	0	0	0	0	0	0	1
	25371	0	0	0	0	0	0	0	0	0
	25372	0	0	0	0	0	0	0	0	0
	25373	0	0	0	0	0	0	0	0	0
11f	25374	0	0	0	0	0	0	0	0	0
	25375	0	0	0	0	0	0	0	0	1
	25376	0	0	0	0	0	0	0	0	2
	25377	0	0	0	0	0	0	0	0	0
	25378	0	0	0	0	0	0	0	0	0
	25379	0	0	0	0	0	0	0	0	0
	25380	0	0	0	0	0	0	0	0	2
	25381	0	0	0	0	0	0	0	0	0
	25382	0	0	0	0	0	0	0	0	0
	25383	0	0	0	0	0	0	0	0	0
	25384	0	0	0	0	0	0	0	1	4
	25385	0	0	0	0	0	0	0	0	0
	25386	0	0	0	0	0	0	0	0	0
	25387	0	0	0	0	0	0	0	0	3
	25388	0	0	0	0	0	0	0	0	0
	25389	0	0	0	0	0	0	0	0	3
	25390	0	0	0	0	0	0	0	0	0
	25391	0	0	0	0	0	0	0	0	0
	25392	0	0	0	0	0	0	0	0	0
	25393	0	0	0	0	0	0	0	0	0

Target Dose: Group 1 - 0 mg/kg/day Groups 2 and 7 - 1 mg/kg/day Groups 3 and 8 - 3 mg/kg/day
Groups 4 and 9 - 10 mg/kg/day Groups 5 and 10 - 30 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 14 (continued): Individual Functional Observation Battery

Day 84 or 85 Relative to Start Date

Neuromuscular:

Group Sex	Animal	Activity (Home Cage)	Activity (Open Field)	Fur Appearance	Unusual Behavior (Home Cage)	Unusual Behavior (Open Field)
1f	25254	0	0	0	0	0
	25255	0	0	0	0	0
	25256	0	0	0	0	0
	25257	0	0	0	0	0
	25258	0	0	0	0	0
	25259	0	0	0	0	0
	25260	0	0	0	0	0
	25261	0	0	0	0	0
	25262	0	0	0	0	0
	25263	0	0	0	0	0
	25264	0	0	0	1	0
	25265	0	0	0	0	0
	25266	0	0	0	0	0
	25267	0	0	0	0	0
	25268	0	0	0	0	0
	25269	0	0	0	0	0
	25270	0	0	1	0	0
	25271	0	0	0	0	0
	25272	0	0	0	0	0
	25273	0	0	0	0	0
7f	25334	0	0	0	0	0
	25335	0	0	0	0	0
	25336	0	0	0	0	0
	25337	0	0	0	0	0
	25338	0	0	0	0	0
	25339	0	0	0	0	0
	25340	0	0	0	0	0
	25341	0	0	0	0	0
	25342	0	0	0	0	0
	25343	0	0	0	0	0

Target Dose: Group 1 - 0 mg/kg/day Groups 2 and 7 - 1 mg/kg/day Groups 3 and 8 - 3 mg/kg/day
Groups 4 and 9 - 10 mg/kg/day Groups 5 and 10 - 30 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 14 (continued): Individual Functional Observation Battery

Day 84 or 85 Relative to Start Date

Neuromuscular:

Group Sex	Animal	Activity (Home Cage)	Activity (Open Field)	Fur Appearance	Unusual Behavior (Home Cage)	Unusual Behavior (Open Field)
8f	25344	0	0	0	0	0
	25345	0	0	0	0	0
	25346	0	0	0	0	0
	25347	0	0	0	0	0
	25348	0	0	0	0	0
	25349	0	0	0	0	0
	25350	0	0	0	0	0
	25351	0	0	0	0	0
	25352	0	0	0	0	0
	25353	0	0	0	0	0
9f	25354	0	0	0	0	0
	25355	0	0	0	0	0
	25356	0	0	0	0	0
	25357	0	0	0	0	0
	25358	0	0	0	0	0
	25359	0	0	0	0	0
	25360	0	0	0	0	0
	25361	0	0	0	0	0
	25362	0	0	0	0	0
	25363	0	0	0	0	0
10f	25364	0	0	0	0	0
	25365	0	0	0	0	0
	25366	0	0	0	0	0
	25367	0	0	0	0	0
	25368	0	0	0	0	0
	25369	0	0	0	0	0
	25370	0	0	0	0	0
	25371	0	0	0	0	0
	25372	0	0	0	0	0
	25373	0	0	1	0	0

Target Dose: Group 1 - 0 mg/kg/day Groups 2 and 7 - 1 mg/kg/day Groups 3 and 8 - 3 mg/kg/day
Groups 4 and 9 - 10 mg/kg/day Groups 5 and 10 - 30 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 14 (continued): Individual Functional Observation Battery

Day 84 or 85 Relative to Start Date

Neuromuscular:

Group Sex	Animal	Activity (Home Cage)	Activity (Open Field)	Fur Appearance	Unusual Behavior (Home Cage)	Unusual Behavior (Open Field)
11f	25374	0	0	0	0	0
	25375	0	0	0	0	0
	25376	0	0	0	0	0
	25377	0	0	0	0	0
	25378	0	0	0	0	0
	25379	0	0	0	0	0
	25380	0	0	0	0	0
	25381	0	0	0	0	0
	25382	0	0	0	0	0
	25383	0	0	0	0	0
	25384	0	0	0	0	0
	25385	0	0	0	0	0
	25386	0	0	0	0	0
	25387	0	0	0	0	0
	25388	0	0	0	0	0
	25389	0	0	0	0	0
	25390	0	0	0	0	0
	25391	0	0	0	0	0
	25392	0	0	0	0	0
	25393	0	0	0	0	0

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 14 (continued): Individual Functional Observation Battery

Day 84 or 85 Relative to Start Date

Neuromuscular (continued):

Group	Sex	Animal	Gait (Home Cage)	Gait (Open Field)	Righting Response	Grooms	Forelimb Grip (kg)	Hindlimb Grip (kg)	Hindlimb Splay (mm)
1	f	25254	0	0	0	4	1.185	0.518	90
		25255	0	0	0	0	1.525	0.558	75
		25256	0	0	0	0	1.255	0.528	70
		25257	0	0	0	0	1.260	0.505	75
		25258	0	0	0	0	1.380	0.638	70
		25259	0	0	0	0	1.363	0.470	65
		25260	0	0	0	0	1.343	0.488	60
		25261	0	0	0	0	1.495	0.540	85
		25262	0	0	0	0	1.200	0.603	55
		25263	0	0	0	0	1.585	0.610	65
		25264	0	0	0	0	1.563	0.773	90
		25265	0	0	0	0	1.630	0.650	75
		25266	0	0	0	4	1.385	0.678	85
		25267	0	0	0	0	1.635	0.838	100
		25268	0	0	0	0	1.555	0.673	80
		25269	0	0	0	2	1.333	0.843	75
		25270	0	0	0	0	1.328	0.550	75
		25271	0	0	0	0	1.418	0.510	70
		25272	0	0	0	1	1.470	0.608	90
		25273	0	0	0	0	1.345	0.650	110
7	f	25334	0	0	0	0	1.340	0.640	100
		25335	0	0	0	0	1.228	0.533	110
		25336	0	0	0	3	1.465	0.730	85
		25337	0	0	0	0	1.343	0.685	70
		25338	0	0	0	0	1.273	0.570	85
		25339	0	0	0	3	1.343	0.678	80
		25340	0	0	0	0	1.375	0.665	65
		25341	0	0	0	0	1.450	0.500	55
		25342	0	0	0	1	1.583	0.543	70
		25343	0	0	0	0	1.635	0.720	75

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 14 (continued): Individual Functional Observation Battery

Day 84 or 85 Relative to Start Date

Neuromuscular (continued):

Group	Sex	Animal	Gait (Home Cage)	Gait (Open Field)	Righting Response	Grooms	Forelimb Grip (kg)	Hindlimb Grip (kg)	Hindlimb Splay (mm)
8	f	25344	0	0	0	1	1.563	0.660	95
		25345	0	0	0	0	1.290	0.550	95
		25346	0	0	0	0	1.600	0.673	90
		25347	0	0	0	0	1.568	0.908	65
		25348	0	0	0	1	1.648	0.700	85
		25349	0	0	0	0	1.243	0.605	80
		25350	0	0	0	0	1.560	0.620	70
		25351	0	0	0	0	1.423	0.623	80
		25352	0	0	0	0	1.395	0.708	70
		25353	0	0	0	0	1.428	0.785	110
9	f	25354	0	0	0	0	1.250	0.553	80
		25355	0	0	0	0	1.498	0.645	120
		25356	0	0	0	1	1.198	0.563	115
		25357	0	0	0	0	1.283	0.553	65
		25358	0	0	0	0	1.528	0.708	100
		25359	0	0	0	0	1.690	0.845	90
		25360	0	0	0	0	1.508	0.568	75
		25361	0	0	0	0	1.418	0.678	60
		25362	0	0	0	0	1.513	0.668	65
		25363	0	0	0	0	1.410	0.685	70
10	f	25364	0	0	0	2	1.525	0.618	100
		25365	0	0	0	0	1.325	0.570	95
		25366	0	0	0	2	1.393	0.635	110
		25367	0	0	0	1	1.283	0.498	90
		25368	0	0	0	0	1.423	0.543	100
		25369	0	0	0	0	1.293	0.550	70
		25370	0	0	0	0	1.415	0.713	80
		25371	0	0	0	1	1.400	0.828	95
		25372	0	0	0	2	1.618	0.538	75
		25373	0	0	0	0	1.365	0.668	90

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 14 (continued): Individual Functional Observation Battery

Day 84 or 85 Relative to Start Date

Neuromuscular (continued):

Group	Sex	Animal	Gait (Home Cage)	Gait (Open Field)	Righting Response	Grooms	Forelimb Grip (kg)	Hindlimb Grip (kg)	Hindlimb Splay (mm)
11	f	25374	0	0	0	0	1.578	0.600	105
		25375	0	0	0	0	1.428	0.670	110
		25376	0	0	0	2	1.373	0.573	105
		25377	0	0	0	0	1.368	0.455	95
		25378	0	0	0	0	1.345	0.643	85
		25379	0	0	0	0	1.635	0.615	70
		25380	0	0	0	0	1.420	0.673	75
		25381	0	0	0	0	1.558	0.655	75
		25382	0	0	0	0	1.435	0.573	70
		25383	0	0	0	0	1.528	0.698	80
		25384	0	0	0	1	1.500	0.560	100
		25385	0	0	0	0	1.523	0.703	70
		25386	0	0	0	0	1.180	0.623	80
		25387	0	0	0	0	1.695	0.678	100
		25388	0	0	0	0	1.533	0.505	80
		25389	0	0	0	0	1.378	0.625	55
		25390	0	0	0	0	1.655	0.693	80
		25391	0	0	0	0	1.453	0.640	60
		25392	0	0	0	0	1.455	0.460	65
		25393	0	0	0	0	1.370	0.625	70

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 14 (continued): Individual Functional Observation Battery

Day 84 or 85 Relative to Start Date

Physiological:					Sensory Motor:			
Group	Sex	Animal	Respiration	SD 85 Body Weight (g)	Approach Response	Auditory Response	Tail Pinch	Pinna Response
1	f	25254	0	309.5	0	0	0	0
		25255	0	270.8	0	0	0	0
		25256	0	238.8	0	0	0	0
		25257	0	275.8	0	0	0	0
		25258	0	344.8	0	0	0	0
		25259	0	254.6	0	0	0	0
		25260	0	297.1	0	0	0	0
		25261	0	340.7	0	0	0	0
		25262	0	290.1	0	0	0	0
		25263	0	308.4	0	0	0	0
		25264	0	269.5	0	0	0	0
		25265	0	291.8	0	0	0	0
		25266	0	280.0	0	0	0	0
		25267	0	316.6	0	0	0	0
		25268	0	294.5	0	0	0	0
		25269	0	296.8	0	0	0	0
		25270	0	299.2	0	0	0	0
		25271	0	311.8	0	0	0	0
		25272	0	316.2	0	0	0	0
		25273	0	323.7	0	0	0	0
7	f	25334	0	246.0	0	0	0	0
		25335	0	283.7	0	0	0	0
		25336	0	326.1	0	0	0	0
		25337	0	322.1	0	0	0	0
		25338	0	292.6	0	0	0	0
		25339	0	309.4	0	0	0	0
		25340	0	258.4	0	0	0	0
		25341	0	287.0	0	0	0	0
		25342	0	308.5	0	0	0	0
		25343	0	310.6	0	0	0	0

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 14 (continued): Individual Functional Observation Battery

Day 84 or 85 Relative to Start Date

Physiological:					Sensory Motor:			
Group	Sex	Animal	Respiration	SD 85 Body Weight (g)	Approach Response	Auditory Response	Tail Pinch	Pinna Response
8	f	25344	0	327.6	0	0	0	0
		25345	0	268.4	0	0	0	0
		25346	0	260.2	0	0	0	0
		25347	0	318.2	0	0	0	0
		25348	0	302.5	0	0	0	0
		25349	0	291.1	0	0	0	0
		25350	0	274.3	0	0	0	0
		25351	0	249.4	0	0	0	0
		25352	0	298.4	0	0	0	0
		25353	0	328.7	0	0	0	0
9	f	25354	0	346.0	0	0	0	0
		25355	0	301.5	0	0	0	0
		25356	0	284.8	0	0	0	0
		25357	0	271.5	0	0	0	0
		25358	0	288.7	0	0	0	0
		25359	0	296.3	0	0	0	0
		25360	0	317.4	0	0	0	0
		25361	0	290.1	0	0	0	0
		25362	0	304.7	0	0	0	0
		25363	0	280.5	0	0	0	0
10	f	25364	0	277.7	0	0	0	0
		25365	0	316.4	0	0	0	0
		25366	0	233.3	0	0	0	0
		25367	0	301.3	0	0	0	0
		25368	0	291.4	0	0	0	0
		25369	0	318.6	0	0	0	0
		25370	0	275.8	0	0	0	0
		25371	0	311.2	0	0	0	0
		25372	0	259.5	0	0	0	0
		25373	0	296.8	0	0	0	0

Target Dose: Group 1 - 0 mg/kg/day Groups 2 and 7 - 1 mg/kg/day Groups 3 and 8 - 3 mg/kg/day
Groups 4 and 9 - 10 mg/kg/day Groups 5 and 10 - 30 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 14 (continued): Individual Functional Observation Battery

Day 84 or 85 Relative to Start Date

Physiological:					Sensory Motor:			
Group	Sex	Animal	Respiration	SD 85 Body Weight (g)	Approach Response	Auditory Response	Tail Pinch	Pinna Response
11	f	25374	0	337.9	0	0	0	0
		25375	0	305.5	0	0	0	0
		25376	0	266.7	0	0	0	0
		25377	0	235.9	0	0	0	0
		25378	0	280.8	0	0	0	0
		25379	0	296.3	0	0	0	0
		25380	0	324.1	0	0	0	0
		25381	0	312.4	0	0	0	0
		25382	0	258.9	0	0	0	0
		25383	0	291.7	0	0	0	0
		25384	0	337.9	0	0	0	0
		25385	0	337.3	0	0	0	0
		25386	0	278.8	0	0	0	0
		25387	0	260.0	0	0	0	0
		25388	0	293.5	0	0	0	0
		25389	0	264.3	0	0	0	0
		25390	0	269.7	0	0	0	0
		25391	0	233.1	0	0	0	0
		25392	0	279.9	0	0	0	0
		25393	0	266.5	0	0	0	0

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

APPENDIX 15: INDIVIDUAL LOCOMOTOR ACTIVITY DATA

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 15: Individual Locomotor Activity Data

Day 89 Relative to Start Date

Group	Sex	Animal	Interval	Basic Movements	Fine Movements	Rearing	Group	Sex	Animal	Interval	Basic Movements	Fine Movements	Rearing
1	m	25234	1	2248	1224	100	1	m	25244	1	2034	854	74
			2	1345	873	51				2	1379	688	72
			3	829	527	27				3	566	372	20
		25235	1	2006	1315	103			25245	1	1864	1073	91
			2	254	158	12				2	713	463	22
			3	1015	694	36				3	190	129	0
		25236	1	2139	913	140			25246	1	1915	1017	102
			2	1857	979	55				2	475	335	48
			3	852	488	18				3	52	41	0
		25237	1	2628	1424	74			25247	1	2643	1442	92
			2	1506	1022	59				2	959	587	92
			3	855	603	34				3	119	82	0
		25238	1	1707	869	77			25248	1	2270	1290	130
			2	676	428	48				2	843	553	116
			3	188	146	3				3	297	185	8
		25239	1	2255	1322	123			25249	1	1802	941	81
			2	981	643	40				2	177	142	83
			3	932	582	102				3	41	34	0
		25240	1	1775	1042	95			25250	1	1373	627	55
			2	1510	936	76				2	596	367	17
			3	1052	718	44				3	233	147	2
		25241	1	1658	821	46			25251	1	1896	1020	172
			2	591	353	27				2	1296	740	119
			3	127	96	1				3	239	179	30
		25242	1	1910	1090	88			25252	1	2515	1412	100
			2	1053	715	46				2	1342	785	92
			3	126	101	5				3	149	112	3
		25243	1	2145	1084	56			25253	1	2239	1007	136
			2	1123	643	25				2	790	486	72
			3	40	28	0				3	475	288	26

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 15 (continued): Individual Locomotor Activity Data

Day 89 Relative to Start Date

Group	Sex	Animal	Interval	Basic Movements	Fine Movements	Rearing	Group	Sex	Animal	Interval	Basic Movements	Fine Movements	Rearing
2	m	25274	1	1912	1270	118	3	m	25284	1	2137	1349	116
			2	1174	856	78				2	734	504	45
			3	935	638	69				3	1284	895	75
		25275	1	2097	1318	71			25285	1	1587	821	65
			2	596	449	20				2	821	468	30
			3	112	101	8				3	1067	643	35
		25276	1	1968	1006	110			25286	1	1822	941	140
			2	715	448	56				2	543	357	43
			3	632	395	48				3	6	6	0
		25277	1	1926	1054	100			25287	1	2393	1239	123
			2	858	554	60				2	1693	972	64
			3	744	507	64				3	430	272	16
		25278	1	2358	1273	172			25288	1	2326	1077	128
			2	1314	757	79				2	767	438	54
			3	873	540	53				3	1432	830	62
		25279	1	2392	1245	130			25289	1	2371	1107	65
			2	834	520	57				2	1463	719	55
			3	656	412	24				3	616	406	23
		25280	1	1556	897	76			25290	1	2397	1337	93
			2	1372	806	57				2	1838	1115	70
			3	1173	754	27				3	741	523	26
		25281	1	2268	1161	135			25291	1	2304	999	107
			2	1338	789	74				2	1234	761	27
			3	351	254	61				3	927	587	38
		25282	1	1959	1012	82			25292	1	2334	1288	104
			2	972	625	44				2	1701	1006	72
			3	283	183	11				3	1061	605	58
		25283	1	2299	1167	84			25293	1	2527	1538	114
			2	754	514	40				2	1050	693	76
			3	190	125	1				3	89	65	0

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 15 (continued): Individual Locomotor Activity Data

Day 89 Relative to Start Date

Group	Sex	Animal	Interval	Basic Movements	Fine Movements	Rearing	Group	Sex	Animal	Interval	Basic Movements	Fine Movements	Rearing
4	m	25294	1	2194	1075	124	5	m	25304	1	2199	1215	77
			2	1032	577	48				2	1028	663	22
			3	677	397	33				3	863	582	68
		25295	1	1914	1089	102			25305	1	2141	1200	115
			2	1063	706	60				2	1489	899	70
			3	945	629	52				3	1003	644	43
		25296	1	2420	1468	84			25306	1	1962	1143	120
			2	806	562	47				2	646	460	42
			3	902	585	46				3	776	561	45
		25297	1	2319	1274	92			25307	1	2233	1097	85
			2	916	557	46				2	927	506	79
			3	1117	748	40				3	851	531	15
		25298	1	2431	1240	101			25308	1	2233	1273	101
			2	830	563	36				2	1290	860	45
			3	196	143	15				3	457	311	25
		25299	1	2417	1108	94			25309	1	1444	669	148
			2	1514	863	60				2	565	294	120
			3	550	326	11				3	362	189	72
		25300	1	1899	1079	117			25310	1	2202	1102	102
			2	641	438	53				2	1261	841	45
			3	381	281	10				3	409	301	31
		25301	1	2166	1256	189			25311	1	2114	1130	138
			2	597	368	80				2	1427	924	96
			3	11	10	0				3	532	319	62
		25302	1	2080	1033	99			25312	1	2035	863	90
			2	1025	591	44				2	1049	608	71
			3	389	275	34				3	802	562	62
		25303	1	2386	1437	128			25313	1	2063	894	186
			2	611	413	54				2	1166	637	129
			3	5	5	0				3	101	87	7

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 15 (continued): Individual Locomotor Activity Data

Day 89 Relative to Start Date

Group	Sex	Animal	Interval	Basic Movements	Fine Movements	Rearing	Group	Sex	Animal	Interval	Basic Movements	Fine Movements	Rearing
6	m	25314	1	2952	1482	102	6	m	25324	1	1749	1062	94
			2	1616	940	54				2	1410	918	72
			3	1107	607	42				3	987	658	35
		25315	1	2004	1047	137			25325	1	2544	1421	115
			2	1649	990	73				2	1675	960	79
			3	906	626	25				3	216	176	20
		25316	1	2212	1224	105			25326	1	2278	1135	159
			2	1316	868	58				2	1812	1050	115
			3	631	452	20				3	1416	853	75
		25317	1	2470	1329	124			25327	1	2183	1208	91
			2	1057	687	37				2	855	584	56
			3	376	277	49				3	240	179	60
		25318	1	2194	1145	117			25328	1	2266	1080	75
			2	897	592	46				2	1708	919	27
			3	488	342	19				3	860	520	26
		25319	1	2537	1205	144			25329	1	2393	1449	118
			2	1566	803	196				2	967	745	70
			3	572	342	95				3	30	30	0
		25320	1	2252	1265	122			25330	1	1996	975	102
			2	1086	682	85				2	1082	547	96
			3	398	279	98				3	547	319	28
		25321	1	2028	1129	70			25331	1	2067	1138	105
			2	1502	855	41				2	1071	675	70
			3	725	446	31				3	198	143	11
		25322	1	2355	1095	100			25332	1	2135	1094	88
			2	859	524	63				2	797	470	29
			3	297	200	3				3	307	208	0
		25323	1	1476	701	65			25333	1	1918	1083	77
			2	975	630	32				2	416	293	15
			3	126	102	4				3	72	63	0

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 15 (continued): Individual Locomotor Activity Data

Day 89 Relative to Start Date

Group	Sex	Animal	Interval	Basic Movements	Fine Movements	Rearing	Group	Sex	Animal	Interval	Basic Movements	Fine Movements	Rearing
1	f	25254	1	2011	854	71	1	f	25264	1	1826	644	80
			2	910	388	25				2	1129	544	30
			3	898	483	21				3	932	535	11
		25255	1	1739	782	62			25265	1	1433	554	62
			2	262	147	7				2	630	295	18
			3	704	372	21				3	486	325	2
		25256	1	2129	616	89			25266	1	1381	434	78
			2	934	354	49				2	569	235	33
			3	823	305	19				3	467	266	32
		25257	1	1868	669	78			25267	1	2269	883	118
			2	1119	485	43				2	1299	524	76
			3	500	205	30				3	1158	475	62
		25258	1	1951	710	98			25268	1	2166	766	108
			2	1113	486	36				2	920	391	50
			3	502	301	22				3	388	168	25
		25259	1	1771	567	84			25269	1	1819	537	130
			2	1489	576	34				2	1444	472	62
			3	915	399	22				3	852	344	28
		25260	1	1966	778	85			25270	1	2071	645	102
			2	1650	680	58				2	1412	499	62
			3	770	341	31				3	1173	432	47
		25261	1	2041	1078	73			25271	1	1615	573	69
			2	760	394	36				2	632	306	18
			3	324	227	10				3	696	358	29
		25262	1	1533	492	89			25272	1	1745	610	83
			2	1075	469	45				2	768	322	75
			3	795	332	61				3	604	257	23
		25263	1	1399	500	84			25273	1	1685	697	69
			2	973	330	81				2	1008	521	36
			3	381	181	33				3	1192	561	34

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 15 (continued): Individual Locomotor Activity Data

Day 89 Relative to Start Date

Group	Sex	Animal	Interval	Basic Movements	Fine Movements	Rearing	Group	Sex	Animal	Interval	Basic Movements	Fine Movements	Rearing
7	f	25334	1	1986	845	78	8	f	25344	1	2043	845	79
			2	1032	520	55				2	1287	661	58
			3	1036	456	43				3	959	493	37
		25335	1	1657	626	62			25345	1	1604	611	68
			2	593	321	21				2	996	459	39
			3	465	224	32				3	888	456	36
		25336	1	1946	728	82			25346	1	1439	419	78
			2	846	408	21				2	958	310	44
			3	173	104	3				3	801	251	48
		25337	1	1870	678	84			25347	1	1815	780	78
			2	1079	427	30				2	907	473	24
			3	843	345	45				3	906	493	19
		25338	1	1969	812	57			25348	1	1778	505	86
			2	1234	631	21				2	1310	452	56
			3	593	363	8				3	632	283	24
		25339	1	1659	518	84			25349	1	1713	520	96
			2	1074	433	68				2	1403	531	66
			3	708	344	14				3	776	359	21
		25340	1	1639	538	61			25350	1	1291	335	63
			2	1200	548	44				2	1158	337	44
			3	552	279	23				3	1105	340	53
		25341	1	1579	548	51			25351	1	1327	356	88
			2	1042	381	31				2	1193	368	56
			3	363	191	8				3	887	299	52
		25342	1	1394	483	60			25352	1	1476	545	80
			2	523	279	31				2	951	428	37
			3	718	309	30				3	417	234	22
		25343	1	1899	722	88			25353	1	2137	838	86
			2	1243	551	64				2	1287	608	67
			3	229	150	16				3	890	413	39

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 15 (continued): Individual Locomotor Activity Data

Day 89 Relative to Start Date

Group	Sex	Animal	Interval	Basic Movements	Fine Movements	Rearing	Group	Sex	Animal	Interval	Basic Movements	Fine Movements	Rearing
9	f	25354	1	1797	625	73	10	f	25364	1	1559	621	119
			2	1122	532	42				2	715	409	26
			3	1018	474	35				3	118	102	0
		25355	1	1722	687	75			25365	1	2198	748	140
			2	1330	596	41				2	1243	533	53
			3	787	382	33				3	1158	532	56
		25356	1	1969	701	88			25366	1	2219	829	104
			2	899	411	66				2	993	443	30
			3	476	280	38				3	773	324	23
		25357	1	1770	542	74			25367	1	1499	830	74
			2	1248	438	47				2	1095	769	60
			3	707	325	26				3	1108	718	43
		25358	1	1757	686	69			25368	1	2070	761	89
			2	965	458	54				2	1456	606	43
			3	851	397	27				3	1106	500	31
		25359	1	1619	572	62			25369	1	1641	520	79
			2	388	210	32				2	1243	465	59
			3	24	24	0				3	1215	517	39
		25360	1	1896	713	91			25370	1	1447	543	74
			2	929	434	47				2	1057	564	26
			3	794	421	48				3	18	15	0
		25361	1	1767	661	116			25371	1	1649	651	66
			2	949	415	74				2	1218	498	39
			3	839	376	47				3	890	437	27
		25362	1	1685	629	91			25372	1	1669	533	72
			2	1169	456	48				2	1137	344	82
			3	1161	479	26				3	690	324	27
		25363	1	1824	720	95			25373	1	1832	580	72
			2	1087	417	41				2	1282	442	52
			3	506	272	18				3	588	267	37

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 15 (continued): Individual Locomotor Activity Data

Day 89 Relative to Start Date

Group	Sex	Animal	Interval	Basic Movements	Fine Movements	Rearing	Group	Sex	Animal	Interval	Basic Movements	Fine Movements	Rearing
11	f	25374	1	1851	745	64	11	f	25384	1	2130	758	130
			2	1207	600	52				2	797	397	59
			3	1209	607	35				3	756	367	22
		25375	1	1868	836	102			25385	1	1772	636	78
			2	1037	558	48				2	1415	575	66
			3	931	468	34				3	839	372	50
		25376	1	1799	625	85			25386	1	1940	656	82
			2	888	375	25				2	1060	406	61
			3	669	300	38				3	769	315	32
		25377	1	1682	504	113			25387	1	1580	587	62
			2	1186	429	58				2	958	311	38
			3	490	173	59				3	686	319	22
		25378	1	1575	563	79			25388	1	1914	618	79
			2	1198	587	38				2	1394	538	39
			3	642	359	29				3	324	222	16
		25379	1	2043	761	90			25389	1	1733	672	73
			2	1453	626	65				2	1025	451	39
			3	755	420	44				3	522	302	18
		25380	1	1717	661	82			25390	1	1785	722	76
			2	902	436	34				2	853	400	35
			3	520	318	32				3	612	294	34
		25381	1	1792	660	79			25391	1	2309	748	97
			2	909	393	63				2	1548	515	51
			3	293	154	34				3	659	276	12
		25382	1	1699	567	76			25392	1	1705	775	71
			2	1310	463	69				2	879	532	18
			3	953	417	30				3	369	216	13
		25383	1	1723	537	89			25393	1	1649	613	75
			2	818	292	36				2	616	290	32
			3	607	314	26				3	712	274	57

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

APPENDIX 16: INDIVIDUAL VAGINAL CYTOLOGY

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 16: Individual Vaginal Cytology

Day Numbers Relative to Start Date

Group	Sex	Animal	15	16	17	18	19	20	21	22	23	24	25	26	27	28	Cycling (Y/N)	Nature (I/R)	Number of Cycles	Cycle Length (Days)
1	f	25254	D	E	M	D	D	E	M	D	D	E	M	D	D	E	Y	R	3	4.0
		25255	E	E	M	D	D	E	M	D	E	E	D	D	D	E	Y	R	3	4.0
		25256	P	E	M	D	P	E	M	D	P	E	M	D	P	E	Y	R	3	4.0
		25257	D	P	E	M	D	P	E	M	D	P	E	M	D	P	Y	R	3	4.0
		25258	D	D	D	E	E	D	D	E	E	D	D	E	E	D	Y	R	2	4.0
		25259	D	E	D	D	P	E	D	D	E	E	D	D	E	E	Y	R	3	4.0
		25260	E	M	D	P	E	D	D	D	E	M	D	D	E	D	Y	R	3	4.0
		25261	E	E	M	D	E	E	M	D	E	E	M	D	E	E	Y	R	3	4.0
		25262	E	M	D	P	E	M	D	P	E	M	D	P	E	M	Y	R	3	4.0
		25263	E	M	D	D	E	D	D	D	E	M	D	D	E	M	Y	R	3	4.0
		25264	D	D	E	E	D	D	D	E	D	D	D	E	D	D	Y	R	2	4.0
		25265	D	D	D	E	E	D	D	D	E	E	D	D	D	E	Y	R	2	4.5
		25266	E	D	D	D	E	D	D	D	E	D	D	D	E	D	Y	R	3	4.0
		25267	P	E	D	D	P	E	D	D	P	E	D	D	P	E	Y	R	3	4.0
		25268	D	E	M	D	D	E	D	D	D	E	D	D	E	E	Y	R	3	4.0
		25269	D	P	E	D	D	P	E	M	D	D	E	M	D	D	Y	R	2	4.0
		25270	E	E	M	D	E	E	M	D	E	E	M	D	E	E	Y	R	3	4.0
		25271	E	D	D	E	E	D	D	E	E	D	D	E	E	D	Y	R	3	4.0
		25272	P	E	M	D	P	E	M	D	P	E	M	D	P	E	Y	R	3	4.0
		25273	D	P	E	D	D	P	E	D	D	P	E	D	D	P	Y	R	3	4.0

D - Diestrus P - Proestrus E - Estrus M - Metestrus
Y - Yes R - Regular

Target Dose: Group 1 - 0 mg/kg/day Group 7 - 1 mg/kg/day Group 8 - 3 mg/kg/day Group 9 - 10 mg/kg/day Group 10 - 30 mg/kg/day
Group 11 - 100 mg/kg

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 16 (continued): Individual Vaginal Cytology

Day Numbers Relative to Start Date

Group	Sex	Animal	15	16	17	18	19	20	21	22	23	24	25	26	27	28	Cycling (Y/N)	Nature (I/R)	Number of Cycles	Cycle Length (Days)
7	f	25334	D	D	P	E	D	D	P	E	M	D	D	E	M	D	Y	R	2	4.0
		25335	D	D	P	E	D	D	E	E	M	D	D	E	D	D	Y	R	2	4.0
		25336	E	M	D	D	E	M	D	E	E	D	D	E	E	M	Y	R	3	4.0
		25337	D	E	M	D	E	E	D	D	E	E	M	D	E	E	Y	R	3	4.0
		25338	E	E	M	D	E	E	M	D	E	E	M	D	E	E	Y	R	3	4.0
		25339	D	D	D	E	M	D	P	E	E	D	D	P	D	D	Y	R	1	5.0
		25340	E	D	D	P	E	D	D	P	E	M	D	P	E	M	Y	R	3	4.0
		25341	D	E	E	M	D	D	E	M	D	D	E	M	D	D	Y	R	2	4.0
		25342	D	E	E	D	D	E	E	D	D	D	E	E	D	D	Y	R	2	4.5
		25343	E	D	D	P	E	D	D	D	E	M	D	P	E	M	Y	R	3	4.0
8	f	25344	D	D	P	E	D	D	D	E	M	D	E	E	M	D	Y	R	2	4.0
		25345	D	E	M	D	E	E	D	D	P	E	D	D	D	P	Y	R	2	4.0
		25346	E	M	D	D	E	D	D	D	D	D	E	D	D	D	Y	I	2	5.0
		25347	E	M	D	D	E	D	D	E	E	M	D	D	E	M	Y	R	3	4.0
		25348	D	D	E	M	D	E	E	M	D	P	E	M	D	D	Y	R	2	4.0
		25349	E	D	D	E	E	D	D	E	E	D	D	E	E	M	Y	R	3	4.0
		25350	D	E	E	D	D	E	E	M	D	E	E	M	D	E	Y	R	3	3.7
		25351	P	E	M	D	P	E	D	D	P	E	M	D	P	E	Y	R	3	4.0
		25352	D	P	E	E	D	D	P	E	M	D	P	E	D	D	Y	R	2	4.5
		25353	D	D	E	E	D	D	E	E	D	D	D	E	D	D	Y	R	2	4.0

D - Diestrus P - Proestrus E - Estrus M - Metestrus
Y - Yes I - Irregular R - Regular

Target Dose: Group 1 - 0 mg/kg/day Group 7 - 1 mg/kg/day Group 8 - 3 mg/kg/day Group 9 - 10 mg/kg/day Group 10 - 30 mg/kg/day
Group 11 - 100 mg/kg

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 16 (continued): Individual Vaginal Cytology

Day Numbers Relative to Start Date

Group	Sex	Animal	15	16	17	18	19	20	21	22	23	24	25	26	27	28	Cycling (Y/N)	Nature (I/R)	Number of Cycles	Cycle Length (Days)
9	f	25354	E	D	D	D	E	E	D	D	D	P	E	D	D	D	Y	R	2	5.0
		25355	D	D	E	D	P	E	D	E	M	D	D	E	E	D	Y	I	3	3.3
		25356	D	D	P	E	D	D	D	E	M	D	E	E	D	D	Y	R	2	4.0
		25357	D	P	E	D	D	P	D	D	D	P	E	D	D	P	Y	R	3	4.0
		25358	D	P	E	M	D	E	E	E	M	D	D	E	D	D	Y	I	2	4.5
		25359	D	P	E	M	D	P	E	M	D	P	E	D	D	E	Y	R	3	3.7
		25360	D	P	E	M	D	E	E	M	D	D	E	E	D	D	Y	R	2	4.5
		25361	M	D	D	E	M	D	D	E	M	D	D	E	M	D	Y	R	3	4.0
		25362	P	E	M	D	P	E	M	D	P	E	M	D	P	E	Y	R	3	4.0
		25363	P	E	D	D	E	E	M	D	E	E	M	D	E	E	Y	R	3	4.0
10	f	25364	E	E	D	D	P	E	D	D	P	E	D	D	P	E	Y	R	3	4.0
		25365	E	D	D	E	E	D	D	P	E	M	D	P	E	D	Y	R	3	4.0
		25366	P	E	M	D	P	E	D	D	P	E	D	D	E	E	Y	R	3	4.0
		25367	E	D	D	P	E	M	D	P	E	M	D	P	E	M	Y	R	3	4.0
		25368	D	P	E	D	D	P	E	D	D	P	E	M	D	P	Y	R	3	4.0
		25369	D	D	D	E	D	D	D	E	D	D	E	E	D	D	Y	R	2	4.0
		25370	P	E	M	D	P	E	D	D	E	E	M	D	E	E	Y	R	3	4.0
		25371	E	E	M	D	E	E	M	D	E	E	M	D	E	E	Y	R	3	4.0
		25372	D	P	E	D	D	E	E	D	D	E	E	D	D	P	Y	R	2	4.0
		25373	D	P	E	M	D	P	E	D	D	P	E	D	D	P	Y	R	3	4.0

D - Diestrus P - Proestrus E - Estrus M - Metestrus
Y - Yes I - Irregular R - Regular

Target Dose: Group 1 - 0 mg/kg/day Group 7 - 1 mg/kg/day Group 8 - 3 mg/kg/day Group 9 - 10 mg/kg/day Group 10 - 30 mg/kg/day
Group 11 - 100 mg/kg

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 16 (continued): Individual Vaginal Cytology

Day Numbers Relative to Start Date

Group	Sex	Animal	15	16	17	18	19	20	21	22	23	24	25	26	27	28	Cycling (Y/N)	Nature (I/R)	Number of Cycles	Cycle Length (Days)
11	f	25374	D	D	P	E	D	D	P	E	D	D	P	E	D	D	Y	R	2	4.0
		25375	M	D	E	E	D	D	D	E	M	D	D	E	D	D	Y	R	2	4.0
		25376	P	E	E	D	D	P	E	M	D	P	E	D	D	E	Y	R	3	3.7
		25377	E	E	M	D	D	E	D	D	E	E	D	D	E	E	Y	R	3	4.0
		25378	D	P	E	M	D	P	E	M	D	P	E	M	D	P	Y	R	3	4.0
		25379	D	P	E	D	D	P	E	D	D	P	E	E	M	D	Y	R	2	4.0
		25380	D	D	E	E	D	D	P	E	D	D	E	E	M	D	Y	R	2	4.0
		25381	D	D	P	E	D	D	P	E	E	D	D	D	E	E	Y	R	2	5.0
		25382	E	D	D	E	E	D	D	E	E	D	D	E	E	D	Y	R	3	4.0
		25383	U	P	E	D	D	P	E	E	M	D	E	E	D	D	Y	R	2	4.5
		25384	E	D	D	P	E	D	D	P	E	M	D	P	E	M	Y	R	3	4.0
		25385	E	E	D	D	E	E	M	D	E	E	M	D	E	E	Y	R	3	4.0
		25386	D	E	D	D	E	E	M	D	E	E	M	D	E	E	Y	R	3	4.0
		25387	D	P	E	E	D	D	D	P	E	D	D	D	D	E	Y	R	2	5.0
		25388	P	E	M	D	P	E	D	D	P	E	D	D	P	E	Y	R	3	4.0
		25389	D	P	E	M	D	D	E	E	M	D	D	E	M	D	Y	R	2	4.5
		25390	P	E	D	D	P	E	M	D	E	E	D	D	E	E	Y	R	3	4.0
		25391	D	E	E	M	D	E	E	M	D	E	E	M	D	E	Y	R	3	3.7
		25392	E	E	D	D	E	E	M	D	D	E	E	D	D	P	Y	R	2	4.5
		25393	D	P	E	D	D	P	E	M	D	P	E	D	D	P	Y	R	3	4.0

D - Diestrus P - Proestrus E - Estrus M - Metestrus
Y - Yes I - Irregular R - Regular

Target Dose: Group 1 - 0 mg/kg/day Group 7 - 1 mg/kg/day Group 8 - 3 mg/kg/day Group 9 - 10 mg/kg/day Group 10 - 30 mg/kg/day
Group 11 - 100 mg/kg

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 16 (continued): Individual Vaginal Cytology

Day Numbers Relative to Start Date

Group	Sex	Animal	72	73	74	75	76	77	78	79	80	81	82	83	84	85	Cycling (Y/N)	Nature (I/R)	Number of Cycles	Cycle Length (Days)
1	f	25254	D	E	M	D	D	E	M	D	D	E	M	D	D	E	Y	R	3	4.0
		25255	D	E	D	D	D	E	E	M	D	D	E	E	D	D	Y	R	2	5.0
		25256	P	E	M	D	D	E	M	D	E	E	M	D	D	E	Y	R	3	4.0
		25257	D	P	E	M	D	P	E	M	D	P	E	D	D	E	Y	R	3	3.7
		25258	E	M	D	E	D	D	D	E	E	M	D	D	E	M	Y	R	3	4.0
		25259	E	E	D	D	E	E	D	D	E	E	M	D	P	E	Y	R	3	4.0
		25260	E	M	D	D	E	M	D	D	E	M	D	P	E	D	Y	R	3	4.0
		25261	E	E	M	D	D	E	M	D	D	E	M	D	E	E	Y	R	3	4.0
		25262	E	M	D	D	E	M	D	D	E	M	D	D	E	M	Y	R	3	4.0
		25263	E	M	D	D	E	M	D	D	E	M	D	D	E	M	Y	R	3	4.0
		25264	D	E	D	D	E	E	E	D	D	E	E	E	D	D	Y	I	2	5.0
		25265	E	E	E	E	E	E	E	E	E	E	E	E	E	E	N	I	-	-
		25266	D	D	D	E	E	M	D	D	D	P	E	D	D	D	Y	R	1	6.0
		25267	E	E	D	D	U	E	D	D	E	E	M	D	E	E	Y	R	3	4.0
		25268	E	E	E	E	E	E	E	E	E	E	E	E	E	E	N	I	-	-
		25269	D	E	E	D	D	D	E	D	D	E	E	D	D	D	Y	R	2	4.0
		25270	E	E	D	D	D	E	D	D	D	E	D	D	D	E	Y	R	3	4.0
		25271	E	E	D	D	E	E	D	D	E	E	D	D	E	E	Y	R	3	4.0
		25272	D	D	P	D	E	M	D	D	P	D	D	D	E	E	Y	R	1	6.0
		25273	D	D	P	E	M	D	E	E	D	E	P	E	M	D	Y	I	3	2.7

D - Diestrus P - Proestrus E - Estrus M - Metestrus
Y - Yes I - Irregular R - Regular

Target Dose: Group 1 - 0 mg/kg/day Group 7 - 1 mg/kg/day Group 8 - 3 mg/kg/day Group 9 - 10 mg/kg/day Group 10 - 30 mg/kg/day
Group 11 - 100 mg/kg

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 16 (continued): Individual Vaginal Cytology

Day Numbers Relative to Start Date

Group	Sex	Animal	72	73	74	75	76	77	78	79	80	81	82	83	84	85	Cycling (Y/N)	Nature (I/R)	Number of Cycles	Cycle Length (Days)
7	f	25334	D	D	P	E	D	D	D	E	M	D	D	E	M	D	Y	R	2	4.0
		25335	D	D	E	E	D	D	E	E	M	D	E	E	M	D	Y	R	2	4.0
		25336	E	E	E	E	E	E	E	E	E	E	E	E	E	E	N	I	-	-
		25337	D	E	M	D	D	E	M	D	D	E	D	D	D	E	Y	R	3	4.0
		25338	D	E	M	D	E	E	M	D	E	E	M	D	D	E	Y	R	3	4.0
		25339	E	M	D	D	P	E	D	D	D	E	E	M	D	D	Y	R	2	5.0
		25340	E	D	D	E	E	D	D	D	E	E	D	D	E	D	Y	R	3	4.0
		25341	D	D	E	M	D	D	E	D	D	D	E	M	D	D	Y	R	2	4.0
		25342	E	E	M	D	D	E	E	D	D	D	P	E	M	D	Y	R	2	5.0
		25343	E	M	D	D	E	M	D	D	E	M	D	D	E	M	Y	R	3	4.0
8	f	25344	D	D	P	E	D	D	E	E	M	D	D	E	M	D	Y	R	2	4.0
		25345	E	E	D	D	E	E	D	D	E	E	M	D	D	E	Y	R	3	4.0
		25346	E	D	D	D	E	E	D	D	D	E	E	D	P	E	Y	R	3	4.3
		25347	E	D	D	D	E	D	D	D	E	D	D	D	E	D	Y	R	3	4.0
		25348	D	D	E	D	D	D	E	M	D	P	E	D	D	D	Y	R	2	4.0
		25349	E	D	D	E	E	D	D	D	E	D	D	D	E	M	Y	R	3	4.0
		25350	D	D	E	M	D	D	E	M	D	E	E	M	D	E	Y	R	3	3.7
		25351	E	E	D	D	E	E	D	D	E	E	M	D	E	E	Y	R	3	4.0
		25352	D	D	E	E	M	D	D	E	M	D	D	E	M	D	Y	R	2	4.0
		25353	D	D	E	E	D	D	D	E	D	D	E	E	M	D	Y	R	2	4.0

D - Diestrus P - Proestrus E - Estrus M - Metestrus
Y - Yes I - Irregular R - Regular

Target Dose: Group 1 - 0 mg/kg/day Group 7 - 1 mg/kg/day Group 8 - 3 mg/kg/day Group 9 - 10 mg/kg/day Group 10 - 30 mg/kg/day
Group 11 - 100 mg/kg

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 16 (continued): Individual Vaginal Cytology

Day Numbers Relative to Start Date

Group	Sex	Animal	72	73	74	75	76	77	78	79	80	81	82	83	84	85	Cycling (Y/N)	Nature (I/R)	Number of Cycles	Cycle Length (Days)
9	f	25354	D	D	P	E	D	E	E	E	D	D	D	E	D	D	Y	I	2	4.0
		25355	D	D	D	P	E	M	D	D	E	M	D	D	E	D	Y	R	2	4.0
		25356	D	D	E	E	D	D	E	E	M	D	D	E	M	D	Y	R	2	4.0
		25357	E	E	M	D	D	E	E	E	E	E	E	E	E	E	Y	I	1	12.0
		25358	E	E	E	E	E	E	E	E	E	E	E	E	E	E	N	I	-	-
		25359	D	P	E	M	D	E	E	M	D	P	E	D	D	D	Y	R	2	4.0
		25360	E	E	E	D	D	D	E	E	D	D	D	E	E	D	Y	I	2	5.0
		25361	D	D	E	E	D	D	D	E	D	D	D	E	D	D	Y	R	2	4.0
		25362	E	E	M	D	E	E	M	D	E	E	M	D	E	E	Y	R	3	4.0
		25363	E	E	D	D	D	E	D	D	E	E	M	D	D	E	Y	R	3	4.0
10	f	25364	E	E	M	D	E	E	M	D	P	E	M	D	D	E	Y	R	3	4.0
		25365	E	M	D	D	E	E	D	E	M	D	D	E	E	D	Y	I	3	4.0
		25366	E	E	D	D	E	E	D	D	P	E	D	D	E	E	Y	R	3	4.0
		25367	E	D	D	E	E	D	D	D	E	E	D	D	E	M	Y	R	3	4.0
		25368	E	D	E	E	E	D	D	E	P	E	D	D	E	E	Y	I	4	3.3
		25369	D	D	D	E	D	D	E	E	M	D	D	E	D	D	Y	R	2	4.0
		25370	D	E	M	D	D	E	E	E	M	D	D	P	E	D	Y	I	2	5.5
		25371	E	M	D	D	E	M	D	D	E	M	D	D	E	E	Y	R	3	4.3
		25372	E	M	D	P	E	E	D	D	E	E	E	E	D	D	Y	I	2	5.5
		25373	D	P	E	D	D	P	E	D	D	P	E	D	D	P	Y	R	3	4.0

D - Diestrus P - Proestrus E - Estrus M - Metestrus
Y - Yes I - Irregular R - Regular

Target Dose: Group 1 - 0 mg/kg/day Group 7 - 1 mg/kg/day Group 8 - 3 mg/kg/day Group 9 - 10 mg/kg/day Group 10 - 30 mg/kg/day
Group 11 - 100 mg/kg

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 16 (continued): Individual Vaginal Cytology

Day Numbers Relative to Start Date

Group	Sex	Animal	72	73	74	75	76	77	78	79	80	81	82	83	84	85	Cycling (Y/N)	Nature (I/R)	Number of Cycles	Cycle Length (Days)
11	f	25374	D	E	M	D	D	E	D	D	D	E	D	P	E	D	Y	R	3	3.7
		25375	D	D	D	E	D	D	D	E	D	D	D	E	D	D	Y	R	2	4.0
		25376	E	M	D	P	E	M	D	E	E	M	D	D	E	M	Y	R	3	4.0
		25377	D	D	D	E	E	E	E	E	E	E	E	E	E	E	N	I	-	-
		25378	D	P	E	M	D	D	E	M	D	P	E	M	D	E	Y	R	3	3.7
		25379	D	D	D	E	E	D	D	D	P	E	D	D	D	P	Y	R	1	5.0
		25380	D	D	E	E	M	D	D	E	D	D	E	E	M	D	Y	R	2	4.0
		25381	E	E	D	E	E	E	E	D	E	E	E	E	E	E	Y	I	2	6.0
		25382	E	M	D	D	E	D	D	D	E	D	D	D	E	D	Y	R	3	4.0
		25383	D	D	D	E	D	D	E	E	D	D	D	E	D	D	Y	R	2	4.0
		25384	E	M	D	D	E	M	D	D	E	M	D	D	E	D	Y	R	3	4.0
		25385	D	E	D	D	D	E	D	D	E	E	D	D	D	E	Y	R	3	4.0
		25386	D	D	E	D	D	E	E	M	D	D	E	M	D	D	Y	R	2	4.0
		25387	E	D	D	D	E	E	D	D	D	P	E	D	D	D	Y	R	2	5.0
		25388	E	E	D	D	D	E	E	E	E	M	D	P	E	M	Y	I	2	5.5
		25389	D	E	D	D	D	E	E	D	D	D	E	M	D	D	Y	R	2	4.5
		25390	E	E	D	D	E	E	M	D	D	E	M	D	D	E	Y	R	3	4.0
		25391	D	E	E	M	D	E	E	M	D	D	E	D	D	E	Y	R	3	3.7
		25392	D	D	D	D	D	D	D	D	D	E	M	D	D	P	Y	I	-	-
		25393	D	E	E	D	D	P	E	D	D	P	E	D	D	D	Y	R	2	4.0

D - Diestrus P - Proestrus E - Estrus M - Metestrus
Y - Yes I - Irregular R - Regular

Target Dose: Group 1 - 0 mg/kg/day Group 7 - 1 mg/kg/day Group 8 - 3 mg/kg/day Group 9 - 10 mg/kg/day Group 10 - 30 mg/kg/day
Group 11 - 100 mg/kg

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 16 (continued): Individual Vaginal Cytology

Day Numbers Relative to Start Date

Group	Sex	Animal	119	Group	Sex	Animal	119
1	f	25264	E	11	f	25384	E
		25265	E			25385	D
		25266	D			25386	E
		25267	E			25387	D
		25268	E			25388	D
		25269	D			25389	D
		25270	D			25390	D
		25271	E			25391	D
		25272	M			25392	D
		25273	D			25393	D

D - Diestrus E - Estrus M - Metestrus

Target Dose: Group 1 - 0 mg/kg/day Group 11 - 100 mg/kg

APPENDIX 17: OPHTHALMOLOGY REPORT

OPHTHALMOLOGY REPORT

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Smithers Avanza Study No. 2410-14374

GROUP DESIGNATION AND MATERIAL AND METHODS

Group Designation

Group designation, treatment, target dose levels, and animal distribution are presented in Text Table 1.

