U.S. ARMY PUBLIC HEALTH COMMAND
5158 Blackhawk Road, Aberdeen Proving Ground, Maryland 21010-5403

TOXICOLOGY STUDY NO. S.0015300-13
PROTOCOL NO. 30-13-07-01
EFFECTS OF ACUTE ORAL 5-AMINOTETRAZOLE (5-AT) EXPOSURE TO RATS *(Rattus norvegicus)*

JANUARY 2015

Prepared by:

Valerie H Adams, Ph.D.

PHC FORM 432-E (MCHB-CS-IP), NOV 12

Approved for public release; distribution unlimited.

Specialty: 500C Toxicity Test

ACKNOWLEDGEMENTS

The author would like to acknowledge the support and encouragement provided to this effort by Mr. Erik Hangeland the director of the U.S. Army Research, Development and Engineering Command, Environmental Acquisition and Logistics Sustainment Program. We also thank Dr. John LaScala of the Environmental Quality Technology Program, Pollution Prevention Team. Several USAPHC personnel contributed to the completion of this study through care of the animals, participation in animal dosing, data collection and necropsy; these include Rebecca Kilby, Robert Sunderland, Dr. William Eck, Dr. Larry Williams, Dr. Will McCain, Dr. Emily Reinke, Dr. Emily Lent, Alicia Shiflett, Allison Jackovitz, Lee Crouse, Terry Hanna, Martha Thompson, Matt Bazar and Mark Way.

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE *(DD-MM-YYYY)*	2. REPORT TYPE	3. DATES COVERED *(From - To)*
12-FEB-2015	Final Technical Report	Aug 2013 - Sept 2013

4. TITLE AND SUBTITLE

Toxicology Study No. S.0015300-13
Effects of Acute Oral 5-aminotetrazole (5-AT) Exposure in Rats

5a. CONTRACT NUMBER

5b. GRANT NUMBER

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)

Adams, Valerie H.

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

U.S. Army Public Health Command
Army Institute of Public Health, Portfolio of Toxicology
5158 Blackhawk Road, MCHB-IP-THE, APG, MD 21010-5403

8. PERFORMING ORGANIZATION REPORT NUMBER

S.0015300-13

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)

U.S. Army Research Development and Engineering Command
Environmental Acquisition and Logistics Sustainment Program
3072 Aberdeen Blvd.
APG, MD 21005

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION/AVAILABILITY STATEMENT

Distribution unlimited.

13. SUPPLEMENTARY NOTES

14. ABSTRACT

5-AT is a potential replacement for perchlorate in pyrotechnic devices. The objectives of this study were to determine the oral acute and subacute toxicity of 5-AT in the rat. 5-AT was not acutely toxic and no mortalities were observed at the limit dose of 2000 milligrams per kilogram (mg/kg) body weight in the acute test. There were no clinical signs of toxicity or morbidity observed in the subacute 14-day study up to 623 mg/kg-day-- the highest dose tested for both male and female rats. Without adverse effects, determination of the LOAEL and derivation of the BMD were not possible. The NOAEL was 623 mg/kg-day, the highest dose used in the subacute exposure test. The acute and subacute tests indicated that 5-AT has low toxicity over a short expose time frame. 5-AT is a less toxic compound than perchlorate and it should be pursued as a replacement. Considering that 5 -AT is also used in the synthesis of two other munition components, 5-nitrotetrazole (5-NT) and copper (I) 5-nitrotetrazolate (DBX-1), a subchronic (90 day) oral study is recommended.

15. SUBJECT TERMS

5-aminotetrazole, perchlorate replacement, oral, toxicity, rat

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			Valerie H Adams
U	U	U	UU	56	19b. TELEPHONE NUMBER *(Include area code)* 410-436-3980

Toxicity Report No. S.0015300-13, August-September 2013

Sponsor

USARDECOM
AMSRD-MSF
Environmental Acquisition and Logistics Sustainment Program
Aberdeen Proving Ground, MD 21005

Study Title

Toxicology Study No. S.0015300-13
Protocol No. 30-13-07-01
Effects of Oral 5 Aminotetrazole (5-AT) Exposure to Rats (*Rattus norvegicus*)

Author

Valerie H. Adams Ph.D.

Study Completed

January 2015

Performing Laboratory

U.S. Army Public Health Command
Portfolio of Toxicology
Health Effects Research Program
MCHB-IP-THE
Aberdeen Proving Ground, MD 21010

Laboratory Project ID

Protocol No. 30-13-07-01

GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT

The study described in this report was conducted in compliance with Title 40 Code of Federal Regulations Part 792, Good Laboratory Practice Standards, except for the following:

1. The test article characterization (purity) was conducted by the manufacturer and it is not known whether the testing was done in compliance with the above regulation.

2. The concentrations of the test article dosing suspensions/solutions for the acute portion of the study were not verified analytically in accordance with Good Laboratory Practice Standards. The accuracy of the data reported is considered sufficient for the purposes of the study.

No deviations from the aforementioned regulation affected the quality or integrity of the study or the interpretation of the results.

Valerie H. Adams, Ph.D.
Study Director
HERP

Jan 30 2015
Date

Table of Contents

Tables

TOXICOLOGY STUDY NO. S.0015300-13
PROTOCOL NO. 30-13-07-01
EFFECTS OF ACUTE ORAL 5-AMINOTETRAZOLE (5-AT) EXPOSURE IN RATS (*RATTUS NORVEGICUS*)

1 Summary

1.1 Objective

The objectives of this study were to determine the oral acute and subacute toxicity of 5-AT in the rat. If adverse effects were observed, the no-observed-adverse-effect-level (NOAEL), lowest-observed-adverse-effect-level (LOAEL), and benchmark dose (BMD) were calculated.

1.2 Purpose

The purpose of this study is to provide environmental and occupational health information for a new potential replacement for perchlorate, an oxidizer used by the Army that is a thyroid-active drinking water contaminant. This information is critical to the research, development, testing, and evaluation (RDT&E) of alternatives under the Environmental Quality Technology (EQT) program and is necessary for work unit program evaluation.

1.3 Conclusions

5-AT was not acutely toxic and no mortalities were observed at the limit dose of 2000 milligrams per kilogram (mg/kg) body weight in the acute test. Without mortalities, the 95 percent CI and slope were not able to be calculated. There were no clinical signs of toxicity or morbidity observed in the subacute 14-day study up to 623 mg/kg-day-- the highest dose tested. No dose-response, statistically significant differences in hematological parameters, clinical chemistry, organ weight changes, body weight changes, food consumption, or DNA damage (micronucleus assay- MNA) were observed. Histopathological findings were negative; no dose or group differences were observed. Without adverse effects, determination of the LOAEL and derivation of the BMD were not possible. The NOAEL was 623 mg/kg-day, the highest dose used in the subacute exposure test.

1.4 Recommendations

5-AT is being considered as a replacement for perchlorate, a very water soluble compound known to disrupt the thyroid system. The acute and subacute tests indicated that 5-AT has low toxicity over a short expose time frame. 5-AT is a less toxic compound than perchlorate and it should be pursued as a replacement. Considering that 5-AT is also used in the synthesis of two other munition components, 5-nitrotetrazole (5-NT) and copper (I) 5-nitrotetrazolate (DBX-1), a subchronic (90 day) oral study is recommended.

2 References

References are listed in Appendix A.

3 Authority

Military Interdepartmental Purchase Request (MIPR) No. 10322305. This toxicological study addresses the environmental safety and occupational health (ESOH) requirements outlined in Army Regulations (AR) (AR 40-5; AR 70-1; AR 200-1) Department of Defense Instruction (DoDI) 4715.4 (DoDI 1998), and

Army Environmental Requirement and Technology Assessment (AERTA) PP-3-02-05, *Compliant Ordnance Lifecycle for Readiness of the Transformation and Objective Forces*, (AERTA 2012). The authority statement is provided in Appendix B.

4 Background

The Army Environmental Quality Technology (EQT) Ordnance Environmental Program (OEP) is dedicated to finding replacements for perchlorate that will reduce or eliminate the health risks from environmental exposure and the adverse ESOH effects. By identifying unacceptable ESOH effects early in the acquisition process, unacceptable replacements can be identified and unnecessary budget expenditures can be greatly reduced.

Perchlorate is a strongly oxidizing compound that is currently fielded by the U.S. Army in explosives and propellants. Perchlorate is known to interfere with iodide uptake in the thyroid gland and as such, states and the USEPA are moving towards setting contaminant levels and other regulations. In addition, perchlorate adversely affects mission readiness and training-associated costs due to site contamination. Thus, there is a need for identifying a suitable replacement for perchlorate. 5-AT is currently used in explosive formulations for airbags and is being tested as a replacement for perchlorate. 5-AT, a high-nitrogen compound, derives its energy from a high heat of formation and releases benign nitrogen gas (N_2) upon combustion (Sabatini and Moretti 2013).

The purpose of this study was to assess the acute and subacute toxicities of 5-AT. This study was composed of two experiments. In the acute experiment, female rats received a single oral dose of 5-AT and were observed for 14 days for signs of toxicity. Results from this experiment were used to calculate the LD_{50} and to determine doses for the subacute experiment in which female and male rats were orally dosed with 5-AT daily for 14 consecutive days. At the end of the 14-day experiment, all animals were euthanized, necropsied and selected organs and tissues were examined for 5-AT-related effects. The data from this study are used to compare the toxicity of 5-AT to other compounds being considered as replacements for currently used explosives.

The conduct, findings and conclusions of the acute and 14-day repeated dose studies performed with 5-AT using rats are reported in this document. The acute study followed the format of a sequential stage-wise probit (SSWP). For the subacute study, the animals were dosed daily for 14 days. The following table identifies the critical dates of the acute and subacute studies.

Table 1. Critical Dates of Acute and 14-Day Studies

Critical Event	**Study**	**Date of Event** (mm/dd/yyyy)
Animal Use Protocol Approved Study Initiation Date	Acute:SSWP/14-Day Subacute	07/24/2013
Animals Received	Acute:SSWP	08/07/2013
	14-Day Subacute	09/03/2013
Study Start	Acute:SSWP	08/12/2013
	14-Day Subacute	09/09/2013
Experimental Start Date	Acute:SSWP	08/13/2013
	14-Day Subacute	09/10/2013

Experimental Completion	Acute:SSWP	08/30/2013
	14-Day Subacute	09/26/2013
Necropsy	Acute:SSWP	08/27/2013, 08/29/2013, 08/30/2013
	14-Day Subacute	09/24/2013, 09/25/2013, 09/26/2013, 09/27/2013
Histopathology Completion	14-Day Subacute	08/16/2014
Study Completion	Acute:SSWP/14-Day Subacute	01/07/2015

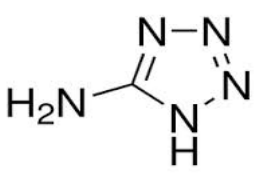
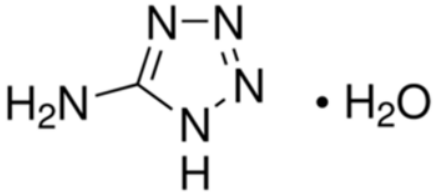
5 Materials

5.1 Test Substance

The test material, 5-aminotetrazole, was purchased from Sigma-Aldrich as 5-aminotetrazole monohydrate, 97 percent; (product number A80602, Lot number STBB9454V). The use of the monohydrate was necessary due the instability of the anhydrous 5-AT. The increase in molecular weight due to the presence of the water molecule was accounted for in the calculations and preparations of the dosing solutions. All doses and dose concentrations report the weight of 5-AT not 5-AT monohydrate. For example, to achieve a 2000 mg weight of 5-AT 2424 mg of 5-AT monohydrate was used. The physicochemical characteristics of the anhydrous and monohydrate 5-AT are listed in Table 2. A certificate of analysis was provided by Sigma-Aldrich. All purity confirmation, concentration verification analysis of the dosing solutions and stability analyses was performed by Army Institute of Public Health (AIPH) Laboratory Sciences Portfolio (LAB)-Client Services Division (CSD)-Method Development Section (MDV).

Table 2. 5-AT Chemical/physical Properties

Name	5-aminotetrazole	5-aminotetrazole monohydrate
Synonym	5-AT or (tetrazol-5-amine)	5-AT
CAS #	4418-61-5	15454-54-3
Physical State	White crystals	White to light yellow crystals
Molecular formula	CH_3N_5	$CH_3N_5 \cdot H_2O$
Molecular weight (g/mol)	85.06	103.08
Solubility	12 g/L	12 g/L

Molecular structure		

The dosing vehicle was food grade Mazola™ corn oil purchased locally. A 5-AT/corn oil stability test was performed prior to the 14-day study. 5-AT was found to be stable in corn oil at room temperature for a minimum of 19 days.

For the acute SSWP experiment, the dosing suspensions were made immediately before dosing by weighing 5-AT doses in individual weigh boats for each rat. Delivery of the test compound was accomplished by adding the appropriate volume of vehicle to the boat then mixing the suspension followed by dosing the entirety of the solution to each rat before adding corn oil to the next boat. The suspension made from corn oil and 5-AT tended to settle out and clog the hub of the gavage needle. For the SSWP-Stage 1, the delivery of the solutions below 2000 mg/kg were delivered without incident; while the 2000 mg/kg dose was divided into 2 doses using the maximum volume of vehicle based on the individual animal weights and delivered 4 hours apart (clearance time of stomach).

5.2 Animals[1]

All studies were conducted using young adult Sprague-Dawley Crl:CD(SD) rats obtained from Charles River Laboratories (Wilmington, MA). Female rats were used for the acute study and at the time of their arrival the animals were 43-50 days old. Male and female rats were used for the 14-day study and at the time of their arrival the animals were 38-42 days old. The Attending Veterinarian examined the animals and found them to be in acceptable health. The animals were quarantined for 5 days after their arrival in this facility. All rats were maintained in a temperature-, relative humidity-, and light-controlled room. The condition ranges were 64 - 79 degrees Fahrenheit (^{o}F) [average =70.1 ^{o}F with no excursions] 30 - 70 percent relative humidity [average = 44.2 percent RH with a period of 3 hours on September 3, 2014 where RH was greater than 70 percent coinciding with the room being cleaned prior to the delivery of the subacute study rats; no other excursions were detected] and a 12-hour light/dark cycle (TOX SOP AP004 2013). A certified pesticide-free rodent chow (Harlan Teklad ®, 8728C Certified Rodent Diet) and drinking quality tap water [most recent test January 2013] were available *ad libitum* (TOX SOP AP004 2013). Rats were pair housed (same sex) in suspended polycarbonate boxes with Diamond Dry Bedding (product number 7070C; Diamond Star Products, WI). For the acute and 14-day study, rats were identified by unique numbers using cage cards and tail markings.

5.3 Quality Assurance

The USAPHC Quality Systems Office audited critical phases of this study. Appendix C provides the dates of these audits along with the audited phase and date reported to Management and the Study Director.

[1] Research was conducted in compliance with DOD and Federal statutes and regulations relating to animals and experiments involving animals and adheres to principles stated in the Guide for the Care and Use of Laboratory Animals, Institute of Laboratory Animal Resources, Commission on Life Sciences, National Research Council, National Academy Press, Washington, DC. 2008. The studies reported herein were performed in animal facilities fully accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International.

5.4 Study Personnel

The names of persons contributing to the performance of these studies are provided in Appendix D.

5.5 Contract Studies

Tissues were preserved, packaged and shipped to Battelle Columbus, OH for processing, slide preparation, staining and histopathological evaluation. Tissues and slides were returned to the USAPHC for archiving.

6. Methods

6.1 Acute Study (Limit Dose)

The objective of the acute study was to identify the oral LD_{50}, 95 percent confidence interval and slope for 5-AT in the female SD rat and set the dosage levels for the subacute (14-day) study. A variation of the SSWP method for LD_{50} determination was used. A total of seven female rats were used for the SSWP phase of this study. Based on the published intraperitoneal LD_{50} of 2500 mg 5-AT/kg in the mouse, four female rats were used in the first stage with each animal receiving a different oral dose (CIDPL 2013). For the first stage, the doses were 61, 195, 625, and 2000 mg 5-AT/kg. The animals were fasted overnight prior to dosing and fasted weights for each animal were obtained. The doses were prepared for each animal based on individual fasted body weight. 5-AT was weighed into separate weigh boats for each animal and mixed with the dosing vehicle immediately before dose delivery (gavage). The vehicle was corn oil for both stages. The maximum dose volumes were 90 percent of the maximum of 10 mL/kg body weight. For the second stage, 3 animals were used to confirm the lack of lethality at the limit dose of 2000 mg 5-AT/kg. Due to the large amount of undissolved 5-AT, the hub of the gavage needle became clogged and made the gavage procedure challenging. To reduce the potential for clogging the gavage needle, the 2000 mg 5-AT/kg doses were divided into two doses delivered 4 hours apart so that effective concentration of 5-AT was lower. The doses were divided so that 60 percent of the 5-AT dose was delivered on the first gavage and the remaining 40 percent was delivered on the second gavage event. Note that 2000 mg 5-AT/kg equated to 2424 mg 5-AT·H_2O/kg being weighed out for use. The increase in total material to accommodate the weight of the water in the formulation likely contributed to the clogging of the gavage needles.

Following the administration of 5-AT, the rats were observed for 14 days. All clinical signs or incidences of death were recorded on a daily basis. The surviving animals were euthanized 14 days after dosing and submitted for gross pathological examination.

6.2 Subacute 14-Day Repeated Oral Dose Toxicity Study

The acute toxicity study data were used to set the dose range for the 14-day repeated oral dose study. The estimated LD_{50} was found to exceed the limit dose test of 2000 mg 5-AT/kg body weight. The dose levels for the subacute study were based on the observation that the LD_{50} was greater than 2000 mg 5-AT/kg. This phase of the study was conducted according to established methods (USAPHC 2011). Fifty-four male and 42 female Sprague-Dawley rats approximately 40 days old upon arrival at the PHC facility were used for this phase of the study. Both male and female rats were used for this phase of the study so that sex specific and testicular toxicity could be evaluated. Weights from all animals were taken the day before the start of the study and the animals were sorted into 7 treatment groups (six 5-AT treatments and one vehicle control) of six male and six female rats each based on body weight such that the weight range was evenly distributed between the groups. The additional 12 male rats were used as positive and negative controls for the micronucleus assay. These rats were maintained with the main study rats.

Three dosing solutions were prepared at the nominal concentrations 80, 20 and 5 mg 5-AT/mL corn oil and the nominal dose groups were 700, 350, 175, 88, 44, 22, and 0 mg 5-AT/kg. These solutions were used for the duration of the 14-day study. The solutions were prepared the day before initiating dosing and were stirred vigorously overnight. The rapid movement of the stir bar crushed the crystalline 5-AT into fine particles and eliminated the clogging of the gavage needle hub that had occurred during the acute experiment. Samples from the three stock solutions (top, middle and bottom of the container) were taken and analyzed by LAB to verify concentrations prior to the first day of dosing. The 80 mg 5-AT/mL solution was also sampled on day 7 and all three solutions were sampled again on day 14 to re-verify the concentrations. Stock solutions were vigorously stirred on a stir plate for a minimum of 15 minutes prior to daily dosing and were stirred continuously during the dosing procedure. For the gavage procedure, the dosing solution was taken from the middle of the column. The doses were delivered daily for 14 days to each rat. The volume of the dose delivered to each rat was calculated from the body weight of the corresponding animal. Stock solutions were sufficiently concentrated so that the dose volume did not exceed 10 mL/kg body weight.

