FINAL REPORT

Study Title

The Hershberger Bioassay (OPPTS 890.1400); Oxybenzone, Octylmethoxycinnamate, Octylsalate, Octocrylene

ILS Project-Study Number

N135-232

Guideline Numbers

OPPTS 890.1400
OECD 441

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Performing Laboratory

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Sponsor

National Institutes of Environmental Health
P.O. Box 12233
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Date of Completion

04 January 2012

STATEMENT OF NO DATA CLAIM OF CONFIDENTIALITY

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Sponsor: National Institutes of Environmental Health

Sponsor Representative: [redacted]

Title: Contract Officer Technical Representative

Signature: [redacted]

Date: 1/4/12

[redacted] 1/4/12

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COMPLIANCE STATEMENT

This study was conducted in accordance with U.S. EPA Good Laboratory Practice Standards, 40 CFR §160 with the following exception:

Flutamide and testosterone propionate were purchased commercially and not analyzed as stated in 40 CFR 160.113(a)(1) of the U.S. EPA GLP requirements, a positive response in the test system following flutamide and/or testosterone propionate administration was evident following statistical analysis of the tissue weights.

Dose formulation analyses were performed at the following laboratories at the request of the sponsor: analysis for Octylmethoxycinnamate with [redacted] as the Study Director at Midwest Research Institute (Kansas City, MO), analysis for Oxybenzone with [redacted] as the Study Director, analysis for Octylsalate with [redacted] as the Study Director, and analysis for Octylcrylene with [redacted] as the Study Director, all at Battelle Memorial Institute (Columbus, OH).

[redacted]

1/4/12
Date

Study Director
Investigative Toxicology Division
Integrated Laboratory Systems, Inc

[redacted]

1/4/2012
Date

Contract Officer Technical Representative

This final report has been reviewed by:

[redacted]

1/4/2012
Date

Study Toxicologist
Investigative Toxicology Division
Integrated Laboratory Systems, Inc

QUALITY ASSURANCE INSPECTION STATEMENT

Laboratory Project ID - Study No.: N135-232

Study Title: The Hershberger Bioassay (OPPTS 890.1400); Oxybenzone, Octylmethoxycinnamate, Octylsalate, Octocrylene

This study was inspected by one or more persons of the Quality Assurance Unit of ILS, Inc., Research Triangle Park, NC, US, and written status reports were submitted on the following dates:

Inspection/Audit:	Date(s) Performed:	Dates Reported to Study Director / Management:
Study Protocol	20 May 2011	20 May 2011/20 May 2011
Dose Formulation Preparation	01 June 2011	01 June 2011/08 June 2011
Data Audit	29 July, 01-03 August 2011	03 August 2011/09 August 2011
Draft Report	21, 24-27 October 2011	28 October 2011/28 October 2011
Final Report	22 November 2011	22 November 2011/22 November 2011
Revised Final Report	04 January 2012	04 January 2012/04 January 2012

[redacted]

Quality Assurance Auditor

01/04/2012

Date

TABLE OF CONTENTS

Tables:

Appendices:

SUMMARY

The purpose of the Hershberger Bioassay was to screen oxybenzone, octylmethoxycinnamate, octylsalate, and octocrylene for their potential androgen agonist/antagonist and 5α-reductase inhibition properties using the castrated rat model (OPPTS 890.1400).

Two hundred eight castrated male Sprague Dawley (SD) rats were allocated to 1 of 26 designated dose groups. To evaluate the test substances for agonist properties, animals were administered 1 of 2 dose levels (320 and 1000 mg/kg or 235 and 750 mg/kg) of test substance, the vehicle control, or an agonist reference substance (TP, 0.4 mg/kg). To evaluate test substances for antagonist properties animals were co-administered 1 of 3 dose levels (100, 320, or 1000 mg/kg or 75, 235, and 750 mg/kg) or FT (3 mg/kg antagonist positive control) with TP.

Animals were dosed for 10 consecutive days via oral gavage (oxybenzone, octylmethoxycinnamate, octylsalate, octocrylene or FT) and in the antagonist group, subcutaneous injection (TP). Approximately 24-hours following the final dose administration, the animals were humanely euthanized; the glans penis, ventral prostate, levator ani plus bulbocavernous muscle (LABC), Cowper's gland, and seminal vesicle with coagulating gland with fluid were excised and weighed. Changes in androgen-dependent tissue weights were evaluated to determine the ability of oxybenzone, octylmethoxycinnamate, octylsalate, and octocrylene to act as androgen agonists/antagonists or inhibitors of 5α-reductase.

Oxybenzone administered at dose levels of 320 or 1000 mg/kg did not change final body weights, body weight gain, or increase any androgen-dependent tissue weights compared to the vehicle control (corn oil) animals in the agonist assay. In the androgen antagonist assay, final body weight and body weight gain were statistically decreased with 1000 mg/kg oxybenzone + TP compared to control rats (vehicle control + TP). Oxybenzone co-administered with TP was associated with a significant decrease in glans penis weight at 1000 mg/kg compared to the control group (p=0.0087), and a marginal decrease in the ventral prostate (p=0.0800), no other tissue weights were different. Multivariate analyses of all tissues indicated no significant difference from the controls.

Octylmethoxycinnamate administered at dose levels of 320 or 1000 mg/kg did not change final body weights, body weight gain, or increase any androgen-dependent tissue weights compared to the vehicle control (corn oil) animals in the agonist assay. Final body weight and body weight gain were not statistically decreased in rats administered octylmethoxycinnamate + TP at any dose level (up to 1000 mg/kg) in the antagonist assay. Co-administration of octylmethoxycinnamate with TP did not cause a significant decrease in androgen-dependent tissue weights, however the Cowper's gland and LABC weights were marginally significant (p=0.0753 and p=0.0692, respectively) following administration with 1000 mg/kg octylmethoxycinnamate + TP. Multivariate analyses of all tissues indicated no significant difference from the controls.

A significant decrease was observed in mean body weight gain in animals administered 750 mg/kg octylsalate compared to vehicle control rats in the agonist assay. Final body weight and androgen-dependent tissue weights were not different than controls at dose levels of 235 and

750 mg/kg in the agonist assay. In the androgen antagonist assay, final body weight and body weight gain were statistically decreased in rats administered 750 mg/kg octylsalate + TP compared to control rats (rats administered vehicle control + TP). Octylsalate (750 mg/kg) co-administered with TP was associated with a significant decrease in mean LABC weight compared to the control group, no other tissue weights were significantly decreased; however, multivariate analysis showed a statistical difference when evaluating all five androgen-dependent tissues. Because reduced growth was observed in only in two tissues, it is unlikely that octylsalate is an androgen antagonist; however, additional screening data could be used in a weight of evidence approach to make that determination.

Octocrylene administered at dose levels of 320 or 1000 mg/kg did not cause any changes in final body weight, body weight gain, or increase any androgen-dependent tissue weights in the agonist assay. Co-administration of octocrylene + TP, at any dose level (up to 1000 mg/kg), did not cause any changes in final body weight, body weight gain, or decreases in androgen-dependent tissue weights in the antagonist assay.

Using the castrated rat model Hershberger Assay (OPPTS 890.1400), oral administration of oxybenzone, octylmethoxycinnamate, and octocrylene up to the limit dose of 1000 mg/kg did not show androgen agonist/antagonist activity, or properties reflective of 5α-reductase inhibition. Oral administration of octylsalate up to 750 mg/kg did not show androgen agonist activity; however, administration of octylsalate + TP at 750 mg/kg shows potential antagonist activity.

INTRODUCTION

1.1 Study Title

The Hershberger Bioassay (OPPTS 890.1400); Oxybenzone, Octylmethoxycinnamate, Octylsalate, Octocrylene

1.2 Laboratory Project Identification

ILS Project No.-Study No.: N135-232

1.3 Background

The Endocrine Disruptor Screening Program (EDSP) reflects a two-tiered approach to implement the statutory testing requirements of FFDCA section 408(p) (21 U.S.C. 346a). U.S. EPA will use the data collected under the EDSP, along with other information to determine if a pesticide, chemical, or other substances, may pose a risk to human health or the environment due to disruption of the endocrine system.

EDSP Tier 1 screening assays will be used to identify substances that have the potential to interact with the estrogen, androgen, or thyroid hormone systems (Test guidelines in the OPPTS 890 series). The determination of the potential of each test substance activity will be made on a weight-of-evidence basis taking into account data from the Tier 1 assays and other available scientifically-relevant information. The fact that a substance may interact with a hormone system, however, does not mean that when the substance is used it will cause adverse effects in humans or ecological systems. The Hershberger Bioassay (OPPTS 890.1400) is used as an *in vivo* screening assay for androgen agonists, androgen antagonists, and 5α-reductase inhibitors and is one of four *in vivo* mammalian assays in the EDSP Tier 1 battery of assays.

1.4 Purpose of the Study

The purpose of the Hershberger Bioassay was to screen oxybenzone, octylmethoxycinnamate, octylsalate, octocrylene for its potential androgen agonist/antagonist activity and 5α-reductase inhibition properties using a castrated rat model (OPPTS 890.1400).

1.5 Sponsor

National Institutes of Environmental Health
P.O. Box 12233
Research Triangle Park, NC 27709

NIEHS Investigator

[redacted]
Telephone No.: [redacted]
Email:

Study Monitor
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1.6 Testing Facility

Integrated Laboratory Systems, Inc (ILS)
Shipping Address: 601 Keystone Park Drive, Suite 100
Durham, NC 27713

Mailing Address: P.O. Box 13501
Research Triangle Park, NC 27709

Study Director
[redacted]
Telephone No.:
Facsimile No.:
E-mail:

1.7 Study Dates

Study Initiation Date: May 23 2011
Animal Arrival Dates: May 23, 2011; June 06, 2011
Experimental Start Date: May 30, 2011
Experimental Termination Date: June 24, 2011

TEST SUBSTANCE

2.1 Test Substance **2-Hydroxy-4-methoxybenzone (Oxybenzone)**

Product Name: 2-Hydroxy-4-methoxybenzophenone

CAS No. 131-57-7

ILS Repository No.: 11-29

Source: Ivy Fine Chemical Corporation

Lot/Batch No.: 20100801

Formula: $C_{14}H_{12}O_3$

Description: Light yellow powder

Purity: 99.9%

Expiration Date: 01 August 2012

Dose Formulation: Test substance for formulations were prepared at ILS one time prior to study start. Oxybenzone formulations were prepared using corn oil as the vehicle at concentrations of 20, 64, or 200 mg/ml and dispensed into 15 mL amber vials that were used for daily dosing throughout the study.

Storage:

Test Substance: Room temperature

Dose Formulation: Room temperature

Stability:

Dose Formulation: Dose formulations prepared in corn oil and held at approximately 5 and 25°C for 42 days were considered stable (Richey, 2011c).

2.2 Test Substance **2-Ethylhexyl p-methoxycinnamate (Octylmethoxycinnamate)**

Product Name: Octyl 4-methoxycinnamate

CAS No. 5466-77-3

ILS Repository No.: 11-32

Source: Acros Organics

Lot/Batch No.: A0293319

Formula: $C_{18}H_{26}O_3$

Description: Clear colorless liquid

Purity: 99.8%

Expiration Date: 04 July 2011

Dose Formulation: Test substance for formulations were prepared at ILS one time prior to study start. Octylmethoxycinnamate formulations were prepared using corn oil as the vehicle at concentrations of 20, 64, or 200 mg/ml and dispensed into

15 mL amber vials that were used for daily dosing throughout the study.

Storage:

Test Substance: Room temperature

Dose Formulation: Stored between 1 and 10°C and protected from light

Stability:

Dose Formulation: Dose formulations prepared in corn oil and held at up to 60°C for 12 days were considered stable (Kroenke, 2011).

2.3 Test Substance **Octyl Salicylate (Octylsalate)**

Product Name: 2-Ethylhexyl salicylate

CAS No. 118-60-5

ILS Repository No.: 11-30

Source: Sigma Aldrich

Lot/Batch No.: 44698PJ

Formula: $C_{15}H_{22}O_3$

Description: Colorless liquid

Purity: 99.6%

Dose Formulation: Test substance for formulations were prepared at ILS one time prior to study start. Octylsalate formulations were prepared using corn oil as the vehicle at concentrations of 15, 47, or 150 mg/ml and dispensed into 15 mL amber vials that were used for daily dosing throughout the study. Dose concentrations were adjusted to correct for purity of octylsalate.

Storage:

Test Substance: Room Temperature

Dose Formulation: Stored between 1 and 10°C and protected from light

Stability:

Dose Formulation: Dose formulations prepared in corn oil and held at approximately 5 and 25°C for 42 days were considered stable (Richey, 2011b).

2.4 Test Substance **2-Ethylhexyl 2-Cyano-3,3-diphenylacrylate (Octocrylene)**

Product Name: 2-Ethylhexyl 2-Cyano-3,3-diphenylacrylate

CAS No. 6197-30-4

ILS Repository No.: 11-31

Source: Sigma Aldrich

Lot/Batch No.: 01697MJ

Formula: $C_{24}H_{27}NO_2$

Description: Yellow viscous liquid

Purity: 99.2%

Dose Formulation: Test substance for formulations were prepared at ILS one time prior to study start. Octocrylene formulations were prepared using corn oil as the vehicle at concentrations of 20, 64, or 200 mg/ml and dispensed into 15 mL amber vials that were used for daily dosing throughout the study. Dose concentrations were adjusted to correct for purity of octocrylene.

Storage:

Test Substance: Room temperature

Dose Formulation: Stored between 1 and 10°C and protected from light

Stability:

Dose Formulation: Dose formulations prepared in corn oil and held and at approximately 5 and 25°C for 42 days were considered stable (Richey, 2011a).

2.5 Reference Substance: Testosterone Propionate (Androgen Agonist)

CAS No. 57-85-2

Source:	Sigma-Aldrich Company
Lot/Batch No.:	048K1328
Formula:	$C_{22}H_{32}O_3$
Description:	White to off-white powder
Purity:	100%
Dose Formulation:	Testosterone propionate was prepared at ILS in corn oil once at a dose level of 0.8 mg/mL and dispensed into vials used daily during the study.
Storage:	
Reference Substance:	Room temperature, protected from light
Dose Formulation:	Between 1-10°C
Stability:	
Dose Formulation:	TP in corn oil held between 1-10°C was shown to be stable for 14 days (Smith, 2011).

2.6 Reference Substance: Flutamide (Androgen Agonist)

CAS No.	13311-84-7
Source:	Sigma-Aldrich Company
Lot/Batch No.:	107K1293
Formula:	$C_{11}H_{11}F_3N_2O_3$
Description:	Yellow powder
Purity:	99.5%
Dose Formulation:	Flutamide was prepared at ILS in corn oil once at a dose level of 0.6 mg/mL and dispensed into vials to be used daily during the study.

Storage:

Reference Substance: Room temperature, protected from light

Dose Formulation: Between 1-10°C

Stability:

Dose Formulation: Flutamide in corn oil stored between 1-10°C was shown to be stable for 42 days (Graves, 2001).

2.7 Vehicle: Corn Oil

CAS No.: 8001-30-7

Source: MP Biomedicals, LLC

Lot/Batch No.: 7862K

Formula: $C_{27}H_{50}O_6$

Description: Yellow oil

Storage:

Vehicle: Room temperature

2.8 Archival Samples

Approximately a 1 g sample of the neat test substance and 1 mg of the reference substances are stored between 0 and -30°C. One mL of the vehicle and each dose formulation is stored between 0 and -30°C until acceptance of the final report; after acceptance of the report by the Sponsor archival dose formulations will be discarded. The archival test substance and reference substance samples will be maintained by ILS for 5 years following submission of the final report to the sponsor.

2.9 Dose Formulation Analysis

Dose formulations were prepared at ILS, sent, and analyzed at Midwest Research Institute (Kansas City, MO) and Battelle Memorial Institute (Columbus, OH) in accordance with GLP regulations as promulgated by the U.S. EPA GLP Regulations (40 CFR Part 160).

Octylmethoxycinnamate:
Midwest Research Institute
Program: NTP Chemistry Support
425 Volker Boulevard
Kansas City, MO 64110-2299

Oxybenzone, Octylsalate and Octocrylene:
Battelle Memorial Institute
TOXBC Test Article Custodian
651 W. Fifth Avenue
Columbus, OH 43201-2693

Three samples (top, middle, and bottom) of the test substance were analyzed for concentration and homogeneity. Concentration results were acceptable if the mean concentration was within 10% of the target concentration. Homogeneity results were acceptable if the coefficient of variation was less than ≤5%.

EXPERIMENTAL DESIGN

3.1 Test System

Species:	Rat, *Rattus norvegicus*
Strain:	Sprague-Dawley Crl:CD®(SD) IGS
Source:	Charles River Laboratories International, Inc. (Raleigh, NC)
Number/Sex:	208/castrated males; surgical manipulation was performed by Charles River Laboratories International, Inc. Rats were postnatal day (PND) 45 at surgery. Note: PND 0 is the day of birth
Date of birth:	02 April 2011 (study 1) and 15 April 2011 (study 2)
Age at arrival:	PND 51 (study 1) and 52 (study 2)
Acclimation:	Animals were acclimated in the study room for at least 7 days.
Age at dose administration:	PND 58/59 (study 1), 59/60 (study 2)
Weight at dose administration:	228.1 – 285.8 grams (study 1) 208.4 – 328.6 grams (study 2)
Identification:	Each animal was uniquely identified by ear punch prior to dose administration. Until the animals were ear punched, they were identified by the temporary numbers located on the animal's cage.

Justification: Animal model used is in accordance with OPPTS 890.1400: Hershberger Bioassay (U.S. EPA, 2009) and OECD Guideline 441 (OECD, 2009).

3.2 Animal Husbandry

All procedures were in compliance with the Animal Welfare Act Regulations, 9 CFR 1-4 and animals were handled and treated according to the *Guide for the Care and Use of Laboratory Animals* (ILAR, 1996).

Housing (pre-allocation): 1 per cage

Housing (post allocation): 2 per cage

Cage Changes: Twice per week

Cage Type: Polycarbonate with micro-isolator top

Cage Size: 23 cm wide by 44 cm long (1012 cm^2 area) and 21 cm high

Bedding: Absorbent heat-treated hardwood bedding (Northeastern Products Corp., Warrensburg, NY)

Diet: Teklad Global 16% Protein Rodent Diet (Teklad Diets, Madison WI) *ad libitum*

Prior to shipment rats were given Autoclaved Purina5L79 Rat and Mouse diet *ad libitum* at Charles River Laboratories International, Inc. A copy of the diet composition is included in the raw data.

Analysis: The manufacturer's analytical results is included in the raw data and reviewed prior to animal arrival. The total genistein equivalent of genistein plus daidzein (as described by Owens et al., 2003) was determined to be 8.0 µg/g of feed.

Water: Reverse osmosis treated tap water (City of Durham, NC) *ad libitum*

Supplied: Glass water bottles with stainless steel sipper tubes

Analysis: The results of the current annual comprehensive chemical analyses of water from National Testing Laboratories, Inc. (Cleveland, OH) were reviewed prior to initiation of the study and are included in the raw data.

Water Bottle Changes: Once per week

Animal Room Conditions:

Temperature:	23-26°C (study 1) 23-27°C (study 2)
Humidity	40-53% (study 1) 37-56% (study 2)
Lighting:	12/12 hour light/dark cycle
Cleaning:	The rooms were sanitized within 15 (study 1)/3 (study 2) days of animal receipt.

Enrichment: None

STUDY DESIGN

4.1 Allocation

The animals for each study were assigned to a dose group using a procedure that allocated animals across groups by body weight such that mean body weight of each group was not statistically different from any other group using analysis of variance [ANOVA, Statistical Analysis System (SAS) version 9.1, SAS Institute, Cary, NC].

4.2 Group Designation

Study 1

Table 1. Androgen Agonist; Group Number, Animal Identification, Dose Group and Level

Group Number	Animal Identification	Test Substance/Control	Test Substance Dose Level (mg/kg/day)
1	01-08	Vehicle Control (Corn Oil)	0
2	09-16	Oxybenzone	320
3	17-24	Oxybenzone	1000
4	25-32	Octylmethoxycinnamate	320
5	33-40	Octylmethoxycinnamate	1000

Table 2. Androgen Antagonist; Group Number, Animal Identification, Dose Group and Level

Group Number	Animal Identification	Test/Reference Substance/Controls	Test/Reference Substance Dose Level (mg/kg/day)
6[§]	41-48	Vehicle Control (corn oil) + TP	0 + 0.4
7	49-56	Oxybenzone + TP	100 + 0.4
8	57-64	Oxybenzone + TP	320 + 0.4
9	65-72	Oxybenzone + TP	1000 + 0.4
10	73-80	Octylmethoxycinnamate + TP	100 + 0.4
11	81-88	Octylmethoxycinnamate + TP	320 + 0.4
12	89-96	Octylmethoxycinnamate + TP	1000 + 0.4
13	97-104	FT + TP (positive control)	3 + 0.4

[§]Group served as the positive control for agonist assay and control in the antagonist assay

Study 2

Table 3. Androgen Agonist; Group Number, Animal Identification, Dose Group and Level

Group Number	Animal Identification	Test Substance/Control	Test Substance Dose Level (mg/kg/day)
14	105-112	Vehicle Control (corn oil)	0
15	113-120	Octylsalate	235
16	121-128	Octylsalate	750
17	129-136	Octocrylene	320
18	137-144	Octocrylene	1000

Table 4. Androgen Antagonist; Group Number, Animal Identification, Dose Group and Level

Group Number	Animal Identification	Test/Reference Substance/Controls	Test/Reference Substance Dose Level (mg/kg/day)
19[§]	145-152	Vehicle control (Corn oil) + TP	0 + 0.4
20	153-160	Octylsalate + TP	75 + 0.4
21	161-168	Octylsalate + TP	235 + 0.4
22	169-176	Octylsalate + TP	750 + 0.4
23	177-184	Octocrylene + TP	100 + 0.4
24	185-192	Octocrylene + TP	320 + 0.4
25	193-200	Octocrylene + TP	1000 + 0.4
26	201-208	FT + TP (Positive control)	3 + 0.4

[§]Group served as the positive control for agonist assay and control in the antagonist assay

4.3 Dose Administration

The test substance, FT, or corn oil (vehicle control) dose formulations were administered by oral gavage at a dose volume of 5 mL/kg body weight. TP dose formulations were administered by subcutaneous injection into the dorsoscapular region at a dose volume of 0.5 mL/kg body weight. In co-administered animals, oral gavage preceded subcutaneous injections.

Study 1
The dose formulations were administered on a staggered start for 10 consecutive days (PND 58/59 through PND 67/68). The first four animals from each group were dosed beginning on PND 58, and the second four animals from each group on PND 59.

Study 2
The dose formulations were administered on a staggered start for 10 consecutive days (PND 59/60 through PND 68/69). The first four animals from each group were dosed beginning on PND 59, and the second four animals from each group on PND 60.

In both studies, dosing occurred 24 hours (± 2 hours) from the previous dose. Dose volume was determined on individual animal daily body weight. The dosing sequence was stratified across dose groups; one animal from each group and then repeated until all animals are dosed.

4.3.1 Justification of Route of Administration
Selection of the route of administration is in accordance with OPPTS 890.1400: Hershberger Bioassay (U.S. EPA, 2009) and OECD Guideline 441 (OECD, 2009).

4.3.2 Justification of Dose Levels
OPPTS 890.1400 specifies to select doses that ensure animal survival and that are without significant toxicity or distress to the animals after ten consecutive days of chemical administration, and the highest dose should not cause a reduction in the final body weight of the animals greater than 10% of control weight.

The octylsalate dose level was selected based on data obtained from a uterotrophic study performed by ILS (Zorrilla, 2011) where body weight loss of ~10% was observed after 3 consecutive days of dosing (1000 mg/kg), therefore 750 mg/kg was defined at the MTD for the Hershberger Bioassay. All other test substances were evaluated up to the limit dose level (1000 mg/kg) due to the LD_{50} and available data of each test substance.

4.4 Disposal of Dose Formulations
Dose formulations were disposed of as hazardous material following dose administration each day.

4.5 In-Life Animal Observations

Mortality/Moribundity:	Twice daily on weekdays, once daily on weekends and holidays.
Clinical Observations:	Observed within 2 days of arrival, again for allocation of animals to study groups, daily prior to dose administration, and prior to euthanasia.

Body Weights: Collected within 2 days of arrival, again for allocation of animals to study groups, daily prior to dose administration, and prior to euthanasia.

4.6 Termination

Scheduled: Twenty-four hours (± 2 hours) after the final dose administration, animals were humanely euthanized by carbon dioxide (CO_2) asphyxiation with death confirmed by cervical dislocation in the same order as they were dosed.

Tissue Collection: Gross observations of the tissues that were excised for tissue weights were recorded.

Tissue Weights: The following tissues were excised, trimmed of excess adhering tissue and fat, and weighed to the nearest 0.0001 g.

1. Ventral Prostate
2. Seminal vesicle and coagulating gland with fluid
3. Levator ani plus bulbocavernous muscle complex
4. Cowper's gland (weighed as a pair)
5. Glans penis

4.7 Statistical Analysis

Descriptive statistics (mean, standard deviation and count) were calculated using MS Excel. Final body weight, body weight gain, and tissue weights were analyzed using SAS version 9.2 (SAS Institute, Cary, NC). Studentized residual plots were used to detect possible outliers and Levene's test was used to assess homogeneity of variance. Heterogeneous data (oxybenzone antagonist assay-seminal vesicle weight; octocrylene antagonist assay - LABC) were transformed (seminal vesicle- logarithm, LABC - logarithm, square root and inverse) and if still heterogeneous, analyzed using the non-parametric Kruskal-Wallis and Dunn's test.

Final body weight, body weight gain, and androgen-dependent tissue weights were analyzed by one-way ANOVA followed by pair wise comparisons using Dunnett's one tailed t test (tissues weights) or Dunnett's two tailed t test (final body weight and body weight gain). Multivariate analysis was performed on antagonist assay data when either 1 of 5 tissue weights was statistically significant as compared to controls, or tissue weights were marginally significant (p=0.05-0.10) as compared to controls. Positive controls were analyzed by the t test procedure. Statistically significant effects were reported when $p < 0.05$.

RESULTS

5.1 Dose Formulation Analysis

Actual concentration and homogeneity results of each dose formulation used in the study were within the acceptance criteria (Appendix II).

Study 1

Table 5. Dose Formulation Results

Dose Group	Nominal Dose Concentration (mg/mL)	Actual Dose Concentration* (mg/mL) [Percent from Nominal[§]]	Grand Standard Deviation* (Homogeneity)	Nominal Dose Level (mg/kg/day)	Actual Dose Level (mg/kg/day)
Oxybenzone[†]	20	20.2 [0.8]	0.3	100	101
Oxybenzone[†]	64	63.9 [0.2]	0.3	320	319.5
Oxybenzone[†]	200	211 [5.3]	1.2	1000	1055
Octylmethoxycinnamate[¥]	20	20.1 [0.5]	1.1	100	100.5
Octylmethoxycinnamate[¥]	64	65.2 [2.0]	3.2	320	326
Octylmethoxycinnamate[¥]	200	202.9 [1.4]	2.4	1000	1014.5

Preparation Dates: 04 May[¥] and 05 May[†] 2011
*Sources: Haney, 2011; Kerns, 2011
[§] Reported as Relative Error (RE) in formulation report
Abbreviations: CV – coefficient of variation

Study 2

Table 6. Dose Formulation Results

Dose Group	Nominal Dose Concentration (mg/mL)	Actual Dose Concentration* (mg/mL) [Percent from Nominal[§]]	Standard Deviation* (Homogeneity)	Nominal Dose Level (mg/kg/day)	Actual Dose Level (mg/kg/day)
Octylsalate[†]	15	14.8 [1.1]	1.0	75	74.0
Octylsalate[†]	47	45.8 [2.6]	2.0	235	229
Octylsalate[†]	150	143 [4.9]	2.7	750	715
Octocrylene[†]	20	19.9 [0.5]	1.3	100	99.5
Octocrylene[†]	64	62.1 [3.0]	0.7	320	311
Octocrylene[†]	200	191 [4.5]	0.5	1000	955

Preparation Date: 01 June[†] 2011
*Sources: Richey, 2011d,e
[§] Reported as Relative Error (RE) in formulation report
Abbreviations: CV – coefficient of variation

5.2 In Life Animal Observations

Study 1

Mortality/Moribundity

Androgen Agonist (Groups 1-6[§])
Animals administered oxybenzone or octylmethoxycinnamate survived to the scheduled study termination with no animals showing signs of moribundity. One vehicle control (corn oil) animal (group 1), was found dead after dosing on day 10 due to gavage error.

Androgen Antagonist (Groups 6[§]-13)
All animals were co-administered vehicle or test substance + TP. Animals administered oxybenzone, octocrylene, and the positive control (FT + TP) all survived to the scheduled termination with no animals showing signs of moribundity. Two animals administered 320 mg/kg octylmethoxycinnamate + TP (group 11) were euthanized on study days 7 and 10 due to abnormal breathing. Both animals had evidence of gavage error. All other animals administered octylmethoxycinnamate + TP were normal.

[§] Group 6 served as the positive control for agonist assay and control in the antagonist assay

Clinical Observations
Individual animal data are listed in Appendix IV.

Androgen Agonist (Groups 1-6[§])
No clinical signs of toxicity were observed in any rats administered oxybenzone.

One rat administered 1000 mg/kg octylmethoxycinnamate exhibited a hunched posture on day 7 and a mass was found on its left shoulder/chest on day 10. All other animals were observed as normal.

Vehicle control (corn oil) animals and those administered vehicle control + TP exhibited no clinical signs of toxicity.

Androgen Antagonist (Groups 6[§]-13)
One rat co-administered 1000 mg/kg oxybenzone + TP exhibited hunched posture on day 8. All other animals administered oxybenzone (100, 320, or 1000 mg/kg + TP) were observed as normal.

One rat co-administered 100 mg/kg octylmethoxycinnamate + TP (group 10) exhibited a hunched posture on study days 8-10, and another displayed minimal hind leg movement on day 3; both rats were observed to be normal on all other study days. One rat administered 320 mg/kg octylmethoxycinnamate + TP (group 11) exhibited rales on day 7, one rat exhibited abnormal breathing rate, lethargy, clear oral discharge, rales, hunched posture, rough coat, and a mass in the thoracic area on day 7. On day 8 oral discharge was no longer observed but other clinical signs remained. A hunched posture and thoracic mass persisted until day 10; both of these animals were euthanized as described above. One rat co-administered 1000 mg/kg octylmethoxycinnamate + TP (group 12) exhibited hunched posture on day 9. All other animals were observed as normal.

Animals administered vehicle control + TP (group 6) or FT + TP (group 13) exhibited no clinical signs of toxicity.

Body Weights
Group mean initial and final body weights and body weight changes for animals euthanized following 10 consecutive days of administration are presented in Table 7 (agonist assay) and Table 8 (antagonist assay). Individual animal data are listed in Appendix V.

Androgen Agonist (Groups 1-6[§], Table 7)
There was no significant decrease in mean body weight or body weight gain for animals administered oxybenzone or octylmethoxycinnamate as compared to controls.

[§] Group 6 served as the positive control for agonist assay and control in the antagonist assay

Androgen Antagonist (Groups 6[§]-13, Table 8)

There was no significant decrease in mean body weight or body weight gain for animals co-administered octylmethoxycinnamate + TP as compared to controls. A significant decrease in mean final body weight and body weight gain was observed in animals co-administered 1000 mg/kg oxybenzone + TP (group 9) as compared to TP controls (group 6). Final body weights were 100.9%, 101.2%, and 92.9% of vehicle control at dose levels of 100, 320, and 1000 mg/kg oxybenzone, respectively.

[§] Group 6 served as the positive control for agonist assay and control in the antagonist assay

Study 1

Table 7. Androgen Agonist; Body Weight Changes

Group Number	Dose Group	Test/Reference Substance Dose Level (mg/kg/day)	n	Initial Mean Body Weight (g) ± SD	Final Mean Body Weight (g) ± SD	Mean Body Weight Gain (g) ± SD	Final Body Weight (% of Control)
1	Vehicle Control (Corn Oil)	0	7[1]	255.5 ± 14.3	302.2 ± 24.9	47.3 ± 16.6	-
2	Oxybenzone	320	8	255.9 ± 17.7	299.0 ± 27.7	43.1 ± 10.6	98.9
3	Oxybenzone	1000	8	258.69 ± 12.4	298.0 ± 20.3	39.4 ± 11.2	98.6
4	Octylmethoxy-cinnamate	320	8	256.8 ± 14.4	313.6 ± 29.4	56.8 ± 17.6	103.8
5	Octylmethoxy-cinnamate	1000	8	257.4 ± 9.3	298.3 ± 14.0	40.9 ± 10.4	98.7
6[§]	Vehicle Control (Corn Oil) + TP (Positive Control)	0 + 0.4	8	259.3 ± 11.9	**335.1 ± 24.1**[†]	**75.8 ± 16.7**[†]	-

Abbreviation: SD- standard deviation, TP- testosterone propionate
[†]Statistically significant ($p<0.05$) compared to the vehicle control mean (t-test)
[§]Group served as the positive control for agonist assay and control in the antagonist assay
[1]One animal found dead prior to necropsy due to gavage error

Table 8. Androgen Antagonist; Body Weight Changes

Group Number	Dose Group	Test/Reference Substance Dose Level (mg/kg/day)	n	Initial Mean Body Weight (g) ± SD	Final Mean Body Weight (g) ± SD	Mean Body Weight Gain (g) ± SD	Final Body Weight (% of Control)
6[§]	Vehicle Control (Corn Oil) + TP	0 + 0.4	8	259.3 ± 11.9	335.1 ± 24.1	75.8 ± 16.7	-
7	Oxybenzone + TP	100 + 0.4	8	257.9 ± 14.2	338.1 ± 17.7	80.2 ± 9.0	100.9
8	Oxybenzone + TP	320 + 0.4	8	260.8 ± 9.5	339.2 ± 15.9	78.4 ± 10.1	101.2
9	Oxybenzone + TP	1000 + 0.4	8	256.8 ± 13.4	**311.2 ± 16.7***	**54.4 ± 12.4***	92.9
10	Octylmethoxy-cinnamate + TP	100 + 0.4	8	259.9 ± 14.7	330.2 ± 42.3	70.3 ± 30.9	98.6
11	Octylmethoxy-cinnamate + TP	320 + 0.4	6[1]	259.4 ± 11.1	343.7 ± 26.5	85.2 ± 23.9	102.6
12	Octylmethoxy-cinnamate + TP	1000 + 0.4	8	259.3 ± 13.3	319.7 ± 24.8	60.5 ± 16.4	95.4
13	FT + TP (Positive Control)	3 + 0.4	8	258.1 ± 14.4	324.0 ± 24.3	65.9 ± 14.2	-

Abbreviation: SD- standard deviation, TP- testosterone propionate, FT-flutamide
*Statistically significant ($p<0.05$) compared to the vehicle control mean (Dunnett's test)
[§]Group served as the positive control for agonist assay and control in the antagonist assay
[1]Two animals euthanized prior to necropsy due to gavage error

Study 2

Mortality/Moribundity

Androgen Agonist (Groups 14-19[§])
Animals administered octylsalate (235 mg/kg) or octocrylene survived to the scheduled study termination with no animals showing signs of moribundity. Two animals administered 750 mg/kg octylsalate (group 16) were found dead, one on study day 5 and one on study day 6, neither showed signs of dose error upon necropsy.

Androgen Antagonist (Groups 19-26[§])
All animals were co-administered vehicle or test substance + TP. Animals administered octocrylene, octylsalate (75 and 235 mg/kg) and the positive control FT all survived to the scheduled termination with no animals showing signs of moribundity. One animal administered 750 mg/kg octylsalate + TP (group 22) was found dead on day 7 with no evidence of gavage error.

Clinical Observations
Individual animal data are listed in Appendix IV.

Androgen Agonist (Groups 14-19[§])
One rat administered 235 mg/kg octylsalate (group 15) developed a scab on the left cheek on day 10, and another rat yellow nasal discharge day 8. All other clinical observations for these animals were normal. One rat administered 750 mg/kg octylsalate (group 16) exhibited an ungroomed appearance on day 9 of dosing, but was normal at all other time points. All other animals were observed as normal.

One rat administered 1000 mg/kg octocrylene (group 18) exhibited heavy salivation on study days 9 and 10 but was observed as normal on all other study days. All other animals were observed as normal.

Animals administered vehicle control + TP (group 19) or FT + TP (group 26) exhibited no clinical signs of toxicity.

Androgen Antagonist (Groups 19-26[§])
One rat co-administered 750 mg/kg octylsalate + TP (group 22) was thin on day 5 and one exhibited an ungroomed appearance on day 9, but both were observed to be normal on all other study days. All other animals were observed as normal.

One rat co-administered 1000 mg/kg octocrylene + TP (group 25) exhibited alopecia and a scab on the right cheek prior to termination but was observed to be normal on all other study days. All other animals were observed as normal.

[§]Group 19 served as the positive control for agonist assay and control in the antagonist assay

Animals administered vehicle control + TP or FT + TP (group 26) exhibited no clinical signs of toxicity.

Body Weights
Group mean initial and final body weights and body weight changes for animals euthanized following 10 consecutive days of administration are presented in Table 9 (agonist assay) and Table 10 (antagonist assay). Individual animal data are listed in Appendix V.

Androgen Agonist (Groups 14-19[§], Table 9)
There was no significant decrease in mean body weight or body weight gain for animals administered octocrylene.

Animals administered 750 mg/kg octylsalate had a significant decrease in mean body weight gain compared to vehicle controls. Final body weights were 97.1% and 86.2% of vehicle control at dose levels of 235 and 750 mg/kg octylsalate, respectively.

Androgen Antagonist (Groups 19-26[§], Table 10)
There was no significant decrease in mean body weight or body weight gain for animals co-administered octocrylene + TP.

Animals co-administered 750 mg/kg octylsalate + TP had significantly decreased final body weight and body weight gain as compared to rats administered TP alone; final body weights were 97.3%, 96.2% and 84.7% of vehicle control at dose levels of 75, 235 and 750 mg/kg octylsalate, respectively.

[§]Group 19 served as the positive control for agonist assay and control in the antagonist assay

Study 2

Table 9. Androgen Agonist; Body Weight Changes

Group Number	Dose Group	Test/Reference Substance Dose Level (mg/kg/day)	n	Initial Mean Body Weight (g) ± SD	Final Mean Body Weight (g) ± SD	Mean Body Weight Gain (g) ± SD	Final Body Weight (% of Control)
14	Vehicle Control (Corn Oil)	0	8	268.7 ± 35.9	319.2 ± 47.8	50.6 ± 16.0	-
15	Octylsalate	235	8	263.9 ± 34.6	310.0 ± 42.3	46.1 ± 12.1	97.1
16	Octylsalate	750	6[1]	270.1 ± 31.8	275.3 ± 25.5	**14.2 ± 13.8***	86.2
17	Octocrylene	320	8	268.7 ± 30.5	321.1 ± 37.4	52.4 ± 11.1	100.6
18	Octocrylene	1000	8	267.4 ± 32.0	320.4 ± 38.5	53.0 ± 10.3	100.4
19[§]	Vehicle Control (Corn Oil) + TP (Positive Control)	0 + 0.4	8	268.9 ± 29.7	353.2 ± 47.7	**86.3 ± 20.9**[†]	-

Abbreviation: SD- standard deviation, TP- testosterone propionate
*Statistically significant ($p<0.05$) compared to the vehicle control mean (Dunnett's test)
[†]Statistically significant ($p<0.05$) compared to the vehicle control mean (t-test)
[§]Group served as the positive control for agonist assay and control in the antagonist assay
[1]Two animals found dead prior to necropsy, undetermined causes of death

Table 10. Androgen Antagonist; Body Weight Changes

Group Number	Dose Group	Test/Reference Substance Dose Level (mg/kg/day)	n	Initial Mean Body Weight (g) ± SD	Final Mean Body Weight (g) ± SD	Mean Body Weight Gain (g) ± SD	Final Body Weight (% of Control)
19[§]	Vehicle Control (Corn Oil) + TP	0 + 0.4	8	268.9 ± 29.7	353.2± 47.7	86.3 ± 20.9	-
20	Octylsalate + TP	75 + 0.4	8	269.0 ± 26.9	343.5 ± 37.8	74.5 ± 18.4	97.3
21	Octylsalate + TP	235 + 0.4	8	267.1 ± 27.3	339.8 ± 38.5	72.7 ± 19.2	96.2
22	Octylsalate + TP	750 + 0.4	7[1]	268.7 ± 28.0	**299.3 ± 42.2***	**24.2 ± 28.9***	84.7
23	Octocrylene + TP	100 + 0.4	8	268.8 ± 27.6	346.6 ± 33.2	77.8 ± 7.8	98.1
24	Octocrylene + TP	320 + 0.4	8	267.4 ± 27.4	351.8 ± 36.7	84.4 ± 14.4	99.6
25	Octocrylene + TP	1000 + 0.4	8	271.5 ± 28.6	342.2 ± 39.3	70.8 ± 13.7	96.9
26	FT + TP (Positive Control)	3 + 0.4	8	268.2 ± 24.5	335.5 ± 32.7	67.4 ± 10.9	-

Abbreviation: SD- standard deviation, TP- testosterone propionate, FT-flutamide
*Statistically significant ($p<0.05$) compared to the vehicle control mean (Dunnett's test)
[§]Group served as the positive control for agonist assay and control in the antagonist assay
[1]One animal found dead prior to necropsy, undetermined cause of death

5.3. Necropsy

Study 1

Gross Observations
The following gross observation was made at necropsy:
Animal 33: fluid filled mass on muscle proximal to front left limb
All other animals were normal.