Text Table 1: Study Information

Group	Treatment	Target Dose (mg/kg/day)	Animal Numbers							
			Main Phase				Recovery Phase			
			N	Males	N	Females	N	Males	N	Females
1	Control	0	10	25234-25243	10	25254-25263	10	25244-25253	10	25264-25273
2	TFM	1	10	25274-25283	-	-	-	-	-	-
3	TFM	3	10	25284-25293	-	-	-	-	-	-
4	TFM	10	10	25294-25303	-	-	-	-	-	-
5	TFM	30	10	25304-25313	-	-	-	-	-	-
6	TFM	100	10	25314-25323	-	-	10	25324-25333	-	-
7	TFM	1	-	-	10	25334-25343	-	-	-	-
8	TFM	3	-	-	10	25344-25353	-	-	-	-
9	TFM	10	-	-	10	25354-25363	-	-	-	-
10	TFM	30	-	-	10	25364-25373	-	-	-	-
11	TFM	100	-	-	10	25374-25383	-	-	10	25384-25393

Material and Methods

Ophthalmology examinations were conducted using an indirect ophthalmoscope and a slit lamp biomicroscope (as needed); the eyes of each animal were examined following administration of a mydriatic solution. Ophthalmology examinations were conducted prior to randomization for all animals and for all surviving animals in Groups 1, 6, and 11 only on Study Days 88/90 (F/M) and 117/118 (F/M).

RESULTS

No visible ocular lesions were noted in any animal.

CONCLUSION

In conclusion, there were no test-article related ocular effects under the conditions of this study.

Holly Atlee, DVM

Holly Atlee, DVM

26 March 2019

Date

APPENDIX 18: CLINICAL AND ANATOMIC PATHOLOGY REPORT

Vet Path Services, Inc.
6450 Castle Drive
Mason, OH 45040

Clinical and Anatomic Pathology Report

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Smithers Avanza Study No. 2410-14374

INTRODUCTION

The purpose of this study was to determine the potential toxicity of 4-nitro-3-(trifluoromethyl)phenol (TFM, test substance) to male and female Sprague Dawley rats when administered continuously for 90-days via drinking water and to determine the persistence or reversibility of any toxic effects over a 28-day recovery period.

EXPERIMENTAL DESIGN AND METHODS

One hundred and sixty (80/sex) Sprague Dawley rats were randomly assigned to 1 of 11 groups and treated as described in Text Table 1.

Text Table 1: Group Designation and Dosage Levels

Group	Treatment	Target Dose (mg/kg/day)	Animal Numbers							
			Main Phase				Recovery Phase			
			N	Males	N	Females	N	Males	N	Females
1	Control	0	10	25234-25243	10	25254-25263	10	25244-25253	10	25264-25273
2	TFM	1	10	25274-25283	-	-	-	-	-	-
3	TFM	3	10	25284-25293	-	-	-	-	-	-
4	TFM	10	10	25294-25303	-	-	-	-	-	-
5	TFM	30	10	25304-25313	-	-	-	-	-	-
6	TFM	100	10	25314-25323	-	-	10	25324-25333	-	-
7	TFM	1	-	-	10	25334-25343	-	-	-	-
8	TFM	3	-	-	10	25344-25353	-	-	-	-
9	TFM	10	-	-	10	25354-25363	-	-	-	-
10	TFM	30	-	-	10	25364-25373	-	-	-	-
11	TFM	100	-	-	10	25374-25383	-	-	10	25384-25393

Control = Deionized Water; - = not applicable.

Blood samples and urine specimens were collected on Study Day (SD) 91 (main phase animals only) or SD 119 (recovery phase animals only).

Full gross necropsy was performed on animals at scheduled timepoints, as required per the study protocol and applicable protocol amendments. All protocol-required tissues were embedded in paraffin,

sectioned, stained (hematoxylin and eosin), and evaluated microscopically by the undersigned board-certified veterinary pathologist.

All summary data tables, individual data appendices, and clinical pathology methods are presented in the final (Smithers Avanza) report for this study.

RESULTS AND DISCUSSION

Mortality

There were no early deaths. Animals were terminated in accordance with the study protocol.

Clinical Pathology

Clinical Chemistry

SD 91

There were no test substance-related changes in clinical chemistry parameters.

Increased mean creatine kinase (CK) in females given 100 mg/kg was not considered test substance-related due to lack of dose-response, absence of similar changes in males, absence of correlating microscopic findings, and lack of statistical significance.

Decreased mean total protein (TPROT) in males given 100 mg/kg was not considered test substance-related due to lack of dose-response, absence of similar changes in females, and absence of correlating microscopic findings.

Increased mean (ALTi) in females given 1 and 100 mg/kg was not considered test substance-related due to lack of dose-response, absence of similar changes in males, and absence of correlating microscopic findings.

SD 119

There were no test substance-related changes in clinical chemistry parameters.

Increased mean calcium (CA) in males given 100 mg/kg was not considered test substance-related due to the absence of a similar change in females, and because the mean value was within the range of historical control data.

Increased mean potassium (K) in females given 100 mg/kg was not considered test substance-related due to the absence of a similar change in males, and because the mean value was within the range of historical control data.

Hematology

SD 91

There were no test substance-related changes in hematology parameters.

Decreased mean absolute eosinophil count (ABSEOS) in males given 100 mg/kg was not considered test substance-related due to the absence of a similar change in females, absence of dose-response, and because the mean value was within the range of historical control data.

SD 119

There were no test substance-related changes in hematology parameters.

Increased mean red blood cell count (RBC), hemoglobin (HGB), and hematocrit (HCT) in females given 100 mg/kg were not considered test substance-related due to the absence of similar changes in males and because the mean values were within the range of historical control data.

Decreased mean platelet count (PLT) and increased mean platelet volume (MPV) in males given 100 mg/kg were not considered test substance-related due to the absence of similar changes in females and because the mean values were within the range of historical control data.

Coagulation

SD 91

There were no test substance-related changes in coagulation parameters.

Decreased mean fibrinogen (FIB) in females given 100 mg/kg was not considered test substance-related due to the lack of dose-response, absence of similar changes in males, and absence of correlating microscopic findings.

SD 119

There were no test substance-related changes in coagulation parameters.

Increased mean activated partial thromboplastin time (APTT) in females given 100 mg/kg, and increased prothrombin time (PT) in males given 100 mg/kg were not considered test substance-related due to the absence of similar changes in the opposite gender, and absence of correlating macroscopic or clinical observations.

Urinalysis

SD 91

There were no test substance-related changes in urinalysis parameters.

Decreased mean specific gravity (SG) in males given 100 mg/kg was not considered test substance-related due to the absence of similar changes in females and because the mean value was within the range of historical control data. Increased mean urobilinogen (URO) in females given 100 mg/kg was not considered test substance-related due to the absence of similar changes in males.

SD 119

There were no test substance-related changes in urinalysis parameters.

Increased mean total urinary volume (TUVOL) in males given 100 mg/kg was not considered test substance-related due to the absence of similar changes in females and because the mean value was within the range of historical control data.

Organ Weight Data

Terminal Necropsy (SD 91)

There were no test substance-related organ weight changes.

Significantly increased mean relative (to body weight) brain weight in males given 100 mg/kg was due to decreased mean body weight in this group. Significantly increased mean relative (to brain weight) thymus weight in females given 10 mg/kg was considered unrelated to TFM and due to individual variation (primarily attributed to an increase in two animals), as there was no dose response, and similar changes were not present in males.

Recovery Necropsy (SD 119)

There were no test substance-related organ weight changes.

Macroscopic Findings

Terminal Necropsy (SD 91)

There were no test substance-related macroscopic observations.

Bilateral, clear fluid-filled distention of the uterus was observed in two females given 10 mg/kg and two females given 30 mg/kg TFM, correlating microscopically with dilation of the uterine lumen. This finding of dilated uterine lumen was also observed microscopically in three control females and one female given 100 mg/kg and was likely due to normal estrous cycle activity (Westwood, 2008).

Recovery Necropsy (SD 119)

There were no test substance-related macroscopic observations.

Small testis correlating with severe hypospermatogenesis was observed in one male (25330) given 100 mg/kg TFM. Hypospermatogenesis is a common incidental finding in Sprague Dawley rats, and was observed in control and high dose males at the terminal necropsy.

Microscopic Findings

Terminal Necropsy (SD 91)

There were no test substance-related microscopic findings.

All microscopic findings at the terminal necropsy are considered unrelated to TFM due to their low incidence rates and/or because they are common findings in Sprague Dawley rats of this age.

SUMMARY

The purpose of this study was to determine the potential toxicity of 4-nitro-3-(trifluoromethyl)phenol (TFM, test substance) when administered continuously for 90-days via drinking water to male and female Sprague Dawley rats and to determine the persistence or reversibility of any toxic effects over a 28-day recovery period.

All animals survived to the scheduled necropsies. There were no test substance-related alterations in clinical pathology parameters at any time point. There were no test substance-related macroscopic observations or organ weight changes at any time point, and there were no test substance-related microscopic findings at the terminal necropsy.

REFERENCE

Westwood, FR. The Female Rat Reproductive Cycle: A Practical Histological Guide to Staging (2008). *Toxicologic Pathology* 36: 375-384.

Roxanne E. Baumgartner, D.V.M., Diplomate, A.C.V.P., A.B.T.
Principal Investigator, Anatomic and Clinical Pathology

21 March 2019
Date

Vet Path Services

Smithers Avanza Study No.: 2410-14374

Study Title: 4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Principal Investigator Compliance Statement

The portion of the study performed by Vet Path Services, Inc. (VPS) was conducted in compliance with the Organisation for Economic Co-operation and Development (OECD), Principles of Good Laboratory Practices (GLP) ENV/MC/CHEM (98) 17, the Environmental Protection Agency TSCA Good Laboratory Practice Standards (40 CFR Part 792), the study protocol, protocol amendment numbers 1-7, applicable Smithers Avanza standard operating procedures and applicable VPS standard operating procedures.

21 March 2019

Roxanne E. Baumgartner, D.V.M., Diplomate, A.C.V.P., A.B.T. Date
Vet Path Services, Inc. (VPS)
6450 Castle Drive
Mason, Ohio 45040

APPENDIX 19: HISTOLOGY REPORT

Vet Path Services
Experience counts

March 25, 2019

Principal Investigator Report

Study Number: 2410-14374
Study Title: 4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Methods and Procedures

Tissues collected at necropsy were received in good condition at Vet Path Services, Inc. on August 1, 2018 and August 29, 2018. Tissues were inventoried in according to VPS SOP 202. The protocol required tissues were trimmed, processed, embedded in paraffin, sectioned, stained with Hematoxylin and Eosin, coverslipped and checked for quality according to all applicable VPS SOPs. Slides were shipped to Dr. Roxanne Baumgartner (Vet Path Services, Inc.) on August 20, 2018, September 11, 2018, and September 12, 2018 for evaluation.

One VPS SOP deviation was reported on March 14, 2019 with no impact to the study.

The portion of the study performed by Vet Path Services, Inc. (VPS) was conducted in compliance with the current OECD Good Laboratory Practice Principles (GLP) (ENV/MC/CHEM(98)17), the Environmental Protection Agency TSCA Good Laboratory Practice Standards (40 CFR Part 792), the study protocol, protocol amendments, and applicable VPS's Standard Operating Procedures (SOPs).

Material Disposition

Upon study completion all residual wet tissues, paraffin blocks, and glass microscopic slides will be transferred to VPS Archives, LLC (6450 Castle Drive, Mason, OH 45040) for long-term GLP-compliant storage.

All remaining study-related materials (original histology data) will be returned to Smithers Avanza (11 Firstfield Road, Suite B, Gaithersburg, MD 20878) upon completion of the evaluation of slides.

Sheree K. Lovelace 3-25-19

Sheree K. Lovelace, LAT, HT (ASCP)
Vet Path Services, Inc.
6450 Castle Drive
Mason, Ohio 45040

Date

Vet Path Services
Experience counts

March 25, 2019

Study Number: 2410-14374
Study Title: 4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Principal Investigator Compliance Statement

The portion of the study performed by Vet Path Services, Inc. (VPS) was conducted in compliance with the current OECD Good Laboratory Practice Principles (GLP) (ENV/MC/CHEM(98)17), the Environmental Protection Agency TSCA Good Laboratory Practice Standards (40 CFR Part 792), the study protocol, protocol amendments, and applicable VPS's Standard Operating Procedures (SOPs).

Sheree K. Lovelace 3-25-19

Sheree K. Lovelace, LAT, HT (ASCP)
Vet Path Services, Inc.
6450 Castle Drive
Mason, Ohio 45040

Date

Vet Path Services
Experience counts

QUALITY ASSURANCE STATEMENT

STUDY IDENTITY: Smithers Avanza Study No. 2410-14374
4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

STUDY DIRECTOR: Caitlin Murphy, PhD, DABT

PRINCIPAL INVESTIGATOR: Sheree K. Lovelace, LAT, HT (ASCP)
Vet Path Services, Inc.
6450 Castle Drive
Mason, Ohio 45040

Study Aspect QA Date	Reported to Principal Investigator and VPS Management	Reported to Study Director and Management
Staining and Coverslipping		
8 August 2018	9 August 2018	9 August 2018
Histology Laboratory Data, Principal Investigator Report and Compliance Statement		
22, 25 March 2019	25 March 2019	25 March 2019

Asheton E. Whitaker
Asheton E. Whitaker, BS
Quality Assurance Specialist

25 march 2019
Date

Vet Path Services, Inc • 6450 Castle Drive • Mason, OH 45040 • (513) 469-0777 • FAX (513) 469-2474

APPENDIX 20: CLINICAL PATHOLOGY HISTORICAL CONTROL DATA

SMITHERS AVANZA

Rat (Sprague Dawley) Historical Data
Clinical Chemistry

Test	Units	Males				Females			
		Mean	SD	N	Range	Mean	SD	N	Range
GLU	mg/dL	102.7	15.2	97	78 - 144	102.0	8.5	101	83 - 120
BUN	mg/dL	19.8	2.3	97	16 - 25	19.5	2.5	101	14 - 25
CREA	mg/dL	0.57	0.09	97	0.4 - 0.8	0.64	0.10	101	0.4 - 0.9
NA	mmol/L	148.8	3.5	96	144 - 175	147.3	4.0	101	143 - 175
K	mmol/L	6.29	0.47	96	5.3 - 7.6	6.01	0.50	101	5.0 - 7.2
CL	mmol/L	103.4	2.2	96	100 - 118	104.1	2.6	101	100 - 120
CA	mg/dL	10.75	0.44	97	9.8 - 11.9	10.59	0.50	101	9.7 - 12.1
PHOS	mg/dL	9.78	1.17	97	7.9 - 13.5	8.96	1.25	101	6.4 - 12.9
CHOL	mg/dL	111.7	13.4	97	86 - 139	105.9	17.1	101	66 - 147
TRIG	mg/dL	31.9	11.8	81	16 - 63	30.4	8.8	100	16 - 53
TPROT	g/dL	6.59	0.34	97	6.0 - 8.2	6.48	0.43	101	5.9 - 8.6
ALB	g/dL	3.19	0.18	97	2.9 - 4.0	3.28	0.21	101	3.0 - 4.2
GLOB	g/dL	3.39	0.21	97	3.1 - 4.2	3.21	0.26	101	2.8 - 4.4
A/G	ratio	0.95	0.07	97	0.8 - 1.1	1.02	0.07	101	0.9 - 1.1
AST	U/L	99.5	15.3	97	73 - 142	95.3	13.2	101	75 - 143
ALT/ALTi	U/L	59.2	12.0	85	40 - 88	46.5	7.8	101	31 - 64
ALKP	U/L	122.2	23.7	97	80 - 173	79.7	13.7	101	56 - 115
TBILI	mg/dL	0.18	0.06	97	0.1 - 0.3	0.19	0.04	101	0.1 - 0.3
CK	U/L	211.3	101.8	97	87 - 604	174.0	79.1	101	96 - 476
GGT	U/L	4.3	2.1	97	1 - 9	4.1	2.1	101	1 - 9

Ranges represent nonparametric 95% interval
Tests were performed using the Siemens Dimension XPand chemistry analyzer

Rat (Sprague Dawley) Historical Data
Hematology

Test	Units	Males				Females			
		Mean	SD	N	Range	Mean	SD	N	Range
RBC	M/uL	8.79	0.32	101	8.23 - 9.65	8.19	0.29	101	7.46 - 8.85
HGB	g/dL	16.06	0.57	101	15 - 17.4	15.40	0.56	101	14.4 - 17.1
HCT	%	52.00	1.61	101	48.0 - 55.3	48.65	2.16	101	44.3 - 53.5
MCV	fL	59.19	1.85	101	55.1 - 63.0	59.53	2.02	101	55.4 - 63.1
MCH	pg	18.27	0.56	101	17.2 - 19.4	18.82	0.57	101	17.9 - 20
MCHC	g/dL	30.86	0.84	101	29.3 - 33.1	31.70	0.86	101	29.7 - 33.5
RDW	%	11.79	0.49	101	10.8 - 12.8	11.00	0.38	101	10.3 - 11.7
ABRETi	10^9/L	204.96	40.19	101	104.7 - 289.5	200.71	39.78	101	111.9 - 294.4
PLT	K/uL	858.5	140.6	98	542 - 1150	914.2	150.8	99	629 - 1268
MPV	fL	8.56	1.11	98	6.7 - 10.8	8.32	1.07	99	6.9 - 10.3
WBC	K/uL	12.07	2.39	101	7.26 - 17.25	8.70	2.38	101	4.22 - 15.49
ABNEUT	K/uL	2.05	0.73	101	0.94 - 3.75	1.21	0.48	101	0.59 - 2.68
ABLYMP	K/uL	9.39	2.06	101	5.63 - 14.06	7.02	1.89	101	3.27 - 11.61
ABMONO	K/uL	0.35	0.15	101	0.11 - 0.75	0.23	0.13	101	0.06 - 0.70
ABSEOS	K/uL	0.11	0.04	101	0.04 - 0.19	0.10	0.04	101	0.04 - 0.20
ABBAS	K/uL	0.08	0.04	101	0.01 - 0.20	0.05	0.03	101	0.01 - 0.12

Ranges represent nonparametric 95% interval
Tests were performed using the Bayer Advia 120 analyzer

Rat (Sprague Dawley) Historical Data Coagulation									
Test	Units	Males				Females			
		Mean	SD	N	Range	Mean	SD	N	Range
PT	sec	14.77	0.92	86	13.1 - 16.3	15.03	1.20	85	13.0 - 17.4
FIB	mg/dL	363.3	44.7	86	285 - 468	298.9	46.6	85	212 - 428
APTT	sec	17.25	2.86	86	11.7 - 23.2	15.56	1.77	85	12.3 - 19.0

Ranges represent nonparametric 95% interval
Tests were performed using the Beckman Coulter ACL 10000 or ACL Elite Pro analyzer

Rat (Sprague Dawley) Historical Data Urinalysis									
Test	Units	Males				Females			
		Mean	SD	N	Range	Mean	SD	N	Range
SG		1.030	0.010	69	1.013 - 1.048	1.025	0.008	81	1.011 - 1.045
UpH		6.58	0.45	83	6.0 - 8.0	6.44	0.4	85	6.0 - 7.5
URO		0.20	0.00	83	0.2 - 0.2	0.20	0.00	85	0.2 - 0.2
TUVOL	mL	8.27	3.74	83	2.5 - 17	7.87	3.44	85	2.0 - 16

Ranges represent nonparametric 95% interval
Volume was manually measured.
Specific gravity was determined with a refractometer.
pH was determined using urinalysis test strips.

APPENDIX 21: INDIVIDUAL CLINICAL CHEMISTRY DATA

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 21: Individual Clinical Chemistry Data

Day Numbers Relative to Start Date

Specimen Disposition:

Day	Group	Sex	Animal	Comment
91	9	f	25359	Specimen Moderately Hemolyzed
	11	f	25382	Specimen Moderately Hemolyzed
119	1	m	25244	Specimen Moderately Hemolyzed
			25245	Specimen Moderately Hemolyzed

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 21 (continued): Individual Clinical Chemistry Data

Day 91 Relative to Start Date

Group	Sex	Animal	GLU mg/dL	BUN mg/dL	CRE2 mg/dL	NA+ mmol/L	K+ mmol/L	CL mmol/L	CA mg/dL	PHOS mg/dL	CHOL mg/dL	TRIG mg/dL
1	m	25234	127	12	0.3	149	6.2	106	11.3	9.7	78	95
		25235	118	13	0.4	149	6.0	103	11.9	8.2	102	105
		25236	123	13	0.4	149	5.8	103	11.8	8.5	89	119
		25237	117	10	0.3	148	6.1	104	11.2	7.7	86	88
		25238	134	13	0.3	148	6.7	104	11.4	8.8	79	71
		25239	125	15	0.5	149	5.6	103	11.9	7.3	85	66
		25240	127	15	0.5	149	5.9	105	11.6	8.3	76	68
		25241	133	8	0.3	148	6.3	104	11.6	8.5	89	112
		25242	139	13	0.4	147	5.6	103	11.3	8.7	112	78
		25243	132	13	0.3	148	6.2	103	11.8	9.3	113	59
2	m	25274	148	14	0.3	147	6.4	104	10.3	8.6	96	85
		25275	139	13	0.4	147	5.8	104	10.7	7.6	113	139
		25276	160	13	0.4	148	5.8	104	10.9	8.6	93	132
		25277	121	17	0.4	149	6.9	104	11.0	9.4	76	139
		25278	135	16	0.3	149	5.8	104	10.9	8.6	83	94
		25279	134	13	0.4	148	6.4	105	10.9	9.3	66	52
		25280	132	15	0.4	148	6.4	104	11.1	8.5	116	187
		25281	165	13	0.4	148	5.9	104	10.7	9.0	61	50
		25282	110	13	0.4	149	6.6	105	10.9	8.8	58	30
		25283	122	14	0.5	151	6.8	105	11.2	8.9	63	31
3	m	25284	119	11	0.3	147	5.9	104	10.6	7.9	92	118
		25285	144	13	0.4	148	6.2	103	10.3	8.3	70	39
		25286	142	12	0.3	148	5.9	105	11.1	8.3	77	84
		25287	109	14	0.3	149	6.3	104	10.1	8.0	75	66
		25288	131	12	0.4	147	6.3	104	10.5	8.6	82	86
		25289	135	10	0.5	148	6.7	104	11.2	10.0	80	97
		25290	114	15	0.4	150	6.5	104	10.6	9.4	83	68
		25291	120	14	0.4	150	6.4	104	10.6	8.7	51	48
		25292	111	12	0.4	148	6.3	103	10.6	8.2	102	61
		25293	120	11	0.5	150	5.7	103	11.4	8.6	77	56

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 21 (continued): Individual Clinical Chemistry Data

Day 91 Relative to Start Date

Group	Sex	Animal	GLU mg/dL	BUN mg/dL	CRE2 mg/dL	NA+ mmol/L	K+ mmol/L	CL mmol/L	CA mg/dL	PHOS mg/dL	CHOL mg/dL	TRIG mg/dL
4	m	25294	130	13	0.2	149	6.4	106	9.8	8.0	65	52
		25295	140	13	0.5	148	5.7	105	10.9	8.0	87	83
		25296	117	14	0.3	148	6.2	104	10.2	8.1	43	81
		25297	132	13	0.3	149	6.7	104	9.2	8.9	66	70
		25298	113	12	0.6	153	5.5	105	10.8	8.6	72	51
		25299	112	11	0.4	150	6.0	105	10.7	8.1	85	67
		25300	154	15	0.6	147	7.0	102	10.8	9.7	137	229
		25301	128	11	0.4	150	5.6	104	11.0	7.9	108	86
		25302	141	11	0.5	149	5.9	103	11.3	8.8	116	71
		25303	116	11	0.3	150	6.3	104	10.5	8.5	96	64
5	m	25304	128	12	0.6	148	5.6	105	10.9	7.9	71	94
		25305	126	12	0.4	148	5.4	103	11.4	8.3	83	95
		25306	115	11	0.3	150	5.9	105	10.8	7.9	65	82
		25307	156	13	0.4	147	6.0	104	11.2	9.7	93	102
		25308	118	11	0.4	149	5.9	103	11.6	8.4	86	71
		25309	130	12	0.4	148	6.6	105	11.2	9.6	76	39
		25310	126	11	0.4	149	5.9	103	11.3	8.0	84	59
		25311	113	11	0.2	148	6.4	104	10.7	9.3	93	110
		25312	140	9	0.3	147	5.9	103	11.6	8.7	100	101
		25313	153	12	0.4	147	5.5	106	11.0	8.7	86	55
6	m	25314	150	11	0.4	150	6.2	107	11.3	8.6	89	55
		25315	138	12	0.4	148	6.3	105	11.2	9.8	98	81
		25316	104	12	0.4	148	6.0	103	11.0	8.1	96	77
		25317	129	12	0.4	145	5.7	103	10.9	7.7	108	91
		25318	129	10	0.5	149	5.9	105	11.6	8.5	84	92
		25319	146	12	0.5	147	7.1	104	11.9	10.7	99	90
		25320	121	10	0.4	147	6.3	103	11.2	8.5	128	70
		25321	136	9	0.4	149	5.8	107	11.2	8.6	52	61
		25322	128	9	0.3	150	5.6	104	11.0	8.2	59	60
		25323	128	13	0.4	148	5.9	104	11.1	8.7	110	43

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 21 (continued): Individual Clinical Chemistry Data

Day 91 Relative to Start Date

Group	Sex	Animal	TPROT g/dL	ALB g/dL	GLOB g/dL	A/G ratio	AST U/L	ALTi U/L	ALPi U/L	TBILI mg/dL	GGT U/L	CK U/L
1	m	25234	6.6	3.1	3.5	0.9	125	59	77	0.2	5	730
		25235	7.4	3.4	4.0	0.9	95	53	101	0.2	5	209
		25236	7.1	3.4	3.7	0.9	99	45	83	0.2	5	225
		25237	6.9	3.1	3.8	0.8	120	41	61	0.2	6	486
		25238	6.8	3.1	3.7	0.8	83	47	80	0.2	3	160
		25239	7.3	3.4	3.9	0.9	82	32	89	0.1	4	151
		25240	6.9	3.2	3.7	0.9	173	48	121	0.1	5	714
		25241	7.3	3.4	3.9	0.9	123	50	62	0.2	5	467
		25242	7.0	3.3	3.7	0.9	102	36	79	0.2	4	371
		25243	7.4	3.4	4.0	0.9	152	51	106	0.2	4	655
2	m	25274	6.8	3.1	3.7	0.8	106	43	72	0.2	4	365
		25275	6.8	3.1	3.7	0.8	89	41	97	0.2	4	202
		25276	6.9	3.1	3.8	0.8	93	44	110	0.2	4	167
		25277	7.2	3.2	4.0	0.8	107	34	54	<0.1	5	417
		25278	7.5	3.4	4.1	0.8	118	33	88	0.2	5	420
		25279	6.6	3.0	3.6	0.8	85	28	91	<0.1	4	129
		25280	7.3	3.3	4.0	0.8	106	31	52	0.2	4	452
		25281	6.9	2.8	4.1	0.7	102	44	66	0.2	5	247
		25282	7.2	3.2	4.0	0.8	113	41	102	0.3	5	245
		25283	7.4	3.1	4.3	0.7	254	110	110	0.1	6	343
3	m	25284	7.0	3.4	3.6	0.9	116	42	78	0.2	4	495
		25285	7.2	3.3	3.9	0.8	93	36	108	0.2	5	142
		25286	7.2	3.3	3.9	0.8	178	40	60	0.2	4	808
		25287	7.0	3.2	3.8	0.8	114	48	71	0.2	4	311
		25288	7.0	3.4	3.6	0.9	155	42	88	0.2	4	586
		25289	7.0	3.2	3.8	0.8	87	56	102	0.1	4	164
		25290	7.1	3.1	4.0	0.8	148	35	93	0.2	4	619
		25291	7.2	3.3	3.9	0.8	137	39	103	0.2	4	593
		25292	7.1	3.3	3.8	0.9	89	31	80	0.2	5	226
		25293	7.2	3.2	4.0	0.8	81	31	84	0.2	4	116

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 21 (continued): Individual Clinical Chemistry Data

Day 91 Relative to Start Date

Group	Sex	Animal	TPROT g/dL	ALB g/dL	GLOB g/dL	A/G ratio	AST U/L	ALTi U/L	ALPi U/L	TBILI mg/dL	GGT U/L	CK U/L
4	m	25294	6.7	3.0	3.7	0.8	131	44	75	0.2	5	401
		25295	6.7	3.0	3.7	0.8	96	36	71	0.1	4	253
		25296	7.0	3.3	3.7	0.9	113	47	101	0.2	4	236
		25297	7.1	3.2	3.9	0.8	368	57	73	0.2	4	2026
		25298	7.1	3.4	3.7	0.9	85	33	68	<0.1	4	180
		25299	7.2	3.3	3.9	0.8	103	34	73	0.2	4	277
		25300	7.7	3.5	4.2	0.8	77	48	82	0.2	4	184
		25301	7.3	3.2	4.1	0.8	90	32	89	0.2	4	204
		25302	7.6	3.5	4.1	0.9	73	32	73	<0.1	4	147
		25303	7.0	3.2	3.8	0.8	129	35	77	0.3	4	521
5	m	25304	6.9	3.2	3.7	0.9	84	39	78	0.2	5	148
		25305	7.1	3.2	3.9	0.8	100	49	67	<0.1	5	282
		25306	6.8	3.2	3.6	0.9	76	35	90	0.2	5	179
		25307	6.7	3.2	3.5	0.9	135	53	83	0.2	5	383
		25308	7.3	3.2	4.1	0.8	162	39	81	<0.1	5	721
		25309	7.0	3.2	3.8	0.8	150	44	70	0.2	5	662
		25310	7.5	3.3	4.2	0.8	109	38	94	0.2	5	424
		25311	7.2	3.2	4.0	0.8	184	44	86	0.3	4	793
		25312	7.8	3.4	4.4	0.8	108	42	78	0.2	5	382
		25313	6.6	2.9	3.7	0.8	91	33	97	0.2	5	174
6	m	25314	6.8	3.1	3.7	0.8	106	49	76	0.2	5	154
		25315	6.4	3.1	3.3	0.9	117	42	82	0.1	6	183
		25316	6.6	3.0	3.6	0.8	137	70	96	0.2	5	200
		25317	6.8	3.2	3.6	0.9	111	42	62	0.2	5	310
		25318	6.6	3.2	3.4	0.9	85	34	91	0.2	5	185
		25319	6.8	3.2	3.6	0.9	159	46	107	0.2	5	512
		25320	6.9	3.3	3.6	0.9	161	42	84	0.2	4	689
		25321	6.7	3.2	3.5	0.9	89	32	122	0.2	6	142
		25322	7.0	3.2	3.8	0.8	100	40	73	0.2	4	209
		25323	6.9	3.1	3.8	0.8	132	30	84	0.1	5	531

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 21 (continued): Individual Clinical Chemistry Data

Day 91 Relative to Start Date

Group	Sex	Animal	GLU mg/dL	BUN mg/dL	CRE2 mg/dL	NA+ mmol/L	K+ mmol/L	CL mmol/L	CA mg/dL	PHOS mg/dL	CHOL mg/dL	TRIG mg/dL
1	f	25254	96	15	0.6	148	5.8	104	11.9	6.7	85	46
		25255	112	15	0.6	147	5.6	103	11.8	6.9	106	43
		25256	107	17	0.6	148	5.3	105	11.4	6.3	116	55
		25257	99	17	0.6	146	5.4	101	12.1	8.0	94	75
		25258	124	12	0.5	146	5.2	102	11.5	8.9	121	47
		25259	109	12	0.5	148	5.6	104	10.1	7.5	82	38
		25260	127	12	0.5	147	5.9	105	12.1	6.6	119	49
		25261	115	12	0.5	148	5.9	103	11.3	7.8	123	46
		25262	135	14	0.6	150	5.3	104	11.3	8.1	102	46
		25263	116	12	0.6	148	5.2	103	12.2	7.7	76	35
7	f	25334	109	12	0.6	146	5.8	101	12.0	6.1	179	75
		25335	117	13	0.4	144	5.6	102	10.7	6.7	124	42
		25336	110	13	0.5	146	4.9	99	11.6	7.3	132	100
		25337	105	12	0.5	149	5.7	105	10.9	7.2	81	32
		25338	102	17	0.6	148	6.4	103	11.3	7.7	100	37
		25339	127	13	0.6	149	4.9	104	11.0	7.8	66	46
		25340	113	13	0.6	146	5.9	101	11.2	8.0	118	36
		25341	107	14	0.6	148	6.0	104	11.5	7.3	109	49
		25342	108	17	0.6	148	5.7	102	11.7	8.2	113	29
		25343	134	13	0.7	146	5.1	101	10.7	6.8	93	38
8	f	25344	115	14	0.6	147	5.5	102	10.6	5.5	83	33
		25345	105	17	0.5	148	6.5	105	10.4	7.3	77	33
		25346	121	17	0.4	146	5.4	103	10.7	6.8	91	37
		25347	126	14	0.5	147	5.0	104	11.7	7.5	100	38
		25348	96	16	0.6	147	6.0	102	12.0	9.1	128	40
		25349	102	12	0.5	148	5.7	103	12.0	7.7	69	53
		25350	101	15	0.6	146	5.7	103	11.7	7.6	94	27
		25351	103	12	0.5	147	6.4	104	11.9	10.6	114	27
		25352	94	13	0.5	148	6.5	104	12.0	7.9	120	29
		25353	117	12	0.5	146	5.6	103	11.9	8.0	96	33

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 21 (continued): Individual Clinical Chemistry Data

Day 91 Relative to Start Date

Group	Sex	Animal	GLU mg/dL	BUN mg/dL	CRE2 mg/dL	NA+ mmol/L	K+ mmol/L	CL mmol/L	CA mg/dL	PHOS mg/dL	CHOL mg/dL	TRIG mg/dL
9	f	25354	146	14	0.6	145	4.9	100	11.2	6.2	144	86
		25355	106	13	0.6	148	5.2	102	11.0	7.2	89	38
		25356	100	13	0.5	147	4.6	102	11.5	6.9	107	38
		25357	120	12	0.3	145	6.2	103	12.1	8.4	122	29
		25358	101	14	0.5	147	5.6	103	12.5	7.8	159	37
		25359	108	14	0.4	146	6.2	102	11.4	9.5	109	40
		25360	124	18	0.7	146	5.8	101	12.2	8.1	106	42
		25361	105	15	0.5	147	5.0	103	11.1	7.4	98	30
		25362	113	11	0.5	149	5.5	104	11.9	7.7	64	39
		25363	104	13	0.5	149	5.7	103	11.1	8.0	89	25
10	f	25364	112	14	0.4	150	6.4	102	11.2	7.3	97	37
		25365	137	13	0.7	147	4.7	102	11.5	7.1	86	40
		25366	102	12	0.5	147	5.7	105	10.6	8.6	105	40
		25367	123	11	0.6	146	6.2	104	11.8	8.6	79	42
		25368	113	14	0.4	147	6.4	103	11.7	7.9	116	52
		25369	137	12	0.4	149	6.1	105	10.9	8.8	114	60
		25370	104	13	0.6	146	6.3	101	12.4	7.5	143	57
		25371	122	13	0.5	147	6.2	104	12.0	8.4	120	52
		25372	106	16	0.5	148	5.9	101	12.1	7.4	133	32
		25373	113	14	0.6	147	5.5	103	12.4	7.9	120	38
11	f	25374	127	16	0.6	147	5.3	102	11.4	6.4	130	35
		25375	118	12	0.6	146	5.9	102	11.9	8.0	131	41
		25376	112	13	0.6	147	5.3	103	11.7	7.5	93	33
		25377	97	19	0.6	147	5.8	103	11.8	8.3	128	27
		25378	112	13	0.6	147	5.7	101	11.1	8.2	105	39
		25379	106	16	0.5	146	6.6	102	11.9	9.5	117	32
		25380	100	10	0.5	147	5.6	102	12.2	7.5	119	57
		25381	118	10	0.5	146	5.4	100	12.2	7.3	108	27
		25382	131	14	0.2	144	6.4	104	11.3	9.5	87	54
		25383	124	10	0.0	145	6.2	104	11.4	8.5	83	34

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 21 (continued): Individual Clinical Chemistry Data

Day 91 Relative to Start Date

Group	Sex	Animal	TPROT g/dL	ALB g/dL	GLOB g/dL	A/G ratio	AST U/L	ALTi U/L	ALPi U/L	TBILI mg/dL	GGT U/L	CK U/L
1	f	25254	8.3	4.1	4.2	1.0	84	30	52	0.2	4	122
		25255	8.5	4.5	4.0	1.1	74	25	60	0.2	4	157
		25256	8.1	3.8	4.3	0.9	165	47	37	0.2	5	195
		25257	8.9	4.5	4.4	1.0	125	37	42	0.3	4	164
		25258	8.3	4.3	4.0	1.1	138	30	45	0.2	5	580
		25259	7.2	3.4	3.8	0.9	83	31	60	0.2	5	141
		25260	8.0	4.2	3.8	1.1	87	24	57	0.1	5	209
		25261	8.0	4.0	4.0	1.0	169	70	33	0.3	4	232
		25262	8.2	4.2	4.0	1.1	76	25	64	0.2	4	151
		25263	8.3	4.2	4.1	1.0	82	26	36	0.2	5	113
7	f	25334	9.3	4.5	4.8	0.9	320	116	58	0.2	5	327
		25335	8.1	4.1	4.0	1.0	198	67	34	0.2	5	628
		25336	9.0	4.7	4.3	1.1	105	36	39	0.2	4	240
		25337	7.8	4.0	3.8	1.1	145	66	31	0.2	5	235
		25338	8.0	4.1	3.9	1.1	112	58	40	0.2	5	198
		25339	7.7	3.8	3.9	1.0	91	31	52	0.2	5	125
		25340	8.2	4.0	4.2	1.0	351	142	75	0.3	5	197
		25341	7.9	3.9	4.0	1.0	352	360	33	0.2	5	134
		25342	8.1	4.2	3.9	1.1	88	28	30	0.2	4	129
		25343	8.0	4.1	3.9	1.1	104	40	41	0.7	5	260
8	f	25344	8.1	4.0	4.1	1.0	118	59	57	0.2	4	110
		25345	7.7	3.6	4.1	0.9	93	28	43	0.1	4	253
		25346	8.7	4.4	4.3	1.0	245	46	32	0.2	4	768
		25347	8.2	4.2	4.0	1.1	101	38	31	0.1	3	142
		25348	7.8	3.6	4.2	0.9	138	50	38	0.2	4	164
		25349	7.8	4.2	3.6	1.2	75	33	34	0.1	3	161
		25350	8.0	4.1	3.9	1.1	74	25	28	0.1	3	130
		25351	7.5	3.7	3.8	1.0	107	34	70	0.2	3	305
		25352	8.1	4.2	3.9	1.1	67	28	31	0.1	4	115
		25353	7.8	3.9	3.9	1.0	91	39	36	0.1	3	158

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 21 (continued): Individual Clinical Chemistry Data

Day 91 Relative to Start Date

Group	Sex	Animal	TPROT g/dL	ALB g/dL	GLOB g/dL	A/G ratio	AST U/L	ALTi U/L	ALPi U/L	TBILI mg/dL	GGT U/L	CK U/L
9	f	25354	8.9	4.5	4.4	1.0	711	337	34	0.2	5	219
		25355	8.6	4.5	4.1	1.1	135	63	47	0.2	4	186
		25356	7.7	3.7	4.0	0.9	80	29	55	0.2	4	120
		25357	8.9	4.4	4.5	1.0	108	60	60	0.2	3	178
		25358	8.6	4.4	4.2	1.0	277	90	32	0.2	3	130
		25359	7.5	3.8	3.7	1.0	149	50	46	0.3	4	363
		25360	9.0	4.7	4.3	1.1	294	128	27	0.2	4	207
		25361	7.4	3.5	3.9	0.9	83	31	38	0.2	5	106
		25362	8.1	4.2	3.9	1.1	72	24	41	0.2	4	177
		25363	7.6	3.7	3.9	0.9	82	37	36	0.2	4	187
10	f	25364	8.9	4.5	4.4	1.0	103	22	40	0.2	4	273
		25365	8.7	4.5	4.2	1.1	106	31	41	0.2	4	278
		25366	7.6	3.5	4.1	0.9	199	29	46	0.3	4	1028
		25367	7.8	3.9	3.9	1.0	90	27	46	0.2	5	161
		25368	8.4	4.0	4.4	0.9	139	51	35	0.3	4	191
		25369	8.3	4.2	4.1	1.0	399	56	30	0.2	5	1193
		25370	9.7	4.9	4.8	1.0	526	306	62	0.2	4	163
		25371	8.1	4.1	4.0	1.0	119	46	27	0.1	3	123
		25372	9.0	4.6	4.4	1.0	216	98	37	0.2	4	129
		25373	8.2	4.1	4.1	1.0	134	50	31	0.2	4	105
11	f	25374	8.8	4.6	4.2	1.1	93	41	45	0.2	4	149
		25375	7.9	4.1	3.8	1.1	154	93	36	0.1	5	215
		25376	7.9	4.0	3.9	1.0	94	39	37	0.2	3	183
		25377	8.1	4.1	4.0	1.0	90	37	79	0.2	4	202
		25378	7.6	3.6	4.0	0.9	155	61	57	0.2	6	195
		25379	8.2	3.9	4.3	0.9	297	174	41	0.2	5	177
		25380	8.3	4.4	3.9	1.1	82	33	31	0.2	6	176
		25381	9.0	4.9	4.1	1.2	242	104	30	0.3	4	112
		25382	7.5	3.8	3.7	1.0	577	58	43	<0.1	5	5143
		25383	7.3	3.6	3.7	1.0	234	43	51	0.2	6	1601

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 21 (continued): Individual Clinical Chemistry Data

Day 119 Relative to Start Date

Group	Sex	Animal	GLU mg/dL	BUN mg/dL	CRE2 mg/dL	NA+ mmol/L	K+ mmol/L	CL mmol/L	CA mg/dL	PHOS mg/dL	CHOL mg/dL	TRIG mg/dL
1	m	25244	107	15	0.5	146	7.0	104	11.0	8.6	111	54
		25245	111	15	0.5	146	6.2	103	10.8	8.9	111	107
		25246	115	12	0.4	148	6.4	103	10.9	8.2	84	120
		25247	108	12	0.5	147	6.1	104	10.8	8.4	89	53
		25248	108	12	0.6	150	5.7	106	10.7	8.5	95	53
		25249	103	12	0.5	149	5.6	104	11.3	8.1	92	199
		25250	104	14	0.4	147	6.6	104	10.7	8.1	110	68
		25251	121	12	0.5	147	6.2	101	11.1	8.4	131	375
		25252	129	11	0.5	147	5.5	104	10.9	7.9	61	119
		25253	111	12	0.4	148	5.7	104	10.8	8.3	106	75
6	m	25324	104	12	0.6	147	7.0	104	11.3	9.0	99	108
		25325	120	13	0.5	148	6.9	104	11.5	10.5	88	108
		25326	90	12	0.5	147	6.6	105	10.9	8.9	99	72
		25327	104	10	0.6	149	6.2	105	10.6	7.2	84	110
		25328	118	12	0.5	149	5.4	102	11.5	9.0	109	68
		25329	116	11	0.5	149	5.7	104	11.2	8.4	99	87
		25330	121	11	0.5	148	6.3	104	11.5	8.6	100	92
		25331	116	10	0.5	148	5.8	104	11.1	7.7	100	154
		25332	114	13	0.5	148	6.3	104	11.1	8.6	74	58
		25333	109	13	0.4	148	5.9	104	11.0	7.4	117	85

Target Dose: Group 1 - 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 21 (continued): Individual Clinical Chemistry Data

Day 119 Relative to Start Date

Group	Sex	Animal	TPROT g/dL	ALB g/dL	GLOB g/dL	A/G ratio	AST U/L	ALTi U/L	ALPi U/L	TBILI mg/dL	GGT U/L	CK U/L
1	m	25244	7.3	3.1	4.2	0.7	125	47	138	0.2	5	244
		25245	7.3	3.3	4.0	0.8	113	71	130	0.2	4	214
		25246	7.3	3.3	4.0	0.8	88	38	93	0.2	4	306
		25247	6.8	3.1	3.7	0.8	97	43	85	<0.1	4	212
		25248	6.7	3.2	3.5	0.9	88	34	68	<0.1	4	146
		25249	6.8	3.2	3.6	0.9	80	33	88	0.1	4	128
		25250	6.6	3.0	3.6	0.8	99	42	73	0.2	4	214
		25251	7.2	3.3	3.9	0.8	89	32	54	0.1	3	160
		25252	6.6	2.9	3.7	0.8	81	38	105	<0.1	5	181
		25253	6.5	3.0	3.5	0.9	82	32	66	0.2	3	158
6	m	25324	7.2	3.1	4.1	0.8	109	42	132	0.3	3	258
		25325	6.9	3.2	3.7	0.9	138	38	80	0.2	5	671
		25326	6.7	3.1	3.6	0.9	140	41	78	0.2	4	533
		25327	6.5	2.9	3.6	0.8	90	39	75	0.1	4	179
		25328	7.1	3.2	3.9	0.8	151	44	84	0.2	4	306
		25329	6.9	3.1	3.8	0.8	81	29	55	<0.1	4	160
		25330	7.3	3.2	4.1	0.8	102	37	99	0.2	4	174
		25331	6.7	3.1	3.6	0.9	88	37	92	<0.1	4	143
		25332	6.8	3.0	3.8	0.8	157	36	103	<0.1	4	627
		25333	6.8	3.0	3.8	0.8	84	31	83	0.2	4	140