Rats were pair housed (same sex) for the duration of the 14-day study. The dosing scheme for the 14-day study consisted of a stagger start over four consecutive days i.e. groups A and B (males), C and D (females). All rats were weighed on group A day -1 (the day prior to the first dosing) and distributed into the A/B (males) and C/D (females) groups by weight for the study. Body weights were recorded for A/B/C/D on days 0 (first dosing day), 3, 7, 13 (last dosing day), and 14 (terminal body weights-fasted). Dosing volumes for each animal were adjusted based on body weights taken on days 0, 3, and 7 so that the rats continued to receive the intended dose. Food consumption based on change in feed container weights was monitored weekly. Water was *ad libitum* and intake was not monitored. Animals were observed daily for clinical signs of toxicity, morbidity and mortality.

The micronucleus assay (MNA)-positive (6 male) and negative control (6 male) rats were housed and maintained with the main study rats. For the MNA, the positive/negative control rats were euthanized on the same days as the male main study rats. The positive control rats were orally gavaged twice--once at 48 and once at 24 hours prior to euthanasia with 200 mg/kg ethylmethyl sulfonate (EMS; Sigma M0880, Lot # BCBK5968V) a known DNA damaging agent. The negative control rats were untreated and served as a negative control for both the EMS and the vehicle (corn oil) treated rats. On the scheduled necropsy day saphenous blood from the MNA control rats and male rats from the three highest dose groups with no mortalities was collected. As no compound related mortalities were observed in any of the dose groups the groups used for the MNA were 177, 313, and 623 mg 5-AT/kg-day. The MNA positive and negative control rats were then euthanized using carbon dioxide gas. Blood collected in support of the MNA was processed according to the MicroFlow Basic Kit ® (Litron Laboratories, Rochester NY) instructions. The prepared samples were then mailed to Litron Laboratories for analysis.

For the main study, approximately 24 hours after the 14th dose, each rat was anesthetized with carbon dioxide gas, 3-4 mLs of blood were collected by intracardiac puncture and the rat was immediately euthanized using carbon dioxide gas. Clinical chemistry and hematology analyses were performed on all samples meeting validation criteria (e.g. volume and quality of sample). The brain, heart, kidneys, liver, spleen, epididymides and testes were removed and weighed for absolute organ weights, organ-to-body weight ratios, and organ-to-brain weight ratios. Gross necropsies were completed on all terminal animals. The following parameters, by test group, were analyzed and compared to the controls: (a) body weight; (b) weight gain; (c) food consumption; (d) absolute organ weight; (e) organ-to-body weight ratio; and (f) organ-to-brain weight ratio. A segment of the epididymides was taken and used for sperm analysis. Collected organs were preserved in 10 percent buffered formalin.

Hematology (Cell-Dyn 3700 Hematology Analyzer, Abbott Laboratories, Abbott Park, Illinois 60064) variables included: white blood cell count (WBC K/mL), WBC differential (K/mL and percent for neutrophils (NEU-%N), lymphocytes (LYM-%L), monocytes (MONO-%M), eosinophils (EOS-%E), basophils (BASO-%B)), red blood cell count (RBC M/mL), hemoglobin (HGB g/dL), hematocrit (HCT %), mean cell volume (MCV fL), mean cell hemoglobin (MCH pg), mean cell hemoglobin

concentration (MCHC g/dL), red blood cell distribution width (RDW %), platelets (PLT K/mL), mean platelet volume (MPV fL), and prothrombin time (PT sec).

Clinical Chemistry (VetTest 8008 Chemistry Analyzer and VetLyte Na, K, Cl Analyzer, IDEXX Laboratories, Inc., One IDEXX Drive, Westbrook, ME 04092) variables included: albumin (ALB g/dL), alkaline phosphatase (ALK P U/L), alanine aminotransferase (ALT U/L), aspartate aminotransferase (AST U/L), blood urea nitrogen (BUN mg/dL), calcium (Ca mg/dL), cholesterol (CHOL mg/dL), creatinine (CREA mg/dL), glucose (GLU mg/dL), globulin (GLOB g/dL), phosphorus (PHOS), total bilirubin (TBIL mg/dL), total protein (TP g/dL), sodium (Na mmol/L), potassium (K mmol/L), and chlorine (Cl mmol/L).

Cauda epididymal sperm counts were determined using a computer-assisted sperm analyzer (TOX IVOS-CASA). The trimmed caudal section was placed in a suitable container containing a measured volume of RPMI-1640 medium warmed to 34-37 °C and minced using a scalpel or scissors to release sperm. The sample was incubated for 5 minutes at 34-37 °C, an aliquot was then removed and diluted 1:1 with RPMI-1640. A chamber of a rat toxicology slide (Leja® or Hamilton Thorne) was loaded with approximately 20 µL of the diluted sperm suspension and the slide was inserted into the sperm analyzer. For each chamber, the image analysis was performed in duplicate. The IVOS-CASA software reported the number (million/mL and million/g tissue) and percent of sperm, motile sperm, and progressive sperm.

Descriptive statistics and statistical analyses were performed using SigmaPlot for Windows Version 12.3, © Systat Software, Inc. 2011). One-factor analysis of variance (ANOVA) was used for data collected at the end of the study. Parametric statistical tests included Dunnett's, Holm-Sidak and Bonferroni. For each analysis, a selection of appropriate tests was provided by the SigmaPlot software and the most rigorous test was chosen. For data that did not meet normality and/or equal variance criteria Kruskal-Wallis rank sum analyses were performed and the non-parametric post test was Dunn's.

7 Results

7.1 Analytical Chemistry

The analytical chemistry results for both phases of the study are provided in Appendix E. In corn oil, 5-AT was not soluble and was stable at room temperature for a 19-day period. For the 14-day study, the nominal concentrations of the dosing solutions were 5, 20, and 80 mg 5-AT/mL corn oil. The measured concentrations were 4.98, 20.2, 71.2 mg 5-AT/mL corn oil. The dose groups were calculated to be 0, 22, 44, 89, 177, 313, and 623 mg 5-AT/kg body weight-day. Doses and concentrations account for the contribution of water weight in the formulation and are reported as mg 5-AT (not 5-AT·H_2O).

7.2 Acute Study Limit Dose Procedure

The SSWP procedure was used to assess the acute toxicity of 5-AT. The first stage used 4 animals, each received one of the following doses: 61, 195, 625, or 2000 mg 5-AT/kg body weight. No animals died at any of the doses for the first stage; thus, the limit dose toxicity test (at 2000 mg 5-AT/kg body weight) was used. Three additional animals were dosed at 2000 mg 5-AT/kg body weight. Two of these animals sustained a gavage related injury that necessitated their early removal from the study. Two additional animals were dosed with 2000 mg/kg body weight to replace the ones removed from study. For all stages and concentrations there was no apparent aversion to the compound and it appeared to be well tolerated. With the exception of the gavage injuries, no clinical signs of distress or discomfort were observed in the dosed animals. For the acute toxicity LD_{50} test, no animals died from compound toxicity at the highest dose tested--2000 mg 5-AT/kg body weight for the limit-dose procedure. Thus, the LD_{50} is greater than the limit dose of 2000 mg 5-AT/kg body wt. Without lethality, the slope and CI for the dose response curve cannot be defined.

7.3 14-Day Repeated Oral Dose Toxicity Study

Summaries of results and raw data for the 14-day oral repeated dose toxicity study are presented in Appendices G-P.

No clinical signs of toxicity were noted in any of the dose groups (0, 22, 44, 89, 177, 313, and 623 mg 5-AT/kg body weight-day) for the duration of the 14 day dosing period. All animals survived until their scheduled necropsy day.

Gross observations at necropsy included pale and or mottled liver (male- 4 instances; two in the corn oil control and two in the highest 5-AT treatment; female- one instance in the highest 5-AT treatment), bedding in the intestinal tract (male- 10 instances; distributed among the 5-AT treatments; female; 28 instances distributed between the treatments and control group), and hydro-uterus in 5 females. None of the observations were considered compound-related. The complete list of observations is provided in Appendix G.

Food consumption was monitored during the study by weighing the food bins before and after adding food on days 0 and 7. Additionally the final food bin weights were taken on day 13. Because the animals were pair housed the consumption per individual rat was calculated based on individual body weights. No differences in food consumption were measured. The food consumption data table is provided in Appendix I.

The body weight of each study animal was obtained on days 0, 3, 7, 13 and 14 of the study. The animals in this study were young and were expected to gain weight during the study. For all dose groups there was an average 11.7(M)/9.3(F) percent decrease in body weights between days 13 and 14 due to overnight fasting. There were no dose-related differences in body weights. The body weight tables for the dose groups and individual animals are provided in Appendix G; the body weight changes and individual data are provided in Appendix H.

The weights of the heart, kidneys, epididymides, liver, spleen, testes (male), ovaries/uterus (female) and thymus were collected at necropsy. The absolute weights and organ/brain weight ratios were analyzed for treatment effects. No differences in absolute brain weight were found between the treatment groups. The organ weights and individual data are in Appendix J; the organ-to-brain weight ratios and individual data are in Appendix K.

Blood was collected from animals on the day of euthanasia and evaluated for total red blood cell and white blood cell counts, packed cell volume, hemoglobin, five-part differential and the following serum chemistries: prothrombin, blood urea nitrogen (BUN), creatinine (CREA), glucose (GLU), total protein (TP), albumin (ALB), cholesterol (CHOL), triglycerides (TRIG), total bilirubin (TBIL), calcium (Ca), globulin (GLOB) alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALK-P), inorganic phosphate (PHOS), electrolytes (Na, K, Cl). No significant dose-related differences among the treatment groups were found in either the hematology or clinical chemistries. Non-treatment-related statistically significant differences between groups are annotated in the summary tables of the appropriate Appendix. The complete data tables for individual animals and group summary data are provided in Appendices L and M.

7.4 Micronucleus Assay (MNA)

Male rats from the 5-AT study (three highest dose groups and the vehicle control) were tested for DNA damage in their peripheral blood. The MNA samples were prepared according to the manufacturer's protocol and shipped to Litron for analysis. The complete contributing scientist report from Litron was archived with the study. The analyses included measuring the frequencies of reticulocytes (RET) and RET-containing micronuclei (MN-RET). Additional control rats were either a) dosed with a known genotoxicant, ethylmethylsulfonide (EMS) as a positive control for peripheral blood DNA damage, or b) untreated and not subject to daily vehicle gavage as a negative

experimental control. The EMS positive control group had a significantly higher percent MN-RET ($p \leq 0.001$) compared to the negative and 5-AT treated groups. There were no significant differences between the negative and 5-AT treated groups ($p=0.785$). The percent RET was reduced in the EMS-treated controls compared to the negative, vehicle and 5-AT treated groups ($p \leq 0.001$) while the negative control group had an increased percent RET compared to the EMS treated, vehicle and 5-AT treatment groups ($0.027 \leq p \geq 0.001$). The vehicle and 5-AT treatments were not significantly different from each other ($0.982 \leq p \geq 0.736$). Taken together the data indicate that 5-AT was not genotoxic to bone marrow in male rats. Only a generalized low level stress response was observed, as evidenced by the reduced RET frequency when compared to untreated negative controls. Summary tables, graphs and individual data are provided in Appendix N.

7.5 Sperm Analysis

For each terminal animal, sperm from a section of epididymides dissected at necropsy was evaluated for total sperm and motility. Of the 42 rats tested, 20 had measurable sperm and 22 did not; these data were not treatment-related. It is believed that the sexual maturation of the rats tested was at the threshold of competence and therefore the sperm analysis was uninformative. The individual and summary data tables are provided in Appendix O.

7.6 Histopathology

Liver, kidney, spleen and heart for the vehicle and highest dose (623 mg 5-AT/kg-day) were submitted to Battelle for routine processing to slides, stained with hematoxylin and eosin, and subjected to histopathological examination. The slides were examined by the pathologist without prior knowledge of the dose group identity. There were no microscopic findings related to exposure of 5-AT. The report is provided in Appendix P.

8 Discussion

An acute and subacute oral toxicity study exposing rats to 5-AT was conducted. 5-AT was not acutely toxic as a single dose at the limit dose of 2000 mg/kg body weight suggesting low potential for acute toxicity.

No toxicity or morbidity were observed in the 14-day repeated dose subacute study at any of the doses tested including the highest treatment of 623 mg/kg-day. Thus, the 14-day NOAEL/NOEL was 623 mg 5-AT/kg-day and no LOAEL/LOEL could be determined.

9 Conclusions

The test article, 5-AT, is a potential replacement for perchlorate in munition formulations. In rats, it is not toxic in either a single or 14-day exposure scenario at the exposure levels used in this study. Based on a lack of short term toxicity, it is a superior substance compared to perchlorate and it should be pursued as a perchlorate replacement.

10 Recommendations

The substitution of 5-AT for perchlorate presents an opportunity to reduce the toxicity of the munition formulations. 5-AT is the parent compound for 5-nitrotetrazole (5-NT) and DBX-1 (Copper (I) 5-nitrotetrazolate). Considering that toxicity testing of DBX-1 is unlikely because it is a primary explosive, conducting a 90-day toxicity test using 5-AT is recommended. The subchronic test of 5-AT will provide data for all three of these tetrazole-compounds.

11 Point of Contact

Dr. Valerie H. Adams, the principle investigator, is the point of contact for this project. She may be reached at 410-436-3980 (commercial).

Submitted by: U.S. Army Public Health Command
Portfolio of Toxicology
Health Effects Research Program (HERP)
MCHB-IP-THE
Aberdeen Proving Ground, MD 21010-5403

Prepared by:

Valerie H. Adams, Ph.D.
Biologist
HERP

Jan 30 2015
Date

Approved by:

Michael Quinn, Ph.D.
Program Manager- HERP

1/30/15
Date

Mark S. Johnson, Ph.D., D.A.B.T.
Director Toxicology Portfolio

2-12-15
Date

APPENDIX A
REFERENCES
Protocol No. 30-13-07-01
Acute Oral Toxicity of 5-AT in Rats

AERTA. 2012. Army Environmental Requirements and Technology Assessments: Requirement PP-3-02-05. In *Compliant Ordnance Lifecycle for Readiness of the Transformation and Objective Forces*. Aberdeen Proving Ground, MD: U.S. Army Environmental Command.

AR 40-5. Preventive Medicine, 25 May 2007.

AR 70-1. Army Aquisition Policy, 31 December 2003.

AR 200-1. Environmental Protection and Enhancement, 31 December 2007.

CIDPL. 2013. *ChemIDplus Lite*. U.S. National Library of Medicine [cited multiple dates, 2013- 2009]. Available from http://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp.

DoDI. 1998. Department of Defense Instruction 4715.4, Pollution Prevention. http://www.dtic.mil/whs/directives/corres/pdf/471504p.pdf.

Sabatini, J. J., and J. D. Moretti. 2013. High-nitrogen-based pyrotechnics: perchlorate-free red- and green-light illuminants based on 5-aminotetrazole. *Chemistry* 19 (38):12839-45.

TOX SOP AP004. Animal Health Technician Duties within the Animal Facility. USAPHC. Aberdeen Proving Ground, MD.

USAPHC. 2011. TOX SOP OT037.003, 14-Day Range Finding and 90-Day Oral Toxicity Study in Rodents. (POC Lee Crouse).

APPENDIX B
AUTHORITY
Protocol No. 30-13-07-01
Acute Oral Toxicity of 5-AT in Rats

Military Interdepartmental Purchase Request (MIPR) No. 10322305

UNCLASSIFIED // APPORVED FOR PUBLIC RLEASE // DISTRIBUTION UNLIMITED

HEADQUARTERS, U.S. ARMY MEDICAL COMMAND
Fort Sam Houston, TX 78234-6007

APPENDIX C

Quality Assurance Statement

For: Toxicology Study No. S.0015656-13, Protocol No. 30-13-07-01, titled "Effects of Effects of Oral 5 Aminotetrazole (5-AT) Exposure to Rats (*Rattus norvegicus*), August–Sept 2013", the following critical phases were audited by the Quality Systems and Regulatory Compliance Office (QSARC), Quality Assurance Unit (QAU):

PRE IN-LIFE PHASE OF THE STUDY

Critical Phase Inspected/Audited	Date Inspected /Audited	Date Reported to Management/SD
Study Protocol Good Laboratory Practice Standards and Animal Care Review	06/11/2013	06/11/2013

IN-LIFE PHASE OF THE STUDY

Critical Phase Inspected/Audited	Date Inspected /Audited	Date Reported to Management/SD
Acute Study - Test System Receipt, Facilities, Husbandry, Veterinary Care and Enrichment.	08/15/2013	08/22/2013
Acute Study - Test Substance Preparation and Administration, Labeling and Post Dose Observations.	08/15/2013	08/22/2013
Sub-Acute 14 Day - Test Substance Preparation and Administration, Labeling and Post Dose Observations	09/12/2013	09/19/2013
Sub-Acute-14 Day-Test System Facilities, Identification, Husbandry, Food & Water Supply & Enrichment	09/12/2013	09/19/2013
Study Personnel Qualifications and Training Records Review	09/24/2013	10/07/2013
14-Day Repeated Dose Test (Sub-acute Study) - Sperm Collection and Analysis	09/25/2013	10/07/2013
14-Day Repeated Dose Test (Sub-acute Study) - Micronucleus Assay Biosample Collection Procedures	09/25/2013	10/07/2013
Sub-Acute study - Anesthesia, Bleeding Technique, Euthanasia, and Necropsy Procedures	09/27/2013	10/09/2013
Clinical chemistry, Hematology and Final In-Life Study Endpoint Criteria	09/27/2013	10/09/2013

APPENDIX C

Quality Assurance Statement

For: Toxicology Study No. S.0015656-13, Protocol No. 30-13-07-01, titled "Effects of Effects of Oral 5 Aminotetrazole (5-AT) Exposure to Rats (*Rattus norvegicus*), August–Sept 2013", the following critical phases were audited by the Quality Systems and Regulatory Compliance Office (QSARC), Quality Assurance Unit (QAU):

POST IN-LIFE PHASE OF THE STUDY

Critical Phase Inspected/Audited	Date Inspected /Audited	Date Reported to Management/SD
LAB Analytical Support - Verification of homogeneity, stability & concentration of dosing solutions	10/16/2013	10/18/2013
Micronucleus Assay Contractor Good Laboratory Practice Protocol Review	10/22/2013	11/01/2013
Contractor Good Laboratory Practice Micronucleus Final Report Review	12/13/2013	12/20/2013
Final Study Report Good Laboratory Practice Standards Review	12/19/2014	12/22/2014
Study Raw Data Good Laboratory Practice Standards Review	12/19/2014	12/22/2014

Note 1: All findings were made known to the Study Director and the Program Manager at the time of the audit/inspection. If there were no findings during the inspection, the inspection was reported to Management and the Study Director on the date shown in the table.

Note 2: In addition to the study specific critical phase inspections listed here, general facility and process based inspection not specifically related to this study are done monthly or annually in accordance with QA Standard Operating Procedure.

Note 3: This report has been audited by the Quality Assurance Unit (QSARC), and is considered to be an accurate account of the data generated and of the procedures followed.

Michael P. Kefauver
Quality Assurance Specialist, QSARC

02/12/2015
Date

APPENDIX D
ARCHIVES AND STUDY PERSONNEL
Protocol No. 30-13-07-01
Acute Oral Toxicity of 5-AT in Rats

D-1. Archives

All raw data, documentation, records (including test system), protocol, and a copy of the final report generated as a result of this study will be archived in the storage facilities of the Toxicology Portfolio, Army Institute of Public Health (AIPH), for a minimum of five (5) years following submission of the final report to the Sponsor. If the report is used to support a regulatory action, it shall, along with all supporting data, be retained indefinitely.