Tissue Weights
Group mean weights of glans penis, Cowper's gland, LABC, ventral prostate, and seminal vesicle for animals euthanized following 10 consecutive days of oxybenzone or octylmethoxycinnamate administration are presented in Tables 11 (agonist assay) and Tables 12 (antagonist assay). Individual animal tissue weight data are listed in Appendix VI.

Androgen Agonist (Groups 1-6[§], Table 11)
Administration of oxybenzone and octylmethoxycinnamate did not affect glans penis, Cowper's gland, LABC, ventral prostate, or seminal vesicle weights in the agonist assay at any dose level. All five androgen-dependent tissue weights were significantly increased in the positive control (vehicle control + TP; group 6) as compared to vehicle control.

Androgen Antagonist (Groups 6-13[§], Table 12)
Oxybenzone co-administered with TP caused a significant decrease in glans penis weight at 1000 mg/kg (group 9) compared to the TP control group (group 6). No significant effect was observed on LABC, Cowper's gland, or seminal vesicle weights, however the decrease in ventral prostate weight was marginally significant (p=0.08, group 9). The Hershberger Bioassay guidelines state a multivariate analysis can be used to evaluate the combined androgen-dependent tissue responses when only one tissue (glans penis) shows a statistically significant response, as is the case with oxybenzone. Since one tissue of the five androgen-dependent tissue weights was significant, and another marginally significant, multivariate analysis was performed on all five androgen-dependent tissues. Multivariate analysis did not show a statistical significant difference with administration of oxybenzone.

Administration of octylmethoxycinnamate + TP did not significantly affect the weights of glans penis, ventral prostate and seminal vesicle compared to controls at any dose level. A decrease in Cowper's gland and LABC weights were marginally significant (p=0.08 and p=0.07 respectively) with administration of 1000 mg/kg octylmethoxycinnamate + TP.

[§]Group 6 served as the positive control for agonist assay and control in the antagonist assay

(group 12), and therefore multivariate analysis was performed on all five androgen-dependent tissues. Multivariate analysis of all five tissue weights did not show a statistical significant difference with administration of octylmethoxycinnamate.

A significant decrease in the weights of glans penis, LABC, Cowper's gland, seminal vesicle, and ventral prostate occurred in the positive control groups, (FT + TP; Group 13) compared to the vehicle control + TP control group (Group 6).

Study 1

Table 11. Androgen Agonist; Absolute Androgen-dependent Tissue Weights

Group Number	Dose Group	Test/Reference Substance Dose Level (mg/kg/day)	n	Mean Glans Penis Weight (mg) ± SD (CV)	Mean Cowper's Gland Weight (mg) ± SD (CV)	Mean LABC Weight (mg) ± SD (CV)	Mean Ventral Prostate Weight (mg) ± SD (CV)	Mean Seminal Vesicle Weight (mg) ± SD (CV)
1	Vehicle Control (Corn Oil)	0	7[1]	47.4 ± 6.1 (13)	5.4 ± 1.5 (27)	133.4 ± 34.9 (26)	15.8 ± 3.1 (19)	31.1 ± 5.3 (17)
2	Oxybenzone	320	8	52.4 ± 7.3 (14)	5.2 ± 2.6 (51)	133.4 ± 19.1 (14)	15.2 ± 3.0 (20)	39.2 ± 9.0 (23)
3	Oxybenzone	1000	8	50.7 ± 5.2 (10)	5.1 ± 1.6 (32)	123.4 ± 32.0 (26)	14.0 ± 1.6 (12)	33.6 ± 9.6 (28)
4	Octylmethoxy-cinnamate	320	8	49.4 ± 7.0 (14)	4.6 ± 1.5 (33)	143.3 ± 28.9 (20)	16.1 ± 2.4 (15)	34.1 ± 6.4 (19)
5	Octylmethoxy-cinnamate	1000	8	50.4 ± 5.9 (12)	5.6 ± 2.0 (35)	129.1 ± 25.6 (20)	15.6 ± 2.8 (18)	33.9 ± 7.6 (22)
6[§]	Vehicle Control (Corn Oil) + TP (Positive Control)	0 + 0.4	8	**92.7 ± 5.0† (5)**	**39.0 ± 5.6† (14)**	**384.5 ± 51.7† (13)**	**186.2 ± 57.2† (31)**	**542.5 ± 63.2† (12)**

Abbreviations: SD - standard deviation; CV – coefficient of variation; LABC-levator ani plus bulbocavernous muscle complex, TP- testosterone propionate

†Statistically significant ($p<0.05$) compared to the vehicle control mean (t-test)

[§]Group served as the positive control for agonist assay and control in the antagonist assay

[1]One animal found dead prior to necropsy due to gavage error

Table 12. Androgen Antagonist; Androgen-dependent Tissue Weights

Group Number	Dose Group	Test/Reference Substance Dose Level (mg/kg/day)	n	Mean Glans Penis Weight (mg) ± SD (CV)	Mean Cowper's Gland Weight (mg) ± SD (CV)	Mean LABC Weight (mg) ± SD (CV)	Mean Ventral Prostate Weight (mg) ± SD (CV)	Mean Seminal Vesicle Weight (mg) ± SD (CV)
6[§]	Vehicle Control (Corn Oil) + TP	0 + 0.4	8	92.7 ± 5.0 (5)	39.0 ± 5.6 (14)	384.5 ± 51.7 (13)	186.2 ± 57.2 (31)	542.5 ± 63.2 (12)
7	Oxybenzone + TP	100 + 0.4	8	95.6 ± 4.7 (5)	38.1 ± 5.2 (14)	419.5 ± 41.9 (10)	206.2 ± 38.6 (19)	594.7 ± 54.5 (9)
8	Oxybenzone + TP	320 + 0.4	8	94.0 ± 4.5 (5)	37.2 ± 5.6 (15)	428.0 ± 55.1 (13)	195.8 ± 32.1 (16)	618.8 ± 97.3 (16)
9	Oxybenzone + TP	1000 + 0.4	8	**87.5 ± 3.8* (4)**	37.3 ± 9.8 (26)	387.9 ± 41.1 (11)	155.0 ± 21.3^ (14)	506.5 ± 39.9 (8)
10	Octylmethoxy-cinnamate + TP	100 + 0.4	8	94.7 ± 7.8 (8)	39.4 ± 5.7 (14)	415.9 ± 46.3 (11)	182.4 ± 47.6 (26)	562.3 ± 74.4 (13)
11	Octylmethoxy-cinnamate + TP	320 + 0.4	6[1]	94.6 ± 3.2 (3)	36.7 ± 7.7 (21)	419.1 ± 42.6 (10)	176.9 ± 47.2 (27)	610.1 ± 99.1 (16)
12	Octylmethoxy-cinnamate + TP	1000 + 0.4	8	91.6 ± 5.0 (5)	32.1 ± 5.0^ (16)	359.4 ± 47.3^ (13)	147.6 ± 39.7 (27)	465.5 ± 80.2 (17)
13	FT + TP (Positive Control)	3 + 0.4	8	**62.5 ± 3.8† (6)**	**12.2 ± 3.9† (32)**	**181.7 ± 25.6† (14)**	**37.0 ± 7.7† (21)**	**58.5 ± 16.7† (28)**

Abbreviations: SD - standard deviation; CV – coefficient of variation; LABC-levator ani plus bulbocavernous muscle complex, TP- testosterone propionate, FT-flutamide

*Statistically significant ($p<0.05$) compared to the vehicle control mean (Dunnett's test)

^Marginal significance ($p>0.05$ and $p<0.10$) compared to the vehicle control group mean (Dunnett's test)

[§]Group served as the positive control for agonist assay and control in the antagonist assay

†Statistically significant ($p<0.05$) compared to the vehicle control mean (t-test)

[1]Two animals euthanized prior to necropsy due to gavage error

Study 2
Gross Observations
No observations were made at necropsy.

Tissue Weights
Group mean weights of glans penis, Cowper's gland, LABC, ventral prostate, and seminal vesicle for animals euthanized following ten consecutive days of octylsalate and octocrylene administration are presented in Tables 13 (agonist assay) and 14 (antagonist assay). Individual animal tissue weight data are listed in Appendix VI.

Androgen Agonist (Groups 14-19[§], Table 13)
Administration of octylsalate and octocrylene did not affect glans penis, Cowper's gland, LABC, ventral prostate, or seminal vesicle weights at any dose level in the agonist assay. All five androgen-dependent tissue weights were significantly increased in the positive control (vehicle control + TP; Group 19) as compared to vehicle control group.

Androgen Antagonist (Groups 19-26[§], Table 14)
Octylsalate co-administered with TP caused a significant decrease in LABC weight at 1000 mg/kg octylsalate + TP (group 22) compared to vehicle + TP controls (group 19, p=0.0004). No significant weight changes occurred in the glans penis, Cowper's gland, ventral prostate, or seminal vesicle.

The Hershberger Bioassay guidelines state a multivariate analysis can used to evaluate the combined androgen-dependent tissue responses when only one tissue (LABC) shows a statistically significant response, as is the case in this study with octylsalate. The conduct of a multivariate analysis was found to show statistical significance from the control group when all five androgen-dependent tissue weights were evaluated. The guidelines also state that in the case of a positive result, all androgen-dependent tissues should display some reduced growth. In this study, the ventral prostate weights are the only other tissue showing some reduced growth. The glans penis, seminal vesicle, and Cowper's gland did not show any reduced growth.

Administration of octocrylene did not affect the weights of any of the five androgen-dependent tissues compared to controls at any dose level.

A significant decrease in the weights of glans penis, LABC, Cowper's gland, seminal vesicle, and ventral prostate occurred in the positive control groups, (FT + TP; Group 26) compared to the vehicle control + TP control group (Group 19).

[§]Group 19 served as the positive control for agonist assay and control in the antagonist assay

Study 2

Table 13. Androgen Agonist; Androgen-dependent Tissue Weights

Group Number	Dose Group	Test/Reference Substance Dose Level (mg/kg/day)	n	Mean Glans Penis Weight (mg) ± SD (CV)	Mean Cowper's Gland Weight (mg) ± SD (CV)	Mean LABC Weight (mg) ± SD (CV)	Mean Ventral Prostate Weight (mg) ± SD (CV)	Mean Seminal Vesicle Weight (mg) ± SD (CV)
14	Vehicle Control (Corn Oil)	0	8	53.0 ± 8.5 (16)	6.7 ± 1.9 (29)	166.4 ± 38.4 (23)	16.6 ± 4.1 (25)	48.1 ± 15.6 (32)
15	Octylsalate	235	8	53.7 ± 5.6 (10)	6.6 ± 2.0 (31)	156.9 ± 40.4 (26)	20.6 ± 9.1 (44)	47.2 ± 10.4 (22)
16	Octylsalate	750	6[1]	52.1 ± 7.9 (15)	6.5 ± 2.9 (44)	137.0 ± 19.8 (14)	20.1 ± 6.8 (34)	38.1 ± 14.6 (38)
17	Octocrylene	320	8	51.7 ± 6.2 (12)	6.1 ± 1.8 (29)	147.1 ± 18.7 (13)	15.4 ± 4.4 (28)	42.3 ± 10.8 (25)
18	Octocrylene	1000	8	57.5 ± 5.2 (9)	7.5 ± 1.4 (18)	151.7 ± 25.9 (17)	18.0 ± 4.1 (23)	41.7 ± 6.9 (17)
19[§]	Vehicle Control (Corn Oil) + TP (Positive Control)	0 + 0.4	8	**85.3 ± 10.6† (12)**	**44.1 ± 9.8† (22)**	**500.5 ± 77.4† (15)**	**197.0 ± 59.1† (30)**	**593.3 ± 193.2† (33)**

Abbreviations: SD - standard deviation; CV – coefficient of variation; LABC-levator ani plus bulbocavernous muscle complex, TP- testosterone propionate

†Statistically significant ($p<0.05$) compared to the vehicle control mean (t-test)

[§]Group served as the positive control for agonist assay and control in the antagonist assay

[1]Two animals found dead prior to necropsy, undetermined causes of death

Table 14. Androgen Antagonist; Androgen-dependent Tissue Weights

Group Number	Dose Group	Test/Reference Substance Dose Level (mg/kg/day)	n	Mean Glans Penis Weight (mg) ± SD (CV)	Mean Cowper's Gland Weight (mg) ± SD (CV)	Mean LABC Weight (mg) ± SD (CV)	Mean Ventral Prostate Weight (mg) ± SD (CV)	Mean Seminal Vesicle Weight (mg) ± SD (CV)
19[§]	Vehicle Control (Corn Oil) + TP	0 + 0.4	8	85.3 ± 10.6 (12)	44.1 ± 9.8 (22)	500.5 ± 77.4 (15)	197.0 ± 59.1 (30)	593.3 ± 193.2 (33)
20	Octylsalate + TP	75 + 0.4	8	98.7 ± 13.2 (13)	42.1 ± 7.1 (17)	490.1 ± 73.8 (15)	176.1 ± 42.7 (24)	550.0 ± 75.5 (14)
21	Octylsalate + TP	235 + 0.4	8	89.5 ± 11.6 (13)	44.0 ± 8.5 (19)	466.1 ± 60.7 (13)	183.6 ± 33.4[2] (18)	618.5 ± 110.3[2] (18)
22	**Octylsalate + TP[∞]**	750 + 0.4	7[1]	87.2 ± 10.7 (12)	46.5 ± 9.5 (20)	**341.4 ± 53.5* (16)**	158.1 ± 36.0 (23)	585.2 ± 160.2 (27)
23	Octocrylene + TP	100 + 0.4	8	88.5 ± 11.2 (13)	42.2 ± 6.1 (14)	500.4 ± 46.6 (9)	191.8 ± 42.8 (22)	584.0 ± 108.0 (18)
24	Octocrylene + TP	320 + 0.4	8	88.5 ± 12.6 (14)	44.9 ± 6.6 (15)	521.4 ± 51.9 (10)	206.2 ± 40.3 (20)	646.8 ± 115.5 (18)
25	Octocrylene + TP	1000 + 0.4	8	89.7 ± 11.5 (13)	44.3 ± 6.6 (15)	443.6 ± 36.2 (8)	176.0 ± 42.8 (24)	601.4 ± 123.2 (20)
26	FT + TP (Positive Control)	3 + 0.4	8	**66.9 ± 8.0† (12)**	**13.8 ± 2.3† (17)**	**225.4 ± 19.3† (9)**	**41.5 ± 13.1† (32)**	**89.8 ± 24.0† (27)**

Abbreviations: SD - standard deviation; CV – coefficient of variation; LABC-levator ani plus bulbocavernous muscle complex, TP- testosterone propionate, FT-flutamide

*Statistically significant ($p<0.05$) compared to the negative control mean (Dunnett's test)

†Statistically significant ($p<0.05$) compared to the negative control mean (t-test)

[§]Group served as the positive control for agonist assay and control in the antagonist assay

[∞]Statistically significant ($p<0.05$) multivariate analysis

[1]One animal found dead prior to necropsy, undetermined cause of death

[2] Mean weights of 7 tissues, one excluded due to possible transcription error

5.4. Performance Criteria

All tissue coefficients of variation (CVs) were below the maximum allowable limits for all test substances in both agonist and antagonist assays (Table 15).

Table 15. Maximum Allowable Coefficient of Variations

Tissue	Androgen Agonist	Androgen Antagonist
Glans Penis	22%	17%
Cowper's Gland	55%	35%
LABC	30%	20%
Ventral Prostate	45%	40%
Seminal Vesicle	40%	40%

Source: U.S. EPA (2009)

CONCLUSION

Two hundred and eight castrated male SD rats were allocated to 1 of 26 designated dose groups. To evaluate the test substances for agonist properties, animals were administered 1 of 2 dose levels (320 and 1000 mg/kg or 235 and 750 mg/kg) of test substance, the vehicle control, or an agonist reference substance (TP, 0.4 mg/kg). To evaluate test substances for antagonist properties animals were co-administered 1 of 3 dose levels (100, 320, and 1000 mg/kg or 75, 235, and 750 mg/kg) or FT (3 mg/kg, antagonist positive control) with TP.

Animals were dosed for 10 consecutive days via oral gavage (oxybenzone, octylmethoxycinnamate, octylsalate, octocrylene or FT) and in the antagonist group, subcutaneous injection (TP). Approximately 24-hours following the final dose administration, the animals were humanely euthanized; the glans penis, ventral prostate, levator ani plus bulbocavernous muscle (LABC), Cowper's gland, and seminal vesicle with coagulating gland with fluid were excised and weighed. Changes in androgen-dependent tissue weights were evaluated to determine the ability of oxybenzone, octylmethoxycinnamate, octylsalate, and octocrylene to act as androgen agonists/antagonists or inhibitors of 5α-reductase.

Oxybenzone administered at dose levels of 320 or 1000 mg/kg did not change final body weights, body weight gain, or increase any androgen-dependent tissue weights compared to the vehicle control (corn oil) animals in the agonist assay. In the androgen antagonist assay, final body weight and body weight gain were statistically decreased with 1000 mg/kg oxybenzone + TP compared to control rats (vehicle control + TP). Oxybenzone co-administered with TP was associated with a significant decrease in glans penis weight at 1000 mg/kg compared to the control group (p=0.0087), and a marginal decrease in the ventral prostate (p=0.0800), no other tissue weights were different. Multivariate analyses of all tissues indicated no significant difference from the controls.

Octylmethoxycinnamate administered at dose levels of 320 or 1000 mg/kg did not change final body weights, body weight gain, or increase any androgen-dependent tissue weights compared to the vehicle control (corn oil) animals in the agonist assay. Final body weight and body weight gain were not statistically decreased in rats administered octylmethoxycinnamate + TP at any dose level (up to 1000 mg/kg) in the antagonist assay. Co-administration of octylmethoxycinnamate with TP did not cause a significant decrease in androgen-dependent tissue weights, however the Cowper's gland and LABC weights were marginally significant (p=0.0753 and p=0.0692 respectively) following administration with 1000 mg/kg octylmethoxycinnamate + TP. Multivariate analyses of all tissues indicated no significant difference from the controls.

A significant decrease was observed in mean body weight gain in animals administered 750 mg/kg octylsalate compared to vehicle control rats in the agonist assay. Final body weight and androgen-dependent tissue weights were not different than controls at dose levels of 235 or 750 mg/kg in the agonist assay. In the androgen antagonist assay, final body weight and body weight gain was statistically decreased in rats administered 750

mg/kg octylsalate + TP compared to control rats (rats administered vehicle control + TP). Octylsalate (750 mg/kg) co-administered with TP was associated with a significant decrease in mean LABC weight as compared to the control group, no other tissue weights were significantly decreased; however, multivariate analysis showed a statistical difference when evaluating all five androgen-dependent tissues. Because reduced growth was observed in only in two tissues, it is unlikely that octylsalate is an androgen antagonist; however, additional screening data could be used in a weight of evidence approach to make that determination.

Octocrylene administered at dose levels of 320 or 1000 mg/kg did not cause any changes in final body weight, body weight gain, or increase any androgen-dependent tissue weights in the agonist assay. Co-administration of octocrylene + TP, at any dose level (up to 1000 mg/kg), did not cause any changes in final body weight, body weight gain, or decreases in androgen-dependent tissue weights in the antagonist assay.

Using the castrated rat model Hershberger Assay (OPPTS 890.1400), oral administration of oxybenzone, octylmethoxycinnamate, and octocrylene up to the limit dose of 1000 mg/kg did not show androgen agonist/antagonist activity, or properties reflective of 5α-reductase inhibition. Oral administration of octylsalate up to 750 mg/kg did not show androgen agonist activity; however, administration of octylsalate + TP at 750 mg/kg shows potential antagonist activity.

REFERENCES

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Richey, J. (2011b) Dose formulation developmental study report Octyl Salicylate. Battelle Project No: G005430-DZZ. NTP ChemTask No: CHEM10925. Unpublished study report prepared by Battelle.

Richey, J. (2011c) Dose formulation developmental study report 2-Hydroxy-4-methoxybenzophenone. Battelle Project No: G005430-EAB. NTP ChemTask No: CHEM10928. Unpublished study report prepared by Battelle.

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KEY PERSONNEL
Study Director:
Study Toxicologist:
Toxicology Study Manager:
Animal Facility Operations Manager:
Necropsy Manager:
Facility Veterinarian:
Health and Safety Manager:

Appendix I:

Certificate of Analysis

N135-232-
[redacted] 57971

From: [redacted]
To:
Subject: C of A for lot 7862K
Date: Tuesday, April 05, 2011 3:18:17 PM
Attachments: ATT00002.jpe

----- Forwarded by [redacted] MPBIO on 04/05/2011 03:12 PM -----

MP Biomedicals, LLC
29525 Fountain Parkway
Solon, Ohio 44139
Telephone: 440/337-1200
Toll Free: 800/854-0530
Fax: 440/337-1180
web: www.mpbio.com

Certificate of Analysis

Product Description: Corn Oil
Catalog Number: 901414
Lot: 7862K

Formula: N/A
CAS #: 8001-30-7
Physical Description: Yellow Oil
Formula Weight: N/A
Storage: Room Temperature

Test	Specification	Result
Identity	Passes	Passes

Color (Lovibond): 1.6

Free Fatty Acid: 0.045%
Peroxide: 0.5 meq/kg
Iodine: 126.85
Cold Test: 5.5 Clear & Brilliant
Additives: None

[redacted]

08/17/2010

[redacted]

MP Biomedicals, LLC.
Technical Director

This is an electronically generated document
mailto:biotech@mpbio.com
http://www.mpbio.com
Online Ordering, MSDSs, certificates of analysis and data sheets now available on our web site
Technical Service: 1-800-279-5490 (440-337-1200) Customer Service: 1-800-854-0530 (440-337-1200)

N135-232
[redacted]
5-19-11

SIGMA-ALDRICH®

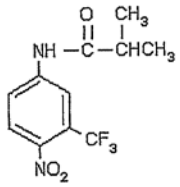
sigma-aldrich.com

3050 Spruce Street,Saint Louis,MO 63103,USA
Website: www.sigmaaldrich.com
Email USA: techserv@sial.com
Outside USA: eurtechserv@sial.com

Certificate of Analysis

Product Name:
Flutamide

Product Number:	**F9397**
Lot Number:	**021M1406V**
Brand:	SIGMA
CAS Number:	13311-84-7
MDL Number:	MFCD00072009
Formula:	C11H11F3N2O3
Formula Weight:	276.21 g/mol
Quality Release Date:	01 MAR 2011



Test	Specification	Result
Appearance (Color)	Yellow	Light Yellow
Appearance (Form)	Powder	Powder
Solubility (Color)	Yellow to Yellow-Green	Yellow - Green
Solubility (Turbidity) 50 mg/mL, EtOH	Clear to Hazy	Clear
Carbon	46.8 - 49.8%	48.0%
Nitrogen	9.8 - 10.4%	10.1%
Purity (TLC)	≥ 99%	100%

[redacted]
[redacted] Manager
Analytical Services
St. Louis, Missouri US

Sigma-Aldrich warrants, that at the time of the quality release or subsequent retest date this product conformed to the information contained in this publication. The current Specification sheet may be available at Sigma-Aldrich.com. For further inquiries, please contact Technical Service. Purchaser must determine the suitability of the product for its particular use. See reverse side of invoice or packing slip for additional terms and conditions of sale.

Version Number: 1

Page 1 of 1

N135-232 Page 1 of 1

[redacted] 5/19/11

Certificate of Analysis

SIGMA-ALDRICH

Product Name	Testosterone propionate, solid
Product Number	T1875
Product Brand	SIGMA
CAS Number	57-85-2
Molecular Formula	$C_{22}H_{32}O_3$
Molecular Weight	344.49

TEST	SPECIFICATION	LOT 048k1328 RESULTS
APPEARANCE	WHITE TO OFF-WHITE POWDER	WHITE POWDER
SOLUBILITY	CLEAR COLORLESS TO FAINT YELLOW SOLUTION AT 50MG/ML IN CHLOROFORM	CLEAR COLORLESS
IR SPECTRUM	CONSISTENT WITH STRUCTURE	CONFORMS
SPECIFIC ROTATION	+82 TO +87 DEG (C=2 IN DIOXANE AT 25DEGC)	+85 DEG *
PURITY BY HPLC	MINIMUM 98%	100.2% *
		* SUPPLIER INFORMATION
QC RELEASE DATE		APRIL 2008

[redacted] Manager
Quality Control
St. Louis, Missouri USA

http://www.sigmaaldrich.com/catalog/CertOfAnalysisPage.do?symbol=T1875&LotNo=048k1328&brandTest=... 5/19/2011

N135-232-
[redacted] 5-1971

CERTIFICATE OF ANALYSIS

Product 29116 **Octyl 4-methoxycinnamate,98%,stabilized**

Specifications

Appearance	CLEAR COLOURLESS TO YELLOW LIQUID
Infrared spectrometry	AUTHENTIC
Seperat. techn. GC	>97.5 %
Acid value	<1 mg KOH/g
Specific abs. A (1%/1cm)	>830 (at 307 to 308 nm in methanol)
Specific gravity	(25/25°C) 1.007 to 1.012
Refractive index	1.5430 to 1.5470 (20°C, 589 nm)
Stabilizer	0.05 to 0.1 % BHT

General Product Data

Version	00
CAS No.	5466-77-3
Molecular weight	290.39
Molecular formula	C18 H26 O3
Linear formula	
Flash point (°C)	193

Lot Specific Data for Lot No.: A0293319

Appearance	CLEAR COLOURLESS LIQUID
Infrared spectrometry	AUTHENTIC
Separat. techn. GC	99.8 %
Acid value	0.1 mg KOH/g
Specific abs. A (1%/1cm)	865 (at 307 to 308 nm in methanol)
Specific gravity	(25/25°C) 1.0096
Refractive index	1.5453 (20°C, 589 nm)
Stabilizer	0.09 % BHT

ACROS ORGANICS

[redacted]

Issued: 10-08-10 [redacted] **Quality Assurance Manager**

Acros Organics Geel West Zone 2, Janssen Pharmaceuticalaan 3a, B-2440 Geel, Belgium Tel +32 14/57.52.11 - Fax +32 14/59.34.34 Internet: http://www.acros.com
1 Reagent Lane, Fair Lawn, NJ 07410,USA Fax 201-796-1329

MRI-NTPThak 1492

A-1

[redacted]

Page 1 of 1

Certificate of Analysis

SIGMA-ALDRICH

Product Name	2-Ethylhexyl salicylate, ≥99%
Product Number	W514500
Product Brand	ALDRICH
CAS Number	118-60-5
Molecular Formula	$(HO)C_6H_4CO_2CH_2CH(C_2H_6)(CH_2)_3CH_3$
Molecular Weight	250.33

TEST	SPECIFICATION	LOT 44698PJ RESULTS
Appearance (Color)	Colorless	Colorless
Appearance (Form)	Liquid	Liquid
Refractive Index at 20 °C	1.500 - 1.504	1.502
Infrared spectrum	Conforms to Structure	Conforms
Purity (GC)	≥99.0 %	99.6 %
Color Test	≤100 APHA	10 APHA
Arsenic (As)	≤3.0 ppm	< 1.0 ppm
Cadmium (Cd)	≤1.0 ppm	< 1.0 ppm
Mercury (Hg)	≤1.0 ppm	< 1.0 ppm
Lead (Pb)	≤10.0 ppm	< 1.0 ppm
Specification Date:		DEC 2008
Date of QC Release:		DEC 2008
Print Date:		DEC 18 2008

[redacted]
Supervisor
Quality Control
Milwaukee, Wisconsin USA

http://www.sigmaaldrich.com/catalog/CertOfAnalysisPage.do?symbol=W514500&LotNo=44698... 8/30/2010

Battelle Study No. G005430-DYM 4

N135-232
[redacted] 51971

Page 1 of 1

Certificate of Analysis

SIGMA-ALDRICH

Product Name	2-Ethylhexyl 2-cyano-3,3-diphenylacrylate, 97%
Product Number	415820
Product Brand	ALDRICH
CAS Number	6197-30-4
Molecular Formula	$(C_6H_5)_2C=C(CN)CO_2CH_2CH(C_2H_5)(CH_2)_3CH_3$
Molecular Weight	361.48

TEST	SPECIFICATION	LOT 01697MJ RESULTS
Appearance (Color)	Yellow	Yellow
Appearance (Form)	Viscous Liquid	Viscous Liquid
Infrared spectrum	Conforms to Structure	Conforms
Purity (GC)	≥96.5 %	99.2 %
Specification Date:		OCT 2008
Date of QC Release:		OCT 2008
Print Date:		OCT 22 2008

[redacted]

[redacted] Supervisor
Quality Control
Milwaukee, Wisconsin USA

http://www.sigmaaldrich.com/catalog/CertOfAnalysisPage.do?symbol=415820&LotNo=01697MJ... 8/30/2010

N135-232
[redacted]5-1911

IVYCHEM

IVY FINE CHEMICALS
http://www.ivychem.com

CERTICATE OF ANALYSIS

Product Name	**2-HYDROXY-4-METHOXYBENZOPHENONE**		
Synonym	Oxybenzone		
Catalog Number	HH13-026		
CAS Number	131-57-7		
Batch Number	20100801	**Quantity**	200 KG
Manu. Date	August 2, 2010	**Expiry Date**	August 1, 2012
Date of Report	August 2, 2010	**Package**	
Quality Specifications	Specifications (In house)		

Test	**Standard**	**Results**
Appearance	Light yellow to green crystalline powder	Light yellow crystalline powder
Assay (HPLC)	98% min	99.92%
Melting Point	62 °C to 65 °C	63.8 °C to 64.8 °C
Loss on Drying	0.5% max	0.07%
Heavy Metals	<= 5 ppm	2.9 ppm
Conclusion: **Conform**		

N135-232 [redacted] 6.24.11

SMITHERS VISCIENT
formerly Smithers Springborn

CERTIFICATE OF ANALYSIS

STUDY INFORMATION

Study Sponsor: Integrated Laboratory Systems, Inc.
Address: 601 Keystone Drive, Suite 100
Durham, North Carolina 27713

Test Substance: Testosterone propionate

SMV Sample ID:	Purity:
CSI-1-30A-A	100%
CSI-1-30A-B	100%
CSI-1-30A-C	100%
Mean	**100%**
Standard Deviation	**0.0%**
% CV	**0.0**

Test Facility: Smithers Viscient
Address: 790 Main Street
Wareham, MA 02571-1037
508-295-2550

Expiration Date: 17 March 2012

Additional information: The percent purity of a 1.00 mg/mL stock solution was determined using high performance liquid chromatography with ultraviolet detection (HPLC/UV). The percent of the active ingredient, testosterone propionate, was determined on 17 March 2011. This data was collected using good laboratory practice standards and was assigned study number 13974.6101. This analysis confirms the original purity of 100.2% since the mean percent purity falls within ± 1% of the original purity.

SMITHERS VISCIENT

[redacted] 6/6/11
Study Director Date

[redacted] 6/6/11
Quality Assurance Auditor Date

NBS-232 [redacted] 10-2611

SMITHERS VISCIENT
formerly Smithers Springborn

CERTIFICATE OF ANALYSIS

STUDY INFORMATION

Study Sponsor: Integrated Laboratory Systems, Inc.
Address: 601 Keystone Drive, Suite 100
Durham, North Carolina 27713

Test Substance: Flutamide
Lot Number: 107k1293
Supplier Name: Integrated Laboratory Systems
Study Number: 13974.6102

SMV Sample ID:	Purity:
4895A-A	99.5%
4895A-B	99.5%
4895A-C	99.5%
Mean	**99.5%**
Standard Deviation	**0.00752%**
% CV	**0.00756**

Test Facility: Smithers Viscient
Address: 790 Main Street
Wareham, MA 02571-1037
508-295-2550

Expiration Date: 15 February 2012

Additional information: The percent purity of a 1.00 mg/mL stock solution was determined using high performance liquid chromatography with ultraviolet detection (HPLC/UV). The percent of the active ingredient, flutamide, was determined on 17 March 2011. This data was collected using good laboratory practice standards and was assigned study number 13974.6102. This analysis confirms the original purity of 99% since the mean percent purity falls within ± 1% of the original purity.

SMITHERS VISCIENT

[redacted] 7/22/11
Study Director Date

[redacted] 20 July 2011
Quality Assurance Auditor Date

Smithers Viscient LLC
www.smithersviscient.com
790 Main Street | Wareham, MA 02571 | p 508.295.2550
2900 Quakenbush Road | Snow Camp, NC 27349 | p 336.376.0141

Appendix II:

Dose Formulation Analysis

Battelle
The Business of Innovation

BATTELLE-FA

Analytical Chemistry Services for the NTP
NIH Contract No.: HHSN273201000016C
Battelle Project No.: G006623-EEB
NTP ChemTask No.: CHEM11267
CAS No.: 131-57-7

FORMULATION ANALYSIS OF 2-HYDROXY-4-METHOXYBENZOPHENONE (HMB) IN CORN OIL

June 9, 2011

Prepared By:

[redacted]
Study Director

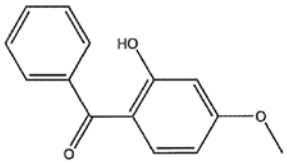
Approved By:

[redacted]
Steven W. Graves, B.S.
Principal Investigator

Submitted to:

[redacted]
National Institute of Environmental Health Sciences
111 T.W. Alexander Drive
P.O. Box 12233
Research Triangle Park, NC 27709-2233

FORMULATION ANALYSIS OF
2-HYDROXY-4-METHOXYBENZOPHENONE (HMB) IN CORN OIL

<table>
<tr><td colspan="2">CAS No.: 131-57-7</td><td>Lot No.: 20100801 [Ivy Fine Chemicals, 99.92% pure by high performance liquid chromatography (HPLC)]</td></tr>
<tr><td colspan="2">Battelle Chemical ID Code: 292</td><td>Samples Analyzed:
<u>Batch</u> — <u>Concentration</u>
N135-11-94-5511A — 0 mg/mL
11-29-1 T — 20 mg/mL
11-29-1 M — 20 mg/mL
11-29-1 B — 20 mg/mL
11-29-2 T — 64 mg/mL
11-29-2 M — 64 mg/mL
11-29-2 B — 64 mg/mL
11-29-3 T — 200 mg/mL
11-29-3 M — 200 mg/mL
11-29-3 B — 200 mg/mL</td></tr>
<tr><td colspan="2">Battelle Task No.: 16-292-FA-314</td><td>Sample Receipt Dates: 5/6 and 5/9/11</td></tr>
<tr><td colspan="2">NTP Task No.: CHEM11267</td><td>Submitter: Integrated Laboratory Systems, Inc. (ILS)</td></tr>
<tr><td colspan="2">Program Supported: TOX</td><td>Study Lab: ILS</td></tr>
<tr><td colspan="2">Analysis Dates: 5/9-5/10/11</td><td>Mix Date: 5/5/11</td></tr>
<tr><td colspan="2">Interim Results Date: 5/11/11</td><td>Receipt Condition: Good</td></tr>
<tr><td colspan="2">SOPs: CSCSPEC.II-051-00, Standard Operating Procedure for the Analysis of 2-Hydroxy-4-Methoxybenzophenone (HMB) Formulations in Corn Oil</td><td>Shipping Container: Total of ten amber glass vials
Storage Conditions (@ Battelle): Room Temperature (~25°C)</td></tr>
<tr><td>Structure
 
</td><td>Mol. Wt.
228.25 g/mol</td><td>Mol. Formula
$HOC_6H_3(OCH_3)COC_6H_5$</td></tr>
</table>

EXECUTIVE SUMMARY

Formulations of 2-hydroxy-4-methoxybenzophenone (HMB) in corn oil at target concentrations of 0, 20, 64, and 200 mg/mL were prepared by ILS and analyzed by Battelle to determine their concentration and homogeneity prior to administration in support of a TOX study.

The concentrations of all formulations containing HMB were within 10 percent of target, the National Toxicology Program (NTP) acceptance limit. The relative standard deviation (RSD) values were also within the specified acceptance limit. They also met the acceptance criteria for homogeneity. The 0 mg/mL formulation contained no detectable HMB. All other quality criteria stated in the SOP were within acceptance limits.

QUALITY ASSURANCE STATEMENT

FORMULATION ANALYSIS OF
2-HYDROXY-4-METHOXYBENZOPHENONE (HMB) IN CORN OIL

NTP ChemTask No.: CHEM11267
Battelle Project No.: G006623-EEB
Battelle Task No.: 16-292-FA-314

Listed below are the phases and/or procedures performed by Battelle that were reviewed by the Quality Assurance Unit (QAU) during performance of the task described in this report. Adverse findings, if any, were reported to the Study Director at the time of review.

Critical Phase Inspected	Date Inspected	Date Reported to Study Director and Management
Formulation analysis	5/9/11	5/10/11
Audit study file	5/24/11	5/24/11
Audit final analytical report	5/24/11	5/24/11

This report reflects the procedures and raw data generated in this study.

In addition to the study-specific audits/inspections cited above, routine inspections of the general facilities and equipment were performed by the QAU and reports were submitted to management as follows:

Facility/Equipment	Date Inspected	Date of Report to Management
Chemistry Technical Center Inspection	12/2, 12/15/08	12/2, 12/22/08
	12/16, 12/23/09	12/16, 12/31/09
	12/28, 12/30/10	12/30/10

[redacted] 6-1-11
Quality Assurance Unit Date

COMPLIANCE STATEMENT

This study was conducted in accordance with the Food and Drug Administration's (FDA's) Good Laboratory Practice (GLP) regulations (21 CFR, Part 58), with the exception of archival of study records at the close of the study. These records are gathered, microfiched, and archived periodically for finalized studies for this program.

[redacted] 6/9/11

Study Director Date

Date Study Initiated (Date Protocol Signed): May 4, 2011
Date Study Completed (Date Final Report Signed): June 9, 2011

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

1.0 INTRODUCTION

This report contains:

- A description of the analyses of the formulations for concentration and homogeneity
- Results from the analysis
- Figures
- Conclusions.

This work was performed at Battelle, 505 King Avenue, Columbus, OH 43201, and supports a TOX study.

2.0 FORMULATION SAMPLES

Formulation samples prepared in corn oil (approximately 10 mL each) were received from ILS on May 6 and May 9, 2011. The samples were formulated on May 5, 2011 with an expiration date of June 17, 2011. They were identified as being from ILS Protocol No. N135-231/232 and had the following concentrations and log numbers.

Table 1. Formulation Samples

Concentration (mg/mL)	ILS Log No.
0	N135-11-94-5511A
20	11-29-1 T
20	11-29-1 M
20	11-29-1 B
64	11-29-2 T
64	11-29-2 M
64	11-29-2 B
200	11-29-3 T
200	11-29-3 M
200	11-29-3 B

All samples that were supplied by ILS in Table 1 were analyzed.

3.0 FORMULATION ANALYSIS FOR CONTENT AND HOMOGENEITY

The formulations were analyzed for HMB according to CSCSPEC.II-051-00, "Standard Operating Procedure for the Analysis of 2-Hydroxy-4-Methoxybenzophenone (HMB) Formulations in Corn Oil." This SOP was based on work originally conducted under the preliminary chemical studies (PCS) task for

HMB, Battelle Study No. G005430-DYS, NTP ChemTask No. CHEM10881 and the dose formulation development (DFD) task for HMB in corn oil, Battelle Study No. G005430-EAB, NTP ChemTask No. CHEM10928. The experimental limit of quantitation (ELOQ) is 0.01 mg/mL, which is the nominal concentration of the lowest standard for this task. This section describes the method, results, and conclusions.

3.1 Preparation of Diluted Vehicle Solution

The diluted vehicle solution was prepared by adding 1 mL of corn oil to a 100-mL volumetric flask and dissolving it in and diluting the flask to volume with acetone. The flask was sealed and the contents mixed well.

3.2 Preparation of Internal Standard (IS)

IS solution was prepared by weighing approximately 250 mg of benzophenone into a 50-mL volumetric flask and dissolving it in and diluting the flask to volume with acetone. The flask was sealed and the contents mixed well.

3.3 Preparation of Standards and Blanks

3.3.1 Stocks

The amounts of HMB shown in Table 2 were weighed into individual 50-mL volumetric flasks. The chemical was dissolved in and the flask diluted to volume with acetone. The flasks were sealed and the contents mixed well.

Table 2. Preparation of Stocks

ID	Target Concentration (mg/mL)	Target Weight (mg)
A	1.25	62.5 ± 2
B	1	50 ± 2

3.3.2 Spiking Solutions

The volumes of A and B indicated in Table 3 were pipetted into individual volumetric flasks. The flasks were diluted to volume with acetone, sealed, and the contents mixed well. A single solution was prepared at all concentrations.

Table 3. Preparation of Spiking Solutions

ID	Target Concentration (mg/mL)	Source	Source Volume (mL)	Final Volume (mL)
C	0.75	A	3	5
D	0.40	B	2	5
E	0.25	A	2	10
F	0.10	B	1	10

3.3.3 Vehicle/Calibration Standards

One (1) mL from each solution A - F was pipetted into individual 10-mL volumetric flasks. One (1) mL of diluted vehicle and 0.1 mL of IS was added to each volumetric flask. The flasks were diluted to volume with acetone, sealed, and the contents mixed well. This produced single vehicle standards at target concentrations of 0.125, 0.1, 0.075, 0.04, 0.025, and 0.01 mg/mL.