Target Dose: Group 1 - 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 21 (continued): Individual Clinical Chemistry Data

Day 119 Relative to Start Date

Group	Sex	Animal	GLU mg/dL	BUN mg/dL	CRE2 mg/dL	NA+ mmol/L	K+ mmol/L	CL mmol/L	CA mg/dL	PHOS mg/dL	CHOL mg/dL	TRIG mg/dL
1	f	25264	113	17	0.7	143	5.2	101	11.3	6.4	122	61
		25265	104	16	0.7	147	6.1	103	11.7	6.3	155	70
		25266	88	17	0.3	141	6.8	101	10.7	7.1	76	69
		25267	117	15	0.7	147	6.1	104	11.6	7.1	105	34
		25268	93	14	0.6	144	5.6	102	12.0	7.2	180	61
		25269	95	17	0.7	147	6.2	104	12.1	8.2	133	49
		25270	100	16	0.7	145	5.0	104	11.4	8.0	70	43
		25271	108	16	0.6	143	5.4	101	11.7	7.2	150	54
		25272	107	12	0.6	146	5.7	102	11.9	7.8	154	56
		25273	129	13	0.3	143	6.6	103	11.7	9.0	84	63
11	f	25384	132	13	0.7	145	6.2	103	12.4	6.3	136	94
		25385	114	13	0.7	144	7.1	103	11.7	7.4	141	87
		25386	101	15	0.6	145	5.7	102	12.1	7.0	160	85
		25387	96	18	0.6	143	6.5	103	11.2	9.4	109	39
		25388	97	11	0.6	145	6.2	102	11.6	7.8	128	40
		25389	95	13	0.6	145	5.9	103	11.7	8.0	88	59
		25390	131	15	0.3	145	6.5	103	11.3	9.1	100	62
		25391	94	14	0.4	144	7.6	104	10.8	10.0	109	53
		25392	95	12	0.3	144	6.9	104	11.5	8.9	99	44
		25393	97	15	0.3	144	6.6	103	12.0	9.6	117	80

Target Dose: Group 1 - 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 21 (continued): Individual Clinical Chemistry Data

Day 119 Relative to Start Date

Group	Sex	Animal	TPROT g/dL	ALB g/dL	GLOB g/dL	A/G ratio	AST U/L	ALTi U/L	ALPi U/L	TBILI mg/dL	GGT U/L	CK U/L
1	f	25264	8.2	4.3	3.9	1.1	499	201	53	0.2	4	229
		25265	8.6	4.8	3.8	1.3	470	99	51	0.2	4	346
		25266	8.5	4.4	4.1	1.1	304	47	41	<0.1	4	1563
		25267	8.2	4.1	4.1	1.0	119	45	60	0.1	4	206
		25268	8.9	4.3	4.6	0.9	841	397	54	0.3	4	444
		25269	9.3	4.6	4.7	1.0	493	264	37	0.3	4	288
		25270	7.4	3.9	3.5	1.1	127	87	58	0.2	3	193
		25271	8.6	4.3	4.3	1.0	117	53	45	0.1	2	184
		25272	8.8	4.5	4.3	1.0	188	104	44	0.2	3	219
		25273	7.5	3.9	3.6	1.1	194	57	51	0.2	3	707
11	f	25384	9.0	4.7	4.3	1.1	115	45	55	0.2	3	270
		25385	8.5	4.4	4.1	1.1	280	130	39	0.2	4	340
		25386	8.8	4.6	4.2	1.1	147	42	45	0.1	4	545
		25387	7.6	3.8	3.8	1.0	325	54	36	0.2	3	501
		25388	8.2	4.0	4.2	1.0	472	134	60	0.2	4	387
		25389	8.1	4.1	4.0	1.0	468	279	53	0.3	5	326
		25390	8.1	4.1	4.0	1.0	252	37	45	0.2	4	1628
		25391	7.5	3.6	3.9	0.9	303	53	46	0.2	4	1696
		25392	7.2	3.4	3.8	0.9	238	117	38	0.2	4	612
		25393	8.1	4.1	4.0	1.0	292	131	40	0.2	4	801

Target Dose: Group 1 - 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

APPENDIX 22: INDIVIDUAL HEMATOLOGY DATA

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 22: Individual Hematology Data

Day Numbers Relative to Start Date

Specimen Disposition:

Day	Group	Sex	Animal	Comment
91	4	m	25297	Sample Clotted
	5	m	25311	Sample Clotted

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 22 (continued): Individual Hematology Data

Day 91 Relative to Start Date

Group	Sex	Animal	RBC M/µL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RDW %	RET %	ABRETi 10^9/L
1	m	25234	8.29	14.5	46.0	55.5	17.5	31.4	15.2	3.4	280.3
		25235	8.93	15.5	50.6	56.7	17.3	30.5	14.5	2.8	249.3
		25236	9.31	15.7	50.7	54.5	16.8	30.9	13.8	2.0	183.0
		25237	8.49	13.9	44.3	52.1	16.4	31.4	16.9	2.7	231.3
		25238	9.30	14.7	47.5	51.0	15.8	31.1	13.9	2.0	182.7
		25239	9.28	14.8	48.8	52.6	16.0	30.4	16.4	2.1	195.8
		25240	8.92	15.1	48.6	54.5	16.9	31.0	12.9	1.7	150.1
		25241	8.89	15.0	47.1	53.0	16.8	31.8	16.1	2.7	237.4
		25242	9.50	16.0	50.9	53.5	16.8	31.4	13.5	1.9	181.5
		25243	8.96	15.5	49.6	55.4	17.3	31.2	13.8	2.5	227.9
2	m	25274	8.59	14.2	45.8	53.4	16.5	31.0	14.9	3.4	290.4
		25275	8.74	14.6	47.7	54.6	16.7	30.7	15.2	2.4	207.1
		25276	9.05	15.5	51.2	56.6	17.1	30.3	13.6	2.0	181.2
		25277	8.91	15.3	48.4	54.3	17.2	31.7	13.7	2.0	181.6
		25278	8.99	14.4	47.8	53.2	16.0	30.2	14.5	2.5	227.8
		25279	8.78	14.5	46.7	53.2	16.5	30.9	14.4	1.8	160.3
		25280	8.66	15.6	50.1	57.8	18.0	31.0	12.6	1.9	163.7
		25281	8.90	14.2	45.3	50.9	15.9	31.2	13.8	2.2	193.9
		25282	9.17	15.1	49.6	54.0	16.5	30.5	13.0	1.8	166.6
		25283	10.78	15.8	52.9	49.1	14.7	30.0	14.0	2.2	232.1
3	m	25284	8.26	14.2	44.1	53.4	17.1	32.1	15.6	2.5	205.4
		25285	8.75	15.3	49.1	56.1	17.5	31.1	13.6	1.8	161.1
		25286	9.00	15.1	48.8	54.2	16.8	31.0	13.7	2.1	187.9
		25287	9.29	16.2	50.9	54.8	17.5	31.9	13.5	1.6	148.7
		25288	9.13	15.3	48.7	53.4	16.7	31.3	13.6	2.5	228.7
		25289	9.05	15.0	48.5	53.6	16.6	30.9	14.4	2.1	187.3
		25290	9.78	15.9	52.5	53.6	16.3	30.3	13.8	2.0	197.0
		25291	9.22	16.2	52.2	56.6	17.5	31.0	13.3	1.4	125.1
		25292	8.95	14.9	46.9	52.4	16.6	31.7	15.2	2.0	176.9
		25293	8.78	14.5	46.4	52.8	16.5	31.2	14.7	1.9	169.4

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 22 (continued): Individual Hematology Data

Day 91 Relative to Start Date

Group	Sex	Animal	RBC M/µL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RDW %	RET %	ABRETi 10^9/L
4	m	25294	8.78	14.8	47.6	54.2	16.9	31.1	13.4	1.8	156.2
		25295	8.48	14.9	47.3	55.8	17.6	31.6	13.1	2.0	172.5
		25296	9.32	15.0	49.1	52.7	16.1	30.5	16.2	2.6	242.9
		25298	9.07	15.3	49.2	54.3	16.9	31.1	13.6	2.1	187.0
		25299	8.51	15.1	48.4	56.9	17.8	31.2	13.9	2.2	185.0
		25300	9.17	15.6	50.5	55.1	17.0	30.9	13.3	2.3	210.3
		25301	8.37	14.2	45.0	53.7	16.9	31.5	14.2	2.2	182.1
		25302	9.61	15.9	51.4	53.5	16.5	30.9	14.4	1.8	175.1
		25303	9.18	15.3	49.1	53.5	16.7	31.2	15.7	2.5	228.6
5	m	25304	8.92	15.1	48.2	54.0	16.9	31.3	12.6	1.9	168.0
		25305	9.04	15.4	48.8	54.0	17.0	31.5	12.8	1.8	160.1
		25306	8.57	15.0	47.9	55.9	17.5	31.4	14.0	2.6	219.1
		25307	8.41	13.9	45.0	53.6	16.6	31.0	15.6	2.4	200.2
		25308	8.66	14.7	48.3	55.8	17.0	30.5	13.5	2.1	180.1
		25309	8.87	15.0	47.8	53.9	16.9	31.4	14.1	2.0	176.0
		25310	9.30	14.3	46.2	49.7	15.4	30.9	15.9	2.2	202.4
		25312	8.89	15.1	48.3	54.4	17.0	31.2	13.9	2.2	197.5
		25313	8.33	13.4	42.8	51.4	16.1	31.2	14.0	2.2	186.6
6	m	25314	8.60	14.5	47.1	54.7	16.9	30.9	12.5	1.5	132.1
		25315	8.45	14.5	46.4	54.9	17.2	31.3	13.7	1.8	153.4
		25316	8.37	14.1	46.1	55.1	16.9	30.6	15.6	2.6	217.7
		25317	8.04	13.2	43.1	53.5	16.4	30.7	14.1	3.1	252.6
		25318	8.35	14.9	48.7	58.3	17.8	30.6	14.1	2.1	173.1
		25319	8.65	15.3	49.9	57.7	17.6	30.6	13.2	2.7	235.4
		25320	8.95	15.1	49.1	54.8	16.9	30.7	12.8	1.8	164.4
		25321	8.76	15.0	48.1	54.9	17.2	31.3	14.3	2.3	205.0
		25322	9.03	15.0	47.8	52.9	16.6	31.3	14.5	2.6	234.2
		25323	9.26	15.4	49.8	53.9	16.6	30.8	14.1	1.5	134.6

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 22 (continued): Individual Hematology Data

Day 91 Relative to Start Date

Group	Sex	Animal	PLT K/µL	MPV fL	WBC K/µL	ABNEUT K/µL	ABLYMP K/µL	ABMONO K/µL	ABSEOS K/µL	ABBAS K/µL
1	m	25234	309	9.4	11.22	2.18	8.35	0.41	0.11	0.07
		25235	557	8.5	13.36	3.23	9.32	0.53	0.12	0.07
		25236	905	7.8	13.78	1.79	11.21	0.45	0.11	0.08
		25237	PClump	PClump	11.53	2.12	8.73	0.37	0.14	0.04
		25238	526	7.3	10.49	1.98	8.07	0.21	0.16	0.02
		25239	647	7.5	10.82	4.48	5.84	0.28	0.13	0.03
		25240	896	6.8	13.21	4.25	7.82	0.90	0.08	0.11
		25241	639	8.2	16.87	3.48	12.39	0.66	0.12	0.13
		25242	757	6.6	14.53	3.50	9.66	0.95	0.16	0.12
		25243	599	7.6	11.58	2.27	8.60	0.41	0.19	0.07
2	m	25274	815	7.8	11.71	2.34	8.79	0.36	0.07	0.07
		25275	946	8.0	13.45	1.93	10.82	0.35	0.17	0.09
		25276	837	7.5	13.56	2.79	10.13	0.35	0.12	0.07
		25277	851	8.1	12.14	2.57	9.18	0.20	0.09	0.05
		25278	677	7.6	12.18	1.50	10.06	0.37	0.11	0.05
		25279	773	8.1	11.78	1.75	9.60	0.23	0.07	0.05
		25280	611	7.8	12.49	1.73	10.16	0.32	0.13	0.07
		25281	909	7.8	16.23	1.71	13.58	0.66	0.09	0.09
		25282	947	7.5	14.27	2.85	10.83	0.38	0.08	0.07
		25283	821	7.6	12.98	2.24	10.21	0.32	0.07	0.07
3	m	25284	747	8.7	8.31	2.11	5.59	0.37	0.13	0.04
		25285	629	7.9	12.66	1.71	10.57	0.15	0.09	0.07
		25286	831	7.6	13.65	3.84	9.07	0.42	0.15	0.07
		25287	690	8.3	13.71	1.64	11.04	0.75	0.12	0.09
		25288	994	6.9	12.76	2.06	10.22	0.25	0.09	0.05
		25289	1025	8.1	11.73	1.34	9.88	0.27	0.09	0.06
		25290	702	8.0	13.59	2.53	10.40	0.38	0.14	0.07
		25291	620	7.2	10.23	3.00	6.75	0.20	0.21	0.04
		25292	1007	7.5	11.43	1.84	9.11	0.25	0.10	0.06
		25293	789	7.4	11.63	2.38	8.72	0.29	0.12	0.04

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 22 (continued): Individual Hematology Data

Day 91 Relative to Start Date

Group	Sex	Animal	PLT K/µL	MPV fL	WBC K/µL	ABNEUT K/µL	ABLYMP K/µL	ABMONO K/µL	ABSEOS K/µL	ABBAS K/µL
4	m	25294	764	8.3	11.61	1.88	9.11	0.37	0.13	0.05
		25295	796	7.6	10.71	2.26	7.89	0.31	0.15	0.05
		25296	838	8.8	10.99	1.72	8.76	0.35	0.06	0.04
		25298	527	8.8	12.28	2.74	9.16	0.19	0.09	0.06
		25299	702	8.4	12.89	2.40	9.93	0.35	0.09	0.07
		25300	948	8.2	10.63	1.40	8.62	0.36	0.11	0.04
		25301	752	7.6	9.00	2.14	6.50	0.23	0.05	0.03
		25302	675	7.9	12.61	2.80	9.01	0.56	0.10	0.07
		25303	550	7.4	17.53	3.40	13.14	0.65	0.11	0.11
5	m	25304	871	8.1	9.66	1.80	7.17	0.45	0.15	0.02
		25305	418	8.2	12.23	2.13	9.49	0.39	0.09	0.06
		25306	704	7.7	9.02	3.23	5.36	0.28	0.08	0.03
		25307	739	7.6	11.30	1.87	8.94	0.28	0.10	0.04
		25308	687	8.5	10.93	2.89	7.59	0.32	0.06	0.04
		25309	615	8.4	14.82	3.24	10.48	0.70	0.09	0.09
		25310	823	7.8	12.93	2.68	9.65	0.31	0.16	0.06
		25312	923	7.6	22.68	8.24	12.89	1.01	0.25	0.14
		25313	1065	8.4	16.44	2.48	13.12	0.42	0.17	0.14
6	m	25314	938	7.6	13.32	2.92	9.78	0.40	0.10	0.06
		25315	913	8.0	11.61	2.57	8.44	0.36	0.14	0.05
		25316	766	8.0	13.16	3.23	9.37	0.39	0.06	0.04
		25317	968	7.9	13.14	4.54	7.86	0.42	0.17	0.06
		25318	956	7.7	13.68	3.24	9.85	0.35	0.07	0.06
		25319	725	7.8	12.72	2.99	9.03	0.48	0.08	0.06
		25320	720	8.2	11.57	4.47	6.46	0.45	0.07	0.03
		25321	837	7.9	11.92	2.84	8.56	0.34	0.06	0.05
		25322	608	7.9	10.30	2.01	7.70	0.40	0.09	0.04
		25323	847	8.1	19.67	1.78	17.26	0.31	0.08	0.12

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 22 (continued): Individual Hematology Data

Day 91 Relative to Start Date

Group	Sex	Animal	RBC M/µL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RDW %	RET %	ABRETi 10^9/L
1	f	25254	7.82	14.2	45.0	57.5	18.2	31.6	11.7	1.5	120.6
		25255	8.42	15.2	47.7	56.6	18.0	31.8	11.7	2.3	189.4
		25256	7.63	13.5	42.9	56.2	17.7	31.4	13.0	2.3	174.8
		25257	8.42	14.6	46.2	54.8	17.4	31.7	11.4	1.3	108.3
		25258	8.52	14.6	47.3	55.5	17.2	31.0	11.7	1.6	139.0
		25259	8.64	15.2	48.6	56.3	17.6	31.3	11.9	2.7	231.0
		25260	7.82	14.6	45.8	58.5	18.7	31.9	12.5	3.3	261.0
		25261	8.21	14.5	46.5	56.6	17.6	31.2	11.6	2.2	179.6
		25262	7.94	14.6	46.5	58.5	18.4	31.5	11.8	1.9	147.1
		25263	7.35	13.7	42.3	57.6	18.7	32.4	12.4	2.1	150.7
7	f	25334	7.90	14.7	46.9	59.4	18.6	31.4	12.5	1.5	120.0
		25335	8.23	15.0	46.8	56.8	18.2	32.0	12.1	2.4	193.6
		25336	7.54	14.0	43.2	57.2	18.6	32.5	12.4	2.4	179.5
		25337	7.77	14.0	43.5	56.0	18.0	32.1	11.8	1.4	110.5
		25338	8.13	14.8	46.3	57.0	18.3	32.0	11.6	1.4	116.3
		25339	8.37	15.2	48.0	57.4	18.2	31.8	11.9	2.1	172.3
		25340	8.97	15.6	48.6	54.2	17.3	32.0	11.5	1.9	166.5
		25341	8.57	14.9	48.2	56.3	17.4	30.9	12.0	1.7	142.5
		25342	8.23	15.0	47.7	57.9	18.2	31.5	11.9	2.4	194.4
		25343	8.44	15.2	47.3	56.0	18.0	32.1	12.1	2.4	198.8
8	f	25344	8.14	14.9	47.1	57.8	18.3	31.7	12.3	1.7	141.7
		25345	7.92	14.0	43.9	55.4	17.6	31.8	11.4	1.9	149.3
		25346	7.79	14.6	45.9	58.9	18.8	31.8	11.6	1.5	119.4
		25347	7.92	13.8	42.9	54.1	17.4	32.2	12.2	1.9	151.0
		25348	9.21	16.3	52.6	57.1	17.7	31.0	11.8	1.8	161.5
		25349	7.80	13.9	43.9	56.3	17.8	31.6	12.3	2.1	164.0
		25350	7.82	14.9	46.4	59.4	19.0	32.0	11.3	1.1	87.1
		25351	7.84	14.6	45.3	57.9	18.6	32.1	11.9	2.4	188.4
		25352	8.62	14.8	46.8	54.3	17.1	31.6	11.5	1.1	93.2
		25353	8.12	14.1	44.1	54.3	17.4	32.0	11.7	1.6	130.0

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 22 (continued): Individual Hematology Data

Day 91 Relative to Start Date

Group	Sex	Animal	RBC M/µL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RDW %	RET %	ABRETi 10^9/L
9	f	25354	7.86	14.5	45.2	57.6	18.4	31.9	12.4	1.9	149.7
		25355	8.94	15.3	48.6	54.3	17.2	31.6	11.9	1.8	161.4
		25356	8.34	15.0	48.0	57.6	18.0	31.3	11.9	2.3	193.6
		25357	8.11	14.4	45.9	56.6	17.7	31.3	12.0	2.0	163.6
		25358	7.73	13.6	43.5	56.3	17.6	31.2	12.0	1.9	143.8
		25359	8.21	14.0	44.5	54.2	17.0	31.4	12.3	1.5	126.8
		25360	7.59	14.2	44.4	58.5	18.7	31.9	11.3	1.7	128.5
		25361	8.34	14.4	45.1	54.1	17.3	31.9	11.5	1.5	121.5
		25362	8.71	15.1	48.6	55.7	17.4	31.2	11.2	1.9	168.4
		25363	8.06	14.4	44.8	55.5	17.9	32.2	11.9	1.6	126.5
10	f	25364	8.13	14.9	47.0	57.7	18.3	31.7	12.4	3.0	241.9
		25365	8.20	14.8	47.0	57.4	18.1	31.5	12.8	2.4	196.1
		25366	8.32	14.8	47.5	57.1	17.7	31.0	12.3	3.6	296.5
		25367	8.83	15.9	50.3	56.9	18.0	31.6	11.4	1.6	145.1
		25368	8.74	15.2	48.4	55.4	17.4	31.4	12.0	2.1	185.4
		25369	7.55	14.1	44.1	58.4	18.7	32.0	11.8	1.6	118.4
		25370	8.71	14.8	47.7	54.8	17.0	31.1	11.8	1.4	120.9
		25371	7.64	13.9	44.5	58.2	18.1	31.2	11.7	2.1	162.3
		25372	8.01	13.8	44.0	55.0	17.3	31.4	11.3	1.8	146.2
		25373	8.83	15.0	48.1	54.4	16.9	31.1	11.7	1.2	107.3
11	f	25374	7.62	14.1	44.6	58.5	18.5	31.6	11.9	1.9	143.7
		25375	8.09	15.0	47.1	58.2	18.5	31.8	11.8	2.5	198.7
		25376	7.74	13.7	42.9	55.5	17.7	31.9	11.5	2.6	199.6
		25377	7.98	13.9	43.6	54.6	17.4	31.8	11.7	1.7	134.5
		25378	8.09	14.5	45.2	55.8	17.9	32.1	11.4	1.3	106.5
		25379	7.74	14.0	44.1	56.9	18.1	31.9	11.9	1.4	109.4
		25380	7.77	14.7	45.8	59.0	18.9	32.1	11.7	2.1	165.1
		25381	7.81	13.6	42.8	54.7	17.4	31.8	12.6	1.8	138.6
		25382	6.69	12.2	37.0	55.3	18.2	33.0	11.8	2.1	141.2
		25383	8.33	15.1	47.2	56.7	18.2	32.1	11.3	1.7	142.2

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 22 (continued): Individual Hematology Data

Day 91 Relative to Start Date

Group	Sex	Animal	PLT K/µL	MPV fL	WBC K/µL	ABNEUT K/µL	ABLYMP K/µL	ABMONO K/µL	ABSEOS K/µL	ABBAS K/µL
1	f	25254	770	7.0	9.17	1.42	7.15	0.42	0.05	0.05
		25255	852	6.9	6.59	0.51	5.66	0.23	0.08	0.05
		25256	985	6.8	4.79	1.07	3.53	0.12	0.02	0.02
		25257	757	7.6	7.11	0.97	5.92	0.13	0.04	0.02
		25258	611	7.6	8.94	1.08	7.49	0.23	0.05	0.04
		25259	927	6.7	8.44	1.40	6.63	0.28	0.04	0.03
		25260	381	8.2	10.02	0.95	8.31	0.56	0.04	0.05
		25261	623	6.9	8.58	1.95	6.35	0.19	0.02	0.04
		25262	624	7.3	7.93	0.77	6.75	0.23	0.06	0.04
		25263	792	6.3	8.88	0.50	8.09	0.16	0.02	0.04
7	f	25334	628	7.2	8.28	1.63	6.08	0.36	0.06	0.04
		25335	544	7.3	9.80	1.99	7.32	0.33	0.06	0.05
		25336	655	7.1	7.71	0.86	6.50	0.22	0.04	0.03
		25337	689	6.8	8.08	0.61	7.20	0.09	0.06	0.03
		25338	921	7.4	9.27	0.85	8.02	0.25	0.05	0.05
		25339	653	6.9	13.46	2.06	10.86	0.36	0.05	0.05
		25340	738	7.6	10.32	1.97	7.92	0.30	0.03	0.03
		25341	696	6.4	7.99	1.32	6.15	0.36	0.06	0.02
		25342	697	7.0	11.13	0.99	9.51	0.43	0.04	0.06
		25343	725	7.1	10.64	0.93	9.29	0.25	0.05	0.05
8	f	25344	916	7.1	5.35	0.86	4.24	0.19	0.04	0.01
		25345	952	7.3	11.64	1.13	10.04	0.28	0.07	0.05
		25346	601	7.5	8.91	0.99	7.28	0.37	0.09	0.03
		25347	861	6.7	8.93	1.63	6.63	0.41	0.07	0.03
		25348	905	7.4	9.07	1.99	6.63	0.24	0.14	0.03
		25349	793	6.7	8.47	1.24	6.87	0.23	0.06	0.04
		25350	718	7.9	6.66	0.68	5.66	0.20	0.04	0.02
		25351	618	6.5	8.23	0.92	7.06	0.15	0.02	0.03
		25352	709	6.5	10.66	1.15	9.08	0.25	0.06	0.05
		25353	636	6.8	9.79	0.99	8.35	0.23	0.09	0.04

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 22 (continued): Individual Hematology Data

Day 91 Relative to Start Date

Group	Sex	Animal	PLT K/µL	MPV fL	WBC K/µL	ABNEUT K/µL	ABLYMP K/µL	ABMONO K/µL	ABSEOS K/µL	ABBAS K/µL
9	f	25354	666	7.8	9.58	2.05	6.90	0.46	0.05	0.04
		25355	746	7.9	11.92	1.84	9.27	0.52	0.04	0.09
		25356	487	7.3	7.57	1.72	5.51	0.26	0.02	0.02
		25357	888	7.6	4.38	1.35	2.81	0.09	0.04	0.01
		25358	795	7.5	8.35	1.99	5.92	0.31	0.03	0.05
		25359	681	6.7	8.69	1.34	6.77	0.30	0.13	0.05
		25360	865	6.6	16.17	1.68	13.62	0.46	0.12	0.10
		25361	800	6.3	9.29	0.64	8.47	0.10	0.03	0.03
		25362	707	6.9	5.73	0.56	4.90	0.18	0.04	0.02
		25363	919	5.7	7.16	1.19	5.69	0.18	0.06	0.02
10	f	25364	853	7.2	5.56	1.22	4.05	0.18	0.03	0.01
		25365	644	7.3	6.60	0.92	5.34	0.27	0.03	0.03
		25366	830	7.4	7.76	1.75	5.72	0.18	0.06	0.02
		25367	776	7.1	12.95	0.96	11.38	0.32	0.11	0.08
		25368	775	7.6	13.90	2.02	11.21	0.38	0.07	0.08
		25369	861	7.0	9.79	1.28	8.08	0.19	0.08	0.06
		25370	683	7.4	11.80	1.64	9.45	0.46	0.12	0.07
		25371	602	6.9	11.02	1.34	9.10	0.38	0.07	0.04
		25372	990	6.9	9.18	1.17	7.48	0.33	0.06	0.03
		25373	855	6.2	9.93	1.84	7.48	0.42	0.11	0.04
11	f	25374	803	7.2	7.48	1.11	6.08	0.17	0.05	0.03
		25375	516	7.8	9.17	1.09	7.62	0.28	0.08	0.04
		25376	774	7.4	8.12	0.76	7.17	0.09	0.03	0.02
		25377	809	7.5	8.47	1.11	7.01	0.24	0.03	0.02
		25378	819	6.6	12.36	0.89	10.89	0.30	0.08	0.06
		25379	600	8.1	10.66	1.61	8.30	0.48	0.14	0.05
		25380	655	6.4	9.37	0.93	8.10	0.24	0.02	0.05
		25381	624	7.4	7.24	0.79	5.90	0.38	0.05	0.03
		25382	PClump	PClump	3.24	0.25	2.84	0.04	0.02	0.08
		25383	444	6.5	10.64	0.76	9.43	0.28	0.07	0.05

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 22 (continued): Individual Hematology Data

Day 119 Relative to Start Date

Group	Sex	Animal	RBC M/µL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RDW %	RET %	ABRETi 10^9/L
1	m	25244	8.97	14.5	47.8	53.3	16.2	30.4	14.2	2.6	236.9
		25245	8.23	13.7	42.8	52.0	16.7	32.1	16.9	2.5	208.1
		25246	9.20	15.8	49.7	54.0	17.2	31.7	14.1	2.0	186.5
		25247	8.19	14.5	46.9	57.3	17.7	31.0	14.5	2.4	193.8
		25248	8.15	14.8	46.9	57.6	18.2	31.6	15.7	2.8	224.6
		25249	8.67	14.7	46.0	53.0	16.9	31.9	14.0	2.2	194.7
		25250	8.28	13.9	44.1	53.2	16.8	31.6	14.0	2.4	198.7
		25251	7.81	14.1	44.5	57.0	18.1	31.8	16.1	3.5	272.5
		25252	8.47	14.8	46.3	54.6	17.4	31.9	14.3	2.3	190.3
		25253	8.17	14.0	44.6	54.6	17.2	31.4	16.8	2.9	240.2
6	m	25324	8.91	15.1	49.0	55.0	16.9	30.8	14.2	2.3	204.9
		25325	8.72	16.1	49.3	56.5	18.4	32.6	14.3	2.3	201.1
		25326	8.08	13.7	43.8	54.3	17.0	31.3	15.0	2.8	228.0
		25327	8.21	14.6	46.2	56.3	17.8	31.6	15.6	2.6	209.4
		25328	8.55	15.3	48.6	56.8	17.9	31.4	14.0	2.0	174.6
		25329	8.73	14.8	47.2	54.0	17.0	31.4	13.9	2.0	176.4
		25330	8.54	14.5	46.7	54.7	17.0	31.0	15.5	2.4	202.4
		25331	8.40	13.8	44.3	52.7	16.4	31.2	15.1	2.4	205.2
		25332	8.48	14.1	45.7	53.9	16.7	30.9	13.7	2.6	219.5
		25333	8.55	14.8	46.5	54.4	17.4	31.9	14.6	2.0	167.6

Target Dose: Group 1 - 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 22 (continued): Individual Hematology Data

Day 119 Relative to Start Date

Group	Sex	Animal	PLT K/µL	MPV fL	WBC K/µL	ABNEUT K/µL	ABLYMP K/µL	ABMONO K/µL	ABSEOS K/µL	ABBAS K/µL
1	m	25244	992	7.8	9.16	1.88	6.91	0.19	0.13	0.03
		25245	984	7.5	11.15	2.58	7.74	0.54	0.13	0.03
		25246	754	7.7	10.40	1.89	7.85	0.39	0.12	0.05
		25247	746	7.7	10.87	1.18	9.16	0.26	0.14	0.05
		25248	953	7.4	10.84	1.75	8.60	0.33	0.04	0.03
		25249	874	7.4	9.72	1.72	7.29	0.49	0.08	0.04
		25250	922	6.9	9.89	1.67	7.88	0.17	0.08	0.03
		25251	921	7.5	15.58	2.96	11.64	0.56	0.16	0.07
		25252	658	7.8	11.04	1.95	8.38	0.52	0.09	0.04
		25253	608	7.3	11.19	3.12	7.41	0.44	0.09	0.04
6	m	25324	698	8.2	9.72	2.20	6.90	0.45	0.09	0.03
		25325	751	7.9	12.38	1.34	10.43	0.35	0.14	0.04
		25326	678	7.4	8.25	2.50	5.29	0.29	0.08	0.02
		25327	513	8.3	10.10	1.42	8.15	0.33	0.09	0.03
		25328	518	8.1	9.46	1.70	7.36	0.24	0.04	0.02
		25329	606	8.2	14.88	4.50	9.78	0.36	0.08	0.07
		25330	842	7.5	15.91	1.75	13.42	0.51	0.11	0.07
		25331	647	8.0	13.88	2.94	10.13	0.56	0.07	0.06
		25332	663	8.0	11.23	2.13	8.53	0.28	0.19	0.04
		25333	618	7.8	13.53	1.82	11.10	0.41	0.08	0.06

Target Dose: Group 1 - 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 22 (continued): Individual Hematology Data

Day 119 Relative to Start Date

Group	Sex	Animal	RBC M/µL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	RDW %	RET %	ABRETi 10^9/L
1	f	25264	7.75	14.0	43.4	56.0	18.0	32.2	12.1	2.3	179.8
		25265	7.33	13.4	40.7	55.6	18.3	32.9	11.9	1.6	113.8
		25266	7.53	13.1	40.9	54.3	17.4	32.0	11.8	2.0	153.9
		25267	7.47	14.5	44.6	59.7	19.5	32.6	12.2	2.4	176.2
		25268	7.77	14.5	44.7	57.5	18.7	32.5	12.1	2.2	168.0
		25269	7.95	14.5	45.9	57.7	18.2	31.5	13.0	1.7	137.5
		25270	7.93	15.0	46.1	58.1	18.9	32.4	11.8	1.9	153.1
		25271	7.33	14.2	42.3	57.7	19.4	33.6	12.7	2.2	162.7
		25272	7.67	14.5	45.4	59.2	18.9	32.0	12.5	2.1	162.1
		25273	6.79	13.3	40.8	60.0	19.6	32.6	12.6	3.3	222.6
11	f	25384	8.13	14.6	45.7	56.2	18.0	32.0	12.1	2.4	192.9
		25385	7.73	14.5	44.2	57.2	18.7	32.7	12.4	2.6	198.5
		25386	8.49	14.9	46.3	54.5	17.5	32.1	12.0	2.1	177.7
		25387	7.90	15.1	46.4	58.8	19.1	32.5	12.2	3.0	234.9
		25388	7.90	15.3	47.5	60.2	19.4	32.3	12.4	2.3	181.9
		25389	7.77	14.4	44.4	57.2	18.6	32.5	11.9	1.9	144.7
		25390	7.27	13.6	42.0	57.7	18.7	32.5	12.1	2.2	161.6
		25391	8.30	15.0	44.5	53.7	18.0	33.6	12.0	1.5	123.7
		25392	8.16	15.0	45.6	55.9	18.4	32.9	11.7	1.3	101.6
		25393	8.48	15.2	46.8	55.2	18.0	32.5	11.9	1.4	116.0

Target Dose: Group 1 - 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 22 (continued): Individual Hematology Data

Day 119 Relative to Start Date

Group	Sex	Animal	PLT K/µL	MPV fL	WBC K/µL	ABNEUT K/µL	ABLYMP K/µL	ABMONO K/µL	ABSEOS K/µL	ABBAS K/µL
1	f	25264	846	8.4	5.73	1.78	3.60	0.27	0.03	0.01
		25265	690	7.9	5.94	1.30	4.06	0.43	0.05	0.02
		25266	175	10.7	3.64	0.54	2.90	0.11	0.04	0.02
		25267	788	7.1	3.91	0.86	2.86	0.12	0.05	0.01
		25268	588	7.6	7.12	1.67	5.02	0.31	0.05	0.02
		25269	660	7.3	5.85	1.30	4.19	0.21	0.11	0.01
		25270	879	7.9	4.16	0.90	3.01	0.16	0.07	0.01
		25271	469	6.9	9.34	1.63	7.13	0.31	0.05	0.04
		25272	728	6.8	7.15	1.00	5.61	0.40	0.06	0.02
		25273	610	7.2	4.91	0.64	3.94	0.18	0.09	0.01
11	f	25384	834	6.8	5.13	0.96	3.87	0.20	0.06	0.01
		25385	728	7.3	6.52	1.27	4.90	0.22	0.07	0.02
		25386	698	7.3	6.98	0.71	6.01	0.19	0.03	0.01
		25387	656	7.3	5.51	0.76	4.44	0.21	0.03	0.01
		25388	551	7.4	6.29	1.36	4.47	0.34	0.05	0.02
		25389	897	7.7	5.33	0.92	3.88	0.39	0.08	0.02
		25390	PClump	PClump	7.13	0.87	5.97	0.11	0.05	0.05
		25391	542	7.8	8.56	2.15	5.97	0.29	0.07	0.03
		25392	531	7.2	10.43	1.10	8.56	0.54	0.12	0.04
		25393	649	7.6	8.54	1.79	6.15	0.43	0.07	0.03

Target Dose: Group 1 - 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

APPENDIX 23: INDIVIDUAL COAGULATION DATA

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 23: Individual Coagulation Data

Day Numbers Relative to Start Date

Specimen Disposition:

Day	Group	Sex	Animal	Comment
91	3	m	25284	Gross Hemolyses
	4	m	25297	Gross Hemolyses
	5	m	25311	No Clot detected
	9	f	25359	Specimen Moderately Hemolyzed
	10	f	25369	Specimen Moderately Hemolyzed
	11	f	25382	Specimen Grossly Hemolyzed
119	1	f	25265	Grossly Hemolyzed
	6	m	25325	Sample Grossly Hemolyzed
	11	f	25388	No clot detected

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 23 (continued): Individual Coagulation Data

Day 91 Relative to Start Date

Group	Sex	Animal	PT sec	APTT sec	FIB mg/dL	Group	Sex	Animal	PT sec	APTT sec	FIB mg/dL
1	m	25234	15.6	21.1	241	4	m	25294	16.5	20.7	309
		25235	16.5	18.5	327			25295	16.4	15.0	286
		25236	16.0	19.3	312			25296	16.6	16.5	292
		25237	15.6	22.1	320			25297	GrsHe	GrsHe	GrsHe
		25238	15.5	14.2	273			25298	16.4	19.3	278
		25239	16.7	26.9	544			25299	15.3	26.6	270
		25240	15.7	22.2	341			25300	15.6	26.1	317
		25241	16.1	38.0	293			25301	15.5	26.1	331
		25242	15.8	20.7	293			25302	15.6	29.4	319
		25243	14.9	26.8	350			25303	15.7	10.9	469
2	m	25274	15.8	15.8	288	5	m	25304	17.2	25.7	357
		25275	15.5	14.5	301			25305	16.2	15.9	365
		25276	16.0	25.2	319			25306	16.7	36.7	337
		25277	16.3	18.0	335			25307	16.8	19.5	332
		25278	16.5	19.8	368			25308	15.9	32.0	408
		25279	16.3	14.7	339			25309	17.3	34.9	98
		25280	16.3	21.4	345			25310	15.6	24.4	349
		25281	17.4	15.1	493			25311	NoClt	NoClt	NoClt
		25282	16.2	28.4	310			25312	15.7	26.7	385
		25283	15.5	32.7	405			25313	17.7	16.1	364
3	m	25284	GrsHe	GrsHe	GrsHe	6	m	25314	17.7	15.2	352
		25285	16.0	25.0	290			25315	17.1	14.0	287
		25286	16.3	15.1	292			25316	15.6	25.3	328
		25287	16.0	23.2	256			25317	16.3	13.4	381
		25288	15.9	16.8	309			25318	16.1	14.6	355
		25289	15.3	16.3	351			25319	15.2	13.2	381
		25290	15.5	18.1	332			25320	15.4	13.5	412
		25291	17.3	18.0	384			25321	15.8	21.2	287
		25292	16.0	19.3	282			25322	16.2	24.7	340
		25293	16.1	17.8	299			25323	16.0	22.2	303

GrsHe = Grossly Hemolyzed
Target Dose: Group 1 - 0 mg/kg/day Groups 2 and 7 - 1 mg/kg/day Groups 3 and 8 - 3 mg/kg/day
Groups 4 and 9 - 10 mg/kg/day Groups 5 and 10 - 30 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 23 (continued): Individual Coagulation Data

Day 91 Relative to Start Date

Group	Sex	Animal	PT sec	APTT sec	FIB mg/dL	Group	Sex	Animal	PT sec	APTT sec	FIB mg/dL
1	f	25254	15.7	25.5	238	9	f	25354	13.6	12.0	219
		25255	14.9	14.3	157			25355	14.8	25.6	248
		25256	15.1	39.6	324			25356	15.6	25.0	206
		25257	14.3	34.7	215			25357	14.4	28.0	222
		25258	14.4	21.2	195			25358	14.0	25.9	199
		25259	15.4	25.9	252			25359	15.9	13.7	196
		25260	14.4	19.0	209			25360	14.5	29.6	196
		25261	14.4	14.1	227			25361	15.0	15.0	227
		25262	15.3	27.0	239			25362	16.7	26.1	210
		25263	15.6	21.4	240			25363	16.7	35.6	239
7	f	25334	13.4	18.3	227	10	f	25364	15.2	27.9	241
		25335	14.3	23.4	248			25365	15.0	14.2	193
		25336	14.1	32.0	223			25366	16.0	16.9	297
		25337	15.2	27.7	202			25367	15.2	25.0	213
		25338	14.5	23.4	188			25368	15.5	16.1	233
		25339	15.5	31.5	253			25369	15.2	12.3	226
		25340	14.9	32.8	204			25370	14.2	28.3	255
		25341	14.6	22.2	233			25371	14.0	18.3	183
		25342	15.3	17.5	166			25372	15.5	29.8	247
		25343	15.6	35.0	200			25373	16.3	34.8	229
8	f	25344	15.1	31.3	208	11	f	25374	14.3	25.3	184
		25345	15.5	26.2	207			25375	15.7	20.3	230
		25346	14.7	23.6	203			25376	15.8	26.0	170
		25347	14.2	16.1	195			25377	16.2	42.7	195
		25348	14.8	28.6	245			25378	16.6	22.1	222
		25349	14.7	16.3	186			25379	15.3	14.3	195
		25350	14.8	29.5	192			25380	14.1	11.4	178
		25351	14.5	32.0	196			25381	14.3	22.6	166
		25352	15.9	16.6	218			25382	GrsHe	GrsHe	GrsHe
		25353	15.7	12.3	186			25383	16.1	19.3	194

UfA – Unsuitable for Analysis

Target Dose: Group 1 – 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 23 (continued): Individual Coagulation Data

Day 119 Relative to Start Date

Group	Sex	Animal	PT sec	APTT sec	FIB mg/dL	Group	Sex	Animal	PT sec	APTT sec	FIB mg/dL
1	m	25244	15.8	29.3	344	1	f	25264	14.4	29.2	162
		25245	15.3	25.8	384			25265	GrsHe	GrsHe	GrsHe
		25246	16.2	22.9	326			25266	14.5	19.8	190
		25247	15.4	23.7	311			25267	14.9	24.4	214
		25248	15.7	29.8	324			25268	14.4	26.6	240
		25249	15.6	24.5	280			25269	15.5	25.8	209
		25250	16.7	18.9	340			25270	14.6	25.8	210
		25251	16.5	21.2	344			25271	12.8	14.3	196
		25252	16.6	22.6	335			25272	13.0	18.8	202
		25253	15.9	27.3	301			25273	14.0	15.0	195
6	m	25324	16.0	34.0	326	11	f	25384	14.9	28.6	228
		25325	GrsHe	GrsHe	GrsHe			25385	15.0	24.6	225
		25326	16.3	18.6	378			25386	14.0	32.1	238
		25327	16.6	30.0	276			25387	14.1	29.1	165
		25328	16.1	24.2	331			25388	NoClt	NoClt	NoClt
		25329	16.5	17.1	336			25389	14.1	29.9	230
		25330	17.1	37.4	421			25390	18.9	43.3	80
		25331	16.8	20.1	333			25391	14.8	21.1	276
		25332	17.9	24.6	131			25392	15.3	20.6	214
		25333	17.2	30.7	284			25393	14.7	28.7	220

GrsHe = Grossly Hemolyzed

Target Dose: Group 1 - 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

APPENDIX 24: INDIVIDUAL URINALYSIS DATA

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 24: Individual Urinalysis Data

Day 91 Relative to Start Date

Group	Sex	Animal	SG	UpH	URO U/dL	TUVol mL	Color	Clarity	BLO	PRO	UGLU
1	m	25234	1.019	8.0	0.2	12.0	YELLOW	CLOUDY	NEGATIVE	1+	NEGATIVE
		25235	1.037	7.0	0.2	10.0	YELLOW	TURBID	NEGATIVE	2+	NEGATIVE
		25236	1.036	7.0	0.2	9.0	YELLOW	CLOUDY	NEGATIVE	2+	NEGATIVE
		25237	1.045	7.5	0.2	6.0	YELLOW	CLOUDY	NEGATIVE	2+	NEGATIVE
		25238	>1.050	7.0	0.2	4.0	DK YELLOW	CLOUDY	NEGATIVE	2+	NEGATIVE
		25239	1.017	7.5	0.2	12.0	YELLOW	CLOUDY	NEGATIVE	1+	NEGATIVE
		25240	1.020	7.0	0.2	1.5	YELLOW	CLOUDY	NEGATIVE	TRACE	NEGATIVE
		25241	1.027	7.5	0.2	10.0	YELLOW	CLOUDY	NEGATIVE	1+	NEGATIVE
		25242	1.020	8.0	0.2	12.0	YELLOW	CLOUDY	NEGATIVE	1+	NEGATIVE
		25243	1.016	8.0	0.2	1.0	YELLOW	SLCLOUDY	NEGATIVE	NEGATIVE	NEGATIVE
2	m	25274	1.021	8.5	0.2	12.0	YELLOW	CLOUDY	NEGATIVE	1+	NEGATIVE
		25275	1.025	7.0	0.2	1.5	YELLOW	CLOUDY	NEGATIVE	1+	NEGATIVE
		25276	1.029	8.5	0.2	8.0	YELLOW	CLOUDY	NEGATIVE	2+	NEGATIVE
		25277	1.025	7.5	0.2	12.0	YELLOW	CLOUDY	NEGATIVE	1+	NEGATIVE
		25278	1.035	8.0	0.2	8.0	YELLOW	CLEAR	NEGATIVE	2+	NEGATIVE
		25279	1.036	6.5	0.2	11.0	YELLOW	CLEAR	NEGATIVE	1+	NEGATIVE
		25280	1.038	6.5	0.2	7.0	YELLOW	CLOUDY	NEGATIVE	2+	NEGATIVE
		25281	>1.050	6.5	0.2	4.0	YELLOW	CLEAR	NEGATIVE	2+	NEGATIVE
		25282	>1.050	7.0	0.2	2.0	YELLOW	CLOUDY	NEGATIVE	NEGATIVE	NEGATIVE
		25283	1.022	7.0	0.2	12.0	YELLOW	CLOUDY	NEGATIVE	1+	NEGATIVE
3	m	25284	1.028	8.0	0.2	10.0	YELLOW	CLOUDY	NEGATIVE	2+	NEGATIVE
		25285	1.013	7.0	0.2	12.0	YELLOW	CLOUDY	NEGATIVE	NEGATIVE	NEGATIVE
		25286	1.026	8.5	0.2	11.0	YELLOW	CLOUDY	NEGATIVE	2+	NEGATIVE
		25287	1.012	7.5	0.2	12.0	YELLOW	CLEAR	NEGATIVE	NEGATIVE	NEGATIVE
		25288	1.023	7.5	0.2	12.0	YELLOW	CLOUDY	NEGATIVE	1+	NEGATIVE
		25289	1.022	6.5	0.2	8.0	YELLOW	CLOUDY	NEGATIVE	1+	NEGATIVE
		25290	1.024	7.0	0.2	12.0	YELLOW	CLOUDY	NEGATIVE	1+	NEGATIVE
		25291	1.019	7.5	0.2	12.0	YELLOW	CLOUDY	NEGATIVE	1+	NEGATIVE
		25292	1.048	7.5	0.2	4.0	YELLOW	CLOUDY	NEGATIVE	2+	NEGATIVE
		25293	1.012	7.5	0.2	12.0	YELLOW	CLOUDY	NEGATIVE	TRACE	NEGATIVE

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 24 (continued): Individual Urinalysis Data