The present study used the laboratory project number: S.0015300-13, Toxicology Study number: S.0015300-13, and protocol number 30-13-07-01 for all filings.

The protocol, raw data, summary data, and the final report pertaining to this study will be physically maintained within Building E-2100, USAPHC. These data may be scanned to a computer disk. Scanned study files will be stored electronically in Room 3010, Building E-2100, USAPHC, Aberdeen Proving Ground (APG), MD, 21010.

Archived SOPs and maintenance and calibration logbooks may be found in Room 1026, Building E-2100, USAPHC, APG, MD, 21010.

Archivist: Martha Thompson

D-2. Personnel

Management: Mark S Johnson, Ph.D, Portfolio Toxicology Director; Michael J Quinn, Ph.D., Program Manager, Health Effects Research Program (HERP)

Study Director: Valerie H Adams, Biologist, HERP.

Quality Assurance: Michael P Kefauver, Chemist, Quality Systems Office.

APPENDIX E
ANALYTICAL DATA
Protocol No. 30-13-07-01
Acute Oral Toxicity of 5-AT in Rats

Acute Study

For all stages of the acute study, the doses were weighed individually for each animal based on the weight of the animal. Doses were mixed with the vehicle and dosed in their entirety to each animal. No analytical data were collected on these doses.

14-day Subacute Study

Stability. The stability test was performed prior to the start of the 14-day study. The anticipated lowest dose was 50 mg/kg-day; therefore the stability of a 8.95 mg/mL 5-AT/corn oil solution was tested. 5-AT remained as a suspension in the corn oil for the duration of the stability test. The 5-AT suspension was prepared on Aug 21, 2013 and analyzed on Sept 9, 2013. DLS obtained 93.3 percent recovery indicating that 5-AT was sufficiently stable for the duration of the study.

Homogeneity. Three dosing solutions were prepared with the final volume sufficient for the entirety of the 14-day study and were vigorously stirred with a stir bar/plate. While stirring, from each of the three containers, 3 - 2 mL samples of solution (top, middle, and bottom of the 5-AT solution column) were withdrawn using the same size gavage needle as used for dosing the animals. DLS verified the concentrations of these samples.

Dose Group	Nominal mg 5-AT/kg-day	Measured mg 5-AT/mL corn oil	Calculated dose mg/kg-day (range) *
1	0	0	0
2	22	--	21.9 (21-22)
3	44	4.98	43.6 (43-44)
4	88	--	88.9 (88-89)
5	175	20.2	176.7 (176-177)
6	350	--	313.2 (311-315)
7	700	71.2	623.1 (622-624)
* determined by analysis of individual body weights and dosing volumes.			

APPENDIX F
SEQUENTIAL STAGEWISE PROBIT: ORAL, RAT, LIMIT DOSE
Protocol No. 30-13-07-01
Acute Oral Toxicity of 5-AT in Rats

Study No. 0.S0015300-13, Protocol No. 30-13-07-01, SOP No 17.08
Chemical Substance: 5-aminotetrazole (5-AT)
Route: Oral Species: Rat (Sprague-Dawley Crl:CD(SD)) Sex: Female
Diluent: Corn Oil

Animal #	Dosing Stage	Weight (g)	Nominal Dose (mg/kg)	Volume (mL)	Exposure Day Signs	Exposure Day Morbidity/mortality
13-0915	1	194	61	1.9	N	N
13-0916	1	179	195	1.7	N	N
13-0917	1	190	625	1.9	N	N
13-0918	1	191	2000	1.9	N	N
13-0919*	2	212	2000	2.1 + 2.1 Split dose	N	N
13-0920	2	189	2000	1.8 + 1.8 Split dose	N	N
13-0921	2	219	2000	2.1 + 2.1 Split dose	N	N
13-0923	2	212	2000	2.0 + 1.8 Split dose	N	N
13-0924*	2	213	2000	2.0 + n/a	N	N

*= animal removed from study due to injury
Study conclusions: 5-AT has an LD_{50} greater than 2000 mg/kg.

APPENDIX G
SUMMARY OF 14-DAY BODY WEIGHTS,
INDIVIDUAL DATA AND NECROPSY GROSS OBSERVATIONS
Protocol No. 30-13-07-01
Acute Oral Toxicity of 5-AT in Rats

Table G-1: Summary male and female 14-day body weights

5-AT mg/kg-day		Day on study body weight; males (g)						5-AT mg/kg-day		Day on study body weight; females (g)					
		-1	0	3	7	13	14			-1	0	3	7	13	14
0	Mean	165	183	208	238	286	274	0	Mean	124	148	168	185	216	204
	SD	5	8	7	9	12	13		SD	8	10	10	8	11	12
	N	6	6	6	6	6	6		N	6	6	6	6	6	6
22	Mean	162	174	202	235	287	274	22	Mean	126	147	168	184	205	197
	SD	5	8	9	11	17	17		SD	12	13	14	14	14	13
	N	6	6	6	6	6	6		N	6	6	6	6	6	6
44	Mean	163	180	206	242	293	280	44	Mean	126	154	173	189	218	207
	SD	9	8	11	15	24	22		SD	7	8	9	9	10	6
	N	6	6	6	6	6	6		N	6	6	6	6	6	6
89	Mean	165	179	207	238	286	275	89	Mean	128	151	170	189	207	194
	SD	5	6	7	10	13	12		SD	12	12	9	6	12	20
	N	6	6	6	6	6	6		N	6	6	6	6	6	6
177	Mean	165	182	208	240	291	279	177	Mean	126	154	173	182	211	202
	SD	4	5	6	7	16	13		SD	10	14	20	13	12	9
	N	6	6	6	6	6	6		N	6	6	6	5	5	5
313	Mean	161	173	200	230	277	268	313	Mean	125	149	169	189	210	203
	SD	7	5	5	8	11	12		SD	12	15	15	14	20	20
	N	6	6	6	6	6	6		N	6	6	6	6	6	6
623	Mean	167	179	206	238	284	272	623	Mean	123	145	167	185	204	198
	SD	11	15	16	19	25	22		SD	11	11	13	18	21	22
	N	6	6	6	6	6	6		N	6	6	6	6	6	6

APPENDIX G
SUMMARY OF 14-DAY BODY WEIGHTS,
INDIVIDUAL DATA AND NECROPSY GROSS OBSERVATIONS
Protocol No. 30-13-07-01
Acute Oral Toxicity of 5-AT in Rats

Table G-2: Individual male and female 14 day body weights

5-AT mg/kg	Animal I.D.	Day on study body weight; males (g)					
		-1	0	3	7	13	14
0	13-0969	162	175	200	228	271	260
	13-0970	167	175	206	241	298	285
	13-0953	163	182	206	234	278	270
	13-0954	163	184	205	238	287	278
	13-0985	174	198	221	253	302	291
	13-0986	163	181	207	231	277	261
22	13-0949	162	170	196	228	274	262
	13-0950	156	163	195	233	294	284
	13-0981	163	172	197	224	271	260
	13-0982	171	185	218	252	314	300
	13-0965	164	178	199	228	275	258
	13-0966	157	176	207	243	294	282
44	13-0973	162	173	204	244	297	285
	13-0974	177	189	220	260	320	306
	13-0957	155	174	199	232	275	266
	13-0958	159	177	202	236	289	270
	13-0989	155	176	193	222	260	249
	13-0990	169	190	218	260	318	303
89	13-0947	167	177	207	235	288	275
	13-0948	166	176	200	230	273	266
	13-0979	171	182	214	249	302	290
	13-0980	160	171	199	226	269	259
	13-0963	159	177	205	238	285	272
	13-0964	169	190	217	249	298	287
177	13-0971	163	173	199	233	279	277
	13-0960	168	183	213	249	314	299
	13-0955	161	182	203	232	272	264
	13-0956	167	187	211	239	288	272
	13-0987	161	180	208	240	287	273
	13-0988	169	187	213	248	306	288
313	13-0945	159	170	199	235	281	267
	13-0946	162	173	201	232	274	262
	13-0977	171	179	208	242	298	290
	13-0978	165	176	201	226	274	269
	13-0961	158	173	200	223	267	261
	13-0962	149	165	191	220	270	258
623	13-0951	157	168	195	228	275	264
	13-0952	167	177	210	239	282	271
	13-0983	154	161	184	214	255	247
	13-0984	171	177	209	246	290	277
	13-0967	184	205	232	270	329	312
	13-0968	166	183	206	230	274	263

5-AT mg/kg	Animal I.D.	Day on study body weight; females (g)					
		-1	0	3	7	13	14
0	13-1021	134	148	170	182	210	197
	13-1022	118	134	161	184	213	197
	13-1007	132	152	173	186	210	198
	13-1008	119	152	166	185	223	209
	13-1035	115	140	154	175	204	196
	13-1036	128	161	184	200	234	227
22	13-1003	114	140	162	182	196	197
	13-1004	134	155	170	189	220	204
	13-1031	132	147	167	180	198	190
	13-1032	111	124	148	163	186	175
	13-1017	141	162	191	205	223	211
	13-1018	123	153	170	185	204	205
44	13-1025	121	146	164	175	213	205
	13-1026	118	145	163	184	210	200
	13-1011	133	158	181	194	214	205
	13-1012	125	159	177	196	236	218
	13-1039	135	165	183	200	220	210
	13-1040	121	148	169	185	212	205
89	13-1001	143	167	182	197	218	207
	13-1002	133	155	166	192	217	200
	13-1029	114	138	157	180	198	191
	13-1030	114	137	162	184	187	155
	13-1015	130	158	174	190	205	204
	13-1016	132	152	176	191	215	204
177	13-1023	115	134	149	168	199	193
	13-1024	125	149	171	191	225	211
	13-1009	135	154	171	183	204	197
	13-1010	140	173	201	(f)	(f)	(f)
	13-1037	123	164	191	198	222	213
	13-1038	117	147	154	171	203	195
313	13-0999	116	141	164	185	221	209
	13-1000	138	155	176	191	218	209
	13-1027	118	138	160	187	204	199
	13-1028	123	141	159	174	179	177
	13-1013	113	144	158	180	199	188
	13-1014	140	177	195	215	238	235
623	13-1005	110	129	150	169	193	181
	13-1006	133	149	176	185	206	197
	13-1033	132	155	179	210	232	228
	13-1034	132	158	180	203	225	219
	13-1019	114	139	154	169	176	174
	13-1020	115	140	165	176	192	186

(f) = fated

APPENDIX G
SUMMARY OF 14-DAY BODY WEIGHTS,
INDIVIDUAL DATA AND NECROPSY GROSS OBSERVATIONS
Protocol No. 30-13-07-01
Acute Oral Toxicity of 5-AT in Rats

Table G-3: Male and female 14-day gross observations at necropsy

5-AT mg/kg	Animal I.D. male	Remarks at Necropsy	5-AT mg/kg-	Animal I.D. female	Remarks at Necropsy
	13-0969	liver mildly mottled, left testes small		13-1021	hydro-uterus; bedding in stomach, intestines and cecum
	13-0970	liver pale, mildly mottled		13-1022	mild hydro-uterus; bedding in cecum
0	13-0953	yellow fluid in stomach	**0**	13-1007	bedding in stomach, throughout intestines and cecum
	13-0954	NGLR		13-1008	bedding in stomach, throughout intestines and cecum
	13-0985	NGLR		13-1035	bedding in stomach, throughout intestines and cecum
	13-0986	NGLR		13-1036	bedding in stomach, throughout intestines and cecum
	13-0949	NGLR		13-1003	mild hydro-uterus; bedding in stomach and intestines
	13-0950	NGLR		13-1004	bedding in stomach, throughout intestines and cecum
22	13-0981	bedding in stomach and cecum	**22**	13-1031	bedding in stomach, throughout intestines and cecum
	13-0982	bedding in stomach, throughout intestines and cecum		13-1032	bedding in intestines and cecum; hydro-uterus; thymus
	13-0965	yellow fluid in stomach		13-1017	bedding in stomach, throughout intestines and cecum
	13-0966	NGLR		13-1018	bedding in stomach, throughout intestines and cecum
	13-0973	NGLR		13-1025	NGLR
	13-0974	blood around nose, lungs congested and dark red,		13-1026	NGLR
44	13-0957	NGLR	**44**	13-1011	bedding in stomach, throughout intestines and cecum
	13-0958	NGLR		13-1012	bedding in stomach, throughout intestines and cecum
	13-0989	bedding in stomach		13-1039	bedding in stomach, throughout intestines and cecum
	13-0990	NGLR		13-1040	NGLR
	13-0947	NGLR		13-1001	bedding in stomach, throughout intestines and cecum
	13-0948	NGLR		13-1002	NGLR
89	13-0979	thymus red spot 0.2 cm; bedding in stomach, throughout intestines and cecum	**89**	13-1029	NGLR
	13-0980	bedding in stomach, throughout intestines and cecum		13-1030	bedding in stomach, throughout intestines and cecum
	13-0963	Bedding in stomach		13-1015	bedding in stomach, throughout intestines and cecum
	13-0964	small testes right and left		13-1016	NGLR
	13-0971	lungs congested, bedding in stomach		13-1023	bedding in stomach, throughout intestines and cecum
	13-0960	bedding in stomach and cecum		13-1024	bedding in stomach, throughout intestines and cecum
	13-0955	NGLR		13-1009	Thymus was in formalin briefly before weighing
177	13-0956	bedding in stomach, throughout intestines and cecum	**177**	13-1010	early death-bedding in stomach, throughout intestines and cecum
	13-0987	NGLR		13-1037	NGLR
	13-0988	bedding in stomach, throughout intestines and cecum		13-1038	hydro-uterus
	13-0945	NGLR		13-0999	bedding in stomach, throughout intestines and cecum
	13-0946	NGLR		13-1000	bedding in stomach and cecum
313	13-0977	yellow fluid in stomach, bedding in cecum	**313**	13-1027	NGLR
	13-0978	NGLR		13-1028	NGLR
	13-0961	NGLR		13-1013	bedding in stomach, throughout intestines and cecum
	13-0962	NGLR		13-1014	bedding in stomach, throughout intestines and cecum
	13-0951	NGLR		13-1005	bedding in stomach, throughout intestines and cecum
	13-0952	blood around nose, lungs dark red, bedding in cecum		13-1006	thymus was in formalin briefly before weighing; bedding in stomach, intestines and cecum
623	13-0983	liver mildly mottled	**623**	13-1033	bedding in stomach, throughout intestines and cecum
	13-0984	pale liver, mildly mottled		13-1034	bedding in stomach, throughout intestines and cecum
	13-0967	NGLR		13-1019	liver slightly mottled; bedding in stomach, intestines and cecum
	13-0968	NGLR		13-1020	NGLR

NGLR = no gross lesion reported

APPENDIX H
SUMMARY OF 14-DAY BODY WEIGHT CHANGES AND INDIVIDUAL DATA
Protocol No. 30-13-07-01
Acute Oral Toxicity of 5-AT in Rats

Table H-1: Summary of 14-day body weight changes

5-AT mg/kg-day		male weight change (g) * Days 0 to 3	3 to 7	7 to 13	13 to 14		female weight change (g) * Days 0 to 3	3 to 7	7 to 13	13 to 14
0	**Mean**	25.0	30.0	48.0	-11.3	**Mean**	20.2	17.3	30.3	-11.7
	SD	3.4	4.0	5.1	2.9	**SD**	5.2	4.4	4.9	3.5
	N	6	6	6	6	**N**	6	6	6	6
22	**Mean**	28.0	32.7	52.3	-12.7	**Mean**	21.2	16.0	20.5	-7.5
	SD	4.7	4.2	7.3	2.5	**SD**	5.0	2.8	5.9	7.1
	N	6	6	6	6	**N**	6	6	6	6
44	**Mean**	26.2	36.3	50.8	-13.3	**Mean**	19.3	16.2	28.5	-10.3
	SD	5.2	5.1	8.6	3.5	**SD**	2.2	3.7	8.7	3.9
	N	6	6	6	6	**N**	6	6	6	6
89	**Mean**	28.2	30.8	48.0	-11.0	**Mean**	18.3	19.5	17.7	-13.2
	SD	2.7	3.1	4.5	2.3	**SD**	5.4	4.8	8.1	10.6
	N	6	6	6	6	**N**	6	6	6	6
177	**Mean**	25.8	32.3	50.8	-12.2	**Mean**	19.3	15.0	28.4	-8.8
	SD	3.1	3.3	9.1	6.0	**SD**	8.0	5.4	5.6	3.1
	N	6	6	6	6	**N**	6	5	5	5
313	**Mean**	27.3	29.7	47.7	-9.5	**Mean**	19.3	20.0	21.2	-7.0
	SD	1.6	5.0	5.0	3.7	**SD**	3.3	4.6	10.4	4.2
	N	6	6	6	6	**N**	6	6	6	6
623	**Mean**	27.5	31.8	46.3	-11.8	**Mean**	22.3	18.0	18.7	-6.5
	SD	4.3	5.3	6.5	3.0	**SD**	4.2	8.2	6.3	3.6
	N	6	6	6	6	**N**	6	6	6	6

* = no statistically significant differences were found between treatment groups.