3.3.4 Preparation of Blanks

Vehicle Blank

A single blank was prepared by pipetting 1 mL of diluted vehicle into a 10-mL volumetric flask and diluting to volume with acetone. The flask was sealed and the contents mixed well.

Vehicle Blank with IS

A single blank with IS was prepared by pipetting 1 mL of diluted vehicle and 0.1 mL of IS into a 10-mL volumetric flask and diluting to volume with acetone. The flask was sealed and the contents mixed well.

3.4 Preparation of Formulation Samples For Analysis

3.4.1 Density Determination

For the 0, 20, and 64 mg/mL formulation concentrations, a tared 5-mL volumetric flask was filled to volume with the formulation. The weight of the filled flask was recorded and divided by five to obtain the density of the formulation. For the 200 mg/mL formulation, a tared 1-mL volumetric flask was filled to volume with formulation. The density of this formulation was the weight of the flask contents.

3.4.2 Preparation of Formulation Samples

All formulation samples had a stir bar added to the container. The 200 mg/mL formulations were shaken and vortexed to ensure a uniform sample. The

formulations were stirred for at least 5 minutes prior to use. If necessary, the contents of the vial were transferred to another amber container to allow sufficient stirring before taking samples.

For each formulation with a concentration equal to or less than 100 mg/mL, a 1-mL aliquot was transferred to three previously tared 10-mL volumetric flasks. The weight of the aliquot was recorded. The flasks were diluted to volume with acetone, sealed, and the contents mixed well.

For each formulation with a concentration of 100 mg/mL or greater, a 1-mL aliquot was transferred to three previously tared 25-mL volumetric flasks. The weight of the aliquot was recorded. A 1.5-mL aliquot of corn oil was added to each flask. The flasks were diluted to volume with acetone, sealed, and the contents mixed well.

A 1-mL aliquot of the diluted formulation was transferred to individual 100-mL volumetric flasks. A 1-mL aliquot of IS was added to each flask. The flasks were diluted to volume with acetone, sealed, and the contents mixed well.

3.5 Analysis

Aliquots of each vehicle standard, blank, and sample were transferred into autosampler vials with minimal headspace and the vials were sealed. Single injections were made from each vial using the gas chromatography (GC) instrumental system with flame ionization detection (FID) as shown in Table 4.

Table 4. GC System

Instrument	Agilent 6890 (Santa Clara, CA)
Data System	Thermo Fisher Scientific Atlas, Version 8.2
Column	Restek (Bellefonte, PA), Rtx-5, 30 m × 0.32 mm (ID), 1.0 µm film thickness
Oven Temperature	80°C, hold for 1 minute, increase at 20°C/minute to 200°C, no hold, increase at 10°C/minute to 280°C, hold for 10 minutes
Hydrogen Flow	28 mL/minute
Air Flow Rate	280 mL/minute
Carrier Flow Rate	Helium at 3 mL/minute
Detector Temperature	280°C
Injector Temperature	260°C
Detector Type	FID
Injection Volume/Mode	1 µL/Splitless
Run Time	25 minutes

Representative overlaid chromatograms from a high and low standard, a blank with IS, and a blank are shown in Figure 1.

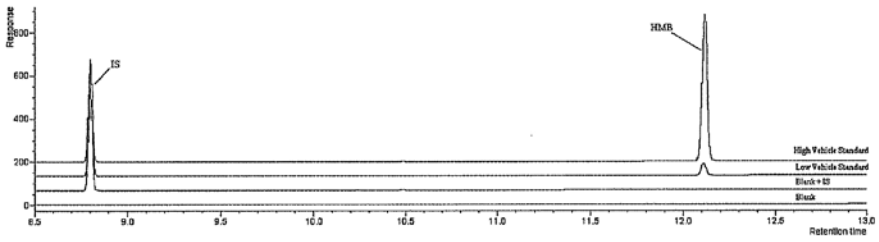


Figure 1. Representative Overlaid Chromatograms

3.6 Calculations

The integration of the HMB and IS peaks done by the chromatography data system was evaluated and manually adjusted, if necessary, to achieve consistent integration. The response ratio of the HMB peak area divided by the IS peak area was calculated. A linear regression equation with 1/x weighting was calculated relating the response ratio of the standards to their nominal concentrations. The determined concentration was calculated for each standard and sample using the regression equation, the response ratio for that standard or sample, the sample weight and density, and any dilution factor for the samples. The relative error (RE) for each standard and sample was calculated by subtracting the target concentration from its determined concentration, dividing the difference by the target concentration, and multiplying the result by 100. The average concentration, average RE, standard deviation, and RSD for each formulation location were calculated using the individual values. The grand average concentration, grand RE, grand standard deviation, and grand RSD for each formulation were calculated using the average concentration for each location.

At least one extra significant figure was carried through all calculations to minimize rounding errors, therefore, the summary statistics presented in the tables may not be exactly reproduced using the rounded input values shown.

3.7 Results

The results of the formulation analyses are shown in Table 5. The 0 mg/mL formulations were all below the limit of quantitation (BLOQ). The standard curve is shown in Figure 2.

Table 5. Corn Oil Homogeneity Formulation Sample Analysis Results

Target Concentration (Sample ID)	Location	Corrected Determined Concentration (mg/mL)	Average Corrected Determined Concentration (mg/mL)	s (mg/mL)	RSD	RE	Avg. RE	Grand Average Concentration (mg/mL)	Grand s (mg/mL)	Grand RSD	Grand RE
20 mg/mL (11-29-1B)	Bottom A	20.3	20.2	0.1	0.5	1.5	0.8	20.2	0.1	0.3	0.8
	Bottom B	20.1				0.5					
	Bottom C	20.1				0.5					
20 mg/mL (11-29-1M)	Middle A	20.2	20.1	0.2	1.0	1.0	0.3				
	Middle B	19.9				-0.5					
	Middle C	20.1				0.5					
20 mg/mL (11-29-1T)	Top A	20.2	20.2	0.1	0.5	1.0	1.0				
	Top B	20.3				1.5					
	Top C	20.1				0.5					
64 mg/mL (11-29-2B)	Bottom A	64.0	64.1	0.2	0.3	0.0	0.1	63.9	0.2	0.3	-0.2
	Bottom B	63.9				-0.2					
	Bottom C	64.3				0.5					
64 mg/mL (11-29-2M)	Middle A	64.2	63.9	0.3	0.5	0.3	-0.2				
	Middle B	63.8				-0.3					
	Middle C	63.6				-0.6					
64 mg/mL (11-29-2T)	Top A	63.8	63.7	0.5	0.8	-0.3	-0.4				
	Top B	64.2				0.3					
	Top C	63.2				-1.3					
200 mg/mL (11-29-3B)	Bottom A	208	208	1	0.5	4.0	4.2	211	2.5	1.2	5.3
	Bottom B	208				4.0					
	Bottom C	209				4.5					
200 mg/mL (11-29-3M)	Middle A	211	211	0	0.0	5.5	5.5				
	Middle B	211				5.5					
	Middle C	211				5.5					
200 mg/mL (11-29-3T)	Top A	214	213	1	0.5	7.0	6.7				
	Top B	213				6.5					
	Top C	213				6.5					

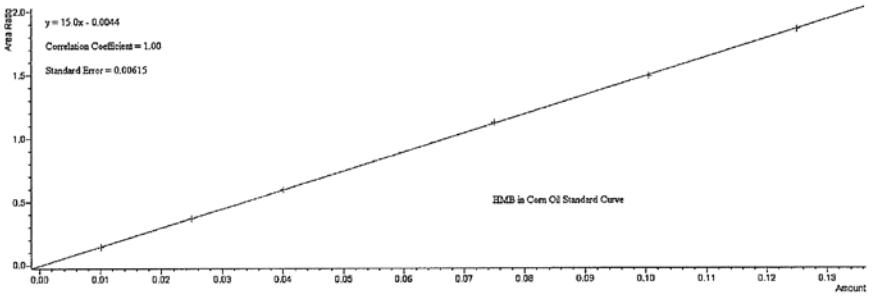


Figure 2. Standard Curve

3.8 Conclusions

The concentrations of all the formulations containing HMB were within 10 percent of target, the NTP acceptance limit. The formulations were also homogeneous. The 0 mg/mL formulation contained no detectable HMB. All other quality criteria stated in the SOP were within acceptance limits.

4.0 ACKNOWLEDGMENTS

[redacted] conducted the analysis. [redacted] wrote the report. [redacted] reviewed the analysis raw data for completeness and accuracy.

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BATTELLE-FA

Analytical Chemistry Services for the NTP
NIH Contract No.: HHSN273201000016C
Battelle Project No.: G006623-EEP
NTP ChemTask No.: CHEM11298
CAS No.: 6197-30-4

FORMULATION ANALYSIS OF
2-ETHYLHEXYL 2-CYANO-3,3-DIPHENYLACRYLATE (OCTOCRYLENE)
IN CORN OIL

June 23, 2011

Prepared By:

[redacted]
Study Director

Approved By:

[redacted]
For Steven W. Graves, B.S.
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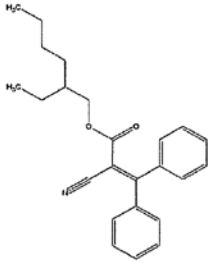
Research Triangle Park, NC 27709-2233

This PDF File is an Exact Copy of the Report
Signature: [redacted]
Date: 6/28/11

FORMULATION ANALYSIS OF
2-ETHYLHEXYL 2-CYANO-3,3-DIPHENYLACRYLATE (OCTOCRYLENE)
IN CORN OIL

<table>
<tr><td colspan="2">CAS No.: 6197-30-4</td><td>Lot No.: 01697MJ (Sigma-Aldrich, 99.2% purity by GC)</td></tr>
<tr><td colspan="2">Battelle Chemical ID Code: 335</td><td>Samples Analyzed:
<u>Batch</u> <u>Concentration</u>
11-31-3T 20 mg/mL
11-31-3M 20 mg/mL
11-31-3B 20 mg/mL
11-31-4T 64 mg/mL
11-31-4M 64 mg/mL
11-31-4B 64 mg/mL
11-31-5T 200 mg/mL
11-31-5M 200 mg/mL
11-31-5B 200 mg/mL</td></tr>
<tr><td colspan="2">Battelle Task No.: 16-335-FA-321</td><td>Sample Receipt Date: 6/2/11</td></tr>
<tr><td colspan="2">NTP Task No.: CHEM11298</td><td>Submitter: Integrated Laboratory Systems, Inc. (ILS)</td></tr>
<tr><td colspan="2">Program Supported: TOX</td><td>Study Lab: ILS</td></tr>
<tr><td colspan="2">Analysis Dates: 6/3-6/4/11</td><td>Mix Date: 6/1/11</td></tr>
<tr><td colspan="2">Interim Results Date: 6/6/11</td><td>Receipt Condition: Samples received on thawed ice packs and warm on receipt. Vial labels soaked due to a broken thawed ice pack, however information on label was still legible, but appear uncompromised.</td></tr>
<tr><td colspan="2" rowspan="2">SOPs: CSCSPEC.II-049-01, Standard Operating Procedure (SOP) for the Analysis of 2-Ethylhexyl 2-Cyano-3,3-Diphenylacrylate (Octocrylene) Formulations in Corn Oil</td><td>Shipping Container: Nine glass vials</td></tr>
<tr><td>Storage Conditions (@ Battelle): Refrigerated (~5°C)</td></tr>
<tr><td>Structure
  </td><td>Mol. Wt.
361.48 g/mol</td><td>Mol. Formula
$C_{24}H_{27}NO_2$</td></tr>
</table>

EXECUTIVE SUMMARY

Formulations of octocrylene in corn oil at target concentrations of 20, 64, and 200 mg/mL were prepared by ILS and analyzed by Battelle to determine their concentration and homogeneity prior to administration in support of a TOX study.

The concentrations of all the formulations containing octocrylene were within 10 percent of target, the National Toxicology Program (NTP) acceptance limit. The relative standard deviation (RSD) values were also within the specified acceptance limit. All formulations were found to be homogeneous. All other quality criteria stated in the SOP were within acceptance limits.

QUALITY ASSURANCE STATEMENT

FORMULATION ANALYSIS OF
2-ETHYLHEXYL 2-CYANO-3,3-DIPHENYLACRYLATE (OCTOCRYLENE)
IN CORN OIL

NTP ChemTask No.: CHEM11298
Battelle Project No.: G006623-EEP
Battelle Task No.: 16-335-FA-321

Listed below are the phases and/or procedures performed by Battelle that were reviewed by the Quality Assurance Unit (QAU) during performance of the task described in this report. Adverse findings, if any, were reported to the study director at the time of review.

Critical Phase Inspected	Date Inspected	Date Reported to Study Director and Management
Formulation analysis	6/3/11	6/3/11
Audit study file	6/15/11	6/15/11
Audit final analytical report	6/15/11	6/15/11

This report reflects the procedures and raw data generated in this study.

In addition to the study-specific audits/inspections cited above, routine inspections of the general facilities and equipment were performed by the QAU and reports were submitted to management as follows:

Facility/Equipment	Date Inspected	Date of Report to Management
Chemistry Technical Center Inspection	12/2, 12/15/08	12/2, 12/22/08
	12/16, 12/23/09	12/16, 12/31/09
	12/28, 12/30/10	12/30/10

[redacted] 6-23-11
Quality Assurance Unit Date

COMPLIANCE STATEMENT

This study was conducted in accordance with the Food and Drug Administration's (FDA's) Good Laboratory Practice (GLP) regulations (21 CFR, Part 58), with the exception of archival of study records at the close of the study. These records are gathered, microfiched, and archived periodically for finalized studies for this program.

[redacted] 6-23-11

Study Director Date

Date Study Initiated (Date Protocol Signed): May 31, 2011
Date Study Completed (Date Final Report Signed): June 23, 2011

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

1.0 INTRODUCTION

This report contains:

- A description of the analyses of the formulations for concentration and homogeneity
- Results from the analysis
- Figures
- Conclusions.

This work was performed at Battelle, 505 King Avenue, Columbus, OH 43201, and supports a TOX study.

2.0 FORMULATION SAMPLES

Formulation samples prepared in corn oil (approximately 10 mL each) were received from ILS on June 2, 2011. The samples were formulated on June 1, 2011 with an expiration date of July 13, 2011. They were identified as being from ILS Protocol No. N135-232 and had the following concentrations and log numbers.

Table 1. Formulation Samples

Concentration (mg/mL)	ILS Log No.
20	11-31-3T
20	11-31-3M
20	11-31-3B
64	11-31-4T
64	11-31-4M
64	11-31-4B
200	11-31-5T
200	11-31-5M
200	11-31-5B

All analysis samples that were supplied by ILS in Table 1 were analyzed.

3.0 FORMULATION ANALYSIS FOR CONTENT AND HOMOGENEITY

The formulations were analyzed for octocrylene according to CSCSPEC.II-049-01, "Standard Operating Procedure (SOP) for the Analysis of 2-Ethylhexyl 2-Cyano-3,3-Diphenylacrylate (Octocrylene) Formulations in Corn Oil." This SOP was based on work originally conducted under the preliminary chemical studies (PCS) task for octocrylene, Battelle Study No. G005430-DYT, NTP ChemTask No. CHEM10882

and the dose formulation developmental (DFD) task for octocrylene in corn oil, Battelle Study No. G005430-DZY, NTP ChemTask No. CHEM10924. The experimental limit of quantitation (ELOQ) is 0.01 mg/mL, which is the nominal concentration of the lowest standard for this task. This section describes the method, results, and conclusions.

3.1 Preparation of Diluted Vehicle Solution

The diluted vehicle solution was prepared by adding 1 mL of corn oil to a 100-mL volumetric flask and dissolving it in and diluting the flask to volume with acetone. The flask was sealed and the contents mixed well.

3.2 Preparation of Internal Standard (IS)

IS solution was prepared by weighing approximately 250 mg of benzophenone into a 50-mL volumetric flask and dissolving it in and diluting the flask to volume with acetone. The flask was sealed and the contents mixed well.

3.3 Preparation of Standards and Blanks

3.3.1 Stocks

The amounts of octocrylene shown in Table 2 were weighed into individual 50-mL volumetric flasks. The chemical was dissolved in and the flasks diluted to volume with acetone. The flasks were sealed and the contents mixed well.

Table 2. Preparation of Stocks

ID	Target Concentration (mg/mL)	Target Weight (mg)
A	1.25	62.50 ± 2
B	1	50.00 ± 2

3.3.2 Spiking Solutions

The volumes of the A and B indicated in Table 3 were pipetted into individual volumetric flasks. The flasks were diluted to volume with acetone, sealed, and the contents mixed well. A single solution was prepared at all concentrations.

Table 3. Preparation of Spiking Solutions

ID	Target Concentration (mg/mL)	Source	Source Volume (mL)	Final Volume (mL)
C	0.75	A	3	5
D	0.40	B	2	5
E	0.25	A	2	10
F	0.10	B	1	10

3.3.3 Vehicle/Calibration Standards

One (1) mL from each solution A to F was pipetted into individual 10-mL volumetric flasks. One (1) mL of diluted vehicle and 0.1 mL of IS was added to each volumetric flask. The flasks were diluted to volume with acetone, sealed, and the contents mixed well. This produced single vehicle standards at target concentrations of 0.125, 0.1, 0.075, 0.04, 0.025, and 0.01 mg/mL.

3.3.4 Preparation of Blanks

Vehicle Blank

A single blank was prepared by pipetting 1 mL of diluted vehicle into a 10-mL volumetric flask and diluting to volume with acetone. The flask was sealed and the contents mixed well.

Vehicle Blank with IS

A single blank with IS was prepared by pipetting 1 mL of diluted vehicle and 0.1 mL of IS into a 10-mL volumetric flask and diluting to volume with acetone. The flask was sealed and the contents mixed well.

3.4 Preparation of Formulation Samples For Analysis

3.4.1 Density Determination

For each formulation concentration, a tared 5-mL volumetric flask was filled to volume with the formulation. The weight of the filled flask was recorded and divided by five to obtain the density of the formulation.

3.4.2 Preparation of Formulation Samples

All formulation samples had a stir bar added to the container. The formulations were stirred for at least 5 minutes prior to use.

For each formulation sample with a concentration less than or equal to 100 mg/mL, a 1-mL aliquot was transferred to three previously tared 10-mL volumetric flasks. The weight of the aliquot was recorded. The flasks were diluted to volume with acetone, sealed, and the contents mixed well.

For each formulation sample with a concentration greater than 100 mg/mL, a 1-mL aliquot was transferred to three previously tared 25-mL volumetric flasks. The weight of the aliquot was recorded. A 1.5-mL aliquot of corn oil was added to each flask. The flasks were diluted to volume with acetone, sealed, and the contents mixed well.

A 1-mL aliquot of each diluted formulation was transferred to individual 100-mL volumetric flasks. A 1-mL aliquot of IS was added to each flask. The flasks were diluted to volume with acetone, sealed, and the contents mixed well.

3.5 Analysis

Aliquots of each vehicle standard, blank, and diluted sample were transferred into autosampler vials with minimal headspace and the vials were sealed. Single injections were made from each vial using the gas chromatography (GC) instrumental system with flame ionization (FID) detection as shown in Table 4.

Table 4. GC System

Instrument	Agilent 6890 (Santa Clara, CA)
Data System	Thermo Fisher Scientific Atlas, Version 8.2
Column	Restek (Bellefonte, PA), Rtx-5, 30 m × 0.32 mm (ID), 1.0 µm film thickness
Oven Temperature	80°C, hold for 1 minute, increase at 20°C/minute to 200°C, no hold, increase at 10°C/minute to 280°C, hold for 10 minutes
Hydrogen Flow	28 mL/minute
Air Flow Rate	280 mL/minute
Nitrogen Makeup Flow	25 mL/minute
Carrier Flow Rate	Helium at 3 mL/minute
Detector Temperature	280°C
Injector Temperature	260°C
Detector Type	FID
Injection Volume	1 µL
Injection Mode	Splitless
Run Time	25 minutes

Representative overlaid chromatograms from a high and low standard, a blank with IS, and a blank are shown in Figure 1.

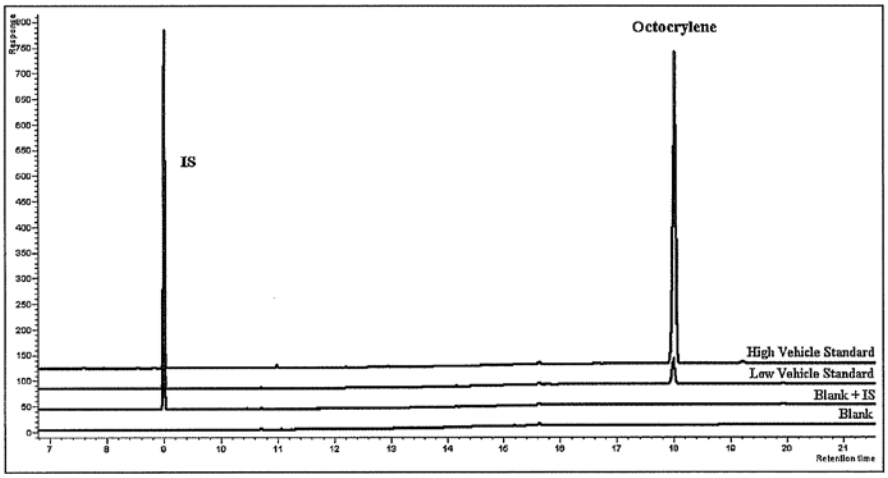


Figure 1. Representative Overlaid Chromatograms

3.6 Calculations

The integration of the octocrylene and IS peaks done by the chromatography data system was evaluated and manually adjusted, if necessary, to achieve consistent integration. The response ratio of the octocrylene peak area divided by the IS peak area was calculated. A linear regression equation with 1/x weighting was calculated relating the response ratio of the standards to their nominal concentrations. The determined concentration was calculated for each standard and sample using the regression equation, the response ratio for that standard or sample, the sample weight and density, and any dilution factor for the samples. The relative error (RE) for each standard and sample was calculated by subtracting the target concentration from its determined concentration, dividing the difference by the target concentration, and multiplying the result by 100. The average concentration, average RE, standard deviation, and RSD for each formulation location were calculated using the individual values. The grand average concentration, grand RE, grand standard deviation, and grand RSD for each formulation were calculated using the average concentration for each location.

At least one extra significant figure was carried through all calculations to minimize rounding errors, therefore, the summary statistics presented in the tables may not be exactly reproduced using the rounded input values shown.

3.7 Results

The results of the formulation analyses are shown in Table 5. The standard curve is shown in Figure 2.

Table 5. Corn Oil Homogeneity Formulation Sample Analysis Results

Target Concentration (Sample ID)	Sample No.	Determined Concentration (mg/mL)	Average Determined Concentration (mg/mL)	s (mg/mL)	RSD	RE	Average RE	Grand Average Determined Concentration (mg/mL)	Grand s (mg/mL)	Grand RSD	Grand RE
20 mg/mL (11-31-3T)	Top A	20.0	20.0	0.0	0.0	0.0	0.0	19.9	0.3	1.3	-0.5
	Top B	20.0				0.0					
	Top C	20.0				0.0					
20 mg/mL (11-31-3M)	Middle A	19.4	19.6	0.2	1.0	-3.0	-1.8				
	Middle B	19.8				-1.0					
	Middle C	19.7				-1.5					
20 mg/mL (11-31-3B)	Bottom A	19.9	20.1	0.2	1.0	-0.5	0.3				
	Bottom B	20.3				1.5					
	Bottom C	20.0				0.0					
64 mg/mL (11-31-4T)	Top A	61.5	61.7	0.2	0.3	-3.9	-3.6	62.1	0.5	0.7	-3.0
	Top B	61.8				-3.4					
	Top C	61.8				-3.4					
64 mg/mL (11-31-4M)	Middle A	64.2	62.6	1.4	2.2	0.3	-2.2				
	Middle B	62.1				-3.0					
	Middle C	61.6				-3.8					
64 mg/mL (11-31-4B)	Bottom A	62.6	62.0	1.1	1.8	-2.2	-3.1				
	Bottom B	60.7				-5.2					
	Bottom C	62.7				-2.0					
200 mg/mL (11-31-5T)	Top A	194	192	3	2.0	-3.0	-4.0	191	1	0.5	-4.5
	Top B	193				-3.5					
	Top C	189				-5.5					
200 mg/mL (11-31-5M)	Middle A	190	190	2	1.0	-5.0	-5.2				
	Middle B	191				-4.5					
	Middle C	188				-6.0					
200 mg/mL (11-31-5B)	Bottom A	191	191	2	1.0	-4.5	-4.7				
	Bottom B	189				-5.5					
	Bottom C	192				-4.0					

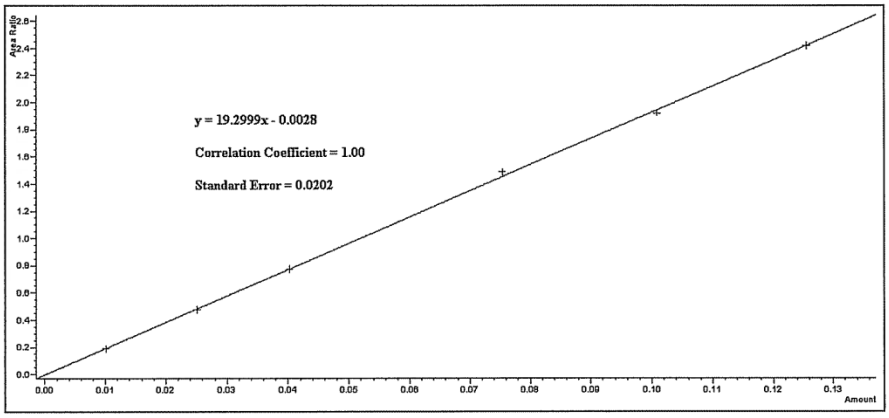


Figure 2. Standard Curve

3.8 Conclusions

The concentrations of all the submitted formulations containing octocrylene were within 10 percent of target, the NTP acceptance limit. The formulations were found to be homogeneous. All other quality criteria stated in the SOP were within acceptance limits.

4.0 ACKNOWLEDGMENTS

[redacted] conducted the analysis. [redacted] wrote the report. [redacted] reviewed the analysis raw data for completeness and accuracy.

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Analytical Chemistry Services for the NTP
NIH Contract No.: HHSN273201000016C
Battelle Project No.: G006623-EEQ
NTP ChemTask No.: CHEM11299
CAS No.: 118-60-5

FORMULATION ANALYSIS OF OCTYL SALICYLATE IN CORN OIL

June 23, 2011

Prepared By:

[redacted]
Study Director

Approved By:

[redacted]
For Steven W. Graves, B.S.
Principal Investigator

Submitted to:

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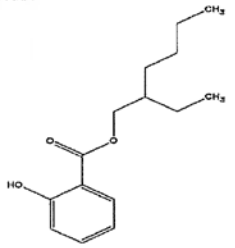
Research Triangle Park, NC 27709-2233

This PDF File is an Exact Copy of the Report.
Signature [redacted]
Date: 06/28/11

FORMULATION ANALYSIS OF OCTYL SALICYLATE IN CORN OIL

CAS No.: 118-60-5		Lot No.: 44698PJ (Sigma-Aldrich, 99.6% purity by GC)
Battelle Chemical ID Code: 336		Samples Analyzed: **Batch** — **Concentration** N135-11-94-6111 — 0 mg/mL 11-30-3T — 15 mg/mL 11-30-3M — 15 mg/mL 11-30-3B — 15 mg/mL 11-30-4T — 47 mg/mL 11-30-4M — 47 mg/mL 11-30-4B — 47 mg/mL 11-30-5T — 150 mg/mL 11-30-5M — 150 mg/mL 11-30-5B — 150 mg/mL
Battelle Task No.: 16-336-FA-322		Sample Receipt Date: 6/2/11
NTP Task No.: CHEM11299		Submitter: Integrated Laboratory Systems, Inc. (ILS)
Program Supported: TOX		Study Lab: ILS
Analysis Dates: 6/3-6/6/11		Mix Date: 6/1/11
Interim Results Date: 6/7/11		Receipt Condition: Received on thawed ice packs and samples warm on receipt
SOPs: CSCSPEC.II-050-01, Standard Operating Procedure (SOP) for the Analysis of Octyl Salicylate Formulations in Corn Oil		Shipping Container: Ten glass vials
		Storage Conditions (@ Battelle): Refrigerated (~5°C)
Structure 	Mol. Wt. 250.33 g/mol	Mol. Formula $C_{15}H_{22}O_3$

EXECUTIVE SUMMARY

Formulations of octyl salicylate in corn oil at target concentrations of 0, 15, 47, and 150 mg/mL were prepared by ILS and analyzed by Battelle to determine their concentration and homogeneity prior to administration in support of a TOX study.

The concentrations of all formulations containing octyl salicylate were within 10 percent of target, the National Toxicology Program (NTP) acceptance limit. The relative standard deviation (RSD) values were also within the specified acceptance limit. All formulations were also found to meet all acceptance criteria for homogeneity. The 0 mg/mL formulation contained no detectable octyl salicylate. All other quality criteria stated in the SOP were within acceptance limits.

QUALITY ASSURANCE STATEMENT

FORMULATION ANALYSIS OF OCTYL SALICYLATE IN CORN OIL

NTP ChemTask No.: CHEM11299
Battelle Project No.: G006623-EEQ
Battelle Task No.: 16-336-FA-322

Listed below are the phases and/or procedures performed by Battelle that were reviewed by the Quality Assurance Unit (QAU) during performance of the task described in this report. Adverse findings, if any, were reported to the study director at the time of review.

Critical Phase Inspected	Date Inspected	Date Reported to Study Director and Management
Formulation analysis	6/3/11	6/3/11
Audit study file	6/15/11	6/15/11
Audit final analytical report	6/15/11	6/15/11

This report reflects the procedures and raw data generated in this study.

In addition to the study-specific audits/inspections cited above, routine inspections of the general facilities and equipment were performed by the QAU and reports were submitted to management as follows:

Facility/Equipment	Date Inspected	Date of Report to Management
Chemistry Technical Center Inspection	12/2, 12/15/08	12/2, 12/22/08
	12/16, 12/23/09	12/16, 12/31/09
	12/28, 12/30/10	12/30/10

[redacted] 6-23-11
Quality Assurance Unit Date

COMPLIANCE STATEMENT

This study was conducted in accordance with the Food and Drug Administration's (FDA's) Good Laboratory Practice (GLP) regulations (21 CFR, Part 58), with the exception of archival of study records at the close of the study. These records are gathered, microfiched, and archived periodically for finalized studies for this program.

[redacted] 6-23-11

Study Director Date

Date Study Initiated (Date Protocol Signed): May 31, 2011
Date Study Completed (Date Final Report Signed): June 23, 2011

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

1.0 INTRODUCTION

This report contains:

- A description of the analyses of the formulations for concentration and homogeneity
- Results from the analysis
- Figures
- Conclusions.

This work was performed at Battelle, 505 King Avenue, Columbus, OH 43201, and supports a TOX study.

2.0 FORMULATION SAMPLES

Formulation samples prepared in corn oil (approximately 10 mL each) were received from ILS on June 2, 2011. The samples were formulated on June 1, 2011 with an expiration date of July 13, 2011. They were identified as being from ILS Protocol No. N135-232 and had the following concentrations and log numbers.

Table 1. Formulation Samples

Concentration (mg/mL)	ILS Log No.
0	N135-11-94-6111
15	11-30-3T
15	11-30-3M
15	11-30-3B
47	11-30-4T
47	11-30-4M
47	11-30-4B
150	11-30-5T
150	11-30-5M
150	11-30-5B

All analysis samples that were supplied by ILS in Table 1 were analyzed.

3.0 FORMULATION ANALYSIS FOR CONTENT AND HOMOGENEITY

The formulations were analyzed for octyl salicylate according to CSCSPEC.II-050-01, "Standard Operating Procedure (SOP) for the Analysis of Octyl Salicylate Formulations in Corn Oil." This SOP was based on work originally conducted under the preliminary chemical studies (PCS) task for octyl salicylate,

Battelle Study No. G005430-DYU, NTP ChemTask No. CHEM10883 and the dose formulation developmental (DFD) task for octyl salicylate in corn oil, Battelle Study No. G005430-DZZ, NTP ChemTask No. CHEM10925. The experimental limit of quantitation (ELOQ) is 0.01 mg/mL, which is the nominal concentration of the lowest standard for this task. This section describes the method, results, and conclusions.

3.1 Preparation of Diluted Vehicle Solution

The diluted vehicle solution was prepared by adding 1 mL of corn oil to a 100-mL volumetric flask and dissolving it in and diluting the flask to volume with acetone. The flask was sealed and the contents mixed well.

3.2 Preparation of Internal Standard (IS)

IS solution was prepared by weighing approximately 500 mg of benzophenone into a 100-mL volumetric flask and dissolving it in and diluting the flask to volume with acetone. The flask was sealed and the contents mixed well.

3.3 Preparation of Standards and Blanks

3.3.1 Stocks

The amounts of octyl salicylate shown in Table 2 were weighed into individual 50-mL volumetric flasks. The chemical was dissolved in and the flask was diluted to volume with acetone. The flasks were sealed and the contents mixed well.

Table 2. Preparation of Stocks

ID	Target Concentration (mg/mL)	Target Weight (mg)
A	1.25	62.50 ± 2
B	1	50.00 ± 2

3.3.2 Spiking Solutions

The volumes of the A and B indicated in Table 3 were pipetted into individual volumetric flasks. The flasks were diluted to volume with acetone, sealed, and the contents mixed well. A single solution was prepared at all concentrations.

Table 3. Preparation of Spiking Solutions

ID	Target Concentration (mg/mL)	Source	Source Volume (mL)	Final Volume (mL)
C	0.75	A	3	5
D	0.40	B	2	5
E	0.25	A	2	10
F	0.10	B	1	10

3.3.3 Vehicle/Calibration Standards

One (1) mL from each solution A through F was pipetted into individual 10-mL volumetric flasks. One (1) mL of diluted vehicle and 0.1 mL of IS was added to each volumetric flask. The flasks were diluted to volume with acetone, sealed, and the contents mixed well. This produced single vehicle standards at target concentrations of 0.125, 0.1, 0.075, 0.04, 0.025, and 0.01 mg/mL.

3.3.4 Preparation of Blanks

Vehicle Blank

A single blank was prepared by pipetting 1 mL of diluted vehicle into a 10-mL volumetric flask and diluting to volume with acetone. The flask was sealed and the contents mixed well.

Vehicle Blank with IS

A single blank with IS was prepared by pipetting 1 mL of diluted vehicle and 0.1 mL of IS into a 10-mL volumetric flask and diluting to volume with acetone. The flask was sealed and the contents mixed well.

3.4 Preparation of Formulation Samples For Analysis

3.4.1 Density Determination

For each formulation concentration, a tared 5-mL volumetric flask was filled to volume with the formulation. The weight of the filled flask was recorded and divided by five to obtain the density of the formulation.

3.4.2 Preparation of Formulation Samples

All formulation samples had a stir bar added to the container. The formulations were stirred for at least 5 minutes prior to use.

For each formulation with a concentration less than or equal to 100 mg/mL, a 1-mL aliquot was transferred to three previously tared 10-mL volumetric flasks. The weight of the aliquot was recorded. The flasks were diluted to volume with acetone, sealed, and the contents mixed well.

For each formulation with a concentration of greater than 100 mg/mL, a 1-mL aliquot was transferred to three previously tared 25-mL volumetric flasks. The weight of the aliquot was recorded. A 1.5-mL aliquot of corn oil was added to each flask. The flasks were diluted to volume with acetone, sealed, and the contents mixed well.

A 1-mL aliquot of each diluted formulation was transferred to individual 100-mL volumetric flasks. A 1-mL aliquot of IS was added to each flask. The flasks were diluted to volume with acetone, sealed, and the contents mixed well.

3.5 Analysis

Aliquots of each vehicle standard, blank, and diluted sample were transferred into autosampler vials with minimal headspace and the vials were sealed. Single injections were made from each vial using the gas chromatography (GC) instrumental system with flame ionization detection (FID) as shown in Table 4.

Table 4. GC System

Instrument	Agilent 6890 (Santa Clara, CA)
Data System	Thermo Fisher Scientific Atlas, Version 8.2
Column	Restek (Bellefonte, PA),Rtx-5, 30 m × 0.32 mm (ID), 1.0 µm film thickness
Oven Temperature	80°C, hold for 1 minute, increase at 20°C/minute to 200°C, no hold, increase at 10°C/minute to 280°C, hold for 10 minutes
Hydrogen Flow	28 mL/minute
Air Flow Rate	280 mL/minute
Nitrogen Makeup Flow	26 mL/minute
Carrier Flow Rate	Helium at 3 mL/minute
Detector Temperature	280°C
Injector Temperature	260°C
Detector Type	FID
Injection Volume	1 µL
Injection Mode	Splitless
Run Time	25 minutes

Representative overlaid chromatograms from a high and low standard, a blank with IS, and a blank are shown in Figure 1.

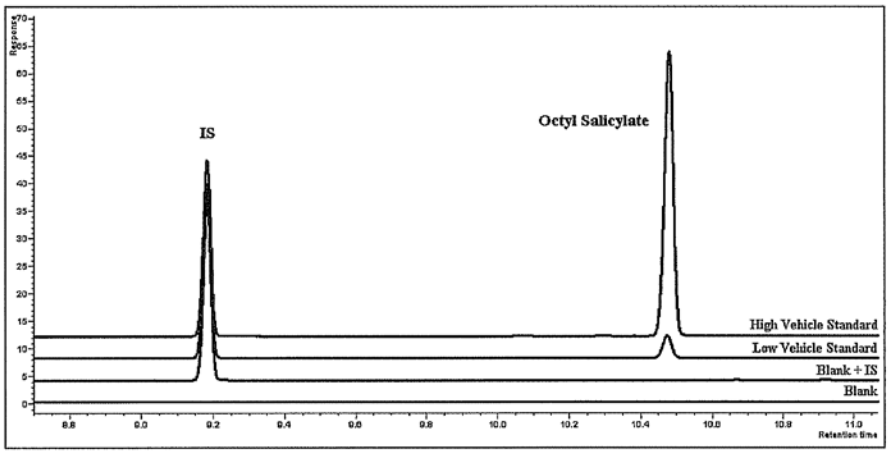


Figure 1. Representative Overlaid Chromatograms

3.6 Calculations

The integration of the octyl salicylate and IS peaks done by the chromatography data system was evaluated and manually adjusted, if necessary, to achieve consistent integration. The response ratio of the octyl salicylate peak area divided by the IS peak area was calculated. A linear regression equation with 1/x weighting was calculated relating the response ratio of the standards to their nominal concentrations. The determined concentration was calculated for each standard and sample using the regression equation, the response ratio for that standard or sample, the sample weight and density, and any dilution factor for the samples. The relative error (RE) for each standard and sample was calculated by subtracting the target concentration from its determined concentration, dividing the difference by the target concentration, and multiplying the result by 100. The average concentration, average RE, standard deviation, and RSD for each formulation location were calculated using the individual values. The grand average concentration, grand RE, grand standard deviation, and grand RSD for each formulation were calculated using the average concentration for each location.

At least one extra significant figure was carried through all calculations to minimize rounding errors, therefore, the summary statistics presented in the tables may not be exactly reproduced using the rounded input values shown.

3.7 Results

The results of the formulation analyses are shown in Table 5. The 0 mg/mL formulations were below the limit of quantitation (BLOQ). The standard curve is shown in Figure 2.

Table 5. Corn Oil Homogeneity Formulation Sample Analysis Results

Target Concentration (Sample ID)	Sample No.	Determined Concentration (mg/mL)	Average Determined Concentration (mg/mL)	s (mg/mL)	RSD	RE	Average RE	Grand Average Determined Concentration (mg/mL)	Grand s (mg/mL)	Grand RSD	Grand RE
15 mg/mL (11-30-3T)	Top A	15.0	15.0	0.0	0.0	0.0	0.0	14.8	0.2	1.0	-1.1
	Top B	15.0				0.0					
	Top C	15.0				0.0					
15 mg/mL (11-30-3M)	Middle A	14.8	14.7	0.1	0.7	-1.3	-1.8				
	Middle B	14.6				-2.7					
	Middle C	14.8				-1.3					
15 mg/mL (11-30-3B)	Bottom A	14.9	14.8	0.1	0.7	-0.7	-1.1				
	Bottom B	14.8				-1.3					
	Bottom C	14.8				-1.3					
47 mg/mL (11-30-4T)	Top A	45.4	45.0	0.4	0.9	-3.4	-4.2	45.8	0.9	2.0	-2.6
	Top B	44.7				-4.9					
	Top C	45.0				-4.3					
47 mg/mL (11-30-4M)	Middle A	47.0	46.8	0.2	0.4	0.0	-0.5				
	Middle B	46.6				-0.9					
	Middle C	46.7				-0.6					
47 mg/mL (11-30-4B)	Bottom A	45.4	45.6	0.2	0.4	-3.4	-2.9				
	Bottom B	45.8				-2.6					
	Bottom C	45.7				-2.8					
150 mg/mL (11-30-5T)	Top A	146	147	1	0.7	-2.7	-2.2	143	4	2.7	-4.9
	Top B	148				-1.3					
	Top C	146				-2.7					
150 mg/mL (11-30-5M)	Middle A	141	140	1	0.7	-6.0	-6.4				
	Middle B	141				-6.0					
	Middle C	139				-7.3					
150 mg/mL (11-30-5B)	Bottom A	140	141	1	0.7	-6.7	-6.2				
	Bottom B	142				-5.3					
	Bottom C	140				-6.7					

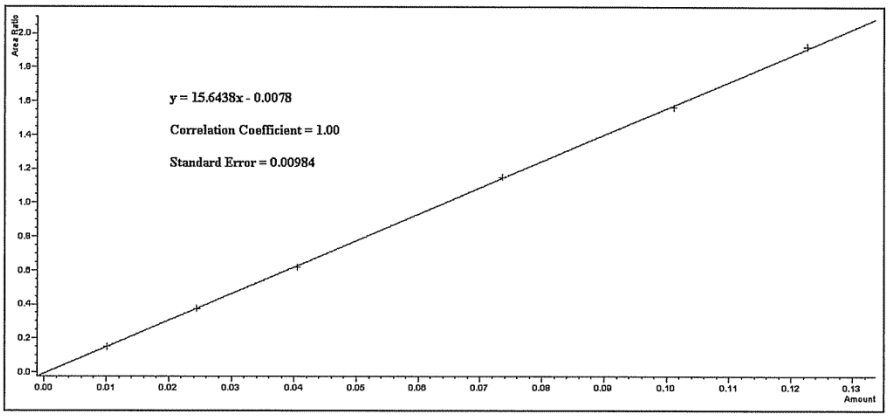


Figure 2. Standard Curve

3.8 Conclusions

The concentrations of all the submitted formulations containing octyl salicylate were within 10 percent of target, the NTP acceptance limit. All formulations were found to be homogeneous. The 0 mg/mL formulation contained no detectable octyl salicylate. All other quality criteria stated in the SOP were within acceptance limits.