Day 91 Relative to Start Date

Group	Sex	Animal	SG	UpH	URO U/dL	TUVol mL	Color	Clarity	BLO	PRO	UGLU
4	m	25294	1.018	7.0	0.2	12.0	YELLOW	CLOUDY	NEGATIVE	TRACE	NEGATIVE
		25295	1.018	7.0	0.2	12.0	YELLOW	CLOUDY	NEGATIVE	1+	NEGATIVE
		25296	1.022	7.5	0.2	12.0	YELLOW	CLOUDY	NEGATIVE	1+	NEGATIVE
		25297	1.018	7.5	0.2	1.5	YELLOW	TURBID	NEGATIVE	1+	NEGATIVE
		25298	1.027	7.5	0.2	11.0	YELLOW	CLOUDY	NEGATIVE	1+	NEGATIVE
		25299	1.018	7.0	0.2	12.0	YELLOW	CLOUDY	NEGATIVE	TRACE	NEGATIVE
		25300	1.031	7.0	0.2	6.0	YELLOW	CLEAR	NEGATIVE	1+	NEGATIVE
		25301	1.022	8.0	0.2	12.0	YELLOW	CLOUDY	NEGATIVE	1+	NEGATIVE
		25302	1.019	8.0	0.2	11.0	YELLOW	CLOUDY	NEGATIVE	1+	NEGATIVE
		25303	1.072	6.0	1.0	2.0	DK YELLOW	CLEAR	NEGATIVE	3+	TRACE
5	m	25304	1.027	7.0	0.2	8.0	YELLOW	CLOUDY	NEGATIVE	1+	NEGATIVE
		25305	1.015	7.5	0.2	12.0	YELLOW	CLOUDY	NEGATIVE	TRACE	NEGATIVE
		25306	1.022	7.5	0.2	12.0	YELLOW	CLOUDY	NEGATIVE	1+	NEGATIVE
		25307	1.015	7.5	0.2	12.0	YELLOW	CLOUDY	NEGATIVE	TRACE	NEGATIVE
		25308	1.023	8.5	0.2	11.0	YELLOW	CLOUDY	NEGATIVE	2+	NEGATIVE
		25309	1.025	7.0	0.2	11.0	YELLOW	CLOUDY	NEGATIVE	1+	NEGATIVE
		25310	1.035	8.0	0.2	5.0	YELLOW	CLOUDY	NEGATIVE	2+	NEGATIVE
		25311	1.010	7.5	0.2	12.0	YELLOW	CLEAR	NEGATIVE	NEGATIVE	NEGATIVE
		25312	1.023	7.0	0.2	10.0	YELLOW	CLOUDY	NEGATIVE	1+	NEGATIVE
		25313	1.014	7.5	0.2	12.0	YELLOW	CLOUDY	NEGATIVE	TRACE	NEGATIVE
6	m	25314	1.010	6.5	0.2	12.0	YELLOW	CLOUDY	1+	NEGATIVE	NEGATIVE
		25315	1.020	6.5	0.2	9.0	YELLOW	CLOUDY	NEGATIVE	TRACE	NEGATIVE
		25316	1.026	7.5	0.2	9.0	YELLOW	CLOUDY	NEGATIVE	1+	NEGATIVE
		25317	1.012	7.0	0.2	12.0	YELLOW	CLEAR	NEGATIVE	NEGATIVE	NEGATIVE
		25318	1.008	7.5	0.2	12.0	YELLOW	CLOUDY	NEGATIVE	NEGATIVE	NEGATIVE
		25319	1.010	7.0	0.2	12.0	YELLOW	CLOUDY	NEGATIVE	NEGATIVE	NEGATIVE
		25320	1.019	6.5	0.2	12.0	YELLOW	CLOUDY	NEGATIVE	1+	NEGATIVE
		25321	1.016	7.0	0.2	12.0	YELLOW	CLOUDY	NEGATIVE	TRACE	NEGATIVE
		25322	1.007	7.0	0.2	12.0	YELLOW	CLEAR	NEGATIVE	NEGATIVE	NEGATIVE
		25323	1.018	6.5	0.2	12.0	YELLOW	CLOUDY	NEGATIVE	TRACE	NEGATIVE

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 24 (continued): Individual Urinalysis Data

Day 91 Relative to Start Date

Group	Sex	Animal	UBILI	NIT	KET	LEU	uRBC HPF	uWBC HPF	EPI HPF	GRAN CA LPF	HYAL CA LPF
1	m	25234	NEGATIVE	POSITIVE	1+	2+	NS	NS	NS	NS	NS
		25235	NEGATIVE	NEGATIVE	1+	1+	NS	NS	NS	NS	NS
		25236	NEGATIVE	NEGATIVE	TRACE	1+	NS	NS	NS	NS	NS
		25237	NEGATIVE	NEGATIVE	1+	1+	NS	NS	NS	NS	NS
		25238	NEGATIVE	NEGATIVE	TRACE	1+	NS	NS	NS	NS	NS
		25239	NEGATIVE	POSITIVE	TRACE	1+	NS	NS	NS	NS	NS
		25240	NEGATIVE	NEGATIVE	NEGATIVE	TRACE	NS	1-3	NS	NS	NS
		25241	NEGATIVE	NEGATIVE	TRACE	1+	NS	NS	NS	NS	NS
		25242	NEGATIVE	NEGATIVE	TRACE	1+	NS	NS	NS	NS	NS
		25243	NEGATIVE	NEGATIVE	TRACE	NEGATIVE	NS	NS	NS	NS	NS
2	m	25274	NEGATIVE	NEGATIVE	TRACE	NEGATIVE	NS	NS	NS	NS	NS
		25275	NEGATIVE	NEGATIVE	TRACE	1+	NS	NS	NS	NS	NS
		25276	NEGATIVE	POSITIVE	1+	1+	NS	NS	NS	NS	NS
		25277	NEGATIVE	NEGATIVE	1+	1+	NS	NS	NS	NS	NS
		25278	NEGATIVE	NEGATIVE	TRACE	1+	NS	NS	NS	NS	NS
		25279	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NS	NS	NS	NS	NS
		25280	NEGATIVE	NEGATIVE	TRACE	TRACE	NS	1-3	NS	NS	NS
		25281	NEGATIVE	NEGATIVE	TRACE	1+	NS	NS	NS	NS	NS
		25282	1+	NEGATIVE	1+	NEGATIVE	NS	NS	NS	NS	NS
		25283	NEGATIVE	NEGATIVE	TRACE	1+	NS	NS	NS	NS	NS
3	m	25284	NEGATIVE	NEGATIVE	1+	1+	NS	NS	NS	NS	NS
		25285	NEGATIVE	NEGATIVE	TRACE	TRACE	NS	NS	NS	NS	NS
		25286	NEGATIVE	NEGATIVE	1+	1+	NS	NS	NS	NS	NS
		25287	NEGATIVE	NEGATIVE	TRACE	NEGATIVE	NS	NS	NS	NS	NS
		25288	NEGATIVE	POSITIVE	TRACE	1+	NS	NS	NS	NS	NS
		25289	NEGATIVE	NEGATIVE	TRACE	TRACE	NS	NS	NS	NS	NS
		25290	NEGATIVE	NEGATIVE	TRACE	1+	NS	NS	NS	NS	NS
		25291	NEGATIVE	NEGATIVE	1+	1+	NS	NS	NS	NS	NS
		25292	NEGATIVE	NEGATIVE	TRACE	1+	NS	NS	NS	NS	NS
		25293	NEGATIVE	NEGATIVE	TRACE	NEGATIVE	NS	NS	NS	NS	NS

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 24 (continued): Individual Urinalysis Data

Day 91 Relative to Start Date

Group	Sex	Animal	UBILI	NIT	KET	LEU	uRBC HPF	uWBC HPF	EPI HPF	GRAN CA LPF	HYAL CA LPF
4	m	25294	NEGATIVE	NEGATIVE	TRACE	TRACE	NS	NS	NS	NS	NS
		25295	NEGATIVE	NEGATIVE	TRACE	1+	NS	NS	NS	NS	NS
		25296	NEGATIVE	POSITIVE	TRACE	1+	NS	NS	NS	NS	NS
		25297	NEGATIVE	POSITIVE	TRACE	1+	NS	NS	NS	NS	NS
		25298	NEGATIVE	NEGATIVE	TRACE	1+	NS	NS	NS	NS	NS
		25299	NEGATIVE	POSITIVE	TRACE	1+	NS	NS	NS	NS	NS
		25300	NEGATIVE	POSITIVE	NEGATIVE	1+	NS	NS	NS	NS	NS
		25301	NEGATIVE	NEGATIVE	NEGATIVE	1+	NS	NS	NS	NS	NS
		25302	NEGATIVE	POSITIVE	TRACE	1+	NS	NS	NS	NS	NS
		25303	1+	NEGATIVE	TRACE	TRACE	NS	NS	NS	NS	NS
5	m	25304	NEGATIVE	NEGATIVE	TRACE	TRACE	NS	NS	NS	NS	NS
		25305	NEGATIVE	NEGATIVE	TRACE	TRACE	NS	NS	NS	NS	NS
		25306	NEGATIVE	NEGATIVE	TRACE	TRACE	NS	NS	NS	NS	NS
		25307	NEGATIVE	NEGATIVE	TRACE	TRACE	NS	NS	NS	NS	NS
		25308	NEGATIVE	POSITIVE	1+	1+	NS	NS	NS	NS	NS
		25309	NEGATIVE	NEGATIVE	TRACE	1+	NS	NS	NS	NS	NS
		25310	NEGATIVE	NEGATIVE	1+	2+	NS	NS	NS	NS	NS
		25311	NEGATIVE	NEGATIVE	TRACE	TRACE	NS	NS	NS	NS	NS
		25312	NEGATIVE	NEGATIVE	TRACE	1+	NS	NS	NS	NS	NS
		25313	NEGATIVE	NEGATIVE	TRACE	TRACE	NS	NS	NS	NS	NS
6	m	25314	NEGATIVE	NEGATIVE	TRACE	TRACE	NS	NS	NS	NS	NS
		25315	NEGATIVE	NEGATIVE	TRACE	1+	NS	NS	NS	NS	NS
		25316	NEGATIVE	NEGATIVE	1+	1+	NS	NS	NS	NS	NS
		25317	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NS	NS	NS	NS	NS
		25318	NEGATIVE	POSITIVE	NEGATIVE	NEGATIVE	NS	NS	NS	NS	NS
		25319	NEGATIVE	POSITIVE	NEGATIVE	TRACE	NS	NS	NS	NS	NS
		25320	NEGATIVE	NEGATIVE	TRACE	1+	NS	NS	NS	NS	NS
		25321	NEGATIVE	NEGATIVE	NEGATIVE	TRACE	NS	NS	NS	NS	NS
		25322	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NS	NS	NS	NS	NS
		25323	NEGATIVE	NEGATIVE	TRACE	TRACE	NS	NS	NS	NS	NS

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 24 (continued): Individual Urinalysis Data

Day 91 Relative to Start Date

Group	Sex	Animal	Amorph HPF	CAO CRYS HPF	TP CRYS HPF	Bacter HPF	Fecal HPF	Mucus HPF	Sperm HPF	Yeast HPF	Othr/Uri HPF
1	m	25234	NS	NS	1-3	3+	1+	NS	1+	NS	NS
		25235	NS	NS	7-10	3+	2+	NS	1+	NS	NS
		25236	NS	NS	4-6	3+	1+	NS	NS	NS	NS
		25237	NS	NS	11-20	3+	1+	NS	NS	NS	NS
		25238	NS	NS	NS	NS	1+	NS	NS	NS	NS
		25239	NS	NS	NS	3+	1+	NS	NS	NS	NS
		25240	NS	NS	1-3	NS	2+	NS	NS	NS	NS
		25241	NS	NS	1-3	NS	1+	NS	NS	NS	NS
		25242	NS	NS	11-20	3+	2+	NS	1+	NS	NS
		25243	NS	NS	NS	NS	1+	NS	NS	NS	NS
2	m	25274	NS	NS	7-10	NS	2+	NS	NS	NS	NS
		25275	NS	NS	NS	NS	1+	NS	NS	NS	NS
		25276	NS	NS	21-40	3+	2+	NS	1+	NS	NS
		25277	NS	NS	11-20	3+	3+	NS	NS	NS	NS
		25278	NS	NS	21-40	3+	2+	NS	NS	NS	NS
		25279	NS	NS	1-3	3+	2+	NS	1+	NS	NS
		25280	NS	NS	1-3	2+	1+	NS	NS	NS	NS
		25281	NS	NS	1-3	NS	2+	NS	1+	NS	NS
		25282	NS	NS	NS	NS	1+	NS	2+	NS	NS
		25283	NS	NS	4-6	3+	1+	NS	NS	NS	NS
3	m	25284	NS	NS	11-20	3+	1+	NS	NS	NS	NS
		25285	NS	NS	NS	NS	NS	NS	NS	NS	NS
		25286	NS	NS	11-20	3+	2+	NS	NS	NS	NS
		25287	NS	NS	4-6	3+	1+	NS	NS	NS	NS
		25288	NS	1-3	7-10	3+	2+	NS	1+	NS	NS
		25289	NS	NS	4-6	3+	1+	NS	NS	NS	NS
		25290	NS	4-6	11-20	3+	1+	NS	NS	NS	NS
		25291	NS	NS	4-6	3+	1+	NS	NS	NS	NS
		25292	NS	NS	7-10	3+	2+	NS	1+	NS	NS
		25293	NS	NS	7-10	3+	2+	NS	NS	NS	NS

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 24 (continued): Individual Urinalysis Data

Day 91 Relative to Start Date

Group	Sex	Animal	Amorph HPF	CAO CRYS HPF	TP CRYS HPF	Bacter HPF	Fecal HPF	Mucus HPF	Sperm HPF	Yeast HPF	Othr/Uri HPF
4	m	25294	NS	NS	11-20	3+	1+	NS	NS	NS	NS
		25295	NS	NS	1-3	3+	1+	NS	NS	NS	NS
		25296	NS	NS	21-40	3+	1+	NS	NS	NS	NS
		25297	NS	NS	NS	3+	1+	NS	NS	NS	NS
		25298	NS	NS	41-50	2+	1+	NS	1+	NS	NS
		25299	NS	NS	NS	1+	1+	NS	NS	NS	NS
		25300	NS	NS	41-50	2+	1+	NS	NS	NS	NS
		25301	NS	NS	NS	2+	1+	NS	NS	NS	NS
		25302	NS	NS	21-40	1+	1+	NS	NS	NS	NS
		25303	NS	NS	NS	1+	1+	NS	1+	NS	NS
5	m	25304	NS	NS	21-40	2+	1+	NS	NS	NS	NS
		25305	NS	NS	11-20	2+	1+	NS	NS	NS	NS
		25306	NS	NS	11-20	3+	1+	NS	NS	NS	NS
		25307	NS	NS	11-20	3+	1+	NS	1+	NS	NS
		25308	NS	NS	21-40	3+	1+	NS	NS	NS	NS
		25309	NS	NS	11-20	3+	1+	NS	NS	NS	NS
		25310	NS	NS	11-20	3+	1+	NS	1+	NS	NS
		25311	NS	NS	7-10	3+	1+	NS	NS	NS	NS
		25312	NS	NS	11-20	3+	1+	NS	NS	NS	NS
		25313	NS	NS	11-20	3+	1+	NS	NS	NS	NS
6	m	25314	NS	NS	NS	3+	1+	NS	NS	NS	NS
		25315	NS	NS	NS	2+	NS	NS	NS	NS	NS
		25316	NS	NS	7-10	3+	1+	NS	NS	NS	NS
		25317	NS	NS	NS	1+	1+	NS	NS	NS	NS
		25318	NS	NS	7-10	3+	1+	NS	NS	NS	NS
		25319	NS	NS	NS	3+	1+	NS	2+	NS	NS
		25320	NS	NS	4-6	2+	NS	NS	NS	NS	NS
		25321	NS	NS	NS	3+	1+	NS	NS	NS	NS
		25322	NS	NS	4-6	3+	1+	NS	NS	NS	NS
		25323	NS	NS	1-3	3+	2+	NS	NS	NS	NS

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 24 (continued): Individual Urinalysis Data

Day 91 Relative to Start Date

Group	Sex	Animal	SG	UpH	URO U/dL	TUVol mL	Color	Clarity	BLO	PRO	UGLU
1	f	25254	1.038	6.5	0.2	4.0	YELLOW	TURBID	NEGATIVE	1+	NEGATIVE
		25255	1.035	7.0	0.2	4.0	YELLOW	CLOUDY	NEGATIVE	1+	NEGATIVE
		25256	1.033	6.5	0.2	4.0	YELLOW	CLEAR	NEGATIVE	1+	NEGATIVE
		25257	1.022	6.5	0.2	8.0	YELLOW	CLEAR	NEGATIVE	TRACE	NEGATIVE
		25258	1.039	6.0	0.2	6.0	YELLOW	CLEAR	NEGATIVE	1+	NEGATIVE
		25259	1.027	6.5	0.2	6.0	YELLOW	CLOUDY	NEGATIVE	TRACE	NEGATIVE
		25260	1.046	7.0	0.2	3.0	YELLOW	CLEAR	NEGATIVE	2+	NEGATIVE
		25261	1.022	7.0	0.2	8.0	YELLOW	CLEAR	NEGATIVE	TRACE	NEGATIVE
		25262	>1.050	7.0	0.2	1.0	YELLOW	SLCLOUDY	NEGATIVE	1+	NEGATIVE
		25263	1.038	6.5	0.2	5.0	YELLOW	CLEAR	NEGATIVE	1+	NEGATIVE
7	f	25334	>1.050	7.5	0.2	1.0	YELLOW	SLCLOUDY	NEGATIVE	1+	NEGATIVE
		25335	1.040	6.5	0.2	3.0	YELLOW	CLOUDY	NEGATIVE	1+	NEGATIVE
		25336	1.045	6.5	0.2	3.0	YELLOW	CLOUDY	NEGATIVE	2+	NEGATIVE
		25337	1.017	7.0	0.2	12.0	YELLOW	CLEAR	NEGATIVE	TRACE	NEGATIVE
		25338	1.020	7.5	0.2	9.0	YELLOW	CLOUDY	NEGATIVE	TRACE	NEGATIVE
		25339	1.040	7.0	0.2	2.0	YELLOW	CLOUDY	NEGATIVE	2+	NEGATIVE
		25340	1.028	6.5	0.2	3.0	YELLOW	CLEAR	NEGATIVE	1+	NEGATIVE
		25341	1.019	8.0	0.2	6.0	YELLOW	CLOUDY	NEGATIVE	TRACE	NEGATIVE
		25342	1.022	6.5	0.2	8.0	YELLOW	CLEAR	NEGATIVE	TRACE	NEGATIVE
		25343	1.035	7.0	0.2	6.0	YELLOW	CLOUDY	NEGATIVE	1+	NEGATIVE
8	f	25344	1.029	6.5	0.2	6.0	YELLOW	CLOUDY	NEGATIVE	TRACE	NEGATIVE
		25345	1.022	7.0	0.2	7.0	YELLOW	CLEAR	NEGATIVE	1+	NEGATIVE
		25346	1.030	6.5	0.2	5.0	YELLOW	CLEAR	NEGATIVE	TRACE	NEGATIVE
		25347	1.027	7.0	0.2	3.0	YELLOW	CLEAR	NEGATIVE	1+	NEGATIVE
		25348	1.016	7.0	0.2	11.0	YELLOW	CLOUDY	NEGATIVE	NEGATIVE	NEGATIVE
		25349	1.015	7.5	0.2	7.0	YELLOW	CLEAR	NEGATIVE	NEGATIVE	NEGATIVE
		25350	1.038	6.5	0.2	4.0	YELLOW	CLEAR	NEGATIVE	1+	NEGATIVE
		25351	1.015	6.5	0.2	12.0	YELLOW	CLOUDY	NEGATIVE	NEGATIVE	NEGATIVE
		25352	1.040	6.0	0.2	2.0	YELLOW	CLEAR	NEGATIVE	1+	NEGATIVE
		25353	1.018	6.5	0.2	8.0	YELLOW	CLEAR	NEGATIVE	NEGATIVE	NEGATIVE

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 24 (continued): Individual Urinalysis Data

Day 91 Relative to Start Date

Group	Sex	Animal	SG	UpH	URO U/dL	TUVol mL	Color	Clarity	BLO	PRO	UGLU
9	f	25354	1.016	7.5	0.2	12.0	YELLOW	CLOUDY	NEGATIVE	NEGATIVE	NEGATIVE
		25355	1.019	7.0	0.2	12.0	YELLOW	CLOUDY	NEGATIVE	TRACE	NEGATIVE
		25356	1.017	6.5	0.2	7.0	YELLOW	CLOUDY	NEGATIVE	NEGATIVE	NEGATIVE
		25357	1.023	6.0	0.2	6.0	YELLOW	CLEAR	NEGATIVE	TRACE	NEGATIVE
		25358	1.015	6.0	0.2	10.0	YELLOW	CLOUDY	NEGATIVE	TRACE	NEGATIVE
		25359	1.019	7.0	0.2	10.0	YELLOW	CLOUDY	NEGATIVE	NEGATIVE	NEGATIVE
		25360	1.029	6.5	0.2	5.0	YELLOW	CLOUDY	NEGATIVE	1+	NEGATIVE
		25361	1.063	6.0	0.2	3.0	DK YELLOW	CLEAR	NEGATIVE	2+	NEGATIVE
		25362	1.031	6.5	0.2	5.0	YELLOW	CLOUDY	NEGATIVE	1+	NEGATIVE
		25363	1.027	6.0	0.2	3.0	YELLOW	CLEAR	NEGATIVE	TRACE	NEGATIVE
10	f	25364	1.031	7.0	0.2	6.0	YELLOW	CLOUDY	NEGATIVE	1+	NEGATIVE
		25365	1.012	7.0	0.2	12.0	YELLOW	CLOUDY	NEGATIVE	NEGATIVE	NEGATIVE
		25366	1.027	6.0	0.2	6.0	YELLOW	CLOUDY	NEGATIVE	TRACE	NEGATIVE
		25367	1.021	7.5	0.2	7.0	YELLOW	CLOUDY	NEGATIVE	TRACE	NEGATIVE
		25368	1.028	6.5	0.2	3.0	YELLOW	CLOUDY	NEGATIVE	TRACE	NEGATIVE
		25369	1.014	6.5	0.2	10.0	YELLOW	CLEAR	NEGATIVE	NEGATIVE	NEGATIVE
		25370	1.036	7.0	0.2	4.0	YELLOW	CLOUDY	NEGATIVE	1+	NEGATIVE
		25371	1.031	6.5	0.2	5.0	YELLOW	CLEAR	NEGATIVE	1+	NEGATIVE
		25372	1.022	7.0	0.2	9.0	YELLOW	CLEAR	NEGATIVE	NEGATIVE	NEGATIVE
		25373	1.015	7.0	0.2	12.0	YELLOW	CLEAR	NEGATIVE	NEGATIVE	NEGATIVE
11	f	25374	>1.050	6.0	1.0	2.0	DK YELLOW	CLOUDY	NEGATIVE	4+	NEGATIVE
		25375	1.010	7.0	0.2	12.0	YELLOW	CLEAR	NEGATIVE	NEGATIVE	NEGATIVE
		25376	1.010	6.5	0.2	12.0	YELLOW	CLOUDY	NEGATIVE	NEGATIVE	NEGATIVE
		25377	1.022	6.0	0.2	6.0	YELLOW	CLEAR	NEGATIVE	NEGATIVE	NEGATIVE
		25378	1.028	6.0	0.2	5.0	YELLOW	CLEAR	NEGATIVE	1+	NEGATIVE
		25379	1.030	7.0	1.0	5.0	DK YELLOW	CLOUDY	NEGATIVE	1+	NEGATIVE
		25380	1.019	6.5	0.2	7.0	YELLOW	CLOUDY	NEGATIVE	NEGATIVE	NEGATIVE
		25381	1.042	6.0	0.2	3.0	YELLOW	CLOUDY	NEGATIVE	2+	NEGATIVE
		25382	>1.050	6.0	0.2	2.0	YELLOW	SLCLOUDY	NEGATIVE	1+	NEGATIVE
		25383	1.015	6.5	0.2	7.0	YELLOW	CLEAR	NEGATIVE	NEGATIVE	NEGATIVE

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 24 (continued): Individual Urinalysis Data

Day 91 Relative to Start Date

Group	Sex	Animal	UBILI	NIT	KET	LEU	uRBC HPF	uWBC HPF	EPI HPF	GRAN CA LPF	HYAL CA LPF
1	f	25254	NEGATIVE	NEGATIVE	NEGATIVE	1+	1-3	NS	NS	NS	NS
		25255	NEGATIVE	POSITIVE	NEGATIVE	1+	NS	NS	NS	NS	NS
		25256	NEGATIVE	NEGATIVE	NEGATIVE	TRACE	NS	1-3	NS	NS	NS
		25257	NEGATIVE	NEGATIVE	NEGATIVE	1+	NS	NS	NS	NS	NS
		25258	NEGATIVE	NEGATIVE	NEGATIVE	TRACE	NS	NS	NS	NS	NS
		25259	NEGATIVE	NEGATIVE	NEGATIVE	TRACE	NS	NS	NS	NS	NS
		25260	NEGATIVE	NEGATIVE	NEGATIVE	1+	NS	NS	NS	NS	NS
		25261	NEGATIVE	NEGATIVE	NEGATIVE	1+	NS	NS	NS	NS	NS
		25262	NEGATIVE	NEGATIVE	TRACE	NEGATIVE	NS	NS	NS	NS	NS
		25263	NEGATIVE	NEGATIVE	NEGATIVE	1+	NS	NS	NS	NS	NS
7	f	25334	1+	NEGATIVE	NEGATIVE	NEGATIVE	NS	NS	NS	NS	NS
		25335	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NS	1-3	NS	NS	NS
		25336	NEGATIVE	NEGATIVE	NEGATIVE	1+	NS	NS	NS	NS	NS
		25337	NEGATIVE	NEGATIVE	NEGATIVE	1+	NS	NS	NS	NS	NS
		25338	NEGATIVE	NEGATIVE	NEGATIVE	1+	NS	NS	NS	NS	NS
		25339	NEGATIVE	NEGATIVE	NEGATIVE	1+	NS	NS	NS	NS	NS
		25340	NEGATIVE	NEGATIVE	NEGATIVE	1+	NS	NS	NS	NS	NS
		25341	NEGATIVE	POSITIVE	NEGATIVE	TRACE	NS	NS	NS	NS	NS
		25342	NEGATIVE	NEGATIVE	NEGATIVE	TRACE	NS	NS	NS	NS	NS
		25343	NEGATIVE	NEGATIVE	NEGATIVE	1+	NS	1-3	NS	NS	NS
8	f	25344	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NS	1-3	NS	NS	NS
		25345	NEGATIVE	NEGATIVE	NEGATIVE	1+	NS	NS	NS	NS	NS
		25346	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NS	NS	NS	NS	NS
		25347	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NS	1-3	NS	NS	NS
		25348	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NS	NS	NS	NS	NS
		25349	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NS	NS	NS	NS	NS
		25350	NEGATIVE	NEGATIVE	NEGATIVE	TRACE	NS	NS	NS	NS	NS
		25351	NEGATIVE	POSITIVE	NEGATIVE	TRACE	NS	NS	NS	NS	NS
		25352	NEGATIVE	NEGATIVE	NEGATIVE	TRACE	NS	NS	NS	NS	NS
		25353	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NS	NS	NS	NS	NS

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 24 (continued): Individual Urinalysis Data

Day 91 Relative to Start Date

Group	Sex	Animal	UBILI	NIT	KET	LEU	uRBC HPF	uWBC HPF	EPI HPF	GRAN CA LPF	HYAL CA LPF
9	f	25354	NEGATIVE	POSITIVE	NEGATIVE	NEGATIVE	NS	NS	NS	NS	NS
		25355	NEGATIVE	NEGATIVE	NEGATIVE	TRACE	NS	NS	NS	NS	NS
		25356	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NS	NS	NS	NS	NS
		25357	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NS	NS	NS	NS	NS
		25358	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NS	NS	NS	NS	NS
		25359	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NS	NS	NS	NS	NS
		25360	NEGATIVE	NEGATIVE	NEGATIVE	1+	NS	1-3	NS	NS	NS
		25361	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NS	1-3	NS	NS	NS
		25362	NEGATIVE	NEGATIVE	NEGATIVE	TRACE	NS	NS	NS	NS	NS
		25363	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NS	NS	NS	NS	NS
10	f	25364	NEGATIVE	POSITIVE	NEGATIVE	1+	NS	NS	NS	NS	NS
		25365	NEGATIVE	POSITIVE	NEGATIVE	TRACE	1-3	NS	NS	NS	NS
		25366	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NS	NS	NS	NS	NS
		25367	NEGATIVE	POSITIVE	NEGATIVE	TRACE	NS	NS	NS	NS	NS
		25368	NEGATIVE	NEGATIVE	NEGATIVE	TRACE	NS	NS	NS	NS	NS
		25369	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NS	NS	NS	NS	NS
		25370	NEGATIVE	NEGATIVE	NEGATIVE	TRACE	NS	NS	NS	NS	NS
		25371	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NS	NS	NS	NS	NS
		25372	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NS	NS	NS	NS	NS
		25373	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NS	NS	NS	NS	NS
11	f	25374	NEGATIVE	NEGATIVE	NEGATIVE	1+	1-3	NS	NS	NS	NS
		25375	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NS	NS	NS	NS	NS
		25376	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NS	NS	NS	NS	NS
		25377	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NS	NS	NS	NS	NS
		25378	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NS	1-3	NS	NS	NS
		25379	1+	NEGATIVE	NEGATIVE	NEGATIVE	NS	NS	NS	NS	NS
		25380	NEGATIVE	NEGATIVE	NEGATIVE	TRACE	NS	NS	NS	NS	NS
		25381	NEGATIVE	NEGATIVE	NEGATIVE	TRACE	NS	NS	NS	NS	NS
		25382	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NS	NS	NS	NS	NS
		25383	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NS	NS	NS	NS	NS

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 24 (continued): Individual Urinalysis Data

Day 91 Relative to Start Date

Group	Sex	Animal	Amorph HPF	CAO CRYS HPF	TP CRYS HPF	Bacter HPF	Fecal HPF	Mucus HPF	Sperm HPF	Yeast HPF	Othr/Uri HPF
1	f	25254	NS	NS	11-20	3+	1+	NS	NS	NS	NS
		25255	NS	NS	21-40	3+	1+	NS	NS	NS	NS
		25256	NS	NS	11-20	2+	1+	NS	NS	NS	NS
		25257	NS	NS	7-10	2+	2+	NS	NS	NS	NS
		25258	NS	NS	4-6	1+	1+	NS	NS	NS	NS
		25259	NS	NS	NS	3+	1+	NS	NS	NS	NS
		25260	NS	NS	21-40	2+	1+	NS	NS	NS	NS
		25261	NS	NS	21-40	3+	1+	NS	NS	NS	NS
		25262	NS	NS	4-6	3+	1+	NS	NS	NS	NS
		25263	NS	NS	1-3	1+	1+	NS	NS	NS	NS
7	f	25334	NS	NS	NS	1+	1+	NS	NS	NS	NS
		25335	NS	NS	1-3	3+	1+	NS	NS	NS	NS
		25336	NS	NS	NS	3+	2+	NS	NS	NS	NS
		25337	NS	NS	1-3	3+	1+	NS	NS	NS	NS
		25338	NS	NS	21-40	3+	1+	NS	NS	NS	NS
		25339	NS	NS	11-20	3+	1+	NS	NS	NS	NS
		25340	NS	NS	NS	1+	1+	NS	NS	NS	NS
		25341	NS	NS	41-50	3+	1+	NS	NS	NS	NS
		25342	NS	NS	NS	3+	1+	NS	NS	NS	NS
		25343	NS	NS	41-50	3+	1+	NS	NS	NS	NS
8	f	25344	NS	NS	NS	2+	1+	NS	NS	NS	NS
		25345	NS	NS	41-50	3+	1+	NS	NS	NS	NS
		25346	NS	NS	NS	1+	1+	NS	NS	NS	NS
		25347	NS	NS	11-20	3+	1+	NS	NS	NS	NS
		25348	NS	NS	4-6	1+	1+	NS	NS	NS	NS
		25349	NS	NS	7-10	3+	1+	NS	NS	NS	NS
		25350	NS	NS	NS	1+	1+	NS	NS	NS	NS
		25351	NS	NS	1-3	3+	1+	NS	NS	NS	NS
		25352	NS	NS	NS	3+	1+	NS	NS	NS	NS
		25353	NS	NS	NS	2+	1+	NS	NS	NS	NS

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 24 (continued): Individual Urinalysis Data

Day 91 Relative to Start Date

Group	Sex	Animal	Amorph HPF	CAO CRYS HPF	TP CRYS HPF	Bacter HPF	Fecal HPF	Mucus HPF	Sperm HPF	Yeast HPF	Othr/Uri HPF
9	f	25354	NS	7-10	21-40	3+	1+	NS	NS	NS	NS
		25355	NS	11-20	21-40	3+	1+	NS	NS	NS	NS
		25356	NS	NS	NS	3+	1+	NS	NS	NS	NS
		25357	NS	NS	NS	3+	2+	NS	NS	NS	NS
		25358	NS	NS	NS	3+	1+	NS	NS	NS	NS
		25359	NS	NS	7-10	3+	1+	NS	NS	NS	NS
		25360	NS	NS	21-40	3+	1+	NS	NS	NS	NS
		25361	NS	NS	NS	1+	2+	NS	NS	NS	NS
		25362	NS	NS	4-6	3+	1+	NS	NS	NS	NS
		25363	NS	NS	NS	3+	1+	NS	NS	NS	NS
10	f	25364	NS	NS	21-40	3+	1+	NS	NS	NS	NS
		25365	NS	NS	NS	NS	1+	NS	NS	NS	NS
		25366	NS	NS	NS	3+	1+	NS	NS	NS	NS
		25367	NS	NS	21-40	3+	1+	NS	NS	NS	NS
		25368	NS	NS	7-10	3+	1+	NS	NS	NS	NS
		25369	NS	NS	NS	3+	2+	NS	NS	NS	NS
		25370	NS	NS	1-3	2+	1+	NS	NS	NS	NS
		25371	NS	NS	7-10	3+	1+	NS	NS	NS	NS
		25372	NS	1-3	7-10	2+	2+	NS	NS	NS	NS
		25373	NS	NS	21-40	3+	1+	NS	NS	NS	NS
11	f	25374	NS	NS	NS	1+	1+	NS	NS	NS	NS
		25375	NS	NS	4-6	3+	1+	NS	NS	NS	NS
		25376	NS	NS	NS	3+	1+	NS	NS	NS	NS
		25377	NS	NS	NS	2+	2+	NS	NS	NS	NS
		25378	NS	NS	NS	1+	2+	NS	NS	NS	NS
		25379	NS	NS	7-10	NS	2+	NS	NS	NS	NS
		25380	NS	NS	NS	3+	1+	NS	NS	NS	NS
		25381	NS	NS	NS	1+	1+	NS	NS	NS	NS
		25382	NS	NS	NS	NS	1+	NS	NS	NS	NS
		25383	NS	NS	11-20	3+	2+	NS	NS	NS	NS

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 24 (continued): Individual Urinalysis Data

Day 119 Relative to Start Date

Group	Sex	Animal	SG	UpH	URO U/dL	TUVol mL	Color	Clarity	BLO	PRO	UGLU
1	m	25244	1.050	6.5	0.2	5.0	YELLOW	CLOUDY	NEGATIVE	2+	NEGATIVE
		25245	1.031	7.0	0.2	5.0	YELLOW	CLOUDY	NEGATIVE	1+	NEGATIVE
		25246	1.016	7.0	0.2	12.0	YELLOW	CLOUDY	NEGATIVE	NEGATIVE	NEGATIVE
		25247	1.022	7.0	0.2	7.0	YELLOW	CLOUDY	NEGATIVE	1+	NEGATIVE
		25248	1.012	7.5	0.2	12.0	YELLOW	CLOUDY	NEGATIVE	1+	NEGATIVE
		25249	1.014	7.0	0.2	12.0	YELLOW	CLOUDY	NEGATIVE	NEGATIVE	NEGATIVE
		25250	1.028	7.5	0.2	9.0	YELLOW	CLOUDY	NEGATIVE	1+	NEGATIVE
		25251	1.009	7.5	0.2	12.0	YELLOW	CLOUDY	NEGATIVE	NEGATIVE	NEGATIVE
		25252	1.026	7.0	0.2	9.0	YELLOW	CLOUDY	NEGATIVE	1+	NEGATIVE
		25253	1.030	7.5	0.2	6.0	YELLOW	CLEAR	NEGATIVE	1+	NEGATIVE
6	m	25324	1.025	7.0	0.2	12.0	YELLOW	CLEAR	NEGATIVE	1+	NEGATIVE
		25325	1.018	7.5	0.2	7.0	YELLOW	CLOUDY	NEGATIVE	TRACE	NEGATIVE
		25326	1.024	7.5	0.2	12.0	YELLOW	CLOUDY	NEGATIVE	1+	NEGATIVE
		25327	1.019	8.5	0.2	12.0	YELLOW	CLOUDY	NEGATIVE	1+	NEGATIVE
		25328	1.011	7.0	0.2	12.0	YELLOW	CLEAR	NEGATIVE	NEGATIVE	NEGATIVE
		25329	1.035	7.0	0.2	10.0	YELLOW	CLOUDY	NEGATIVE	1+	NEGATIVE
		25330	1.014	7.0	0.2	12.0	YELLOW	CLOUDY	NEGATIVE	NEGATIVE	NEGATIVE
		25331	1.019	8.0	0.2	12.0	YELLOW	CLOUDY	NEGATIVE	1+	NEGATIVE
		25332	1.011	8.0	0.2	12.0	YELLOW	CLOUDY	NEGATIVE	NEGATIVE	NEGATIVE
		25333	1.027	7.0	0.2	12.0	YELLOW	CLOUDY	NEGATIVE	1+	NEGATIVE

Target Dose: Group 1 - 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 24 (continued): Individual Urinalysis Data

Day 119 Relative to Start Date

Group	Sex	Animal	UBILI	NIT	KET	LEU	uRBC HPF	uWBC HPF	EPI HPF	GRAN CA LPF	HYAL CA LPF
1	m	25244	NEGATIVE	NEGATIVE	1+	1+	NS	NS	NS	NS	NS
		25245	NEGATIVE	POSITIVE	1+	1+	NS	NS	NS	NS	NS
		25246	NEGATIVE	NEGATIVE	1+	TRACE	NS	NS	NS	NS	NS
		25247	NEGATIVE	NEGATIVE	1+	2+	NS	NS	NS	NS	NS
		25248	NEGATIVE	POSITIVE	1+	1+	NS	NS	NS	NS	NS
		25249	NEGATIVE	NEGATIVE	TRACE	NEGATIVE	NS	NS	NS	NS	NS
		25250	NEGATIVE	NEGATIVE	TRACE	1+	NS	NS	NS	NS	NS
		25251	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NS	NS	NS	NS	NS
		25252	NEGATIVE	NEGATIVE	TRACE	NEGATIVE	NS	NS	NS	NS	NS
		25253	NEGATIVE	NEGATIVE	1+	TRACE	NS	NS	NS	NS	NS
6	m	25324	NEGATIVE	NEGATIVE	1+	TRACE	NS	NS	NS	NS	NS
		25325	NEGATIVE	NEGATIVE	TRACE	NEGATIVE	NS	NS	NS	NS	NS
		25326	NEGATIVE	NEGATIVE	TRACE	1+	NS	NS	NS	NS	NS
		25327	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NS	NS	NS	NS	NS
		25328	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NS	NS	NS	NS	NS
		25329	NEGATIVE	NEGATIVE	1+	1+	NS	NS	NS	NS	NS
		25330	NEGATIVE	NEGATIVE	TRACE	NEGATIVE	NS	NS	NS	NS	NS
		25331	NEGATIVE	POSITIVE	NEGATIVE	1+	NS	NS	NS	NS	NS
		25332	NEGATIVE	POSITIVE	TRACE	NEGATIVE	NS	NS	NS	NS	NS
		25333	NEGATIVE	NEGATIVE	1+	1+	NS	NS	NS	NS	NS

Target Dose: Group 1 - 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 24 (continued): Individual Urinalysis Data

Day 119 Relative to Start Date

Group	Sex	Animal	Amorph HPF	CAO CRYS HPF	TP CRYS HPF	Bacter HPF	Fecal HPF	Mucus HPF	Sperm HPF	Yeast HPF	Othr/Uri HPF
1	m	25244	NS	NS	NS	1+	1+	NS	NS	NS	NS
		25245	NS	NS	1-3	3+	2+	NS	1+	NS	NS
		25246	NS	NS	1-3	3+	1+	NS	1+	NS	NS
		25247	NS	NS	4-6	3+	1+	NS	NS	NS	NS
		25248	NS	NS	1-3	3+	1+	NS	1+	NS	NS
		25249	NS	NS	NS	3+	1+	NS	1+	NS	NS
		25250	NS	NS	NS	2+	2+	NS	NS	NS	NS
		25251	NS	NS	1-3	3+	1+	NS	1+	NS	NS
		25252	NS	NS	4-6	3+	1+	NS	NS	NS	NS
		25253	NS	NS	4-6	3+	1+	NS	NS	NS	NS
6	m	25324	NS	NS	1-3	3+	1+	NS	2+	NS	NS
		25325	NS	NS	4-6	3+	1+	NS	1+	NS	NS
		25326	NS	NS	4-6	3+	1+	NS	2+	NS	NS
		25327	NS	NS	7-10	3+	1+	NS	1+	NS	NS
		25328	NS	NS	7-10	3+	1+	NS	1+	NS	NS
		25329	NS	NS	4-6	3+	1+	NS	NS	NS	NS
		25330	NS	NS	1-3	3+	1+	NS	NS	NS	NS
		25331	NS	NS	41-50	3+	1+	NS	1+	NS	NS
		25332	NS	NS	1-3	3+	1+	NS	NS	NS	NS
		25333	NS	NS	4-6	3+	2+	NS	1+	NS	NS

Target Dose: Group 1 - 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 24 (continued): Individual Urinalysis Data

Day 119 Relative to Start Date

Group	Sex	Animal	SG	UpH	URO U/dL	TUVol mL	Color	Clarity	BLO	PRO	UGLU
1	f	25264	1.040	6.5	0.2	3.0	YELLOW	CLOUDY	NEGATIVE	1+	NEGATIVE
		25265	1.017	6.5	0.2	7.0	YELLOW	CLOUDY	NEGATIVE	NEGATIVE	NEGATIVE
		25266	1.016	8.0	0.2	12.0	YELLOW	TURBID	NEGATIVE	NEGATIVE	NEGATIVE
		25267	1.011	7.0	0.2	12.0	YELLOW	CLOUDY	NEGATIVE	NEGATIVE	NEGATIVE
		25268	1.020	7.0	0.2	9.0	YELLOW	CLOUDY	NEGATIVE	NEGATIVE	NEGATIVE
		25269	1.026	6.0	0.2	7.0	YELLOW	CLOUDY	NEGATIVE	TRACE	NEGATIVE
		25270	1.027	6.0	0.2	7.0	YELLOW	CLOUDY	NEGATIVE	TRACE	NEGATIVE
		25271	NSS	NSS	NSS	NSS	NSS	NSS	NSS	NSS	NSS
		25272	1.043	6.0	0.2	3.0	YELLOW	CLOUDY	NEGATIVE	1+	NEGATIVE
		25273	1.012	7.5	0.2	12.0	YELLOW	CLOUDY	NEGATIVE	NEGATIVE	NEGATIVE
11	f	25384	1.012	7.0	0.2	12.0	YELLOW	CLOUDY	NEGATIVE	TRACE	NEGATIVE
		25385	1.013	6.0	0.2	4.0	YELLOW	CLEAR	NEGATIVE	NEGATIVE	NEGATIVE
		25386	1.024	7.0	0.2	6.0	YELLOW	CLOUDY	NEGATIVE	NEGATIVE	NEGATIVE
		25387	1.020	7.5	0.2	7.0	YELLOW	CLOUDY	NEGATIVE	NEGATIVE	NEGATIVE
		25388	1.017	7.0	0.2	12.0	YELLOW	CLEAR	NEGATIVE	TRACE	NEGATIVE
		25389	1.017	6.5	0.2	7.0	YELLOW	CLOUDY	NEGATIVE	NEGATIVE	NEGATIVE
		25390	1.016	6.5	0.2	12.0	YELLOW	CLOUDY	NEGATIVE	NEGATIVE	NEGATIVE
		25391	1.010	7.0	0.2	12.0	YELLOW	CLOUDY	NEGATIVE	NEGATIVE	NEGATIVE
		25392	1.005	7.0	0.2	12.0	YELLOW	CLEAR	NEGATIVE	NEGATIVE	NEGATIVE
		25393	1.017	8.0	0.2	11.0	YELLOW	CLOUDY	NEGATIVE	NEGATIVE	NEGATIVE

Target Dose: Group 1 - 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 24 (continued): Individual Urinalysis Data

Day 119 Relative to Start Date

Group	Sex	Animal	UBILI	NIT	KET	LEU	uRBC HPF	uWBC HPF	EPI HPF	GRAN CA LPF	HYAL CA LPF
1	f	25264	NEGATIVE	NEGATIVE	TRACE	TRACE	NS	NS	NS	NS	NS
		25265	NEGATIVE	NEGATIVE	NEGATIVE	TRACE	NS	NS	NS	NS	NS
		25266	NEGATIVE	POSITIVE	NEGATIVE	TRACE	NS	NS	NS	NS	NS
		25267	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NS	NS	NS	NS	NS
		25268	NEGATIVE	POSITIVE	NEGATIVE	NEGATIVE	NS	NS	NS	NS	NS
		25269	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NS	NS	NS	NS	NS
		25270	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NS	NS	NS	NS	NS
		25271	NSS	NSS	NSS	NSS	NSS	NSS	NSS	NSS	NSS
		25272	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NS	1-3	NS	NS	NS
		25273	NEGATIVE	POSITIVE	NEGATIVE	NEGATIVE	NS	NS	NS	NS	NS
11	f	25384	NEGATIVE	NEGATIVE	NEGATIVE	TRACE	NS	NS	NS	NS	NS
		25385	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NS	NS	NS	NS	NS
		25386	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	1-3	NS	NS	NS	NS
		25387	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NS	NS	NS	NS	NS
		25388	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NS	1-3	NS	NS	NS
		25389	NEGATIVE	NEGATIVE	NEGATIVE	TRACE	NS	NS	NS	NS	NS
		25390	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NS	NS	NS	NS	NS
		25391	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NS	NS	NS	NS	NS
		25392	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NS	NS	NS	NS	NS
		25393	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NS	NS	NS	NS	NS

Target Dose: Group 1 - 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 24 (continued): Individual Urinalysis Data

Day 119 Relative to Start Date

Group	Sex	Animal	Amorph HPF	CAO CRYS HPF	TP CRYS HPF	Bacter HPF	Fecal HPF	Mucus HPF	Sperm HPF	Yeast HPF	Othr/Uri HPF
1	f	25264	NS	NS	NS	2+	1+	NS	NS	NS	NS
		25265	NS	NS	NS	3+	1+	NS	NS	NS	NS
		25266	NS	NS	NS	3+	2+	NS	NS	NS	NS
		25267	NS	NS	1-3	3+	1+	NS	NS	NS	NS
		25268	NS	NS	NS	3+	1+	NS	NS	NS	NS
		25269	NS	NS	NS	3+	1+	NS	NS	NS	NS
		25270	NS	NS	NS	2+	1+	NS	NS	NS	NS
		25271	NSS	NSS	NSS	NSS	NSS	NSS	NSS	NSS	NSS
		25272	NS	NS	NS	1+	1+	NS	NS	NS	NS
		25273	NS	NS	1-3	3+	1+	NS	NS	NS	NS
11	f	25384	NS	NS	NS	3+	1+	NS	NS	NS	NS
		25385	NS	NS	NS	3+	1+	NS	NS	NS	NS
		25386	NS	NS	1-3	3+	2+	NS	NS	NS	NS
		25387	NS	NS	11-20	3+	1+	NS	NS	NS	NS
		25388	NS	NS	NS	3+	1+	NS	NS	NS	NS
		25389	NS	NS	NS	1+	1+	NS	NS	NS	NS
		25390	NS	NS	1-3	3+	1+	NS	NS	NS	NS
		25391	NS	NS	1-3	3+	1+	NS	NS	NS	NS
		25392	NS	NS	NS	3+	1+	NS	NS	NS	NS
		25393	NS	NS	21-40	3+	1+	NS	NS	NS	NS

Target Dose: Group 1 - 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

APPENDIX 25: INDIVIDUAL GROSS PATHOLOGY OBSERVATIONS

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 25: Individual Gross Pathology Observations