APPENDIX H
SUMMARY OF 14-DAY BODY WEIGHT CHANGES AND INDIVIDUAL DATA
Protocol No. 30-13-07-01
Acute Oral Toxicity of 5-AT in Rats

Table H-2: Individual data for male and female 14-day body weight changes

5-AT mg/kg	Animal I.D.	Day on study body weight; males (g)				Animal I.D.	Day on study body weight; females (g)			
		0-3	3-7	7-13	13-14		0-3	3-7	7-13	13-14
0	13-0969	25	28	43	-11	13-1021	22	12	28	-13
	13-0970	31	35	57	-13	13-1022	27	23	29	-16
	13-0953	24	28	44	-8	13-1007	21	13	24	-12
	13-0954	21	33	49	-9	13-1008	14	19	38	-14
	13-0985	23	32	49	-11	13-1035	14	21	29	-8
	13-0986	26	24	46	-16	13-1036	23	16	34	-7
22	13-0949	26	32	46	-12	13-1003	22	20	14	1
	13-0950	32	38	61	-10	13-1004	15	19	31	-16
	13-0981	25	27	47	-11	13-1031	20	13	18	-8
	13-0982	33	34	62	-14	13-1032	24	15	23	-11
	13-0965	21	29	47	-17	13-1017	29	14	18	-12
	13-0966	31	36	51	-12	13-1018	17	15	19	1
44	13-0973	31	40	53	-12	13-1025	18	11	38	-8
	13-0974	31	40	60	-14	13-1026	18	21	26	-10
	13-0957	25	33	43	-9	13-1011	23	13	20	-9
	13-0958	25	34	53	-19	13-1012	18	19	40	-18
	13-0989	17	29	38	-11	13-1039	18	17	20	-10
	13-0990	28	42	58	-15	13-1040	21	16	27	-7
89	13-0947	30	28	53	-13	13-1001	15	15	21	-11
	13-0948	24	30	43	-7	13-1002	11	26	25	-17
	13-0979	32	35	53	-12	13-1029	19	23	18	-7
	13-0980	28	27	43	-10	13-1030	25	22	3	-32
	13-0963	28	33	47	-13	13-1015	16	16	15	-1
	13-0964	27	32	49	-11	13-1016	24	15	24	-11
177	13-0971	26	34	46	-2	13-1023	15	19	31	-6
	13-0960	30	36	65	-15	13-1024	22	20	34	-14
	13-0955	21	29	40	-8	13-1009	17	12	21	-7
	13-0956	24	28	49	-16	13-1010	28	(f)	(f)	(f)
	13-0987	28	32	47	-14	13-1037	27	7	24	-9
	13-0988	26	35	58	-18	13-1038	7	17	32	-8
313	13-0945	29	36	46	-14	13-0999	23	21	36	-12
	13-0946	28	31	42	-12	13-1000	21	15	27	-9
	13-0977	29	34	56	-8	13-1027	22	27	17	-5
	13-0978	25	25	48	-5	13-1028	18	15	5	-2
	13-0961	27	23	44	-6	13-1013	14	22	19	-11
	13-0962	26	29	50	-12	13-1014	18	20	23	-3
623	13-0951	27	33	47	-11	13-1005	21	19	24	-12
	13-0952	33	29	43	-11	13-1006	27	9	21	-9
	13-0983	23	30	41	-8	13-1033	24	31	22	-4
	13-0984	32	37	44	-13	13-1034	22	23	22	-6
	13-0967	27	38	59	-17	13-1019	15	15	7	-2
	13-0968	23	24	44	-11	13-1020	25	11	16	-6

(f)= fated

APPENDIX I
SUMMARY OF 14-DAY FOOD CONSUMPTION AND INDIVIDUAL DATA
Protocol No. 30-13-07-01
Acute Oral Toxicity of 5-AT in Rats

Table I-1: Summary of male and female food consumption over 14 day study

5-AT mg/kg-day	Males	total food consumed (g) per rat *	average daily food intake (g) per rat *	5-AT mg/kg-day	Females	total food consumed (g) per rat *	average daily food intake (g) per rat *
0	**Mean**	295	21	**0**	**Mean**	230	16
	SD	14	1		**SD**	14	1
	N	6	6		**N**	6	6
22	**Mean**	318	23	**22**	**Mean**	225	16
	SD	20	1		**SD**	13	1
	N	6	6		**N**	6	6
44	**Mean**	308	22	**44**	**Mean**	229	16
	SD	31	2		**SD**	6	0
	N	6	6		**N**	6	6
89	**Mean**	307	22	**89**	**Mean**	228	16
	SD	15	1		**SD**	15	1
	N	6	6		**N**	6	6
177	**Mean**	302	22	**177**	**Mean**	227	16
	SD	21	1		**SD**	13	1
	N	6	6		**N**	4	4
313	**Mean**	302	22	**313**	**Mean**	235	17
	SD	12	1		**SD**	24	2
	N	6	6		**N**	6	6
623	**Mean**	292	21	**623**	**Mean**	215	15
	SD	20	1		**SD**	33	2
	N	6	6		**N**	6	6

* = no statistically significant differences between treatment groups were found.

APPENDIX I
SUMMARY OF 14-DAY FOOD CONSUMPTION AND INDIVIDUAL DATA
Protocol No. 30-13-07-01
Acute Oral Toxicity of 5-AT in Rats

Table I-2: Individual data for male food consumption over 14-day study

5-AT mg/kg-day	Male I.D.*	Terminal body wts (g)	fractional rat wt per cage	food bin weights (g) per cage				food consumed per cage			total food consumed per rat**	average daily food intake (g) per rat
				Day 0 (full)	Day 7 (empty)	Day 7 (full)	Day 13 (empty)	Day 0-7	Day 7-13	Day 0-13		
0	13-0953	270	0.493	1162.2	834.4	1128.6	856.4	327.8	272.2	600	295.6	21.1
	13-0954	278	0.507								304.4	21.7
	13-0969	260	0.477	1197.4	888.6	1181.2	899.4	308.8	281.8	590.6	281.8	20.1
	13-0970	285	0.523								308.8	22.1
	13-0985	291	0.527	1165.4	856.4	1143.4	871.6	309	271.8	580.8	306.2	21.9
	13-0986	261	0.473								274.6	19.6
22	13-0949	262	0.480	1189	861.6	1217.6	905.4	327.4	312.2	639.6	306.9	21.9
	13-0950	284	0.520								332.7	23.8
	13-0965	258	0.478	1170.2	839.8	1154	862.2	330.4	291.8	622.2	297.3	21.2
	13-0966	282	0.522								324.9	23.2
	13-0981	260	0.464	1203	873.6	1176.2	860.4	329.4	315.8	645.2	299.6	21.4
	13-0982	300	0.536								345.6	24.7
44	13-0957	266	0.496	1175.2	864	1174.2	896.6	311.2	277.6	588.8	292.2	20.9
	13-0958	270	0.504								296.6	21.2
	13-0973	285	0.482	1229.6	875.2	1189.6	866.8	354.4	322.8	677.2	326.6	23.3
	13-0974	306	0.518								350.6	25.0
	13-0989	249	0.451	1193.2	883.8	1115.8	842.4	309.4	273.4	582.8	262.9	18.8
	13-0990	303	0.549								319.9	22.9
89	13-0947	275	0.508	1168.4	851.2	1173.8	893.6	317.2	280.2	597.4	303.7	21.7
	13-0948	266	0.492								293.7	21.0
	13-0963	272	0.487	1176	840	1165	869.4	336	295.6	631.6	307.3	22.0
	13-0964	287	0.513								324.3	23.2
	13-0979	290	0.528	1190.4	869.4	1144.2	852	321	292.2	613.2	323.9	23.1
	13-0980	259	0.472								289.3	20.7
177	13-0955	264	0.493	1184.2	882.8	1139.2	883.8	301.4	255.4	556.8	274.2	19.6
	13-0956	272	0.507								282.6	20.2
	13-0960	299	0.519	1224.6	900.6	1182	870	324	312	636	330.1	23.6
	13-0971	277	0.481								305.9	21.8
	13-0987	273	0.487	1205	873.4	1140.4	855.8	331.6	284.6	616.2	299.9	21.4
	13-0988	288	0.513								316.3	22.6
313	13-0945	267	0.505	1151.6	830.8	1190	906.4	320.8	283.6	604.4	305.1	21.8
	13-0946	262	0.495								299.3	21.4
	13-0961	261	0.503	1171.9	859.6	1127.6	857.8	312.3	269.8	582.1	292.7	20.9
	13-0962	258	0.497								289.4	20.7
	13-0977	290	0.519	1208.2	883.6	1201.2	900	324.6	301.2	625.8	324.7	23.2
	13-0978	269	0.481								301.1	21.5
623	13-0951	264	0.493	1196.6	896.2	1188.6	916.6	300.4	272	572.4	282.5	20.2
	13-0952	271	0.507								289.9	20.7
	13-0967	312	0.543	1154.2	842.4	1177	889.4	311.8	287.6	599.4	325.2	23.2
	13-0968	263	0.457								274.2	19.6
	13-0983	247	0.471	1180.4	867	1162.6	895	313.4	267.6	581	273.9	19.6
	13-0984	277	0.529								307.1	21.9

* = animals were pair housed; ** = based on the fractional wieght of each rat per pair

APPENDIX I
SUMMARY OF 14-DAY FOOD CONSUMPTION AND INDIVIDUAL DATA
Protocol No. 30-13-07-01
Acute Oral Toxicity of 5-AT in Rats

Table I-3: Individual data for female food consumption over 14-day study

5-AT mg/kg-day	Female I.D.*	Terminal body wts (g)	fractional rat wt per cage	food bin weights (g) per cage				food consumed per cage			total food consumed (g) per rat**	average daily food intake (g) per rat
				Day 0 (full)	Day 7 (empty)	Day 7 (full)	Day 13 (empty)	Day 0-7	Day 7-13	Day 0-13		
0	13-1007	198	0.486	1198	944.2	1070.4	864.2	253.8	206.2	460	223.8	16.0
	13-1008	209	0.514								236.2	16.9
	13-1021	197	0.500	1182.2	935	1041.4	843.2	247.2	198.2	445.4	222.7	15.9
	13-1022	197	0.500								222.7	15.9
	13-1035	196	0.463	1119	850.8	1021.4	813.6	268.2	207.8	476	220.6	15.8
	13-1036	227	0.537								255.4	18.2
22	13-1003	197	0.491	1162.8	902.2	1022.4	819.6	260.6	202.8	463.4	227.7	16.3
	13-1004	204	0.509								235.7	16.8
	13-1017	211	0.507	1178	921.6	1025.6	817.8	256.4	207.8	464.2	235.4	16.8
	13-1018	205	0.493								228.8	16.3
	13-1031	190	0.521	1145.4	911.8	1005	818.2	233.6	186.8	420.4	218.8	15.6
	13-1032	175	0.479								201.6	14.4
44	13-1011	205	0.485	1157.4	901.4	1061.4	854.4	256	207	463	224.4	16.0
	13-1012	218	0.515								238.6	17.0
	13-1025	205	0.506	1183.6	930.6	1048.6	845.6	253	203	456	230.8	16.5
	13-1026	200	0.494								225.2	16.1
	13-1039	210	0.506	1131	877.4	1002.4	802.2	253.6	200.2	453.8	229.6	16.4
	13-1040	205	0.494								224.2	16.0
89	13-1001	207	0.509	1185.4	935.8	1034.4	834	249.6	200.4	450	228.9	16.3
	13-1002	200	0.491								221.1	15.8
	13-1015	204	0.500	1169	920.8	1004	796.4	248.2	207.6	455.8	227.9	16.3
	13-1016	204	0.500								227.9	16.3
	13-1029	191	0.552	1187.6	925.4	1063.8	866.4	262.2	197.4	459.6	253.7	18.1
	13-1030	155	0.448								205.9	14.7
177	13-1009	197	nd	1153.6	984.8	984.8	896.4	168.8	88.4	257.2	nd	nd
	13-1010	(f)	(f)								(f)	(f)
	13-1023	193	0.478	1205.6	962	1092	890.8	243.6	201.2	444.8	212.5	15.2
	13-1024	211	0.522								232.3	16.6
	13-1037	213	0.522	1151	881	1017.4	825.2	270	192.2	462.2	241.3	17.2
	13-1038	195	0.478								220.9	15.8
313	13-0999	209	0.500	1180	918	1060	833.6	262	226.4	488.4	244.2	17.4
	13-1000	209	0.500								244.2	17.4
	13-1013	188	0.444	1151.6	884.4	1036.4	813.6	267.2	222.8	490	217.8	15.6
	13-1014	235	0.556								272.2	19.4
	13-1027	199	0.529	1179.2	940.8	1076.8	884.2	238.4	192.6	431	228.1	16.3
	13-1028	177	0.471								202.9	14.5
623	13-1005	181	0.479	1175.8	943.4	1074.4	900	232.4	174.4	406.8	194.8	13.9
	13-1006	197	0.521								212.0	15.1
	13-1019	174	0.483	1174	964.6	1056.4	891.8	209.4	164.6	374	180.8	12.9
	13-1020	186	0.517								193.2	13.8
	13-1033	228	0.510	1185.4	893.4	1011.4	793.2	292	218.2	510.2	260.2	18.6
	13-1034	219	0.490								250.0	17.9

* = animals were paired housed; ** = based on the fractional wieght of each rat per pair; nd=no data; (f)= fated

APPENDIX J
SUMMARY OF 14-DAY ORGAN WEIGHTS AND INDIVIDUAL DATA
Protocol No. 30-13-07-01
Acute Oral Toxicity of 5-AT in Rats

Table J-1: Summary of male 14-day organ weights

5-AT mg/kg-day		Organ/tissue weights; Male absolute weights (g) *								
		adrenals	brain	heart	kidneys	epis.	liver	spleen	testes	thymus
0	Mean	0.043	1.903	1.181	2.218	0.504	10.806	0.699	2.539	0.534
	SD	0.014	0.035	0.094	0.168	0.126	0.950	0.122	0.230	0.109
	N	6	6	6	6	6	6	6	6	6
22	Mean	0.040	1.914	1.138	2.346	0.500	10.793	0.713	2.668	0.629
	SD	0.008	0.101	0.109	0.172	0.116	1.576	0.126	0.396	0.130
	N	6	6	6	6	6	6	6	6	6
44	Mean	0.040	1.938	1.112	2.281	0.523	10.456	0.663	2.614	0.613
	SD	0.009	0.110	0.098	0.222	0.091	1.283	0.034	0.309	0.086
	N	6	6	6	6	6	6	6	6	6
89	Mean	0.045	1.922	1.147	2.314	0.547	10.131	0.779	2.255	0.569
	SD	0.010	0.067	0.089	0.179	0.083	0.961	0.190	0.805	0.123
	N	6	6	6	6	6	6	6	6	6
177	Mean	0.055	1.927	1.196	2.321	0.514	10.224	0.701	2.721	0.579
	SD	0.016	0.065	0.055	0.187	0.082	0.755	0.109	0.297	0.157
	N	6	6	6	6	6	6	6	6	6
313	Mean	0.047	1.886	1.149	2.204	0.532	9.813	0.711	2.710	0.583
	SD	0.009	0.045	0.061	0.207	0.093	0.938	0.104	0.255	0.116
	N	6	6	6	6	6	6	6	6	6
623	Mean	0.039	1.907	1.113	2.142	0.516	9.952	0.567	2.648	0.566
	SD	0.015	0.050	0.069	0.197	0.084	1.096	0.110	0.208	0.165
	N	6	6	6	6	6	6	6	6	6

*** = no statistically significant differences found between treatment groups; epis. = epididymides**

APPENDIX J
SUMMARY OF 14-DAY ORGAN WEIGHTS AND INDIVIDUAL DATA
Protocol No. 30-13-07-01
Acute Oral Toxicity of 5-AT in Rats

Table J-2: Summary of female 14-day organ weights

5-AT mg/kg-day		Organ/tissue weights; Female absolute weights (g) *								
		adrenals	brain	heart	kidneys	liver	ovaries	spleen	thymus	uterus
0	Mean	0.052	1.812	0.941	1.785	8.153	0.118	0.548	0.596	0.513
	SD	0.007	0.099	0.067	0.089	0.675	0.007	0.103	0.055	0.231
	N	6	6	6	6	6	6	6	6	6
22	Mean	0.057	1.821	0.952	1.744	8.314	0.142	0.528	0.583	0.302
	SD	0.010	0.075	0.126	0.186	1.077	0.037	0.119	0.101	0.038
	N	6	6	6	6	6	6	6	6	6
44	Mean	0.057	1.830	1.003	1.806	8.610	0.125	0.543	0.619	0.431
	SD	0.007	0.075	0.127	0.149	0.850	0.027	0.104	0.074	0.216
	N	6	6	5	6	6	6	6	6	6
89	Mean	0.054	1.801	0.900	1.692	7.564	0.130	0.486	0.592	0.314
	SD	0.008	0.080	0.085	0.094	0.262	0.013	0.046	0.118	0.077
	N	6	6	6	6	6	6	6	6	6
177	Mean	0.055	1.815	0.859	1.585	7.855	0.116	0.517	0.615	0.469
	SD	0.012	0.095	0.075	0.101	0.732	0.005	0.080	0.128	0.058
	N	5	5	5	5	5	5	5	5	5
313	Mean	0.057	1.818	0.918	1.760	8.516	0.127	0.556	0.615	0.339
	SD	0.017	0.036	0.154	0.156	1.468	0.015	0.066	0.217	0.134
	N	6	6	6	6	6	6	6	6	6
623	Mean	0.054	1.823	0.857	1.716	8.091	0.134	0.529	0.547	0.362
	SD	0.019	0.063	0.075	0.156	1.094	0.017	0.153	0.124	0.051
	N	6	6	6	6	6	6	6	6	6

*** = no statistically significant differences found between treatment groups.**

APPENDIX J
SUMMARY OF 14-DAY ORGAN WEIGHTS AND INDIVIDUAL DATA
Protocol No. 30-13-07-01
Acute Oral Toxicity of 5-AT in Rats

Table J-3: Individual data of male 14-day organ weights

5-AT mg/kg - day	Animal I.D.	Terminal BW (g)	Absolute Organ/tissue weights; males (g)								
			adrenals	brain	heart	kidneys	epis.	liver	spleen	testes	thymus
0	13-0969	260	0.035	1.851	1.085	2.094	0.404	9.086	0.597	2.101	0.559
	13-0970	285	0.040	1.908	1.199	2.255	0.387	11.321	0.646	2.622	0.692
	13-0953	270	0.033	1.941	1.173	2.064	0.425	10.638	0.550	2.468	0.515
	13-0954	278	0.049	1.872	1.342	2.128	0.497	11.855	0.838	2.654	0.564
	13-0985	291	0.068	1.919	1.198	2.521	0.612	11.202	0.838	2.683	0.354
	13-0986	261	0.032	1.928	1.090	2.245	0.698	10.733	0.726	2.704	0.518
22	13-0949	262	0.036	1.821	1.094	2.382	0.518	9.530	0.706	3.050	0.625
	13-0950	284	0.051	1.999	1.199	2.133	0.285	12.286	0.833	1.925	0.617
	13-0981	260	0.036	1.918	0.955	2.183	0.504	9.549	0.625	2.677	0.487
	13-0982	300	0.047	2.064	1.194	2.539	0.556	12.413	0.882	2.899	0.571
	13-0965	258	0.029	1.862	1.116	2.306	0.503	9.035	0.545	2.836	0.874
	13-0966	282	0.039	1.817	1.268	2.534	0.631	11.947	0.684	2.618	0.599
44	13-0973	285	0.049	1.827	1.146	2.398	0.494	11.166	0.652	3.044	0.504
	13-0974	306	0.047	1.966	1.037	2.587	0.531	11.196	0.645	2.856	0.685
	13-0957	266	0.037	2.018	1.053	1.956	0.413	8.658	0.609	2.292	0.732
	13-0958	270	0.047	1.777	1.155	2.108	0.629	10.162	0.698	2.568	0.612
	13-0989	249	0.034	1.998	1.008	2.303	0.626	9.426	0.674	2.662	0.611
	13-0990	303	0.026	2.044	1.271	2.331	0.442	12.129	0.698	2.261	0.536
89	13-0947	275	0.050	2.036	1.167	2.147	0.556	9.691	0.867	2.731	0.772
	13-0948	266	0.034	1.865	1.024	2.054	0.530	9.143	0.626	2.405	0.479
	13-0979	290	0.050	1.936	1.279	2.438	0.645	10.555	0.697	2.674	0.645
	13-0980	259	0.042	1.844	1.077	2.501	0.471	9.548	1.127	2.312	0.488
	13-0963	272	0.059	1.916	1.148	2.309	0.635	10.013	0.712	2.754	0.451
	13-0964	287	0.032	1.934	1.189	2.433	0.442	11.838	0.646	0.655	0.578
177	13-0971	277	0.042	1.907	1.175	2.093	0.538	9.911	0.638	2.861	0.606
	13-0960	299	0.061	1.983	1.143	2.382	0.357	11.433	0.823	2.428	0.767
	13-0955	264	0.055	1.861	1.254	2.364	0.587	10.123	0.716	2.956	0.360
	13-0956	272	0.082	1.880	1.248	2.246	0.520	9.184	0.518	2.544	0.558
	13-0987	273	0.047	1.901	1.127	2.206	0.570	10.060	0.779	3.117	0.452
	13-0988	288	0.040	2.030	1.228	2.635	0.513	10.635	0.729	2.418	0.729
313	13-0945	267	0.057	1.937	1.169	1.818	0.360	10.520	0.797	2.290	0.633
	13-0946	262	0.039	1.814	1.247	2.211	0.592	9.174	0.796	2.770	0.773
	13-0977	290	0.056	1.893	1.172	2.392	0.512	11.123	0.807	2.665	0.531
	13-0978	269	0.045	1.877	1.100	2.218	0.559	9.733	0.616	2.643	0.433
	13-0961	261	0.049	1.867	1.075	2.207	0.623	9.843	0.683	3.061	0.529
	13-0962	258	0.035	1.927	1.128	2.379	0.548	8.482	0.569	2.831	0.601
623	13-0951	264	0.026	1.886	1.089	1.892	0.469	11.076	0.554	2.596	0.483
	13-0952	271	0.039	1.914	1.208	2.287	0.562	9.273	0.394	2.426	0.657
	13-0983	247	0.027	1.835	1.043	1.929	0.402	8.509	0.605	2.718	0.552
	13-0984	277	0.032	1.984	1.188	2.162	0.502	9.555	0.737	2.716	0.473
	13-0967	312	0.066	1.931	1.094	2.391	0.511	11.379	0.550	2.987	0.845
	13-0968	263	0.045	1.893	1.055	2.188	0.649	9.917	0.559	2.446	0.383

epis = epididymides

APPENDIX J
SUMMARY OF 14-DAY ORGAN WEIGHTS AND INDIVIDUAL DATA
Protocol No. 30-13-07-01
Acute Oral Toxicity of 5-AT in Rats