4.0 ACKNOWLEDGMENTS

[redacted] conducted the analysis. [redacted] wrote the report. [redacted] reviewed the analysis raw data for completeness and accuracy.

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BATTELLE-FA

Analytical Chemistry Services for the NTP
NIH Contract No.: HHSN273201000016C
Battelle Project No.: G006623-EEP
NTP ChemTask No.: CHEM11298
CAS No.: 6197-30-4

FORMULATION ANALYSIS OF
2-ETHYLHEXYL 2-CYANO-3,3-DIPHENYLACRYLATE (OCTOCRYLENE)
IN CORN OIL

June 23, 2011

Prepared By:

[redacted]
Study Director

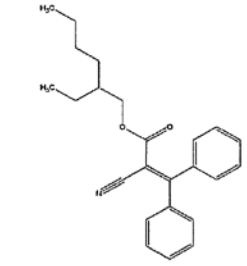
Approved By:

[redacted]
For Steven W. Graves, B.S.
Principal Investigator

Submitted to:

[redacted]
National Institute of Environmental Health Sciences
111 T.W. Alexander Drive
P.O. Box 12233
Research Triangle Park, NC 27709-2233

FORMULATION ANALYSIS OF
2-ETHYLHEXYL 2-CYANO-3,3-DIPHENYLACRYLATE (OCTOCRYLENE)
IN CORN OIL

<table>
<tr><td colspan="2">CAS No.: 6197-30-4</td><td>Lot No.: 01697MJ (Sigma-Aldrich, 99.2% purity by GC)</td></tr>
<tr><td colspan="2">Battelle Chemical ID Code: 335</td><td>Samples Analyzed:
<u>Batch</u> <u>Concentration</u>
11-31-3T 20 mg/mL
11-31-3M 20 mg/mL
11-31-3B 20 mg/mL
11-31-4T 64 mg/mL
11-31-4M 64 mg/mL
11-31-4B 64 mg/mL
11-31-5T 200 mg/mL
11-31-5M 200 mg/mL
11-31-5B 200 mg/mL</td></tr>
<tr><td colspan="2">Battelle Task No.: 16-335-FA-321</td><td>Sample Receipt Date: 6/2/11</td></tr>
<tr><td colspan="2">NTP Task No.: CHEM11298</td><td>Submitter: Integrated Laboratory Systems, Inc. (ILS)</td></tr>
<tr><td colspan="2">Program Supported: TOX</td><td>Study Lab: ILS</td></tr>
<tr><td colspan="2">Analysis Dates: 6/3-6/4/11</td><td>Mix Date: 6/1/11</td></tr>
<tr><td colspan="2">Interim Results Date: 6/6/11</td><td>Receipt Condition: Samples received on thawed ice packs and warm on receipt. Vial labels soaked due to a broken thawed ice pack, however information on label was still legible, but appear uncompromised.</td></tr>
<tr><td colspan="2" rowspan="2">SOPs: CSCSPEC.II-049-01, Standard Operating Procedure (SOP) for the Analysis of 2-Ethylhexyl 2-Cyano-3,3-Diphenylacrylate (Octocrylene) Formulations in Corn Oil</td><td>Shipping Container: Nine glass vials</td></tr>
<tr><td>Storage Conditions (@ Battelle): Refrigerated (~5°C)</td></tr>
<tr><td>Structure
  </td><td>Mol. Wt.
361.48 g/mol</td><td>Mol. Formula
$C_{24}H_{27}NO_2$</td></tr>
</table>

EXECUTIVE SUMMARY

Formulations of octocrylene in corn oil at target concentrations of 20, 64, and 200 mg/mL were prepared by ILS and analyzed by Battelle to determine their concentration and homogeneity prior to administration in support of a TOX study.

The concentrations of all the formulations containing octocrylene were within 10 percent of target, the National Toxicology Program (NTP) acceptance limit. The relative standard deviation (RSD) values were also within the specified acceptance limit. All formulations were found to be homogeneous. All other quality criteria stated in the SOP were within acceptance limits.

QUALITY ASSURANCE STATEMENT

FORMULATION ANALYSIS OF
2-ETHYLHEXYL 2-CYANO-3,3-DIPHENYLACRYLATE (OCTOCRYLENE)
IN CORN OIL

NTP ChemTask No.: CHEM11298
Battelle Project No.: G006623-EEP
Battelle Task No.: 16-335-FA-321

Listed below are the phases and/or procedures performed by Battelle that were reviewed by the Quality Assurance Unit (QAU) during performance of the task described in this report. Adverse findings, if any, were reported to the study director at the time of review.

Critical Phase Inspected	Date Inspected	Date Reported to Study Director and Management
Formulation analysis	6/3/11	6/3/11
Audit study file	6/15/11	6/15/11
Audit final analytical report	6/15/11	6/15/11

This report reflects the procedures and raw data generated in this study.

In addition to the study-specific audits/inspections cited above, routine inspections of the general facilities and equipment were performed by the QAU and reports were submitted to management as follows:

Facility/Equipment	Date Inspected	Date of Report to Management
Chemistry Technical Center Inspection	12/2, 12/15/08	12/2, 12/22/08
	12/16, 12/23/09	12/16, 12/31/09
	12/28, 12/30/10	12/30/10

[redacted] 6-23-11
Quality Assurance Unit Date

COMPLIANCE STATEMENT

This study was conducted in accordance with the Food and Drug Administration's (FDA's) Good Laboratory Practice (GLP) regulations (21 CFR, Part 58), with the exception of archival of study records at the close of the study. These records are gathered, microfiched, and archived periodically for finalized studies for this program.

[redacted] 6-23-11

Study Director Date

Date Study Initiated (Date Protocol Signed): May 31, 2011
Date Study Completed (Date Final Report Signed): June 23, 2011

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

1.0 INTRODUCTION

This report contains:

- A description of the analyses of the formulations for concentration and homogeneity
- Results from the analysis
- Figures
- Conclusions.

This work was performed at Battelle, 505 King Avenue, Columbus, OH 43201, and supports a TOX study.

2.0 FORMULATION SAMPLES

Formulation samples prepared in corn oil (approximately 10 mL each) were received from ILS on June 2, 2011. The samples were formulated on June 1, 2011 with an expiration date of July 13, 2011. They were identified as being from ILS Protocol No. N135-232 and had the following concentrations and log numbers.

Table 1. Formulation Samples

Concentration (mg/mL)	ILS Log No.
20	11-31-3T
20	11-31-3M
20	11-31-3B
64	11-31-4T
64	11-31-4M
64	11-31-4B
200	11-31-5T
200	11-31-5M
200	11-31-5B

All analysis samples that were supplied by ILS in Table 1 were analyzed.

3.0 FORMULATION ANALYSIS FOR CONTENT AND HOMOGENEITY

The formulations were analyzed for octocrylene according to CSCSPEC.II-049-01, "Standard Operating Procedure (SOP) for the Analysis of 2-Ethylhexyl 2-Cyano-3,3-Diphenylacrylate (Octocrylene) Formulations in Corn Oil." This SOP was based on work originally conducted under the preliminary chemical studies (PCS) task for octocrylene, Battelle Study No. G005430-DYT, NTP ChemTask No. CHEM10882

and the dose formulation developmental (DFD) task for octocrylene in corn oil, Battelle Study No. G005430-DZY, NTP ChemTask No. CHEM10924. The experimental limit of quantitation (ELOQ) is 0.01 mg/mL, which is the nominal concentration of the lowest standard for this task. This section describes the method, results, and conclusions.

3.1 Preparation of Diluted Vehicle Solution

The diluted vehicle solution was prepared by adding 1 mL of corn oil to a 100-mL volumetric flask and dissolving it in and diluting the flask to volume with acetone. The flask was sealed and the contents mixed well.

3.2 Preparation of Internal Standard (IS)

IS solution was prepared by weighing approximately 250 mg of benzophenone into a 50-mL volumetric flask and dissolving it in and diluting the flask to volume with acetone. The flask was sealed and the contents mixed well.

3.3 Preparation of Standards and Blanks

3.3.1 Stocks

The amounts of octocrylene shown in Table 2 were weighed into individual 50-mL volumetric flasks. The chemical was dissolved in and the flasks diluted to volume with acetone. The flasks were sealed and the contents mixed well.

Table 2. Preparation of Stocks

ID	Target Concentration (mg/mL)	Target Weight (mg)
A	1.25	62.50 ± 2
B	1	50.00 ± 2

3.3.2 Spiking Solutions

The volumes of the A and B indicated in Table 3 were pipetted into individual volumetric flasks. The flasks were diluted to volume with acetone, sealed, and the contents mixed well. A single solution was prepared at all concentrations.

Table 3. Preparation of Spiking Solutions

ID	Target Concentration (mg/mL)	Source	Source Volume (mL)	Final Volume (mL)
C	0.75	A	3	5
D	0.40	B	2	5
E	0.25	A	2	10
F	0.10	B	1	10

3.3.3 Vehicle/Calibration Standards

One (1) mL from each solution A to F was pipetted into individual 10-mL volumetric flasks. One (1) mL of diluted vehicle and 0.1 mL of IS was added to each volumetric flask. The flasks were diluted to volume with acetone, sealed, and the contents mixed well. This produced single vehicle standards at target concentrations of 0.125, 0.1, 0.075, 0.04, 0.025, and 0.01 mg/mL.

3.3.4 Preparation of Blanks

Vehicle Blank

A single blank was prepared by pipetting 1 mL of diluted vehicle into a 10-mL volumetric flask and diluting to volume with acetone. The flask was sealed and the contents mixed well.

Vehicle Blank with IS

A single blank with IS was prepared by pipetting 1 mL of diluted vehicle and 0.1 mL of IS into a 10-mL volumetric flask and diluting to volume with acetone. The flask was sealed and the contents mixed well.

3.4 Preparation of Formulation Samples For Analysis

3.4.1 Density Determination

For each formulation concentration, a tared 5-mL volumetric flask was filled to volume with the formulation. The weight of the filled flask was recorded and divided by five to obtain the density of the formulation.

3.4.2 Preparation of Formulation Samples

All formulation samples had a stir bar added to the container. The formulations were stirred for at least 5 minutes prior to use.

For each formulation sample with a concentration less than or equal to 100 mg/mL, a 1-mL aliquot was transferred to three previously tared 10-mL volumetric flasks. The weight of the aliquot was recorded. The flasks were diluted to volume with acetone, sealed, and the contents mixed well.

For each formulation sample with a concentration greater than 100 mg/mL, a 1-mL aliquot was transferred to three previously tared 25-mL volumetric flasks. The weight of the aliquot was recorded. A 1.5-mL aliquot of corn oil was added to each flask. The flasks were diluted to volume with acetone, sealed, and the contents mixed well.

A 1-mL aliquot of each diluted formulation was transferred to individual 100-mL volumetric flasks. A 1-mL aliquot of IS was added to each flask. The flasks were diluted to volume with acetone, sealed, and the contents mixed well.

3.5 Analysis

Aliquots of each vehicle standard, blank, and diluted sample were transferred into autosampler vials with minimal headspace and the vials were sealed. Single injections were made from each vial using the gas chromatography (GC) instrumental system with flame ionization (FID) detection as shown in Table 4.

Table 4. GC System

Instrument	Agilent 6890 (Santa Clara, CA)
Data System	Thermo Fisher Scientific Atlas, Version 8.2
Column	Restek (Bellefonte, PA), Rtx-5, 30 m × 0.32 mm (ID), 1.0 µm film thickness
Oven Temperature	80°C, hold for 1 minute, increase at 20°C/minute to 200°C, no hold, increase at 10°C/minute to 280°C, hold for 10 minutes
Hydrogen Flow	28 mL/minute
Air Flow Rate	280 mL/minute
Nitrogen Makeup Flow	25 mL/minute
Carrier Flow Rate	Helium at 3 mL/minute
Detector Temperature	280°C
Injector Temperature	260°C
Detector Type	FID
Injection Volume	1 µL
Injection Mode	Splitless
Run Time	25 minutes

Representative overlaid chromatograms from a high and low standard, a blank with IS, and a blank are shown in Figure 1.

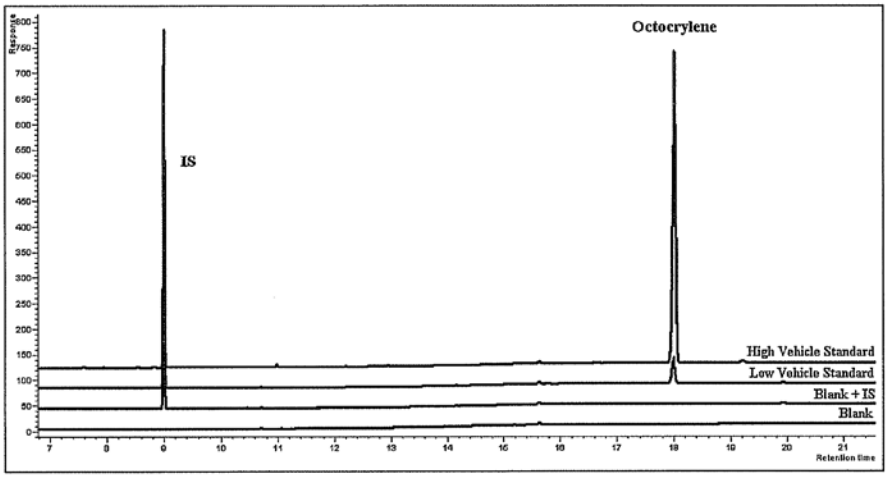


Figure 1. Representative Overlaid Chromatograms

3.6 Calculations

The integration of the octocrylene and IS peaks done by the chromatography data system was evaluated and manually adjusted, if necessary, to achieve consistent integration. The response ratio of the octocrylene peak area divided by the IS peak area was calculated. A linear regression equation with 1/x weighting was calculated relating the response ratio of the standards to their nominal concentrations. The determined concentration was calculated for each standard and sample using the regression equation, the response ratio for that standard or sample, the sample weight and density, and any dilution factor for the samples. The relative error (RE) for each standard and sample was calculated by subtracting the target concentration from its determined concentration, dividing the difference by the target concentration, and multiplying the result by 100. The average concentration, average RE, standard deviation, and RSD for each formulation location were calculated using the individual values. The grand average concentration, grand RE, grand standard deviation, and grand RSD for each formulation were calculated using the average concentration for each location.

At least one extra significant figure was carried through all calculations to minimize rounding errors, therefore, the summary statistics presented in the tables may not be exactly reproduced using the rounded input values shown.

3.7 Results

The results of the formulation analyses are shown in Table 5. The standard curve is shown in Figure 2.

Table 5. Corn Oil Homogeneity Formulation Sample Analysis Results

Target Concentration (Sample ID)	Sample No.	Determined Concentration (mg/mL)	Average Determined Concentration (mg/mL)	s (mg/mL)	RSD	RE	Average RE	Grand Average Determined Concentration (mg/mL)	Grand s (mg/mL)	Grand RSD	Grand RE
20 mg/mL (11-31-3T)	Top A	20.0	20.0	0.0	0.0	0.0	0.0	19.9	0.3	1.3	-0.5
	Top B	20.0				0.0					
	Top C	20.0				0.0					
20 mg/mL (11-31-3M)	Middle A	19.4	19.6	0.2	1.0	-3.0	-1.8				
	Middle B	19.8				-1.0					
	Middle C	19.7				-1.5					
20 mg/mL (11-31-3B)	Bottom A	19.9	20.1	0.2	1.0	-0.5	0.3				
	Bottom B	20.3				1.5					
	Bottom C	20.0				0.0					
64 mg/mL (11-31-4T)	Top A	61.5	61.7	0.2	0.3	-3.9	-3.6	62.1	0.5	0.7	-3.0
	Top B	61.8				-3.4					
	Top C	61.8				-3.4					
64 mg/mL (11-31-4M)	Middle A	64.2	62.6	1.4	2.2	0.3	-2.2				
	Middle B	62.1				-3.0					
	Middle C	61.6				-3.8					
64 mg/mL (11-31-4B)	Bottom A	62.6	62.0	1.1	1.8	-2.2	-3.1				
	Bottom B	60.7				-5.2					
	Bottom C	62.7				-2.0					
200 mg/mL (11-31-5T)	Top A	194	192	3	2.0	-3.0	-4.0	191	1	0.5	-4.5
	Top B	193				-3.5					
	Top C	189				-5.5					
200 mg/mL (11-31-5M)	Middle A	190	190	2	1.0	-5.0	-5.2				
	Middle B	191				-4.5					
	Middle C	188				-6.0					
200 mg/mL (11-31-5B)	Bottom A	191	191	2	1.0	-4.5	-4.7				
	Bottom B	189				-5.5					
	Bottom C	192				-4.0					

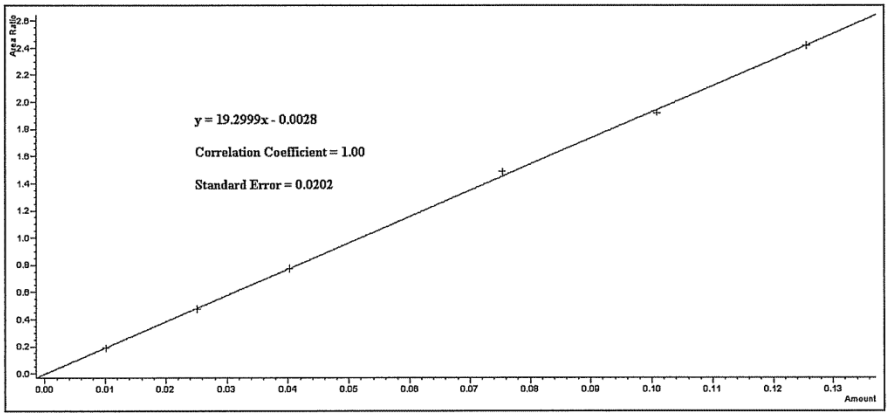


Figure 2. Standard Curve

3.8 Conclusions

The concentrations of all the submitted formulations containing octocrylene were within 10 percent of target, the NTP acceptance limit. The formulations were found to be homogeneous. All other quality criteria stated in the SOP were within acceptance limits.

4.0 ACKNOWLEDGMENTS

[redacted]onducted the analysis. [redacted]wrote the report. [redacted] reviewed the analysis raw data for completeness and accuracy.

Appendix III:

Dose Times, Volume and Dose Administration

					Day 1 (30 & 31 May 2011)			Day 2 (31 May & 1 June 2011)			Day 3 (1 & 2 June 2011)			Day 4 (2 & 3 June 2011)			Day 5 (3 & 4 June 2011)		
Group No.:	Animal No.	Test Substance/Dose Level	Actual Dose Concentration (mg/ml)	Age of Animal (PND)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)
1	01	Corn Oil Control	0	58	10:02	1.3	0	10:15	1.3	0	10:08	1.3	0	9:51	1.3	0	9:20	1.3	0
1	02		0	58	10:18	1.2	0	10:28	1.2	0	10:18	1.3	0	10:03	1.3	0	9:32	1.4	0
1	03		0	58	10:31	1.4	0	10:39	1.4	0	10:26	1.4	0	10:14	1.4	0	9:46	1.4	0
1	04		0	58	10:42	1.2	0	10:48	1.2	0	10:34	1.3	0	10:24	1.3	0	9:58	1.3	0
1	05*		0	59	11:00	1.3	0	10:44	1.3	0	10:37	1.3	0	10:11	1.3	0	10:28	1.4	0
1	06		0	59	11:14	1.3	0	10:55	1.4	0	10:47	1.4	0	10:25	1.4	0	10:39	1.5	0
1	07		0	59	11:29	1.4	0	11:05	1.4	0	10:58	1.4	0	10:42	1.4	0	10:55	1.5	0
1	08		0	59	11:40	1.2	0	11:17	1.2	0	11:09	1.2	0	10:55	1.2	0	11:09	1.2	0

*Found dead due to dosing error

Day 6 (4 & 5 June 2011)			Day 7 (5 & 6 June 2011)			Day 8 (6 & 7 June 2011)			Day 9 (7 & 8 June 2011)			Day 10 (8 & 9 June 2011)			Day 11 (9 & 10 June 2011)	
Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Death	Time From Last Administration
9:34	1.4	0	9:29	1.4	0	10:40	1.4	0	10:35	1.4	0	10:02	1.5	0	8:38	22:36
9:47	1.4	0	9:41	1.4	0	10:53	1.5	0	10:47	1.5	0	10:11	1.6	0	10:17	24:06
9:59	1.4	0	9:54	1.5	0	11:05	1.5	0	10:58	1.5	0	10:23	1.5	0	11:21	24:58
10:11	1.3	0	10:04	1.3	0	11:18	1.4	0	11:11	1.4	0	10:33	1.4	0	12:21	25:48
10:25	1.4	0	11:32	1.4	0	11:23	1.4	0	10:48	1.5	0	10:12	1.5	0	15:41	5:29
10:36	1.5	0	11:45	1.5	0	11:35	1.6	0	10:59	1.6	0	10:24	1.6	0	9:11	22:47
10:49	1.5	0	11:58	1.6	0	11:48	1.6	0	11:16	1.6	0	10:35	1.6	0	10:06	23:31
11:00	1.2	0	12:10	1.3	0	12:00	1.3	0	11:26	1.3	0	10:48	1.3	0	11:12	24:24

					Day 1 (30 & 31 May 2011)			Day 2 (31 May & 1 June 2011)			Day 3 (1 & 2 June 2011)			Day 4 (2 & 3 June 2011)			Day 5 (3 & 4 June 2011)		
Group No.:	Animal No.	Test Substance/Dose Level	Actual Dose Concentration (mg/ml)	Age of Animal (PND)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)
2	09	Oxybenzone (320 mg/kg)	63.9	58	10:04	1.1	308.2	10:16	1.2	328.4	10:09	1.2	324.5	9:52	1.2	321.1	9:21	1.1	306.8
2	10		63.9	58	10:19	1.3	331.1	10:29	1.3	324.1	10:18	1.3	320.6	10:04	1.3	314.7	9:33	1.3	325.0
2	11		63.9	58	10:31	1.2	308.8	10:39	1.2	307.2	10:26	1.3	323.7	10:15	1.3	317.3	9:47	1.3	317.8
2	12		63.9	58	10:42	1.3	317.3	10:49	1.3	310.8	10:34	1.4	329.6	10:24	1.4	324.8	9:59	1.4	326.3
2	13		63.9	59	11:01	1.3	317.2	10:45	1.3	313.0	10:37	1.4	328.2	10:12	1.4	327.7	10:29	1.4	314.7
2	14		63.9	59	11:14	1.4	313.0	10:55	1.5	327.6	10:48	1.5	321.6	10:27	1.5	320.9	10:40	1.5	313.1
2	15		63.9	59	11:29	1.2	317.4	11:05	1.2	310.9	10:58	1.2	308.4	10:43	1.3	329.6	10:56	1.3	327.2
2	16		63.9	59	11:40	1.3	309.0	11:17	1.4	322.3	11:10	1.4	313.9	10:56	1.5	327.4	11:09	1.5	323.7

Day 6 (4 & 5 June 2011)			Day 7 (5 & 6 June 2011)			Day 8 (6 & 7 June 2011)			Day 9 (7 & 8 June 2011)			Day 10 (8 & 9 June 2011)			Day 11 (9 & 10 June 2011)	
Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Death	Time From Last Administration
9:35	1.2	314.9	9:30	1.2	309.4	10:40	1.2	309.2	10:36	1.2	308.4	10:02	1.3	329.0	8:50	22:48
9:47	1.4	330.5	9:41	1.4	324.2	10:53	1.4	323.8	10:47	1.4	318.0	10:12	1.4	312.4	10:25	24:13
9:59	1.4	330.2	9:54	1.4	323.0	11:06	1.4	321.6	10:58	1.4	320.5	10:23	1.4	315.1	11:24	25:01
10:12	1.4	313.7	10:05	1.5	329.8	11:18	1.5	326.5	11:12	1.5	316.3	10:34	1.5	314.6	12:25	25:51
10:25	1.4	308.7	11:32	1.5	323.7	11:24	1.5	321.4	10:49	1.5	316.1	10:13	1.5	309.6	8:14	22:01
10:37	1.6	325.8	11:46	1.6	321.3	11:35	1.6	317.7	10:59	1.7	328.7	10:24	1.7	324.2	9:15	22:51
10:50	1.3	321.2	11:59	1.3	316.0	11:48	1.3	317.5	11:16	1.3	313.8	10:35	1.3	312.5	10:10	23:35
11:01	1.5	314.2	12:11	1.5	309.9	12:00	1.6	329.4	11:27	1.6	317.2	10:49	1.5	309.4	11:17	24:28

					Day 1 (30 & 31 May 2011)			Day 2 (31 May & 1 June 2011)			Day 3 (1 & 2 June 2011)			Day 4 (2 & 3 June 2011)			Day 5 (3 & 4 June 2011)		
Group No.:	Animal No.	Test Substance/Dose Level	Actual Dose Concentration (mg/ml)	Age of Animal (PND)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)
3	17	Oxybenzone (1000 mg/kg)	211	58	10:05	1.4	1077.3	10:17	1.3	1029.7	10:09	1.4	1075.4	9:52	1.4	1034.3	9:22	1.4	1078.9
3	18		211	58	10:20	1.2	1033.5	10:39	1.2	1062.5	10:19	1.2	1056.8	10:04	1.3	1080.3	9:34	1.2	1072.0
3	19		211	58	10:32	1.3	1041.0	10:40	1.3	1044.6	10:27	1.3	1082.1	10:15	1.3	1047.7	9:48	1.3	1021.2
3	20		211	58	10:43	1.3	1076.5	10:50	1.3	1085.0	10:34	1.3	1069.8	10:25	1.3	1043.8	10:00	1.4	1085.2
3	21		211	59	11:01	1.4	1084.8	10:45	1.3	1019.7	10:38	1.4	1082.8	10:13	1.4	1047.5	10:29	1.4	1037.2
3	22		211	59	11:15	1.3	1051.8	10:56	1.3	1062.4	10:48	1.3	1020.1	10:29	1.4	1049.0	10:41	1.4	1027.5
3	23		211	59	11:30	1.2	1063.4	11:06	1.2	1063.9	10:59	1.2	1043.7	10:44	1.2	1025.1	10:57	1.2	1030.9
3	24		211	59	11:41	1.3	1056.2	11:20	1.3	1037.8	11:10	1.3	1026.2	10:57	1.4	1071.8	11:10	1.4	1040.5

Day 6 (4 & 5 June 2011)			Day 7 (5 & 6 June 2011)			Day 8 (6 & 7 June 2011)			Day 9 (7 & 8 June 2011)			Day 10 (8 & 9 June 2011)			Day 11 (9 & 10 June 2011)	
Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Death	Time From Last Administration
9:36	1.5	1068.2	9:31	1.5	1043.5	10:41	1.5	1030.9	10:36	1.6	1081.7	10:03	1.6	1058.6	8:59	22:56
9:48	1.3	1059.1	9:42	1.3	750.5	10:54	1.3	1028.9	10:48	1.4	1083.6	10:12	1.4	1041.6	10:30	24:18
10:00	1.4	1087.2	9:55	1.4	1062.6	11:06	1.4	1060.3	10:59	1.4	1051.6	10:24	1.4	1036.9	11:27	25:03
10:13	1.4	1081.3	10:06	1.4	1059.2	11:19	1.4	1042.7	11:13	1.4	1037.6	10:36	1.5	1083.9	12:29	25:53
10:26	1.4	1050.5	11:33	1.5	1088.4	11:24	1.5	1085.4	10:50	1.5	1056.1	10:13	1.5	1046.3	8:20	22:07
10:38	1.4	1030.0	11:46	1.5	1072.9	11:36	1.5	1070.3	11:00	1.5	1041.5	10:25	1.5	1049.4	9:20	22:55
10:50	1.2	1025.1	11:59	1.2	1016.9	11:49	1.2	1016.1	11:17	1.3	1090.2	10:36	1.3	1089.4	10:15	23:39
11:02	1.4	1028.2	12:11	1.5	1062.8	12:01	1.5	1075.1	11:27	1.5	1061.4	10:49	1.5	1044.6	11:22	24:33

					Day 1 (30 & 31 May 2011)			Day 2 (31 May & 1 June 2011)			Day 3 (1 & 2 June 2011)			Day 4 (2 & 3 June 2011)			Day 5 (3 & 4 June 2011)		
Group No.:	Animal No.	Test Substance/Dose Level	Actual Dose Concentration (mg/ml)	Age of Animal (PND)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)
4	25	Octylmethoxycinnamate (320 mg/kg)	65.2	58	10:06	1.3	335.9	10:17	1.3	329.8	10:10	1.3	320.7	9:53	1.4	336.2	9:23	1.4	331.9
4	26		65.2	58	10:20	1.2	316.9	10:30	1.2	314.0	10:19	1.3	334.5	10:05	1.3	333.8	9:35	1.3	327.1
4	27		65.2	58	10:33	1.2	327.9	10:40	1.2	323.3	10:27	1.3	337.0	10:16	1.3	330.7	9:48	1.3	323.5
4	28		65.2	58	10:43	1.3	325.6	10:50	1.3	320.8	10:35	1.3	314.2	10:26	1.4	332.9	10:01	1.4	327.2
4	29		65.2	59	11:02	1.3	323.8	10:45	1.3	316.3	10:39	1.4	330.0	10:14	1.4	322.8	10:30	1.4	316.6
4	30		65.2	59	11:16	1.4	327.9	10:56	1.4	318.3	10:49	1.5	332.5	10:31	1.5	323.3	10:43	1.6	332.9
4	31		65.2	59	11:31	1.4	333.3	11:07	1.4	323.8	10:59	1.5	334.5	10:44	1.5	327.0	10:58	1.6	334.5
4	32		65.2	59	11:41	1.2	322.6	11:21	1.2	322.4	11:11	1.3	338.6	10:57	1.3	329.0	11:11	1.3	319.5

Day 6 (4 & 5 June 2011)			Day 7 (5 & 6 June 2011)			Day 8 (6 & 7 June 2011)			Day 9 (7 & 8 June 2011)			Day 10 (8 & 9 June 2011)			Day 11 (9 & 10 June 2011)	
Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Death	Time From Last Administration
9:37	1.4	322.3	9:31	1.4	316.4	10:41	1.5	334.5	10:37	1.5	328.9	10:04	1.5	316.3	9:06	23:02
9:48	1.3	322.4	9:43	1.3	320.7	10:54	1.3	318.6	10:48	1.3	315.6	10:13	1.4	334.8	10:35	24:22
10:01	1.3	319.1	9:55	1.4	335.1	11:07	1.4	332.9	10:59	1.4	331.3	10:25	1.4	324.7	11:32	25:07
10:14	1.4	320.3	10:07	1.4	318.4	11:19	1.5	337.1	11:13	1.5	335.5	10:36	1.5	328.5	12:33	25:57
10:27	1.5	332.9	11:33	1.5	328.7	11:25	1.5	324.3	10:50	1.5	316.4	10:14	1.6	335.0	8:25	22:11
10:39	1.6	333.2	11:47	1.6	324.9	11:36	1.7	334.9	11:01	1.7	327.7	10:26	1.7	324.9	9:24	22:58
10:51	1.6	330.0	12:00	1.7	321.2	11:49	1.7	333.4	11:18	1.7	322.7	10:37	1.7	318.3	10:20	23:43
11:02	1.4	336.6	12:12	1.4	335.6	12:01	1.4	329.6	11:28	1.4	319.5	10:50	1.5	336.5	11:33	24:43

					Day 1 (30 & 31 May 2011)			Day 2 (31 May & 1 June 2011)			Day 3 (1 & 2 June 2011)			Day 4 (2 & 3 June 2011)			Day 5 (3 & 4 June 2011)		
Group No.:	Animal No.	Test Substance/Dose Level	Actual Dose Concentration (mg/ml)	Age of Animal (PND)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)
5	33	Octylmethoxycinnamate (1000 mg/kg)	202.9	58	10:06	1.3	1013.7	10:19	1.3	1002.9	10:10	1.3	989.0	9:54	1.4	1042.0	9:24	1.3	1000.6
5	34		202.9	58	10:21	1.4	1043.2	10:30	1.4	1049.7	10:20	1.4	1032.2	10:05	1.4	1012.7	9:36	1.4	1024.4
5	35		202.9	58	10:33	1.2	976.3	10:41	1.3	1044.6	10:28	1.3	1020.4	10:16	1.4	1052.1	9:49	1.4	1040.9
5	36		202.9	58	10:44	1.2	1004.9	10:50	1.2	1000.7	10:35	1.2	996.6	10:26	1.2	979.0	10:01	1.3	1023.2
5	37		202.9	59	11:04	1.3	1033.6	10:46	1.3	1027.9	10:40	1.3	1011.0	10:15	1.3	1003.7	10:31	1.4	1045.5
5	38		202.9	59	11:16	1.3	1000.6	10:57	1.3	986.8	10:49	1.4	1035.2	10:32	1.3	979.1	10:44	1.4	1025.9
5	39		202.9	59	11:31	1.3	1038.9	11:07	1.3	1053.4	11:00	1.3	1049.6	10:45	1.2	976.7	10:59	1.3	998.8
5	40		202.9	59	11:42	1.3	1004.8	11:22	1.3	995.4	11:11	1.4	1051.3	10:58	1.3	999.1	11:11	1.4	993.9

Day 6 (4 & 5 June 2011)			Day 7 (5 & 6 June 2011)			Day 8 (6 & 7 June 2011)			Day 9 (7 & 8 June 2011)			Day 10 (8 & 9 June 2011)			Day 11 (9 & 10 June 2011)	
Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Death	Time From Last Administration
9:37	1.4	991.5	9:32	1.3	997.2	10:42	1.3	1016.8	10:37	1.3	1001.4	10:04	1.4	1034.1	9:14	23:10
9:49	1.5	1047.7	9:44	1.5	1034.5	10:55	1.5	1019.6	10:49	1.5	1000.5	10:14	1.5	990.7	10:38	24:24
10:02	1.4	1035.6	9:56	1.4	1005.9	11:08	1.4	999.2	11:00	1.4	985.0	10:26	1.5	1044.4	11:38	25:12
10:14	1.3	998.8	10:09	1.3	1000.3	11:20	1.3	983.8	11:14	1.3	983.5	10:37	1.4	1034.1	12:38	26:01
10:28	1.4	1024.7	11:34	1.4	1021.8	11:26	1.4	997.1	10:51	1.5	1034.1	10:15	1.5	1024.1	8:30	22:15
10:40	1.4	998.1	11:47	1.4	990.4	11:37	1.4	985.3	11:02	1.5	1029.3	10:26	1.5	1009.1	9:29	23:03
10:52	1.3	1001.8	12:00	1.3	989.8	11:50	1.4	1048.6	11:19	1.4	1025.9	10:38	1.4	1018.1	10:25	23:47
11:02	1.4	985.0	12:13	1.4	984.3	12:02	1.5	1038.7	11:29	1.5	1015.2	10:51	1.5	1017.2	11:37	24:46

					Day 1 (30 & 31 May 2011)		Day 2 (31 May & 1 June 2011)		Day 3 (1 & 2 June 2011)		Day 4 (2 & 3 June 2011)		Day 5 (3 & 4 June 2011)	
Group No.:	Animal No.	Test Substance/Dose Level	Dose Route	Age of Animal (PND)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Time of Administration (Hour:Minute)	Volume Administered (mL)
6	41	Corn Oil (0 mg/kg) & Testosterone Propionate (0.4 mg/kg)	Gavage	58	10:09	1.3	10:20	1.3	10:12	1.3	9:55	1.4	9:25	1.2
			Subcutaneous			0.13		0.13		0.13		0.14		0.12
6	42		Gavage	58	10:22	1.3	10:31	1.3	10:20	1.3	10:06	1.4	9:37	1.4
			Subcutaneous			0.13		0.13		0.13		0.14		0.14
6	43		Gavage	58	10:34	1.3	10:41	1.3	10:28	1.3	10:17	1.3	9:50	1.4
			Subcutaneous			0.13		0.13		0.13		0.13		0.14
6	44		Gavage	58	10:45	1.2	10:51	1.3	10:36	1.3	10:27	1.4	10:02	1.4
			Subcutaneous			0.12		0.13		0.13		0.14		0.14
6	45		Gavage	59	11:05	1.4	10:48	1.4	10:40	1.5	10:16	1.5	10:32	1.6
			Subcutaneous			0.14		0.14		0.15		0.15		0.16
6	46		Gavage	59	11:21	1.3	10:58	1.3	10:50	1.4	10:33	1.4	10:47	1.5
			Subcutaneous			0.13		0.13		0.14		0.14		0.15
6	47		Gavage	59	11:32	1.2	11:08	1.3	11:01	1.3	10:46	1.4	11:00	1.4
			Subcutaneous			0.12		0.13		0.13		0.14		0.14
6	48		Gavage	59	11:43	1.4	11:22	1.4	11:13	1.5	10:59	1.5	11:12	1.6
			Subcutaneous			0.14		0.14		0.15		0.15		0.16

Day 6 (4 & 5 June 2011)		Day 7 (5 & 6 June 2011)		Day 8 (6 & 7 June 2011)		Day 9 (7 & 8 June 2011)		Day 10 (8 & 9 June 2011)		Day 11 (9 & 10 June 2011)	
Time of Administration (Hour:Minute)	Volume Administered (mL)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Time of Death	Time From Last Administration
9:38	1.4	9:34	1.5	10:43	1.5	10:38	1.5	10:05	1.6	9:23	23:18
	0.14		0.15		0.15		0.15		0.16		
9:50	1.4	9:45	1.5	10:56	1.5	10:50	1.5	10:15	1.5	10:44	24:29
	0.14		0.15		0.15		0.15		0.15		
10:03	1.4	9:57	1.5	11:09	1.5	11:01	1.5	10:26	1.6	11:42	25:16
	0.14		0.15		0.15		0.15		0.16		
10:15	1.4	10:10	1.5	11:21	1.5	11:15	1.5	10:38	1.5	12:42	26:04
	0.14		0.15		0.15		0.15		0.15		
10:29	1.6	11:36	1.7	11:27	1.7	10:52	1.8	10:15	1.8	8:34	22:19
	0.16		0.17		0.17		0.18		0.18		
10:40	1.5	11:49	1.5	11:38	1.6	11:03	1.6	10:27	1.6	9:34	23:07
	0.15		0.15		0.16		0.16		0.16		
10:53	1.5	12:01	1.5	11:51	1.6	11:19	1.6	10:39	1.7	10:40	24:01
	0.15		0.15		0.16		0.16		0.17		
11:03	1.6	12:14	1.6	12:03	1.7	11:29	1.7	10:52	1.8	11:42	24:50
	0.16		0.16		0.17		0.17		0.18		

						Day 1 (30 & 31 May 2011)			Day 2 (31 May & 1 June 2011)			Day 3 (1 & 2 June 2011)			Day 4 (2 & 3 June 2011)			Day 5 (3 & 4 June 2011)		
Group No.:	Animal No.	Test Substance/Dose Level	Dose Route	Actual Dose Concentration (mg/ml)	Age of Animal (PND)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)
7	49	Oxybenzone (100 mg/kg) & Testosterone Propionate (0.4 mg/kg)	Gavage	20.2	59	10:11	1.4	101.4	10:21	1.4	102.0	10:13	1.5	107.0	9:56	1.5	104.8	9:26	1.6	109.2
			Subcutaneous				0.14			0.14			0.15			0.15			0.16	
7	50		Gavage		59	10:23	1.3	91.7	10:32	1.3	90.7	10:21	1.4	93.6	10:07	1.4	90.8	9:38	1.5	93.9
			Subcutaneous				0.13			0.13			0.14			0.14			0.15	
7	51		Gavage		59	10:35	1.2	84.0	10:42	1.2	83.2	10:29	1.3	88.5	10:18	1.3	87.4	9:51	1.4	91.4
			Subcutaneous				0.12			0.12			0.13			0.13			0.14	
7	52		Gavage		59	10:46	1.3	97.8	10:52	1.3	96.7	10:37	1.4	102.8	10:29	1.4	101.3	10:03	1.5	105.5
			Subcutaneous				0.13			0.13			0.14			0.14			0.15	
7	53		Gavage		60	11:07	1.2	90.7	10:49	1.2	88.8	10:41	1.3	95.1	10:17	1.3	92.6	10:33	1.3	89.8
			Subcutaneous				0.12			0.12			0.13			0.13			0.13	
7	54		Gavage		60	11:22	1.4	108.1	10:58	1.4	104.9	10:51	1.5	114.3	10:34	1.5	112.0	10:48	1.6	116.5
			Subcutaneous				0.14			0.14			0.15			0.15			0.16	
7	55		Gavage		60	11:33	1.3	88.4	11:09	1.3	89.1	11:02	1.3	87.9	10:47	1.4	93.1	11:01	1.4	89.2
			Subcutaneous				0.13			0.13			0.13			0.14			0.14	
7	56		Gavage		60	11:44	1.3	92.8	11:23	1.3	92.4	11:13	1.4	98.1	10:59	1.4	95.6	11:13	1.5	100.3
			Subcutaneous				0.13			0.13			0.14			0.14			0.15	