Day Numbers Relative to Start Date

Animal No.	Mode Of Death	Death Day	(Week)	Observation(s)
Group: 1 Sex: Male				
25234	TERMINAL KILL	91	(13)	No Visible Lesions
25235	TERMINAL KILL	91	(13)	No Visible Lesions
25236	TERMINAL KILL	91	(13)	No Visible Lesions
25237	TERMINAL KILL	91	(13)	No Visible Lesions
25238	TERMINAL KILL	91	(13)	No Visible Lesions
25239	TERMINAL KILL	91	(13)	No Visible Lesions
25240	TERMINAL KILL	91	(13)	No Visible Lesions
25241	TERMINAL KILL	91	(13)	No Visible Lesions
25242	TERMINAL KILL	91	(13)	No Visible Lesions
25243	TERMINAL KILL	91	(13)	No Visible Lesions
25244	RECOVERY KILL	119	(17)	No Visible Lesions
25245	RECOVERY KILL	119	(17)	No Visible Lesions
25246	RECOVERY KILL	119	(17)	No Visible Lesions
25247	RECOVERY KILL	119	(17)	No Visible Lesions
25248	RECOVERY KILL	119	(17)	No Visible Lesions
25249	RECOVERY KILL	119	(17)	No Visible Lesions
25250	RECOVERY KILL	119	(17)	No Visible Lesions
25251	RECOVERY KILL	119	(17)	No Visible Lesions
25252	RECOVERY KILL	119	(17)	No Visible Lesions
25253	RECOVERY KILL	119	(17)	skin; no correlate with clinical observation
				Any remaining protocol required tissues, which have been examined, have no visible lesions

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 25 (continued): Individual Gross Pathology Observations

Day Numbers Relative to Start Date

Animal No.	Mode Of Death	Death Day	(Week)	Observation(s)
Group: 2 Sex: Male				
25274	TERMINAL KILL	91	(13)	skin; no correlate with clinical observation
				Any remaining protocol required tissues, which have been examined, have no visible lesions
25275	TERMINAL KILL	91	(13)	No Visible Lesions
25276	TERMINAL KILL	91	(13)	No Visible Lesions
25277	TERMINAL KILL	91	(13)	No Visible Lesions
25278	TERMINAL KILL	91	(13)	No Visible Lesions
25279	TERMINAL KILL	91	(13)	No Visible Lesions
25280	TERMINAL KILL	91	(13)	No Visible Lesions
25281	TERMINAL KILL	91	(13)	No Visible Lesions
25282	TERMINAL KILL	91	(13)	No Visible Lesions
25283	TERMINAL KILL	91	(13)	No Visible Lesions
Group: 3 Sex: Male				
25284	TERMINAL KILL	91	(13)	No Visible Lesions
25285	TERMINAL KILL	91	(13)	No Visible Lesions
25286	TERMINAL KILL	91	(13)	No Visible Lesions
25287	TERMINAL KILL	91	(13)	No Visible Lesions
25288	TERMINAL KILL	91	(13)	No Visible Lesions
25289	TERMINAL KILL	91	(13)	No Visible Lesions
25290	TERMINAL KILL	91	(13)	No Visible Lesions
25291	TERMINAL KILL	91	(13)	No Visible Lesions
25292	TERMINAL KILL	91	(13)	No Visible Lesions
25293	TERMINAL KILL	91	(13)	No Visible Lesions

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 25 (continued): Individual Gross Pathology Observations

Day Numbers Relative to Start Date

Animal No.	Mode Of Death	Death Day	Death (Week)	Observation(s)
Group: 4 Sex: Male				
25294	TERMINAL KILL	91	(13)	No Visible Lesions
25295	TERMINAL KILL	91	(13)	skin; no correlate with clinical observation
				Any remaining protocol required tissues, which have been examined, have no visible lesions
25296	TERMINAL KILL	91	(13)	skin; no correlate with clinical observation
				Any remaining protocol required tissues, which have been examined, have no visible lesions
25297	TERMINAL KILL	91	(13)	No Visible Lesions
25298	TERMINAL KILL	91	(13)	skin; no correlate with clinical observation
				Any remaining protocol required tissues, which have been examined, have no visible lesions
25299	TERMINAL KILL	91	(13)	No Visible Lesions
25300	TERMINAL KILL	91	(13)	No Visible Lesions
25301	TERMINAL KILL	91	(13)	No Visible Lesions
25302	TERMINAL KILL	91	(13)	No Visible Lesions
25303	TERMINAL KILL	91	(13)	No Visible Lesions
Group: 5 Sex: Male				
25304	TERMINAL KILL	91	(13)	No Visible Lesions
25305	TERMINAL KILL	91	(13)	No Visible Lesions
25306	TERMINAL KILL	91	(13)	No Visible Lesions
25307	TERMINAL KILL	91	(13)	No Visible Lesions
25308	TERMINAL KILL	91	(13)	No Visible Lesions
25309	TERMINAL KILL	91	(13)	No Visible Lesions
25310	TERMINAL KILL	91	(13)	No Visible Lesions
25311	TERMINAL KILL	91	(13)	No Visible Lesions
25312	TERMINAL KILL	91	(13)	No Visible Lesions
25313	TERMINAL KILL	91	(13)	No Visible Lesions

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 25 (continued): Individual Gross Pathology Observations

Day Numbers Relative to Start Date

Animal No.	Mode Of Death	Death Day	Death (Week)	Observation(s)
Group: 6 Sex: Male				
25314	TERMINAL KILL	91	(13)	No Visible Lesions
25315	TERMINAL KILL	91	(13)	No Visible Lesions
25316	TERMINAL KILL	91	(13)	No Visible Lesions
25317	TERMINAL KILL	91	(13)	No Visible Lesions
25318	TERMINAL KILL	91	(13)	No Visible Lesions
25319	TERMINAL KILL	91	(13)	No Visible Lesions
25320	TERMINAL KILL	91	(13)	No Visible Lesions
25321	TERMINAL KILL	91	(13)	No Visible Lesions
25322	TERMINAL KILL	91	(13)	No Visible Lesions
25323	TERMINAL KILL	91	(13)	No Visible Lesions
25324	RECOVERY KILL	119	(17)	No Visible Lesions
25325	RECOVERY KILL	119	(17)	No Visible Lesions
25326	RECOVERY KILL	119	(17)	No Visible Lesions
25327	RECOVERY KILL	119	(17)	No Visible Lesions
25328	RECOVERY KILL	119	(17)	No Visible Lesions
25329	RECOVERY KILL	119	(17)	No Visible Lesions
25330	RECOVERY KILL	119	(17)	testis; small; right: 25x10x10mm Any remaining protocol required tissues, which have been examined, have no visible lesions
25331	RECOVERY KILL	119	(17)	No Visible Lesions
25332	RECOVERY KILL	119	(17)	No Visible Lesions
25333	RECOVERY KILL	119	(17)	No Visible Lesions

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 25 (continued): Individual Gross Pathology Observations

Day Numbers Relative to Start Date

Animal No.	Mode Of Death	Death Day	Death (Week)	Observation(s)
Group: 1 Sex: Female				
25254	TERMINAL KILL	91	(13)	skin; no correlate with clinical observation
				Any remaining protocol required tissues, which have been examined, have no visible lesions
25255	TERMINAL KILL	91	(13)	No Visible Lesions
25256	TERMINAL KILL	91	(13)	No Visible Lesions
25257	TERMINAL KILL	91	(13)	No Visible Lesions
25258	TERMINAL KILL	91	(13)	No Visible Lesions
25259	TERMINAL KILL	91	(13)	No Visible Lesions
25260	TERMINAL KILL	91	(13)	No Visible Lesions
25261	TERMINAL KILL	91	(13)	No Visible Lesions
25262	TERMINAL KILL	91	(13)	No Visible Lesions
25263	TERMINAL KILL	91	(13)	No Visible Lesions
25264	RECOVERY KILL	119	(17)	No Visible Lesions
25265	RECOVERY KILL	119	(17)	No Visible Lesions
25266	RECOVERY KILL	119	(17)	skin; no correlate with clinical observation
				Any remaining protocol required tissues, which have been examined, have no visible lesions
25267	RECOVERY KILL	119	(17)	No Visible Lesions
25268	RECOVERY KILL	119	(17)	No Visible Lesions
25269	RECOVERY KILL	119	(17)	No Visible Lesions
25270	RECOVERY KILL	119	(17)	No Visible Lesions
25271	RECOVERY KILL	119	(17)	No Visible Lesions
25272	RECOVERY KILL	119	(17)	No Visible Lesions
25273	RECOVERY KILL	119	(17)	No Visible Lesions

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 25 (continued): Individual Gross Pathology Observations

Day Numbers Relative to Start Date

Animal No.	Mode Of Death	Death Day	Death (Week)	Observation(s)
Group: 7 Sex: Female				
25334	TERMINAL KILL	91	(13)	No Visible Lesions
25335	TERMINAL KILL	91	(13)	No Visible Lesions
25336	TERMINAL KILL	91	(13)	No Visible Lesions
25337	TERMINAL KILL	91	(13)	No Visible Lesions
25338	TERMINAL KILL	91	(13)	No Visible Lesions
25339	TERMINAL KILL	91	(13)	No Visible Lesions
25340	TERMINAL KILL	91	(13)	No Visible Lesions
25341	TERMINAL KILL	91	(13)	No Visible Lesions
25342	TERMINAL KILL	91	(13)	No Visible Lesions
25343	TERMINAL KILL	91	(13)	No Visible Lesions
Group: 8 Sex: Female				
25344	TERMINAL KILL	91	(13)	No Visible Lesions
25345	TERMINAL KILL	91	(13)	No Visible Lesions
25346	TERMINAL KILL	91	(13)	No Visible Lesions
25347	TERMINAL KILL	91	(13)	No Visible Lesions
25348	TERMINAL KILL	91	(13)	No Visible Lesions
25349	TERMINAL KILL	91	(13)	No Visible Lesions
25350	TERMINAL KILL	91	(13)	No Visible Lesions
25351	TERMINAL KILL	91	(13)	No Visible Lesions
25352	TERMINAL KILL	91	(13)	No Visible Lesions
25353	TERMINAL KILL	91	(13)	No Visible Lesions

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 25 (continued): Individual Gross Pathology Observations

Day Numbers Relative to Start Date

Animal No.	Mode Of Death	Death Day	Death (Week)	Observation(s)
Group: 9 Sex: Female				
25354	TERMINAL KILL	91	(13)	No Visible Lesions
25355	TERMINAL KILL	91	(13)	No Visible Lesions
25356	TERMINAL KILL	91	(13)	No Visible Lesions
25357	TERMINAL KILL	91	(13)	No Visible Lesions
25358	TERMINAL KILL	91	(13)	No Visible Lesions
25359	TERMINAL KILL	91	(13)	No Visible Lesions
25360	TERMINAL KILL	91	(13)	No Visible Lesions
25361	TERMINAL KILL	91	(13)	No Visible Lesions
25362	TERMINAL KILL	91	(13)	uterus; distention; fluid-filled; bilateral: Clear
				Any remaining protocol required tissues, which have been examined, have no visible lesions
25363	TERMINAL KILL	91	(13)	uterus; distention; fluid-filled; bilateral: Clear
				Any remaining protocol required tissues, which have been examined, have no visible lesions
Group: 10 Sex: Female				
25364	TERMINAL KILL	91	(13)	No Visible Lesions
25365	TERMINAL KILL	91	(13)	No Visible Lesions
25366	TERMINAL KILL	91	(13)	uterus; distention; fluid-filled; bilateral: Clear
				Any remaining protocol required tissues, which have been examined, have no visible lesions
25367	TERMINAL KILL	91	(13)	No Visible Lesions
25368	TERMINAL KILL	91	(13)	skin; no correlate with clinical observation
				uterus; distention; fluid-filled; bilateral: Clear
				Any remaining protocol required tissues, which have been examined, have no visible lesions
25369	TERMINAL KILL	91	(13)	No Visible Lesions
25370	TERMINAL KILL	91	(13)	No Visible Lesions
25371	TERMINAL KILL	91	(13)	No Visible Lesions
25372	TERMINAL KILL	91	(13)	No Visible Lesions
25373	TERMINAL KILL	91	(13)	No Visible Lesions

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 25 (continued): Individual Gross Pathology Observations

Day Numbers Relative to Start Date

Animal No.	Mode Of Death	Death Day	(Week)	Observation(s)
Group: 11 Sex: Female				
25374	TERMINAL KILL	91	(13)	No Visible Lesions
25375	TERMINAL KILL	91	(13)	No Visible Lesions
25376	TERMINAL KILL	91	(13)	No Visible Lesions
25377	TERMINAL KILL	91	(13)	No Visible Lesions
25378	TERMINAL KILL	91	(13)	No Visible Lesions
25379	TERMINAL KILL	91	(13)	No Visible Lesions
25380	TERMINAL KILL	91	(13)	No Visible Lesions
25381	TERMINAL KILL	91	(13)	skin; no correlate with clinical observation
				Any remaining protocol required tissues, which have been examined, have no visible lesions
25382	TERMINAL KILL	91	(13)	No Visible Lesions
25383	TERMINAL KILL	91	(13)	No Visible Lesions
25384	RECOVERY KILL	119	(17)	No Visible Lesions
25385	RECOVERY KILL	119	(17)	No Visible Lesions
25386	RECOVERY KILL	119	(17)	No Visible Lesions
25387	RECOVERY KILL	119	(17)	No Visible Lesions
25388	RECOVERY KILL	119	(17)	No Visible Lesions
25389	RECOVERY KILL	119	(17)	skin; no correlate with clinical observation
				Any remaining protocol required tissues, which have been examined, have no visible lesions
25390	RECOVERY KILL	119	(17)	No Visible Lesions
25391	RECOVERY KILL	119	(17)	No Visible Lesions
25392	RECOVERY KILL	119	(17)	No Visible Lesions
25393	RECOVERY KILL	119	(17)	No Visible Lesions

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

APPENDIX 26: INDIVIDUAL ORGAN WEIGHT DATA

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 26: Individual Organ Weight Data

Day 91 Relative to Start Date

			TBW	--- Brain ---		---- Adrenal Gland -----			------- Heart ---------			------- Kidneys -------		
Group	Sex	Animal	g	Abs	%TBW	Abs	%TBW	/BR	Abs	%TBW	/BR	Abs	%TBW	/BR
1	m	25234	589.6	2.160	0.3664	0.0603	0.0102	0.0279	1.817	0.3082	0.8412	3.590	0.6089	1.6620
		25235	658.0	2.152	0.3271	0.0616	0.0094	0.0286	1.738	0.2641	0.8076	3.952	0.6006	1.8364
		25236	558.5	2.269	0.4063	0.0573	0.0103	0.0253	1.678	0.3004	0.7395	3.003	0.5377	1.3235
		25237	618.6	1.923	0.3109	0.0618	0.0100	0.0321	1.625	0.2627	0.8450	3.440	0.5561	1.7889
		25238	532.3	2.367	0.4447	0.0424	0.0080	0.0179	1.459	0.2741	0.6164	2.952	0.5546	1.2471
		25239	611.7	2.290	0.3744	0.0480	0.0078	0.0210	1.797	0.2938	0.7847	2.960	0.4839	1.2926
		25240	584.9	2.178	0.3724	0.0652	0.0111	0.0299	1.670	0.2855	0.7668	2.769	0.4734	1.2713
		25241	577.5	2.138	0.3702	0.0525	0.0091	0.0246	1.803	0.3122	0.8433	2.745	0.4753	1.2839
		25242	601.4	2.236	0.3718	0.0605	0.0101	0.0271	1.511	0.2512	0.6758	3.245	0.5396	1.4513
		25243	578.0	2.269	0.3926	0.0509	0.0088	0.0224	1.733	0.2998	0.7638	3.208	0.5550	1.4138
2	m	25274	649.2	2.176	0.3352	0.0590	0.0091	0.0271	1.725	0.2657	0.7927	2.882	0.4439	1.3244
		25275	749.9	2.523	0.3364	0.0581	0.0077	0.0230	2.043	0.2724	0.8098	3.431	0.4575	1.3599
		25276	624.0	2.263	0.3627	0.0329	0.0053	0.0145	1.622	0.2599	0.7167	3.634	0.5824	1.6058
		25277	619.2	2.304	0.3721	0.0611	0.0099	0.0265	1.654	0.2671	0.7179	3.895	0.6290	1.6905
		25278	603.5	2.252	0.3732	0.0542	0.0090	0.0241	2.215	0.3670	0.9836	2.861	0.4741	1.2704
		25279	557.3	2.112	0.3790	0.0636	0.0114	0.0301	1.589	0.2851	0.7524	3.216	0.5771	1.5227
		25280	599.2	2.181	0.3640	0.0512	0.0085	0.0235	1.919	0.3203	0.8799	3.352	0.5594	1.5369
		25281	607.5	2.505	0.4123	0.0574	0.0094	0.0229	1.814	0.2986	0.7242	3.129	0.5151	1.2491
		25282	503.9	2.241	0.4447	0.0442	0.0088	0.0197	1.525	0.3026	0.6805	2.884	0.5723	1.2869
		25283	525.7	2.390	0.4546	0.0402	0.0076	0.0168	1.545	0.2939	0.6464	3.135	0.5963	1.3117

Organ weight data are presented as terminal body weights (TBW, g), absolute weights (Abs, g), organ-to-body weight percentages (%TBW) and organ-to-brain weight ratios (/BR).

Target Dose: Group 1 - 0 mg/kg/day Groups 2 and 7 - 1 mg/kg/day Groups 3 and 8 - 3 mg/kg/day
Groups 4 and 9 - 10 mg/kg/day Groups 5 and 10 - 30 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 26 (continued): Individual Organ Weight Data

Day 91 Relative to Start Date

			TBW	--- Brain ---		---- Adrenal Gland -----			------- Heart ---------			------- Kidneys -------		
Group	Sex	Animal	g	Abs	%TBW	Abs	%TBW	/BR	Abs	%TBW	/BR	Abs	%TBW	/BR
3	m	25284	573.3	2.451	0.4275	0.0482	0.0084	0.0197	1.744	0.3042	0.7115	3.091	0.5392	1.2611
		25285	485.2	2.300	0.4740	0.0417	0.0086	0.0181	1.441	0.2970	0.6265	3.180	0.6554	1.3826
		25286	685.8	2.274	0.3316	0.0615	0.0090	0.0270	2.084	0.3039	0.9164	3.346	0.4879	1.4714
		25287	535.3	2.274	0.4248	0.0439	0.0082	0.0193	1.585	0.2961	0.6970	2.725	0.5091	1.1983
		25288	565.8	2.317	0.4095	0.0595	0.0105	0.0257	1.768	0.3125	0.7631	3.014	0.5327	1.3008
		25289	550.3	2.281	0.4145	0.0539	0.0098	0.0236	1.947	0.3538	0.8536	3.327	0.6046	1.4586
		25290	597.6	2.195	0.3673	0.0541	0.0091	0.0246	1.854	0.3102	0.8446	3.799	0.6357	1.7308
		25291	558.4	2.290	0.4101	0.0442	0.0079	0.0193	1.663	0.2978	0.7262	3.131	0.5607	1.3672
		25292	616.8	2.279	0.3695	0.0362	0.0059	0.0159	1.592	0.2581	0.6986	3.124	0.5065	1.3708
		25293	615.4	2.232	0.3627	0.0482	0.0078	0.0216	1.918	0.3117	0.8593	3.565	0.5793	1.5972
4	m	25294	538.6	2.114	0.3925	0.0415	0.0077	0.0196	1.696	0.3149	0.8023	3.350	0.6220	1.5847
		25295	593.8	2.241	0.3774	0.0734	0.0124	0.0328	1.707	0.2875	0.7617	3.336	0.5618	1.4886
		25296	476.6	2.182	0.4578	0.0484	0.0102	0.0222	1.548	0.3248	0.7094	2.782	0.5837	1.2750
		25297	549.5	2.259	0.4111	0.0657	0.0120	0.0291	1.827	0.3325	0.8088	2.950	0.5369	1.3059
		25298	552.8	2.223	0.4021	0.0627	0.0113	0.0282	1.658	0.2999	0.7458	3.165	0.5725	1.4238
		25299	536.6	2.194	0.4089	0.0463	0.0086	0.0211	1.548	0.2885	0.7056	3.270	0.6094	1.4904
		25300	715.1	2.441	0.3414	0.0639	0.0089	0.0262	2.218	0.3102	0.9086	3.452	0.4827	1.4142
		25301	632.3	2.196	0.3473	0.0457	0.0072	0.0208	1.838	0.2907	0.8370	3.407	0.5388	1.5515
		25302	538.5	2.179	0.4046	0.0595	0.0110	0.0273	1.845	0.3426	0.8467	3.114	0.5783	1.4291
		25303	610.1	2.154	0.3531	0.0484	0.0079	0.0225	2.017	0.3306	0.9364	3.756	0.6156	1.7437

Organ weight data are presented as terminal body weights (TBW, g), absolute weights (Abs, g), organ-to-body weight percentages (%TBW) and organ-to-brain weight ratios (/BR).

Target Dose: Group 1 - 0 mg/kg/day Groups 2 and 7 - 1 mg/kg/day Groups 3 and 8 - 3 mg/kg/day
Groups 4 and 9 - 10 mg/kg/day Groups 5 and 10 - 30 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 26 (continued): Individual Organ Weight Data

Day 91 Relative to Start Date

			TBW	--- Brain ---		---- Adrenal Gland -----			------- Heart ---------			------- Kidneys -------		
Group	Sex	Animal	g	Abs	%TBW	Abs	%TBW	/BR	Abs	%TBW	/BR	Abs	%TBW	/BR
5	m	25304	496.9	2.083	0.4192	0.0490	0.0099	0.0235	1.516	0.3051	0.7278	2.540	0.5112	1.2194
		25305	541.5	2.367	0.4371	0.0540	0.0100	0.0228	1.709	0.3156	0.7220	3.258	0.6017	1.3764
		25306	544.0	2.285	0.4200	0.0489	0.0090	0.0214	1.905	0.3502	0.8337	3.532	0.6493	1.5457
		25307	545.1	2.204	0.4043	0.0537	0.0099	0.0244	1.532	0.2810	0.6951	2.601	0.4772	1.1801
		25308	610.9	2.324	0.3804	0.0538	0.0088	0.0231	1.907	0.3122	0.8206	3.554	0.5818	1.5293
		25309	560.3	2.262	0.4037	0.0496	0.0089	0.0219	1.598	0.2852	0.7065	3.430	0.6122	1.5164
		25310	595.2	2.221	0.3732	0.0459	0.0077	0.0207	1.588	0.2668	0.7150	3.076	0.5168	1.3850
		25311	588.2	2.188	0.3720	0.0667	0.0113	0.0305	1.955	0.3324	0.8935	3.019	0.5133	1.3798
		25312	595.8	2.411	0.4047	0.0486	0.0082	0.0202	1.829	0.3070	0.7586	3.584	0.6015	1.4865
		25313	572.0	2.303	0.4026	0.0805	0.0141	0.0350	1.843	0.3222	0.8003	2.640	0.4615	1.1463
6	m	25314	497.2	2.309	0.4644	0.0556	0.0112	0.0241	1.538	0.3093	0.6661	3.056	0.6146	1.3235
		25315	524.8	2.324	0.4428	0.0638	0.0122	0.0275	1.399	0.2666	0.6020	2.732	0.5206	1.1756
		25316	540.9	2.377	0.4395	0.0584	0.0108	0.0246	1.887	0.3489	0.7939	3.009	0.5563	1.2659
		25317	681.1	2.037	0.2991	0.0530	0.0078	0.0260	1.647	0.2418	0.8085	3.509	0.5152	1.7226
		25318	504.4	2.227	0.4415	0.0529	0.0105	0.0238	1.474	0.2922	0.6619	2.785	0.5521	1.2506
		25319	541.0	2.437	0.4505	0.0431	0.0080	0.0177	1.579	0.2919	0.6479	3.290	0.6081	1.3500
		25320	616.8	2.418	0.3920	0.0464	0.0075	0.0192	1.737	0.2816	0.7184	3.628	0.5882	1.5004
		25321	533.1	2.126	0.3988	0.0620	0.0116	0.0292	1.717	0.3221	0.8076	2.917	0.5472	1.3721
		25322	529.3	2.199	0.4155	0.0397	0.0075	0.0181	1.586	0.2996	0.7212	2.748	0.5192	1.2497
		25323	399.0	2.038	0.5108	0.0361	0.0090	0.0177	1.198	0.3003	0.5878	2.229	0.5586	1.0937

Organ weight data are presented as terminal body weights (TBW, g), absolute weights (Abs, g), organ-to-body weight percentages (%TBW) and organ-to-brain weight ratios (/BR).

Target Dose: Group 1 - 0 mg/kg/day Groups 2 and 7 - 1 mg/kg/day Groups 3 and 8 - 3 mg/kg/day
Groups 4 and 9 - 10 mg/kg/day Groups 5 and 10 - 30 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 26 (continued): Individual Organ Weight Data

Day 91 Relative to Start Date

			Liver			Spleen			Thymus			Thyroid		
Group	Sex	Animal	Abs	%TBW	/BR	Abs	%TBW	/BR	Abs	%TBW	/BR	Abs	%TBW	/BR
1	m	25234	14.870	2.5220	6.8843	1.172	0.1988	0.5426	0.604	0.1024	0.2796	0.0467	0.0079	0.0216
		25235	15.839	2.4071	7.3601	1.215	0.1847	0.5646	0.751	0.1141	0.3490	0.0291	0.0044	0.0135
		25236	14.093	2.5234	6.2111	1.076	0.1927	0.4742	0.311	0.0557	0.1371	0.0264	0.0047	0.0116
		25237	16.681	2.6966	8.6745	0.885	0.1431	0.4602	0.499	0.0807	0.2595	0.0342	0.0055	0.0178
		25238	12.627	2.3722	5.3346	0.836	0.1571	0.3532	0.363	0.0682	0.1534	0.0245	0.0046	0.0104
		25239	15.500	2.5339	6.7686	0.760	0.1242	0.3319	0.302	0.0494	0.1319	0.0318	0.0052	0.0139
		25240	12.755	2.1807	5.8563	0.808	0.1381	0.3710	0.334	0.0571	0.1534	0.0304	0.0052	0.0140
		25241	14.786	2.5603	6.9158	0.883	0.1529	0.4130	0.517	0.0895	0.2418	0.0222	0.0038	0.0104
		25242	13.759	2.2878	6.1534	0.688	0.1144	0.3077	0.496	0.0825	0.2218	0.0495	0.0082	0.0221
		25243	13.908	2.4062	6.1296	1.024	0.1772	0.4513	0.408	0.0706	0.1798	0.0213	0.0037	0.0094
2	m	25274	14.199	2.1872	6.5253	0.987	0.1520	0.4536	0.618	0.0952	0.2840	0.0301	0.0046	0.0138
		25275	18.300	2.4403	7.2533	1.493	0.1991	0.5918	0.685	0.0913	0.2715	0.0287	0.0038	0.0114
		25276	16.441	2.6348	7.2651	0.813	0.1303	0.3593	0.555	0.0889	0.2452	0.0355	0.0057	0.0157
		25277	18.137	2.9291	7.8720	1.154	0.1864	0.5009	0.521	0.0841	0.2261	0.0503	0.0081	0.0218
		25278	17.331	2.8717	7.6958	0.824	0.1365	0.3659	0.428	0.0709	0.1901	0.0275	0.0046	0.0122
		25279	13.308	2.3879	6.3011	0.965	0.1732	0.4569	0.370	0.0664	0.1752	0.0274	0.0049	0.0130
		25280	16.001	2.6704	7.3365	1.005	0.1677	0.4608	0.423	0.0706	0.1939	0.0245	0.0041	0.0112
		25281	12.558	2.0672	5.0132	1.206	0.1985	0.4814	0.310	0.0510	0.1238	0.0435	0.0072	0.0174
		25282	10.829	2.1490	4.8322	0.823	0.1633	0.3672	0.264	0.0524	0.1178	0.0240	0.0048	0.0107
		25283	15.719	2.9901	6.5770	1.257	0.2391	0.5259	0.410	0.0780	0.1715	0.0357	0.0068	0.0149

Organ weight data are presented as terminal body weights (TBW, g), absolute weights (Abs, g), organ-to-body weight percentages (%TBW) and organ-to-brain weight ratios (/BR).

Target Dose: Group 1 - 0 mg/kg/day Groups 2 and 7 - 1 mg/kg/day Groups 3 and 8 - 3 mg/kg/day
Groups 4 and 9 - 10 mg/kg/day Groups 5 and 10 - 30 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 26 (continued): Individual Organ Weight Data

Day 91 Relative to Start Date

			Liver			Spleen			Thymus			Thyroid		
Group	Sex	Animal	Abs	%TBW	/BR	Abs	%TBW	/BR	Abs	%TBW	/BR	Abs	%TBW	/BR
3	m	25284	14.772	2.5767	6.0269	0.957	0.1669	0.3905	0.566	0.0987	0.2309	0.0527	0.0092	0.0215
		25285	11.386	2.3467	4.9504	0.890	0.1834	0.3870	0.305	0.0629	0.1326	0.0205	0.0042	0.0089
		25286	16.415	2.3936	7.2186	1.109	0.1617	0.4877	0.373	0.0544	0.1640	0.0291	0.0042	0.0128
		25287	11.760	2.1969	5.1715	1.058	0.1976	0.4653	0.407	0.0760	0.1790	0.0246	0.0046	0.0108
		25288	14.251	2.5187	6.1506	1.012	0.1789	0.4368	0.485	0.0857	0.2093	0.0320	0.0057	0.0138
		25289	12.913	2.3465	5.6611	0.893	0.1623	0.3915	0.357	0.0649	0.1565	0.0256	0.0047	0.0112
		25290	16.070	2.6891	7.3212	0.993	0.1662	0.4524	0.460	0.0770	0.2096	0.0269	0.0045	0.0123
		25291	11.893	2.1298	5.1934	0.829	0.1485	0.3620	0.279	0.0500	0.1218	0.0265	0.0047	0.0116
		25292	15.368	2.4916	6.7433	0.793	0.1286	0.3480	0.372	0.0603	0.1632	0.0277	0.0045	0.0122
		25293	14.853	2.4136	6.6546	0.899	0.1461	0.4028	0.235	0.0382	0.1053	0.0275	0.0045	0.0123
4	m	25294	12.363	2.2954	5.8482	0.890	0.1652	0.4210	0.338	0.0628	0.1599	0.0167	0.0031	0.0079
		25295	13.648	2.2984	6.0901	0.940	0.1583	0.4195	0.307	0.0517	0.1370	0.0232	0.0039	0.0104
		25296	11.333	2.3779	5.1939	0.907	0.1903	0.4157	0.305	0.0640	0.1398	0.0269	0.0056	0.0123
		25297	13.926	2.5343	6.1647	1.274	0.2318	0.5640	0.199	0.0362	0.0881	0.0194	0.0035	0.0086
		25298	13.297	2.4054	5.9816	0.942	0.1704	0.4238	0.455	0.0823	0.2047	0.0417	0.0075	0.0188
		25299	12.913	2.4064	5.8856	0.945	0.1761	0.4307	0.183	0.0341	0.0834	0.0254	0.0047	0.0116
		25300	19.960	2.7912	8.1770	1.023	0.1431	0.4191	0.496	0.0694	0.2032	0.0341	0.0048	0.0140
		25301	16.280	2.5747	7.4135	1.118	0.1768	0.5091	0.433	0.0685	0.1972	0.0296	0.0047	0.0135
		25302	13.271	2.4644	6.0904	0.890	0.1653	0.4084	0.404	0.0750	0.1854	0.0276	0.0051	0.0127
		25303	14.530	2.3816	6.7456	0.984	0.1613	0.4568	0.485	0.0795	0.2252	0.0364	0.0060	0.0169

Organ weight data are presented as terminal body weights (TBW, g), absolute weights (Abs, g), organ-to-body weight percentages (%TBW) and organ-to-brain weight ratios (/BR).

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 26 (continued): Individual Organ Weight Data

Day 91 Relative to Start Date

			Liver			Spleen			Thymus			Thyroid		
Group	Sex	Animal	Abs	%TBW	/BR	Abs	%TBW	/BR	Abs	%TBW	/BR	Abs	%TBW	/BR
5	m	25304	10.831	2.1797	5.1997	0.804	0.1618	0.3860	0.264	0.0531	0.1267	0.0307	0.0062	0.0147
		25305	14.243	2.6303	6.0173	0.830	0.1533	0.3507	0.446	0.0824	0.1884	0.0243	0.0045	0.0103
		25306	14.715	2.7050	6.4398	0.972	0.1787	0.4254	0.448	0.0824	0.1961	0.0247	0.0045	0.0108
		25307	11.410	2.0932	5.1770	0.699	0.1282	0.3172	0.321	0.0589	0.1456	0.0188	0.0034	0.0085
		25308	14.183	2.3217	6.1028	0.991	0.1622	0.4264	0.328	0.0537	0.1411	0.0242	0.0040	0.0104
		25309	12.582	2.2456	5.5623	1.026	0.1831	0.4536	0.308	0.0550	0.1362	0.0209	0.0037	0.0092
		25310	14.801	2.4867	6.6641	0.905	0.1520	0.4075	0.484	0.0813	0.2179	0.0329	0.0055	0.0148
		25311	14.166	2.4084	6.4744	0.972	0.1652	0.4442	0.423	0.0719	0.1933	0.0251	0.0043	0.0115
		25312	14.885	2.4983	6.1738	1.201	0.2016	0.4981	0.582	0.0977	0.2414	0.0304	0.0051	0.0126
		25313	13.229	2.3128	5.7442	1.147	0.2005	0.4980	0.475	0.0830	0.2063	0.0253	0.0044	0.0110
6	m	25314	10.333	2.0782	4.4751	0.802	0.1613	0.3473	0.284	0.0571	0.1230	0.0291	0.0059	0.0126
		25315	11.083	2.1119	4.7689	0.898	0.1711	0.3864	0.455	0.0867	0.1958	0.0356	0.0068	0.0153
		25316	12.482	2.3076	5.2512	0.882	0.1631	0.3711	0.332	0.0614	0.1397	0.0225	0.0042	0.0095
		25317	17.334	2.5450	8.5096	1.369	0.2010	0.6721	0.544	0.0799	0.2671	0.0445	0.0065	0.0218
		25318	12.288	2.4362	5.5177	0.943	0.1870	0.4234	0.277	0.0549	0.1244	0.0293	0.0058	0.0132
		25319	13.197	2.4394	5.4153	0.852	0.1575	0.3496	0.519	0.0959	0.2130	0.0524	0.0097	0.0215
		25320	15.720	2.5486	6.5012	0.739	0.1198	0.3056	0.436	0.0707	0.1803	0.0568	0.0092	0.0235
		25321	11.985	2.2482	5.6373	0.944	0.1771	0.4440	0.343	0.0643	0.1613	0.0202	0.0038	0.0095
		25322	11.916	2.2513	5.4188	0.724	0.1368	0.3292	0.341	0.0644	0.1551	0.0285	0.0054	0.0130
		25323	8.316	2.0842	4.0805	0.500	0.1253	0.2453	0.318	0.0797	0.1560	0.0195	0.0049	0.0096

Organ weight data are presented as terminal body weights (TBW, g), absolute weights (Abs, g), organ-to-body weight percentages (%TBW) and organ-to-brain weight ratios (/BR).

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 26 (continued): Individual Organ Weight Data

Day 91 Relative to Start Date

			Testes						Testes		
Group	Sex	Animal	Abs	%TBW	/BR	Group	Sex	Animal	Abs	%TBW	/BR
1	m	25234	5.380	0.9125	2.4907	3	m	25284	5.279	0.9208	2.1538
		25235	5.475	0.8321	2.5441			25285	4.752	0.9794	2.0661
		25236	4.815	0.8621	2.1221			25286	5.635	0.8217	2.4780
		25237	5.070	0.8196	2.6365			25287	5.457	1.0194	2.3997
		25238	5.169	0.9711	2.1838			25288	4.807	0.8496	2.0747
		25239	5.610	0.9171	2.4498			25289	4.763	0.8655	2.0881
		25240	5.701	0.9747	2.6175			25290	5.908	0.9886	2.6916
		25241	4.686	0.8114	2.1918			25291	5.388	0.9649	2.3528
		25242	5.292	0.8799	2.3667			25292	5.045	0.8179	2.2137
		25243	5.392	0.9329	2.3764			25293	5.164	0.8391	2.3136
2	m	25274	5.518	0.8500	2.5358	4	m	25294	5.086	0.9443	2.4059
		25275	5.889	0.7853	2.3341			25295	5.297	0.8921	2.3637
		25276	5.396	0.8647	2.3844			25296	5.175	1.0858	2.3717
		25277	5.527	0.8926	2.3989			25297	4.685	0.8526	2.0739
		25278	3.811	0.6315	1.6923			25298	3.230	0.5843	1.4530
		25279	5.256	0.9431	2.4886			25299	5.017	0.9350	2.2867
		25280	5.589	0.9327	2.5626			25300	4.940	0.6908	2.0238
		25281	5.702	0.9386	2.2762			25301	5.631	0.8906	2.5642
		25282	5.499	1.0913	2.4538			25302	5.183	0.9625	2.3786
		25283	5.430	1.0329	2.2720			25303	5.488	0.8995	2.5478

Organ weight data are presented as terminal body weights (TBW, g), absolute weights (Abs, g), organ-to-body weight percentages (%TBW) and organ-to-brain weight ratios (/BR).

Target Dose: Group 1 - 0 mg/kg/day Groups 2 and 7 - 1 mg/kg/day Groups 3 and 8 - 3 mg/kg/day
Groups 4 and 9 - 10 mg/kg/day Groups 5 and 10 - 30 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 26 (continued): Individual Organ Weight Data

Day 91 Relative to Start Date

			Testes						Testes		
Group	Sex	Animal	Abs	%TBW	/BR	Group	Sex	Animal	Abs	%TBW	/BR
5	m	25304	4.711	0.9481	2.2616	6	m	25314	4.584	0.9220	1.9853
		25305	5.174	0.9555	2.1859			25315	5.031	0.9587	2.1648
		25306	5.345	0.9825	2.3392			25316	5.426	1.0031	2.2827
		25307	4.720	0.8659	2.1416			25317	5.703	0.8373	2.7997
		25308	5.368	0.8787	2.3098			25318	5.044	1.0000	2.2649
		25309	5.647	1.0079	2.4965			25319	5.277	0.9754	2.1654
		25310	5.285	0.8879	2.3796			25320	3.664	0.5940	1.5153
		25311	5.768	0.9806	2.6362			25321	4.918	0.9225	2.3133
		25312	5.805	0.9743	2.4077			25322	4.613	0.8715	2.0978
		25313	6.098	1.0661	2.6479			25323	3.631	0.9100	1.7816

Organ weight data are presented as terminal body weights (TBW, g), absolute weights (Abs, g), organ-to-body weight percentages (%TBW) and organ-to-brain weight ratios (/BR).

Target Dose: Group 1 - 0 mg/kg/day Groups 2 and 7 - 1 mg/kg/day Groups 3 and 8 - 3 mg/kg/day
Groups 4 and 9 - 10 mg/kg/day Groups 5 and 10 - 30 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 26 (continued): Individual Organ Weight Data

Day 91 Relative to Start Date

			TBW	--- Brain ---		---- Adrenal Gland -----			------- Heart ---------			------- Kidneys -------		
Group	Sex	Animal	g	Abs	%TBW	Abs	%TBW	/BR	Abs	%TBW	/BR	Abs	%TBW	/BR
1	f	25254	293.7	2.069	0.7045	0.0647	0.0220	0.0313	1.060	0.3609	0.5123	1.823	0.6207	0.8811
		25255	254.5	2.073	0.8145	0.0629	0.0247	0.0303	0.958	0.3764	0.4621	1.636	0.6428	0.7892
		25256	230.8	1.752	0.7591	0.0451	0.0195	0.0257	1.017	0.4406	0.5805	1.600	0.6932	0.9132
		25257	268.8	1.972	0.7336	0.0620	0.0231	0.0314	1.102	0.4100	0.5588	1.766	0.6570	0.8955
		25258	331.8	2.173	0.6549	0.0619	0.0187	0.0285	0.878	0.2646	0.4040	1.738	0.5238	0.7998
		25259	238.5	1.971	0.8264	0.0453	0.0190	0.0230	1.033	0.4331	0.5241	1.907	0.7996	0.9675
		25260	283.9	2.160	0.7608	0.0423	0.0149	0.0196	0.973	0.3427	0.4505	1.612	0.5678	0.7463
		25261	332.5	1.939	0.5832	0.0680	0.0205	0.0351	1.056	0.3176	0.5446	1.921	0.5777	0.9907
		25262	278.3	2.116	0.7603	0.0618	0.0222	0.0292	1.359	0.4883	0.6422	1.780	0.6396	0.8412
		25263	291.6	2.110	0.7236	0.0696	0.0239	0.0330	0.801	0.2747	0.3796	1.685	0.5778	0.7986
7	f	25334	240.7	2.125	0.8828	0.0518	0.0215	0.0244	0.738	0.3066	0.3473	1.560	0.6481	0.7341
		25335	273.2	2.079	0.7610	0.0562	0.0206	0.0270	1.044	0.3821	0.5022	1.739	0.6365	0.8365
		25336	316.2	2.134	0.6749	0.0647	0.0205	0.0303	1.061	0.3355	0.4972	1.830	0.5787	0.8575
		25337	307.2	1.993	0.6488	0.0614	0.0200	0.0308	1.025	0.3337	0.5143	1.724	0.5612	0.8650
		25338	283.6	1.990	0.7017	0.0421	0.0148	0.0212	0.929	0.3276	0.4668	1.497	0.5279	0.7523
		25339	295.4	1.969	0.6666	0.0662	0.0224	0.0336	0.953	0.3226	0.4840	1.524	0.5159	0.7740
		25340	247.1	1.985	0.8033	0.0567	0.0229	0.0286	0.830	0.3359	0.4181	1.648	0.6669	0.8302
		25341	281.8	1.963	0.6966	0.0477	0.0169	0.0243	0.982	0.3485	0.5003	1.629	0.5781	0.8299
		25342	295.8	1.965	0.6643	0.0502	0.0170	0.0255	1.052	0.3556	0.5354	1.772	0.5991	0.9018
		25343	298.6	1.997	0.6688	0.0638	0.0214	0.0319	1.143	0.3828	0.5724	1.730	0.5794	0.8663

Organ weight data are presented as terminal body weights (TBW, g), absolute weights (Abs, g), organ-to-body weight percentages (%TBW) and organ-to-brain weight ratios (/BR).

Target Dose: Group 1 - 0 mg/kg/day Groups 2 and 7 - 1 mg/kg/day Groups 3 and 8 - 3 mg/kg/day
Groups 4 and 9 - 10 mg/kg/day Groups 5 and 10 - 30 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 26 (continued): Individual Organ Weight Data

Day 91 Relative to Start Date

			TBW	--- Brain ---		---- Adrenal Gland -----			------- Heart ---------			------- Kidneys -------		
Group	Sex	Animal	g	Abs	%TBW	Abs	%TBW	/BR	Abs	%TBW	/BR	Abs	%TBW	/BR
8	f	25344	316.7	2.012	0.6353	0.0732	0.0231	0.0364	1.001	0.3161	0.4975	1.836	0.5797	0.9125
		25345	256.4	1.966	0.7668	0.0462	0.0180	0.0235	0.962	0.3752	0.4893	1.728	0.6739	0.8789
		25346	258.1	1.654	0.6408	0.0482	0.0187	0.0291	0.934	0.3619	0.5647	1.641	0.6358	0.9921
		25347	303.5	1.969	0.6488	0.0550	0.0181	0.0279	0.945	0.3114	0.4799	1.713	0.5644	0.8700
		25348	293.9	2.096	0.7132	0.0509	0.0173	0.0243	0.942	0.3205	0.4494	1.673	0.5692	0.7982
		25349	278.3	1.944	0.6985	0.0522	0.0188	0.0269	0.973	0.3496	0.5005	1.533	0.5508	0.7886
		25350	269.2	2.015	0.7485	0.0411	0.0153	0.0204	1.004	0.3730	0.4983	1.689	0.6274	0.8382
		25351	247.1	2.032	0.8223	0.0630	0.0255	0.0310	0.911	0.3687	0.4483	1.706	0.6904	0.8396
		25352	291.3	2.038	0.6996	0.0511	0.0175	0.0251	0.965	0.3313	0.4735	1.599	0.5489	0.7846
		25353	319.8	2.279	0.7126	0.0533	0.0167	0.0234	1.163	0.3637	0.5103	1.839	0.5750	0.8069
9	f	25354	343.8	2.170	0.6312	0.0644	0.0187	0.0297	1.222	0.3554	0.5631	2.179	0.6338	1.0041
		25355	287.9	2.079	0.7221	0.0502	0.0174	0.0241	0.964	0.3348	0.4637	1.760	0.6113	0.8466
		25356	274.9	1.936	0.7043	0.0623	0.0227	0.0322	1.064	0.3870	0.5496	1.773	0.6450	0.9158
		25357	264.3	1.993	0.7541	0.0611	0.0231	0.0307	1.108	0.4192	0.5559	1.616	0.6114	0.8108
		25358	279.1	1.854	0.6643	0.0592	0.0212	0.0319	0.885	0.3171	0.4773	1.827	0.6546	0.9854
		25359	295.0	1.961	0.6647	0.0650	0.0220	0.0331	0.879	0.2980	0.4482	1.624	0.5505	0.8281
		25360	302.3	2.141	0.7082	0.0551	0.0182	0.0257	0.833	0.2756	0.3891	1.580	0.5227	0.7380
		25361	284.3	1.882	0.6620	0.0573	0.0202	0.0304	0.857	0.3014	0.4554	1.648	0.5797	0.8757
		25362	289.0	1.920	0.6644	0.0588	0.0203	0.0306	0.827	0.2862	0.4307	1.606	0.5557	0.8365
		25363	269.3	1.941	0.7208	0.0596	0.0221	0.0307	0.888	0.3297	0.4575	1.651	0.6131	0.8506

Organ weight data are presented as terminal body weights (TBW, g), absolute weights (Abs, g), organ-to-body weight percentages (%TBW) and organ-to-brain weight ratios (/BR).

Target Dose: Group 1 - 0 mg/kg/day Groups 2 and 7 - 1 mg/kg/day Groups 3 and 8 - 3 mg/kg/day
Groups 4 and 9 - 10 mg/kg/day Groups 5 and 10 - 30 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 26 (continued): Individual Organ Weight Data

Day 91 Relative to Start Date

			TBW	--- Brain ---		---- Adrenal Gland -----			------- Heart ---------			------- Kidneys -------		
Group	Sex	Animal	g	Abs	%TBW	Abs	%TBW	/BR	Abs	%TBW	/BR	Abs	%TBW	/BR
10	f	25364	264.6	2.033	0.7683	0.0613	0.0232	0.0302	1.020	0.3855	0.5017	1.836	0.6939	0.9031
		25365	308.8	2.100	0.6801	0.0628	0.0203	0.0299	1.095	0.3546	0.5214	1.931	0.6253	0.9195
		25366	227.1	2.054	0.9044	0.0700	0.0308	0.0341	0.778	0.3426	0.3788	1.611	0.7094	0.7843
		25367	287.4	1.987	0.6914	0.0617	0.0215	0.0311	1.108	0.3855	0.5576	1.776	0.6180	0.8938
		25368	279.7	1.849	0.6611	0.0518	0.0185	0.0280	0.872	0.3118	0.4716	1.733	0.6196	0.9373
		25369	304.5	2.037	0.6690	0.0491	0.0161	0.0241	0.806	0.2647	0.3957	1.776	0.5833	0.8719
		25370	267.1	2.028	0.7593	0.0448	0.0168	0.0221	1.067	0.3995	0.5261	1.989	0.7447	0.9808
		25371	299.2	2.076	0.6939	0.0721	0.0241	0.0347	0.933	0.3118	0.4494	1.907	0.6374	0.9186
		25372	252.7	1.934	0.7653	0.0482	0.0191	0.0249	0.969	0.3835	0.5010	1.603	0.6343	0.8289
		25373	294.8	2.004	0.6798	0.0553	0.0188	0.0276	1.035	0.3511	0.5165	1.671	0.5668	0.8338
11	f	25374	328.2	2.040	0.6216	0.0697	0.0212	0.0342	1.247	0.3800	0.6113	2.144	0.6533	1.0510
		25375	296.4	1.960	0.6613	0.0415	0.0140	0.0212	1.170	0.3947	0.5969	1.819	0.6137	0.9281
		25376	254.2	1.969	0.7746	0.0489	0.0192	0.0248	1.030	0.4052	0.5231	1.939	0.7628	0.9848
		25377	226.0	2.049	0.9066	0.0454	0.0201	0.0222	0.901	0.3987	0.4397	1.491	0.6597	0.7277
		25378	271.9	2.137	0.7860	0.0392	0.0144	0.0183	1.003	0.3689	0.4693	2.069	0.7609	0.9682
		25379	296.6	1.967	0.6632	0.0739	0.0249	0.0376	1.045	0.3523	0.5313	2.063	0.6955	1.0488
		25380	315.8	2.016	0.6384	0.0455	0.0144	0.0226	1.267	0.4012	0.6285	2.062	0.6529	1.0228
		25381	304.7	1.944	0.6380	0.0723	0.0237	0.0372	1.168	0.3833	0.6008	2.355	0.7729	1.2114
		25382	253.0	2.004	0.7921	0.0617	0.0244	0.0308	0.903	0.3569	0.4506	1.746	0.6901	0.8713
		25383	285.6	1.911	0.6691	0.0702	0.0246	0.0367	0.879	0.3078	0.4600	1.321	0.4625	0.6913

Organ weight data are presented as terminal body weights (TBW, g), absolute weights (Abs, g), organ-to-body weight percentages (%TBW) and organ-to-brain weight ratios (/BR).