Table J-4: Individual data of female 14-day organ weights

5-AT mg/kg-day	Animal I.D.	Terminal BW (g)	Absolute Organ/tissue weights- females (g)								
			adrenals	brain	heart	kidneys	liver	ovaries	spleen	thymus	uterus
0	13-1021	197	0.057	1.73	1.05	1.922	8.23	0.109	0.543	0.655	0.934
	13-1022	197	0.055	1.87	0.91	1.856	7.87	0.123	0.501	0.573	0.481
	13-1007	198	0.048	1.77	0.890	1.686	8.44	0.109	0.418	0.527	0.271
	13-1008	209	0.042	1.8	1.000	1.735	8.74	0.125	0.672	0.544	0.504
	13-1035	196	0.061	1.73	0.88	1.727	6.94	0.118	0.484	0.644	0.542
	13-1036	227	0.048	1.98	0.92	1.784	8.69	0.124	0.667	0.635	0.344
22	13-1003	197	0.066	1.83	0.99	1.843	8.29	0.101	0.56	0.745	0.286
	13-1004	204	0.058	1.86	1.12	1.81	9.77	0.135	0.669	0.614	0.368
	13-1031	190	0.055	1.79	0.84	1.699	7.56	0.112	0.442	0.478	0.299
	13-1032	175	0.06	1.68	0.78	1.458	6.69	0.198	0.398	0.488	0.254
	13-1017	211	0.063	1.89	1.04	2.001	8.88	0.174	0.662	0.631	0.288
	13-1018	205	0.038	1.87	0.94	1.653	8.7	0.132	0.438	0.539	0.314
44	13-1025	205	0.069	1.72	n.d.	1.964	8.49	0.135	0.538	0.736	0.703
	13-1026	200	0.054	1.85	0.92	1.706	8.09	0.107	0.704	0.62	0.286
	13-1011	205	0.049	1.87	0.93	1.779	7.89	0.107	0.418	0.663	0.282
	13-1012	218	0.059	1.93	1.2	2.017	10.3	0.173	0.575	0.533	0.711
	13-1039	210	0.052	1.85	1.06	1.7	8.38	0.123	0.58	0.612	0.345
	13-1040	205	0.059	1.76	0.91	1.667	8.54	0.103	0.445	0.551	0.258
89	13-1001	207	0.043	1.76	1.01	1.854	7.91	0.122	0.538	0.584	0.285
	13-1002	200	0.057	1.86	1	1.591	7.41	0.146	0.549	0.695	0.454
	13-1029	191	0.052	1.77	0.85	1.647	7.35	0.144	0.446	0.524	0.266
	13-1030	155	0.059	1.71	0.81	1.695	7.89	0.127	0.468	0.771	0.352
	13-1015	204	0.065	1.93	0.86	1.632	7.44	0.115	0.447	0.469	0.27
	13-1016	204	0.045	1.78	0.87	1.733	7.38	0.124	0.467	0.507	0.257
177	13-1023	193	0.055	1.71	0.77	1.61	8.59	0.119	0.518	0.712	0.479
	13-1024	211	0.064	1.86	0.94	1.628	7.71	0.119	0.568	0.759	0.445
	13-1009	197	0.069	1.89	0.79	1.419	6.84	0.107	0.388	0.449	0.386
	13-1010 (f)	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	13-1037	213	0.04	1.9	0.92	1.578	7.6	0.116	0.596	0.529	0.543
	13-1038	195	0.049	1.72	0.88	1.69	8.54	0.119	0.513	0.626	0.493
313	13-0999	209	0.024	1.76	1.15	1.82	10.3	0.107	0.607	0.48	0.603
	13-1000	209	0.058	1.82	0.89	1.8	9.27	0.12	0.637	0.528	0.282
	13-1027	199	0.063	1.82	0.9	1.586	7.85	0.15	0.557	0.658	0.291
	13-1028	177	0.057	1.82	0.67	1.648	6.38	0.12	0.446	0.468	0.286
	13-1013	188	0.064	1.81	0.92	1.686	7.65	0.124	0.556	0.518	0.232
	13-1014	235	0.073	1.88	0.98	2.02	9.65	0.139	0.532	1.035	0.342
623	13-1005	181	0.075	1.86	0.85	1.694	7.2	0.125	0.484	0.559	0.42
	13-1006	197	0.035	1.77	0.88	1.555	8.39	0.122	0.412	0.508	0.284
	13-1033	228	0.056	1.72	0.87	1.766	9.5	0.137	0.705	0.638	0.326
	13-1034	219	0.062	1.89	0.98	1.985	9.2	0.167	0.733	0.701	0.394
	13-1019	174	0.069	1.84	0.75	1.723	6.96	0.129	0.47	0.538	0.394
	13-1020	186	0.029	1.85	0.81	1.575	7.3	0.124	0.369	0.34	0.354

(f)= fated; ND= no data

APPENDIX K
SUMMARY OF 14-DAY ORGAN-TO-BRAIN WEIGHT RATIOS AND INDIVIDUAL DATA
Protocol No. 30-13-07-01
Acute Oral Toxicity of 5-AT in Rats

Table K-1: Summary male 14-day organ to brain weight ratios

5-AT mg/kg-day		Summary Organ/tissue weights -Males; normalized to brain weight*							
		adrenals	heart	kidneys	epis.	liver	spleen	testes	thymus
0	Mean	0.023	0.621	1.165	0.264	5.677	0.368	1.333	0.281
	SD	0.007	0.053	0.083	0.064	0.482	0.065	0.110	0.059
	N	6	6	6	6	6	6	6	6
22	Mean	0.021	0.596	1.229	0.263	5.633	0.371	1.400	0.330
	SD	0.003	0.064	0.117	0.067	0.706	0.052	0.238	0.076
	N	6	6	6	6	6	6	6	6
44	Mean	0.021	0.575	1.180	0.271	5.411	0.343	1.356	0.317
	SD	0.006	0.064	0.129	0.057	0.732	0.030	0.212	0.042
	N	6	6	6	6	6	6	6	6
89	Mean	0.023	0.597	1.206	0.284	5.273	0.406	1.174	0.295
	SD	0.005	0.038	0.111	0.042	0.482	0.106	0.414	0.054
	N	6	6	6	6	6	6	6	6
177	Mean	0.028	0.621	1.204	0.268	5.303	0.363	1.416	0.299
	SD	0.009	0.039	0.073	0.048	0.291	0.053	0.189	0.073
	N	6	6	6	6	6	6	6	6
313	Mean	0.025	0.610	1.170	0.283	5.204	0.378	1.439	0.310
	SD	0.005	0.041	0.118	0.053	0.484	0.058	0.153	0.066
	N	6	6	6	6	6	6	6	6
623	Mean	0.020	0.583	1.122	0.270	5.217	0.297	1.389	0.296
	SD	0.008	0.027	0.090	0.043	0.552	0.055	0.108	0.085
	N	6	6	6	6	6	6	6	6

*** no statistically significant findings; epis.= epididymides**

APPENDIX K
SUMMARY OF 14-DAY ORGAN-TO-BRAIN WEIGHT RATIOS AND INDIVIDUAL DATA
Protocol No. 30-13-07-01
Acute Oral Toxicity of 5-AT in Rats

Table K-2: Summary female 14-day organ to brain weight ratios

5-AT mg/kg-day	Summary data Organ/tissue weights; Females normalized to brain weight *								
		adrenals	heart	kidneys	liver	ovaries	spleen	thymus	uterus
0	Mean	0.029	0.521	0.988	4.503	0.065	0.302	0.330	0.287
	SD	0.005	0.051	0.071	0.349	0.003	0.050	0.037	0.139
	N	6	6	6	6	6	6	6	6
22	Mean	0.031	0.521	0.956	4.554	0.078	0.289	0.319	0.165
	SD	0.006	0.053	0.073	0.439	0.023	0.058	0.050	0.017
	N	6	6	6	6	6	6	6	6
44	Mean	0.031	0.541	0.988	4.706	0.068	0.297	0.340	0.236
	SD	0.005	0.056	0.088	0.411	0.013	0.054	0.050	0.120
	N	6	5	6	6	6	6	6	6
89	Mean	0.030	0.500	0.942	4.209	0.072	0.270	0.330	0.174
	SD	0.004	0.047	0.081	0.294	0.008	0.027	0.074	0.042
	N	6	6	6	6	6	6	6	6
177	Mean	0.031	0.474	0.876	4.352	0.064	0.285	0.341	0.259
	SD	0.006	0.039	0.092	0.623	0.006	0.045	0.080	0.037
	N	5	5	5	5	5	5	5	5
313	Mean	0.031	0.505	0.968	4.687	0.070	0.306	0.337	0.187
	SD	0.009	0.090	0.079	0.830	0.008	0.039	0.112	0.078
	N	6	6	6	6	6	6	6	6
623	Mean	0.030	0.470	0.942	4.452	0.074	0.291	0.301	0.198
	SD	0.010	0.043	0.081	0.699	0.009	0.087	0.069	0.023
	N	6	6	6	6	6	6	6	6

* = no statistically significant differences between treatment groups were found.

APPENDIX K
SUMMARY OF 14-DAY ORGAN-TO-BRAIN WEIGHT RATIOS AND INDIVIDUAL DATA
Protocol No. 30-13-07-01
Acute Oral Toxicity of 5-AT in Rats

Table K-3: Individual male 14-day organ to brain weight ratios

5-AT mg/kg-day	Animal I.D.	Individual Organ/tissue weights; Males normalized to brain weight (g/g brain weight)							
		adrenals	heart	kidneys	epis.	liver	spleen	testes	thymus
0	13-0969	0.019	0.586	1.131	0.218	4.909	0.323	1.135	0.302
	13-0970	0.021	0.628	1.182	0.203	5.933	0.339	1.374	0.363
	13-0953	0.017	0.604	1.063	0.219	5.481	0.283	1.272	0.265
	13-0954	0.026	0.717	1.137	0.265	6.333	0.448	1.418	0.301
	13-0985	0.035	0.624	1.314	0.319	5.837	0.437	1.398	0.184
	13-0986	0.017	0.565	1.164	0.362	5.567	0.377	1.402	0.269
22	13-0949	0.020	0.601	1.308	0.284	5.233	0.388	1.675	0.343
	13-0950	0.026	0.600	1.067	0.143	6.146	0.417	0.963	0.309
	13-0981	0.019	0.498	1.138	0.263	4.979	0.326	1.396	0.254
	13-0982	0.023	0.578	1.230	0.269	6.014	0.427	1.405	0.277
	13-0965	0.016	0.599	1.238	0.270	4.852	0.293	1.523	0.469
	13-0966	0.021	0.698	1.395	0.347	6.575	0.376	1.441	0.330
44	13-0973	0.027	0.627	1.313	0.270	6.112	0.357	1.666	0.276
	13-0974	0.024	0.527	1.316	0.270	5.695	0.328	1.453	0.348
	13-0957	0.018	0.522	0.969	0.205	4.290	0.302	1.136	0.363
	13-0958	0.026	0.650	1.186	0.354	5.719	0.393	1.445	0.344
	13-0989	0.017	0.505	1.153	0.313	4.718	0.337	1.332	0.306
	13-0990	0.013	0.622	1.140	0.216	5.934	0.341	1.106	0.262
89	13-0947	0.025	0.573	1.055	0.273	4.760	0.426	1.341	0.379
	13-0948	0.018	0.549	1.101	0.284	4.902	0.336	1.290	0.257
	13-0979	0.026	0.661	1.259	0.333	5.452	0.360	1.381	0.333
	13-0980	0.023	0.584	1.356	0.255	5.178	0.611	1.254	0.265
	13-0963	0.031	0.599	1.205	0.331	5.226	0.372	1.437	0.235
	13-0964	0.017	0.615	1.258	0.229	6.121	0.334	0.339	0.299
177	13-0971	0.022	0.616	1.098	0.282	5.197	0.335	1.500	0.318
	13-0960	0.031	0.576	1.201	0.180	5.766	0.415	1.224	0.387
	13-0955	0.030	0.674	1.270	0.315	5.440	0.385	1.588	0.193
	13-0956	0.044	0.664	1.195	0.277	4.885	0.276	1.353	0.297
	13-0987	0.025	0.593	1.160	0.300	5.292	0.410	1.640	0.238
	13-0988	0.020	0.605	1.298	0.253	5.239	0.359	1.191	0.359
313	13-0945	0.029	0.604	0.939	0.186	5.431	0.411	1.182	0.327
	13-0946	0.021	0.687	1.219	0.326	5.057	0.439	1.527	0.426
	13-0977	0.030	0.619	1.264	0.270	5.876	0.426	1.408	0.281
	13-0978	0.024	0.586	1.182	0.298	5.185	0.328	1.408	0.231
	13-0961	0.026	0.576	1.182	0.334	5.272	0.366	1.640	0.283
	13-0962	0.018	0.585	1.235	0.284	4.402	0.295	1.469	0.312
623	13-0951	0.014	0.577	1.003	0.249	5.873	0.294	1.376	0.256
	13-0952	0.020	0.631	1.195	0.294	4.845	0.206	1.268	0.343
	13-0983	0.015	0.568	1.051	0.219	4.637	0.330	1.481	0.301
	13-0984	0.016	0.599	1.090	0.253	4.816	0.371	1.369	0.238
	13-0967	0.034	0.567	1.238	0.265	5.893	0.285	1.547	0.438
	13-0968	0.024	0.557	1.156	0.343	5.239	0.295	1.292	0.202

epis. = epididymides

APPENDIX K
SUMMARY OF 14-DAY ORGAN-TO-BRAIN WEIGHT RATIOS AND INDIVIDUAL DATA
Protocol No. 30-13-07-01
Acute Oral Toxicity of 5-AT in Rats

Table K-4: Individual female 14-day organ to brain weight ratios

5-AT mg/kg-day	Animal I.D.	Individual Organ/tissue weights; Females normalized to brain weight (g/g brain weight)							
		adrenals	heart	kidneys	liver	ovaries	spleen	thymus	uterus
0	13-1021	0.033	0.606	1.114	4.772	0.063	0.315	0.380	0.541
	13-1022	0.029	0.488	0.992	4.208	0.066	0.268	0.306	0.257
	13-1007	0.027	0.504	0.955	4.781	0.062	0.237	0.298	0.153
	13-1008	0.023	0.555	0.963	4.852	0.069	0.373	0.302	0.280
	13-1035	0.035	0.508	1.000	4.017	0.068	0.280	0.373	0.314
	13-1036	0.024	0.465	0.901	4.390	0.063	0.337	0.321	0.174
22	13-1003	0.036	0.542	1.006	4.524	0.055	0.306	0.407	0.156
	13-1004	0.031	0.599	0.972	5.245	0.072	0.359	0.330	0.198
	13-1031	0.031	0.466	0.947	4.212	0.062	0.246	0.266	0.167
	13-1032	0.036	0.465	0.867	3.978	0.118	0.237	0.290	0.151
	13-1017	0.033	0.554	1.062	4.708	0.092	0.351	0.335	0.153
	13-1018	0.020	0.503	0.885	4.658	0.071	0.234	0.289	0.168
44	13-1025	0.040	ND	1.141	4.932	0.078	0.312	0.427	0.408
	13-1026	0.029	0.496	0.922	4.372	0.058	0.381	0.335	0.155
	13-1011	0.026	0.498	0.952	4.219	0.057	0.224	0.355	0.151
	13-1012	0.031	0.623	1.047	5.331	0.090	0.299	0.277	0.369
	13-1039	0.028	0.575	0.918	4.528	0.066	0.313	0.331	0.186
	13-1040	0.034	0.514	0.948	4.856	0.059	0.253	0.313	0.147
89	13-1001	0.024	0.572	1.051	4.483	0.069	0.305	0.331	0.162
	13-1002	0.031	0.538	0.855	3.981	0.078	0.295	0.373	0.244
	13-1029	0.029	0.479	0.929	4.147	0.081	0.252	0.296	0.150
	13-1030	0.035	0.472	0.994	4.626	0.074	0.274	0.452	0.206
	13-1015	0.034	0.446	0.846	3.857	0.060	0.232	0.243	0.140
	13-1016	0.025	0.492	0.976	4.160	0.070	0.263	0.286	0.145
177	13-1023	0.032	0.452	0.943	5.032	0.070	0.303	0.417	0.281
	13-1024	0.034	0.504	0.874	4.140	0.064	0.305	0.408	0.239
	13-1009	0.037	0.418	0.751	3.618	0.057	0.205	0.238	0.204
	13-1010	(f)	(f)	(f)	(f)	(f)	(f)	(f)	(f)
	13-1037	0.021	0.483	0.831	4.000	0.061	0.314	0.278	0.286
	13-1038	0.029	0.511	0.983	4.970	0.069	0.298	0.364	0.287
313	13-0999	0.014	0.650	1.033	5.846	0.061	0.344	0.272	0.342
	13-1000	0.032	0.487	0.987	5.080	0.066	0.349	0.289	0.155
	13-1027	0.035	0.497	0.871	4.314	0.082	0.306	0.362	0.160
	13-1028	0.031	0.367	0.906	3.508	0.066	0.245	0.257	0.157
	13-1013	0.035	0.508	0.932	4.228	0.069	0.307	0.286	0.128
	13-1014	0.039	0.524	1.077	5.146	0.074	0.284	0.552	0.182
623	13-1005	0.040	0.456	0.910	3.866	0.067	0.260	0.300	0.226
	13-1006	0.020	0.499	0.878	4.740	0.069	0.233	0.287	0.160
	13-1033	0.033	0.506	1.026	5.514	0.080	0.409	0.370	0.189
	13-1034	0.033	0.517	1.051	4.871	0.088	0.388	0.371	0.209
	13-1019	0.037	0.410	0.936	3.780	0.070	0.255	0.292	0.214
	13-1020	0.016	0.435	0.850	3.942	0.067	0.199	0.184	0.191

(f)= fated; ND= no data

APPENDIX L
SUMMARY OF 14-DAY CLINICAL CHEMISTRY AND INDIVIDUAL DATA
Protocol No. 30-13-07-01
Acute Oral Toxicity of 5-AT in Rats