Day 6 (4 & 5 June 2011)			Day 7 (5 & 6 June 2011)			Day 8 (6 & 7 June 2011)			Day 9 (7 & 8 June 2011)			Day 10 (8 & 9 June 2011)			Day 11 (9 & 10 June 2011)	
Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Death	Time From Last Administration
9:40	1.6	106.7	9:35	1.6	104.4	10:44	1.7	110.7	10:39	1.7	108.8	10:05	1.8	118.7	9:30	23:25
	0.16			0.16			0.17			0.17			0.18			
9:52	1.5	91.6	9:46	1.5	89.6	10:58	1.5	87.3	10:51	1.6	91.4	10:16	1.6	94.1	10:47	24:31
	0.15			0.15			0.15			0.16			0.16			
10:04	1.4	90.4	9:58	1.5	96.2	11:11	1.5	94.5	11:02	1.6	97.9	10:27	1.6	96.7	11:48	25:21
	0.14			0.15			0.15			0.16			0.16			
10:16	1.5	101.6	10:11	1.5	99.5	11:22	1.6	105.0	11:16	1.6	101.9	10:39	1.6	98.8	12:46	26:07
	0.15			0.15			0.16			0.16			0.16			
10:30	1.4	94.9	11:37	1.4	92.6	11:28	1.4	89.9	10:53	1.5	93.3	10:17	1.5	94.0	8:38	22:21
	0.14			0.14			0.14			0.15			0.15			
10:41	1.6	114.8	11:50	1.7	121.1	11:40	1.7	116.6	11:04	1.7	114.8	10:28	1.8	124.1	9:38	23:10
	0.16			0.17			0.17			0.17			0.18			
10:54	1.5	94.0	12:03	1.5	93.2	11:52	1.5	90.5	11:20	1.6	96.3	10:40	1.6	95.5	10:43	24:03
	0.15			0.15			0.15			0.16			0.16			
11:04	1.5	97.3	12:15	1.5	96.5	12:04	1.6	99.4	11:30	1.6	97.9	10:53	1.7	103.5	11:47	24:54
	0.15			0.15			0.16			0.16			0.17			

						Day 1 (30 & 31 May 2011)			Day 2 (31 May & 1 June 2011)			Day 3 (1 & 2 June 2011)			Day 4 (2 & 3 June 2011)			Day 5 (3 & 4 June 2011)		
Group No.:	Animal No.	Test Substance/Dose Level	Dose Route	Actual Dose Concentration (mg/ml)	Age of Animal (PND)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)
8	57	Oxybenzone (320 mg/kg) & Testosterone Propionate (0.4 mg/kg)	Gavage	63.9	59	10:12	1.3	303.7	10:22	1.3	293.2	10:13	1.4	311.3	9:57	1.4	309.7	9:27	1.4	303.8
			Subcutaneous				0.13			0.13			0.14			0.14			0.14	
8	58		Gavage		59	10:24	1.3	325.6	10:33	1.3	321.9	10:22	1.3	314.9	10:08	1.4	334.6	9:40	1.4	330.2
			Subcutaneous				0.13			0.13			0.13			0.14			0.14	
8	59		Gavage		59	10:36	1.3	324.9	10:43	1.3	320.2	10:30	1.4	330.8	10:19	1.5	360.5	9:51	1.6	378.1
			Subcutaneous				0.13			0.13			0.14			0.15			0.16	
8	60		Gavage		59	10:47	1.3	299.8	10:54	1.3	294.2	10:38	1.3	286.3	10:30	1.4	300.9	10:04	1.4	298.1
			Subcutaneous				0.13			0.13			0.13			0.14			0.14	
8	61		Gavage		60	11:09	1.4	318.6	10:50	1.4	314.2	10:42	1.4	311.7	10:18	1.5	323.4	10:34	1.5	317.8
			Subcutaneous				0.14			0.14			0.14			0.15			0.15	
8	62		Gavage		60	11:23	1.4	325.5	10:59	1.4	321.0	10:52	1.5	342.0	10:35	1.5	333.0	10:49	1.6	347.3
			Subcutaneous				0.14			0.14			0.15			0.15			0.16	
8	63		Gavage		60	11:34	1.3	274.4	11:09	1.3	268.7	11:03	1.4	283.4	10:48	1.4	277.7	11:02	1.4	269.5
			Subcutaneous				0.13			0.13			0.14			0.14			0.14	
8	64		Gavage		60	11:45	1.3	275.9	11:24	1.3	270.2	11:14	1.3	264.8	11:00	1.4	280.0	11:15	1.4	276.6
			Subcutaneous				0.13			0.13			0.13			0.14			0.14	

Day 6 (4 & 5 June 2011)			Day 7 (5 & 6 June 2011)			Day 8 (6 & 7 June 2011)			Day 9 (7 & 8 June 2011)			Day 10 (8 & 9 June 2011)			Day 11 (9 & 10 June 2011)	
Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Death	Time From Last Administration
9:41	1.5	317.1	9:35	1.5	313.9	10:46	1.6	327.0	10:40	1.6	318.5	10:06	1.6	314.9	9:37	23:31
	0.15			0.15			0.16			0.16			0.16			
9:52	1.5	342.8	9:47	1.5	339.2	10:58	1.5	336.2	10:52	1.5	326.9	10:17	1.6	346.5	10:51	0:34
	0.15			0.15			0.15			0.15			0.16			
10:05	1.6	371.4	9:58	1.6	367.0	11:12	1.6	365.3	11:04	1.7	380.6	10:28	1.7	376.4	11:53	25:25
	0.16			0.16			0.16			0.17			0.17			
10:17	1.4	291.4	10:12	1.5	307.9	11:23	1.5	303.2	11:17	1.5	293.9	10:39	1.5	289.7	12:50	26:11
	0.14			0.15			0.15			0.15			0.15			
10:31	1.5	310.6	11:38	1.6	325.4	11:29	1.6	310.4	10:54	1.7	325.8	10:18	1.7	319.6	8:43	22:25
	0.15			0.16			0.16			0.17			0.17			
10:42	1.6	344.2	11:51	1.6	341.7	11:41	1.7	353.4	11:05	1.7	348.7	10:29	1.8	361.0	9:43	23:14
	0.16			0.16			0.17			0.17			0.18			
10:55	1.5	282.4	12:04	1.5	280.3	11:53	1.6	291.6	11:20	1.6	286.2	10:42	1.6	282.7	10:47	24:05
	0.15			0.15			0.16			0.16			0.16			
11:05	1.5	288.0	12:16	1.5	282.7	12:05	1.5	278.5	11:30	1.6	290.8	10:54	1.6	287.2	11:53	24:59
	0.15			0.15			0.15			0.16			0.16			

						Day 1 (30 & 31 May 2011)			Day 2 (31 May & 1 June 2011)			Day 3 (1 & 2 June 2011)			Day 4 (2 & 3 June 2011)			Day 5 (3 & 4 June 2011)		
Group No.:	Animal No.	Test Substance/Dose Level	Dose Route	Actual Dose Concentration (mg/ml)	Age of Animal (PND)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)
9	65	Oxybenzone (1000 mg/kg) & Testosterone Propionate (0.4 mg/kg)	Gavage	211	59	10:13	1.3	1037.8	10:23	1.3	1028.1	10:14	1.3	1030.8	9:58	1.4	1079.7	9:28	1.4	1057.6
			Subcutaneous				0.13			0.13			0.13			0.14			0.14	
9	66		Gavage		59	10:25	1.2	1033.0	10:34	1.2	1019.3	10:23	1.3	1087.6	10:10	1.3	1057.0	9:41	1.4	1092.5
			Subcutaneous				0.12			0.12			0.13			0.13			0.14	
9	67		Gavage		59	10:37	1.2	1030.5	10:44	1.2	1073.8	10:31	1.2	1039.8	10:20	1.3	1091.1	9:53	1.3	1053.4
			Subcutaneous				0.12			0.12			0.12			0.13			0.13	
9	68		Gavage		59	10:48	1.2	1062.5	10:55	1.2	1042.8	10:38	1.2	1024.3	10:31	1.3	1055.0	10:06	1.4	1084.8
			Subcutaneous				0.12			0.12			0.12			0.13			0.14	
9	69		Gavage		60	11:10	1.3	1055.4	10:51	1.3	1077.4	10:43	1.3	1053.8	10:20	1.4	1091.2	10:35	1.4	1063.0
			Subcutaneous				0.13			0.13			0.13			0.14			0.14	
9	70		Gavage		60	11:24	1.3	1041.8	11:01	1.3	1026.2	10:53	1.3	1037.4	10:37	1.4	1057.3	10:50	1.4	1049.8
			Subcutaneous				0.13			0.13			0.13			0.14			0.14	
9	71		Gavage		60	11:35	1.3	1064.0	11:10	1.3	1066.1	11:04	1.3	1071.9	10:50	1.3	1020.1	11:03	1.3	1027.7
			Subcutaneous				0.13			0.13			0.13			0.13			0.13	
9	72		Gavage		60	11:47	1.4	1054.2	11:25	1.5	1088.4	11:16	1.5	1090.3	11:01	1.5	1052.2	11:15	1.5	1023.9
			Subcutaneous				0.14			0.15			0.15			0.15			0.15	

Day 6 (4 & 5 June 2011)			Day 7 (5 & 6 June 2011)			Day 8 (6 & 7 June 2011)			Day 9 (7 & 8 June 2011)			Day 10 (8 & 9 June 2011)			Day 11 (9 & 10 June 2011)	
Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Death	Time From Last Administration
9:42	1.5	1090.3	9:36	1.5	1079.5	10:47	1.5	1070.3	10:41	1.5	1058.5	10:07	1.5	1033.6	9:44	23:37
	0.15			0.15			0.15			0.15			0.15			
9:54	1.4	1074.2	9:49	1.4	1040.5	11:00	1.5	1088.0	10:53	1.5	1067.1	10:18	1.5	1032.6	10:45	24:27
	0.14			0.14			0.15			0.15			0.15			
10:06	1.3	1065.7	10:00	1.3	1021.2	11:13	1.4	1085.2	11:06	1.4	1056.5	10:28	1.4	1034.7	11:58	25:30
	0.13			0.13			0.14			0.14			0.14			
10:18	1.4	1072.2	10:13	1.4	1036.1	11:24	1.4	1025.7	11:19	1.5	1091.0	10:40	1.5	1065.3	12:54	26:14
	0.14			0.14			0.14			0.15			0.15			
10:32	1.4	1031.4	11:40	1.5	1080.2	11:30	1.5	1059.2	10:55	1.5	1037.0	10:19	1.6	1084.8	8:47	22:28
	0.14			0.15			0.15			0.15			0.16			
10:45	1.4	1023.6	11:52	1.5	1089.1	11:42	1.5	1068.5	11:06	1.5	1064.6	10:31	1.5	1053.2	9:48	23:17
	0.14			0.15			0.15			0.15			0.15			
10:56	1.3	1019.3	12:05	1.4	1069.1	11:54	1.4	1051.6	11:21	1.4	1034.3	10:43	1.4	1021.4	10:51	24:08
	0.13			0.14			0.14			0.14			0.14			
11:06	1.6	1069.4	12:17	1.6	1061.3	12:06	1.6	1045.2	11:31	1.7	1075.9	10:55	1.7	1067.2	11:57	25:02
	0.16			0.16			0.16			0.17			0.17			

						Day 1 (30 & 31 May 2011)			Day 2 (31 May & 1 June 2011)			Day 3 (1 & 2 June 2011)			Day 4 (2 & 3 June 2011)			Day 5 (3 & 4 June 2011)		
Group No.:	Animal No.	Test Substance/Dose Level	Dose Route	Actual Dose Concentration (mg/ml)	Age of Animal (PND)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)
10	73	Octylmethoxycinnamate (100 mg/kg) & Testosterone Propionate (0.4 mg/kg)	Gavage	20.1	59	10:14	1.3	101.0	10:24	1.3	97.4	10:15	1.4	102.3	9:59	1.4	97.2	9:29	1.5	101.1
			Subcutaneous				0.13			0.13			0.14			0.14			0.15	
10	74		Gavage		59	10:26	1.3	101.2	10:35	1.3	99.1	10:23	1.4	102.9	10:11	1.4	98.9	9:42	1.5	104.0
			Subcutaneous				0.13			0.13			0.14			0.14			0.15	
10	75		Gavage		59	10:38	1.3	102.7	10:45	1.3	102.5	10:31	1.3	97.6	10:21	1.4	101.8	9:54	1.5	103.1
			Subcutaneous				0.13			0.13			0.13			0.14			0.15	
10	76		Gavage		59	10:48	1.2	96.7	10:55	1.3	101.2	10:40	1.3	98.6	10:32	1.4	103.3	10:07	1.4	99.3
			Subcutaneous				0.12			0.13			0.13			0.14			0.14	
10	77		Gavage		60	11:11	1.4	103.9	10:52	1.4	101.7	10:44	1.4	98.3	10:21	1.5	100.5	10:36	1.5	98.9
			Subcutaneous				0.14			0.14			0.14			0.15			0.15	
10	78		Gavage		60	11:25	1.4	99.0	11:02	1.5	103.5	10:54	1.5	99.7	10:38	1.6	103.1	10:51	1.6	99.7
			Subcutaneous				0.14			0.15			0.15			0.16			0.16	
10	79		Gavage		60	11:36	1.2	102.3	11:12	1.2	100.9	11:05	1.2	100.0	10:51	1.2	99.4	11:05	1.3	104.3
			Subcutaneous				0.12			0.12			0.12			0.12			0.13	
10	80		Gavage		60	11:48	1.3	97.6	11:26	1.4	103.3	11:16	1.4	99.2	11:02	1.4	99.6	11:16	1.5	101.6
			Subcutaneous				0.13			0.14			0.14			0.14			0.15	

Day 6 (4 & 5 June 2011)			Day 7 (5 & 6 June 2011)			Day 8 (6 & 7 June 2011)			Day 9 (7 & 8 June 2011)			Day 10 (8 & 9 June 2011)			Day 11 (9 & 10 June 2011)	
Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Death	Time From Last Administration
9:43	1.5	98.8	9:37	1.6	100.4	10:48	1.6	98.6	10:42	1.7	103.3	10:08	1.7	99.1	9:50	23:42
	0.15			0.16			0.16			0.17			0.17			
9:55	1.5	100.9	9:50	1.5	98.1	11:01	1.6	102.5	10:54	1.6	100.5	10:19	1.7	99.7	10:58	24:39
	0.15			0.15			0.16			0.16			0.17			
10:07	1.5	102.2	10:01	1.6	103.5	11:14	1.6	102.1	11:07	1.6	99.8	10:29	1.7	102.8	12:03	25:34
	0.15			0.16			0.16			0.16			0.17			
10:19	1.5	103.0	10:13	1.5	100.3	11:26	1.4	102.6	11:20	1.3	98.5	10:41	1.3	97.1	12:58	26:17
	0.15			0.15			0.14			0.13			0.13			
10:33	1.6	101.9	11:41	1.6	100.0	11:31	1.6	98.0	10:56	1.7	101.2	10:20	1.7	100.6	8:53	22:33
	0.16			0.16			0.16			0.17			0.17			
10:46	1.7	101.9	11:53	1.7	100.6	11:43	1.3	103.1	11:07	1.8	99.4	10:32	1.8	97.9	9:52	23:20
	0.17			0.17			0.13			0.18			0.18			
10:57	1.3	102.7	12:06	1.3	100.8	11:55	1.3	98.8	11:22	1.3	97.0	10:44	1.4	102.6	10:56	24:12
	0.13			0.13			0.13			0.13			0.14			
11:07	1.5	98.9	12:18	1.5	97.4	12:07	1.6	101.5	11:32	1.6	98.1	10:55	1.6	97.7	12:01	25:06
	0.15			0.15			0.16			0.16			0.16			

						Day 1 (30 & 31 May 2011)			Day 2 (31 May & 1 June 2011)			Day 3 (1 & 2 June 2011)			Day 4 (2 & 3 June 2011)			Day 5 (3 & 4 June 2011)		
Group No.:	Animal No.	Test Substance/Dose Level	Dose Route	Actual Dose Concentration (mg/ml)	Age of Animal (PND)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)
11	81	Octylmethoxycinnamate (320 mg/kg) & Testosterone Propionate (0.4 mg/kg)	Gavage	65.2	59	10:15	1.2	326.3	10:26	1.2	325.2	10:16	1.2	313.8	10:00	1.3	334.8	9:30	1.3	316.2
			Subcutaneous				0.12			0.12			0.12			0.13			0.13	
11	82		Gavage		59	10:28	1.2	315.2	10:36	1.2	313.7	10:24	1.3	325.2	10:12	1.4	334.4	9:43	1.4	318.0
			Subcutaneous				0.12			0.12			0.13			0.14			0.14	
11	83		Gavage		59	10:39	1.4	335.5	10:46	1.4	325.9	10:32	1.4	317.9	10:21	1.5	325.7	9:55	1.4	317.3
			Subcutaneous				0.14			0.14			0.14			0.15			0.14	
11	84[#]		Gavage		59	10:49	1.3	319.6	10:56	1.3	318.6	10:41	1.4	331.2	10:33	1.4	316.3	10:08	1.4	328.7
			Subcutaneous				0.13			0.13			0.14			0.14			0.14	
11	85		Gavage		60	11:11	1.3	322.8	10:53	1.3	314.5	10:45	1.4	325.1	10:22	1.5	334.7	10:37	1.5	319.9
			Subcutaneous				0.13			0.13			0.14			0.15			0.15	
11	86[^]		Gavage		60	11:26	1.3	327.5	11:03	1.3	321.8	10:55	1.4	337.0	10:38	1.4	326.7	10:52	1.4	317.6
			Subcutaneous				0.13			0.13			0.14			0.14			0.14	
11	87		Gavage		60	11:37	1.4	336.5	11:14	1.3	323.6	11:06	1.4	337.7	10:53	1.4	324.4	11:06	1.4	315.4
			Subcutaneous				0.14			0.13			0.14			0.14			0.14	
11	88		Gavage		60	11:49	1.3	329.4	11:28	1.4	330.0	11:18	1.5	336.7	11:04	1.5	323.0	11:16	1.6	332.0
			Subcutaneous				0.13			0.14			0.15			0.15			0.16	

[#]Moribund sacrifice due to dosing error

[^]Humane sacrifice due to dosing error

Day 6 (4 & 5 June 2011)			Day 7 (5 & 6 June 2011)			Day 8 (6 & 7 June 2011)			Day 9 (7 & 8 June 2011)			Day 10 (8 & 9 June 2011)			Day 11 (9 & 10 June 2011)	
Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Death	Time From Last Administration
9:44	1.4	331.3	9:38	1.4	323.7	10:50	1.4	318.8	10:43	1.5	334.4	10:09	1.5	324.8	9:57	23:48
	0.14			0.14			0.14			0.15			0.15			
9:56	1.5	329.1	9:51	1.5	321.8	11:02	1.6	335.9	10:55	1.6	322.4	10:20	1.7	334.1	11:03	24:43
	0.15			0.15			0.16			0.16			0.17			
10:08	1.6	330.6	10:01	1.6	323.2	11:15	1.6	316.7	11:08	1.7	333.0	10:30	1.7	319.0	12:08	25:38
	0.16			0.16			0.16			0.17			0.17			
10:20	1.5	318.0	10:15	1.4	326.9										23:44	13:29
	0.15			0.14												
10:34	1.6	331.9	11:42	1.6	325.2	11:32	1.6	317.4	10:56	1.7	331.7	10:21	1.7	316.9	8:57	22:36
	0.16			0.16			0.16			0.17			0.17			
10:47	1.3	235.1	11:55	1.2	317.7	11:45	1.2	333.8	11:13	1.1	325.1		1	312.0	10:20	23:07
	0.13			0.12			0.12			0.11			0.1			
10:58	1.5	331.9	12:07	1.5	330.3	11:56	1.5	320.4	11:23	1.6	332.7	10:45	1.6	328.6	10:59	24:14
	0.15			0.15			0.15			0.16			0.16			
11:08	1.6	319.4	12:19	1.7	335.5	12:08	1.7	320.8	11:33	1.8	329.6	10:56	1.8	322.1	12:05	25:09
	0.16			0.17			0.17			0.18			0.18			

						Day 1 (30 & 31 May 2011)			Day 2 (31 May & 1 June 2011)			Day 3 (1 & 2 June 2011)			Day 4 (2 & 3 June 2011)			Day 5 (3 & 4 June 2011)		
Group No.:	Animal No.	Test Substance/Dose Level	Dose Route	Actual Dose Concentration (mg/ml)	Age of Animal (PND)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)
12	89	Octylmethoxycinnamate (1000 mg/kg) & Testosterone Propionate (0.4 mg/kg)	Gavage	202.9	59	10:16	1.3	1014.1	10:27	1.3	1025.5	10:17	1.3	1000.6	10:01	1.4	1021.1	9:31	1.4	1027.0
			Subcutaneous				0.13			0.13			0.13			0.14			0.14	
12	90		Gavage		59	10:29	1.2	999.5	10:37	1.2	1007.8	10:25	1.3	1053.8	10:13	1.3	1018.8	9:44	1.3	1017.6
			Subcutaneous				0.12			0.12			0.13			0.13			0.13	
12	91		Gavage		59	10:40	1.2	1035.6	10:47	1.2	1039.6	10:33	1.2	1018.7	10:22	1.2	986.9	9:56	1.2	1043.2
			Subcutaneous				0.12			0.12			0.12			0.12			0.12	
12	92		Gavage		59	10:51	1.3	982.0	10:57	1.3	999.9	10:41	1.4	1042.0	10:34	1.4	1027.0	10:09	1.3	1015.3
			Subcutaneous				0.13			0.13			0.14			0.14			0.13	
12	93		Gavage		60	11:12	1.3	1015.3	10:53	1.3	1012.9	10:46	1.3	994.6	10:23	1.3	983.5	10:38	1.4	1019.6
			Subcutaneous				0.13			0.13			0.13			0.13			0.14	
12	94		Gavage		60	11:27	1.3	993.5	11:04	1.4	1049.4	10:56	1.4	1002.0	10:40	1.4	987.7	10:53	1.5	992.3
			Subcutaneous				0.13			0.14			0.14			0.14			0.15	
12	95		Gavage		60	11:38	1.4	1038.2	11:15	1.4	1022.5	11:07	1.4	1003.4	10:54	1.4	1048.6	11:07	1.5	1016.9
			Subcutaneous				0.14			0.14			0.14			0.14			0.15	
12	96		Gavage		60	11:50	1.3	984.2	11:28	1.3	1011.4	11:18	1.3	977.7	11:05	1.3	994.6	11:17	1.4	1005.9
			Subcutaneous				0.13			0.13			0.13			0.13			0.14	

Day 6 (4 & 5 June 2011)			Day 7 (5 & 6 June 2011)			Day 8 (6 & 7 June 2011)			Day 9 (7 & 8 June 2011)			Day 10 (8 & 9 June 2011)			Day 11 (9 & 10 June 2011)	
Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Death	Time From Last Administration
9:45	1.5	1048.4	9:39	1.5	1019.9	10:51	1.5	994.0	10:44	1.6	1037.5	10:10	1.6	1014.5	10:03	23:53
	0.15			0.15			0.15			0.16			0.16			
9:57	1.4	1023.3	9:52	1.4	999.5	11:03	1.5	1070.1	10:56	1.5	1035.9	10:21	1.5	1025.8	11:07	24:46
	0.14			0.14			0.15			0.15			0.15			
10:10	1.3	1021.2	10:02	1.3	1022.0	11:16	1.5	1184.7	11:10	1.3	998.0	10:31	1.3	988.6	12:14	25:43
	0.13			0.13			0.15			0.13			0.13			
10:21	1.5	1049.5	10:23	1.5	1041.6	11:29	1.5	1033.1	11:21	1.5	997.9	10:43	1.5	990.1	13:01	26:18
	0.15			0.15			0.15			0.15			0.15			
10:34	1.4	1016.7	11:43	1.4	1008.7	11:33	1.4	984.6	10:57	1.5	1023.7	10:22	1.5	1002.1	9:01	22:39
	0.14			0.14			0.14			0.15			0.15			
10:47	1.6	1029.0	11:56	1.6	1016.7	11:46	1.6	987.3	11:14	1.7	1005.0	10:33	1.8	1037.3	9:57	23:24
	0.16			0.16			0.16			0.17			0.18			
10:59	1.5	997.9	12:08	1.5	995.3	11:58	1.6	1029.9	11:24	1.6	1019.0	10:46	1.6	1008.5	11:03	24:17
	0.15			0.15			0.16			0.16			0.16			
11:09	1.5	1028.9	12:20	1.5	1021.0	12:09	1.5	1001.8	11:34	1.5	983.7	10:56	1.6	1044.9	12:09	25:13
	0.15			0.15			0.15			0.15			0.16			

					Day 1 (30 & 31 May 2011)		Day 2 (31 May & 1 June 2011)		Day 3 (1 & 2 June 2011)		Day 4 (2 & 3 June 2011)		Day 5 (3 & 4 June 2011)	
Group No.:	Animal No.	Test Substance/Dose Level	Dose Route	Age of Animal (PND)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Time of Administration (Hour:Minute)	Volume Administered (mL)
13	97	Flutamide (3 mg/kg) & Testosterone Propionate (0.4 mg/kg)	Gavage	59	10:17	1.2	10:28	1.2	10:17	1.3	10:02	1.3	9:32	1.4
			Subcutaneous			0.12		0.12		0.13		0.13		0.14
13	98		Gavage	59	10:30	1.2	10:38	1.3	10:25	1.3	10:14	1.3	9:45	1.4
			Subcutaneous			0.12		0.13		0.13		0.13		0.14
13	99		Gavage	59	10:41	1.2	10:48	1.3	10:33	1.3	10:23	1.4	9:57	1.4
			Subcutaneous			0.12		0.13		0.13		0.14		0.14
13	100[+]		Gavage	59	+	1.3	10:58	1.3	10:42	1.3	10:35	1.4	10:10	1.4
			Subcutaneous			0.13		0.13		0.13		0.14		0.14
13	101		Gavage	60	11:13	1.4	10:54	1.4	10:47	1.5	10:24	1.5	10:39	1.6
			Subcutaneous			0.14		0.14		0.15		0.15		0.16
13	102		Gavage	60	11:27	1.4	11:04	1.4	10:57	1.4	10:41	1.5	10:55	1.5
			Subcutaneous			0.14		0.14		0.14		0.15		0.15
13	103		Gavage	60	11:39	1.4	11:16	1.4	11:09	1.4	10:55	1.4	11:08	1.5
			Subcutaneous			0.14		0.14		0.14		0.14		0.15
13	104		Gavage	60	11:50	1.4	11:29	1.3	11:20	1.3	11:06	1.2	11:18	1.3
			Subcutaneous			0.14		0.13		0.13		0.12		0.13

[+]Animal was not dosed due to technician error. See Deviation 1

Day 6 (4 & 5 June 2011)		Day 7 (5 & 6 June 2011)		Day 8 (6 & 7 June 2011)		Day 9 (7 & 8 June 2011)		Day 10 (8 & 9 June 2011)		Day 11 (9 & 10 June 2011)	
Time of Administration (Hour:Minute)	Volume Administered (mL)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Time of Death	Time From Last Administration
9:46	1.4	9:40	1.4	10:52	1.5	10:46	1.5	10:10	1.5	10:10	24:00
	0.14		0.14		0.15		0.15		0.15		
9:58	1.4	9:52	1.4	11:05	1.5	10:57	1.5	10:22	1.5	11:11	24:49
	0.14		0.14		0.15		0.15		0.15		
10:11	1.4	10:03	1.5	11:17	1.5	11:11	1.5	10:32	1.6	12:18	25:46
	0.14		0.15		0.15		0.15		0.16		
10:22	1.4	10:23	1.5	11:30	1.5	11:22	1.5	10:44	1.5	13:05	26:21
	0.14		0.15		0.15		0.15		0.15		
10:36	1.6	11:45	1.7	11:34	1.7	10:58	1.7	10:23	1.8	9:07	22:44
	0.16		0.17		0.17		0.17		0.18		
10:49	1.6	11:57	1.6	11:47	1.6	11:14	1.7	10:34	1.7	10:01	23:27
	0.16		0.16		0.16		0.17		0.17		
11:00	1.5	12:09	1.6	11:59	1.5	11:25	1.5	10:47	1.6	11:08	24:21
	0.15		0.16		0.15		0.15		0.16		
11:10	1.3	12:22	1.3	12:10	1.3	11:34	1.3	10:58	1.4	12:13	25:15
	0.13		0.13		0.13		0.13		0.14		

					Day 1 (13 & 14 June 2011)			Day 2 (14 & 15 June 2011)			Day 3 (15 & 16 June 2011)			Day 4 (16 & 17 June 2011)			Day 5 (17 & 18 June 2011)		
Group No.	Animal No.	Test Substance/Dose Level	Actual Dose Concentration (mg/ml)	Age of Animal (PND)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)
14	105	Corn Oil Control	0	59	10:03	1.0	0	10:01	1.1	0	9:59	1.1	0	10:10	1.1	0	10:04	1.1	0
14	106		0	59	10:14	1.2	0	10:11	1.2	0	10:10	1.3	0	10:25	1.3	0	10:17	1.3	0
14	107		0	59	10:23	1.3	0	10:21	1.3	0	10:22	1.3	0	10:39	1.4	0	10:33	1.4	0
14	108		0	59	10:32	1.3	0	10:32	1.3	0	10:33	1.4	0	10:57	1.4	0	10:48	1.4	0
14	109		0	60	10:47	1.4	0	10:43	1.4	0	11:12	1.4	0	11:05	1.4	0	10:10	1.5	0
14	110		0	60	11:01	1.5	0	10:55	1.5	0	11:27	1.6	0	11:23	1.6	0	10:17	1.6	0
14	111		0	60	11:13	1.4	0	11:09	1.4	0	11:42	1.5	0	11:42	1.5	0	10:26	1.5	0
14	112		0	60	11:25	1.6	0	11:24	1.7	0	11:56	1.7	0	11:57	1.8	0	10:36	1.8	0

Day 6 (18 & 19 June 2011)			Day 7 (19 & 20 June 2011)			Day 8 (20 & 21 June 2011)			Day 9 (21 & 22 June 2011)			Day 10 (22 & 23 June 2011)			Day 11 (23 & 24 June 2011)	
Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Death	Time From Last Administration
9:22	1.1	0	9:20	1.2	0	10:00	1.2	0	10:36	1.2	0	10:03	1.2	0	8:05	22:02
9:31	1.3	0	9:28	1.4	0	10:16	1.4	0	10:47	1.4	0	10:13	1.4	0	9:04	22:51
9:40	1.4	0	9:37	1.4	0	10:32	1.5	0	10:57	1.5	0	10:23	1.5	0	10:02	23:39
9:49	1.4	0	9:47	1.4	0	10:47	1.4	0	11:08	1.4	0	10:33	1.5	0	11:11	24:38
10:02	1.5	0	11:03	1.5	0	11:22	1.5	0	10:45	1.5	0	10:04	1.6	0	8:07	22:03
10:11	1.6	0	11:19	1.7	0	11:36	1.7	0	10:56	1.7	0	10:13	1.7	0	9:04	22:51
10:20	1.5	0	11:37	1.6	0	11:48	1.6	0	11:08	1.6	0	10:26	1.6	0	10:15	23:49
10:29	1.9	0	11:55	1.9	0	12:03	1.9	0	11:19	2.0	0	10:37	2.0	0	11:13	24:36

					Day 1 (13 & 14 June 2011)			Day 2 (14 & 15 June 2011)			Day 3 (15 & 16 June 2011)			Day 4 (16 & 17 June 2011)			Day 5 (17 & 18 June 2011)		
Group No.	Animal No.	Test Substance/Dose Level	Actual Dose Concentration (mg/ml)	Age of Animal (PND)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)
15	113	Octylsalate (235 mg/kg)	45.8	59	10:03	1.0	218.5	10:01	1.0	221.5	10:00	1.1	236.3	10:11	1.1	231.1	10:05	1.1	228.5
15	114		45.8	59	10:14	1.2	223.0	10:12	1.2	223.1	10:11	1.3	235.9	10:26	1.3	228.9	10:18	1.3	224.2
15	115		45.8	59	10:23	1.3	226.7	10:22	1.3	228.1	10:22	1.3	221.6	10:40	1.3	220.8	10:33	1.4	232.3
15	116		45.8	59	10:32	1.2	231.5	10:33	1.2	229.8	10:33	1.2	223.1	10:58	1.3	232.2	10:49	1.3	230.3
15	117		45.8	60	10:48	1.3	222.7	10:44	1.3	224.1	11:13	1.4	228.1	11:06	1.4	227.8	10:10	1.4	224.1
15	118		45.8	60	11:01	1.4	236.6	10:56	1.4	233.7	11:28	1.4	225.8	11:24	1.4	223.6	10:17	1.5	235.0
15	119		45.8	60	11:14	1.5	233.4	11:10	1.5	236.7	11:43	1.5	228.2	11:43	1.5	224.7	10:27	1.5	222.5
15	120		45.8	60	11:26	1.6	227.2	11:24	1.6	230.0	11:58	1.6	223.3	11:59	1.7	228.5	10:37	1.7	228.2

Day 6 (18 & 19 June 2011)			Day 7 (19 & 20 June 2011)			Day 8 (20 & 21 June 2011)			Day 9 (21 & 22 June 2011)			Day 10 (22 & 23 June 2011)			Day 11 (23 & 24 June 2011)	
Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Death	Time From Last Administration
9:23	1.1	226.5	9:20	1.1	220.7	10:01	1.2	236.5	10:37	1.2	236.4	10:04	1.2	3762.4	8:10	22:06
9:32	1.4	236.4	9:29	1.4	231.4	10:17	1.4	225.6	10:47	1.4	223.7	10:13	1.5	3774.1	9:08	22:55
9:41	1.4	231.4	9:37	1.4	230.0	10:33	1.4	224.8	10:57	1.4	222.6	10:23	1.5	3534.6	10:18	23:55
9:49	1.3	231.9	9:47	1.3	226.7	10:48	1.3	223.8	11:09	1.3	225.4	10:33	1.4	3614.7	11:14	24:41
10:03	1.4	224.1	11:04	1.5	234.4	11:22	1.5	234.0	10:46	1.5	227.0	10:04	1.5	3486.4	8:12	22:08
10:12	1.5	232.1	11:20	1.6	233.0	11:37	1.6	234.3	10:56	1.6	230.3	10:14	1.6	3422.0	9:08	22:54
10:21	1.5	223.9	11:39	1.6	233.2	11:49	1.6	234.3	11:09	1.6	228.6	10:26	1.6	3511.4	10:18	23:52
10:30	1.7	228.5	11:57	1.8	232.9	12:04	1.8	228.6	11:20	1.8	224.5	10:38	1.8	3363.1	11:17	24:39

					Day 1 (13 & 14 June 2011)			Day 2 (14 & 15 June 2011)			Day 3 (15 & 16 June 2011)			Day 4 (16 & 17 June 2011)			Day 5 (17 & 18 June 2011)		
Group No.	Animal No.	Test Substance/Dose Level	Actual Dose Concentration (mg/ml)	Age of Animal (PND)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)
16	121	Octylsalate (750 mg/kg)	143	59	10:04	1.1	704.7	10:02	1.1	725.2	10:00	1.1	723.9	10:12	1.1	713.4	10:06	1.1	703.8
16	122		143	0:00	10:14	1.3	735.4	10:12	1.2	702.4	10:12	1.2	710.6	10:27	1.2	698.1	10:19	1.2	708.8
16	123		143	59	10:24	1.2	692.2	10:22	1.2	717.7	10:23	1.2	726.5	10:41	1.2	737.7	10:35	1.1	693.0
16	124		143	59	10:33	1.3	707.7	10:33	1.3	726.7	10:34	1.3	735.7	10:59	1.3	709.3	10:50	1.3	700.2
16	125*		143	60	10:48	1.3	694.7	10:44	1.3	695.5	11:15	1.3	721.4	11:08	1.2	688.9			
16	126		143	60	11:02	1.4	696.6	10:56	1.5	738.6	11:29	1.4	702.5	11:25	1.4	707.2	10:19	1.3	693.7
16	127		143	60	11:15	1.5	733.1	11:11	1.4	710.4	11:44	1.4	711.7	11:44	1.4	720.9	10:28	1.4	726.4
16	128*		143	60	11:27	1.6	700.1	11:25	1.6	731.2	11:59	1.5	702.4	12:00	1.5	720.3	10:38	1.4	711.2

*Animal found dead prior to termination

Day 6 (18 & 19 June 2011)			Day 7 (19 & 20 June 2011)			Day 8 (20 & 21 June 2011)			Day 9 (21 & 22 June 2011)			Day 10 (22 & 23 June 2011)			Day 11 (23 & 24 June 2011)	
Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Death	Time From Last Administration
9:24	1.3	741.2	9:21	1.1	707.0	10:03	1.2	730.2	10:37	1.2	735.2	10:05	1.2	720.4	8:15	22:10
9:33	1.1	700.7	9:29	1.2	692.5	10:18	1.3	716.1	10:48	1.3	723.3	10:14	1.3	701.0	9:12	22:58
9:42	1.1	688.1	9:38	1.2	733.0	10:34	1.3	743.6	10:58	1.3	741.8	10:24	1.3	739.2	10:23	23:59
9:50	1.3	691.6	9:48	1.4	736.3	10:49	1.4	709.4	11:09	1.4	704.4	10:34	1.5	726.6	11:18	24:44
10:12	1.3	706.6	11:22	1.3	700.5	11:37	1.3	720.0	10:57	1.3	691.8	10:14	1.4	729.6	9:12	22:58
10:21	1.4	702.5	11:41	1.5	722.5	11:49	1.5	728.4	11:09	1.5	705.1	10:28	1.5	709.6	10:22	23:54

					Day 1 (13 & 14 June 2011)			Day 2 (14 & 15 June 2011)			Day 3 (15 & 16 June 2011)			Day 4 (16 & 17 June 2011)			Day 5 (17 & 18 June 2011)		
Group No.	Animal No.	Test Substance/Dose Level	Actual Dose Concentration (mg/ml)	Age of Animal (PND)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)
17	129	Octocrylene (320 mg/kg)	62.1	59	10:05	1.1	311.2	10:02	1.1	309.2	10:01	1.1	297.3	10:13	1.2	318.3	10:07	1.2	311.5
17	130		62.1	59	10:15	1.2	302.2	10:13	1.2	301.3	10:12	1.3	314.5	10:28	1.3	303.5	10:20	1.4	317.9
17	131		62.1	59	10:24	1.3	318.8	10:23	1.3	314.2	10:24	1.3	307.4	10:43	1.3	300.7	10:36	1.4	318.9
17	132		62.1	59	10:33	1.3	312.1	10:34	1.3	310.1	10:34	1.3	305.3	11:00	1.4	313.9	10:51	1.4	312.6
17	133		62.1	60	10:49	1.4	319.5	10:45	1.4	307.8	11:16	1.4	302.8	11:10	1.5	316.1	10:10	1.5	318.1
17	134		62.1	60	11:03	1.4	301.8	10:57	1.5	319.2	11:30	1.5	307.7	11:27	1.5	303.0	10:19	1.6	315.8
17	135		62.1	60	11:15	1.6	316.3	11:11	1.6	311.1	11:44	1.6	303.9	11:45	1.6	304.6	10:29	1.7	316.2
17	136		62.1	60	11:28	1.5	313.1	11:25	1.5	312.7	11:59	1.6	317.3	12:01	1.6	315.0	10:39	1.6	310.1

Day 6 (18 & 19 June 2011)			Day 7 (19 & 20 June 2011)			Day 8 (20 & 21 June 2011)			Day 9 (21 & 22 June 2011)			Day 10 (22 & 23 June 2011)			Day 11 (23 & 24 June 2011)	
Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Death	Time From Last Administration
9:25	1.2	305.2	9:21	1.2	300.5	10:04	1.3	320.1	10:38	1.3	313.8	10:05	1.3	311.6	8:20	22:15
9:33	1.4	314.5	9:30	1.4	305.9	10:19	1.5	318.5	10:48	1.5	318.1	10:15	1.5	309.7	9:16	23:01
9:42	1.4	315.9	9:39	1.4	308.4	10:35	1.4	302.7	10:58	1.4	301.5	10:24	1.5	318.6	10:27	24:03
9:50	1.4	310.5	9:48	1.4	304.0	10:50	1.5	320.7	11:10	1.5	319.3	10:34	1.5	313.1	11:22	24:48
10:04	1.5	310.3	11:06	1.5	303.5	11:25	1.5	307.5	10:46	1.6	317.9	10:05	1.6	314.3	8:18	22:13
10:13	1.6	309.6	11:23	1.6	307.1	11:38	1.6	305.3	10:57	1.7	314.9	10:15	1.7	310.5	9:16	23:01
10:22	1.7	309.0	11:42	1.8	317.8	11:50	1.8	316.4	11:10	1.8	309.0	10:28	1.8	302.5	10:25	23:57
10:30	1.6	303.3	11:58	1.7	316.6	12:04	1.7	317.2	11:21	1.7	307.4	10:38	1.7	303.8	11:22	24:44