Target Dose: Group 1 - 0 mg/kg/day Groups 2 and 7 - 1 mg/kg/day Groups 3 and 8 - 3 mg/kg/day
Groups 4 and 9 - 10 mg/kg/day Groups 5 and 10 - 30 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 26 (continued): Individual Organ Weight Data

Day 91 Relative to Start Date

			Liver			Spleen			Thymus			Thyroid		
Group	Sex	Animal	Abs	%TBW	/BR	Abs	%TBW	/BR	Abs	%TBW	/BR	Abs	%TBW	/BR
1	f	25254	7.183	2.4457	3.4717	0.677	0.2305	0.3272	0.322	0.1096	0.1556	0.3376	0.1149	0.1632
		25255	6.363	2.5002	3.0695	0.500	0.1965	0.2412	0.320	0.1257	0.1544	0.0171	0.0067	0.0082
		25256	5.937	2.5724	3.3887	0.494	0.2140	0.2820	0.215	0.0932	0.1227	0.0142	0.0062	0.0081
		25257	7.250	2.6972	3.6765	0.475	0.1767	0.2409	0.212	0.0789	0.1075	0.0191	0.0071	0.0097
		25258	7.914	2.3852	3.6420	0.568	0.1712	0.2614	0.318	0.0958	0.1463	0.0277	0.0083	0.0127
		25259	7.087	2.9715	3.5956	0.559	0.2344	0.2836	0.208	0.0872	0.1055	0.0137	0.0057	0.0070
		25260	7.260	2.5572	3.3611	0.594	0.2092	0.2750	0.297	0.1046	0.1375	0.0178	0.0063	0.0082
		25261	8.108	2.4385	4.1815	0.742	0.2232	0.3827	0.313	0.0941	0.1614	0.0254	0.0076	0.0131
		25262	7.718	2.7733	3.6474	0.559	0.2009	0.2642	0.303	0.1089	0.1432	0.0143	0.0051	0.0068
		25263	7.588	2.6022	3.5962	0.605	0.2075	0.2867	0.305	0.1046	0.1445	0.0340	0.0117	0.0161
7	f	25334	5.914	2.4570	2.7831	0.424	0.1762	0.1995	0.327	0.1359	0.1539	0.0394	0.0164	0.0185
		25335	6.845	2.5055	3.2924	0.506	0.1852	0.2434	0.395	0.1446	0.1900	0.0254	0.0093	0.0122
		25336	9.158	2.8963	4.2915	0.533	0.1686	0.2498	0.356	0.1126	0.1668	0.0180	0.0057	0.0084
		25337	7.093	2.3089	3.5590	0.610	0.1986	0.3061	0.263	0.0856	0.1320	0.0160	0.0052	0.0080
		25338	6.684	2.3568	3.3588	0.674	0.2377	0.3387	0.374	0.1319	0.1879	0.0179	0.0063	0.0090
		25339	6.814	2.3067	3.4606	0.573	0.1940	0.2910	0.344	0.1165	0.1747	0.0223	0.0075	0.0113
		25340	6.918	2.7997	3.4851	0.506	0.2048	0.2549	0.341	0.1380	0.1718	0.0210	0.0085	0.0106
		25341	6.892	2.4457	3.5110	0.479	0.1700	0.2440	0.353	0.1253	0.1798	0.0211	0.0075	0.0107
		25342	6.947	2.3485	3.5354	0.559	0.1890	0.2845	0.308	0.1041	0.1567	0.0188	0.0064	0.0096
		25343	7.401	2.4786	3.7061	0.544	0.1822	0.2724	0.341	0.1142	0.1708	0.0249	0.0083	0.0125

Organ weight data are presented as terminal body weights (TBW, g), absolute weights (Abs, g), organ-to-body weight percentages (%TBW) and organ-to-brain weight ratios (/BR).

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 26 (continued): Individual Organ Weight Data

Day 91 Relative to Start Date

			Liver			Spleen			Thymus			Thyroid		
Group	Sex	Animal	Abs	%TBW	/BR	Abs	%TBW	/BR	Abs	%TBW	/BR	Abs	%TBW	/BR
8	f	25344	7.308	2.3075	3.6322	0.535	0.1689	0.2659	0.277	0.0875	0.1377	0.0124	0.0039	0.0062
		25345	6.029	2.3514	3.0666	0.603	0.2352	0.3067	0.335	0.1307	0.1704	0.0155	0.0060	0.0079
		25346	6.744	2.6129	4.0774	0.509	0.1972	0.3077	0.163	0.0632	0.0985	0.0151	0.0059	0.0091
		25347	7.748	2.5529	3.9350	0.476	0.1568	0.2417	0.396	0.1305	0.2011	0.0164	0.0054	0.0083
		25348	7.401	2.5182	3.5310	0.605	0.2059	0.2886	0.251	0.0854	0.1198	0.0156	0.0053	0.0074
		25349	7.179	2.5796	3.6929	0.538	0.1933	0.2767	0.335	0.1204	0.1723	0.0202	0.0073	0.0104
		25350	6.464	2.4012	3.2079	0.575	0.2136	0.2854	0.270	0.1003	0.1340	0.0122	0.0045	0.0061
		25351	6.560	2.6548	3.2283	0.551	0.2230	0.2712	0.322	0.1303	0.1585	0.0154	0.0062	0.0076
		25352	6.596	2.2643	3.2365	0.498	0.1710	0.2444	0.247	0.0848	0.1212	0.0200	0.0069	0.0098
		25353	8.401	2.6270	3.6863	0.669	0.2092	0.2935	0.286	0.0894	0.1255	0.0230	0.0072	0.0101
9	f	25354	10.570	3.0745	4.8710	0.605	0.1760	0.2788	0.412	0.1198	0.1899	0.0188	0.0055	0.0087
		25355	7.006	2.4335	3.3699	0.645	0.2240	0.3102	0.415	0.1441	0.1996	0.0172	0.0060	0.0083
		25356	7.249	2.6370	3.7443	0.615	0.2237	0.3177	0.420	0.1528	0.2169	0.0213	0.0077	0.0110
		25357	7.175	2.7147	3.6001	0.513	0.1941	0.2574	0.346	0.1309	0.1736	0.0133	0.0050	0.0067
		25358	8.011	2.8703	4.3209	0.567	0.2032	0.3058	0.365	0.1308	0.1969	0.0213	0.0076	0.0115
		25359	6.280	2.1288	3.2024	0.662	0.2244	0.3376	0.283	0.0959	0.1443	0.0177	0.0060	0.0090
		25360	7.451	2.4648	3.4801	0.535	0.1770	0.2499	0.429	0.1419	0.2004	0.0336	0.0111	0.0157
		25361	8.119	2.8558	4.3140	0.653	0.2297	0.3470	0.216	0.0760	0.1148	0.0143	0.0050	0.0076
		25362	6.520	2.2561	3.3958	0.489	0.1692	0.2547	0.297	0.1028	0.1547	0.0222	0.0077	0.0116
		25363	6.099	2.2648	3.1422	0.518	0.1924	0.2669	0.292	0.1084	0.1504	0.0178	0.0066	0.0092

Organ weight data are presented as terminal body weights (TBW, g), absolute weights (Abs, g), organ-to-body weight percentages (%TBW) and organ-to-brain weight ratios (/BR).

Target Dose: Group 1 - 0 mg/kg/day Groups 2 and 7 - 1 mg/kg/day Groups 3 and 8 - 3 mg/kg/day
Groups 4 and 9 - 10 mg/kg/day Groups 5 and 10 - 30 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 26 (continued): Individual Organ Weight Data

Day 91 Relative to Start Date

			Liver			Spleen			Thymus			Thyroid		
Group	Sex	Animal	Abs	%TBW	/BR	Abs	%TBW	/BR	Abs	%TBW	/BR	Abs	%TBW	/BR
10	f	25364	7.472	2.8239	3.6754	0.525	0.1984	0.2582	0.370	0.1398	0.1820	0.0219	0.0083	0.0108
		25365	8.121	2.6299	3.8671	0.585	0.1894	0.2786	0.262	0.0848	0.1248	0.0146	0.0047	0.0070
		25366	5.781	2.5456	2.8145	0.427	0.1880	0.2079	0.255	0.1123	0.1241	0.0266	0.0117	0.0130
		25367	6.814	2.3709	3.4293	0.625	0.2175	0.3145	0.362	0.1260	0.1822	0.0181	0.0063	0.0091
		25368	7.143	2.5538	3.8632	0.539	0.1927	0.2915	0.347	0.1241	0.1877	0.0215	0.0077	0.0116
		25369	7.347	2.4128	3.6068	0.478	0.1570	0.2347	0.466	0.1530	0.2288	0.0375	0.0123	0.0184
		25370	8.053	3.0150	3.9709	0.534	0.1999	0.2633	0.286	0.1071	0.1410	0.0163	0.0061	0.0080
		25371	9.315	3.1133	4.4870	0.611	0.2042	0.2943	0.427	0.1427	0.2057	0.0211	0.0071	0.0102
		25372	6.957	2.7531	3.5972	0.404	0.1599	0.2089	0.288	0.1140	0.1489	0.0217	0.0086	0.0112
		25373	6.880	2.3338	3.4331	0.549	0.1862	0.2740	0.287	0.0974	0.1432	0.0156	0.0053	0.0078
11	f	25374	9.039	2.7541	4.4309	0.543	0.1654	0.2662	0.303	0.0923	0.1485	0.0158	0.0048	0.0077
		25375	7.166	2.4177	3.6561	0.598	0.2018	0.3051	0.312	0.1053	0.1592	0.0135	0.0046	0.0069
		25376	6.680	2.6279	3.3926	0.592	0.2329	0.3007	0.220	0.0865	0.1117	0.0150	0.0059	0.0076
		25377	5.435	2.4049	2.6525	0.557	0.2465	0.2718	0.300	0.1327	0.1464	0.0139	0.0062	0.0068
		25378	6.363	2.3402	2.9775	0.599	0.2203	0.2803	0.340	0.1250	0.1591	0.0204	0.0075	0.0095
		25379	7.714	2.6008	3.9217	0.557	0.1878	0.2832	0.279	0.0941	0.1418	0.0126	0.0042	0.0064
		25380	8.785	2.7818	4.3576	0.761	0.2410	0.3775	0.385	0.1219	0.1910	0.0176	0.0056	0.0087
		25381	8.746	2.8704	4.4990	0.484	0.1588	0.2490	0.326	0.1070	0.1677	0.0152	0.0050	0.0078
		25382	7.204	2.8474	3.5948	0.568	0.2245	0.2834	0.196	0.0775	0.0978	0.0194	0.0077	0.0097
		25383	6.283	2.1999	3.2878	0.566	0.1982	0.2962	0.370	0.1296	0.1936	0.0283	0.0099	0.0148

Organ weight data are presented as terminal body weights (TBW, g), absolute weights (Abs, g), organ-to-body weight percentages (%TBW) and organ-to-brain weight ratios (/BR).

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 26 (continued): Individual Organ Weight Data

Day 91 Relative to Start Date

			Ovary			Uterus			Mammary Gland		
Group	Sex	Animal	Abs	%TBW	/BR	Abs	%TBW	/BR	Abs	%TBW	/BR
1	f	25254	0.1478	0.0503	0.0714	0.672	0.2288	0.3248	0.3938	0.1341	0.1903
		25255	0.1279	0.0503	0.0617	0.868	0.3411	0.4187	0.7651	0.3006	0.3691
		25256	0.0660	0.0286	0.0377	0.799	0.3462	0.4561	0.1409	0.0610	0.0804
		25257	0.0623	0.0232	0.0316	0.748	0.2783	0.3793	0.1820	0.0677	0.0923
		25258	0.1512	0.0456	0.0696	0.674	0.2031	0.3102	0.7937	0.2392	0.3653
		25259	0.0869	0.0364	0.0441	0.620	0.2600	0.3146	0.2786	0.1168	0.1413
		25260	0.0733	0.0258	0.0339	0.568	0.2001	0.2630	0.6828	0.2405	0.3161
		25261	0.1398	0.0420	0.0721	0.947	0.2848	0.4884	1.5495	0.4660	0.7991
		25262	0.0713	0.0256	0.0337	0.634	0.2278	0.2996	0.1662	0.0597	0.0785
		25263	0.1270	0.0436	0.0602	0.674	0.2311	0.3194	1.2026	0.4124	0.5700
7	f	25334	0.0889	0.0369	0.0418	0.575	0.2389	0.2706	0.4829	0.2006	0.2272
		25335	0.1386	0.0507	0.0667	0.515	0.1885	0.2477	0.6405	0.2344	0.3081
		25336	0.0665	0.0210	0.0312	0.737	0.2331	0.3454	9.7194	3.0738	4.5545
		25337	0.1702	0.0554	0.0854	0.830	0.2702	0.4165	0.4218	0.1373	0.2116
		25338	0.0786	0.0277	0.0395	0.529	0.1865	0.2658	0.3153	0.1112	0.1584
		25339	0.1529	0.0518	0.0777	0.555	0.1879	0.2819	1.0433	0.3532	0.5299
		25340	0.1418	0.0574	0.0714	0.572	0.2315	0.2882	0.8758	0.3544	0.4412
		25341	0.1217	0.0432	0.0620	0.526	0.1867	0.2680	0.4463	0.1584	0.2274
		25342	0.1008	0.0341	0.0513	0.471	0.1592	0.2397	0.5825	0.1969	0.2964
		25343	0.1182	0.0396	0.0592	0.571	0.1912	0.2859	0.4052	0.1357	0.2029

Organ weight data are presented as terminal body weights (TBW, g), absolute weights (Abs, g), organ-to-body weight percentages (%TBW) and organ-to-brain weight ratios (/BR).

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 26 (continued): Individual Organ Weight Data

Day 91 Relative to Start Date

			Ovary			Uterus			Mammary Gland		
Group	Sex	Animal	Abs	%TBW	/BR	Abs	%TBW	/BR	Abs	%TBW	/BR
8	f	25344	0.1305	0.0412	0.0649	0.522	0.1648	0.2594	0.9779	0.3088	0.4860
		25345	0.0681	0.0266	0.0346	0.929	0.3623	0.4725	0.2090	0.0815	0.1063
		25346	0.1013	0.0392	0.0612	0.765	0.2964	0.4625	0.3790	0.1468	0.2291
		25347	0.1584	0.0522	0.0804	0.748	0.2465	0.3799	1.4494	0.4776	0.7361
		25348	0.1307	0.0445	0.0624	0.508	0.1728	0.2424	0.5564	0.1893	0.2655
		25349	0.0910	0.0327	0.0468	0.649	0.2332	0.3338	0.5254	0.1888	0.2703
		25350	0.1030	0.0383	0.0511	0.490	0.1820	0.2432	0.5005	0.1859	0.2484
		25351	0.1058	0.0428	0.0521	0.996	0.4031	0.4902	0.3350	0.1356	0.1649
		25352	0.1080	0.0371	0.0530	0.535	0.1837	0.2625	7.3683	2.5295	3.6155
		25353	0.0877	0.0274	0.0385	0.688	0.2151	0.3019	0.4924	0.1540	0.2161
9	f	25354	0.0864	0.0251	0.0398	0.744	0.2164	0.3429	0.4232	0.1231	0.1950
		25355	0.1169	0.0406	0.0562	0.749	0.2602	0.3603	0.8573	0.2978	0.4124
		25356	0.1273	0.0463	0.0658	0.600	0.2183	0.3099	0.7235	0.2632	0.3737
		25357	0.0745	0.0282	0.0374	0.698	0.2641	0.3502	0.5817	0.2201	0.2919
		25358	0.0934	0.0335	0.0504	0.578	0.2071	0.3118	1.0965	0.3929	0.5914
		25359	0.1097	0.0372	0.0559	0.772	0.2617	0.3937	0.5351	0.1814	0.2729
		25360	0.1480	0.0490	0.0691	0.666	0.2203	0.3111	1.1117	0.3677	0.5192
		25361	0.1383	0.0486	0.0735	0.533	0.1875	0.2832	0.3054	0.1074	0.1623
		25362	0.1111	0.0384	0.0579	0.931	0.3221	0.4849	1.3346	0.4618	0.6951
		25363	0.1182	0.0439	0.0609	0.782	0.2904	0.4029	1.0517	0.3905	0.5418

Organ weight data are presented as terminal body weights (TBW, g), absolute weights (Abs, g), organ-to-body weight percentages (%TBW) and organ-to-brain weight ratios (/BR).

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 26 (continued): Individual Organ Weight Data

Day 91 Relative to Start Date

			Ovary			Uterus			Mammary Gland		
Group	Sex	Animal	Abs	%TBW	/BR	Abs	%TBW	/BR	Abs	%TBW	/BR
10	f	25364	0.0809	0.0306	0.0398	0.620	0.2343	0.3050	0.1375	0.0520	0.0676
		25365	0.0950	0.0308	0.0452	0.812	0.2630	0.3867	0.6038	0.1955	0.2875
		25366	0.0924	0.0407	0.0450	1.080	0.4756	0.5258	0.4906	0.2160	0.2389
		25367	0.1141	0.0397	0.0574	0.650	0.2262	0.3271	0.4306	0.1498	0.2167
		25368	0.0731	0.0261	0.0395	0.959	0.3429	0.5187	0.4898	0.1751	0.2649
		25369	0.1317	0.0433	0.0647	0.608	0.1997	0.2985	0.5507	0.1809	0.2703
		25370	0.1066	0.0399	0.0526	0.627	0.2347	0.3092	0.4047	0.1515	0.1996
		25371	0.0769	0.0257	0.0370	0.568	0.1898	0.2736	1.4527	0.4855	0.6998
		25372	0.0318	0.0126	0.0164	0.719	0.2845	0.3718	0.2249	0.0890	0.1163
		25373	0.0626	0.0212	0.0312	0.518	0.1757	0.2585	0.5780	0.1961	0.2884
11	f	25374	0.1111	0.0339	0.0545	0.619	0.1886	0.3034	0.4340	0.1322	0.2127
		25375	0.1099	0.0371	0.0561	0.628	0.2119	0.3204	0.4072	0.1374	0.2078
		25376	0.0979	0.0385	0.0497	0.831	0.3269	0.4220	0.2137	0.0841	0.1085
		25377	0.0321	0.0142	0.0157	0.458	0.2027	0.2235	0.2147	0.0950	0.1048
		25378	0.0923	0.0339	0.0432	0.588	0.2163	0.2752	0.1680	0.0618	0.0786
		25379	0.1384	0.0467	0.0704	0.588	0.1982	0.2989	0.4448	0.1500	0.2261
		25380	0.0624	0.0198	0.0310	0.758	0.2400	0.3760	0.5034	0.1594	0.2497
		25381	0.1040	0.0341	0.0535	0.682	0.2238	0.3508	0.4749	0.1559	0.2443
		25382	0.0768	0.0304	0.0383	0.510	0.2016	0.2545	0.4078	0.1612	0.2035
		25383	0.1309	0.0458	0.0685	0.535	0.1873	0.2800	0.6942	0.2431	0.3633

Organ weight data are presented as terminal body weights (TBW, g), absolute weights (Abs, g), organ-to-body weight percentages (%TBW) and organ-to-brain weight ratios (/BR).

Target Dose: Group 1 - 0 mg/kg/day; Groups 2 and 7 - 1 mg/kg/day; Groups 3 and 8 - 3 mg/kg/day; Groups 4 and 9 - 10 mg/kg/day; Groups 5 and 10 - 30 mg/kg/day; Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 26 (continued): Individual Organ Weight Data

Day 119 Relative to Start Date

			TBW	--- Brain ---		---- Adrenal Gland -----			------- Heart ---------		
Group	Sex	Animal	g	Abs	%TBW	Abs	%TBW	/BR	Abs	%TBW	/BR
1	m	25244	497.5	2.118	0.4257	0.0412	0.0083	0.0195	1.416	0.2846	0.6686
		25245	635.5	2.152	0.3386	0.0380	0.0060	0.0177	1.631	0.2566	0.7579
		25246	697.8	2.227	0.3191	0.0634	0.0091	0.0285	2.082	0.2984	0.9349
		25247	662.8	2.253	0.3399	0.0606	0.0091	0.0269	2.059	0.3107	0.9139
		25248	644.5	2.333	0.3620	0.0537	0.0083	0.0230	1.706	0.2647	0.7312
		25249	577.1	2.409	0.4174	0.0536	0.0093	0.0222	1.420	0.2461	0.5895
		25250	486.0	2.088	0.4296	0.0413	0.0085	0.0198	1.599	0.3290	0.7658
		25251	788.9	2.388	0.3027	0.0682	0.0086	0.0286	2.199	0.2787	0.9209
		25252	671.6	2.184	0.3252	0.0560	0.0083	0.0256	1.758	0.2618	0.8049
		25253	639.1	2.204	0.3449	0.0459	0.0072	0.0208	1.986	0.3107	0.9011
6	m	25324	629.9	2.251	0.3574	0.0588	0.0093	0.0261	1.719	0.2729	0.7637
		25325	681.0	2.326	0.3416	0.0643	0.0094	0.0276	1.990	0.2922	0.8555
		25326	725.9	2.295	0.3162	0.0566	0.0078	0.0247	2.113	0.2911	0.9207
		25327	636.9	2.300	0.3611	0.0678	0.0106	0.0295	1.789	0.2809	0.7778
		25328	623.4	2.317	0.3717	0.0573	0.0092	0.0247	1.741	0.2793	0.7514
		25329	658.2	2.287	0.3475	0.0585	0.0089	0.0256	2.008	0.3051	0.8780
		25330	621.3	2.179	0.3507	0.0572	0.0092	0.0263	1.839	0.2960	0.8440
		25331	655.4	2.236	0.3412	0.0498	0.0076	0.0223	1.936	0.2954	0.8658
		25332	538.1	2.034	0.3780	0.0462	0.0086	0.0227	1.855	0.3447	0.9120
		25333	656.0	2.308	0.3518	0.0466	0.0071	0.0202	2.034	0.3101	0.8813

Organ weight data are presented as terminal body weights (TBW, g), absolute weights (Abs, g), organ-to-body weight percentages (%TBW) and organ-to-brain weight ratios (/BR).

Target Dose: Group 1 - 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 26 (continued): Individual Organ Weight Data

Day 119 Relative to Start Date

			Kidneys			Liver			Spleen		
Group	Sex	Animal	Abs	%TBW	/BR	Abs	%TBW	/BR	Abs	%TBW	/BR
1	m	25244	2.436	0.4896	1.1501	11.684	2.3485	5.5165	1.147	0.2306	0.5415
		25245	2.761	0.4345	1.2830	14.191	2.2330	6.5943	0.761	0.1197	0.3536
		25246	3.740	0.5360	1.6794	17.284	2.4769	7.7611	1.158	0.1660	0.5200
		25247	4.184	0.6313	1.8571	16.564	2.4991	7.3520	1.178	0.1777	0.5229
		25248	3.582	0.5558	1.5354	15.234	2.3637	6.5298	0.931	0.1445	0.3991
		25249	2.788	0.4831	1.1573	14.332	2.4835	5.9494	0.883	0.1530	0.3665
		25250	2.463	0.5068	1.1796	10.495	2.1595	5.0263	1.024	0.2107	0.4904
		25251	3.814	0.4835	1.5972	19.467	2.4676	8.1520	1.468	0.1861	0.6147
		25252	3.312	0.4932	1.5165	17.512	2.6075	8.0183	1.033	0.1538	0.4730
		25253	3.075	0.4811	1.3952	14.743	2.3068	6.6892	1.042	0.1630	0.4728
6	m	25324	3.313	0.5260	1.4718	14.550	2.3099	6.4638	1.141	0.1811	0.5069
		25325	3.285	0.4824	1.4123	14.230	2.0896	6.1178	0.977	0.1435	0.4200
		25326	3.936	0.5422	1.7150	17.598	2.4243	7.6680	1.287	0.1773	0.5608
		25327	3.330	0.5228	1.4478	14.227	2.2338	6.1857	0.956	0.1501	0.4157
		25328	3.267	0.5241	1.4100	14.974	2.4020	6.4627	0.886	0.1421	0.3824
		25329	3.609	0.5483	1.5780	16.151	2.4538	7.0621	1.253	0.1904	0.5479
		25330	3.231	0.5200	1.4828	14.451	2.3259	6.6319	0.998	0.1606	0.4580
		25331	3.177	0.4847	1.4208	16.609	2.5342	7.4280	1.117	0.1704	0.4996
		25332	2.983	0.5544	1.4666	13.020	2.4196	6.4012	1.010	0.1877	0.4966
		25333	2.996	0.4567	1.2981	15.410	2.3491	6.6768	1.132	0.1726	0.4905

Organ weight data are presented as terminal body weights (TBW, g), absolute weights (Abs, g), organ-to-body weight percentages (%TBW) and organ-to-brain weight ratios (/BR).

Target Dose: Group 1 - 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 26 (continued): Individual Organ Weight Data

Day 119 Relative to Start Date

			Thymus			Thyroid			Testes		
Group	Sex	Animal	Abs	%TBW	/BR	Abs	%TBW	/BR	Abs	%TBW	/BR
1	m	25244	0.289	0.0581	0.1364	0.0299	0.0060	0.0141	4.137	0.8316	1.9533
		25245	0.337	0.0530	0.1566	0.0308	0.0048	0.0143	4.814	0.7575	2.2370
		25246	0.375	0.0537	0.1684	0.0329	0.0047	0.0148	4.863	0.6969	2.1837
		25247	0.283	0.0427	0.1256	0.0285	0.0043	0.0126	5.838	0.8808	2.5912
		25248	0.303	0.0470	0.1299	0.0298	0.0046	0.0128	5.525	0.8573	2.3682
		25249	0.466	0.0807	0.1934	0.0242	0.0042	0.0100	4.524	0.7839	1.8780
		25250	0.362	0.0745	0.1734	0.0229	0.0047	0.0110	5.283	1.0870	2.5302
		25251	0.458	0.0581	0.1918	0.0331	0.0042	0.0139	6.290	0.7973	2.6340
		25252	0.471	0.0701	0.2157	0.0272	0.0041	0.0125	4.914	0.7317	2.2500
		25253	0.324	0.0507	0.1470	0.0253	0.0040	0.0115	5.878	0.9197	2.6670
6	m	25324	0.579	0.0919	0.2572	0.0396	0.0063	0.0176	5.349	0.8492	2.3763
		25325	0.285	0.0419	0.1225	0.0292	0.0043	0.0126	5.653	0.8301	2.4304
		25326	0.470	0.0647	0.2048	0.0285	0.0039	0.0124	5.686	0.7833	2.4776
		25327	0.437	0.0686	0.1900	0.0341	0.0054	0.0148	5.526	0.8676	2.4026
		25328	0.243	0.0390	0.1049	0.0268	0.0043	0.0116	5.475	0.8782	2.3630
		25329	0.284	0.0431	0.1242	0.0270	0.0041	0.0118	4.885	0.7422	2.1360
		25330	0.325	0.0523	0.1492	0.0267	0.0043	0.0123	3.825	0.6156	1.7554
		25331	0.389	0.0594	0.1740	0.0322	0.0049	0.0144	4.947	0.7548	2.2124
		25332	0.266	0.0494	0.1308	0.0220	0.0041	0.0108	4.817	0.8952	2.3682
		25333	0.457	0.0697	0.1980	0.0320	0.0049	0.0139	5.631	0.8584	2.4398

Organ weight data are presented as terminal body weights (TBW, g), absolute weights (Abs, g), organ-to-body weight percentages (%TBW) and organ-to-brain weight ratios (/BR).

Target Dose: Group 1 - 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 26 (continued): Individual Organ Weight Data

Day 119 Relative to Start Date

			TBW	--- Brain ---		---- Adrenal Gland -----			------- Heart ---------		
Group	Sex	Animal	g	Abs	%TBW	Abs	%TBW	/BR	Abs	%TBW	/BR
1	f	25264	270.2	2.016	0.7461	0.0388	0.0144	0.0192	1.089	0.4030	0.5402
		25265	306.0	1.939	0.6337	0.0527	0.0172	0.0272	1.395	0.4559	0.7194
		25266	288.3	2.074	0.7194	0.0621	0.0215	0.0299	1.056	0.3663	0.5092
		25267	333.7	2.295	0.6877	0.0562	0.0168	0.0245	1.187	0.3557	0.5172
		25268	293.5	1.971	0.6716	0.0481	0.0164	0.0244	1.232	0.4198	0.6251
		25269	311.3	2.233	0.7173	0.0649	0.0208	0.0291	1.058	0.3399	0.4738
		25270	314.4	2.102	0.6686	0.0673	0.0214	0.0320	1.122	0.3569	0.5338
		25271	344.0	2.281	0.6631	0.0641	0.0186	0.0281	1.227	0.3567	0.5379
		25272	327.9	1.991	0.6072	0.0602	0.0184	0.0302	1.215	0.3705	0.6102
		25273	372.7	2.127	0.5707	0.0746	0.0200	0.0351	1.263	0.3389	0.5938
11	f	25384	375.5	1.988	0.5294	0.0413	0.0110	0.0208	1.239	0.3300	0.6232
		25385	355.1	2.149	0.6052	0.0547	0.0154	0.0255	1.238	0.3486	0.5761
		25386	298.2	2.116	0.7096	0.0595	0.0200	0.0281	0.904	0.3032	0.4272
		25387	280.7	2.020	0.7196	0.0637	0.0227	0.0315	1.079	0.3844	0.5342
		25388	305.6	1.976	0.6466	0.0516	0.0169	0.0261	1.231	0.4028	0.6230
		25389	270.6	2.036	0.7524	0.0495	0.0183	0.0243	1.212	0.4479	0.5953
		25390	281.4	2.067	0.7345	0.0580	0.0206	0.0281	1.039	0.3692	0.5027
		25391	253.8	2.021	0.7963	0.0575	0.0227	0.0285	1.006	0.3964	0.4978
		25392	306.2	1.808	0.5905	0.0571	0.0186	0.0316	0.998	0.3259	0.5520
		25393	296.8	2.049	0.6904	0.0614	0.0207	0.0300	1.190	0.4009	0.5808

Organ weight data are presented as terminal body weights (TBW, g), absolute weights (Abs, g), organ-to-body weight percentages (%TBW) and organ-to-brain weight ratios (/BR).

Target Dose: Group 1 - 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 26 (continued): Individual Organ Weight Data

Day 119 Relative to Start Date

			Kidneys			Liver			Spleen		
Group	Sex	Animal	Abs	%TBW	/BR	Abs	%TBW	/BR	Abs	%TBW	/BR
1	f	25264	1.804	0.6677	0.8948	7.737	2.8634	3.8378	0.512	0.1895	0.2540
		25265	1.719	0.5618	0.8865	7.879	2.5748	4.0634	0.484	0.1582	0.2496
		25266	1.739	0.6032	0.8385	6.867	2.3819	3.3110	0.521	0.1807	0.2512
		25267	1.861	0.5577	0.8109	7.975	2.3899	3.4749	0.611	0.1831	0.2662
		25268	1.975	0.6729	1.0020	8.784	2.9928	4.4566	0.714	0.2433	0.3623
		25269	1.877	0.6030	0.8406	8.300	2.6662	3.7170	0.573	0.1841	0.2566
		25270	1.647	0.5239	0.7835	7.353	2.3387	3.4981	0.643	0.2045	0.3059
		25271	1.996	0.5802	0.8751	9.669	2.8108	4.2389	0.743	0.2160	0.3257
		25272	1.986	0.6057	0.9975	9.080	2.7691	4.5605	0.572	0.1744	0.2873
		25273	2.018	0.5415	0.9488	9.598	2.5753	4.5125	0.677	0.1816	0.3183
11	f	25384	2.107	0.5611	1.0599	9.831	2.6181	4.9452	0.563	0.1499	0.2832
		25385	1.867	0.5258	0.8688	8.699	2.4497	4.0479	0.593	0.1670	0.2759
		25386	1.576	0.5285	0.7448	8.318	2.7894	3.9310	0.607	0.2036	0.2869
		25387	1.851	0.6594	0.9163	7.227	2.5746	3.5777	0.577	0.2056	0.2856
		25388	2.149	0.7032	1.0876	8.598	2.8135	4.3512	0.628	0.2055	0.3178
		25389	1.686	0.6231	0.8281	7.048	2.6046	3.4617	0.545	0.2014	0.2677
		25390	2.050	0.7285	0.9918	7.498	2.6645	3.6275	0.631	0.2242	0.3053
		25391	1.556	0.6131	0.7699	6.312	2.4870	3.1232	0.604	0.2380	0.2989
		25392	2.001	0.6535	1.1067	7.095	2.3171	3.9242	0.735	0.2400	0.4065
		25393	2.080	0.7008	1.0151	7.968	2.6846	3.8887	0.742	0.2500	0.3621

Organ weight data are presented as terminal body weights (TBW, g), absolute weights (Abs, g), organ-to-body weight percentages (%TBW) and organ-to-brain weight ratios (/BR).

Target Dose: Group 1 - 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 26 (continued): Individual Organ Weight Data

Day 119 Relative to Start Date

			Thymus			Thyroid		
Group	Sex	Animal	Abs	%TBW	/BR	Abs	%TBW	/BR
1	f	25264	0.210	0.0777	0.1042	0.0151	0.0056	0.0075
		25265	0.305	0.0997	0.1573	0.0167	0.0055	0.0086
		25266	0.252	0.0874	0.1215	0.0268	0.0093	0.0129
		25267	0.231	0.0692	0.1007	0.0133	0.0040	0.0058
		25268	0.225	0.0767	0.1142	0.0297	0.0101	0.0151
		25269	0.231	0.0742	0.1034	0.0167	0.0054	0.0075
		25270	0.289	0.0919	0.1375	0.0242	0.0077	0.0115
		25271	0.298	0.0866	0.1306	0.0202	0.0059	0.0089
		25272	0.331	0.1009	0.1662	0.0249	0.0076	0.0125
		25273	0.395	0.1060	0.1857	0.0246	0.0066	0.0116
11	f	25384	0.448	0.1193	0.2254	0.0251	0.0067	0.0126
		25385	0.240	0.0676	0.1117	0.0194	0.0055	0.0090
		25386	0.292	0.0979	0.1380	0.0159	0.0053	0.0075
		25387	0.285	0.1015	0.1411	0.0215	0.0077	0.0106
		25388	0.265	0.0867	0.1341	0.0171	0.0056	0.0087
		25389	0.210	0.0776	0.1031	0.0179	0.0066	0.0088
		25390	0.267	0.0949	0.1292	0.0236	0.0084	0.0114
		25391	0.309	0.1217	0.1529	0.0196	0.0077	0.0097
		25392	0.327	0.1068	0.1809	0.0172	0.0056	0.0095
		25393	0.257	0.0866	0.1254	0.0249	0.0084	0.0122

Organ weight data are presented as terminal body weights (TBW, g), absolute weights (Abs, g), organ-to-body weight percentages (%TBW) and organ-to-brain weight ratios (/BR).

Target Dose: Group 1 - 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 26 (continued): Individual Organ Weight Data

Day 119 Relative to Start Date

			Ovaries			Uterus			Mammary Gland		
Group	Sex	Animal	Abs	%TBW	/BR	Abs	%TBW	/BR	Abs	%TBW	/BR
1	f	25264	0.0395	0.0146	0.0196	0.834	0.3087	0.4137	0.1247	0.0462	0.0619
		25265	0.0848	0.0277	0.0437	0.798	0.2608	0.4116	0.1763	0.0576	0.0909
		25266	0.1217	0.0422	0.0587	0.713	0.2473	0.3438	0.2606	0.0904	0.1257
		25267	0.0918	0.0275	0.0400	0.860	0.2577	0.3747	0.3062	0.0918	0.1334
		25268	0.0491	0.0167	0.0249	0.981	0.3342	0.4977	0.2928	0.0998	0.1486
		25269	0.1018	0.0327	0.0456	0.608	0.1953	0.2723	1.1136	0.3577	0.4987
		25270	0.1228	0.0391	0.0584	1.001	0.3184	0.4762	0.3421	0.1088	0.1627
		25271	0.0440	0.0128	0.0193	0.915	0.2660	0.4011	0.4583	0.1332	0.2009
		25272	0.0929	0.0283	0.0467	0.567	0.1729	0.2848	0.5301	0.1617	0.2662
		25273	0.1283	0.0344	0.0603	0.864	0.2318	0.4062	1.8193	0.4881	0.8553
11	f	25384	0.1097	0.0292	0.0552	0.838	0.2232	0.4215	1.1185	0.2979	0.5626
		25385	0.0709	0.0200	0.0330	0.791	0.2228	0.3681	0.2807	0.0790	0.1306
		25386	0.1084	0.0364	0.0512	0.898	0.3011	0.4244	1.2483	0.4186	0.5899
		25387	0.1200	0.0428	0.0594	0.591	0.2105	0.2926	0.2962	0.1055	0.1466
		25388	0.1722	0.0563	0.0871	0.632	0.2068	0.3198	0.3043	0.0996	0.1540
		25389	0.0430	0.0159	0.0211	0.755	0.2790	0.3708	0.2612	0.0965	0.1283
		25390	0.1261	0.0448	0.0610	0.851	0.3024	0.4117	1.0865	0.3861	0.5256
		25391	0.4563	0.1798	0.2258	0.522	0.2057	0.2583	0.3277	0.1291	0.1621
		25392	0.1291	0.0422	0.0714	0.533	0.1741	0.2948	0.4097	0.1338	0.2266
		25393	0.0904	0.0305	0.0441	0.540	0.1819	0.2635	0.4159	0.1401	0.2030

Organ weight data are presented as terminal body weights (TBW, g), absolute weights (Abs, g), organ-to-body weight percentages (%TBW) and organ-to-brain weight ratios (/BR).

Target Dose: Group 1 - 0 mg/kg/day Groups 6 and 11 - 100 mg/kg/day

APPENDIX 27: INDIVIDUAL HISTOPATHOLOGY OBSERVATIONS

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 27: Individual Histopathology Observations

Animal No.: 25234 Group: 1 Sex: Male Species: Rat Strain: Sprague Dawley
Test Substance: TFM Dose: Group 1; 0 mg/kg/day Route: Drinking Water Study Type: Subchronic
Date of Death: 07/25/2018 Study Day (Week): 91 (13) Mode of Death: TERMINAL KILL
Date of Necropsy: 07/25/2018 ** NECROPSY COMPLETE ** ** EXAMINATION COMPLETE **

Histo Pathology Observations: Correlated with:

epididymis;
infiltrate, mononuclear cell; minimal

kidney;
chronic progressive nephropathy; minimal

pancreas;
infiltrate, mononuclear cell; minimal

The following tissues were within normal limits:

adrenal gland	aorta	bone with marrow - femur		bone with marrow - sternum		brain
cecum	colon	duodenum	esophagus	eye	harderian gland	heart
ileum	jejunum	lacrimal gland	liver	lung	lymph node - mandibular	
lymph node - mesenteric		mandibular salivary gland		nerve - sciatic	nerve - optic	parathyroid gland
pituitary	prostate	rectum	seminal vesicle	skeletal muscle	skin	spinal cord - cervical
spinal cord - thoracic		spinal cord - lumbar	spleen	stomach	testis	thymus
thyroid gland	tongue	trachea	urinary bladder			

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 27 (continued): Individual Histopathology Observations

Animal No.: 25235 Group: 1 Sex: Male Species: Rat Strain: Sprague Dawley
Test Substance: TFM Dose: Group 1; 0 mg/kg/day Route: Drinking Water Study Type: Subchronic
Date of Death: 07/25/2018 Study Day (Week): 91 (13) Mode of Death: TERMINAL KILL
Date of Necropsy: 07/25/2018 ** NECROPSY COMPLETE ** ** EXAMINATION COMPLETE **

Histo Pathology Observations:	Correlated with:
harderian gland; infiltrate, mononuclear cell; minimal	
kidney; infiltrate, mononuclear cell; minimal	
parathyroid gland; Only One of Pair Present; recut slide examined	
prostate; infiltrate, mononuclear cell; minimal	

The following tissues were within normal limits:

adrenal gland	aorta	bone with marrow - femur		bone with marrow - sternum		brain
cecum	colon	duodenum	epididymis	esophagus	eye	heart
ileum	jejunum	lacrimal gland	liver	lung	lymph node - mandibular	
lymph node - mesenteric		mandibular salivary gland		nerve - sciatic	nerve - optic	pancreas
parathyroid gland	pituitary	rectum	seminal vesicle	skeletal muscle	skin	spinal cord - cervical
spinal cord - thoracic		spinal cord - lumbar	spleen	stomach	testis	thymus
thyroid gland	tongue	trachea	urinary bladder			

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 27 (continued): Individual Histopathology Observations

Animal No.: 25236 Group: 1 Sex: Male Species: Rat Strain: Sprague Dawley
Test Substance: TFM Dose: Group 1; 0 mg/kg/day Route: Drinking Water Study Type: Subchronic
Date of Death: 07/25/2018 Study Day (Week): 91 (13) Mode of Death: TERMINAL KILL
Date of Necropsy: 07/25/2018 ** NECROPSY COMPLETE ** ** EXAMINATION COMPLETE **

Histo Pathology Observations: Correlated with:

kidney;
chronic progressive nephropathy; minimal

parathyroid gland;
Only One of Pair Present; recut slide examined

prostate;
infiltrate, mononuclear cell; minimal
exudate; luminal; minimal

stomach;
ectasia; glandular; minimal; glandular stomach

testis;
hypospermatogenesis; minimal

The following tissues were within normal limits:

adrenal gland	aorta	bone with marrow - femur		bone with marrow - sternum		brain
cecum	colon	duodenum	epididymis	esophagus	eye	harderian gland
heart	ileum	jejunum	lacrimal gland	liver	lung	lymph node - mandibular
lymph node - mesenteric		mandibular salivary gland		nerve - sciatic	nerve - optic	pancreas
parathyroid gland	pituitary	rectum	seminal vesicle	skeletal muscle	skin	spinal cord - cervical
spinal cord - thoracic		spinal cord - lumbar	spleen	thymus	thyroid gland	tongue
trachea	urinary bladder					

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 27 (continued): Individual Histopathology Observations

Animal No.: 25237 Group: 1 Sex: Male Species: Rat Strain: Sprague Dawley
Test Substance: TFM Dose: Group 1; 0 mg/kg/day Route: Drinking Water Study Type: Subchronic
Date of Death: 07/25/2018 Study Day (Week): 91 (13) Mode of Death: TERMINAL KILL
Date of Necropsy: 07/25/2018 ** NECROPSY COMPLETE ** ** EXAMINATION COMPLETE **

Histo Pathology Observations: Correlated with:

adrenal gland;
medulla not present; recut slide examined

lacrimal gland;
infiltrate, mononuclear cell; minimal

parathyroid gland;
Only One of Pair Present; recut slide examined

The following tissues were within normal limits:

adrenal gland	aorta	bone with marrow - femur		bone with marrow - sternum		brain
cecum	colon	duodenum	epididymis	esophagus	eye	harderian gland
heart	ileum	jejunum	kidney	liver	lung	lymph node - mandibular
lymph node - mesenteric		mandibular salivary gland		nerve - sciatic	nerve - optic	pancreas
parathyroid gland	pituitary	prostate	rectum	seminal vesicle	skeletal muscle	skin
spinal cord - cervical		spinal cord - thoracic		spinal cord - lumbar	spleen	stomach
testis	thymus	thyroid gland	tongue	trachea	urinary bladder	

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 27 (continued): Individual Histopathology Observations

Animal No.: 25238 Group: 1 Sex: Male Species: Rat Strain: Sprague Dawley
Test Substance: TFM Dose: Group 1; 0 mg/kg/day Route: Drinking Water Study Type: Subchronic
Date of Death: 07/25/2018 Study Day (Week): 91 (13) Mode of Death: TERMINAL KILL
Date of Necropsy: 07/25/2018 ** NECROPSY COMPLETE ** ** EXAMINATION COMPLETE **

Histo Pathology Observations: Correlated with:

epididymis;
infiltrate, mononuclear cell; minimal

kidney;
chronic progressive nephropathy; minimal

lung;
alveolar macrophages; minimal

nerve - optic;
Only One of Pair Present; recut slide examined

prostate;
exudate; luminal; minimal

The following tissues were within normal limits:

adrenal gland	aorta	bone with marrow - femur		bone with marrow - sternum		brain
cecum	colon	duodenum	esophagus	eye	harderian gland	heart
ileum	jejunum	lacrimal gland	liver	lymph node - mandibular		lymph node - mesenteric
mandibular salivary gland		nerve - sciatic	nerve - optic	pancreas	parathyroid gland	pituitary
rectum	seminal vesicle	skeletal muscle	skin	spinal cord - cervical		spinal cord - thoracic
spinal cord - lumbar	spleen	stomach	testis	thymus	thyroid gland	tongue
trachea	urinary bladder					

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 27 (continued): Individual Histopathology Observations

Animal No.: 25239 Group: 1 Sex: Male Species: Rat Strain: Sprague Dawley
Test Substance: TFM Dose: Group 1; 0 mg/kg/day Route: Drinking Water Study Type: Subchronic
Date of Death: 07/25/2018 Study Day (Week): 91 (13) Mode of Death: TERMINAL KILL
Date of Necropsy: 07/25/2018 ** NECROPSY COMPLETE ** ** EXAMINATION COMPLETE **

Histo Pathology Observations:	Correlated with:
heart;	
infiltrate, mononuclear cell; minimal; myocardium	
degeneration / necrosis; minimal; myocardium	
kidney;	
chronic progressive nephropathy; minimal	
parathyroid gland;	
Only One of Pair Present; recut slide examined	
prostate;	
infiltrate, mononuclear cell; minimal	
skeletal muscle;	
infiltrate, mononuclear cell; minimal	

The following tissues were within normal limits:

adrenal gland	aorta	bone with marrow - femur		bone with marrow - sternum		brain
cecum	colon	duodenum	epididymis	esophagus	eye	harderian gland
ileum	jejunum	lacrimal gland	liver	lung	lymph node - mandibular	
lymph node - mesenteric		mandibular salivary gland		nerve - sciatic	nerve - optic	pancreas
parathyroid gland	pituitary	rectum	seminal vesicle	skin	spinal cord - cervical	
spinal cord - thoracic		spinal cord - lumbar	spleen	stomach	testis	thymus
thyroid gland	tongue	trachea	urinary bladder			

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 27 (continued): Individual Histopathology Observations

Animal No.: 25240 Group: 1 Sex: Male Species: Rat Strain: Sprague Dawley
Test Substance: TFM Dose: Group 1; 0 mg/kg/day Route: Drinking Water Study Type: Subchronic
Date of Death: 07/25/2018 Study Day (Week): 91 (13) Mode of Death: TERMINAL KILL
Date of Necropsy: 07/25/2018 ** NECROPSY COMPLETE ** ** EXAMINATION COMPLETE **