Table L-1: Summary data of male 14-day clinical chemistry parameters

5-AT mg/kg-day *		ALB	ALKP	ALT	AST	BUN	CA	CHOL	CREA	GLOB	GLU	PHOS	TP	TRIG	Na	K	Cl
0	**Mean**	3.0	557.2	81.7	110.0	10.5	11.2	100.0	0.7	3.1	167.8	15.0	6.1	85.7	152.3	8.9	104.3
	SD	0.15	134.55	14.25	19.85	3.73	0.58	13.02	0.13	0.15	58.70	1.37	0.24	27.27	0.82	1.41	1.37
	N	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
22	**Mean**	2.9	541.2	83.2	110.5	12.8	11.2	98.0	0.6	3.0	134.8	14.2	5.9	135.8	152.0	9.4	104.5
	SD	0.16	96.86	9.20	11.64	3.97	0.29	17.74	0.12	0.10	50.22	1.14	0.20	115.99	1.10	1.12	0.55
	N	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
44	**Mean**	2.9	523.5	72.2	108.5	11.8	11.4	98.7	0.7	3.1	160.2	13.4	6.0	90.3	151.0	9.6	103.8
	SD	0.13	97.22	11.09	17.49	4.17	0.38	16.55	0.08	0.23	58.74	1.27	0.34	23.42	0.63	1.90	1.72
	N	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
89	**Mean**	2.9	504.5	82.5	104.5	16.3	11.6	109.0	0.6	3.0	175.2	13.8	5.9	95.8	151.0	10.3	105.0
	SD	0.18	95.83	12.96	9.40	3.14	0.30	10.33	0.18	0.12	47.63	1.13	0.13	28.82	1.41	1.61	1.10
	N	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
177	**Mean**	3.0	595.3	83.5	112.2	11.5	11.2	103.2	0.6	3.0	163.3	13.2	6.0	89.7	151.2	8.1	104.2
	SD	0.08	139.89	14.65	16.96	2.88	0.38	17.58	0.10	0.11	51.34	1.27	0.14	92.76	1.94	1.23	1.33
	N	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
313	**Mean**	3.0	509.0	73.2	110.7	12.7	11.1	110.8	0.6	3.0	139.2	13.9	6.0	71.8	151.7	8.6	104.8
	SD	0.09	79.72	6.94	12.88	2.25	0.14	13.32	0.16	0.08	42.58	0.92	0.08	13.76	2.07	1.03	1.83
	N	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
623	**Mean**	3.0	537.2	81.0	110.5	11.8	11.3	95.8	0.6	3.1	166.2	13.9	6.0	62.3	150.2	9.3	104.7
	SD	0.19	80.21	9.59	15.71	3.37	0.36	11.84	0.14	0.12	49.66	0.90	0.17	18.61	1.17	0.91	0.82
	N	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6

* no statistically significant differences noted between treatments

APPENDIX L
SUMMARY OF 14-DAY CLINICAL CHEMISTRY AND INDIVIDUAL DATA
Protocol No. 30-13-07-01
Acute Oral Toxicity of 5-AT in Rats

Table L-2: Summary data of female 14-day clinical chemistry parameters

5-AT mg/kg-day		ALB	ALKP*	ALT	AST	BUN*	CA	CHOL	CREA	GLOB	GLU	PHOS	TP	TRIG	Na	K	Cl
0	**Mean**	3.1	283.8	74.7	104.5	15.7	11.0	58.5	0.6	3.0	100.8	13.2	6.1	40.7	150.8	9.7	106.0
	SD	0.15	55.36	19.11	20.04	4.27	0.09	11.17	0.08	0.19	11.39	1.03	0.22	8.21	1.94	1.42	1.26
	N	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
22	**Mean**	3.4	265.5	55.4	111.5	16.0	11.0	69.0	0.7	3.0	73.6	16.4	6.4	39.4	151.2	9.9	107.0
	SD	0.29	52.14	9.79	40.90	2.55	0.95	15.73	0.08	0.10	4.28	1.74	0.28	7.06	0.84	2.17	0.71
	N	5	4	5	4	5	4	5	4	5	5	4	5	5	5	4	5
44	**Mean**	3.1	**330.8**	60.8	102.2	14.0	10.8	72.3	0.7	3.0	87.8	13.6	6.1	46.0	150.3	9.2	106.2
	SD	0.15	**105.31**	14.54	14.03	4.38	0.48	11.76	0.14	0.14	23.19	1.63	0.20	12.41	1.75	0.91	1.47
	N	6	**6**	6	6	6	6	6	6	6	6	6	6	6	6	6	6
89	**Mean**	3.3	246.3	55.2	113.8	17.2	11.0	70.3	0.6	3.1	84.0	13.5	6.4	38.5	151.7	9.4	106.3
	SD	0.10	34.23	8.82	40.24	2.04	0.54	19.21	0.14	0.15	12.23	1.71	0.19	4.76	0.52	1.02	0.52
	N	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
177	**Mean**	3.1	240.4	59.0	94.2	13.8	11.1	63.6	0.7	3.0	91.2	13.4	6.1	50.0	150.6	8.9	105.4
	SD	0.17	32.75	9.06	14.27	2.17	0.34	11.24	0.13	0.10	24.77	1.70	0.17	17.56	0.89	1.79	1.52
	N	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
313	**Mean**	3.2	225.3	58.5	114.5	**22.3**	11.0	62.0	0.7	3.1	85.8	13.2	6.3	39.3	149.5	9.4	104.8
	SD	0.08	20.32	3.11	46.58	**1.26**	0.15	15.43	0.06	0.21	15.02	1.22	0.26	2.22	1.29	1.26	1.26
	N	4	4	4	4	**4**	4	4	4	4	4	4	4	4	4	4	4
623	**Mean**	3.5	216.2	69.8	312.2	20.2	11.4	65.2	0.7	3.2	87.7	14.8	6.6	45.8	149.2	10.1	104.7
	SD	0.33	51.33	11.92	278.16	7.00	0.52	23.16	0.27	0.19	24.91	2.65	0.51	14.85	1.94	2.19	1.86
	N	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6

***= "bolded" group statistically different**

APPENDIX L
SUMMARY OF 14-DAY CLINICAL CHEMISTRY AND INDIVIDUAL DATA
Protocol No. 30-13-07-01
Acute Oral Toxicity of 5-AT in Rats

Table L-3: Individual data of male 14-day clinical chemistry parameters

5-AT mg/kg-day	Animal I.D.	ALB	ALKP	ALT	AST	BUN	CA	CHOL	CREA	GLOB	GLU	PHOS	TP	TRIG	Na	K	Cl
0	13- 953	3.1	775	85	104	9	11.1	123	0.5	3.4	216	15.8	6.5	125	152	7.4	104
	13- 954	2.9	497	77	144	16	10.6	103	0.8	3.1	93	14.5	6.1	100	153	8.0	105
	13- 969	2.9	600	98	117	12	11.5	103	0.6	3.0	201	14.3	5.9	67	153	9.6	106
	13- 970	2.9	606	92	108	5	11.8	89	0.7	3.0	239	16.8	5.9	56	153	10.9	104
	13- 985	3.2	387	57	84	12	11.7	94	0.8	3.1	137	15.6	6.2	64	151	9.9	105
	13- 986	2.8	478	81	103	9	10.4	88	0.8	3.1	121	12.9	5.9	102	152	7.7	102
22	13- 949	2.7	464	78	116	7	11.4	100	0.7	3.2	155	14.3	5.8	66	152	10.7	105
	13- 950	2.9	526	78	115	11	11.4	76	0.6	3.0	110	14.9	5.9	81	152	9.6	104
	13- 965	3.0	549	83	102	14	10.8	104	0.5	3.0	129	12.5	6.0	65	151	8.7	104
	13- 966	2.7	540	101	98	12	11.3	79	0.6	2.9	220	13.5	5.6	52	151	7.8	104
	13- 981	2.9	720	83	129	14	10.9	106	0.5	3.0	70	14.0	6.0	211	152	9.1	105
	13- 982	3.1	448	76	103	19	11.5	123	0.8	3.1	125	15.8	6.2	340	154	10.6	105
44	13- 957	2.7	636	90	122	14	10.8	84	0.6	2.9	73	12.0	5.6	110	151	8.1	105
	13- 958	3.0	426	63	123	10	11.6	109	0.7	3.4	139	15.3	6.4	117	151	11.7	106
	13- 973	2.9	479	70	106	7	11.5	92	0.7	3.0	155	13.5	5.9	102	151	9.2	104
	13- 974	3.0	543	73	124	10	11.2	127	0.6	3.3	144	14.4	6.3	78	151	12.2	104
	13- 989	2.8	422	59	93	11	11.5	85	0.6	2.8	209	12.9	5.6	55	152	7.7	103
	13- 990	3.0	635	78	83	19	11.9	95	0.8	3.1	241	12.3	6.1	80	150	8.7	101
89	13- 947	3.1	610	93	106	18	11.9	121	0.8	2.9	197	14.9	6.0	123	150	9.2	103
	13- 948	3.0	569	87	104	13	11.6	113	0.4	2.9	214	13.0	5.8	73	151	8.3	105
	13- 963	2.9	444	92	99	20	11.0	98	0.6	3.1	197	14.4	6.0	70	153	10.8	105
	13- 964	3.0	385	65	95	18	11.5	106	0.8	3.0	82	14.7	6.0	77	151	12.7	106
	13- 979	2.8	589	67	101	12	11.6	119	0.4	3.2	189	13.5	6.0	139	152	9.4	105
	13- 980	2.6	430	91	122	17	11.7	97	0.6	3.1	172	12.0	5.7	93	149	11.3	106
177	13- 955	3.1	444	75	131	9	10.8	91	0.5	3.1	118	13.0	6.2	33	153	7.7	105
	13- 956	3.1	678	105	95	16	11.4	137	0.4	2.8	207	11.5	5.9	66	148	7.1	102
	13- 960	2.9	538	64	102	8	11.7	104	0.6	3.0	235	14.6	5.9	39	153	9.9	105
	13- 971	3.1	798	89	125	11	11.5	91	0.7	3.1	155	14.5	6.2	277	152	9.3	105
	13- 987	3.0	659	76	94	12	10.8	103	0.6	3.0	165	12.1	6.0	61	150	6.8	103
	13- 988	3.0	455	92	126	13	11.1	93	0.6	3.0	100	13.7	6.0	62	151	7.8	105
313	13- 945	3.0	523	70	114	13	10.9	106	0.6	3.0	134	13.4	6.0	97	151	7.5	104
	13- 946	2.9	434	82	135	16	10.9	116	0.6	3.0	92	13.0	5.9	68	154	7.7	108
	13- 961	3.0	455	82	104	12	11.0	97	0.6	3.0	129	14.6	6.1	67	152	8.0	104
	13- 962	3.1	627	67	105	9	11.2	107	0.3	2.9	188	14.0	6.0	75	152	9.6	103
	13- 977	3.1	440	68	99	13	11.2	104	0.5	2.9	192	12.9	6.0	56	148	8.7	104
	13- 978	2.9	575	70	107	13	11.1	135	0.8	3.1	100	15.2	5.9	68	153	10.0	106
623	13- 951	2.8	639	90	105	16	11.4	97	0.7	3.1	115	15.2	5.9	65	150	9.1	105
	13- 952	2.9	582	93	138	14	11.2	104	0.6	3.2	131	13.6	6.1	72	149	10.1	103
	13- 967	3.3	525	68	103	12	11.5	100	0.4	2.9	213	14.7	6.2	73	152	10.0	105
	13- 968	2.9	575	80	108	12	10.7	86	0.7	3.0	154	12.7	5.9	84	151	8.6	105
	13- 983	2.8	492	73	117	6	11.0	110	0.8	3.0	143	13.9	5.8	35	149	7.9	105
	13- 984	3.0	410	82	92	11	11.7	78	0.6	3.2	241	13.5	6.2	45	150	10.0	105

APPENDIX L
SUMMARY OF 14-DAY CLINICAL CHEMISTRY AND INDIVIDUAL DATA
Protocol No. 30-13-07-01
Acute Oral Toxicity of 5-AT in Rats

Table L-4: Individual data of female 14-day clinical chemistry parameters

5-AT mg/kg-day	Animal I.D.	ALB	ALKP	ALT	AST	BUN	CA	CHOL	CREA	GLOB	GLU	PHOS	TP	TRIG	Na	K	Cl
0	13- 1007	3.2	231	63	75	16	11.1	64	0.5	3.2	122	14.9	6.4	33	151	10.0	105
	13- 1008	2.8	368	95	107	13	10.9	65	0.6	3.0	100	13.0	5.8	41	152	8.7	105
	13- 1021	3.0	216	55	102	21	11.0	56	0.7	3.1	104	13.3	6.0	31	152	8.7	107
	13- 1022	3.2	301	59	129	9	11.1	40	0.6	2.7	92	13.4	5.9	39	152	12.2	108
	13- 1035	3.1	307	100	123	19	10.9	54	0.6	3.0	92	11.8	6.1	52	151	8.5	106
	13- 1036	3.0	280	76	91	16	11.0	72	0.7	3.2	95	12.6	6.2	48	147	10.2	105
22	13- 1003	3.7	ND	64	ND	12	ND	72	ND	2.9	76	ND	6.6	34	152	7.8	107
	13- 1004	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	13- 1017	3.0	284	52	108	19	9.8	55	0.6	3.1	78	14.5	6.1	36	150	8.8	108
	13- 1018	3.2	320	53	90	16	10.8	51	0.7	2.9	69	15.4	6.1	33	151	10.1	107
	13- 1031	3.6	262	42	78	16	12.0	88	0.7	3.1	76	18.4	6.7	46	151	ND	107
	13- 1032	3.4	196	66	170	17	11.5	79	0.8	3.0	69	17.1	6.5	48	152	12.8	106
44	13- 1011	3.0	294	58	86	15	10.1	86	0.6	3.0	106	11.3	6.1	66	150	8.0	106
	13- 1012	3.3	196	39	87	10	10.7	65	0.6	3.0	125	13.3	6.3	37	153	8.6	105
	13- 1025	3.1	325	68	108	9	10.5	71	0.5	2.7	77	12.1	5.8	54	148	10.7	105
	13- 1026	3.2	440	76	110	21	11.3	87	0.7	2.9	73	15.3	6.1	48	149	9.3	105
	13- 1039	2.9	261	74	122	16	11.0	58	0.7	3.0	63	15.0	5.9	35	151	9.0	108
	13- 1040	3.2	469	50	100	13	11.3	67	0.9	3.1	83	14.5	6.3	36	151	9.4	108
89	13- 1001	3.4	273	50	83	18	11.2	59	0.7	3.1	96	12.3	6.5	40	152	9.3	106
	13- 1002	3.2	266	48	156	14	10.0	65	0.4	3.0	92	10.9	6.2	38	152	7.5	107
	13- 1015	3.2	214	58	174	16	11.3	72	0.6	3.2	71	15.5	6.4	36	151	10.1	107
	13- 1016	3.3	217	48	85	18	11.5	50	0.7	3.3	97	13.9	6.6	33	152	9.6	106
	13- 1029	3.4	291	56	91	20	11.2	106	0.8	3.0	75	15.0	6.4	47	152	9.5	106
	13- 1030	3.2	217	71	94	17	10.8	70	0.6	2.9	73	13.3	6.1	37	151	10.4	106
177	13- 1009	3.2	271	60	87	17	10.7	70	0.5	2.9	118	11.1	6.1	42	150	6.8	106
	13- 1023	3.1	247	58	97	12	11.0	78	0.6	2.9	83	13.7	6.0	40	150	9.0	103
	13- 1024	3.2	233	45	85	12	10.9	64	0.6	3.1	116	12.8	6.2	51	151	7.4	105
	13- 1037	3.0	263	70	118	13	11.6	49	0.8	3.1	62	15.8	6.2	80	152	10.5	106
	13- 1038	2.8	188	62	84	15	11.1	57	0.8	3.0	77	13.5	5.8	37	150	10.8	107
	13- 1010	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
313	13- 999	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	13- 1000	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	13- 1013	3.2	216	57	82	22	11.2	85	0.7	3.1	95	14.9	6.3	40	150	10.0	105
	13- 1014	3.2	202	58	75	24	10.9	56	0.6	3.3	102	12.0	6.5	36	149	7.5	105
	13- 1027	3.1	235	63	125	21	11.1	52	0.7	2.8	72	13.2	5.9	40	148	9.8	103
	13- 1028	3.3	248	56	176	22	10.9	55	0.6	3.1	74	12.8	6.4	41	151	10.2	106
623	13- 1005	3.2	169	66	410	13	10.7	47	0.3	3.0	102	11.3	6.2	39	149	7.0	105
	13- 1006	3.7	180	69	371	21	11.7	41	0.7	3.2	79	18.5	6.9	38	152	9.6	105
	13- 1019	3.2	245	62	101	29	11.2	52	0.9	3.1	58	15.8	6.3	39	148	11.8	106
	13- 1020	3.2	298	60	87	15	10.8	76	0.6	3.0	124	12.8	6.2	41	151	8.2	105
	13- 1033	3.5	232	69	106	15	11.8	72	1.1	3.1	98	13.7	6.6	42	148	11.3	101
	13- 1034	4.0	173	93	798	28	11.9	103	0.8	3.5	65	16.5	7.5	76	147	12.6	106

ND= no data

APPENDIX M
SUMMARY OF 14-DAY HEMATOLOGY AND INDIVIDUAL DATA
Protocol No. 30-13-07-01
Acute Oral Toxicity of 5-AT in Rats

Table M-1: Summary data for male hematology parameters

		Hematology Parameters; males summary data *																					
		WBC	NEU		LYM		MONO		EOS		BASO		RBC	HGB	HCT	MCV	MCH	MCHC	RDW	PLT	MPV
5-AT mg/kg-day		(K/uL)	(K/uL)	(%N)	(K/uL)	(%L)	(K/uL)	(%M)	(K/uL)	(%E)	(K/uL)	(%B)	(MuL)	(g/dL)	(%)	(fL)	(pg)	(g/dL)	(%)	(K/uL)	(fL)
0	Mean	13.82	1.55	12.14	11.42	81.50	0.30	2.33	0.08	0.57	0.48	3.46	7.65	15.45	43.45	56.85	20.23	35.60	16.75	1170.67	5.41
	SD	4.75	0.59	6.55	4.45	8.40	0.17	1.55	0.04	0.25	0.33	1.71	0.43	0.79	2.08	1.81	0.67	0.64	0.98	299.57	0.41
	N	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
22	Mean	10.58	0.98	9.60	8.65	80.62	0.46	4.72	0.07	0.63	0.41	4.44	7.22	15.22	44.58	58.96	21.10	35.76	16.50	1124.40	5.08
	SD	2.85	0.15	2.04	2.99	6.32	0.12	1.81	0.02	0.23	0.21	2.89	0.35	0.40	4.14	1.65	0.59	0.42	1.21	473.11	0.26
	N	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
44	Mean	12.65	1.20	10.54	9.98	77.35	0.75	6.21	0.05	0.37	0.67	5.55	7.49	15.53	43.50	58.05	20.72	35.70	16.78	859.83	5.24
	SD	3.34	0.49	6.46	3.58	9.25	0.21	2.14	0.04	0.17	0.13	1.78	0.49	1.13	3.37	1.73	0.58	0.56	0.58	387.30	0.37
	N	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
89	Mean	12.07	1.15	9.72	10.09	82.35	0.38	3.71	0.06	0.54	0.41	3.68	7.70	15.70	43.68	56.72	20.37	35.93	16.52	1289.50	5.34
	SD	2.77	0.17	1.67	3.12	7.29	0.34	3.57	0.02	0.19	0.23	2.37	0.39	0.79	2.33	1.72	0.60	0.15	1.32	254.11	0.33
	N	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
177	Mean	16.10	1.77	10.87	12.98	80.65	0.53	3.35	0.07	0.41	0.74	4.28	7.55	15.63	44.37	58.87	20.70	35.18	16.07	792.83	5.86
	SD	3.31	0.65	2.68	2.89	6.46	0.28	1.84	0.04	0.19	0.37	2.75	0.46	0.89	2.02	1.48	0.20	0.88	0.92	610.36	0.99
	N	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
313	Mean	12.39	1.18	10.73	10.20	80.25	0.41	4.01	0.09	0.81	0.49	4.21	7.37	15.08	42.08	57.18	20.48	35.87	16.53	1285.17	4.93
	SD	4.11	0.37	4.89	4.17	9.35	0.27	2.90	0.06	0.53	0.21	1.95	0.32	0.70	1.59	0.97	0.69	0.67	0.89	166.04	0.20
	N	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
623	Mean	12.91	1.16	8.67	10.57	82.04	0.57	4.49	0.07	0.57	0.53	4.23	7.49	15.48	43.04	57.54	20.68	35.94	16.88	1248.80	5.06
	SD	2.33	0.61	3.60	1.85	3.56	0.19	1.41	0.02	0.19	0.08	1.25	0.42	0.44	1.34	1.53	0.64	0.40	0.53	122.29	0.41
	N	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5

*=no statistically significant differences between treatment groups were found.