					Day 1 (13 & 14 June 2011)			Day 2 (14 & 15 June 2011)			Day 3 (15 & 16 June 2011)			Day 4 (16 & 17 June 2011)			Day 5 (17 & 18 June 2011)		
Group No.	Animal No.	Test Substance/Dose Level	Actual Dose Concentration (mg/ml)	Age of Animal (PND)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)
18	137	Octocrylene (1000 mg/kg)	191	59	10:05	1.1	967.8	10:03	1.1	962.9	10:02	1.1	946.0	10:14	1.2	984.1	10:08	1.2	961.0
18	138		191	59	10:15	1.2	987.1	10:13	1.2	953.0	10:13	1.2	948.7	10:29	1.3	980.3	10:21	1.3	982.2
18	139		191	59	10:25	1.3	962.4	10:23	1.3	981.4	10:24	1.3	940.2	10:44	1.4	975.2	10:36	1.4	969.5
18	140		191	59	10:34	1.3	948.4	10:35	1.3	948.1	10:35	1.4	967.4	11:01	1.4	939.9	10:51	1.5	985.6
18	141		191	60	10:50	1.4	963.3	10:46	1.4	960.1	11:17	1.4	923.0	11:11	1.5	975.8	10:11	1.5	986.6
18	142		191	60	11:03	1.4	934.3	10:57	1.5	987.3	11:30	1.5	965.9	11:28	1.5	939.0	10:20	1.6	983.9
18	143		191	60	11:16	1.5	983.2	11:12	1.5	971.8	11:46	1.5	948.0	11:46	1.5	931.7	10:29	1.6	981.4
18	144		191	60	11:28	1.6	970.2	11:26	1.6	958.0	12:01	1.6	942.0	12:02	1.7	973.9	10:39	1.7	965.8

Day 6 (18 & 19 June 2011)			Day 7 (19 & 20 June 2011)			Day 8 (20 & 21 June 2011)			Day 9 (21 & 22 June 2011)			Day 10 (22 & 23 June 2011)			Day 11 (23 & 24 June 2011)	
Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Death	Time From Last Administration
9:25	1.2	952.6	9:22	1.2	933.2	10:05	1.3	974.5	10:38	1.3	991.6	10:06	1.3	976.8	8:25	22:19
9:34	1.3	959.1	9:30	1.3	948.4	10:20	1.3	932.8	10:49	1.3	950.6	10:15	1.3	921.0	9:21	23:06
9:42	1.4	949.2	9:39	1.4	935.9	10:36	1.4	924.9	10:59	1.4	932.4	10:25	1.5	965.9	10:30	24:05
9:51	1.5	983.2	9:50	1.5	941.8	10:51	1.5	925.7	11:10	1.6	968.3	10:35	1.6	951.7	11:26	24:51
10:04	1.5	974.2	11:08	1.5	955.3	11:25	1.5	940.3	10:47	1.6	983.3	10:05	1.6	974.5	8:22	22:17
10:14	1.6	967.1	11:24	1.6	944.4	11:39	1.6	952.0	10:58	1.7	967.5	10:16	1.7	969.8	9:21	23:05
10:22	1.7	941.7	11:43	1.6	943.2	11:51	1.6	935.7	11:10	1.6	930.0	10:29	1.7	975.7	10:30	24:01
10:33	1.6	968.0	11:59	1.7	937.4	12:05	1.8	959.3	11:22	1.8	947.1	10:39	1.8	933.5	11:25	24:46

						Day 1 (13 & 14 June 2011)		Day 2 (14 & 15 June 2011)		Day 3 (15 & 16 June 2011)		Day 4 (16 & 17 June 2011)		Day 5 (17 & 18 June 2011)	
Group No.	Animal No.	Test Substance/Dose Level	Dose Route	Age of Animal (PND)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Time of Administration (Hour:Minute)
19	145	Corn Oil (0 mg/kg) & Testosterone Propionate (0.4 mg/kg)	Gavage	59	10:06	1.1	10:04	1.1	10:02	1.2	10:16	1.2	10:09	1.2	9:25
			Subcutaneous			0.11		0.11		0.12		0.12		0.12	
19	146		Gavage	59	10:16	1.2	10:14	1.3	10:14	1.3	10:30	1.3	10:22	1.4	9:34
			Subcutaneous			0.12		0.13		0.13		0.13		0.14	
19	147		Gavage	59	10:26	1.3	10:24	1.3	10:25	1.4	10:45	1.5	10:38	1.5	9:43
			Subcutaneous			0.13		0.13		0.14		0.15		0.15	
19	148		Gavage	59	10:34	1.3	10:36	1.3	10:36	1.4	11:02	1.4	10:53	1.5	9:52
			Subcutaneous			0.13		0.13		0.14		0.14		0.15	
19	149		Gavage	60	10:51	1.4	10:47	1.4	11:17	1.4	11:12	1.5	10:12	1.5	10:05
			Subcutaneous			0.14		0.14		0.14		0.15		0.15	
19	150		Gavage	60	11:04	1.4	10:58	1.4	11:31	1.5	11:29	1.5	10:21	1.6	10:14
			Subcutaneous			0.14		0.14		0.15		0.15		0.16	
19	151		Gavage	60	11:17	1.4	11:13	1.5	11:47	1.5	11:47	1.6	10:30	1.6	10:23
			Subcutaneous			0.14		1.5		0.15		0.16		0.16	
19	152		Gavage	60	11:29	1.6	11:27	1.6	12:02	1.7	12:03	1.7	10:40	1.8	10:34
			Subcutaneous			0.16		0.16		0.17		0.17		0.18	

Day 6 (18 & 19 June 2011)		Day 7 (19 & 20 June 2011)		Day 8 (20 & 21 June 2011)		Day 9 (21 & 22 June 2011)		Day 10 (22 & 23 June 2011)		Day 11 (23 & 24 June 2011)
Volume Administered (mL)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Time of Death	Time From Last Administration
1.3	9:22	1.3	10:07	1.3	10:39	1.3	10:07	1.3	8:29	22:22
0.13		0.13		0.13		0.13		0.13		
1.4	9:31	1.5	10:21	1.5	10:50	1.5	10:16	1.6	9:26	23:10
0.14		0.15		0.15		0.15		0.16		
1.6	9:40	1.7	10:37	1.7	11:00	1.7	10:26	1.8	10:35	24:09
0.16		0.17		0.17		0.17		0.18		
1.5	9:51	1.5	10:52	1.6	11:12	1.6	10:36	1.6	11:30	24:54
0.15		0.15		0.16		0.16		0.16		
1.5	11:09	1.6	11:26	1.6	10:48	1.6	10:06	1.7	8:26	22:20
0.15		0.16		0.16		0.16		0.17		
1.6	11:26	1.7	11:40	1.7	10:58	1.7	10:17	1.8	9:27	23:10
0.16		0.17		0.17		0.17		0.18		
1.7	11:44	1.7	11:53	1.8	11:12	1.8	10:30	1.8	10:34	24:04
0.17		0.17		0.18		0.18		0.18		
1.9	12:01	1.9	12:08	2.0	11:22	2.1	10:39	2.1	11:29	24:50
0.19		0.19		0.20		0.21		0.21		

						Day 1 (13 & 14 June 2011)			Day 2 (14 & 15 June 2011)			Day 3 (15 & 16 June 2011)			Day 4 (16 & 17 June 2011)			Day 5 (17 & 18 June 2011)		
Group No.:	Animal No.	Test Substance/Dose Level	Dose Route	Actual Dose Concentration (mg/ml)	Age of Animal (PND)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)
20	153	Octylsalate (75 mg/kg) & Testosterone Propionate (0.4 mg/kg)	Gavage	14.8	59	10:07	1.1	72.0	10:05	1.2	77.2	10:03	1.2	74.5	10:17	1.2	71.1	10:10	1.3	76.4
			Subcutaneous				0.11			0.12			0.12			0.12			0.13	
20	154		Gavage		59	10:17	1.2	73.4	10:15	1.2	73.0	10:15	1.2	71.5	10:31	1.3	75.5	10:23	1.3	74.2
			Subcutaneous				0.12			0.12			0.12			0.13			0.13	
20	155		Gavage		59	10:26	1.3	74.7	10:25	1.3	73.8	10:26	1.4	76.7	10:47	1.4	73.9	10:39	1.4	72.5
			Subcutaneous				0.13			0.13			0.14			0.14			0.14	
20	156		Gavage		59	10:35	1.3	72.9	10:37	1.3	72.1	10:37	1.4	74.3	11:03	1.5	75.5	10:54	1.5	73.5
			Subcutaneous				0.13			0.13			0.14			0.15			0.15	
20	157		Gavage		60	10:52	1.4	75.2	10:48	1.4	74.4	11:19	1.5	76.2	11:14	1.5	74.2	10:12	1.5	73.9
			Subcutaneous				0.14			0.14			0.15			0.15			0.15	
20	158		Gavage		60	11:05	1.5	76.4	11:00	1.5	75.2	11:32	1.5	71.9	11:31	1.6	74.8	10:21	1.6	72.7
			Subcutaneous				0.15			0.15			0.15			0.16			0.16	
20	159		Gavage		60	11:18	1.5	76.5	11:15	1.5	72.6	11:48	1.6	74.8	11:48	1.7	76.2	10:31	1.7	74.0
			Subcutaneous				0.15			0.15			0.16			0.17			0.17	
20	160		Gavage		60	11:30	1.5	72.5	11:28	1.5	71.8	12:03	1.6	73.7	12:04	1.6	71.9	10:41	1.7	74.7
			Subcutaneous				0.15			0.15			0.16			0.16			0.17	

Day 6 (18 & 19 June 2011)			Day 7 (19 & 20 June 2011)			Day 8 (20 & 21 June 2011)			Day 9 (21 & 22 June 2011)			Day 10 (22 & 23 June 2011)			Day 11 (23 & 24 June 2011)	
Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Death	Time From Last Administration
9:26	1.3	73.9	9:23	1.3	72.4	10:08	1.4	75.2	10:40	1.4	75.2	10:08	1.4	74.5	8:34	22:58
	0.13			0.13			0.14			0.14			0.14			
9:35	1.3	73.4	9:32	1.4	76.3	10:22	1.4	74.6	10:50	1.4	74.4	10:17	1.4	72.4	9:30	23:13
	0.13			0.14			0.14			0.14			0.14			
9:44	1.5	76.3	9:41	1.5	73.5	10:38	1.5	71.8	11:01	1.6	75.7	10:27	1.6	74.0	10:39	24:12
	0.15			0.15			0.15			0.16			0.16			
9:53	1.5	71.9	9:52	1.6	74.5	10:53	1.7	75.1	11:13	1.7	74.5	10:38	1.8	75.8	11:34	24:56
	0.15			0.16			0.17			0.17			0.18			
10:05	1.5	72.1	11:10	1.6	76.1	11:27	1.6	76.1	10:49	1.6	73.4	10:07	1.6	72.9	8:31	22:24
	0.15			0.16			0.16			0.16			0.16			
10:15	1.7	75.9	11:27	1.7	74.5	11:41	1.7	74.2	11:02	1.7	72.0	10:19	1.8	75.1	9:32	23:13
	0.17			0.17			0.17			0.17			0.18			
10:24	1.8	75.7	11:46	1.8	75.1	11:54	1.8	73.4	11:13	1.9	74.7	10:31	1.9	74.2	10:38	24:07
	0.18			0.18			0.18			0.19			0.19			
10:34	1.7	72.2	12:03	1.8	75.2	12:10	1.8	75.1	11:23	1.8	74.0	10:40	1.8	72.8	11:33	24:53
	0.17			0.18			0.18			0.18			0.18			

						Day 1 (13 & 14 June 2011)			Day 2 (14 & 15 June 2011)			Day 3 (15 & 16 June 2011)			Day 4 (16 & 17 June 2011)			Day 5 (17 & 18 June 2011)		
Group No.:	Animal No.	Test Substance/Dose Level	Dose Route	Actual Dose Concentration (mg/ml)	Age of Animal (PND)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)
21	161	Octylsalate (235 mg/kg) & Testosterone Propionate (0.4 mg/kg)	Gavage	45.8	59	10:08	1.1	221.4	10:06	1.2	237.8	10:04	1.2	229.6	10:18	1.2	226.1	10:11	1.3	236.5
			Subcutaneous				0.11			0.12			0.12			0.12			0.13	
21	162		Gavage		59	10:18	1.2	227.8	10:16	1.2	223.4	10:16	1.3	226.0	10:32	1.4	236.2	10:25	1.4	226.3
			Subcutaneous				0.12			0.12			0.13			0.14			0.14	
21	163		Gavage		59	10:27	1.3	231.0	10:26	1.3	234.8	10:27	1.3	228.4	10:48	1.3	220.7	10:40	1.4	230.2
			Subcutaneous				0.13			0.13			0.13			0.13			0.14	
21	164		Gavage		59	10:36	1.3	228.5	10:39	1.3	232.9	10:37	1.3	222.5	11:04	1.4	232.6	10:55	1.4	229.1
			Subcutaneous				0.13			0.13			0.13			0.14			0.14	
21	165		Gavage		60	10:54	1.4	236.8	10:49	1.4	236.4	11:20	1.4	227.6	11:15	1.5	235.0	10:13	1.5	234.2
			Subcutaneous				0.14			0.14			0.14			0.15			0.15	
21	166		Gavage		60	11:07	1.4	235.3	11:01	1.4	233.7	11:34	1.4	229.7	11:32	1.4	225.3	10:22	1.5	230.7
			Subcutaneous				0.14			0.14			0.14			0.14			0.15	
21	167		Gavage		60	11:19	1.5	234.6	11:16	1.5	231.8	11:49	1.5	222.2	11:50	1.6	233.2	10:31	1.6	246.1
			Subcutaneous				1.15			0.15			0.15			0.16			0.16	
21	168		Gavage		60	11:31	1.6	250.3	11:29	1.6	229.9	12:04	1.7	230.6	12:05	1.7	227.3	10:42	1.8	255.8
			Subcutaneous				0.16			0.16			0.17			0.17			0.18	

Day 6 (18 & 19 June 2011)			Day 7 (19 & 20 June 2011)			Day 8 (20 & 21 June 2011)			Day 9 (21 & 22 June 2011)			Day 10 (22 & 23 June 2011)			Day 11 (23 & 24 June 2011)	
Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Death	Time From Last Administration
9:27	1.3	231.1	9:24	1.3	224.8	10:09	1.4	236.0	10:41	1.4	234.1	10:09	1.4	225.5	8:39	23:03
	0.13			0.13			0.14			0.14			0.14			
9:35	1.5	236.4	9:33	1.5	226.6	10:23	1.6	233.7	10:51	1.6	233.5	10:18	1.6	226.1	9:34	23:16
	0.15			0.15			0.16			0.16			0.16			
9:45	1.5	235.8	9:41	1.5	229.1	10:39	1.5	225.8	11:02	1.6	235.1	10:28	1.6	229.2	10:45	24:17
	0.15			0.15			0.15			0.16			0.16			
9:53	1.4	227.3	9:53	1.4	222.8	10:55	1.5	231.2	11:15	1.5	226.7	10:39	1.5	226.9	11:39	25:00
	0.14			0.14			0.15			0.15			0.15			
10:06	1.5	226.1	11:11	1.6	233.2	11:28	1.6	236.4	10:50	1.6	229.6	10:08	1.6	227.9	8:35	22:27
	0.15			0.16			0.16			0.16			0.16			
10:16	1.5	228.6	11:28	1.5	222.8	11:42	1.6	234.0	11:03	1.6	232.2	10:20	1.6	225.5	9:37	23:17
	0.15			0.15			0.16			0.16			0.16			
10:25	1.7	233.7	11:48	1.7	226.3	11:55	1.7	224.2	11:14	1.8	228.0	10:32	1.8	225.2	10:43	24:11
	0.17			0.17			0.17			0.18			0.18			
10:35	1.8	227.2	12:04	1.9	232.4	12:12	1.9	226.8	11:25	2.0	230.0	10:41	2.0	226.8	11:37	24:56
	0.18			0.19			0.19			0.20			0.20			

						Day 1 (13 & 14 June 2011)			Day 2 (14 & 15 June 2011)			Day 3 (15 & 16 June 2011)			Day 4 (16 & 17 June 2011)			Day 5 (17 & 18 June 2011)		
Group No.:	Animal No.	Test Substance/Dose Level	Dose Route	Actual Dose Concentration (mg/ml)	Age of Animal (PND)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)
22	169*	Octylsalate (750 mg/kg) & Testosterone Propionate (0.4 mg/kg)	Gavage	143	59	10:09	1.1	702.5	10:07	1.1	693.9	10:05	1.1	706.0	10:20	1.1	693.0	10:12	1.1	741.3
			Subcutaneous				0.11			0.11			0.11			0.11			0.11	
22	170		Gavage		59	10:19	1.2	706.5	10:17	1.2	737.7	10:17	1.2	742.9	10:34	1.2	729.3	10:26	1.2	712.9
			Subcutaneous				0.12			0.12			0.12			0.12			0.12	
22	171		Gavage		59	10:29	1.3	719.1	10:27	1.3	731.6	10:28	1.2	689.2	10:50	1.2	700.7	10:41	1.2	707.6
			Subcutaneous				0.13			0.13			0.12			0.12			0.12	
22	172		Gavage		59	10:36	1.3	703.9	10:40	1.3	740.0	10:38	1.2	706.8	11:05	1.2	713.5	10:57	1.2	738.1
			Subcutaneous				0.13			0.13			0.12			0.12			0.12	
22	173		Gavage		60	10:55	1.4	735.2	10:50	1.4	738.2	11:21	1.4	721.4	11:17	1.4	718.3	10:13	1.4	708.2
			Subcutaneous				0.14			0.14			0.14			0.14			0.14	
22	174		Gavage		60	11:08	1.4	710.4	11:03	1.4	736.3	11:35	1.3	693.7	11:34	1.3	716.1	10:23	1.3	728.2
			Subcutaneous				0.14			0.14			0.13			0.13			0.13	
22	175		Gavage		60	11:20	1.5	728.1	11:18	1.5	739.1	11:50	1.4	712.7	11:51	1.4	735.8	10:32	1.4	712.7
			Subcutaneous				0.15			0.15			0.14			0.14			0.14	
22	176		Gavage		60	11:33	1.6	734.0	11:30	1.6	721.8	12:05	1.6	814.5	12:07	1.6	726.6	10:43	1.6	717.2
			Subcutaneous				0.16			0.16			0.16			0.16			0.16	

*Animal found dead prior to termination

Day 6 (18 & 19 June 2011)			Day 7 (19 & 20 June 2011)			Day 8 (20 & 21 June 2011)			Day 9 (21 & 22 June 2011)			Day 10 (22 & 23 June 2011)			Day 11 (23 & 24 June 2011)	
Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Death	Time From Last Administration
9:28	1.0	695.2														0:00
	0.10															
9:37	1.2	708.2	9:34	1.3	740.9	10:26	1.3	724.8	10:52	1.3	715.0	10:19	1.3	697.0	9:39	23:20
	0.12			0.13			0.13			0.13			0.13			
9:45	1.2	729.9	9:43	1.2	704.7	10:41	1.3	715.8	11:03	1.3	689.3	10:28	1.4	720.1	10:49	24:21
	0.12			0.12			0.13			0.13			0.14			
9:55	1.1	715.0	9:54	1.1	692.6	10:57	1.2	731.1	11:16	1.2	730.5	10:40	1.2	720.7	11:43	25:03
	0.11			0.11			0.12			0.12			0.12			
10:07	1.4	721.7	11:13	1.4	695.6	11:29	1.5	721.5	10:51	1.5	694.0	10:09	1.5	708.2	8:41	22:32
	0.14			0.14			0.15			0.15			0.15			
10:16	1.2	697.6	11:30	1.3	705.2	11:43	1.3	714.7	11:04	1.3	699.9	10:21	1.2	693.6	9:42	23:21
	0.12			0.13			0.13			0.13			0.12			
10:26	1.4	698.5	11:49	1.5	721.7	11:56	1.5	715.2	11:15	1.5	707.9	10:32	1.5	696.4	10:48	24:16
	0.14			0.15			0.15			0.15			0.15			
10:36	1.6	710.6	12:05	1.7	732.4	12:13	1.7	700.4	11:26	1.8	728.8	10:42	1.8	705.8	11:43	25:01
	0.16			0.17			0.17			0.18			0.18			

						Day 1 (13 & 14 June 2011)			Day 2 (14 & 15 June 2011)			Day 3 (15 & 16 June 2011)			Day 4 (16 & 17 June 2011)			Day 5 (17 & 18 June 2011)		
Group No.:	Animal No.	Test Substance/Dose Level	Dose Route	Actual Dose Concentration (mg/ml)	Age of Animal (PND)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)
23	177	Octocrylene (100 mg/kg) & Testosterone Propionate (0.4 mg/kg)	Gavage	19.9	59	10:10	1.2	103.0	10:08	1.2	101.7	10:06	1.2	97.5	10:21	1.3	99.9	10:13	1.3	96.0
			Subcutaneous				0.12			0.12			0.12			0.13			0.13	
23	178		Gavage		59	10:19	1.2	100.0	10:18	1.2	99.7	10:18	1.3	102.8	10:35	1.3	99.0	10:28	1.4	103.0
			Subcutaneous				0.12			0.12			0.13			0.13			0.14	
23	179		Gavage		59	10:30	1.3	102.0	10:28	1.3	100.3	10:29	1.3	97.0	10:51	1.4	101.8	10:43	1.4	99.8
			Subcutaneous				0.13			0.13			0.13			0.14			0.14	
23	180		Gavage		59	10:37	1.3	99.3	10:41	1.3	97.5	10:39	1.4	101.0	11:07	1.4	97.1	10:59	1.5	100.5
			Subcutaneous				0.13			0.13			0.14			0.14			0.15	
23	181		Gavage		60	10:56	1.4	100.8	10:51	1.4	100.0	11:22	1.4	96.3	11:18	1.5	100.3	10:14	1.5	98.8
			Subcutaneous				0.14			0.14			0.14			0.15			0.15	
23	182		Gavage		60	11:09	1.4	99.7	11:04	1.4	97.8	11:36	1.5	100.8	11:35	1.5	98.2	10:23	1.6	102.3
			Subcutaneous				0.14			0.14			0.15			0.15			0.16	
23	183		Gavage		60	11:21	1.5	98.9	11:19	1.5	96.8	11:52	1.6	99.5	11:52	1.7	102.0	10:33	1.7	100.8
			Subcutaneous				0.15			0.15			0.16			0.17			0.17	
23	184		Gavage		60	11:34	1.5	97.0	11:31	1.6	101.4	12:07	1.6	97.8	12:08	1.7	102.2	10:44	1.7	99.4
			Subcutaneous				0.15			0.16			0.16			0.17			0.17	

Day 6 (18 & 19 June 2011)			Day 7 (19 & 20 June 2011)			Day 8 (20 & 21 June 2011)			Day 9 (21 & 22 June 2011)			Day 10 (22 & 23 June 2011)			Day 11 (23 & 24 June 2011)	
Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Death	Time From Last Administration
9:29	1.4	101.8	9:25	1.4	99.1	10:11	1.5	101.9	10:42	1.5	100.7	10:10	1.5	98.7	8:44	20:44
	0.14			0.14			0.15			0.15			0.15			
9:38	1.4	101.9	9:34	1.4	100.0	10:27	1.4	96.7	10:53	1.5	102.6	10:19	1.5	99.8	9:45	23:26
	0.14			0.14			0.14			0.15			0.15			
9:46	1.4	97.5	9:44	1.5	101.7	10:42	1.5	98.5	11:04	1.5	98.2	10:29	1.6	101.4	10:53	24:24
	0.14			0.15			0.15			0.15			0.16			
9:56	1.5	99.0	9:54	1.6	101.7	10:58	1.6	98.7	11:17	1.6	98.1	10:41	1.7	101.8	11:47	25:06
	0.15			0.16			0.16			0.16			0.17			
10:08	1.6	101.8	11:14	1.6	99.4	11:30	1.6	97.3	10:52	1.7	101.2	10:09	1.7	98.6	8:46	22:37
	0.16			0.16			0.16			0.17			0.17			
10:17	1.6	99.0	11:32	1.6	97.1	11:44	1.6	96.9	11:05	1.7	100.2	10:22	1.7	98.4	9:47	23:25
	0.16			0.16			0.16			0.17			0.17			
10:27	1.7	98.2	11:51	1.8	100.5	11:57	1.8	100.2	11:16	1.9	102.2	10:33	1.9	100.3	10:53	24:20
	0.17			0.18			0.18			0.19			0.19			
10:37	1.8	102.1	12:07	1.8	98.2	12:16	1.4	102.7	11:26	1.9	101.5	10:43	1.9	100.0	11:48	25:05
	0.18			0.18			0.14			0.19			0.19			

						Day 1 (13 & 14 June 2011)			Day 2 (14 & 15 June 2011)			Day 3 (15 & 16 June 2011)			Day 4 (16 & 17 June 2011)			Day 5 (17 & 18 June 2011)		
Group No.:	Animal No.	Test Substance/Dose Level	Dose Route	Actual Dose Concentration (mg/ml)	Age of Animal (PND)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)
24	185	Octocrylene (320 mg/kg) & Testosterone Propionate (0.4 mg/kg)	Gavage	62.1	59	10:11	1.2	318.3	10:09	1.2	311.3	10:07	1.3	322.8	10:22	1.3	310.0	10:14	1.3	304.1
			Subcutaneous				0.12			0.12			0.13			0.13			0.13	
24	186		Gavage		59	10:20	1.2	309.5	10:19	1.2	303.8	10:19	1.3	317.1	10:36	1.3	303.2	10:29	1.4	317.2
			Subcutaneous				0.12			0.12			0.13			0.13			0.14	
24	187		Gavage		59	10:30	1.2	299.2	10:29	1.3	311.8	10:30	1.3	307.0	10:52	1.4	317.9	10:45	1.4	307.5
			Subcutaneous				0.12			0.13			0.13			0.14			0.14	
24	188		Gavage		59	10:38	1.3	308.4	10:43	1.3	304.8	10:40	1.4	314.3	11:08	1.4	305.2	11:00	1.5	321.0
			Subcutaneous				0.13			0.13			0.14			0.14			0.15	
24	189		Gavage		60	10:57	1.3	309.1	10:52	1.3	300.6	11:23	1.4	307.3	11:19	1.4	301.5	10:15	1.5	315.7
			Subcutaneous				0.13			0.13			0.14			0.14			0.15	
24	190		Gavage		60	11:10	1.4	305.1	11:06	1.4	304.7	11:37	1.5	316.8	11:37	1.5	310.0	10:24	1.5	303.6
			Subcutaneous				0.14			0.14			0.15			0.15			0.15	
24	191		Gavage		60	11:22	1.5	314.1	11:20	1.5	310.2	11:53	1.6	316.0	11:54	1.6	307.4	10:34	1.6	301.3
			Subcutaneous				0.15			0.15			0.16			0.16			0.16	
24	192		Gavage		60	11:35	1.6	319.7	11:32	1.6	313.6	12:08	1.7	319.9	12:10	1.7	310.3	10:45	1.7	301.7
			Subcutaneous				0.16			0.16			0.17			0.17			0.17	

Day 6 (18 & 19 June 2011)			Day 7 (19 & 20 June 2011)			Day 8 (20 & 21 June 2011)			Day 9 (21 & 22 June 2011)			Day 10 (22 & 23 June 2011)			Day 11 (23 & 24 June 2011)	
Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Death	Time From Last Administration
9:29	1.4	317.8	9:36	1.4	307.8	10:12	1.5	320.1	10:44	1.5	318.8	10:11	1.5	305.7	8:48	20:48
	0.14			0.14			0.15			0.15			0.15			
9:38	1.4	310.4	9:35	1.5	319.1	10:28	1.5	312.1	10:54	1.5	308.9	10:21	1.6	318.7	9:49	23:28
	0.14			0.15			0.15			0.15			0.16			
9:47	1.5	320.8	9:44	1.5	308.2	10:43	1.6	319.8	11:05	1.6	311.4	10:30	1.7	317.7	10:58	24:28
	0.15			0.15			0.16			0.16			0.17			
9:57	1.5	313.8	9:55	1.5	302.8	10:59	1.6	314.4	11:18	1.6	308.7	10:42	1.7	316.1	11:51	25:09
	0.15			0.15			0.16			0.16			0.17			
10:09	1.5	316.6	11:15	1.6	316.3	11:32	1.6	313.3	10:53	1.6	305.8	10:10	1.6	301.7	8:50	22:40
	0.15			0.16			0.16			0.16			0.16			
10:18	1.5	301.1	11:33	1.6	304.6	11:45	1.6	302.7	11:06	1.6	301.4	10:23	1.7	310.4	9:51	23:28
	0.15			0.16			0.16			0.16			0.17			
10:27	1.7	307.9	11:52	1.8	315.1	11:58	1.8	314.9	11:17	1.9	318.2	10:34	1.9	313.3	10:57	24:23
	0.17			0.18			0.18			0.19			0.19			
10:38	1.8	310.2	12:08	1.9	315.0	12:17	1.9	310.2	11:28	2.0	312.5	10:44	2.0	308.6	11:53	25:09
	0.18			0.19			0.19			0.20			0.20			

						Day 1 (13 & 14 June 2011)			Day 2 (14 & 15 June 2011)			Day 3 (15 & 16 June 2011)			Day 4 (16 & 17 June 2011)			Day 5 (17 & 18 June 2011)		
Group No.:	Animal No.	Test Substance/Dose Level	Dose Route	Actual Dose Concentration (mg/ml)	Age of Animal (PND)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)
25	193	Octocrylene (1000 mg/kg) & Testosterone Propionate (0.4 mg/kg)	Gavage	191	59	10:12	1.2	953.8	10:10	1.2	961.4	10:08	1.2	922.7	10:23	1.3	970.3	10:16	1.3	935.2
			Subcutaneous				0.12			0.12			0.12			0.13			0.13	
25	194		Gavage		59	10:21	1.2	959.0	10:20	1.2	930.6	10:20	1.2	919.7	10:37	1.3	959.8	10:30	1.3	945.5
			Subcutaneous				0.12			0.12			0.12			0.13			0.13	
25	195		Gavage		59	10:31	1.3	988.5	10:30	1.3	893.6	10:31	1.3	965.4	10:54	1.3	929.6	10:46	1.4	960.1
			Subcutaneous				0.13			0.13			0.13			0.13			0.14	
25	196		Gavage		59	10:39	1.3	951.3	10:44	1.3	935.9	10:41	1.4	984.5	11:09	1.4	961.2	11:01	1.4	929.8
			Subcutaneous				0.13			0.13			0.14			0.14			0.14	
25	197		Gavage		60	10:58	1.4	979.1	10:53	1.4	937.6	11:25	1.5	957.9	11:21	1.5	934.4	10:15	1.6	965.6
			Subcutaneous				0.14			0.14			0.15			0.15			0.16	
25	198		Gavage		60	11:11	1.4	926.9	11:07	1.5	979.2	11:39	1.5	936.0	11:38	1.5	926.6	10:25	1.5	936.6
			Subcutaneous				0.14			0.15			0.15			0.15			0.15	
25	199		Gavage		60	11:23	1.5	939.0	11:22	1.6	982.6	11:54	1.6	947.6	11:55	1.7	971.3	10:35	1.7	947.2
			Subcutaneous				0.15			0.16			0.16			0.17			0.17	
25	200		Gavage		60	11:36	1.6	975.1	11:33	1.6	971.4	12:09	1.6	929.7	12:12	1.7	951.6	10:46	1.7	930.6
			Subcutaneous				0.16			0.16			0.16			0.17			0.17	

Day 6 (18 & 19 June 2011)			Day 7 (19 & 20 June 2011)			Day 8 (20 & 21 June 2011)			Day 9 (21 & 22 June 2011)			Day 10 (22 & 23 June 2011)			Day 11 (23 & 24 June 2011)	
Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Actual Dose Received (mg/kg)	Time of Death	Time From Last Administration
9:30	1.3	939.8	9:27	1.4	978.4	10:14	1.4	960.5	10:45	1.4	969.5	10:12	1.4	957.1	8:54	23:18
	0.13			0.14			0.14			0.14			0.14			
9:39	1.3	932.1	9:35	1.4	977.0	10:30	1.4	945.5	10:55	1.4	947.6	10:21	1.5	979.8	9:54	23:33
	0.13			0.14			0.14			0.14			0.15			
9:47	1.4	942.2	9:45	1.4	934.6	10:44	1.5	969.5	11:06	1.5	961.7	10:31	1.5	934.1	11:02	24:31
	0.14			0.14			0.15			0.15			0.15			
9:58	1.5	977.5	9:56	1.5	955.6	11:00	1.5	935.1	11:19	1.6	980.7	10:43	1.6	952.3	11:56	25:13
	0.15			0.15			0.15			0.16			0.16			
10:10	1.6	943.5	11:17	1.7	956.7	11:34	1.7	956.1	10:54	1.7	939.5	10:11	1.8	975.6	8:55	22:44
	0.16			0.17			0.17			0.17			0.18			
10:19	1.6	959.2	11:34	1.6	936.3	11:46	1.7	982.7	11:07	1.7	953.3	10:24	1.7	943.9	9:55	23:31
	0.16			0.16			0.17			0.17			0.17			
10:28	1.8	969.0	11:53	1.8	953.9	12:00	1.8	937.6	11:18	1.9	957.3	10:35	1.9	931.9	11:01	24:26
	0.18			0.18			0.18			0.19			0.19			
10:39	1.8	976.1	12:09	1.8	948.9	12:18	1.8	949.2	11:29	1.9	969.3	10:45	1.9	960.6	11:57	25:12
	0.18			0.18			0.18			0.19			0.19			

					Day 1 (13 & 14 June 2011)		Day 2 (14 & 15 June 2011)		Day 3 (15 & 16 June 2011)		Day 4 (16 & 17 June 2011)		Day 5 (17 & 18 June 2011)	
Group No.:	Animal No.	Test Substance/Dose Level	Dose Route	Age of Animal (PND)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Time of Administration (Hour:Minute)	Volume Administered (mL)
26	201	Flutamide (3 mg/kg) & Testosterone Propionate (0.4 mg/kg)	Gavage	59	10:13	1.2	10:11	1.2	10:09	1.2	10:24	1.3	10:17	1.3
			Subcutaneous			0.12		0.12		0.12		0.13		0.13
26	202		Gavage	59	10:22	1.2	10:20	1.2	10:21	1.3	10:39	1.3	10:32	1.3
			Subcutaneous			0.12		0.12		0.13		0.13		0.13
26	203		Gavage	59	10:32	1.3	10:32	1.3	10:32	1.3	10:56	1.4	10:47	1.4
			Subcutaneous			0.13		0.13		0.13		0.14		0.14
26	204		Gavage	59	10:40	1.3	10:45	1.3	10:42	1.3	11:10	1.4	11:03	1.4
			Subcutaneous			0.13		0.13		0.13		0.14		0.14
26	205		Gavage	60	11:00	1.4	10:54	1.4	11:27	1.5	11:22	1.5	10:16	1.5
			Subcutaneous			0.14		0.14		0.15		0.15		0.15
26	206		Gavage	60	11:12	1.4	11:08	1.4	11:41	1.5	11:40	1.5	10:25	1.5
			Subcutaneous			0.14		0.14		0.15		0.15		0.15
26	207		Gavage	60	11:24	1.5	11:23	1.5	11:56	1.6	11:56	1.6	10:35	1.6
			Subcutaneous			0.15		0.15		0.16		0.16		0.16
26	208		Gavage	60	11:36	1.5	11:34	1.5	12:10	1.6	12:12	1.6	10:47	1.7
			Subcutaneous			0.15		0.15		0.16		0.16		0.17

Day 6 (18 & 19 June 2011)		Day 7 (19 & 20 June 2011)		Day 8 (20 & 21 June 2011)		Day 9 (21 & 22 June 2011)		Day 10 (22 & 23 June 2011)		Day 11 (23 & 24 June 2011)	
Time of Administration (Hour:Minute)	Volume Administered (mL)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Time of Administration (Hour:Minute)	Volume Administered (mL)	Time of Death	Time From Last Administration
9:31	1.3	9:27	1.4	10:15	1.4	10:46	1.4	10:12	1.4	8:58	22:46
	0.13		0.14		0.14		0.14		0.14		
9:40	1.4	9:36	1.4	10:31	1.4	10:56	1.4	10:22	1.5	9:58	23:36
	0.14		0.14		0.14		0.14		0.15		
9:48	1.5	9:46	1.5	10:46	1.5	11:07	1.5	10:32	1.6	11:07	24:35
	0.15		0.15		0.15		0.15		0.16		
9:59	1.4	9:57	1.4	11:01	1.5	11:20	1.5	10:44	1.5	0:00	13:16
	0.14		0.14		0.15		0.15		0.15		
10:11	1.6	11:18	1.6	11:35	1.7	10:55	1.7	10:12	1.7	9:00	22:48
	0.16		0.16		0.17		0.17		0.17		
10:19	1.6	11:36	1.6	11:47	1.6	11:07	1.7	10:25	1.7	10:01	23:36
	0.16		0.16		0.16		0.17		0.17		
10:29	1.7	11:55	1.7	12:01	1.8	11:19	1.8	10:36	1.8	11:07	24:31
	0.17		0.17		0.18		0.18		0.18		
10:39	1.7	12:11	1.7	12:20	1.8	11:30	1.8	10:45	1.9	0:01	13:16
	0.17		0.17		0.18		0.18		0.19		

Appendix IV:

Clinical Observations

				Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Terminal
Group No.:	**Animal No.**	**Sex**	**Treatment/Dose Level**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**
1	01	M	Corn Oil Control	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
1	02	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
1	03	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
1	04	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
1	05	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
1	06	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
1	07	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
1	08	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal

Group No.:	**Animal No.**	**Sex**	**Treatment/Dose Level**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**
2	09	M	Oxybenzone (320 mg/kg)	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
2	10	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
2	11	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
2	12	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
2	13	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
2	14	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
2	15	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
2	16	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal

Group No.:	**Animal No.**	**Sex**	**Treatment/Dose Level**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**
3	17	M	Oxybenzone (1000 mg/kg)	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
3	18	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
3	19	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
3	20	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
3	21	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
3	22	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
3	23	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
3	24	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal

Group No.:	**Animal No.**	**Sex**	**Treatment/Dose Level**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**
4	25	M	Octyl Methoxycinnamate (320 mg/kg)	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
4	26	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
4	27	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
4	28	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
4	29	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
4	30	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
4	31	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
4	32	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal

Group No.:	Animal No.	Sex	Treatment/Dose Level	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation
5	33	M	Octyl Methoxycinnamate (1000 mg/kg)	Normal	Normal	Normal	Normal	Normal	Normal	Hunched Posture	Normal	Normal	Mass(Left
5	34	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
5	35	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
5	36	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
5	37	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
5	38	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
5	39	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
5	40	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal

Group No.:	Animal No.	Sex	Treatment/Dose Level	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation
6	41	M	Corn Oil (0 mg/kg) & Testosterone Propionate (0.4 mg/kg)	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
6	42	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
6	43	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
6	44	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
6	45	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
6	46	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
6	47	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
6	48	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal

Group No.:	Animal No.	Sex	Treatment/Dose Level	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation
7	49	M	Oxybenzone (100 mg/kg) & Testosterone Propionate (0.4 mg/kg)	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
7	50	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
7	51	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
7	52	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
7	53	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
7	54	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
7	55	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
7	56	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal

Group No.:	Animal No.	Sex	Treatment/Dose Level	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation
8	57	M	Oxybenzone (320 mg/kg) & Testosterone Propionate (0.4 mg/kg)	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
8	58	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
8	59	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
8	60	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
8	61	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
8	62	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
8	63	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
8	64	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal

Group No.:	Animal No.	Sex	Treatment/Dose Level	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation
9	65	M	Oxybenzone (1000 mg/kg) & Testosterone Propionate (0.4 mg/kg)	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
9	66	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
9	67	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
9	68	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
9	69	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Hunched Posture	Normal	Normal	Normal
9	70	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
9	71	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
9	72	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal

Group No.:	Animal No.	Sex	Treatment/Dose Level	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation
10	73	M	Octyl Methoxycinnamate (100 mg/kg) & Testosterone Propionate (0.4 mg/kg)	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
10	74	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
10	75	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
10	76	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Hunched Posture	Hunched Posture	Hunched Posture	Normal
10	77	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
10	78	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
10	79	M		Normal	Normal	Minimal Hind Leg Movement	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
10	80	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal

Group No.:	Animal No.	Sex	Treatment/Dose Level	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation
11	81	M	Octyl Methoxycinnamate (320 mg/kg) & Testosterone Propionate (0.4 mg/kg)	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
11	82	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
11	83	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
11	84[#]	M		Normal	Normal	Normal	Normal	Normal	Normal	Rales				
11	85	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
11	86^	M		Normal	Normal	Normal	Normal	Normal	Normal	Abnormal Breathing Rate (Shallow), Lethargic, Oral Discharge (Clear), Rales, Hunched Posture, Rough Coat, Mass in Thoracic Area 10x10x10mm	Rales, Hunched Posture, Rough Coat, Abnormal Breathing Rate (Shallow), Decreased Movement, Mass (10x10x10mm thoracic area)	Mass(Ventral Chest and Left Shoulder 1x1cm), Hunched Posture	Mass(Ventral Chest and Left Shoulder 1x1cm), Hunched Posture, Thin	
11	87	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
11	88	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal

[#]Moribund sacrifice due to dosing error

^Humane sacrifice due to dosing error

Group No.:	Animal No.	Sex	Treatment/Dose Level	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation
12	89	M	Octyl Methoxycinnamate (1000 mg/kg) & Testosterone Propionate (0.4 mg/kg)	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
12	90	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
12	91	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Hunched Posture	Normal	Normal
12	92	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
12	93	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
12	94	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
12	95	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
12	96	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal

Group No.:	Animal No.	Sex	Treatment/Dose Level	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation
13	97	M	Flutamide (3 mg/kg) & Testosterone Propionate (0.4 mg/kg)	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
13	98	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
13	99	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
13	100	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
13	101	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
13	102	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
13	103	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
13	104	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal

				Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Terminal
Group No.:	**Animal No.**	**Sex**	**Treatment/Dose Level**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**
14	105	M	Corn Oil Control	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
14	106	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
14	107	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
14	108	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
14	109	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
14	110	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
14	111	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
14	112	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal

Group No.:	**Animal No.**	**Sex**	**Treatment/Dose Level**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**
15	113	M	Octylsalate (235 mg/kg)	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
15	114	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
15	115	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Scab on left cheek	Normal
15	116	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
15	117	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Nasal Discharge (Yellow)	Normal	Normal	Normal
15	118	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
15	119	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
15	120	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal

Group No.:	**Animal No.**	**Sex**	**Treatment/Dose Level**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**
16	121	M	Octylsalate (750 mg/kg)	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
16	122	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
16	123	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
16	124	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
16	125*	M		Normal	Normal	Normal	Normal							
16	126	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Ungroomed Appearance	Normal	Normal
16	127	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
16	128*	M		Normal	Normal	Normal	Normal	Normal						

Group No.:	**Animal No.**	**Sex**	**Treatment/Dose Level**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**	**Clinical Observation**
17	129	M	Octocrylene (320 mg/kg)	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
17	130	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
17	131	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
17	132	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
17	133	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
17	134	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
17	135	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
17	136	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal

Group No.:	Animal No.	Sex	Treatment/Dose Level	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation
18	137	M	Octocrylene (1000 mg/kg)	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
18	138	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
18	139	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
18	140	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Heavy Salivation prior to dosing	Heavy Salivation prior to dosing	Normal
18	141	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
18	142	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
18	143	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
18	144	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal

Group No.:	Animal No.	Sex	Treatment/Dose Level	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation
19	145	M	Corn Oil (0 mg/kg) & Testosterone Propionate (0.4 mg/kg)	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
19	146	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
19	147	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
19	148	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
19	149	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
19	150	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
19	151	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
19	152	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal

Group No.:	Animal No.	Sex	Treatment/Dose Level	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation
20	153	M	Octylsalate (75 mg/kg) & Testosterone Propionate (0.4 mg/kg)	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
20	154	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
20	155	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
20	156	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
20	157	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
20	158	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
20	159	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
20	160	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal

Group No.:	Animal No.	Sex	Treatment/Dose Level	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation
21	161	M	Octylsalate (235 mg/kg) & Testosterone Propionate (0.4 mg/kg)	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
21	162	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
21	163	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
21	164	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
21	165	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
21	166	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
21	167	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
21	168	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal

Group No.:	Animal No.	Sex	Treatment/Dose Level	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation
22	169*	M	Octylsalate (750 mg/kg) & Testosterone Propionate (0.4 mg/kg)	Normal	Normal	Normal	Normal	Thin	Normal					
22	170	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
22	171	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
22	172	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
22	173	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
22	174	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Ungroomed Appearance	Normal	Normal
22	175	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
22	176	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal

Group No.:	Animal No.	Sex	Treatment/Dose Level	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation
23	177	M	Octocrylene (100 mg/kg) & Testosterone Propionate (0.4 mg/kg)	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
23	178	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
23	179	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
23	180	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
23	181	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
23	182	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
23	183	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
23	184	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal

Group No.:	Animal No.	Sex	Treatment/Dose Level	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation
24	185	M	Octocrylene (320 mg/kg) & Testosterone Propionate (0.4 mg/kg)	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
24	186	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
24	187	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
24	188	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
24	189	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
24	190	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
24	191	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
24	192	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal

Group No.:	Animal No.	Sex	Treatment/Dose Level	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation
25	193	M	Octocrylene (1000 mg/kg) & Testosterone Propionate (0.4 mg/kg)	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
25	194	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
25	195	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
25	196	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
25	197	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
25	198	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
25	199	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Alopecia and scab on right cheek
25	200	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal

Group No.:	Animal No.	Sex	Treatment/Dose Level	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation	Clinical Observation
26	201	M	Flutamide (3 mg/kg) & Testosterone Propionate (0.4 mg/kg)	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
26	202	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
26	203	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
26	204	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
26	205	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
26	206	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
26	207	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
26	208	M		Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal

*Animals found dead prior to termination

Appendix V:

Body Weight Data

				Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Terminal		
Group No.:	Animal No.	Sex	Treatment/Dose Level	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	% of Control	Body Weight Gain (g)
1	01	M	Corn Oil Control	254.1	257.4	261.5	265.4	268.5	274.3	275.7	280.3	284.0	290.5	294.1		40.0
1	02	M		243.2	248.5	256.1	264.1	270.3	280.3	286.2	296.5	298.6	314.2	315.0		71.8
1	03	M		273.6	275.7	278.9	286.2	287.2	288.9	294.8	297.0	298.2	301.8	307.3		33.7
1	04	M		245.6	248.6	251.7	258.0	265.3	268.2	266.4	273.3	275.7	280.1	284.9		39.3
1	05*	M		259.1	265.6	269.6	269.4	273.2	274.5	278.9	281.5	290.7	292.5			
1	06	M		264.4	276.4	282.1	288.3	296.8	296.0	305.4	311.3	320.1	324.5	322.3		57.9
1	07	M		270.9	277.3	285.1	288.7	294.5	301.7	310.1	311.4	322.6	328.3	332.6		61.7
1	08	M		232.8	238.0	238.9	239.2	242.7	246.5	250.3	250.8	254.3	256.4	259.2		26.4
			Mean	**255.5**	**260.9**	**265.5**	**269.9**	**274.8**	**278.8**	**283.5**	**287.8**	**293.0**	**298.5**	**302.2**		**47.3**
			St. dev.	**14.3**	**15.1**	**16.3**	**17.3**	**17.8**	**17.4**	**20.0**	**20.5**	**22.5**	**24.0**	**24.9**		**16.6**
			Count	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**7**		**7**

*Found dead due to dosing error

Group No.:	Animal No.	Sex	Treatment/Dose Level	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	% of Control	Body Weight Gain (g)
2	09	M	Oxybenzone (320 mg/kg)	228.1	233.5	236.3	238.8	229.1	243.5	247.8	248.0	248.6	252.5	257.3	85.1	29.2
2	10	M		250.9	256.3	259.1	264.0	255.6	270.7	275.9	276.3	281.3	286.4	290.2	96.0	39.3
2	11	M		248.3	249.6	256.6	261.8	261.4	270.9	277.0	278.2	279.1	283.9	288.1	95.3	39.8
2	12	M		261.8	267.3	271.4	275.4	274.2	285.2	290.6	293.6	303.0	304.7	312.9	103.5	51.1
2	13	M		261.9	265.4	272.6	273.0	284.3	289.8	296.1	298.2	303.2	309.6	315.8	104.5	53.9
2	14	M		285.8	292.6	298.0	298.7	306.1	313.8	318.2	321.8	330.5	335.1	342.6	113.4	56.8
2	15	M		241.6	246.6	248.6	252.0	253.9	258.6	262.9	261.6	264.7	265.8	270.6	89.5	29.0
2	16	M		268.8	277.6	285.0	292.8	296.1	305.1	309.3	310.4	322.3	309.8	314.7	104.1	45.9
			Mean	**255.9**	**261.1**	**266.0**	**269.6**	**270.1**	**279.7**	**284.7**	**286.0**	**291.6**	**293.5**	**299.0**	**98.9**	**43.1**
			St. dev.	**17.7**	**18.7**	**19.9**	**19.9**	**25.1**	**23.5**	**23.5**	**24.7**	**28.2**	**26.7**	**27.7**	**9.2**	**10.6**
			Count	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**

Group No.:	Animal No.	Sex	Treatment/Dose Level	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	% of Control	Body Weight Gain (g)
3	17	M	Oxybenzone (1000 mg/kg)	274.2	266.4	274.7	285.6	273.8	296.3	303.3	307.0	312.1	318.9	322.4	106.7	48.2
3	18	M		245.0	238.3	239.6	253.9	236.2	259.0	365.5	266.6	272.6	283.6	285.4	94.4	40.4
3	19	M		263.5	262.6	253.5	261.8	268.6	271.7	278.0	278.6	280.9	284.9	292.4	96.8	28.9
3	20	M		254.8	252.8	256.4	262.8	272.2	273.2	278.9	283.3	284.7	292.0	295.9	97.9	41.1
3	21	M		272.3	269.0	272.8	282.0	284.8	281.2	290.8	291.6	299.7	302.5	308.2	102.0	35.9
3	22	M		260.8	258.2	268.9	281.6	287.5	286.8	295.0	295.7	303.9	301.6	310.1	102.6	49.3
3	23	M		238.1	238.0	242.6	247.0	245.6	247.0	249.0	249.2	251.6	251.8	257.4	85.2	19.3
3	24	M		259.7	264.3	267.3	275.6	283.9	287.3	297.8	294.4	298.2	303.0	312.0	103.2	52.3
			Mean	**258.6**	**256.2**	**259.5**	**268.8**	**269.1**	**275.3**	**294.8**	**283.3**	**288.0**	**292.3**	**298.0**	**98.6**	**39.4**
			St. dev.	**12.4**	**12.2**	**13.5**	**14.4**	**18.8**	**16.2**	**33.2**	**18.4**	**19.6**	**19.9**	**20.3**	**6.7**	**11.2**
			Count	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**

Group No.:	Animal No.	Sex	Treatment/Dose Level	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	% of Control	Body Weight Gain (g)
4	25	M	Octyl Methoxycinnamate (320 mg/kg)	252.3	257.0	264.3	271.5	275.0	283.2	288.5	292.4	297.4	309.2	313.2	103.6	60.9
4	26	M		246.9	249.2	253.4	253.9	259.1	262.9	264.3	266.0	268.6	272.6	275.5	91.2	28.6
4	27	M		238.6	242.0	251.5	256.3	262.0	265.6	272.4	274.2	275.5	281.1	288.2	95.4	49.6
4	28	M		260.3	264.2	269.8	274.2	279.0	285.0	286.7	290.1	291.5	297.7	302.4	100.1	42.1
4	29	M		261.8	268.0	276.6	282.8	288.3	293.8	297.5	301.6	309.1	311.4	322.6	106.8	60.8
4	30	M		278.4	286.8	294.1	302.5	313.4	313.1	321.1	331.0	338.2	341.2	349.7	115.7	71.3
4	31	M		273.9	281.9	292.4	299.1	311.9	316.1	345.1	332.5	343.5	348.2	360.1	119.2	86.2
4	32	M		242.5	242.7	250.3	257.6	265.3	271.2	272.0	276.9	285.7	290.6	297.0	98.3	54.5
			Mean	**256.8**	**261.5**	**269.1**	**274.7**	**281.8**	**286.4**	**293.5**	**295.6**	**301.2**	**306.5**	**313.6**	**103.8**	**56.8**
			St. dev.	**14.4**	**16.9**	**17.6**	**18.9**	**21.3**	**20.3**	**27.4**	**25.0**	**27.5**	**27.0**	**29.4**	**9.7**	**17.6**
			Count	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**

Group No.:	Animal No.	Sex	Treatment/Dose Level	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	% of Control	Body Weight Gain (g)
5	33	M	Octyl Methoxycinnamate (1000 mg/kg)	260.2	263.0	266.7	272.6	263.6	286.5	264.5	259.4	263.4	274.7	282.8	93.6	22.6
5	34	M		272.3	270.6	275.2	280.5	277.3	290.5	294.2	298.5	304.2	307.2	316.1	104.6	43.8
5	35	M		249.4	252.5	258.5	270.0	272.9	274.3	282.4	284.3	288.4	291.4	300.2	99.3	50.8
5	36	M		242.3	243.3	244.3	248.7	257.8	264.1	263.7	268.1	268.2	274.7	281.4	93.1	39.1
5	37	M		255.2	256.6	260.9	262.8	271.7	277.2	278.0	284.9	294.3	297.2	306.9	101.6	51.7
5	38	M		263.6	267.3	274.4	269.4	276.9	284.6	286.8	288.3	295.7	301.6	311.4	103.0	47.8
5	39	M		253.9	250.4	251.3	249.3	264.1	263.3	266.5	270.9	276.9	279.0	282.7	93.5	28.8
5	40	M		262.5	265.0	270.2	264.0	285.8	288.4	288.6	293.0	299.8	299.2	304.8	100.9	42.3
			Mean	**257.4**	**258.6**	**262.7**	**264.7**	**271.3**	**278.6**	**278.1**	**280.9**	**286.4**	**290.6**	**298.3**	**98.7**	**40.9**
			St. dev.	**9.3**	**9.4**	**11.1**	**11.1**	**9.1**	**10.7**	**11.9**	**13.4**	**15.1**	**12.8**	**14.0**	**4.6**	**10.4**
			Count	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**

Group No.:	Animal No.	Sex	Treatment/Dose Level	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	% of Control	Body Weight Gain (g)
6	41	M	Corn Oil (0 mg/kg) & Testosterone Propionate (0.4 mg/kg)	252.5	254.4	266.9	276.3	236.0	287.2	299.7	305.1	309.2	318.2	326.7		74.2
6	42	M		257.1	250.8	267.1	279.1	286.0	287.6	294.7	296.1	300.4	304.0	306.7		49.6
6	43	M		253.6	256.4	264.5	266.8	278.8	287.4	294.6	298.7	302.7	311.9	321.4		67.8
6	44	M		247.4	251.6	263.3	273.0	273.2	280.2	290.9	293.3	295.8	302.6	312.9		65.5
6	45	M		280.3	287.3	293.2	307.7	318.7	327.3	334.7	343.6	355.9	363.6	375.2		94.9
6	46	M		262.5	269.8	275.6	285.8	292.9	299.3	304.9	310.3	318.5	323.4	329.6		67.1
6	47	M		248.0	254.4	269.6	280.9	286.5	298.8	302.8	310.7	321.9	334.2	344.9		96.9
6	48	M		273.2	278.9	290.7	300.3	311.6	320.2	329.0	334.2	346.1	353.7	363.2		90.0
			Mean	**259.3**	**263.0**	**273.9**	**283.7**	**285.5**	**298.5**	**306.4**	**311.5**	**318.8**	**326.5**	**335.1**		**75.8**
			St. dev.	**11.9**	**13.9**	**11.8**	**13.8**	**25.3**	**16.9**	**16.4**	**18.2**	**21.9**	**22.5**	**24.1**		**16.7**
			Count	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**		**8**

Group No.:	Animal No.	Sex	Treatment/Dose Level	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	% of Control	Body Weight Gain (g)
7	49	M	Oxybenzone (100 mg/kg) & Testosterone Propionate (0.4 mg/kg)	270.4	281.0	290.2	297.2	311.2	321.5	327.7	331.6	340.7	354.2	360.2	107.5	89.8
7	50	M		268.3	268.9	277.2	288.8	296.9	297.8	302.1	304.6	313.3	323.8	334.7	99.9	66.4
7	51	M		240.8	248.2	256.2	268.0	280.3	288.5	201.0	308.0	314.8	321.6	330.8	98.7	90.0
7	52	M		255.7	264.0	272.2	287.2	295.9	302.4	306.2	311.8	320.9	328.1	338.2	100.9	82.5
7	53	M		235.5	239.6	252.6	259.0	268.4	274.7	280.2	283.7	298.4	302.4	309.8	92.5	74.3
7	54	M		276.0	286.4	295.0	306.6	316.2	320.6	330.3	338.2	348.2	355.6	364.1	108.7	88.1
7	55	M		254.6	256.4	268.5	277.1	284.2	296.1	299.7	306.8	314.3	319.8	325.7	97.2	71.1
7	56	M		261.9	265.3	274.6	285.7	294.2	303.8	309.6	315.2	326.2	333.1	341.2	101.8	79.3
			Mean	**257.9**	**263.7**	**273.3**	**283.7**	**293.4**	**300.7**	**294.6**	**312.5**	**322.1**	**329.8**	**338.1**	**100.9**	**80.2**
			St. dev.	**14.2**	**15.7**	**14.7**	**15.3**	**15.8**	**15.6**	**41.0**	**16.8**	**16.0**	**17.8**	**17.7**	**5.3**	**9.0**
			Count	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**

Group No.:	Animal No.	Sex	Treatment/Dose Level	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	% of Control	Body Weight Gain (g)
8	57	M	Oxybenzone (320 mg/kg) & Testosterone Propionate (0.4 mg/kg)	260.1	265.9	272.2	280.5	288.8	297.1	306.8	317.4	323.6	328.8	335.9	100.2	75.8
8	58	M		256.4	263.0	269.8	276.0	286.2	295.2	302.9	300.9	308.9	317.2	325.4	97.1	69.0
8	59	M		262.3	266.2	280.9	293.7	312.2	317.1	323.2	326.6	340.8	344.7	354.3	105.7	92.0
8	60	M		252.1	255.5	261.0	273.4	275.6	282.4	291.3	293.8	302.0	304.6	312.6	93.3	60.5
8	61	M		275.7	286.2	289.1	301.5	293.7	304.0	314.5	320.4	331.0	340.7	352.2	105.1	76.5
8	62	M		274.2	283.8	294.7	301.1	311.2	320.9	327.4	337.2	349.1	352.7	360.4	107.6	86.2
8	63	M		252.8	261.2	272.3	281.8	283.5	300.1	307.5	315.1	324.4	329.7	336.9	100.5	84.1
8	64	M		252.5	255.3	267.5	280.1	285.5	293.9	304.1	309.5	320.6	325.0	335.7	100.2	83.2
			Mean	**260.8**	**267.1**	**275.9**	**286.0**	**292.1**	**301.3**	**309.7**	**315.1**	**325.1**	**330.4**	**339.2**	**101.2**	**78.4**
			St. dev.	**9.5**	**11.8**	**11.4**	**11.1**	**13.1**	**12.6**	**11.6**	**13.8**	**15.5**	**15.5**	**15.9**	**4.7**	**10.1**
			Count	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**

Group No.:	Animal No.	Sex	Treatment/Dose Level	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	% of Control	Body Weight Gain (g)
9	65	M	Oxybenzone (1000 mg/kg) & Testosterone Propionate (0.4 mg/kg)	264.3	266.8	266.1	273.6	279.3	290.3	293.2	295.7	299.0	306.2	313.7	93.6	49.4
9	66	M		245.1	248.4	252.2	259.5	270.4	275.0	283.9	290.9	296.6	306.5	315.5	94.2	70.4
9	67	M		245.7	235.8	243.5	251.4	260.4	257.4	268.6	272.2	279.6	285.5	293.2	87.5	47.5
9	68	M		238.3	242.8	247.2	260.0	272.3	275.5	285.1	288.0	290.1	297.1	303.5	90.6	65.2
9	69	M		259.9	254.6	260.3	270.7	277.9	286.4	293.0	298.8	305.2	311.2	319.9	95.5	60.0
9	70	M		263.3	267.3	264.4	279.4	281.4	288.6	290.6	296.2	297.3	300.5	303.1	90.5	39.8
9	71	M		257.8	257.3	255.9	268.9	266.9	269.1	276.3	280.9	285.6	289.2	295.7	88.2	37.9
9	72	M		280.2	290.8	290.3	300.8	309.1	315.7	318.1	323.0	333.4	336.1	345.2	103.0	65.0
			Mean	**256.8**	**258.0**	**260.0**	**270.5**	**277.2**	**282.3**	**288.6**	**293.2**	**298.4**	**304.0**	**311.2**	**92.9**	**54.4**
			St. dev.	**13.4**	**17.2**	**14.6**	**15.1**	**14.6**	**17.4**	**14.6**	**14.9**	**16.3**	**15.7**	**16.7**	**5.0**	**12.4**
			Count	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**

Group No.:	Animal No.	Sex	Treatment/Dose Level	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	% of Control	Body Weight Gain (g)
10	73	M		258.8	268.4	275.1	289.6	298.2	305.3	320.2	326.3	330.7	344.8	352.8	105.3	94.0
10	74	M	Octyl	258.1	263.8	273.5	284.6	290.0	298.8	307.4	313.7	320.1	342.9	333.6	99.6	75.5
10	75	M	Methoxycinnamate	254.5	255.0	267.6	276.3	292.3	294.9	310.6	315.1	322.2	332.5	338.9	101.1	84.4
10	76	M	(100 mg/kg) &	249.4	258.3	264.9	272.3	283.5	292.6	300.5	274.4	265.3	269.0	256.8	76.6	7.4
10	77	M	Testosterone	270.8	276.8	286.4	299.9	304.8	315.5	321.7	328.0	337.8	339.8	351.8	105.0	81.0
10	78	M	Propionate	284.3	291.3	302.4	312.0	322.6	335.2	339.7	253.4	363.9	369.4	387.2	115.6	102.9
10	79	M	(0.4 mg/kg)	235.7	239.0	241.2	242.6	250.6	254.5	259.3	264.5	269.3	274.3	278.6	83.1	42.9
10	80	M		267.6	272.3	283.6	282.6	296.8	304.9	309.4	316.9	327.7	329.2	342.2	102.1	74.6
			Mean	**259.9**	**265.6**	**274.3**	**282.5**	**292.4**	**300.2**	**308.6**	**299.0**	**317.1**	**325.2**	**330.2**	**98.6**	**70.3**
			St. dev.	**14.7**	**15.7**	**17.9**	**20.6**	**20.5**	**22.9**	**23.2**	**29.9**	**33.6**	**35.2**	**42.3**	**12.6**	**30.9**
			Count	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**

Group No.:	Animal No.	Sex	Treatment/Dose Level	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	% of Control	Body Weight Gain (g)
11	81	M		239.8	240.6	249.3	253.2	268.1	275.5	282.0	286.3	292.5	301.1	303.8	90.7	64.0
11	82	M	Octyl	248.2	249.4	260.6	273.0	287.0	297.2	303.9	310.6	323.6	331.8	340.2	101.5	92.0
11	83	M	Methoxycinnamate	272.1	280.1	287.1	300.3	287.7	315.5	322.8	329.4	332.9	347.5	356.2	106.3	84.1
11	84[#]	M	(320 mg/kg) &	265.2	266.0	275.6	288.6	277.7	307.5	279.2						
11	85	M	Testosterone	262.6	269.5	280.8	292.2	305.7	314.3	320.8	328.7	334.2	349.8	362.9	108.3	100.3
11	86^	M	Propionate	258.8	263.4	270.9	279.4	287.4	360.6	246.3	234.4	220.6	209.0			
11	87	M	(0.4 mg/kg)	271.3	261.9	270.3	281.4	289.4	294.7	296.1	305.2	313.6	317.5	323.9	96.7	52.6
11	88	M		257.3	276.6	290.5	302.8	314.2	326.6	330.4	345.5	356.1	364.4	375.3	112.0	118.0
			Mean	**259.4**	**263.4**	**273.1**	**283.9**	**289.7**	**311.5**	**297.7**	**305.7**	**310.5**	**317.3**	**343.7**	**102.6**	**85.2**
			St. dev.	**11.1**	**13.2**	**13.6**	**16.1**	**14.6**	**25.2**	**28.0**	**36.9**	**44.2**	**52.3**	**26.5**	**7.9**	**23.9**
			Count	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**7**	**7**	**7**	**6**	**6**	**6**

[#]Moribund sacrifice due to dosing error

^Humane sacrifice due to dosing error

Group No.:	Animal No.	Sex	Treatment/Dose Level	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	% of Control	Body Weight Gain (g)
12	89	M		260.1	257.2	263.6	278.2	276.6	290.3	298.4	306.2	312.9	320.0	327.1	97.6	67.0
12	90	M	Octyl	243.6	241.6	250.3	258.9	259.2	277.6	284.2	284.4	293.8	296.7	305.2	91.1	61.6
12	91	M	Methoxycinnamate	235.1	234.2	239.0	246.7	233.4	258.3	258.1	256.9	264.3	266.8	273.6	81.7	38.5
12	92	M	(1000 mg/kg) &	268.6	263.8	272.6	276.6	259.8	290.0	292.2	294.6	305.0	307.4	320.2	95.6	51.6
12	93	M	Testosterone	259.8	260.4	265.2	268.2	278.6	279.4	281.6	288.5	297.3	303.7	315.7	94.2	55.9
12	94	M	Propionate	265.5	270.7	283.5	287.6	306.7	315.5	319.3	328.8	343.2	352.1	360.8	107.7	95.3
12	95	M	(0.4 mg/kg)	273.6	277.8	283.1	270.9	299.3	305.0	305.8	315.2	318.6	321.9	333.7	99.6	60.1
12	96	M		268.0	260.8	269.8	265.2	282.4	295.8	298.1	303.8	309.4	310.7	321.6	96.0	53.6
			Mean	**259.3**	**258.3**	**265.9**	**269.0**	**274.5**	**289.0**	**292.2**	**297.3**	**305.6**	**309.9**	**319.7**	**95.4**	**60.5**
			St. dev.	**13.3**	**14.3**	**15.3**	**12.6**	**23.5**	**17.6**	**18.3**	**21.8**	**22.6**	**24.2**	**24.8**	**7.4**	**16.4**
			Count	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**

Group No.:	Animal No.	Sex	Treatment/Dose Level	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	% of Control	Body Weight Gain (g)
13	97	M		239.8	248.6	256.8	260.8	270.4	278.9	285.3	293.6	298.8	305.9	316.2	94.4	76.4
13	98	M	Flutamide	249.4	257.8	262.3	268.8	276.7	282.9	289.1	292.6	294.4	300.1	310.8	92.8	61.4
13	99	M	(3 mg/kg) &	249.8	255.7	263.5	270.8	278.9	287.8	295.6	301.6	308.2	311.2	317.2	94.7	67.4
13	100	M	Testosterone	260.4	263.5	268.2	275.8	280.6	285.6	291.1	293.3	298.0	306.1	311.0	92.8	50.6
13	101	M	Propionate	275.6	285.4	296.0	302.1	313.5	324.0	331.0	340.4	344.5	350.7	360.8	107.7	85.2
13	102	M	(0.4 mg/kg)	273.0	277.6	288.0	299.5	307.1	315.1	318.7	326.9	332.9	338.6	350.1	104.5	77.1
13	103	M		272.9	277.5	286.3	282.1	306.1	305.4	315.6	306.2	299.9	329.8	339.3	101.3	66.4
13	104	M		243.5	250.8	252.6	248.0	261.6	266.3	268.7	261.9	254.1	278.1	286.2	85.4	42.7
			Mean	**258.1**	**264.6**	**271.7**	**276.0**	**286.9**	**293.3**	**299.4**	**302.1**	**303.9**	**315.1**	**324.0**	**96.7**	**65.9**
			St. dev.	**14.4**	**13.8**	**16.1**	**18.4**	**19.3**	**19.6**	**20.6**	**23.8**	**27.1**	**23.3**	**24.3**	**7.3**	**14.2**
			Count	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**

				Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Terminal		
Group No.:	Animal No.	Sex	Treatment/Dose Level	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	% of Control	Body Weight Gain (g)
14	105	M	Corn Oil Control	208.4	210.4	212.3	217.5	221.2	222.1	231.6	237.1	235.2	239.4	249.9		41.5
14	106	M		244.8	249.8	252.8	260.3	261.8	267.9	272.3	278.3	278.2	282.5	286.7		41.9
14	107	M		250.1	252.1	259.4	270.8	274.8	278.2	286.4	290.4	292.7	294.8	304.2		54.1
14	108	M		267.5	267.1	273.3	279.0	277.8	278.4	282.9	289.4	287.4	295.9	299.7		32.2
14	109	M		271.2	273.1	283.6	286.6	290.3	292.4	301.5	299.4	305.6	311.7	319.3		48.1
14	110	M		291.6	298.8	310.4	315.2	321.4	326.2	334.4	333.1	344.3	349.2	361.6		70.0
14	111	M		287.2	289.8	296.8	301.0	301.9	305.8	312.2	314.6	315.8	320.4	325.7		38.5
14	112	M		328.6	337.1	346.9	357.1	357.7	371.1	378.5	385.9	390.0	397.6	406.8		78.2
			Mean	**268.7**	**272.3**	**279.4**	**285.9**	**288.4**	**292.8**	**300.0**	**303.5**	**306.2**	**311.4**	**319.2**		**50.6**
			St. dev.	**35.9**	**37.8**	**40.5**	**41.0**	**40.7**	**43.8**	**43.8**	**43.5**	**46.2**	**47.0**	**47.8**		**16.0**
			Count	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**		**8**

Group No.:	Animal No.	Sex	Treatment/Dose Level	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	% of Control	Body Weight Gain (g)
15	113	M	Octylsalate (235 mg/kg)	209.6	206.8	213.2	218.0	220.5	222.4	228.3	232.4	232.5	237.8	240.6	75.4	31.0
15	114	M		246.5	246.3	252.4	260.1	265.6	271.2	277.1	284.2	286.6	294.5	299.3	93.8	52.8
15	115	M		262.6	261.0	268.7	269.7	276.0	277.1	278.8	285.2	288.1	291.2	300.2	94.0	37.6
15	116	M		237.4	239.2	246.3	256.4	258.5	256.7	262.6	266.1	264.1	270.3	275.9	86.4	38.5
15	117	M		267.3	265.7	281.1	281.5	286.1	286.1	293.1	293.6	302.6	306.8	313.3	98.1	46.0
15	118	M		271.0	274.4	284.0	286.8	292.4	296.0	314.5	312.8	318.2	324.2	337.0	105.6	66.0
15	119	M		294.3	290.3	301.0	305.8	308.8	306.8	314.3	312.8	320.6	325.6	332.0	104.0	37.7
15	120	M		322.6	318.6	328.2	340.8	341.2	340.8	353.9	360.7	367.2	369.4	381.5	119.5	58.9
			Mean	**263.9**	**262.8**	**271.9**	**277.4**	**281.1**	**282.1**	**290.3**	**293.5**	**297.5**	**302.5**	**310.0**	**97.1**	**46.1**
			St. dev.	**34.6**	**33.8**	**35.3**	**36.4**	**35.8**	**35.1**	**38.0**	**37.6**	**40.3**	**39.5**	**42.3**	**13.3**	**12.1**
			Count	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**

Group No.:	Animal No.	Sex	Treatment/Dose Level	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	% of Control	Body Weight Gain (g)
16	121	M	Octylsalate (750 mg/kg)	223.2	216.9	217.3	220.5	223.5	250.8	222.5	235.0	233.4	238.2	244.6	76.6	21.4
16	122	M		252.8	244.3	241.5	245.8	242.1	224.5	247.8	259.6	257.0	265.2	269.9	84.5	17.1
16	123	M		247.9	239.1	236.2	232.6	227.0	228.6	234.1	250.0	250.6	251.5	250.8	78.6	2.9
16	124	M		262.7	255.8	252.7	262.1	265.5	268.8	271.9	282.2	284.2	295.2	294.7	92.3	32.0
16	125*	M		267.6	267.3	257.7	249.1									
16	126	M		287.4	290.4	285.0	283.1	268.0	263.1	265.4	258.2	268.7	274.4	280.8	88.0	-6.6
16	127	M		292.6	281.8	281.3	277.7	275.6	285.0	296.9	294.5	304.2	302.3	311.0	97.4	18.4
16	128*	M		326.8	312.9	305.4	297.8	281.5								
			Mean	**270.1**	**263.6**	**259.6**	**258.6**	**254.7**	**253.5**	**256.4**	**263.3**	**266.4**	**271.1**	**275.3**	**86.2**	**14.2**
			St. dev.	**31.8**	**31.0**	**29.1**	**26.4**	**23.6**	**23.6**	**27.1**	**21.7**	**25.2**	**24.8**	**25.5**	**8.0**	**13.8**
			Count	**8**	**8**	**8**	**8**	**7**	**6**	**6**	**6**	**6**	**6**	**6**	**6**	**6**

*Animal found dead prior to termination

Group No.:	Animal No.	Sex	Treatment/Dose Level	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	% of Control	Body Weight Gain (g)
17	129	M	Octocrylene (320 mg/kg)	219.5	220.9	229.8	234.1	239.2	244.2	248.0	252.2	257.3	259.1	266.4	83.4	46.9
17	130	M		246.6	247.3	256.7	266.0	273.5	276.4	284.2	292.5	292.8	300.8	307.8	96.4	61.2
17	131	M		253.2	256.9	262.6	268.5	272.6	275.2	281.9	287.2	288.4	292.4	299.2	93.7	46.0
17	132	M		258.7	260.3	264.4	277.0	278.1	280.0	286.0	290.5	291.7	297.5	303.6	95.1	44.9
17	133	M		272.1	282.5	287.1	294.7	292.8	300.2	306.9	302.9	312.6	316.1	306.3	95.9	34.2
17	134	M		288.1	291.8	302.7	307.4	314.6	320.9	323.5	325.5	335.2	340.0	343.7	107.7	55.6
17	135	M		314.1	319.4	326.9	326.2	333.9	341.7	351.7	353.3	361.8	369.5	379.7	118.9	65.6
17	136	M		297.5	297.9	313.1	315.4	320.4	327.6	333.4	332.8	343.4	347.5	362.0	113.4	64.5
			Mean	**268.7**	**272.1**	**280.4**	**286.2**	**290.6**	**295.8**	**302.0**	**304.6**	**310.4**	**315.4**	**321.1**	**100.6**	**52.4**
			St. dev.	**30.5**	**31.6**	**32.7**	**30.5**	**31.1**	**32.7**	**33.5**	**31.6**	**34.5**	**35.4**	**37.4**	**11.7**	**11.1**
			Count	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**

Group No.:	Animal No.	Sex	Treatment/Dose Level	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	% of Control	Body Weight Gain (g)
18	137	M	Octocrylene (1000 mg/kg)	217.1	218.2	222.1	232.9	238.5	240.6	245.6	254.8	250.4	254.2	265.4	83.1	48.3
18	138	M		232.2	240.5	241.6	253.3	252.8	258.9	261.8	266.2	261.2	269.6	273.6	85.7	41.4
18	139	M		258.0	253.0	264.1	274.2	275.8	281.7	285.7	289.1	286.8	296.6	303.7	95.1	45.7
18	140	M		261.8	261.9	276.4	284.5	290.7	291.4	304.2	309.5	315.6	321.1	329.5	103.2	67.7
18	141	M		277.6	278.5	289.7	293.6	290.4	294.1	299.9	304.7	310.8	313.6	323.6	101.4	46.0
18	142	M		286.2	290.2	296.6	305.1	310.6	316.0	323.6	321.0	335.6	334.8	346.5	108.5	60.3
18	143	M		291.4	294.8	302.2	307.5	311.4	344.8	324.0	326.6	328.6	332.8	339.1	106.2	47.7
18	144	M		315.0	319.0	324.4	333.4	336.2	315.7	346.4	358.4	363.0	368.3	381.6	119.5	66.6
			Mean	**267.4**	**269.5**	**277.1**	**285.6**	**288.3**	**292.9**	**298.9**	**303.8**	**306.5**	**311.4**	**320.4**	**100.4**	**53.0**
			St. dev.	**32.0**	**32.5**	**33.5**	**32.0**	**32.1**	**33.3**	**33.6**	**33.5**	**38.2**	**37.0**	**38.5**	**12.1**	**10.3**
			Count	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**

Group No.:	Animal No.	Sex	Treatment/Dose Level	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	% of Control	Body Weight Gain (g)
19	145	M	Corn Oil (0 mg/kg) & Testosterone Propionate (0.4 mg/kg)	220.3	223.2	230.8	238.2	244.4	252.6	255.3	263.3	264.8	266.0	272.8		52.5
19	146	M		244.7	252.0	255.4	267.4	274.4	282.7	292.9	301.3	302.3	313.4	323.7		79.0
19	147	M		263.2	267.5	282.6	298.6	309.5	316.8	330.8	339.5	343.8	359.7	372.8		109.6
19	148	M		261.0	268.0	272.4	284.5	290.5	295.9	301.5	311.9	313.2	322.6	332.2		71.2
19	149	M		271.4	271.6	283.6	292.0	296.0	305.6	315.0	316.5	324.6	333.0	344.0		72.6
19	150	M		282.8	287.8	298.3	304.4	311.8	320.8	332.6	334.9	346.1	355.6	366.0		83.2
19	151	M		288.0	297.7	309.9	322.3	328.2	337.8	347.1	350.5	362.2	366.6	378.0		90.0
19	152	M		319.6	328.5	337.2	349.5	362.6	376.9	388.8	398.6	412.8	419.0	436.1		116.5
			Mean	**268.9**	**274.5**	**283.8**	**294.6**	**302.2**	**311.1**	**320.5**	**327.1**	**333.7**	**342.0**	**353.2**		**84.3**
			St. dev.	**29.7**	**31.3**	**32.7**	**33.6**	**35.4**	**37.1**	**39.7**	**39.6**	**44.0**	**44.9**	**47.7**		**20.9**
			Count	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**		**8**

Group No.:	Animal No.	Sex	Treatment/Dose Level	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	% of Control	Body Weight Gain (g)
20	153	M	Octylsalate (75 mg/kg) & Testosterone Propionate (0.4 mg/kg)	226.1	230.1	238.5	249.7	251.7	260.2	265.8	275.7	275.5	278.1	291.3	82.5	65.2
20	154	M		241.9	243.3	248.4	255.0	259.3	262.0	271.4	277.9	278.5	286.2	293.5	83.1	51.6
20	155	M		257.4	260.6	270.2	280.3	285.7	290.9	301.9	309.0	312.7	320.1	334.5	94.7	77.1
20	156	M		264.1	266.7	278.8	294.0	302.1	308.9	317.8	334.8	337.8	351.6	359.9	101.9	95.8
20	157	M		275.7	278.6	291.2	299.3	300.4	307.9	311.2	311.3	322.5	324.9	331.3	93.8	55.6
20	158	M		290.4	295.1	308.6	316.4	325.7	331.6	337.5	338.9	349.3	354.8	365.4	103.5	75.0
20	159	M		290.3	305.9	316.4	330.2	339.9	351.9	354.9	363.1	376.6	379.1	395.2	111.9	104.9
20	160	M		306.2	309.1	321.3	329.2	336.7	348.3	354.4	354.9	360.2	365.9	377.2	106.8	71.0
			Mean	**269.0**	**273.7**	**284.2**	**294.3**	**300.2**	**307.7**	**314.4**	**320.7**	**326.6**	**332.6**	**343.5**	**97.3**	**74.5**
			St. dev.	**26.9**	**28.8**	**30.8**	**31.1**	**33.4**	**35.5**	**34.1**	**32.9**	**36.7**	**36.8**	**37.8**	**10.7**	**18.4**
			Count	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**

Group No.:	Animal No.	Sex	Treatment/Dose Level	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	% of Control	Body Weight Gain (g)
21	161	M	Octylsalate (235 mg/kg) & Testosterone Propionate (0.4 mg/kg)	227.6	231.1	239.4	243.1	251.8	257.6	264.8	271.7	273.9	284.3	290.7	82.3	63.1
21	162	M		241.3	246.0	263.4	271.5	283.4	290.6	303.2	313.6	313.9	324.1	336.5	95.3	95.2
21	163	M		257.7	253.6	260.7	269.8	278.5	291.3	299.9	304.3	311.7	319.7	335.5	95.0	77.8
21	164	M		260.6	255.7	267.6	275.7	279.9	282.1	287.8	297.2	303.0	302.8	305.7	86.6	45.1
21	165	M		270.8	271.2	281.7	292.3	293.4	303.9	314.2	310.0	319.2	321.5	332.4	94.1	61.6
21	166	M		272.5	274.4	279.2	284.6	297.8	300.5	308.4	313.2	315.6	325.0	329.1	93.2	56.6
21	167	M		292.8	296.4	309.2	314.2	322.3	333.2	344.1	347.3	361.6	366.1	375.3	106.3	82.5
21	168	M		313.5	318.8	337.6	342.5	352.6	362.8	374.4	383.7	398.2	403.9	413.0	116.9	99.5
			Mean	**267.1**	**268.4**	**279.9**	**286.7**	**295.0**	**302.8**	**312.1**	**317.6**	**324.6**	**330.9**	**339.8**	**96.2**	**72.7**
			St. dev.	**27.3**	**28.4**	**30.8**	**30.3**	**30.6**	**32.3**	**33.8**	**33.9**	**38.2**	**37.5**	**38.5**	**10.9**	**19.2**
			Count	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**