Histo Pathology Observations: Correlated with:

kidney;
infiltrate, mononuclear cell; minimal

lymph node - mandibular;
sinus erythrocytosis; minimal

pancreas;
infiltrate, mononuclear cell; minimal

parathyroid gland;
Only One of Pair Present; recut slide examined

prostate;
infiltrate, mononuclear cell; minimal

stomach;
ectasia; glandular; minimal; glandular stomach

The following tissues were within normal limits:

adrenal gland	aorta	bone with marrow - femur		bone with marrow - sternum		brain
cecum	colon	duodenum	epididymis	esophagus	eye	harderian gland
heart	ileum	jejunum	lacrimal gland	liver	lung	lymph node - mesenteric
mandibular salivary gland		nerve - sciatic	nerve - optic	parathyroid gland	pituitary	rectum
seminal vesicle	skeletal muscle	skin	spinal cord - cervical		spinal cord - thoracic	
spinal cord - lumbar	spleen	testis	thymus	thyroid gland	tongue	trachea
urinary bladder						

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 27 (continued): Individual Histopathology Observations

Animal No.: 25241 Group: 1 Sex: Male Species: Rat Strain: Sprague Dawley
Test Substance: TFM Dose: Group 1; 0 mg/kg/day Route: Drinking Water Study Type: Subchronic
Date of Death: 07/25/2018 Study Day (Week): 91 (13) Mode of Death: TERMINAL KILL
Date of Necropsy: 07/25/2018 ** NECROPSY COMPLETE ** ** EXAMINATION COMPLETE **

Histo Pathology Observations:	Correlated with:
heart;	
infiltrate, mononuclear cell; minimal; myocardium	
degeneration / necrosis; minimal; myocardium	
lacrimal gland;	
alteration; harderian gland; mild	
liver;	
infiltrate, mononuclear cell; minimal	
lung;	
infiltrate, mononuclear cell; perivascular; minimal	
pancreas;	
inflammation; chronic; minimal	
parathyroid gland;	
recut slide examined	
prostate;	
infiltrate, mononuclear cell; minimal	
stomach;	
ectasia; glandular; minimal; glandular stomach	
testis;	
hypospermatogenesis; minimal	

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 27 (continued): Individual Histopathology Observations

Animal No.: 25241 Group: 1 Sex: Male Species: Rat Strain: Sprague Dawley
Test Substance: TFM Dose: Group 1; 0 mg/kg/day Route: Drinking Water Study Type: Subchronic
Date of Death: 07/25/2018 Study Day (Week): 91 (13) Mode of Death: TERMINAL KILL
Date of Necropsy: 07/25/2018 ** NECROPSY COMPLETE ** ** EXAMINATION COMPLETE **

The following tissues were within normal limits:

adrenal gland	aorta	bone with marrow - femur		bone with marrow - sternum		brain
cecum	colon	duodenum	epididymis	esophagus	eye	harderian gland
ileum	jejunum	kidney	lymph node - mandibular		lymph node - mesenteric	
mandibular salivary gland		nerve - sciatic	nerve - optic	pituitary	rectum	seminal vesicle
skeletal muscle	skin	spinal cord - cervical		spinal cord - thoracic		spinal cord - lumbar
spleen	thymus	thyroid gland	tongue	trachea	urinary bladder	

The following tissues have not been examined:

parathyroid gland; not present

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 27 (continued): Individual Histopathology Observations

Animal No.: 25242 Group: 1 Sex: Male Species: Rat Strain: Sprague Dawley
Test Substance: TFM Dose: Group 1; 0 mg/kg/day Route: Drinking Water Study Type: Subchronic
Date of Death: 07/25/2018 Study Day (Week): 91 (13) Mode of Death: TERMINAL KILL
Date of Necropsy: 07/25/2018 ** NECROPSY COMPLETE ** ** EXAMINATION COMPLETE **

Histo Pathology Observations: Correlated with:

epididymis;
infiltrate, mononuclear cell; minimal

nerve - optic;
Only One of Pair Present; recut slide examined

spinal cord - cervical;
not found in wet tissue

spinal cord - thoracic;
not found in wet tissue

spinal cord - lumbar;
not found in wet tissue

stomach;
ectasia; glandular; mild; glandular stomach

The following tissues were within normal limits:

adrenal gland	aorta	bone with marrow - femur		bone with marrow - sternum		brain
cecum	colon	duodenum	esophagus	eye	harderian gland	heart
ileum	jejunum	kidney	lacrimal gland	liver	lung	lymph node - mandibular
lymph node - mesenteric		mandibular salivary gland		nerve - sciatic	nerve - optic	pancreas
parathyroid gland	pituitary	prostate	rectum	seminal vesicle	skeletal muscle	skin
spleen	testis	thymus	thyroid gland	tongue	trachea	urinary bladder

The following tissues have not been examined:

spinal cord - cervical; not present
spinal cord - thoracic; not present
spinal cord - lumbar; not present

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 27 (continued): Individual Histopathology Observations

Animal No.: 25243 Group: 1 Sex: Male Species: Rat Strain: Sprague Dawley
Test Substance: TFM Dose: Group 1; 0 mg/kg/day Route: Drinking Water Study Type: Subchronic
Date of Death: 07/25/2018 Study Day (Week): 91 (13) Mode of Death: TERMINAL KILL
Date of Necropsy: 07/25/2018 ** NECROPSY COMPLETE ** ** EXAMINATION COMPLETE **

Histo Pathology Observations:	Correlated with:
epididymis;	
infiltrate, mononuclear cell; minimal	
heart;	
infiltrate, mononuclear cell; minimal; myocardium	
degeneration / necrosis; minimal; myocardium	
liver;	
infiltrate, mononuclear cell; minimal	
prostate;	
infiltrate, mononuclear cell; minimal	

The following tissues were within normal limits:

adrenal gland	aorta	bone with marrow - femur		bone with marrow - sternum		brain
cecum	colon	duodenum	esophagus	eye	harderian gland	ileum
jejunum	kidney	lacrimal gland	lung	lymph node - mandibular		lymph node - mesenteric
mandibular salivary gland		nerve - sciatic	nerve - optic	pancreas	parathyroid gland	pituitary
rectum	seminal vesicle	skeletal muscle	skin	spinal cord - cervical		spinal cord - thoracic
spinal cord - lumbar	spleen	stomach	testis	thymus	thyroid gland	tongue
trachea	urinary bladder					

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 27 (continued): Individual Histopathology Observations

Animal No.: 25254 Group: 1 Sex: Female Species: Rat Strain: Sprague Dawley
Test Substance: TFM Dose: Group 1; 0 mg/kg/day Route: Drinking Water Study Type: Subchronic
Date of Death: 07/26/2018 Study Day (Week): 91 (13) Mode of Death: TERMINAL KILL
Date of Necropsy: 07/26/2018 ** NECROPSY COMPLETE ** ** EXAMINATION COMPLETE **

Histo Pathology Observations: Correlated with:

harderian gland;
infiltrate, mononuclear cell; minimal

liver;
necrosis; hepatocellular; minimal
infiltrate, mononuclear cell; minimal

lung;
infiltrate, mononuclear cell; interstitial; minimal

The following tissues were within normal limits:

adrenal gland	aorta	bone with marrow - femur		bone with marrow - sternum		brain
cecum	cervix	colon	duodenum	esophagus	eye	heart
ileum	jejunum	kidney	lacrimal gland	lymph node - mandibular		lymph node - mesenteric
mammary gland	mandibular salivary gland		nerve - sciatic	nerve - optic	ovary	pancreas
parathyroid gland	pituitary	rectum	skeletal muscle	skin	spinal cord - cervical	
spinal cord - thoracic		spinal cord - lumbar	spleen	stomach	thymus	thyroid gland
tongue	trachea	urinary bladder	uterus	vagina		

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 27 (continued): Individual Histopathology Observations

Animal No.: 25255 Group: 1 Sex: Female Species: Rat Strain: Sprague Dawley
Test Substance: TFM Dose: Group 1; 0 mg/kg/day Route: Drinking Water Study Type: Subchronic
Date of Death: 07/26/2018 Study Day (Week): 91 (13) Mode of Death: TERMINAL KILL
Date of Necropsy: 07/26/2018 ** NECROPSY COMPLETE ** ** EXAMINATION COMPLETE **

Histo Pathology Observations:	Correlated with:
lung;	
infiltrate, mononuclear cell; interstitial; minimal	
ovary;	
cyst(s), follicular; present, no grade assigned	
parathyroid gland;	
Only One of Pair Present; recut slide examined	
uterus;	
dilation; mild; lumen	

The following tissues were within normal limits:

adrenal gland	aorta	bone with marrow - femur		bone with marrow - sternum		brain
cecum	cervix	colon	duodenum	esophagus	eye	harderian gland
heart	ileum	jejunum	kidney	lacrimal gland	liver	lymph node - mandibular
lymph node - mesenteric		mammary gland	mandibular salivary gland		nerve - sciatic	nerve - optic
pancreas	parathyroid gland	pituitary	rectum	skeletal muscle	skin	spinal cord - cervical
spinal cord - thoracic		spinal cord - lumbar	spleen	stomach	thymus	thyroid gland
tongue	trachea	urinary bladder	vagina			

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 27 (continued): Individual Histopathology Observations

Animal No.: 25256 Group: 1 Sex: Female Species: Rat Strain: Sprague Dawley
Test Substance: TFM Dose: Group 1; 0 mg/kg/day Route: Drinking Water Study Type: Subchronic
Date of Death: 07/26/2018 Study Day (Week): 91 (13) Mode of Death: TERMINAL KILL
Date of Necropsy: 07/26/2018 ** NECROPSY COMPLETE ** ** EXAMINATION COMPLETE **

Histo Pathology Observations: Correlated with:

brain;
olfactory bulbs not examined; not found in wet tissue

kidney;
mineralization; tubular; minimal; corticomedullary junction

lacrimal gland;
infiltrate, mononuclear cell; minimal

liver;
infiltrate, mononuclear cell; minimal

nerve - optic;
Only One of Pair Present; recut slide examined

pancreas;
infiltrate, mononuclear cell; minimal

uterus;
dilation; mild; lumen

The following tissues were within normal limits:

adrenal gland	aorta	bone with marrow - femur		bone with marrow - sternum		brain
cecum	cervix	colon	duodenum	esophagus	eye	harderian gland
heart	ileum	jejunum	lung	lymph node - mandibular		lymph node - mesenteric
mammary gland	mandibular salivary gland		nerve - sciatic	nerve - optic	ovary	parathyroid gland
pituitary	rectum	skeletal muscle	skin	spinal cord - cervical		spinal cord - thoracic
spinal cord - lumbar	spleen	stomach	thymus	thyroid gland	tongue	trachea
urinary bladder	vagina					

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 27 (continued): Individual Histopathology Observations

Animal No.: 25257 Group: 1 Sex: Female Species: Rat Strain: Sprague Dawley
Test Substance: TFM Dose: Group 1; 0 mg/kg/day Route: Drinking Water Study Type: Subchronic
Date of Death: 07/26/2018 Study Day (Week): 91 (13) Mode of Death: TERMINAL KILL
Date of Necropsy: 07/26/2018 ** NECROPSY COMPLETE ** ** EXAMINATION COMPLETE **

Histo Pathology Observations: Correlated with:

brain;
one olfactory lobe not examined; one not found in wet tissue

nerve - optic;
Only One of Pair Present; recut slide examined

The following tissues were within normal limits:

adrenal gland	aorta	bone with marrow - femur		bone with marrow - sternum		brain
cecum	cervix	colon	duodenum	esophagus	eye	harderian gland
heart	ileum	jejunum	kidney	lacrimal gland	liver	lung
lymph node - mandibular		lymph node - mesenteric		mammary gland	mandibular salivary gland	
nerve - sciatic	nerve - optic	ovary	pancreas	parathyroid gland	pituitary	rectum
skeletal muscle	skin	spinal cord - cervical		spinal cord - thoracic		spinal cord - lumbar
spleen	stomach	thymus	thyroid gland	tongue	trachea	urinary bladder
uterus	vagina					

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 27 (continued): Individual Histopathology Observations

Animal No.: 25258 Group: 1 Sex: Female Species: Rat Strain: Sprague Dawley
Test Substance: TFM Dose: Group 1; 0 mg/kg/day Route: Drinking Water Study Type: Subchronic
Date of Death: 07/26/2018 Study Day (Week): 91 (13) Mode of Death: TERMINAL KILL
Date of Necropsy: 07/26/2018 ** NECROPSY COMPLETE ** ** EXAMINATION COMPLETE **

Histo Pathology Observations: Correlated with:

harderian gland;
infiltrate, mononuclear cell; minimal

parathyroid gland;
recut slide examined

stomach;
ectasia; glandular; minimal; glandular stomach

The following tissues were within normal limits:

adrenal gland	aorta	bone with marrow - femur		bone with marrow - sternum		brain
cecum	cervix	colon	duodenum	esophagus	eye	heart
ileum	jejunum	kidney	lacrimal gland	liver	lung	lymph node - mandibular
lymph node - mesenteric		mammary gland	mandibular salivary gland		nerve - sciatic	nerve - optic
ovary	pancreas	pituitary	rectum	skeletal muscle	skin	spinal cord - cervical
spinal cord - thoracic		spinal cord - lumbar	spleen	thymus	thyroid gland	tongue
trachea	urinary bladder	uterus	vagina			

The following tissues have not been examined:

parathyroid gland; not present

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 27 (continued): Individual Histopathology Observations

Animal No.: 25259 Group: 1 Sex: Female Species: Rat Strain: Sprague Dawley
Test Substance: TFM Dose: Group 1; 0 mg/kg/day Route: Drinking Water Study Type: Subchronic
Date of Death: 07/26/2018 Study Day (Week): 91 (13) Mode of Death: TERMINAL KILL
Date of Necropsy: 07/26/2018 ** NECROPSY COMPLETE ** ** EXAMINATION COMPLETE **

Histo Pathology Observations: Correlated with:

brain;
olfactory bulbs not examined; not found in wet tissue

nerve - optic;
not found in wet tissue

The following tissues were within normal limits:

adrenal gland	aorta	bone with marrow - femur		bone with marrow - sternum		brain
cecum	cervix	colon	duodenum	esophagus	eye	harderian gland
heart	ileum	jejunum	kidney	lacrimal gland	liver	lung
lymph node - mandibular		lymph node - mesenteric		mammary gland	mandibular salivary gland	
nerve - sciatic	ovary	pancreas	parathyroid gland	pituitary	rectum	skeletal muscle
skin	spinal cord - cervical		spinal cord - thoracic		spinal cord - lumbar	spleen
stomach	thymus	thyroid gland	tongue	trachea	urinary bladder	uterus
vagina						

The following tissues have not been examined:

nerve - optic; not present

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 27 (continued): Individual Histopathology Observations

Animal No.: 25260 Group: 1 Sex: Female Species: Rat Strain: Sprague Dawley
Test Substance: TFM Dose: Group 1; 0 mg/kg/day Route: Drinking Water Study Type: Subchronic
Date of Death: 07/26/2018 Study Day (Week): 91 (13) Mode of Death: TERMINAL KILL
Date of Necropsy: 07/26/2018 ** NECROPSY COMPLETE ** ** EXAMINATION COMPLETE **

Histo Pathology Observations:	Correlated with:
harderian gland;	
infiltrate, mononuclear cell; minimal	
liver;	
necrosis; hepatocellular; minimal	
infiltrate, mononuclear cell; minimal	
parathyroid gland;	
Only One of Pair Present; recut slide examined	

The following tissues were within normal limits:

adrenal gland	aorta	bone with marrow - femur		bone with marrow - sternum		brain
cecum	cervix	colon	duodenum	esophagus	eye	heart
ileum	jejunum	kidney	lacrimal gland	lung	lymph node - mandibular	
lymph node - mesenteric		mammary gland	mandibular salivary gland		nerve - sciatic	nerve - optic
ovary	pancreas	parathyroid gland	pituitary	rectum	skeletal muscle	skin
spinal cord - cervical		spinal cord - thoracic		spinal cord - lumbar	spleen	stomach
thymus	thyroid gland	tongue	trachea	urinary bladder	uterus	vagina

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 27 (continued): Individual Histopathology Observations

Animal No.: 25261 Group: 1 Sex: Female Species: Rat Strain: Sprague Dawley
Test Substance: TFM Dose: Group 1; 0 mg/kg/day Route: Drinking Water Study Type: Subchronic
Date of Death: 07/26/2018 Study Day (Week): 91 (13) Mode of Death: TERMINAL KILL
Date of Necropsy: 07/26/2018 ** NECROPSY COMPLETE ** ** EXAMINATION COMPLETE **

Histo Pathology Observations: Correlated with:

stomach;
infiltrate, mononuclear cell; minimal; glandular stomach; submucosa

The following tissues were within normal limits:

adrenal gland	aorta	bone with marrow - femur		bone with marrow - sternum		brain
cecum	cervix	colon	duodenum	esophagus	eye	harderian gland
heart	ileum	jejunum	kidney	lacrimal gland	liver	lung
lymph node - mandibular		lymph node - mesenteric		mammary gland	mandibular salivary gland	
nerve - sciatic	nerve - optic	ovary	pancreas	parathyroid gland	pituitary	rectum
skeletal muscle	skin	spinal cord - cervical		spinal cord - thoracic		spinal cord - lumbar
spleen	thymus	thyroid gland	tongue	trachea	urinary bladder	uterus
vagina						

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 27 (continued): Individual Histopathology Observations

Animal No.: 25262 Group: 1 Sex: Female Species: Rat Strain: Sprague Dawley
Test Substance: TFM Dose: Group 1; 0 mg/kg/day Route: Drinking Water Study Type: Subchronic
Date of Death: 07/26/2018 Study Day (Week): 91 (13) Mode of Death: TERMINAL KILL
Date of Necropsy: 07/26/2018 ** NECROPSY COMPLETE ** ** EXAMINATION COMPLETE **

Histo Pathology Observations:	Correlated with:
harderian gland; infiltrate, mononuclear cell; minimal	
lacrimal gland; infiltrate, mononuclear cell; minimal	
liver; vacuolation; hepatocellular; mild	
uterus; dilation; moderate; lumen	

The following tissues were within normal limits:

adrenal gland	aorta	bone with marrow - femur		bone with marrow - sternum		brain
cecum	cervix	colon	duodenum	esophagus	eye	heart
ileum	jejunum	kidney	lung	lymph node - mandibular		lymph node - mesenteric
mammary gland	mandibular salivary gland		nerve - sciatic	nerve - optic	ovary	pancreas
parathyroid gland	pituitary	rectum	skeletal muscle	skin	spinal cord - cervical	
spinal cord - thoracic		spinal cord - lumbar	spleen	stomach	thymus	thyroid gland
tongue	trachea	urinary bladder	vagina			

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 27 (continued): Individual Histopathology Observations

Animal No.: 25263 Group: 1 Sex: Female Species: Rat Strain: Sprague Dawley
Test Substance: TFM Dose: Group 1; 0 mg/kg/day Route: Drinking Water Study Type: Subchronic
Date of Death: 07/26/2018 Study Day (Week): 91 (13) Mode of Death: TERMINAL KILL
Date of Necropsy: 07/26/2018 ** NECROPSY COMPLETE ** ** EXAMINATION COMPLETE **

Histo Pathology Observations: Correlated with:

lung;
alveolar macrophages; minimal

parathyroid gland;
Only One of Pair Present; recut slide examined

The following tissues were within normal limits:

adrenal gland	aorta	bone with marrow - femur		bone with marrow - sternum		brain
cecum	cervix	colon	duodenum	esophagus	eye	harderian gland
heart	ileum	jejunum	kidney	lacrimal gland	liver	lymph node - mandibular
lymph node - mesenteric		mammary gland	mandibular salivary gland		nerve - sciatic	nerve - optic
ovary	pancreas	parathyroid gland	pituitary	rectum	skeletal muscle	skin
spinal cord - cervical		spinal cord - thoracic		spinal cord - lumbar	spleen	stomach
thymus	thyroid gland	tongue	trachea	urinary bladder	uterus	vagina

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 27 (continued): Individual Histopathology Observations

Animal No.: 25314 Group: 6 Sex: Male Species: Rat Strain: Sprague Dawley
Test Substance: TFM Dose: Group 6; 100 mg/kg/day Route: Drinking Water Study Type: Subchronic
Date of Death: 07/25/2018 Study Day (Week): 91 (13) Mode of Death: TERMINAL KILL
Date of Necropsy: 07/25/2018 ** NECROPSY COMPLETE ** ** EXAMINATION COMPLETE **

Histo Pathology Observations: Correlated with:

epididymis;
infiltrate, mononuclear cell; minimal

heart;
infiltrate, mononuclear cell; minimal; myocardium

liver;
infiltrate, mononuclear cell; minimal

stomach;
ectasia; glandular; minimal; glandular stomach

The following tissues were within normal limits:

adrenal gland	aorta	bone with marrow - femur		bone with marrow - sternum		brain
cecum	colon	duodenum	esophagus	eye	harderian gland	ileum
jejunum	kidney	lacrimal gland	lung	lymph node - mandibular		lymph node - mesenteric
mandibular salivary gland		nerve - sciatic	nerve - optic	pancreas	parathyroid gland	pituitary
prostate	rectum	seminal vesicle	skeletal muscle	skin	spinal cord - cervical	
spinal cord - thoracic		spinal cord - lumbar	spleen	testis	thymus	thyroid gland
tongue	trachea	urinary bladder				

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 27 (continued): Individual Histopathology Observations

Animal No.: 25315 Group: 6 Sex: Male Species: Rat Strain: Sprague Dawley
Test Substance: TFM Dose: Group 6; 100 mg/kg/day Route: Drinking Water Study Type: Subchronic
Date of Death: 07/25/2018 Study Day (Week): 91 (13) Mode of Death: TERMINAL KILL
Date of Necropsy: 07/25/2018 ** NECROPSY COMPLETE ** ** EXAMINATION COMPLETE **

Histo Pathology Observations:	Correlated with:
bone with marrow - femur; not found in wet tissue	
heart; infiltrate, mononuclear cell; minimal; myocardium	
lacrimal gland; Only One of Pair Present; one not found in wet tissue	

The following tissues were within normal limits:

adrenal gland	aorta	bone with marrow - sternum		brain	cecum	colon
duodenum	epididymis	esophagus	eye	harderian gland	ileum	jejunum
kidney	lacrimal gland	liver	lung	lymph node - mandibular		lymph node - mesenteric
mandibular salivary gland		nerve - sciatic	nerve - optic	pancreas	parathyroid gland	pituitary
prostate	rectum	seminal vesicle	skeletal muscle	skin	spinal cord - cervical	
spinal cord - thoracic		spinal cord - lumbar	spleen	stomach	testis	thymus
thyroid gland	tongue	trachea	urinary bladder			

The following tissues have not been examined:

bone with marrow - femur; not present

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 27 (continued): Individual Histopathology Observations

Animal No.: 25316 Group: 6 Sex: Male Species: Rat Strain: Sprague Dawley
Test Substance: TFM Dose: Group 6; 100 mg/kg/day Route: Drinking Water Study Type: Subchronic
Date of Death: 07/25/2018 Study Day (Week): 91 (13) Mode of Death: TERMINAL KILL
Date of Necropsy: 07/25/2018 ** NECROPSY COMPLETE ** ** EXAMINATION COMPLETE **

Histo Pathology Observations:	Correlated with:
eye;	
dysplasia; minimal; retina	
testis;	
hypospermatogenesis; minimal	

The following tissues were within normal limits:

adrenal gland	aorta	bone with marrow - femur		bone with marrow - sternum		brain
cecum	colon	duodenum	epididymis	esophagus	harderian gland	heart
ileum	jejunum	kidney	lacrimal gland	liver	lung	lymph node - mandibular
lymph node - mesenteric		mandibular salivary gland		nerve - sciatic	nerve - optic	pancreas
parathyroid gland	pituitary	prostate	rectum	seminal vesicle	skeletal muscle	skin
spinal cord - cervical		spinal cord - thoracic		spinal cord - lumbar	spleen	stomach
thymus	thyroid gland	tongue	trachea	urinary bladder		

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 27 (continued): Individual Histopathology Observations

Animal No.: 25317 Group: 6 Sex: Male Species: Rat Strain: Sprague Dawley
Test Substance: TFM Dose: Group 6; 100 mg/kg/day Route: Drinking Water Study Type: Subchronic
Date of Death: 07/25/2018 Study Day (Week): 91 (13) Mode of Death: TERMINAL KILL
Date of Necropsy: 07/25/2018 ** NECROPSY COMPLETE ** ** EXAMINATION COMPLETE **

Histo Pathology Observations: Correlated with:

epididymis;
infiltrate, mononuclear cell; minimal

heart;
degeneration / necrosis; minimal; myocardium
infiltrate, mononuclear cell; minimal; myocardium

kidney;
cyst; present, no grade assigned; medulla

pancreas;
infiltrate, mononuclear cell; minimal

parathyroid gland;
Only One of Pair Present; recut slide examined

prostate;
infiltrate, mononuclear cell; minimal

stomach;
ectasia; glandular; minimal; glandular stomach

thyroid gland;
Only One of Pair Present; recut slide examined

The following tissues were within normal limits:

adrenal gland	aorta	bone with marrow - femur		bone with marrow - sternum		brain
cecum	colon	duodenum	esophagus	eye	harderian gland	ileum
jejunum	lacrimal gland	liver	lung	lymph node - mandibular		lymph node - mesenteric
mandibular salivary gland		nerve - sciatic	nerve - optic	parathyroid gland	pituitary	rectum
seminal vesicle	skeletal muscle	skin	spinal cord - cervical		spinal cord - thoracic	
spinal cord - lumbar	spleen	testis	thymus	thyroid gland	tongue	trachea
urinary bladder						

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 27 (continued): Individual Histopathology Observations

Animal No.: 25318 Group: 6 Sex: Male Species: Rat Strain: Sprague Dawley
Test Substance: TFM Dose: Group 6; 100 mg/kg/day Route: Drinking Water Study Type: Subchronic
Date of Death: 07/25/2018 Study Day (Week): 91 (13) Mode of Death: TERMINAL KILL
Date of Necropsy: 07/25/2018 ** NECROPSY COMPLETE ** ** EXAMINATION COMPLETE **

Histo Pathology Observations:	Correlated with:
epididymis; infiltrate, mononuclear cell; minimal	
lymph node - mandibular; sinus erythrocytosis; mild	

The following tissues were within normal limits:

adrenal gland	aorta	bone with marrow - femur		bone with marrow - sternum		brain
cecum	colon	duodenum	esophagus	eye	harderian gland	heart
ileum	jejunum	kidney	lacrimal gland	liver	lung	lymph node - mesenteric
mandibular salivary gland		nerve - sciatic	nerve - optic	pancreas	parathyroid gland	pituitary
prostate	rectum	seminal vesicle	skeletal muscle	skin	spinal cord - cervical	
spinal cord - thoracic		spinal cord - lumbar	spleen	stomach	testis	thymus
thyroid gland	tongue	trachea	urinary bladder			

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 27 (continued): Individual Histopathology Observations

Animal No.: 25319 Group: 6 Sex: Male Species: Rat Strain: Sprague Dawley
Test Substance: TFM Dose: Group 6; 100 mg/kg/day Route: Drinking Water Study Type: Subchronic
Date of Death: 07/25/2018 Study Day (Week): 91 (13) Mode of Death: TERMINAL KILL
Date of Necropsy: 07/25/2018 ** NECROPSY COMPLETE ** ** EXAMINATION COMPLETE **

Histo Pathology Observations: Correlated with:

liver;
vacuolation; hepatocellular; mild

pancreas;
atrophy; acinar cell; focal; minimal

parathyroid gland;
Only One of Pair Present; recut slide examined

prostate;
infiltrate, mononuclear cell; minimal

The following tissues were within normal limits:

adrenal gland	aorta	bone with marrow - femur		bone with marrow - sternum		brain
cecum	colon	duodenum	epididymis	esophagus	eye	harderian gland
heart	ileum	jejunum	kidney	lacrimal gland	lung	lymph node - mandibular
lymph node - mesenteric		mandibular salivary gland		nerve - sciatic	nerve - optic	parathyroid gland
pituitary	rectum	seminal vesicle	skeletal muscle	skin	spinal cord - cervical	
spinal cord - thoracic		spinal cord - lumbar	spleen	stomach	testis	thymus
thyroid gland	tongue	trachea	urinary bladder			

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 27 (continued): Individual Histopathology Observations

Animal No.: 25320 Group: 6 Sex: Male Species: Rat Strain: Sprague Dawley
Test Substance: TFM Dose: Group 6; 100 mg/kg/day Route: Drinking Water Study Type: Subchronic
Date of Death: 07/25/2018 Study Day (Week): 91 (13) Mode of Death: TERMINAL KILL
Date of Necropsy: 07/25/2018 ** NECROPSY COMPLETE ** ** EXAMINATION COMPLETE **

Histo Pathology Observations:	Correlated with:
adrenal gland; Only One of Pair Present; questionable tissue submitted for one; recut slide examined	
pancreas; inflammation; chronic; mild	
testis; hypospermatogenesis; moderate	

The following tissues were within normal limits:

adrenal gland	aorta	bone with marrow - femur		bone with marrow - sternum		brain
cecum	colon	duodenum	epididymis	esophagus	eye	harderian gland
heart	ileum	jejunum	kidney	lacrimal gland	liver	lung
lymph node - mandibular		lymph node - mesenteric		mandibular salivary gland		nerve - sciatic
nerve - optic	parathyroid gland	pituitary	prostate	rectum	seminal vesicle	skeletal muscle
skin	spinal cord - cervical		spinal cord - thoracic		spinal cord - lumbar	spleen
stomach	thymus	thyroid gland	tongue	trachea	urinary bladder	

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 27 (continued): Individual Histopathology Observations

Animal No.: 25321 Group: 6 Sex: Male Species: Rat Strain: Sprague Dawley
Test Substance: TFM Dose: Group 6; 100 mg/kg/day Route: Drinking Water Study Type: Subchronic
Date of Death: 07/25/2018 Study Day (Week): 91 (13) Mode of Death: TERMINAL KILL
Date of Necropsy: 07/25/2018 ** NECROPSY COMPLETE ** ** EXAMINATION COMPLETE **

Histo Pathology Observations:	Correlated with:
epididymis;	
vacuolation; epithelial; minimal	
parathyroid gland;	
Only One of Pair Present; recut slide examined	
prostate;	
infiltrate, mononuclear cell; minimal	
exudate; luminal; minimal	

The following tissues were within normal limits:

adrenal gland	aorta	bone with marrow - femur		bone with marrow - sternum		brain
cecum	colon	duodenum	esophagus	eye	harderian gland	heart
ileum	jejunum	kidney	lacrimal gland	liver	lung	lymph node - mandibular
lymph node - mesenteric		mandibular salivary gland		nerve - sciatic	nerve - optic	pancreas
parathyroid gland	pituitary	rectum	seminal vesicle	skeletal muscle	skin	spinal cord - cervical
spinal cord - thoracic		spinal cord - lumbar	spleen	stomach	testis	thymus
thyroid gland	tongue	trachea	urinary bladder			

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 27 (continued): Individual Histopathology Observations

Animal No.: 25322 Group: 6 Sex: Male Species: Rat Strain: Sprague Dawley
Test Substance: TFM Dose: Group 6; 100 mg/kg/day Route: Drinking Water Study Type: Subchronic
Date of Death: 07/25/2018 Study Day (Week): 91 (13) Mode of Death: TERMINAL KILL
Date of Necropsy: 07/25/2018 ** NECROPSY COMPLETE ** ** EXAMINATION COMPLETE **

Histo Pathology Observations:	Correlated with:
epididymis;	
infiltrate, mononuclear cell; minimal	
prostate;	
infiltrate, mononuclear cell; minimal	
stomach;	
ectasia; glandular; minimal; glandular stomach	

The following tissues were within normal limits:

adrenal gland	aorta	bone with marrow - femur		bone with marrow - sternum		brain
cecum	colon	duodenum	esophagus	eye	harderian gland	heart
ileum	jejunum	kidney	lacrimal gland	liver	lung	lymph node - mandibular
lymph node - mesenteric		mandibular salivary gland		nerve - sciatic	nerve - optic	pancreas
parathyroid gland	pituitary	rectum	seminal vesicle	skeletal muscle	skin	spinal cord - cervical
spinal cord - thoracic		spinal cord - lumbar	spleen	testis	thymus	thyroid gland
tongue	trachea	urinary bladder				

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 27 (continued): Individual Histopathology Observations

Animal No.: 25323 Group: 6 Sex: Male Species: Rat Strain: Sprague Dawley
Test Substance: TFM Dose: Group 6; 100 mg/kg/day Route: Drinking Water Study Type: Subchronic
Date of Death: 07/25/2018 Study Day (Week): 91 (13) Mode of Death: TERMINAL KILL
Date of Necropsy: 07/25/2018 ** NECROPSY COMPLETE ** ** EXAMINATION COMPLETE **

Histo Pathology Observations:	Correlated with:
kidney;	
inflammation; chronic active; focal; mild	
lung;	
metaplasia; osseus; minimal	
infiltrate, mononuclear cell; interstitial; minimal	

The following tissues were within normal limits:

adrenal gland	aorta	bone with marrow - femur		bone with marrow - sternum		brain
cecum	colon	duodenum	epididymis	esophagus	eye	harderian gland
heart	ileum	jejunum	lacrimal gland	liver	lymph node - mandibular	
lymph node - mesenteric		mandibular salivary gland		nerve - sciatic	nerve - optic	pancreas
parathyroid gland	pituitary	prostate	rectum	seminal vesicle	skeletal muscle	skin
spinal cord - cervical		spinal cord - thoracic		spinal cord - lumbar	spleen	stomach
testis	thymus	thyroid gland	tongue	trachea	urinary bladder	

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 27 (continued): Individual Histopathology Observations

Animal No.: 25330 Group: 6 Sex: Male Species: Rat Strain: Sprague Dawley
Test Substance: TFM Dose: Group 6; 100 mg/kg/day Route: Drinking Water Study Type: Subchronic
Date of Death: 08/22/2018 Study Day (Week): 119 (17) Mode of Death: RECOVERY KILL
Date of Necropsy: 08/22/2018 ** NECROPSY COMPLETE ** ** EXAMINATION COMPLETE **

Histo Pathology Observations:	Correlated with:
testis;	
hypospermatogenesis; severe	testis; small; right (G)

The following tissues were within normal limits:

None

Codes Used:

(G) = Gross Finding

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 27 (continued): Individual Histopathology Observations

Animal No.: 25362 Group: 9 Sex: Female Species: Rat Strain: Sprague Dawley
Test Substance: TFM Dose: Group 9; 10 mg/kg/day Route: Drinking Water Study Type: Subchronic
Date of Death: 07/26/2018 Study Day (Week): 91 (13) Mode of Death: TERMINAL KILL
Date of Necropsy: 07/26/2018 ** NECROPSY COMPLETE ** ** EXAMINATION COMPLETE **

Histo Pathology Observations:	Correlated with:
uterus;	
dilation; marked; lumen	uterus; distention; fluid-filled; bilateral (G)

The following tissues were within normal limits:

None

Codes Used:

(G) = Gross Finding

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 27 (continued): Individual Histopathology Observations

Animal No.: 25363 Group: 9 Sex: Female Species: Rat Strain: Sprague Dawley
Test Substance: TFM Dose: Group 9; 10 mg/kg/day Route: Drinking Water Study Type: Subchronic
Date of Death: 07/26/2018 Study Day (Week): 91 (13) Mode of Death: TERMINAL KILL
Date of Necropsy: 07/26/2018 ** NECROPSY COMPLETE ** ** EXAMINATION COMPLETE **

Histo Pathology Observations:	Correlated with:
uterus;	
dilation; mild; lumen	uterus; distention; fluid-filled; bilateral (G)

The following tissues were within normal limits:

None

Codes Used:

(G) = Gross Finding

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 27 (continued): Individual Histopathology Observations

Animal No.: 25366 Group: 10 Sex: Female Species: Rat Strain: Sprague Dawley
Test Substance: TFM Dose: Group 10; 30 mg/kg/day Route: Drinking Water Study Type: Subchronic
Date of Death: 07/26/2018 Study Day (Week): 91 (13) Mode of Death: TERMINAL KILL
Date of Necropsy: 07/26/2018 ** NECROPSY COMPLETE ** ** EXAMINATION COMPLETE **

Histo Pathology Observations:	Correlated with:
uterus;	
dilation; moderate; lumen	uterus; distention; fluid-filled; bilateral (G)

The following tissues were within normal limits:

None

Codes Used:

(G) = Gross Finding

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 27 (continued): Individual Histopathology Observations

Animal No.: 25368 Group: 10 Sex: Female Species: Rat Strain: Sprague Dawley
Test Substance: TFM Dose: Group 10; 30 mg/kg/day Route: Drinking Water Study Type: Subchronic
Date of Death: 07/26/2018 Study Day (Week): 91 (13) Mode of Death: TERMINAL KILL
Date of Necropsy: 07/26/2018 ** NECROPSY COMPLETE ** ** EXAMINATION COMPLETE **

Histo Pathology Observations:	Correlated with:
uterus;	
dilation; severe; lumen	uterus; distention; fluid-filled; bilateral (G)

The following tissues were within normal limits:

None

Codes Used:

(G) = Gross Finding

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 27 (continued): Individual Histopathology Observations

Animal No.: 25374 Group: 11 Sex: Female Species: Rat Strain: Sprague Dawley
Test Substance: TFM Dose: Group 11; 100 mg/kg/day Route: Drinking Water Study Type: Subchronic
Date of Death: 07/26/2018 Study Day (Week): 91 (13) Mode of Death: TERMINAL KILL
Date of Necropsy: 07/26/2018 ** NECROPSY COMPLETE ** ** EXAMINATION COMPLETE **

Histo Pathology Observations: Correlated with:

brain;
olfactory lobes not examined; not found in wet tissue

liver;
vacuolation; hepatocellular; minimal

ovary;
cyst(s), follicular; present, no grade assigned

pancreas;
infiltrate, mononuclear cell; minimal

stomach;
ectasia; glandular; minimal; glandular stomach

The following tissues were within normal limits:

adrenal gland	aorta	bone with marrow - femur		bone with marrow - sternum		brain
cecum	cervix	colon	duodenum	esophagus	eye	harderian gland
heart	ileum	jejunum	kidney	lacrimal gland	lung	lymph node - mandibular
lymph node - mesenteric		mammary gland	mandibular salivary gland		nerve - sciatic	nerve - optic
parathyroid gland	pituitary	rectum	skeletal muscle	skin	spinal cord - cervical	
spinal cord - thoracic		spinal cord - lumbar	spleen	thymus	thyroid gland	tongue
trachea	urinary bladder	uterus	vagina			

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 27 (continued): Individual Histopathology Observations

Animal No.: 25375 Group: 11 Sex: Female Species: Rat Strain: Sprague Dawley
Test Substance: TFM Dose: Group 11; 100 mg/kg/day Route: Drinking Water Study Type: Subchronic
Date of Death: 07/26/2018 Study Day (Week): 91 (13) Mode of Death: TERMINAL KILL
Date of Necropsy: 07/26/2018 ** NECROPSY COMPLETE ** ** EXAMINATION COMPLETE **

Histo Pathology Observations: Correlated with:

brain;
one olfactory bulb not examined; not found in wet tissue

lung;
alveolar macrophages; minimal

The following tissues were within normal limits:

adrenal gland	aorta	bone with marrow - femur		bone with marrow - sternum		brain
cecum	cervix	colon	duodenum	esophagus	eye	harderian gland
heart	ileum	jejunum	kidney	lacrimal gland	liver	lymph node - mandibular
lymph node - mesenteric		mammary gland	mandibular salivary gland		nerve - sciatic	nerve - optic
ovary	pancreas	parathyroid gland	pituitary	rectum	skeletal muscle	skin
spinal cord - cervical		spinal cord - thoracic		spinal cord - lumbar	spleen	stomach
thymus	thyroid gland	tongue	trachea	urinary bladder	uterus	vagina

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 27 (continued): Individual Histopathology Observations

Animal No.: 25376 Group: 11 Sex: Female Species: Rat Strain: Sprague Dawley
Test Substance: TFM Dose: Group 11; 100 mg/kg/day Route: Drinking Water Study Type: Subchronic
Date of Death: 07/26/2018 Study Day (Week): 91 (13) Mode of Death: TERMINAL KILL
Date of Necropsy: 07/26/2018 ** NECROPSY COMPLETE ** ** EXAMINATION COMPLETE **

Histo Pathology Observations:	Correlated with:
harderian gland;	
infiltrate, mononuclear cell; minimal	
kidney;	
mineralization; tubular; minimal; corticomedullary junction	
infiltrate, mononuclear cell; minimal	
liver;	
infiltrate, mononuclear cell; minimal	
parathyroid gland;	
recut slide examined	
uterus;	
dilation; moderate; lumen	

The following tissues were within normal limits:

adrenal gland	aorta	bone with marrow - femur		bone with marrow - sternum		brain
cecum	cervix	colon	duodenum	esophagus	eye	heart
ileum	jejunum	lacrimal gland	lung	lymph node - mandibular		lymph node - mesenteric
mammary gland	mandibular salivary gland		nerve - sciatic	nerve - optic	ovary	pancreas
pituitary	rectum	skeletal muscle	skin	spinal cord - cervical		spinal cord - thoracic
spinal cord - lumbar	spleen	stomach	thymus	thyroid gland	tongue	trachea
urinary bladder	vagina					

The following tissues have not been examined:

parathyroid gland; not present

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 27 (continued): Individual Histopathology Observations

Animal No.: 25377 Group: 11 Sex: Female Species: Rat Strain: Sprague Dawley
Test Substance: TFM Dose: Group 11; 100 mg/kg/day Route: Drinking Water Study Type: Subchronic
Date of Death: 07/26/2018 Study Day (Week): 91 (13) Mode of Death: TERMINAL KILL
Date of Necropsy: 07/26/2018 ** NECROPSY COMPLETE ** ** EXAMINATION COMPLETE **

Histo Pathology Observations:	Correlated with:
lacrimal gland; infiltrate, mononuclear cell; minimal	

The following tissues were within normal limits:

adrenal gland	aorta	bone with marrow - femur		bone with marrow - sternum		brain
cecum	cervix	colon	duodenum	esophagus	eye	harderian gland
heart	ileum	jejunum	kidney	liver	lung	lymph node - mandibular
lymph node - mesenteric		mammary gland	mandibular salivary gland		nerve - sciatic	nerve - optic
ovary	pancreas	parathyroid gland	pituitary	rectum	skeletal muscle	skin
spinal cord - cervical		spinal cord - thoracic		spinal cord - lumbar	spleen	stomach
thymus	thyroid gland	tongue	trachea	urinary bladder	uterus	vagina

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 27 (continued): Individual Histopathology Observations

Animal No.: 25378 Group: 11 Sex: Female Species: Rat Strain: Sprague Dawley
Test Substance: TFM Dose: Group 11; 100 mg/kg/day Route: Drinking Water Study Type: Subchronic
Date of Death: 07/26/2018 Study Day (Week): 91 (13) Mode of Death: TERMINAL KILL
Date of Necropsy: 07/26/2018 ** NECROPSY COMPLETE ** ** EXAMINATION COMPLETE **

Histo Pathology Observations: Correlated with:

None

The following tissues were within normal limits:

adrenal gland	aorta	bone with marrow - femur		bone with marrow - sternum		brain
cecum	cervix	colon	duodenum	esophagus	eye	harderian gland
heart	ileum	jejunum	kidney	lacrimal gland	liver	lung
lymph node - mandibular		lymph node - mesenteric		mammary gland	mandibular salivary gland	
nerve - sciatic	nerve - optic	ovary	pancreas	parathyroid gland	pituitary	rectum
skeletal muscle	skin	spinal cord - cervical		spinal cord - thoracic		spinal cord - lumbar
spleen	stomach	thymus	thyroid gland	tongue	trachea	urinary bladder
uterus	vagina					

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 27 (continued): Individual Histopathology Observations

Animal No.: 25379 Group: 11 Sex: Female Species: Rat Strain: Sprague Dawley
Test Substance: TFM Dose: Group 11; 100 mg/kg/day Route: Drinking Water Study Type: Subchronic
Date of Death: 07/26/2018 Study Day (Week): 91 (13) Mode of Death: TERMINAL KILL
Date of Necropsy: 07/26/2018 ** NECROPSY COMPLETE ** ** EXAMINATION COMPLETE **

Histo Pathology Observations: Correlated with:

brain;
one olfactory bulb not examined; not found in wet tissue

lacrimal gland;
infiltrate, mononuclear cell; minimal

liver;
infiltrate, mononuclear cell; mild

parathyroid gland;
Only One of Pair Present; recut slide examined

pituitary;
infiltrate; lymphocyte; focal; minimal; pars distalis

The following tissues were within normal limits:

adrenal gland	aorta	bone with marrow - femur		bone with marrow - sternum		brain
cecum	cervix	colon	duodenum	esophagus	eye	harderian gland
heart	ileum	jejunum	kidney	lung	lymph node - mandibular	
lymph node - mesenteric		mammary gland	mandibular salivary gland		nerve - sciatic	nerve - optic
ovary	pancreas	parathyroid gland	rectum	skeletal muscle	skin	spinal cord - cervical
spinal cord - thoracic		spinal cord - lumbar	spleen	stomach	thymus	thyroid gland
tongue	trachea	urinary bladder	uterus	vagina		

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 27 (continued): Individual Histopathology Observations

Animal No.: 25380 Group: 11 Sex: Female Species: Rat Strain: Sprague Dawley
Test Substance: TFM Dose: Group 11; 100 mg/kg/day Route: Drinking Water Study Type: Subchronic
Date of Death: 07/26/2018 Study Day (Week): 91 (13) Mode of Death: TERMINAL KILL
Date of Necropsy: 07/26/2018 ** NECROPSY COMPLETE ** ** EXAMINATION COMPLETE **

Histo Pathology Observations:	Correlated with:
brain;	
one olfactory bulb not examined; not found in wet tissue	
heart;	
infiltrate, mononuclear cell; minimal; myocardium	
liver;	
vacuolation; hepatocellular; mild	
mandibular salivary gland;	
hyperplasia; lymphoid; moderate	
parathyroid gland;	
Only One of Pair Present; recut slide examined	
vagina;	
mucification; epithelial; mild	

The following tissues were within normal limits:

adrenal gland	aorta	bone with marrow - femur		bone with marrow - sternum		brain
cecum	cervix	colon	duodenum	esophagus	eye	harderian gland
ileum	jejunum	kidney	lacrimal gland	lung	lymph node - mandibular	
lymph node - mesenteric		mammary gland	nerve - sciatic	nerve - optic	ovary	pancreas
parathyroid gland	pituitary	rectum	skeletal muscle	skin	spinal cord - cervical	
spinal cord - thoracic		spinal cord - lumbar	spleen	stomach	thymus	thyroid gland
tongue	trachea	urinary bladder	uterus			

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 27 (continued): Individual Histopathology Observations

Animal No.: 25381 Group: 11 Sex: Female Species: Rat Strain: Sprague Dawley
Test Substance: TFM Dose: Group 11; 100 mg/kg/day Route: Drinking Water Study Type: Subchronic
Date of Death: 07/26/2018 Study Day (Week): 91 (13) Mode of Death: TERMINAL KILL
Date of Necropsy: 07/26/2018 ** NECROPSY COMPLETE ** ** EXAMINATION COMPLETE **

Histo Pathology Observations:	Correlated with:
kidney;	
chronic progressive nephropathy; minimal	
liver;	
necrosis; hepatocellular; minimal	
pancreas;	
infiltrate, mononuclear cell; minimal	
urinary bladder;	
urothelium not examined; not in plane of section; recut slide examined	

The following tissues were within normal limits:

adrenal gland	aorta	bone with marrow - femur		bone with marrow - sternum		brain
cecum	cervix	colon	duodenum	esophagus	eye	harderian gland
heart	ileum	jejunum	lacrimal gland	lung	lymph node - mandibular	
lymph node - mesenteric		mammary gland	mandibular salivary gland		nerve - sciatic	nerve - optic
ovary	parathyroid gland	pituitary	rectum	skeletal muscle	skin	spinal cord - cervical
spinal cord - thoracic		spinal cord - lumbar	spleen	stomach	thymus	thyroid gland
tongue	trachea	urinary bladder	uterus	vagina		

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 27 (continued): Individual Histopathology Observations

Animal No.: 25382 Group: 11 Sex: Female Species: Rat Strain: Sprague Dawley
Test Substance: TFM Dose: Group 11; 100 mg/kg/day Route: Drinking Water Study Type: Subchronic
Date of Death: 07/26/2018 Study Day (Week): 91 (13) Mode of Death: TERMINAL KILL
Date of Necropsy: 07/26/2018 ** NECROPSY COMPLETE ** ** EXAMINATION COMPLETE **

Histo Pathology Observations:	Correlated with:
liver;	
infiltrate, mononuclear cell; minimal	

The following tissues were within normal limits:

adrenal gland	aorta	bone with marrow - femur		bone with marrow - sternum		brain
cecum	cervix	colon	duodenum	esophagus	eye	harderian gland
heart	ileum	jejunum	kidney	lacrimal gland	lung	lymph node - mandibular
lymph node - mesenteric		mammary gland	mandibular salivary gland		nerve - sciatic	nerve - optic
ovary	pancreas	parathyroid gland	pituitary	rectum	skeletal muscle	skin
spinal cord - cervical		spinal cord - thoracic		spinal cord - lumbar	spleen	stomach
thymus	thyroid gland	tongue	trachea	urinary bladder	uterus	vagina

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Appendix 27 (continued): Individual Histopathology Observations

Animal No.: 25383 Group: 11 Sex: Female Species: Rat Strain: Sprague Dawley
Test Substance: TFM Dose: Group 11; 100 mg/kg/day Route: Drinking Water Study Type: Subchronic
Date of Death: 07/26/2018 Study Day (Week): 91 (13) Mode of Death: TERMINAL KILL
Date of Necropsy: 07/26/2018 ** NECROPSY COMPLETE ** ** EXAMINATION COMPLETE **

Histo Pathology Observations:	Correlated with:
heart;	
infiltrate, mononuclear cell; minimal; myocardium	
liver;	
infiltrate, mononuclear cell; minimal	

The following tissues were within normal limits:

adrenal gland	aorta	bone with marrow - femur		bone with marrow - sternum		brain
cecum	cervix	colon	duodenum	esophagus	eye	harderian gland
ileum	jejunum	kidney	lacrimal gland	lung	lymph node - mandibular	
lymph node - mesenteric		mammary gland	mandibular salivary gland		nerve - sciatic	nerve - optic
ovary	pancreas	parathyroid gland	pituitary	rectum	skeletal muscle	skin
spinal cord - cervical		spinal cord - thoracic		spinal cord - lumbar	spleen	stomach
thymus	thyroid gland	tongue	trachea	urinary bladder	uterus	vagina

APPENDIX 28: PROTOCOL, AMENDMENTS, AND DEVIATIONS

SMITHERS AVANZA

Smithers Avanza's contract research laboratories support the pharmaceutical, agrochemical, and chemical industries

STUDY PROTOCOL

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

Smithers Avanza Study No. 2410-14374

APPROVALS:

Caitlin Murphy, PhD, DABT
Study Director
Smithers Avanza

18 Apr 2018
Date

Michael A. Dorato, PhD, DABT, Fellow ATS
Test Facility Management
Smithers Avanza

18 Apr 2018
Date

STEPHEN LANTZ Digitally signed by STEPHEN LANTZ
Date: 2018.04.17 16:29:06 -05'00'

Stephen R. Lantz, PhD
Sponsor Representative
U.S. Geological Survey

4/17/2018
Date

www.smithersavanza.com
info@smithrsavanza.com

Smithers Avanza
Toxicology Services
11-B Firstfield Road
Gaithersburg, MD 20878
Tel: 1.240.364.6360
Fax: 1.240.787.3020

PROTOCOL

1.0 STUDY TITLE

4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period

2.0 PURPOSE

The purpose of this study is to determine the potential toxicity of 4-nitro-3-(trifluoromethyl)phenol (TFM) when administered continuously for 90-days via drinking water to male and female Sprague Dawley rats and to determine the persistence or reversibility of any toxic effects over a 28-day recovery period.