APPENDIX M
SUMMARY OF 14-DAY HEMATOLOGY AND INDIVIDUAL DATA
Protocol No. 30-13-07-01
Acute Oral Toxicity of 5-AT in Rats

Table M-2: Summary data for female hematology parameters

5-AT mg/kg-day		Hematology Parameters; females summary data *																			
		WBC	NEU		LYM		MONO		EOS		BASO		RBC	HGB	HCT	MCV	MCH	MCHC	RDW	PLT	MPV
		(K/uL)	(K/uL)	(%N)	(K/uL)	(%L)	(K/uL)	(%M)	(K/uL)	(%E)	(K/uL)	(%B)	(M/uL)	(g/dL)	(%)	(fL)	(pg)	(g/dL)	(%)	(K/uL)	(fL)
0	**Mean**	7.01	0.41	5.87	6.20	88.12	0.17	2.54	0.03	0.41	0.21	3.05	7.72	16.07	45.25	58.63	20.82	35.52	15.90	1280.17	5.31
	SD	3.00	0.17	0.80	2.78	3.95	0.12	2.07	0.02	0.09	0.10	1.52	0.53	0.86	2.43	1.30	0.37	0.50	0.56	138.16	0.33
	N	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
22	**Mean**	6.33	0.27	4.30	5.76	90.90	0.16	2.47	0.05	0.69	0.09	1.57	7.66	16.05	44.70	58.63	21.05	35.93	15.73	742.00	5.55
	SD	0.53	0.10	1.80	0.63	3.54	0.11	1.57	0.02	0.20	0.10	1.84	0.93	1.42	3.52	2.74	0.83	0.48	0.21	577.27	0.15
	N	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4
44	**Mean**	7.81	0.40	5.11	7.08	90.40	0.11	1.49	0.05	0.60	0.18	2.38	7.45	15.68	44.10	59.20	21.05	35.58	15.63	1204.50	5.47
	SD	3.04	0.18	0.92	2.81	2.44	0.14	1.76	0.03	0.16	0.09	0.94	0.36	0.77	2.19	1.06	0.40	0.56	1.07	137.33	0.31
	N	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
89	**Mean**	7.60	0.32	4.54	6.88	89.28	0.19	2.92	0.05	0.76	0.17	2.50	7.20	15.37	41.98	58.40	21.37	**36.62**	15.80	877.97	5.56
	SD	3.46	0.17	3.22	3.43	5.28	0.23	3.38	0.03	0.38	0.12	1.88	0.48	0.92	2.42	2.05	0.99	**0.72**	0.80	514.14	0.62
	N	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	**6**	6	6	6
177	**Mean**	8.28	0.35	4.12	7.52	90.95	0.15	1.81	0.05	0.57	0.21	2.54	7.31	15.43	43.00	58.73	21.08	35.90	15.28	1250.75	5.07
	SD	0.80	0.16	1.55	0.54	3.37	0.10	1.08	0.06	0.59	0.09	0.90	0.24	0.79	2.36	2.38	0.76	0.22	0.63	72.19	0.39
	N	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4
313	**Mean**	8.42	0.36	4.15	7.60	90.33	0.18	2.11	0.08	0.41	0.25	3.02	7.67	16.10	44.15	57.70	21.00	36.45	16.08	1369.25	5.60
	SD	1.41	0.14	1.25	1.27	3.36	0.14	1.57	0.09	0.17	0.12	1.34	0.75	1.06	3.53	1.22	0.68	0.70	1.07	150.24	0.29
	N	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4
623	**Mean**	6.76	0.42	6.46	5.89	86.18	0.20	3.39	0.02	0.47	0.24	3.54	7.65	16.00	44.80	58.38	20.84	35.70	15.14	1026.80	5.70
	SD	4.07	0.24	2.95	3.70	4.29	0.10	1.14	0.02	0.35	0.17	0.81	0.72	2.04	5.75	2.55	0.85	0.35	0.81	342.38	0.52
	N	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5

*= means significantly different from other treatment groups are in **bold**

APPENDIX M
SUMMARY OF 14-DAY HEMATOLOGY AND INDIVIDUAL DATA
Protocol No. 30-13-07-01
Acute Oral Toxicity of 5-AT in Rats

Table M-3: Individual data for male hematology parameters

NOTES	Necrospy	Sample	5-AT Dose	WBC	NEU		LYM		MONO		EOS		BASO	
(ND = NO DATA)	Date	ID	(mg/kg-d)	(K/uL)	(K/uL)	(%N)	(K/uL)	(%L)	(K/uL)	(%M)	(K/uL)	(%E)	(K/uL)	(%B)
	25-Sep-13	13- 953	0	20.9	1.5	7.1	17.9	85.6	0.4	1.9	0.2	0.7	1.0	4.6
	25-Sep-13	13- 954	0	9.3	0.7	7.5	8.3	89.4	0.1	0.7	0.0	0.2	0.2	2.3
	24-Sep-13	13- 969	0	17.0	2.2	13.1	14.5	85.3	0.1	0.6	0.1	0.5	0.1	0.5
	24-Sep-13	13- 970	0	15.4	1.4	8.8	12.8	82.8	0.5	3.0	0.1	0.5	0.8	4.9
	25-Sep-13	13- 985	0	9.0	2.2	24.6	5.9	65.5	0.4	4.6	0.1	0.9	0.4	4.4
	25-Sep-13	13- 986	0	11.3	1.3	11.7	9.1	80.4	0.4	3.2	0.1	0.6	0.5	4.1
	24-Sep-13	13- 949	22	9.8	0.9	9.5	7.7	79.3	0.5	5.3	0.0	0.3	0.5	5.6
	24-Sep-13	13- 950	22	7.4	0.8	10.2	5.5	74.7	0.5	6.1	0.1	1.0	0.6	8.1
	25-Sep-13	13- 966	22	13.2	1.1	8.6	11.0	83.6	0.5	4.2	0.1	0.6	0.4	3.1
	24-Sep-13	13- 981	22	8.7	1.1	12.6	6.5	75.5	0.5	6.2	0.1	0.6	0.4	5.1
	24-Sep-13	13- 982	22	13.9	1.0	7.1	12.5	90.0	0.3	1.8	0.1	0.7	0.0	0.4
	25-Sep-13	13- 957	44	14.4	1.5	10.6	11.2	78.0	0.8	5.7	0.0	0.3	0.8	5.5
	25-Sep-13	13- 958	44	10.5	0.7	6.8	8.6	81.5	0.7	6.3	0.0	0.2	0.6	5.2
	24-Sep-13	13- 973	44	8.7	1.9	22.2	5.5	62.9	0.5	6.2	0.0	0.4	0.7	8.3
	24-Sep-13	13- 974	44	13.1	0.9	6.6	11.1	84.7	0.6	4.8	0.0	0.3	0.5	3.5
	25-Sep-13	13- 989	44	11.1	1.4	12.7	7.7	70.0	1.1	10.2	0.0	0.4	0.8	6.8
	25-Sep-13	13- 990	44	18.1	0.8	4.3	15.8	87.0	0.7	4.0	0.1	0.7	0.7	4.0
	24-Sep-13	13- 947	89	16.3	1.3	7.7	14.7	89.8	0.1	0.3	0.1	0.5	0.3	1.7
	24-Sep-13	13- 948	89	10.0	1.0	10.1	7.7	77.0	0.6	5.6	0.1	0.6	0.7	6.6
	25-Sep-13	13- 963	89	10.2	0.9	8.9	8.7	85.3	0.2	2.3	0.0	0.4	0.3	3.0
	25-Sep-13	13- 964	89	11.5	1.4	11.9	9.2	80.1	0.4	3.7	0.1	0.7	0.4	3.8
	24-Sep-13	13- 979	89	9.7	1.1	11.3	7.0	71.9	1.0	9.8	0.1	0.8	0.7	6.3
	24-Sep-13	13- 980	89	14.7	1.2	8.4	13.2	90.0	0.1	0.6	0.0	0.2	0.1	0.8
	25-Sep-13	13- 955	177	11.6	1.1	9.4	9.4	81.3	0.4	3.7	0.0	0.3	0.6	2.6
	25-Sep-13	13- 956	177	20.8	2.2	10.7	17.2	82.8	0.5	2.6	0.1	0.6	0.7	3.3
	24-Sep-13	13- 960	177	15.2	1.0	6.5	13.9	91.0	0.1	0.6	0.1	0.6	0.2	1.3
	24-Sep-13	13- 971	177	13.9	1.7	12.4	10.0	72.3	0.8	6.0	0.0	0.1	1.3	9.1
	25-Sep-13	13- 987	177	16.4	2.0	12.0	13.3	81.0	0.4	2.7	0.1	0.4	0.6	3.8
	25-Sep-13	13- 988	177	18.7	2.7	14.2	14.1	75.5	0.8	4.4	0.1	0.4	1.0	5.5
	24-Sep-13	13- 945	313	15.1	0.8	5.3	13.3	88.3	0.4	2.3	0.1	0.6	0.5	3.5
	24-Sep-13	13- 946	313	13.9	0.9	6.6	12.0	86.1	0.4	2.7	0.1	0.5	0.6	4.0
	25-Sep-13	13- 961	313	16.5	1.3	7.8	14.8	90.2	0.0	0.2	0.0	0.1	0.3	1.8
	25-Sep-13	13- 962	313	5.2	0.9	17.6	3.6	70.7	0.3	6.6	0.0	0.9	0.2	4.3
	24-Sep-13	13- 977	313	13.4	1.7	12.8	10.4	77.9	0.6	4.2	0.1	1.1	0.5	4.0
	24-Sep-13	13- 978	313	10.3	1.5	14.3	7.0	68.3	0.8	8.0	0.2	1.7	0.8	7.7
	24-Sep-13	13- 951	623	9.1	0.5	5.1	7.5	81.7	0.6	6.1	0.1	0.8	0.6	6.4
ND - Sample clotted	24-Sep-13	13- 952	623	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	25-Sep-13	13- 967	623	15.1	1.6	10.6	12.0	79.2	0.8	5.5	0.1	0.5	0.6	4.2
	25-Sep-13	13- 968	623	14.3	1.9	13.5	11.2	78.2	0.6	3.9	0.1	0.8	0.5	3.7
	24-Sep-13	13- 983	623	12.4	1.1	8.9	10.4	84.3	0.3	2.5	0.1	0.5	0.5	3.9
	24-Sep-13	13- 984	623	13.6	0.7	5.3	11.8	86.8	0.6	4.5	0.0	0.4	0.4	3.1

APPENDIX M
SUMMARY OF 14-DAY HEMATOLOGY AND INDIVIDUAL DATA
Protocol No. 30-13-07-01
Acute Oral Toxicity of 5-AT in Rats

Table M-3 continued: Individual data for male hematology parameters

NOTES (ND = NO DATA)	Necrospy Date	Sample ID	5-AT Dose (mg/kg-d)	RBC (M/uL)	HGB (g/dL)	HCT (%)	MCV (fL)	MCH (pg)	MCHC (g/dL)	RDW (%)	PLT (K/uL)	MPV (fL)
	25-Sep-13	13- 953	0	7.2	15.3	43.0	59.9	21.3	35.6	18.6	811	6.1
	25-Sep-13	13- 954	0	7.2	14.5	41.5	57.6	20.1	35.0	16.3	808	5.3
	24-Sep-13	13- 969	0	7.9	16.0	43.8	55.7	20.4	36.6	16.8	1285	5.5
	24-Sep-13	13- 970	0	8.3	16.7	47.4	57.2	20.2	35.3	16.6	1513	5.6
	25-Sep-13	13- 985	0	7.6	15.3	42.3	55.9	20.2	36.1	16.5	1409	5.2
	25-Sep-13	13- 986	0	7.8	14.9	42.7	54.8	19.2	35.0	15.7	1198	4.9
	24-Sep-13	13- 949	22	7.0	15.2	51.8	59.3	21.5	36.3	15.9	1561	4.9
	24-Sep-13	13- 950	22	7.4	15.3	42.5	57.6	20.8	36.0	18.5	1465	5.4
	25-Sep-13	13- 966	22	7.0	15.1	42.4	61.0	21.8	35.7	15.3	1300	5.0
	24-Sep-13	13- 981	22	7.0	14.7	41.9	59.9	21.1	35.2	16.4	876	5.3
	24-Sep-13	13- 982	22	7.8	15.8	44.3	57.0	20.3	35.6	16.4	420	4.8
	25-Sep-13	13- 957	44	6.9	14.3	39.8	57.5	20.6	35.9	16.5	1235	5.3
	25-Sep-13	13- 958	44	8.2	17.2	49.0	59.7	20.9	35.0	15.9	163	5.9
	24-Sep-13	13- 973	44	7.2	15.4	43.6	60.2	21.3	35.3	16.9	800	4.8
	24-Sep-13	13- 974	44	8.0	16.5	45.6	57.2	20.6	36.1	17.5	918	5.0
	25-Sep-13	13- 989	44	7.4	14.5	41.0	55.5	19.7	35.4	16.6	842	5.2
	25-Sep-13	13- 990	44	7.2	15.3	42.0	58.2	21.2	36.5	17.3	1201	5.2
	24-Sep-13	13- 947	89	7.7	15.5	43.0	55.9	20.1	36.0	15.7	1328	5.3
	24-Sep-13	13- 948	89	7.3	14.9	41.3	56.5	20.4	36.1	15.3	1355	5.3
	25-Sep-13	13- 963	89	8.3	16.3	45.6	54.7	19.6	35.8	17.5	1406	5.6
	25-Sep-13	13- 964	89	8.0	16.9	47.0	58.9	21.2	36.0	17.8	822	5.8
	24-Sep-13	13- 979	89	7.5	15.7	44.0	58.7	20.9	35.7	15.0	1248	5.0
	24-Sep-13	13- 980	89	7.4	14.9	41.2	55.6	20.0	36.0	17.8	1578	5.0
	25-Sep-13	13- 955	177	7.4	15.4	44.8	60.5	20.8	34.4	14.9	151	5.1
	25-Sep-13	13- 956	177	8.2	17.1	46.8	56.8	20.7	36.5	15.3	1364	5.0
	24-Sep-13	13- 960	177	7.2	15.1	42.0	58.4	21.0	35.9	17.5	1438	5.6
	24-Sep-13	13- 971	177	8.0	16.3	46.6	58.4	20.4	34.9	16.5	146	7.7
	25-Sep-13	13- 987	177	7.4	15.2	43.0	58.4	20.6	35.2	15.9	1208	5.8
	25-Sep-13	13- 988	177	7.1	14.7	43.0	60.7	20.7	34.2	16.3	450	6.0
	24-Sep-13	13- 945	313	6.9	14.1	39.5	57.3	20.4	35.7	17.8	1423	5.2
	24-Sep-13	13- 946	313	7.6	14.8	42.3	56.1	19.6	35.0	16.5	1006	5.0
	25-Sep-13	13- 961	313	7.6	15.6	43.7	57.3	20.5	35.7	16.7	1324	4.7
	25-Sep-13	13- 962	313	7.6	15.1	42.5	56.0	19.9	35.6	15.1	1217	4.8
	24-Sep-13	13- 977	313	7.0	14.8	41.0	58.4	21.1	36.2	16.9	1270	4.8
	24-Sep-13	13- 978	313	7.5	16.1	43.5	58.0	21.4	37.0	16.2	1471	5.1
	24-Sep-13	13- 951	623	7.7	15.5	43.7	56.8	20.1	35.4	17.3	1170	4.8
ND - Sample clotted	24-Sep-13	13- 952	623	ND	ND	ND	ND	ND	ND	ND	ND	ND
	25-Sep-13	13- 967	623	7.7	15.8	43.9	57.0	20.5	36.0	17.1	1356	5.7
	25-Sep-13	13- 968	623	8.0	16.0	44.4	55.9	20.1	36.0	16.8	1117	4.8
	24-Sep-13	13- 983	623	6.9	14.9	41.5	59.9	21.5	35.8	17.2	1202	4.8
	24-Sep-13	13- 984	623	7.2	15.2	41.7	58.1	21.2	36.5	16.0	1399	5.2

APPENDIX M
SUMMARY OF 14-DAY HEMATOLOGY AND INDIVIDUAL DATA
Protocol No. 30-13-07-01
Acute Oral Toxicity of 5-AT in Rats