3.0 SPONSOR INFORMATION

3.1 Name and Address

U.S. Geological Survey (USGS)
2630 Fanta Reed Road
La Crosse, WI 54603

3.2 Sponsor Representative

Stephen R. Lantz, PhD
Chemist
U.S. Geological Survey (USGS)
2630 Fanta Reed Road
La Crosse, WI 54603
Phone: (608) 781-6326
Email: slantz@usgs.gov

3.3 Alternate Sponsor Contact

Kim Fredricks, PhD
Biologist, Quality Assurance Officer
U.S. Geological Survey (USGS)
2630 Fanta Reed Road
La Crosse, WI 54603
Phone: (608) 781-6287
Email: kfredricks@usgs.gov

4.0 SMITHERS AVANZA STUDY DIRECTOR

4.1 Study Director

Caitlin Murphy, PhD, DABT
11 Firstfield Road
Gaithersburg, MD 20878-1704
Phone: (240) 364-6316
FAX: (240) 787-3020
Email: Caitlin.murphy@smithers.com

5.0 TEST FACILITY

5.1 Corporate Office and Clinical Pathology

Smithers Avanza Toxicology Services
(Smithers Avanza)
11 Firstfield Road
Gaithersburg, MD 20878

5.2	**Vivarium and Formulation Analysis**	Smithers Avanza 15 Firstfield Road Gaithersburg, MD 20878

6.0 TEST SITES

6.1	**Histology and Pathology Evaluation**	Vet Path Services, Inc. (VPS) 6450 Castle Drive Mason, OH 45040

7.0 ARCHIVE FACILITIES

7.1	**Chemicals**	Smithers Avanza 15 Firstfield Road Gaithersburg, MD 20878
7.2	**Histology and Tissue Specimens**	VPS Archives, LLC 6450 Castle Drive Mason, OH 45040
7.3	**Data**	
7.3.1.	**Paper Records**	Iron Mountain, Inc. 4451 Georgia Pacific Blvd. Suites L&M Frederick, MD 21704
7.3.2.	**Electronic Media**	Iron Mountain, Inc. 8928 McGaw Ct. Columbia, MD 21045

8.0 PRINCIPAL INVESTIGATORS

8.1	**Clinical Pathology Evaluation and Anatomic Pathology**	Roxanne Baumgartner, DVM, DACVP, DABT VPS Phone: (513) 469-0777 Fax: (513) 469-3378 Email: rbaumgartner@vetpathservicesinc.com
8.2	**Histology**	Sheree K. Lovelace, LAT, HT (ASCP) VPS Phone: (513) 469-0777 ext. 222 Email: slovelace@vetpathservicesinc.com

9.0 QUALITY ASSURANCE CONTACT INFORMATION

9.1 Test Facility/Lead QA

Peggy Miller
Phone: 240-364-6350
Email: peggy.miller@smithers.com

9.2 VPS (Histology)

Karen McClelland, BA (or designee)
Phone: 513-469-0777 ext. 232
Email: kmcclelland@vetpathservicesinc.com

10.0 CONTRIBUTING SCIENTISTS

10.1 Formulation Analysis

Surubhi Kalathur, MS
Smithers Avanza

10.2 Ophthalmology

Holly Atlee, DVM
Smithers Avanza

11.0 REGULATORY INFORMATION

11.1 Compliance

This study will be conducted according to the protocol, Smithers Avanza's Standard Operating Procedures (SOPs, and in compliance with the current OECD Good Laboratory Practice Principles (GLP) (ENV/MC/CHEM(98)17) and Environmental Protection Agency TSCA Good Laboratory Practice Standards (40 CFR Part 792).

Portions of the study performed by the subcontractor(s) will be performed according to the protocol and the subcontractor(s) SOPs and in compliance with the noted regulations.

Any portions of the study performed by the Sponsors will be performed according to the protocol and the Sponsor's SOPs and may not be in compliance with the noted regulations.

11.2 Quality Assurance

The Quality Assurance Unit (QAU) of Smithers Avanza will audit this study in accordance with the protocol, amendment(s), SOPs and referenced GLP(s). The Smithers Avanza QAU will audit all data generated by the Testing Facility, the pathology report and pathology data generated by VPS.

VPS will conduct appropriate phase inspection(s) and audit the histology PI report. All inspection reports will be submitted to the Study Director.

All other portions of the study performed by the Sponsor or subcontractor(s) (except as indicated above) will be verified by their QAUs. All inspection reports will be submitted to the Study Director.

11.3 Data Collection System

Electronic data, which includes but is not limited to, randomization, animal husbandry and enrichment, dose formulations and dispensing, dose administration, cageside and clinical observations, physical examinations, body weights, body weight changes, water consumption, food consumption, clinical pathology, organ weights, gross and microscopic pathology observations, and statistical analysis will be collected/analyzed using Provantis™ 8 (Instem LSS, Limited; Stone, UK). Environmental monitoring data will be collected using Rees Environmental Monitoring System (Rees Scientific Corporation, Trenton, NJ).

Electronic data for dose analysis will be collected using Empower 2 Build 2154 (Waters Corporation, Milford, MA).

Information on electronic data collection systems/processes utilized by the Sponsor or subcontractor(s) (if any) will be provided to Smithers Avanza or outlined in their final reports.

11.4 Record Retention

All study data (including data generated by VPS), chemical archive samples, preserved tissues, blocks, and slides, and communications concerning the conduct of the study will be retained in the designated archives for a period of 5 years following issuance of the final report.

Following the 5-year contract, the Sponsor will be contacted to determine disposition of study materials; additional charges will be applied for disposition of these materials. All electronic data and records regarding disposition of study materials will be maintained by Smithers Avanza.

Study data generated by the Sponsor or other subcontractor(s) (except those indicated above) will be archived for a 5-year period by the Sponsor or subcontractor(s).

11.5 Justification for Study Design, Species, Number on Study, Route of Administration, and Dose Levels

This study follows U.S. EPA Guideline OPPTS 870.3100: 90–Day Oral Toxicity in Rodents and OECD Guidelines for the Testing of Chemicals, Test No 408: Repeated Dose 90-Day Oral Toxicity Study in Rodents.

The rat is selected because it is a standard species for use in toxicology studies. Rats are also being used as a rodent species per current EPA and OECD guidelines.

This study was designed to use the fewest number of animals possible, consistent with the objective of the study, the scientific needs of the Sponsor, contemporary scientific standards, and in consideration of applicable regulatory requirements cited previously in this protocol.

The oral route via drinking water is selected because it is the anticipated route of potential human exposure.

The dose levels were selected based on subchronic studies in dogs, rats, and hamsters conducted in the early 1970s prior to the development of study guidelines and GLP standards. Test material used in previous studies likely contained toxicologically active impurities which could have influenced findings.

Consistent findings of decreased body weight gain and inconsistent findings of decreased gonad weight, ovarian lesions, spleen congestion, increased leukocytes, and reduced hemoglobin were noted but not considered significant by study personnel. In a 1971 subchronic rat study (WARF Institute, Inc., Madison, Wisconsin, U.S. Department of the Interior, Bureau of Sport Fisheries & Wildlife, Contract No. 14-16-0008-620), rats were exposed to TFM through diet for 90 days, a trend of smaller than control gonads were observed in almost all treated female groups of rats; however, considered of no biological significance. Feeding rats with 500, 900, 1620, 2916, and 5248 ppm TFM-fortified diet (approximately 50, 90, 162, 292, and 525 mg/kg/day respectively) for 90 days resulted in no biologically significant difference among treated groups when compared with the control groups of animals regarding body weight, feed consumption or clinical pathology. Insignificant findings for increased leukocytes and decreased female gonad weight occurred as low as 50 mg/kg/day. Insignificant findings for decreased male gonad weight occurred as low as 90 mg/kg/day. Findings of decreased female and male body weight occurred as low as 292 and 525 mg/kg/day, respectively. The proposed dosage levels are expected to cause some organ weight alterations, but no adverse effect to animals when provided in drinking water.

12.0 PROPOSED STUDY TIMETABLE

12.1	**Study Initiation Date**	Date Study Director signs protocol
12.2	**Receipt of Animals**	April 19, 2018
12.3	**Experimental Start Date**	Date of animal receipt
12.4	**First Day of Dosing**	April 26, 2018 (males) April 27, 2018 (females)
12.5	**Last Day of Dosing**	July 24, 2018 (males) July 25, 2018 (females)
12.6	**Necropsy**	Main phase: July 25, 2018 (males) July 26, 2018 (females) Recovery phase: August 22, 2018 (males) August 23, 2018 (females)
12.7	**Experimental Completion Date**	Date of last data collection
12.8	**Submission of Unaudited Draft Report**	November 5, 2018
12.9	**Submission of Audited Draft Report**	November 15, 2018
12.10	**Study Completion Date**	Date Study Director signs final report

13.0 TEST AND VEHICLE/CONTROL SUBSTANCES (NEAT MATERIAL)

13.1 Identification and Supplier

13.1.1. Test Substance

The test substance, 4-nitro-3-(trifluoromethyl)phenol (TFM) (CAS #88-30-2), Lot LAM170517A-Extract, will be supplied by the Sponsor or Sponsor's designee. A certificate of analysis (CoA) for each lot or batch of the test substance and the MSDS (or equivalent) will be provided.

13.1.2. Vehicle/Control Substance

The vehicle/control substance, deionized water, will be provided by a vendor/supplier. A certificate of analysis (CoA) for each lot or batch of the vehicle/control substance and the MSDS (or equivalent), will be provided by the vendor/supplier.

13.2 Purity and Stability

13.2.1. Test Substance

The purity and/or other characteristics that appropriately define the test substance, and stability information for the neat test substance, are the responsibility of the Sponsor or the Sponsor's designee The information provided by USGS indicates that the purity of Lot LAM170517A-Extract is 80.59% (see Certificate of Analysis) with the remaining balance primarily water. The test substance is yellow-orange, clear liquid.

13.2.2. Vehicle/Control Substance

The purity and/or other characteristics that appropriately define the vehicle/control substance, and stability information for the neat vehicle/control substance, will be provided by the vendor/supplier.

13.3 Storage Conditions

13.3.1. Test Substance

The neat test substance will be stored under conditions set to maintain room temperature unless otherwise stated in receipt paperwork.

13.3.2. Vehicle/Control Substance

The neat vehicle/control substance, deionized water will be stored under conditions set to maintain room temperature unless otherwise stated in receipt paperwork.

13.4 Reserve Samples and Disposition

13.4.1. Test Substance

Reserve samples [1 mL] of the neat test substance will be taken and stored under the same conditions as the bulk material(s).

13.4.2. Test Substance Disposition

All empty test substance containers will be disposed after the end of the in-life phase.

All remaining test substance will be retained for use on subsequent studies or disposed in accordance with company SOPs.

13.4.3. Control Substance/Vehicle

Reserve samples [1 mL] of each lot of the neat control substance will be taken and stored under the same conditions as the bulk material(s).

13.4.4. Control Substance/Vehicle Disposition

All empty control substance containers will be disposed after the end of the in-life phase.

All remaining control substance supplied by Smithers Avanza will be returned to Smithers Avanza stock and/or discarded at the discretion of Smithers Avanza.

14.0 DOSE FORMULATION, SAMPLING, AND ANALYSIS

14.1 Formulation

14.2 Formulation of Control Substance/Vehicle

14.2.1. Frequency

No formulation is required.

14.2.2. Procedure

The control substance/vehicle will be used as received.

14.2.3. Disposition

Remaining formulations (following dosing and sampling) will be discarded.

14.3 Formulation of Test Substance

14.3.1. Frequency

Formulations will be prepared for each week of dosing for administration within the period of established stability. Test material-fortified deionized water will be prepared for each week of dose administration (approximately weekly). Week-1 and 2 deionized water mixture concentrations will be based on water consumption data previously collected at the test facility. The following week's admix concentrations will be determined based upon water consumption and bodyweight data obtained during the prior week.

14.3.2. Procedure

Formulations will be prepared according to the mixing method approved by the Study Director. The dose formulation calculations will be adjusted based on test substance purity (80.59%).

Prepared formulations will be maintained at room temperature during storage and dosing.

14.3.3. Disposition

Remaining formulations (following dosing and sampling) will be discarded.

14.4 Sampling and Analysis

14.4.1. Procedure

Samples will be collected and analyzed as outlined in the table below; some samples may be collected and analyzed concurrently as appropriate following authorization of the Study Director. Samples will be stored at room temperature prior to analysis and analyzed using Smithers Avanza Analytical Method Number 0296.

Table 1: Analytical Sampling and Analysis Requirements

Sample Type	Concentrations to Sample	Sample Volume (mL)	Number of Samples per Concentration			Intervals
			Collect	Analyze	Backup	
Stability	Lowest and Highest TFM Solutions (only)	10	2	1	1	Week 1[1]
Concentration Verification	All (includes control)	10	2	1	1	Weeks 1, 8, 13

[1]Samples collected from similarly prepared water bottles maintained at room temperature for at least 7 days.

All results must meet acceptance criteria (90-110%) as outlined in the analytical method and/or company SOPs. Additional samples may be collected and/or analyzed at the discretion of the Study Director if desired. The formulations will be considered stable in the animal watering bottle configuration if the difference between Time-zero analysis and after storage in the bottle for at least 7 days is ≤10%.

Homogeneity - Test substance formulations are solutions; therefore, homogeneity sampling and analysis is not required.

Stability - Stability of solutions stored in the animal watering bottle configuration will be addressed during week 1. Chemical stability of TFM mixtures which encompass formulation concentrations, storage conditions, and conditions of use has been determined to be at least 28 days. The information will be included in the final report.

Following analysis, a Contributing Scientist Report will be submitted to the Study Director.

14.5 Dose Formulation Sample Disposition

Following receipt of analytical results, unused samples will be discarded following authorization of the Study Director.

15.0 TEST SYSTEM AND HUSBANDRY

15.1 Animals

15.1.1. Animal Information

The animal requirements for this study are presented below.

Table 2: Animal Information

Species/ Strain	Source	Number per Sex		Age	Weight
		Ordered	Needed	(at initiation of dosing)	
Sprague Dawley Rat	Charles River Breeding Labs; Raleigh, NC	88	80	7-8 weeks	At least 150 g

Note: Actual age and weight may vary and will be documented.

15.1.2. Identification

Each animal will be identified by ear tag.

15.1.3. Animal Welfare

Smithers Avanza's Institutional Animal Care and Use Committee (IACUC) will review this protocol for its compliance with provisions of the USDA Animal Welfare Act, the Public Health Service Policy on Humane Care and Use of Laboratory Animals and the U.S. Interagency Research Animal Committee Principles for the Utilization and Care of Research Animals, prior to authorizing its execution.

The Study Director may consult with the Sponsor prior to deciding an animal's disposition. The Smithers Avanza veterinarian and/or the Study Director, however, reserve the right in case of extreme emergencies regarding treatment or euthanasia of a study animal.

15.2 Husbandry

15.2.1. Husbandry Information

The husbandry requirements for this study are presented below.

Table 3: Husbandry Information

Housing		Feed (Frequency and Type)	Water
Per Cage	Cage Description		
Paired	Polycarbonate with SaniChip certified hardwood bedding	*Ad libitum*, unless noted otherwise. Certified Global Teklad Laboratory 2018 Diet (pellets)	Deionized water (fortified with or without test substance) via clear glass water bottles[a]

Note: Each cage will be labeled with a cage card displaying pertinent study information.
[a]Animal room light will be filtered to block certain UV light spectra to reduce potential photodegradation of the test substance.

15.2.2. Bedding and Feed Analysis and Contaminant Evaluation

Bedding is analyzed by the manufacturer for acceptable limits of heavy metals, aflatoxins, bacteria, yeasts, molds and organophosphates prior to certification. Feed is analyzed by the manufacturer for concentrations of specified heavy metals, aflatoxin, chlorinated hydrocarbons, and organophosphates.

Certification specifications (bedding), and certificates of nutrient and contaminant analyses (feed) are on file at Smithers Avanza. Available information indicates that no substance is likely to be present in the bedding or feed at a concentration likely to influence the outcome of this study.

15.2.3. Environment

Animals will be housed in a controlled environment as noted below.

Table 4: Environment

Temperature Range	Humidity Range	Light Cycle (light/dark)	Room Air Changes (per hour)
20 to 26ºC	30 to 70%	12 hour/12 hour	10 (minimum)

Temperature and humidity are monitored and recorded continuously in each animal room by an environmental monitoring system. In the event of a system failure, manual recording will be performed (once daily) as defined in the Standard Operating Procedures. Light cycle interruptions for study-related events will be documented. Animal room light will be filtered to block certain UV light spectra to reduce potential photodegradation of the test substance.

15.2.4. Environment Enrichment

Non-plastic environmental enrichment will be provided and documented.

16.0 PROCEDURES FOR ALL ANIMALS PRIOR TO INITIATION OF DOSING

Animals will be acclimated to the facility for at least 5 days prior to the first dose. During that time, animals will be evaluated as shown in the following table.

Table 5: Evaluations Prior to Initiation of Dosing

Procedure	Frequency
Cageside Observations (mortality, moribundity, and general health)	≥ Twice daily
Physical Examinations (skin and fur characteristics, eye and mucous membranes, respiratory, circulatory, autonomic and central nervous systems, somatomotor and behavior patterns)	At least once prior to randomization. Unscheduled observations will be recorded.
Body Weight	At least once prior to randomization
Ophthalmologic Examination[a]	Prior to randomization

[a]Ophthalmologic examinations will be conducted by a veterinarian using an indirect ophthalmoscope and slit lamp (as needed); animals will be administered a mydriatic solution prior to examination.

Animals considered unsuitable for the study, based on the data collected up to the time of randomization, will be excluded from the randomization pool.

16.1 Randomization

Animals suitable for study will be assigned to study groups using computer generated random numbers. Males and females will be randomized separately. Following randomization, the mean body weight for each group will not be statistically different ($p \leq 0.05$) from the control value. Permanent animal numbers will be assigned following randomization. Animals assigned to study may also be excluded prior to initiation of dosing (and replaced with a suitable animal not originally assigned to study) if necessary.

17.0 STUDY DESIGN

17.1 Group Designation and Dosage Levels

Animals will be assigned to groups as noted in the table below.

Table 6: Group Designation and Dosage Levels

Group	Treatment	Target Dose[a] (mg/kg/day)	Number of Animals (main phase)		Number of Animals (recovery phase)[b]	
			Males	Females	Males	Females
1	Control	0	10	10	10	10
2	TFM	1	10	---	---	---
3	TFM	3	10	---	---	---
4	TFM	10	10	---	---	---
5	TFM	30	10	---	---	---
6	TFM	100	10	---	10	---
7	TFM	1	---	10	---	---
8	TFM	3	---	10	---	---
9	TFM	10	---	10	---	---
10	TFM	30	---	10	---	---
11	TFM	100	---	10	---	10

[a]Week-1 & 2 TFM fortification will be based on the data previously collected. Concentrations after week 2 will be based on bodyweight and water consumption data from 2 weeks prior.
[b]During the recovery phase, animals will be provided with non-fortified deionized water.

17.2 Dosing Information

17.2.1. Method of Administration

All animals will be dosed via deionized drinking water provided ad libitum in clear glass water bottles with neoprene stoppers. Neoprene stoppers and dosing solution will be changed weekly.

Test Material Intake (TMI) will be calculated weekly for each animal using test material concentrations in the drinking water, body weights, and measured water consumption data. The achieved dose for each animal through the entire study will be calculated by averaging weekly TMI for each animal. Achieved dose for each dose group will be calculated as an average of individual animal achieved doses within each group.

17.2.2. Frequency

Animals will be dosed continuously with control (non-fortified) or test material-fortified deionized water for at least 90 consecutive days. The first day of dosing will be designated as Study Day (SD) 1. During the recovery phase, all animals will be administered non-fortified deionized water for at least 28 days.

17.3 Observations of Animals Starting on Study Day 1

Animals will be observed and data will be recorded as indicated in the following table.

Table 7: Observations of Animals Starting on Day 1

Procedure	Frequency
Cageside Observations (mortality, moribundity, and general health)	≥ twice daily
Physical Examinations (skin and fur characteristics, eye and mucous membranes, respiratory, circulatory, autonomic and central nervous systems, somatomotor and behavior patterns)	SD 1 (prior to initiation of dosing). Weekly thereafter. Prior to necropsy. Unscheduled observations will be recorded.
Body Weights	SD1 (prior to initiation of dosing). Weekly thereafter. At time of unscheduled termination. Day prior to necropsy (unfasted). Prior to necropsy (fasted).
Water Consumption - Quantitative	Weekly
Food Consumption - Quantitative	Weekly
Vaginal Cytology	Weeks 3 & 4 (daily) Weeks 7 & 8 (daily; if effects observed in weeks 3 & 4) Weeks 11 & 12 (daily) Weeks 15 & 16 (daily; recovery animals, if effects observed)
Ophthalmologic Examinations	Prior to scheduled necropsy (within 3 days) control and high dose groups only[a]
Functional Observational Battery (FOB) including Grip Strength	Once during final two weeks of dosing
Locomotor Activity	Once during final two weeks of dosing

[a]Animals in the lower doses will be examined if ocular effects noted at the high dose.

Ophthalmologic examinations will be conducted by a veterinarian using an indirect ophthalmoscope and slit lamp (as needed); animals will be administered a mydriatic solution prior to examination. Following examination, a Contributing Scientist Report will be submitted to the Study Director.

17.4 Clinical Pathology

Blood will be collected from main and recovery phase animals as noted in the following table.

Table 8: Sample Collection Requirements

Procedure	Timepoints	Sample Volume	Collection Device
Chemistry	Prior to Scheduled Termination (only animals scheduled for necropsy)	At least 1.0 mL	Serum separator tubes
Hematology		At least 1.0 mL	Tubes containing K_2EDTA
Coagulation		At least 1.8 mL	Tubes containing sodium citrate
Urinalysis		Up to 12 mL	Metabolism Cage

Animals will be fasted prior to collection. Blood will be collected via cardiac puncture under 70%CO_2/ 30%O_2 inhalant anesthesia. Blood will also be collected from moribund animals prior to euthanasia, if possible.

Following collection, samples will be transferred to the Clinical Pathology Laboratory for analysis. The required clinical pathology assays are listed in the following table.

Table 9: Clinical Pathology Assays

Chemistry		
albumin/globulin (A/G) ratio	chloride	potassium
alanine aminotransferase	creatinine	sodium
albumin	creatine kinase	total bilirubin
alkaline phosphatase	gamma-glutamyl transferase	total protein
aspartate aminotransferase	globulin	triglycerides
calcium	glucose	urea nitrogen
cholesterol	phosphorus	

Hematology		
cellular morphology	leukocyte differential count	mean platelet volume
erythrocyte count	reticulocyte count	red cell distribution width
hematocrit	mean corpuscular hemoglobin	platelet count
hemoglobin	mean corpuscular hemoglobin conc.	
leukocyte count	mean corpuscular volume	

Coagulation		
activated partial thromboplastin time	prothrombin time	fibrinogen

Urinalysis		
bilirubin	microscopic examination of sediment	specific gravity
color and appearance	nitrites	urobilinogen
glucose	occult blood	volume
ketones	pH	
leukocytes	protein	

17.5 Termination

17.5.1. Unscheduled

Animals found dead or euthanized as moribund will be weighed and subjected to full gross necropsy as described below; moribund animals will be euthanized by carbon dioxide inhalation and exsanguinated prior to necropsy.

17.5.2. Scheduled

Animals will be euthanized by carbon dioxide inhalation and exsanguinated prior to necropsy as outlined in the following table.

Table 10: Necropsy Schedule

Group	SD 91	SD 119
1	10/sex	All surviving
2	All surviving	-
3	All surviving	-
4	All surviving	-
5	All surviving	-
6	10 males	All surviving
7	All surviving	-
8	All surviving	-
9	All surviving	-
10	All surviving	-
11	10 females	All surviving

17.6 Postmortem Procedures

17.6.1. Gross Necropsy

Animals will be necropsied as close as possible to the time of sacrifice or discovery. Gross necropsy will include examination of the external surface of the body, all orifices, and the cranial, thoracic, and abdominal cavities and their contents.

17.6.2. Bone Marrow Collection

Two bone marrow smears will be prepared from the left femur of all scheduled necropsy and moribund animals. Slides will be air-dried, fixed in methanol, and retained for possible future evaluation. If analysis is not required, then unstained slides will be discarded.

17.6.3. Organ Weights and Tissue Preservation

The organs (sex appropriate) listed in table below will be weighed as soon as possible from all animals at scheduled necropsy. Paired organs will be weighed together. Animal identification, gross lesions and tissues (sex appropriate) required to be collected will be preserved in 10% neutral buffered formalin (NBF) with the exception of eyes, associated ocular tissue, testes, and epididymides of all scheduled and moribund animals, which will be initially fixed in modified Davidson's fixative and subsequently transferred to NBF. The tissues from all animals found dead will be preserved in NBF only.

17.6.4. Histopathology

The tissues (sex appropriate) identified in the table below from main phase animals in the control and high dose study groups and gross lesions (regardless of group or phase) will be embedded in paraffin, sectioned, stained with hematoxylin and eosin, and examined microscopically by a board-certified veterinary pathologist.

If there is an unscheduled death, tissues from each animal found dead or euthanized moribund (regardless of group) may be embedded in paraffin, sectioned, stained with hematoxylin and eosin, and examined microscopically by a board-certified veterinary pathologist. These additional evaluations will be added by amendment.

Table 11: Organ Weights (OW), Tissue Preservation (TP), and Histopathology Examination (HE) List

Tissue	OW	TP	HE
adrenal gland	X	X	X
aorta		X	X
bone with marrow-femur		X	X
bone with marrow-sternum		X	X
brain	X	X	X
cecum		X	X
cervix	with uterus	X	X
colon		X	X
duodenum		X	X
epididymis	with testis	X	X
esophagus		X	X
eye		X	X
harderian gland		X	X
heart	X	X	X
ileum		X	X
jejunum		X	X
kidney	X	X	X
lacrimal gland		X	X
liver	X	X	X
lung		X	X
mammary gland (females)	X	X	X
mandibular lymph node		X	X
mandibular salivary gland		X	X

Tissue	OW	TP	HE
mesenteric lymph node		X	X
optic nerve		X	X
ovary	X	X	X
pancreas		X	X
parathyroid gland	with thyroid	X	X
pituitary		X	X
prostate		X	X
rectum		X	X
sciatic nerve		X	X
seminal vesicle		X	X
skeletal muscle		X	X
skin		X	X
spinal cord		X	X
spleen	X	X	X
stomach		X	X
testis	X	X	X
thymus	X	X	X
thyroid gland	X	X	X
tongue		X	X
trachea		X	X
urinary bladder		X	X
uterus	X	X	X
vagina		X	X
gross lesions (incl. masses)		X	X

The presence of test-substance-related lesions in the main phase high dose group identified by histopathological examination may require microscopic examination of the affected target tissue(s) in all animals from the main phase lower dose groups and the affected target tissue(s) in the recovery phase group(s). These additional evaluations will be added by amendment.

Following analysis, a report will be written which meets the regulatory requirements outlined in the compliance section of this protocol (as appropriate) and submitted to the Study Director.

18.0 PROPOSED STATISTICAL ANALYSES

Descriptive statistics (mean, standard deviation, and N) will be presented for all measurement data.

18.1 Body Weight, Body Weight Change, Food Consumption, Absolute and Relative Organ Weights, and Clinical Pathology

Quantitative data will be evaluated as outlined in ATTACHMENT 1.

19.0 FINAL REPORT

A report will be prepared which accurately describes the methods used in the generation and analysis of the data and meets the regulatory requirements previously noted. All final reports provided by subcontractors will be included in the final study report. Draft reports will be provided to the Sponsor for review and comment. Note: The Study Director may finalize the report 60 days after submission of the draft report if no comments are received.

At finalization, an electronic copy of the final report will be submitted to the Sponsor.

20.0 REFERENCE

U.S. EPA 1988. Recommendations for and Documentation of Biological Values for Use in Risk Assessment. EPA/600/6-87/008

ATTACHMENT 1

Descriptive statistics (number of observations, mean, and standard deviation) will be calculated and presented for all measurement data and shown in the summary tables. Data from quantitative variables from treated groups will be compared statistically to the data of the control group using one-way analysis of variance (ANOVA) techniques (1). Groups with three or more observations will be included in the analysis; in a case where the control group has less than 3, no analysis will be performed. Sexes will be analyzed separately.

Prior to performing the ANOVA, the untransformed data will be tested to determine if the data are normally distributed and have homogeneous variances among all groups. A Shapiro-Wilk test (2) will be used to test normality, followed by Levene's test (3) to test the hypothesis of homogeneity of variances. If either the normality or homogeneity test fail, as indicated by a Shapiro-Wilk or Levene's test p-value ≤0.01, the data will be transformed using a log transformation (4) and both the Shapiro-Wilk and Levene's tests will be repeated using the log-transformed values. If the results from either the Shapiro-Wilk or Levene's test on the log-transformed data fail, the data will be transformed using a rank transformation (5, mean ranks) and a Kruskal-Wallis (6) ANOVA will be performed on the rank values. If both the Shapiro-Wilk and the Levene's tests are not statistically significant, the ANOVA will be performed on the untransformed or log-transformed data, respectively.

Dunnett's t-test (7) will be used to determine if differences exist between the control and treated group(s). Group comparisons will be evaluated at the 5% two-tailed probability level.

References:

1 – Neter, J., Wasserman, W., and M.H. Kutner (1985). Applied Linear Statistical Models, 2nd ed. Richard D. Irwin, Inc. Homewood, IL 60430.

2 – Shapiro, S. S. and Wilk, M. B. (1965). "An analysis of variance test for normality (complete samples)", Biometrika, 52, 3 and 4, pages 591-611.

3 – Levene, Howard (1960). "Robust tests for equality of variances". in Ingram Olkin, Harold Hotelling et al. Contributions to Probability and Statistics: Essays in Honor of Harold Hotelling. Stanford University Press. pp. 278–292.

4 – Steel G.D. and J.H. Torrie, (1960). Principles and Procedures of Statistics, McGraw-Hill Book Company, Inc. New York, New York.

5 – Conover, W. J., & Iman, R. L. (1976). On some alternative procedures using ranks for the analysis of experimental designs. Communications in Statistics, A5, 1349-1368.

6 – Kruskal, W.H. and Wallis, W.A. (1952) Use of ranks in one-criterion variance analysis. J. Am. Statist. Assoc., 47, 583-6217.

7 – Dunnett, C.W. (1955). A multiple comparison procedure for comparing several treatments with a control. J. Am. Statist. Assoc., 60, 573-83.

SMITHERS AVANZA

PROTOCOL AMENDMENT

Study Number:	2410-14374	Amendment Number:	1
Study Title:	4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period		

1. Subject: Subject: Section 14.4.1 Procedure

Add the following (bold text is added):

Samples will be collected and analyzed from the Group 7-10 formulations prepared for replacement of the dosing solution on SD 11 (Females).

Group 11 dosing solutions collected after administration to Females on SD 1-7 will be diluted using 0.1% Formic Acid in water and in deionized water (control of test in 0.1% formic acid). The pH of each diluted solution will be recorded and both dilutions will be analyzed.

Justification: Due to out of specification results from the initial analysis of Group 7-10, replacement formulations will be prepared and samples will be analyzed to confirm concentration within acceptance criteria for the replacement formulation. At the request of the Sponsor, the highest TFM (group 11) solution is being diluted in acidified 0.1% formic acid to determine the potential effect of solution pH on analysis as the Sponsor suspects that a pH change may be interfering with the percent recovery.

Effective date is date protocol amendment directives (PAD) issued (07 May 2018).

2. Subject: Table 1: Analytical Sampling and Analysis Requirements

Change the table to the following (bold text is added):

Sample Type	Concentrations to Sample	Sample Volume (mL)	Number of Samples per Concentration			Intervals
			Collect	Analyze	Backup	
Stability	Lowest and Highest TFM Solutions (only)	10	2	1	1	Week 1[1] **[2]**
Concentration Verification	All (includes control)	10	2	1	1	Weeks 1, **2,** 8, 13

[1]Samples collected from similarly prepared water bottles maintained at room temperature for at least 7 days.
[2]Samples will be collected and analyzed from the control and highest TFM solution from a single water bottle used for dosing of the animals for at least 7 days

SMITHERS AVANZA

PROTOCOL AMENDMENT

Study Number:	2410-14374	Amendment Number:	1
Study Title:	4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period		

Justification: Due the results from the initial samples collected from the highest TFM solution water bottle prepared and analyzed during week 1, additional samples are being collected to confirm stability. The control samples is being collected and analyzed to determine if there is an influence of the stopper on the control sample. Due to a color change in solution, i.e. freshly prepared dosing solution lighter in color than dosing solution after 1 week in water bottles, additional samples are being collected to confirm concentration.

Effective date is date protocol amendment directives (PAD) issued (03 and 04 May 2018).

3. Subject: Section 17.2.1 Method of Administration

Add the following to the first paragraph (bold text is added):

On SD 11 (females) the dosing solution will be changed for Groups 7 to 10.

Justification: Due to out of specification analytical results for Group 7-10 of the week 2 dosing solutions, new freshly mixed dosing solution formulations will be prepared and dosing solutions for Groups 7-10 will be discarded and replaced with new dosing solution prepared on 07 May 2018.

Effective date is date protocol amendment directives (PAD) issued (07 May 2018).

SMITHERS AVANZA

PROTOCOL AMENDMENT

Study Number:	2410-14374	Amendment Number:	1
Study Title:	4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period		

Approvals:

Caitlin Murphy, PhD, DABT
Study Director

15 May 2018
Date

STEPHEN LANTZ Digitally signed by STEPHEN LANTZ
Date: 2018.05.15 11:53:55 -05'00'

Stephen R. Lantz, PhD
Sponsor Representative

5/15/2018
Date

SMITHERS AVANZA

PROTOCOL AMENDMENT

Study Number:	2410-14374	Amendment Number:	2
Study Title:	4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period		

1. Subject: Subject: Section 14.4.1 Procedure

Add the following (bold text is added):

Samples (10 mL) will be collected prior to dose administration from formulations prepared for week 4 dosing solutions (Groups 1, ~~2, 4~~ 9 and 11). After the week 4 dosing solutions have been in water bottles for at least 4 days additional samples (10 mL) will be collected from a representative bottle in each of the above groups. Used stoppers (from a representative bottle in each of the above groups) and unused stoppers will be collected. The samples and the stoppers will be sent to the Sponsor at the below address for potential analysis.

Steve Lantz PhD, Chemist
Aquatic Ecosystem Health Branch
Upper Midwest Environmental Sciences Center
U.S. Geological Survey
2630 Fanta Reed Road
La Crosse, WI 54603
Office: 608-781-6326

(1) 7 and 9 due to error groups 7 and 9 will be collected rather than 2 and 4 CM 21 May 18

Justification: Due to the stability results of the high dose solutions in the water bottle, additional samples are being collected and sent to the Sponsor for potential analysis of the degradation product.

Effective date is date protocol amendment directives (PAD) issued (16 May 2018).

2. Subject: Section 14.4.1 Procedure

Add to the stability section the following (bold text is added):

Samples will be collected and analyzed from similarly prepared water bottles at a mid-dose and the high-dose levels that are maintained at room temperature for at least 1, 4, and 7 days (2)

Justification: Due the results from the samples collected from the highest TFM solution water bottle prepared and analyzed, additional samples are being collected to confirm stability.

3. Subject: Section 17.2.1 Method of Administration

Add the following to the first paragraph (bold text is added):

(2) 0, was not initially included. CM 21 May 2018

SMITHERS AVANZA

PROTOCOL AMENDMENT

Study Number:	2410-14374	Amendment Number:	2
Study Title:	4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period		

When water in-progress refills are conducted dosing solutions will be discarded and completely refilled.

Justification: Due to concentration changes of the dosing solutions after 7 days in water bottles the dosing solutions will be discarded and replaced twice weekly, while the stoppers will be changed once weekly.

SMITHERS AVANZA

PROTOCOL AMENDMENT

Study Number:	2410-14374	Amendment Number:	2
Study Title:	4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period		

Approvals:

Caitlin Murphy, PhD, DABT
Study Director

18 May 2018
Date

STEPHEN LANTZ Digitally signed by STEPHEN LANTZ
Date: 2018.05.18 12:11:22 -05'00'

Stephen R. Lantz, PhD
Sponsor Representative

Date

SMITHERS AVANZA

PROTOCOL AMENDMENT

Study Number:	2410-14374	Amendment Number:	3
Study Title:	4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period		

1. **Subject: Section 4.1 (Effective May 22, 2018 to May 28, 2018)**
   Change the Study Director to:

4.1 Study Director

C. Steven Godin, PhD, DABT
11 Firstfield Road
Gaithersburg, MD 20878-1704
Phone: (240) 364-6336
FAX: (240) 787-3020
Email: steve.godin@smithers.com

Justification: Temporary change in personnel due to availability.

Study Director Approval: **Sponsor Approval:**

SMITHERS AVANZA

PROTOCOL AMENDMENT

Study Number:	2410-14374	Amendment Number:	3
Study Title:	4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period		

Approvals:

C. Steven Godin, PhD, DABT
Study Director

21 May 2018
Date

STEPHEN LANTZ Digitally signed by STEPHEN LANTZ
Date: 2018.05.18 12:14:02 -05'00'

Stephen R. Lantz, PhD
Sponsor Representative

Date

Management Approval:

Michael A. Dorato, PhD, DABT, Fellow ATS
Executive Vice President

21 May 2018
Date

SMITHERS AVANZA

PROTOCOL AMENDMENT

Study Number:	2410-14374	Amendment Number:	4
Study Title:	4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period		

1. Subject: Subject: Section 14.4.1 Procedure

Add the following to the stability section (bold text and table are added, strikethrough text is deleted):

Chemical stability of TFM mixtures which encompass formulation concentrations **(up to 2 mg/mL),** storage conditions, and conditions of use has been determined to be at least 28 days. **Formulations concentrations may exceed those previously determined for stability and additional testing to encompass the stability data will be collected and analyzed as described in the below table. At the same time stability of the solution at the high concentration (3.5 mg/mL) from similarly prepared water bottles maintained at room temperature will be tested. Samples and testing will be conducted in accordance with all parameters previously explored under study number 2410-14256.** The information will be included in the final report.

Sample Solution	Conditions	
High (3.5 mg/mL)	T_0	--
	Day 4	Room Temp at 21±5°C, protected from light
	Day 10	Room Temp at 21±5°C, protected from light
	Day 28	Room Temp at 21±5°C, protected from light
Water Bottle (3.5 mg/mL)	Day 1	Room Temp at 21±5°C, protected from light
	Day 4	Room Temp at 21±5°C, protected from light
	Day 7	Room Temp at 21±5°C, protected from light

Justification: The range of solution stability is being expanded in case the formulations concentration exceeds the previously established stability data.

SMITHERS AVANZA

PROTOCOL AMENDMENT

Study Number:	2410-14374	Amendment Number:	4
Study Title:	4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period		

Approvals:

Caitlin Murphy, PhD, DABT
Study Director

07 Jun 2018
Date

STEPHEN LANTZ Digitally signed by STEPHEN LANTZ
Date: 2018.06.06 14:41:54 -05'00'

Stephen R. Lantz, PhD
Sponsor Representative

6/6/2018
Date

SMITHERS AVANZA

PROTOCOL AMENDMENT

Study Number:	2410-14374	Amendment Number:	5
Study Title:	4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period		

Subject: Subject: Section 14.4.1 Procedure

Add the following to the stability section (bold text and table are added, strikethrough text is deleted):

Samples (2 mL, duplicate) of dosing solution from week 10 will be collected from Groups 2, 3, 4, 5, and 6. The samples will be collected from similarly prepared water bottles that replicate the conditions of use. The samples will be collected and analyzed at day 0, day 1, day 4 (prior to and after refilling dosing solutions), and day 7.

Justification: Due to the analytical results that indicate changes in concentration after dosing solution is in water bottles, additional samples are being collected that correspond to the conditions used during the study.

SMITHERS AVANZA

PROTOCOL AMENDMENT

Study Number:	2410-14374	Amendment Number:	5
Study Title:	4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period		

Approvals:

Caitlin Murphy, PhD, DABT
Study Director

27 Jun 2018
Date

STEPHEN LANTZ Digitally signed by STEPHEN LANTZ
Date: 2018.06.27 12:47:50 -05'00'

Stephen R. Lantz, PhD
Sponsor Representative

6/27/2018
Date

SMITHERS AVANZA

PROTOCOL AMENDMENT

Study Number:	2410-14374	Amendment Number:	6
Study Title:	4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period		

Subject: Subject: Table 7 Observation of Animals Starting on Day 1

Add the following to the table (bold and underlined text are added):

Procedure	Frequency
Cageside Observations (mortality, moribundity, and general health)	≥ twice daily
Physical Examinations (skin and fur characteristics, eye and mucous membranes, respiratory, circulatory, autonomic and central nervous systems, somatomotor and behavior patterns)	SD 1 (prior to initiation of dosing). Weekly thereafter. Prior to necropsy. Unscheduled observations will be recorded.
Body Weights	SD1 (prior to initiation of dosing). Weekly thereafter. At time of unscheduled termination. Day prior to necropsy (unfasted). Prior to necropsy (fasted).
Water Consumption - Quantitative	Weekly
Food Consumption - Quantitative	Weekly
Vaginal Cytology	Weeks 3 & 4 (daily) Weeks 7 & 8 (daily; if effects observed in weeks 3 & 4) Weeks 11 & 12 (daily) Weeks 15 & 16 (daily; recovery animals, if effects observed) **Prior to necropsy (recovery animals only)**
Ophthalmologic Examinations	Prior to scheduled necropsy (within 3 days) control and high dose groups only[a]
Functional Observational Battery (FOB) including Grip Strength	Once during final two weeks of dosing
Locomotor Activity	Once during final two weeks of dosing

Justification: Due the results from week 11 and 12 estrus cycling, the Sponsor has requested the addition of a vaginal cytology sample prior to necropsy to provide information on the stage of estrus at necropsy.

SMITHERS AVANZA

PROTOCOL AMENDMENT

Study Number:	2410-14374	Amendment Number:	6
Study Title:	4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period		

Approvals:

Caitlin Murphy, PhD, DABT
Study Director

10 Aug 18
Date

STEPHEN LANTZ

Digitally signed by STEPHEN LANTZ
Date: 2018.08.10 09:01:47 -05'00'

Stephen R. Lantz, PhD
Sponsor Representative

8/10/2018
Date

SMITHERS AVANZA

PROTOCOL AMENDMENT

Study Number:	2410-14374	Amendment Number:	7
Study Title:	4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period		

1. **Subject: Subject: 3.1 Name and Address**
Add the following to the Sponsor information (bold/underlined text are added):

On behalf of:

U.S. Fish and Wildlife Service
Lake Champlain Fish and Wildlife Conservation Office
11 Lincoln Street
Essex Junction, Vermont 05452

Justification: Sponsor request

2. **Subject: Subject: 13.4.2 Test Substance Disposition**
Change to the the following (bold/underlined text are added and bold/strikethrough is deleted):

All empty test substance containers will be disposed after the end of the in-life phase.

All remaining test substance will be ~~**retained for use on subsequent studies or disposed in accordance with company SOPs.**~~ **returned to the Sponsor at the following address:**

C/O Justin Schueller
U.S. Geological Survey (USGS)
2630 Fanta Reed Road
La Crosse, WI 54603

Justification: Sponsor request

SMITHERS AVANZA

PROTOCOL AMENDMENT

Study Number:	2410-14374	Amendment Number:	7
Study Title:	4-Nitro-3-(trifluoromethyl)phenol (TFM): 90-Day Oral Toxicity Study Following Administration via Drinking Water to Sprague Dawley Rats with a 28-Day Recovery Period		

Approvals:

Caitlin Murphy, PhD, DABT
Study Director

04 Mar 2019
Date

Stephen R. Lantz, PhD
Sponsor Representative

3/1/2019
Date

Appendix 28 (continued): Protocol, Amendments, and Deviations

The following deviations from the protocol were noted:

Samples of Groups 1, 2, and 4 were not prepared from dosing bottles on Day 4 of Week 4 prior to the contents being discarded and replaced. As a result, samples of Groups 1, 7, 9, and 11 were prepared on 22May2018 to represent the control, low, mid, and high dose concentrations.

Samples for Day 4 of the mix for Week 10 (prior to and after refilling dosing solutions) were inadvertently not collected from water bottles from Groups 2, 3, 4, 5, and 6.

Some clinical pathology tests were not conducted due to clotted sample, technical error, insufficient specimen volume, or other reasons. These tests are identified with the individual clinical pathology data.

Some tissues were not microscopically examined, or only one of a paired organ was examined, due to sectioning difficulties, technical errors, or other reasons. Non-examined tissues are identified with the individual histopathology data.

The above-mentioned deviations did not impact this study, nor did they affect the quality or integrity of the study or the interpretation of the results in this report.