Table M-4: Individual data for female hematology parameters

NOTES	Necrospy	Sample	5-AT Dose	WBC	NEU		LYM		MONO		EOS		BASO	
(ND = NO DATA)	Date	ID	(mg/kg-d)	(K/uL)	(K/uL)	(%N)	(K/uL)	(%L)	(K/uL)	(%M)	(K/uL)	(%E)	(K/uL)	(%B)
	26-Sep-13	13- 1021	0	9.3	0.5	5.2	8.5	92.0	0.0	0.3	0.0	0.4	0.2	2.0
	26-Sep-13	13- 1022	0	2.0	0.1	6.0	1.8	90.9	0.0	1.2	0.0	0.3	0.0	1.6
	27-Sep-13	13- 1007	0	5.2	0.3	6.2	4.3	81.6	0.3	6.3	0.0	0.5	0.3	5.4
	27-Sep-13	13- 1008	0	7.2	0.4	5.6	6.4	87.8	0.2	2.6	0.0	0.4	0.3	3.5
	27-Sep-13	13- 1035	0	10.2	0.5	5.0	9.3	90.7	0.2	2.0	0.1	0.5	0.2	1.8
	27-Sep-13	13- 1036	0	8.2	0.6	7.2	7.0	85.7	0.2	2.9	0.0	0.3	0.3	4.0
	26-Sep-13	13- 1003	22	6.7	0.3	5.2	6.0	89.1	0.3	3.9	0.1	0.7	0.1	0.8
No sample	26-Sep-13	13- 1004	22	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	26-Sep-13	13- 1031	22	6.7	0.1	1.7	6.3	93.6	0.2	3.4	0.0	0.7	0.0	0.6
	26-Sep-13	13- 1032	22	6.3	0.3	4.5	5.9	94.1	0.0	0.4	0.0	0.4	0.0	0.6
ND - Sample clotted	27-Sep-13	13- 1017	22	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	27-Sep-13	13- 1018	22	5.6	0.3	5.8	4.9	86.8	0.1	2.1	0.1	0.9	0.2	4.3
	26-Sep-13	13- 1025	44	7.9	0.3	3.8	6.8	86.6	0.4	4.9	0.0	0.6	0.3	4.1
	26-Sep-13	13- 1026	44	7.4	0.3	4.4	6.8	92.5	0.0	0.4	0.1	0.7	0.1	2.0
	27-Sep-13	13- 1011	44	8.2	0.4	5.0	7.7	93.0	0.0	0.3	0.0	0.3	0.1	1.4
	27-Sep-13	13- 1012	44	2.7	0.2	5.7	2.4	89.2	0.0	1.7	0.0	0.7	0.1	2.7
	27-Sep-13	13- 1039	44	12.2	0.6	5.3	11.2	91.7	0.0	0.3	0.1	0.8	0.2	2.0
	27-Sep-13	13- 1040	44	8.5	0.5	6.4	7.6	89.4	0.1	1.5	0.0	0.5	0.2	2.2
	26-Sep-13	13- 1001	89	13.9	0.6	4.0	13.1	93.9	0.0	0.2	0.1	0.6	0.2	1.2
	26-Sep-13	13- 1002	89	5.2	0.1	2.3	4.9	93.5	0.1	1.9	0.0	0.2	0.1	2.2
	26-Sep-13	13- 1029	89	6.8	0.2	2.9	5.6	82.2	0.5	8.1	0.1	0.8	0.4	6.1
	26-Sep-13	13- 1030	89	6.5	0.2	3.6	5.6	86.1	0.4	6.3	0.1	1.0	0.2	3.0
	27-Sep-13	13- 1015	89	4.3	0.5	11.0	3.7	85.6	0.0	0.5	0.1	1.3	0.1	1.6
	27-Sep-13	13- 1016	89	9.0	0.3	3.4	8.4	94.4	0.1	0.6	0.1	0.6	0.1	1.0
	26-Sep-13	13- 1023	177	7.5	0.2	2.4	6.9	92.8	0.2	2.2	0.0	0.3	0.2	2.3
	26-Sep-13	13- 1024	177	7.7	0.3	3.3	7.2	92.8	0.1	1.6	0.0	0.3	0.2	2.1
	27-Sep-13	13- 1009	177	9.1	0.5	5.7	7.9	85.9	0.3	3.0	0.1	1.4	0.4	3.9
ND - Sample clotted	27-Sep-13	13- 1037	177	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	27-Sep-13	13- 1038	177	8.8	0.4	5.1	8.1	92.3	0.0	0.4	0.0	0.2	0.2	1.9
		13- 1010	177	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
No sample	26-Sep-13	13- 999	313	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
No sample	26-Sep-13	13- 1000	313	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	26-Sep-13	13- 1027	313	8.6	0.4	5.1	7.6	88.8	0.2	2.3	0.2	0.2	0.3	3.6
	26-Sep-13	13- 1028	313	9.8	0.5	4.8	9.1	93.2	0.0	0.4	0.0	0.3	0.1	1.4
	27-Sep-13	13- 1013	313	8.9	0.4	4.4	7.6	86.3	0.4	4.1	0.1	0.6	0.4	4.5
	27-Sep-13	13- 1014	313	6.5	0.2	2.3	6.0	93.0	0.1	1.7	0.0	0.4	0.2	2.6
	26-Sep-13	13- 1005	623	6.1	0.6	10.4	4.9	81.6	0.2	3.8	0.1	0.8	0.2	3.4
No sample	26-Sep-13	13- 1006	623	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	26-Sep-13	13- 1033	623	12.6	0.6	4.7	11.2	88.5	0.3	2.6	0.0	0.2	0.5	4.0
	26-Sep-13	13- 1034	623	1.4	0.1	5.0	1.2	86.0	0.1	4.7	0.0	0.9	0.0	3.4
	27-Sep-13	13- 1019	623	8.0	0.3	3.5	7.3	92.1	0.1	1.9	0.0	0.3	0.2	2.4
	27-Sep-13	13- 1020	623	5.9	0.5	8.7	4.8	82.7	0.2	3.9	0.0	0.2	0.3	4.5

APPENDIX M
SUMMARY OF 14-DAY HEMATOLOGY AND INDIVIDUAL DATA
Protocol No. 30-13-07-01
Acute Oral Toxicity of 5-AT in Rats

Table M-4 continued: Individual data for female hematology parameters

NOTES (ND = NO DATA)	Necrospy Date	Sample ID	5-AT Dose (mg/kg-d)	RBC (M/uL)	HGB (g/dL)	HCT (%)	MCV (fL)	MCH (pg)	MCHC (g/dL)	RDW (%)	PLT (K/uL)	MPV (fL)
	26-Sep-13	13- 1021	0	7.9	16.4	45.6	57.5	20.7	35.9	16.2	1227	4.8
	26-Sep-13	13- 1022	0	7.3	15.3	42.7	58.5	20.9	35.8	15.7	1102	5.4
	27-Sep-13	13- 1007	0	8.5	17.3	48.2	56.9	20.5	36.0	16.7	1515	5.8
	27-Sep-13	13- 1008	0	7.7	16.1	46.0	59.6	20.8	35.0	15.0	1280	5.2
	27-Sep-13	13- 1035	0	7.0	14.9	42.0	60.4	21.5	35.6	15.9	1225	5.3
	27-Sep-13	13- 1036	0	8.0	16.4	47.0	58.9	20.5	34.8	15.9	1332	5.3
	26-Sep-13	13- 1003	22	6.5	14.2	40.0	62.0	22.0	35.5	15.9	152	5.7
No sample	26-Sep-13	13- 1004	22	ND	ND	ND	ND	ND	ND	ND	ND	ND
	26-Sep-13	13- 1031	22	8.2	16.5	46.1	56.2	20.1	35.9	15.9	588	5.7
	26-Sep-13	13- 1032	22	8.5	17.6	48.3	56.6	20.7	36.6	15.5	695	5.4
ND - Sample clotted	27-Sep-13	13- 1017	22	ND	ND	ND	ND	ND	ND	ND	ND	ND
	27-Sep-13	13- 1018	22	7.4	15.9	44.4	59.7	21.4	35.7	15.6	1533	5.4
	26-Sep-13	13- 1025	44	7.5	15.9	43.7	58.1	21.2	36.5	16.8	1318	5.8
	26-Sep-13	13- 1026	44	8.0	16.9	47.3	59.3	21.1	35.6	16.1	1240	5.2
	27-Sep-13	13- 1011	44	6.9	14.5	40.5	58.5	20.9	35.8	14.7	1322	5.0
	27-Sep-13	13- 1012	44	7.2	15.6	43.9	60.9	21.7	35.6	16.8	1199	5.7
	27-Sep-13	13- 1039	44	7.6	15.5	44.3	58.5	20.5	35.1	14.4	947	5.5
	27-Sep-13	13- 1040	44	7.5	15.7	44.9	59.9	20.9	34.9	15.0	1201	5.6
	26-Sep-13	13- 1001	89	7.1	15.7	43.2	60.9	22.2	36.5	16.5	1272	4.9
	26-Sep-13	13- 1002	89	6.5	13.7	37.9	58.0	20.9	36.1	14.9	622	5.7
	26-Sep-13	13- 1029	89	7.2	16.3	43.7	60.6	22.6	37.3	15.6	1266	5.1
	26-Sep-13	13- 1030	89	7.7	15.9	42.9	56.1	20.7	37.0	16.1	1397	5.6
	27-Sep-13	13- 1015	89	6.9	15.0	40.2	58.5	21.8	37.3	14.9	96	6.7
	27-Sep-13	13- 1016	89	7.8	15.6	44.0	56.3	20.0	35.5	16.8	615	5.4
	26-Sep-13	13- 1023	177	7.5	15.8	44.0	58.9	21.1	35.9	15.4	1314	5.4
	26-Sep-13	13- 1024	177	7.5	16.3	45.6	60.4	21.7	35.8	15.4	1147	5.4
	27-Sep-13	13- 1009	177	7.2	14.5	40.1	55.3	20.0	36.2	14.4	1276	4.8
ND - Sample clotted	27-Sep-13	13- 1037	177	ND	ND	ND	ND	ND	ND	ND	ND	ND
	27-Sep-13	13- 1038	177	7.0	15.1	42.3	60.3	21.5	35.7	15.9	1266	4.7
		13- 1010	177	ND	ND	ND	ND	ND	ND	ND	ND	ND
No sample	26-Sep-13	13- 999	313	ND	ND	ND	ND	ND	ND	ND	ND	ND
No sample	26-Sep-13	13- 1000	313	ND	ND	ND	ND	ND	ND	ND	ND	ND
	26-Sep-13	13- 1027	313	8.3	16.8	47.3	57.3	20.3	35.5	16.2	1345	5.5
	26-Sep-13	13- 1028	313	8.3	17.1	46.9	56.5	20.6	36.4	17.4	1170	6.0
	27-Sep-13	13- 1013	313	7.3	15.7	42.3	57.6	21.3	37.1	15.9	1516	5.3
	27-Sep-13	13- 1014	313	6.8	14.8	40.1	59.4	21.8	36.8	14.8	1446	5.7
	26-Sep-13	13- 1005	623	6.7	13.1	36.5	54.2	19.4	35.8	15.0	1008	5.8
No sample	26-Sep-13	13- 1006	623	ND	ND	ND	ND	ND	ND	ND	ND	ND
	26-Sep-13	13- 1033	623	8.5	18.1	50.3	58.9	21.2	36.0	15.7	475	5.5
	26-Sep-13	13- 1034	623	8.1	17.6	49.2	60.4	21.6	35.7	15.4	1054	6.5
	27-Sep-13	13- 1019	623	7.7	16.3	46.5	60.4	21.2	35.1	15.8	1210	5.5
	27-Sep-13	13- 1020	623	7.2	14.9	41.5	58.0	20.8	35.9	13.8	1387	5.2

APPENDIX N
SUMMARY OF 14-DAY MICRONUCLEUS ASSAY AND INDIVIDUAL DATA
Protocol No. 30-13-07-01
Acute Oral Toxicity of 5-AT in Rats

Table N-1: Summary percent reticulocyte data

% RET Summary						
	Controls [a/c]		5-AT mg/kg-day [b]			
	untreated	+ EMS	0	177	313	623
Mean	3.842	1.15	2.577	2.795	2.927	2.933
SD	0.646	0.26	0.476	0.673	0.457	0.344
N	6	6	6	6	6	6

a= untreated group significantly different from b and c
b= no significant differences between treatment groups; statistically different from a and c
c= EMS group significantly different from a and b

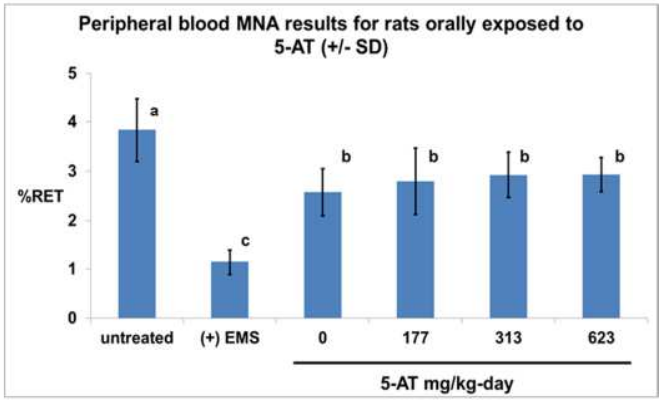
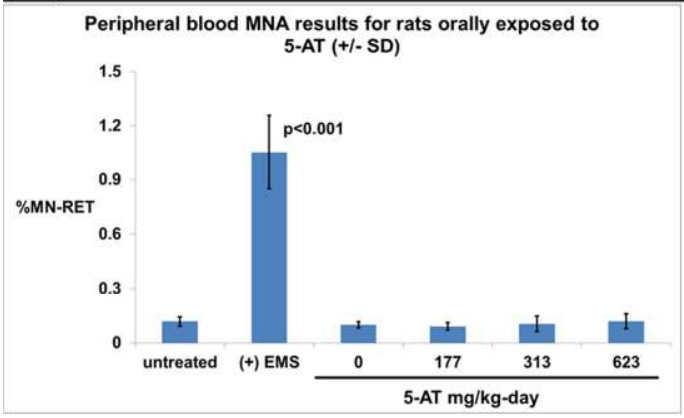


Table N-2: Summary percent micronucleated reticulocyte data

% MN-RET Summary						
	Controls		5-AT mg/kg-day			
	untreated	+EMS	0	177	313	623
Mean	0.118	1.053 ***	0.1	0.09	0.105	0.118
SD	0.0256	0.204	0.0167	0.021	0.0423	0.0417
N	6	6	6	6	6	6

***= p <0.001



APPENDIX N
SUMMARY OF 14-DAY MICRONUCLEUS ASSAY AND INDIVIDUAL DATA
Protocol No. 30-13-07-01
Acute Oral Toxicity of 5-AT in Rats

Table N-2: Individual male MNA data

Treatment	Animal I.D.	Day *	No. NCE[1]	No. MN-NCE[2]	No. RET[3]	No. MN-RET[4]	%RET[a]	%MN-RET[b]
0	13-0969	1	973555	153	19980	20	2.01	0.10
	13-0970	1	845247	63	19984	16	2.31	0.08
	13-0953	2	575202	59	19982	18	3.36	0.09
	13-0954	2	673358	52	19981	19	2.88	0.10
	13-0985	2	782143	60	19981	19	2.49	0.10
	13-0986	2	809640	60	19975	25	2.41	0.13
177	13-0971	1	665899	60	19980	20	2.92	0.10
	13-0960	1	502695	13	19981	19	3.83	0.10
	13-0955	2	913319	41	19983	17	2.14	0.09
	13-0956	2	838957	68	19982	18	2.33	0.09
	13-0987	2	863557	25	19990	10	2.26	0.05
	13-0988	2	588528	48	19978	22	3.29	0.11
313	13-0945	1	580393	30	19984	16	3.33	0.08
	13-0946	1	894187	85	19988	12	2.19	0.06
	13-0977	1	619619	45	19967	33	3.13	0.17
	13-0978	1	615620	65	19974	26	3.15	0.13
	13-0961	2	770860	33	19976	24	2.53	0.12
	13-0962	2	599203	44	19986	14	3.23	0.07
623	13-0951	1	726147	75	19961	39	2.68	0.20
	13-0952	1	732031	74	19978	22	2.66	0.11
	13-0983	1	546688	45	19983	17	3.53	0.09
	13-0984	1	691346	40	19983	17	2.81	0.09
	13-0967	2	612745	62	19981	19	3.16	0.10
	13-0968	2	704698	80	19977	23	2.76	0.12
untreated negative control	13-0975	1	573452	34	19982	18	3.37	0.09
	13-0976	1	692317	77	19970	30	2.81	0.15
	13-0991	2	442759	33	19975	25	4.32	0.13
	13-0992	2	489203	32	19979	21	3.93	0.11
	13-0995	2	472946	24	19983	17	4.06	0.09
	13-0996	2	418919	34	19972	28	4.56	0.14
positive EMS control	13-0993	1	1690121	176	19820	180	1.17	0.90
	13-0994	1	1866570	299	19800	200	1.06	1.00
	13-0997	2	1429057	118	19848	152	1.38	0.76
	13-0998	2	1307730	117	19775	225	1.51	1.13
	13-0959	2	2036037	270	19748	252	0.97	1.26
	13-0972	2	2439799	147	19747	253	0.81	1.27

* Day 1 = Sept 24, 2013 Day 2 = Sept 25, 2013; [1] NCE = normochromatic erythrocytes;
[2] MN-NCE = micronucleated normochromatic erythrocytes; [3] RET = young (high CD71-positive) reticulocytes; [4] MN-RET = young (high CD71-positive) micronucleated reticulocytes; [a] % RET = frequency (%) of young (high CD71-positive) reticulocytes; calculated as [(Number of RET + Number of MN-RET)/ (Number of NCE + Number of MN-NCE + Number of RET + Number of MN-RET)] x 100; [b] % MN-RET = frequency (%) of young (high CD71-positive) micronucleated reticulocytes; calculated as [Number of MN-RET/(Number of RET + Number of MN-RET)] x 100

APPENDIX O
SUMMARY OF 14-DAY SPERM ANALYSIS AND INDIVIDUAL DATA
Protocol No. 30-13-07-01
Acute Oral Toxicity of 5-AT in Rats
Table O-1: Assessment of presence or absence of sperm from male rats treated for 14 days with 5-AT; data is insufficient for further analysis

5AT mg/kg-day	Animal #	tissue weight (g)	sperm y/n	M sperm/ gram	% motile average	% progressive average
0	13- 953	0.024	n	-	-	-
	13- 954	0.027	n	-	-	-
	13- 969	0.017	n	-	-	-
	13- 970	0.015	n	-	-	-
	13- 985	0.024	y	30.8	67	9.5
	13- 986	0.029	y	19.45	2	0.5
22	13- 949	0.024	y	66.9	93	27
	13- 950	0.017	n	-	-	-
	13- 965	0.028	y	52.55	88.5	26
	13- 966	0.03	n	-	-	-
	13- 981	0.019	n	-	-	-
	13- 982	0.019	n	-	-	-
44	13- 957	0.018	n	-	-	-
	13- 958	0.027	y	18.05	0	0
	13- 973	0.019	y	91.7	91.5	25.5
	13- 974	0.017	y	46.1	86	24
	13- 989	0.032	n	-	-	-
	13- 990	0.099	n	-	-	-
89	13- 947	0.036	n	-	-	-
	13- 948	0.027	n	-	-	-
	13- 963	0.041	y	17	0	0
	13- 964	0.018	n	-	-	-
	13- 979	0.026	y	13.15	0.5	0
	13- 980	0.027	n	-	-	-
177	13- 955	0.024	n	-	-	-
	13- 956	0.025	y	69.8	95	31.5
	13- 960	0.016	n	-	-	-
	13- 971	0.028	y	64.45	93.5	29
	13- 987	0.022	n	-	-	-
	13- 988	0.028	y	15.75	4.5	0
313	13- 945	0.022	n	-	-	-
	13- 946	0.019	y	113.8	80.5	22
	13- 961	0.024	n	-	-	-
	13- 962	0.022	y	29.85	59	14
	13- 977	0.02	n	-	-	-
	13- 978	0.02	y	27.75	78.5	22.5
623	13- 951	0.015	y	20.8	28.5	10.5
	13- 952	0.019	y	30.3	0	0
	13- 967	0.02	y	26.15	79.5	18
	13- 968	0.033	n	-	-	-
	13- 983	0.028	y	32.05	87.5	23.5
	13- 984	0.032	y	12.5	2.5	0

M=million

APPENDIX P
HISTOLOGY REPORT (IN ARCHIVE EDITION ONLY)
Protocol No. 30-13-07-01
Acute Oral Toxicity of 5-AT in Rats

APPENDIX Q
STUDY PROTOCOL AND MODIFICATIONS (IN ARCHIVE EDITION ONLY)
Protocol No. 30-13-07-01
Acute Oral Toxicity of 5-AT in Rats