Group No.:	Animal No.	Sex	Treatment/Dose Level	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	% of Control	Body Weight Gain (g)
22	169*	M	Octylsalate (750 mg/kg) & Testosterone Propionate (0.4 mg/kg)	223.9	226.7	222.8	227.0	212.2	205.7							
22	170	M		242.9	232.6	231.0	235.3	240.7	242.3	250.9	256.5	260.0	266.7	274.8	77.8	31.9
22	171	M		258.5	254.1	249.0	244.9	242.5	235.1	243.5	259.7	269.7	278.0	286.3	81.1	27.8
22	172	M		264.1	251.2	242.8	240.5	232.5	220.0	227.1	234.7	234.9	238.1	249.9	70.8	-14.2
22	173	M		272.3	271.2	277.5	278.7	282.7	277.4	287.8	297.3	309.1	302.9	320.9	90.9	48.6
22	174	M		281.8	271.9	268.0	259.6	255.3	246.0	263.6	260.1	265.6	247.4	270.4	76.6	-11.4
22	175	M		294.6	290.2	280.9	272.1	280.9	286.6	297.2	299.9	303.0	308.0	316.7	89.7	22.1
22	176	M		311.7	317.0	320.8	314.9	319.0	322.0	331.9	347.1	353.2	364.7	376.0	106.5	64.3
			Mean	**268.7**	**264.4**	**261.6**	**259.1**	**258.2**	**254.4**	**271.7**	**279.3**	**285.1**	**286.5**	**299.3**	**84.7**	**24.2**
			St. dev.	**28.0**	**29.9**	**31.9**	**28.8**	**34.1**	**38.3**	**36.1**	**37.9**	**39.4**	**43.2**	**42.2**	**12.0**	**28.9**
			Count	**8**	**8**	**8**	**8**	**8**	**8**	**7**	**7**	**7**	**7**	**7**	**7**	**7**

*Animal found dead prior to termination

Group No.:	Animal No.	Sex	Treatment/Dose Level	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	% of Control	Body Weight Gain (g)
23	177	M	Octocrylene (100 mg/kg) & Testosterone Propionate (0.4 mg/kg)	231.9	234.7	244.9	258.9	269.5	273.8	281.0	292.8	296.3	302.3	309.5	87.6	77.6
23	178	M		238.7	239.6	251.7	261.4	270.6	273.3	278.6	288.1	291.0	299.1	306.0	86.6	67.3
23	179	M		253.7	257.8	266.7	273.8	279.1	285.8	293.5	302.9	304.1	313.9	319.1	90.3	65.4
23	180	M		260.6	265.4	275.8	286.8	296.9	301.5	313.1	322.6	324.7	332.3	344.2	97.5	83.6
23	181	M		276.5	278.5	289.3	297.6	302.1	312.9	320.3	327.4	334.3	343.1	356.2	100.8	79.7
23	182	M		279.3	285.0	296.2	304.1	311.2	321.6	327.9	328.7	337.6	343.7	359.0	101.6	79.7
23	183	M		301.8	308.4	319.9	331.7	335.7	344.5	356.4	357.6	370.0	376.8	390.0	110.4	88.2
23	184	M		307.8	314.0	325.5	331.1	340.3	350.8	364.6	271.3	372.4	378.0	388.9	110.1	81.1
			Mean	**268.8**	**272.9**	**283.8**	**293.2**	**300.7**	**308.0**	**316.9**	**311.4**	**328.8**	**336.2**	**346.6**	**98.1**	**77.8**
			St. dev.	**27.6**	**29.2**	**29.6**	**28.4**	**27.4**	**30.0**	**32.3**	**27.7**	**31.2**	**30.6**	**33.2**	**9.4**	**7.8**
			Count	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**

Group No.:	Animal No.	Sex	Treatment/Dose Level	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	% of Control	Body Weight Gain (g)
24	185	M	Octocrylene (320 mg/kg) & Testosterone Propionate (0.4 mg/kg)	234.1	239.4	250.1	260.4	265.5	273.6	282.5	291.0	292.2	304.7	312.1	88.4	78.0
24	186	M		240.8	245.3	254.6	266.3	274.1	280.1	291.9	298.5	301.6	311.8	319.2	90.4	78.4
24	187	M		249.1	258.9	263.0	273.5	282.7	290.4	302.2	310.7	319.1	332.3	344.2	97.5	95.1
24	188	M		261.8	264.9	276.6	284.9	290.2	296.8	307.6	316.0	321.9	334.0	335.7	95.0	73.9
24	189	M		261.2	268.6	282.9	288.4	295.1	294.2	314.1	317.1	324.9	329.3	340.4	96.4	79.2
24	190	M		285.0	285.3	294.0	300.5	306.8	309.4	326.2	328.2	329.7	340.1	351.3	99.5	66.3
24	191	M		296.6	300.3	314.4	323.2	329.8	342.9	354.7	355.0	370.8	376.6	388.9	110.1	92.3
24	192	M		310.8	316.8	330.0	340.2	349.9	360.4	374.6	380.4	397.5	402.4	422.4	119.6	111.6
			Mean	**267.4**	**272.4**	**283.2**	**292.2**	**299.3**	**306.0**	**319.2**	**324.6**	**332.2**	**341.4**	**351.8**	**99.6**	**84.4**
			St. dev.	**27.4**	**26.7**	**28.4**	**27.9**	**28.5**	**30.5**	**31.4**	**29.7**	**35.1**	**32.7**	**36.7**	**10.4**	**14.4**
			Count	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**

Group No.:	Animal No.	Sex	Treatment/Dose Level	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	% of Control	Body Weight Gain (g)
25	193	M	Octocrylene (1000 mg/kg) & Testosterone Propionate (0.4 mg/kg)	240.3	238.4	248.4	255.9	265.5	264.2	273.3	278.4	275.8	279.4	291.8	82.6	51.5
25	194	M		239.0	246.3	249.2	258.7	262.6	266.4	273.7	282.8	282.2	292.4	301.9	85.5	62.9
25	195	M		251.2	256.5	257.2	267.1	278.5	283.8	286.1	295.5	297.9	306.7	319.1	90.3	67.9
25	196	M		261.0	265.3	271.6	278.2	287.6	293.1	299.8	306.4	311.6	320.9	322.8	91.4	61.8
25	197	M		273.1	285.2	299.1	306.6	316.5	323.9	339.4	339.6	345.6	352.4	359.4	101.8	86.3
25	198	M		288.5	292.6	306.1	309.2	305.9	318.6	326.4	330.4	340.6	344.0	356.7	101.0	68.2
25	199	M		305.1	311.0	322.5	334.3	342.8	354.8	360.4	366.7	379.1	389.4	399.0	113.0	93.9
25	200	M		313.4	314.6	328.7	341.2	348.9	352.2	362.3	362.2	374.4	377.8	386.9	109.5	73.5
			Mean	**271.5**	**276.2**	**285.4**	**293.9**	**301.0**	**307.1**	**315.2**	**320.3**	**325.9**	**332.9**	**342.2**	**96.9**	**70.8**
			St. dev.	**28.6**	**28.9**	**32.8**	**33.6**	**33.2**	**35.8**	**36.9**	**34.5**	**40.0**	**39.7**	**39.3**	**11.1**	**13.7**
			Count	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**

Group No.:	Animal No.	Sex	Treatment/Dose Level	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	Body Weight (g)	% of Control	Body Weight Gain (g)
26	201	M	Flutamide (3 mg/kg) & Testosterone Propionate (0.4 mg/kg)	236.9	242.2	249.5	259.0	263.5	266.9	273.9	282.3	281.5	287.6	293.4	83.1	56.5
26	202	M		238.8	242.6	250.2	258.6	268.4	272.3	281.4	287.9	289.1	298.1	303.2	85.8	64.4
26	203	M		257.3	257.0	266.3	276.6	288.7	290.1	298.4	305.7	308.7	319.3	330.3	93.5	73.0
26	204	M		258.6	258.3	268.0	271.4	279.5	282.3	287.5	292.2	295.9	301.6	306.4	86.7	47.8
26	205	M		278.2	284.0	296.9	302.2	305.7	315.1	322.3	330.6	337.2	345.3	354.8	100.5	76.6
26	206	M		276.1	280.3	295.7	297.4	301.8	312.4	319.3	324.4	331.8	335.1	343.0	97.1	66.9
26	207	M		300.4	307.5	315.0	321.8	328.9	338.7	343.4	351.5	359.7	365.8	373.1	105.6	72.7
26	208	M		299.0	301.6	312.2	321.2	331.2	341.9	346.7	359.6	367.4	374.8	379.9	107.6	80.9
			Mean	**268.2**	**271.7**	**281.7**	**288.5**	**296.0**	**302.5**	**309.1**	**316.8**	**321.4**	**328.5**	**335.5**	**95.0**	**67.4**
			St. dev.	**24.5**	**25.4**	**26.5**	**25.8**	**25.6**	**28.9**	**27.9**	**29.4**	**32.5**	**32.2**	**32.7**	**9.3**	**10.9**
			Count	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**

Appendix VI:

Tissue Weight Data

Group No.:	Animal No.:	Sex	Treatment/Dose Level	Glans Penis Weight (g)	Ventral Prostate Weight (g)	Seminal Vesicle Weight (g)	Cowper's Gland Weight (g)	LABC Weight (g)
1	01	M	Corn Oil Control	0.0495	0.0154	0.0320	0.0042	0.1558
1	02	M		0.0499	0.0198	0.0253	0.0039	0.1653
1	03	M		0.0556	0.0197	0.0392	0.0077	0.1194
1	04	M		0.0529	0.0138	0.0340	0.0051	0.1135
1	05*	M						
1	06	M		0.0407	0.0146	0.0254	0.0072	0.1358
1	07	M		0.0422	0.0162	0.0271	0.0053	0.1718
1	08	M		0.0411	0.0114	0.0344	0.0047	0.0725
			Mean	**0.0474**	**0.0158**	**0.0311**	**0.0054**	**0.1334**
			St. dev.	**0.0061**	**0.0031**	**0.0053**	**0.0015**	**0.0349**
			CV	**12.7643**	**19.3380**	**17.0297**	**26.8321**	**26.1400**

*Found dead due to dosing error

Group No.:	Animal No.:	Sex	Treatment/Dose Level	Glans Penis Weight (g)	Ventral Prostate Weight (g)	Seminal Vesicle Weight (g)	Cowper's Gland Weight (g)	LABC Weight (g)
2	09	M	Oxybenzone (320 mg/kg)	0.0584	0.0183	0.0474	0.0087	0.1656
2	10	M		0.0501	0.0133	0.0313	0.0045	0.1298
2	11	M		0.0633	0.0130	0.0523	0.0099	0.1340
2	12	M		0.0522	0.0180	0.0316	0.0043	0.1459
2	13	M		0.0521	0.0149	0.0484	0.0041	0.1265
2	14	M		0.0464	0.0155	0.0362	0.0036	0.1371
2	15	M		0.0566	0.0185	0.0374	0.0033	0.0975
2	16	M		0.0399	0.0102	0.0286	0.0028	0.1307
			Mean	**0.0524**	**0.0152**	**0.0392**	**0.0052**	**0.1334**
			St. dev.	**0.0073**	**0.0030**	**0.0090**	**0.0026**	**0.0191**
			CV	**13.8834**	**19.5586**	**23.0136**	**51.2478**	**14.3476**

Group No.:	Animal No.:	Sex	Treatment/Dose Level	Glans Penis Weight (g)	Ventral Prostate Weight (g)	Seminal Vesicle Weight (g)	Cowper's Gland Weight (g)	LABC Weight (g)
3	17	M	Oxybenzone (1000 mg/kg)	0.0518	0.0147	0.0273	0.0050	0.1338
3	18	M		0.0505	0.0161	0.0338	0.0042	0.1512
3	19	M		0.0559	0.0154	0.0534	0.0089	0.1293
3	20	M		0.0565	0.0121	0.0374	0.0051	0.1521
3	21	M		0.0475	0.0156	0.0252	0.0041	0.1333
3	22	M		0.0533	0.0121	0.0267	0.0037	0.1077
3	23	M		0.0498	0.0135	0.0387	0.0048	0.0523
3	24	M		0.0403	0.0126	0.0266	0.0046	0.1276
			Mean	**0.0507**	**0.0140**	**0.0336**	**0.0051**	**0.1234**
			St. dev.	**0.0052**	**0.0016**	**0.0096**	**0.0016**	**0.0320**
			CV	**10.2190**	**11.7105**	**28.4123**	**32.2266**	**25.9091**

Group No.:	Animal No.:	Sex	Treatment/Dose Level	Glans Penis Weight (g)	Ventral Prostate Weight (g)	Seminal Vesicle Weight (g)	Cowper's Gland Weight (g)	LABC Weight (g)
4	25	M	Octyl Methoxycinnamate (320 mg/kg)	0.0483	0.0206	0.0328	0.0069	0.1770
4	26	M		0.0541	0.0177	0.0436	0.0053	0.1304
4	27	M		0.0511	0.0153	0.0296	0.0057	0.1424
4	28	M		0.0570	0.0134	0.0401	0.0040	0.1515
4	29	M		0.0457	0.0173	0.0342	0.0049	0.1475
4	30	M		0.0417	0.0136	0.0350	0.0049	0.1743
4	31	M		0.0582	0.0148	0.0354	0.0023	0.1387
4	32	M		0.0390	0.0161	0.0224	0.0027	0.0843
			Mean	**0.0494**	**0.0161**	**0.0341**	**0.0046**	**0.1433**
			St. dev.	**0.0070**	**0.0024**	**0.0064**	**0.0015**	**0.0289**
			CV	**14.1639**	**14.8698**	**18.7758**	**33.3947**	**20.1805**

Group No.:	Animal No.:	Sex	Treatment/Dose Level	Glans Penis Weight (g)	Ventral Prostate Weight (g)	Seminal Vesicle Weight (g)	Cowper's Gland Weight (g)	LABC Weight (g)
5	33	M	Octyl Methoxycinnamate (1000 mg/kg)	0.0527	0.0187	0.0332	0.0054	0.1223
5	34	M		0.0585	0.0204	0.0260	0.0061	0.1636
5	35	M		0.0553	0.0122	0.0391	0.0083	0.1602
5	36	M		0.0463	0.0126	0.0293	0.0086	0.0968
5	37	M		0.0461	0.0157	0.0340	0.0053	0.1332
5	38	M		0.0482	0.0153	0.0497	0.0041	0.1330
5	39	M		0.0409	0.0147	0.0277	0.0035	0.0928
5	40	M		0.0549	0.0154	0.0324	0.0036	0.1309
			Mean	**0.0504**	**0.0156**	**0.0339**	**0.0056**	**0.1291**
			St. dev.	**0.0059**	**0.0028**	**0.0076**	**0.0020**	**0.0256**
			CV	**11.7599**	**17.8012**	**22.3223**	**35.2050**	**19.8564**

Group No.:	Animal No.:	Sex	Treatment/Dose Level	Glans Penis Weight (g)	Ventral Prostate Weight (g)	Seminal Vesicle Weight (g)	Cowper's Gland Weight (g)	LABC Weight (g)
6	41	M	Corn Oil (0 mg/kg) & Testosterone Propionate (0.4 mg/kg)	0.0921	0.1861	0.5094	0.0401	0.3935
6	42	M		0.0907	0.1276	0.4481	0.0384	0.4146
6	43	M		0.0977	0.1546	0.6165	0.0414	0.4372
6	44	M		0.0951	0.1394	0.4637	0.0358	0.3644
6	45	M		0.0961	0.2056	0.5741	0.0406	0.4296
6	46	M		0.0827	0.1574	0.5620	0.0307	0.3140
6	47	M		0.0898	0.2129	0.5543	0.0352	0.3044
6	48	M		0.0974	0.3061	0.6115	0.0496	0.4179
			Mean	**0.0927**	**0.1862**	**0.5425**	**0.0390**	**0.3845**
			St. dev.	**0.0050**	**0.0572**	**0.0632**	**0.0056**	**0.0517**
			CV	**5.4272**	**30.7274**	**11.6533**	**14.2464**	**13.4456**

Group No.:	Animal No.:	Sex	Treatment/Dose Level	Glans Penis Weight (g)	Ventral Prostate Weight (g)	Seminal Vesicle Weight (g)	Cowper's Gland Weight (g)	LABC Weight (g)
7	49	M	Oxybenzone (100 mg/kg) & Testosterone Propionate (0.4 mg/kg)	0.0951	0.2081	0.6164	0.0479	0.4551
7	50	M		0.0902	0.1273	0.6275	0.0418	0.4220
7	51	M		0.0929	0.2071	0.6449	0.0328	0.4493
7	52	M		0.0919	0.1762	0.5696	0.0315	0.4035
7	53	M		0.1010	0.2440	0.4964	0.0391	0.4594
7	54	M		0.0959	0.2342	0.5894	0.0371	0.3540
7	55	M		0.1041	0.2149	0.5514	0.0384	0.4490
7	56	M		0.0935	0.2377	0.6620	0.0360	0.3637
			Mean	**0.0956**	**0.2062**	**0.5947**	**0.0381**	**0.4195**
			St. dev.	**0.0047**	**0.0386**	**0.0545**	**0.0052**	**0.0419**
			CV	**4.9440**	**18.7035**	**9.1643**	**13.6065**	**9.9859**

Group No.:	Animal No.:	Sex	Treatment/Dose Level	Glans Penis Weight (g)	Ventral Prostate Weight (g)	Seminal Vesicle Weight (g)	Cowper's Gland Weight (g)	LABC Weight (g)
8	57	M	Oxybenzone (320 mg/kg) & Testosterone Propionate (0.4 mg/kg)	0.0866	0.1828	0.6794	0.0371	0.4856
8	58	M		0.0960	0.2099	0.6936	0.0445	0.4923
8	59	M		0.0946	0.1564	0.5435	0.0375	0.4598
8	60	M		0.0893	0.1752	0.6303	0.0339	0.4615
8	61	M		0.0982	0.2268	0.7721	0.0420	0.4184
8	62	M		0.0923	0.2044	0.4861	0.0296	0.3487
8	63	M		0.0946	0.2482	0.5184	0.0426	0.3941
8	64	M		0.1002	0.1627	0.6273	0.0302	0.3636
			Mean	**0.0940**	**0.1958**	**0.6188**	**0.0372**	**0.4280**
			St. dev.	**0.0045**	**0.0321**	**0.0973**	**0.0056**	**0.0551**
			CV	**4.7679**	**16.4034**	**15.7303**	**15.1908**	**12.8771**

Group No.:	Animal No.:	Sex	Treatment/Dose Level	Glans Penis Weight (g)	Ventral Prostate Weight (g)	Seminal Vesicle Weight (g)	Cowper's Gland Weight (g)	LABC Weight (g)
9	65	M	Oxybenzone (1000 mg/kg) & Testosterone Propionate (0.4 mg/kg)	0.0826	0.1416	0.4757	0.0381	0.4103
9	66	M		0.0871	0.1632	0.4990	0.0388	0.3472
9	67	M		0.0824	0.1392	0.4526	0.0489	0.4159
9	68	M		0.0922	0.1609	0.5839	0.0208	0.4363
9	69	M		0.0931	0.1593	0.5054	0.0509	0.4141
9	70	M		0.0874	0.1315	0.5161	0.0347	0.3115
9	71	M		0.0876	0.1995	0.5335	0.0291	0.3820
9	72	M		0.0877	0.1449	0.4861	0.0374	0.3862
			Mean	**0.0875**	**0.1550**	**0.5065**	**0.0373**	**0.3879**
			St. dev.	**0.0038**	**0.0213**	**0.0399**	**0.0098**	**0.0411**
			CV	**4.3979**	**13.7590**	**7.8753**	**26.1763**	**10.6041**

Group No.:	Animal No.:	Sex	Treatment/Dose Level	Glans Penis Weight (g)	Ventral Prostate Weight (g)	Seminal Vesicle Weight (g)	Cowper's Gland Weight (g)	LABC Weight (g)
10	73	M	Octyl Methoxycinnamate (100 mg/kg) & Testosterone Propionate (0.4 mg/kg)	0.1097	0.1677	0.5614	0.0423	0.5009
10	74	M		0.0954	0.2032	0.5528	0.0403	0.4080
10	75	M		0.0969	0.1389	0.4748	0.0405	0.4458
10	76	M		0.0927	0.1817	0.6184	0.0324	0.3626
10	77	M		0.0961	0.1708	0.5678	0.0442	0.4505
10	78	M		0.0937	0.2435	0.6439	0.0429	0.3925
10	79	M		0.0812	0.1081	0.4394	0.0289	0.3916
10	80	M		0.0919	0.2452	0.6401	0.0439	0.3755
			Mean	**0.0947**	**0.1824**	**0.5623**	**0.0394**	**0.4159**
			St. dev.	**0.0078**	**0.0476**	**0.0744**	**0.0057**	**0.0463**
			CV	**8.2510**	**26.1092**	**13.2296**	**14.3873**	**11.1258**

Group No.:	Animal No.:	Sex	Treatment/Dose Level	Glans Penis Weight (g)	Ventral Prostate Weight (g)	Seminal Vesicle Weight (g)	Cowper's Gland Weight (g)	LABC Weight (g)
11	81	M	Octyl Methoxycinnamate (320 mg/kg) & Testosterone Propionate (0.4 mg/kg)	0.0950	0.1701	0.6642	0.0493	0.4894
11	82	M		0.0928	0.1400	0.5365	0.0381	0.4123
11	83	M		0.0928	0.1532	0.4588	0.0268	0.3888
11	84[#]	M						
11	85	M		0.0998	0.2700	0.6259	0.0334	0.3860
11	86[^]	M						
11	87	M		0.0963	0.1549	0.6345	0.0328	0.3867
11	88	M		0.0907	0.1730	0.7405	0.0398	0.4513
			Mean	**0.0946**	**0.1769**	**0.6101**	**0.0367**	**0.4191**
			St. dev.	**0.0032**	**0.0472**	**0.0991**	**0.0077**	**0.0426**
			CV	**3.4027**	**26.6834**	**16.2409**	**20.9097**	**10.1733**

[#]Moribund sacrifice due to dosing error

[^]Humane sacrifice due to dosing error

Group No.:	Animal No.:	Sex	Treatment/Dose Level	Glans Penis Weight (g)	Ventral Prostate Weight (g)	Seminal Vesicle Weight (g)	Cowper's Gland Weight (g)	LABC Weight (g)
12	89	M	Octyl Methoxycinnamate (1000 mg/kg) & Testosterone Propionate (0.4 mg/kg)	0.0904	0.1454	0.5463	0.0330	0.3725
12	90	M		0.0878	0.1090	0.3165	0.0235	0.3039
12	91	M		0.0976	0.1248	0.5352	0.0384	0.4484
12	92	M		0.0853	0.1777	0.4306	0.0340	0.3553
12	93	M		0.0935	0.2245	0.5272	0.0297	0.3899
12	94	M		0.0881	0.1472	0.4708	0.0386	0.3357
12	95	M		0.0904	0.1008	0.5026	0.0293	0.3053
12	96	M		0.0999	0.1512	0.3946	0.0301	0.3639
			Mean	**0.0916**	**0.1476**	**0.4655**	**0.0321**	**0.3594**
			St. dev.	**0.0050**	**0.0397**	**0.0802**	**0.0050**	**0.0473**
			CV	**5.4998**	**26.9077**	**17.2335**	**15.7178**	**13.1486**

Group No.:	Animal No.:	Sex	Treatment/Dose Level	Glans Penis Weight (g)	Ventral Prostate Weight (g)	Seminal Vesicle Weight (g)	Cowper's Gland Weight (g)	LABC Weight (g)
13	97	M	Flutamide (3 mg/kg) & Testosterone Propionate (0.4 mg/kg)	0.0583	0.0440	0.0642	0.0199	0.1966
13	98	M		0.0710	0.0480	0.0626	0.0130	0.1969
13	99	M		0.0600	0.0311	0.0302	0.0080	0.1871
13	100	M		0.0616	0.0352	0.0492	0.0114	0.1738
13	101	M		0.0612	0.0278	0.0533	0.0080	0.1468
13	102	M		0.0620	0.0278	0.0592	0.0137	0.1628
13	103	M		0.0627	0.0419	0.0597	0.0097	0.1624
13	104	M		0.0631	0.0399	0.0898	0.0140	0.2273
			Mean	**0.0625**	**0.0370**	**0.0585**	**0.0122**	**0.1817**
			St. dev.	**0.0038**	**0.0077**	**0.0167**	**0.0039**	**0.0256**
			CV	**6.0271**	**20.6987**	**28.4844**	**32.1018**	**14.0639**

Group No.:	Animal No.:	Sex	Treatment/Dose Level	Glans Penis Weight (g)	Ventral Prostate Weight (g)	Seminal Vesicle Weight (g)	Cowper's Gland Weight (g)	LABC Weight (g)
14	105	M	Corn Oil Control	0.0365	0.0091	0.0199	0.0028	0.0993
14	106	M		0.0559	0.0192	0.0442	0.0067	0.1520
14	107	M		0.0629	0.0196	0.0435	0.0060	0.1805
14	108	M		0.0614	0.0142	0.0664	0.0063	0.1893
14	109	M		0.0524	0.0162	0.0439	0.0081	0.1674
14	110	M		0.0499	0.0170	0.0567	0.0077	0.1639
14	111	M		0.0481	0.0146	0.0419	0.0065	0.1454
14	112	M		0.0571	0.0228	0.0683	0.0094	0.2330
			Mean	**0.0530**	**0.0166**	**0.0481**	**0.0067**	**0.1664**
			St. dev.	**0.0085**	**0.0041**	**0.0156**	**0.0019**	**0.0384**
			CV	**15.9390**	**25.0159**	**32.4425**	**28.9010**	**23.0781**

Group No.:	Animal No.:	Sex	Treatment/Dose Level	Glans Penis Weight (g)	Ventral Prostate Weight (g)	Seminal Vesicle Weight (g)	Cowper's Gland Weight (g)	LABC Weight (g)
15	113	M	Octylsalate (235 mg/kg)	0.0464	0.0423	0.0328	0.0052	0.1121
15	114	M		0.0540	0.0150	0.0386	0.0042	0.1217
15	115	M		0.0440	0.0170	0.0536	0.0056	0.1615
15	116	M		0.0569	0.0159	0.0448	0.0065	0.1541
15	117	M		0.0567	0.0194	0.0622	0.0072	0.1807
15	118	M		0.0545	0.0224	0.0372	0.0102	0.1125
15	119	M		0.0598	0.0178	0.0568	0.0051	0.1879
15	120	M		0.0571	0.0152	0.0514	0.0086	0.2250
			Mean	**0.0537**	**0.0206**	**0.0472**	**0.0066**	**0.1569**
			St. dev.	**0.0056**	**0.0091**	**0.0104**	**0.0020**	**0.0404**
			CV	**10.3519**	**44.0948**	**22.1286**	**30.5781**	**25.7274**

Group No.:	Animal No.:	Sex	Treatment/Dose Level	Glans Penis Weight (g)	Ventral Prostate Weight (g)	Seminal Vesicle Weight (g)	Cowper's Gland Weight (g)	LABC Weight (g)
16	121	M	Octylsalate (750 mg/kg)	0.0453	0.0157	0.0291	0.0037	0.1186
16	122	M		0.0484	0.0323	0.0180	0.0027	0.1315
16	123	M		0.0494	0.0137	0.0352	0.0090	0.1234
16	124	M		0.0467	0.0200	0.0385	0.0093	0.1258
16	125*	M						
16	126	M		0.0562	0.0161	0.0483	0.0058	0.1684
16	127	M		0.0663	0.0228	0.0596	0.0087	0.1542
16	128*	M						
			Mean	**0.0521**	**0.0201**	**0.0381**	**0.0065**	**0.1370**
			St. dev.	**0.0079**	**0.0068**	**0.0146**	**0.0029**	**0.0198**
			CV	**15.2448**	**33.9229**	**38.1967**	**44.1991**	**14.4573**

*Animal found dead prior to termination

Group No.:	Animal No.:	Sex	Treatment/Dose Level	Glans Penis Weight (g)	Ventral Prostate Weight (g)	Seminal Vesicle Weight (g)	Cowper's Gland Weight (g)	LABC Weight (g)
17	129	M	Octocrylene (320 mg/kg)	0.0456	0.0066	0.0286	0.0047	0.1319
17	130	M		0.0491	0.0135	0.0309	0.0046	0.1291
17	131	M		0.0541	0.0182	0.0476	0.0085	0.1766
17	132	M		0.0453	0.0168	0.0376	0.0048	0.1392
17	133	M		0.0453	0.0152	0.0449	0.0053	0.1456
17	134	M		0.0601	0.0183	0.0570	0.0089	0.1415
17	135	M		0.0591	0.0209	0.0558	0.0070	0.1370
17	136	M		0.0551	0.0135	0.0359	0.0050	0.1759
			Mean	**0.0517**	**0.0154**	**0.0423**	**0.0061**	**0.1471**
			St. dev.	**0.0062**	**0.0044**	**0.0108**	**0.0018**	**0.0187**
			CV	**11.9771**	**28.3671**	**25.4989**	**29.1680**	**12.7252**

Group No.:	Animal No.:	Sex	Treatment/Dose Level	Glans Penis Weight (g)	Ventral Prostate Weight (g)	Seminal Vesicle Weight (g)	Cowper's Gland Weight (g)	LABC Weight (g)
18	137	M	Octocrylene (1000 mg/kg)	0.0488	0.0150	0.0265	0.0090	0.1516
18	138	M		0.0533	0.0235	0.0412	0.0078	0.1309
18	139	M		0.0585	0.0110	0.0472	0.0093	0.1853
18	140	M		0.0615	0.0148	0.0425	0.0065	0.1037
18	141	M		0.0647	0.0215	0.0486	0.0086	0.1749
18	142	M		0.0606	0.0190	0.0451	0.0057	0.1459
18	143	M		0.0539	0.0200	0.0385	0.0065	0.1531
18	144	M		0.0589	0.0192	0.0439	0.0065	0.1681
			Mean	**0.0575**	**0.0180**	**0.0417**	**0.0075**	**0.1517**
			St. dev.	**0.0052**	**0.0041**	**0.0069**	**0.0014**	**0.0259**
			CV	**8.9776**	**22.7303**	**16.6300**	**18.2207**	**17.0977**

Group No.:	Animal No.:	Sex	Treatment/Dose Level	Glans Penis Weight (g)	Ventral Prostate Weight (g)	Seminal Vesicle Weight (g)	Cowper's Gland Weight (g)	LABC Weight (g)
19	145	M	Corn Oil (0 mg/kg) & Testosterone Propionate (0.4 mg/kg)	0.0890	0.1524	0.5243	0.0319	0.4278
19	146	M		0.0754	0.2060	0.5370	0.0475	0.4368
19	147	M		0.0759	0.1455	0.2891	0.0265	0.4397
19	148	M		0.0732	0.5357#	0.1843#	0.0437	0.4250
19	149	M		0.0805	0.1619	0.4706	0.0533	0.5227
19	150	M		0.0905	0.1821	0.7538	0.0477	0.6092
19	151	M		0.0972	0.2132	0.7345	0.0531	0.5508
19	152	M		0.1009	0.3176	0.8437	0.0488	0.5919
			Mean	**0.0853**	**0.1970**	**0.5933**	**0.0441**	**0.5005**
			St. dev.	**0.0106**	**0.0591**	**0.1932**	**0.0098**	**0.0774**
			CV	**12.3835**	**30.0254**	**32.5618**	**22.2199**	**15.4644**

#Data excluded due to possible transcription error

Group No.:	Animal No.:	Sex	Treatment/Dose Level	Glans Penis Weight (g)	Ventral Prostate Weight (g)	Seminal Vesicle Weight (g)	Cowper's Gland Weight (g)	LABC Weight (g)
20	153	M	Octylsalate (75 mg/kg) & Testosterone Propionate (0.4 mg/kg)	0.0783	0.1557	0.4187	0.0329	0.3614
20	154	M		0.0824	0.1234	0.5393	0.0383	0.4656
20	155	M		0.0906	0.1755	0.4922	0.0347	0.4092
20	156	M		0.1121	0.1866	0.5301	0.0447	0.5170
20	157	M		0.1099	0.1728	0.6463	0.0510	0.5513
20	158	M		0.1020	0.1481	0.5670	0.0377	0.4972
20	159	M		0.1032	0.2693	0.6454	0.0502	0.5473
20	160	M		0.1107	0.1773	0.5611	0.0474	0.5716
			Mean	**0.0987**	**0.1761**	**0.5500**	**0.0421**	**0.4901**
			St. dev.	**0.0132**	**0.0427**	**0.0755**	**0.0071**	**0.0738**
			CV	**13.4239**	**24.2717**	**13.7229**	**16.8596**	**15.0623**

Group No.:	Animal No.:	Sex	Treatment/Dose Level	Glans Penis Weight (g)	Ventral Prostate Weight (g)	Seminal Vesicle Weight (g)	Cowper's Gland Weight (g)	LABC Weight (g)
21	161	M	Octylsalate (235 mg/kg) & Testosterone Propionate (0.4 mg/kg)	0.0737	0.5374#	0.1438#	0.0419	0.3784
21	162	M		0.0861	0.1801	0.5318	0.0279	0.4384
21	163	M		0.0938	0.1917	0.6071	0.0453	0.4365
21	164	M		0.0791	0.1573	0.4804	0.0486	0.4545
21	165	M		0.0859	0.1579	0.5483	0.0398	0.4503
21	166	M		0.0866	0.2118	0.7443	0.0467	0.4747
21	167	M		0.1018	0.1470	0.7769	0.0578	0.5839
21	168	M		0.1089	0.2394	0.6407	0.0439	0.5123
			Mean	**0.0895**	**0.1836**	**0.6185**	**0.0440**	**0.4661**
			St. dev.	**0.0116**	**0.0334**	**0.1103**	**0.0085**	**0.0607**
			CV	**12.9279**	**18.1715**	**17.8407**	**19.2490**	**13.0255**

#Data excluded due to possible transcription error

Group No.:	Animal No.:	Sex	Treatment/Dose Level	Glans Penis Weight (g)	Ventral Prostate Weight (g)	Seminal Vesicle Weight (g)	Cowper's Gland Weight (g)	LABC Weight (g)
22	169*	M	Octylsalate (750 mg/kg) & Testosterone Propionate (0.4 mg/kg)					
22	170	M		0.0929	0.1607	0.5556	0.0424	0.3634
22	171	M		0.0925	0.2057	0.4179	0.0374	0.3375
22	172	M		0.0722	0.1460	0.4550	0.0580	0.2759
22	173	M		0.0831	0.1284	0.5780	0.0374	0.3245
22	174	M		0.1044	0.1643	0.6967	0.0544	0.3329
22	175	M		0.0777	0.1041	0.5083	0.0388	0.3094
22	176	M		0.0873	0.1973	0.8847	0.0569	0.4463
			Mean	**0.0872**	**0.1581**	**0.5852**	**0.0465**	**0.3414**
			St. dev.	**0.0107**	**0.0360**	**0.1602**	**0.0095**	**0.0535**
			CV	**12.2904**	**22.7981**	**27.3705**	**20.4999**	**15.6709**

*Animal found dead prior to termination

Group No.:	Animal No.:	Sex	Treatment/Dose Level	Glans Penis Weight (g)	Ventral Prostate Weight (g)	Seminal Vesicle Weight (g)	Cowper's Gland Weight (g)	LABC Weight (g)
23	177	M	Octocrylene (100 mg/kg) & Testosterone Propionate (0.4 mg/kg)	0.0754	0.2482	0.4740	0.0489	0.4318
23	178	M		0.0892	0.1710	0.6055	0.0371	0.4726
23	179	M		0.1019	0.1966	0.7944	0.0408	0.5824
23	180	M		0.0755	0.1543	0.5699	0.0479	0.4745
23	181	M		0.0836	0.1640	0.6418	0.0328	0.5028
23	182	M		0.0855	0.1363	0.5847	0.0441	0.4998
23	183	M		0.1063	0.2504	0.4397	0.0373	0.4920
23	184	M		0.0909	0.2135	0.5618	0.0483	0.5475
			Mean	**0.0885**	**0.1918**	**0.5840**	**0.0422**	**0.5004**
			St. dev.	**0.0112**	**0.0428**	**0.1080**	**0.0061**	**0.0466**
			CV	**12.6369**	**22.2972**	**18.4982**	**14.4178**	**9.3022**

Group No.:	Animal No.:	Sex	Treatment/Dose Level	Glans Penis Weight (g)	Ventral Prostate Weight (g)	Seminal Vesicle Weight (g)	Cowper's Gland Weight (g)	LABC Weight (g)
24	185	M	Octocrylene (320 mg/kg) & Testosterone Propionate (0.4 mg/kg)	0.0744	0.1577	0.5661	0.0411	0.4833
24	186	M		0.0745	0.2321	0.6430	0.0513	0.4779
24	187	M		0.0873	0.2110	0.4735	0.0443	0.4762
24	188	M		0.0985	0.2088	0.6124	0.0492	0.5429
24	189	M		0.0790	0.1340	0.6194	0.0339	0.4614
24	190	M		0.0850	0.2163	0.6776	0.0411	0.5702
24	191	M		0.1048	0.2432	0.8691	0.0546	0.5683
24	192	M		0.1043	0.2464	0.7135	0.0433	0.5907
			Mean	**0.0885**	**0.2062**	**0.6468**	**0.0449**	**0.5214**
			St. dev.	**0.0126**	**0.0403**	**0.1155**	**0.0066**	**0.0519**
			CV	**14.2590**	**19.5317**	**17.8495**	**14.7495**	**9.9487**

Group No.:	Animal No.:	Sex	Treatment/Dose Level	Glans Penis Weight (g)	Ventral Prostate Weight (g)	Seminal Vesicle Weight (g)	Cowper's Gland Weight (g)	LABC Weight (g)
25	193	M	Octocrylene (1000 mg/kg) & Testosterone Propionate (0.4 mg/kg)	0.0967	0.2326	0.7136	0.0375	0.4433
25	194	M		0.0898	0.1290	0.6433	0.0469	0.4441
25	195	M		0.0935	0.1670	0.4511	0.0403	0.3911
25	196	M		0.0894	0.1993	0.7106	0.0382	0.4412
25	197	M		0.0795	0.1048	0.4027	0.0375	0.4425
25	198	M		0.0701	0.1975	0.5356	0.0529	0.4162
25	199	M		0.0899	0.2105	0.6447	0.0514	0.4519
25	200	M		0.1090	0.1671	0.7092	0.0493	0.5183
			Mean	**0.0897**	**0.1760**	**0.6014**	**0.0443**	**0.4436**
			St. dev.	**0.0115**	**0.0428**	**0.1232**	**0.0066**	**0.0362**
			CV	**12.8048**	**24.3356**	**20.4794**	**14.8388**	**8.1566**

Group No.:	Animal No.:	Sex	Treatment/Dose Level	Glans Penis Weight (g)	Ventral Prostate Weight (g)	Seminal Vesicle Weight (g)	Cowper's Gland Weight (g)	LABC Weight (g)
26	201	M	Flutamide (3 mg/kg) & Testosterone Propionate (0.4 mg/kg)	0.0787	0.0381	0.1368	0.0142	0.2119
26	202	M		0.0679	0.0426	0.1016	0.0153	0.2127
26	203	M		0.0595	0.0275	0.0552	0.0085	0.2390
26	204	M		0.0738	0.0235	0.0918	0.0150	0.2427
26	205	M		0.0546	0.0331	0.0762	0.0135	0.1894
26	206	M		0.0625	0.0544	0.0730	0.0138	0.2419
26	207	M		0.0727	0.0573	0.0925	0.0161	0.2396
26	208	M		0.0652	0.0551	0.0915	0.0136	0.2262
			Mean	**0.0669**	**0.0415**	**0.0898**	**0.0138**	**0.2254**
			St. dev.	**0.0080**	**0.0131**	**0.0240**	**0.0023**	**0.0193**
			CV	**11.9886**	**31.6444**	**26.7013**	**16.7971**	**8.5466**

Appendix VII:

Study Protocol

Study Title
The Hershberger Bioassay (OPPTS 890.1400);

Oxybenzone
Octylmethoxycinnamate
Octylsalate
Octocrylene

ILS Project-Study Numbers
N135-232

Performing Laboratory
Integrated Laboratory Systems, Inc.
601 Keystone Park Drive, Suite 100
Durham, NC27713

Sponsor
National Toxicology Program
National Institute of Environmental Health Sciences

ILS Project No.N135 – Study No.:232; The Hershberger Bioassay (OPPTS 890.1400); Oxybenzone, Octylmethoxycinnamate, Octylsalate, Octocrylene

Study Protocol Approval

[redacted] 5/23/11
Date

Chief, Toxicology Branch
National Toxicology Program, NIEHS

Approval received by email, original maintained in study notebook [redacted] 5/23/11
Date

[redacted]
Contract Office Technical Representative
National Toxicology Program, NIEHS

[redacted] 5/23/11
Date

Study Director
Investigative Toxicology Division
Integrated Laboratory Systems, Inc.

[redacted] 5/23/11
Date

Study Toxicologist
Investigative Toxicology Division
Integrated Laboratory Systems, Inc.

TABLE OF CONTENTS

INTRODUCTION

1.1 Background

The Endocrine Disruptor Screening Program (EDSP) reflects a two-tiered approach to implement the statutory testing requirements of FFDCA section 408(p) (21 U.S.C. 346a). EPA will use the data collected under the EDSP, along with other information to determine if a pesticide chemical, or other substances, may pose a risk to human health or the environment due to disruption of the endocrine system.

EDSP Tier I screening assays will be used to identify substances that have the potential to interact with the estrogen, androgen, or thyroid hormone (Test guidelines in the OPPTS 890 series). The determination of the potential of each test substance activity will be made on a weight-of-evidence basis taking into account data from the Tier 1 assays and other scientifically relevant information available. The fact that a substance may interact with a hormone system, however, does not mean that when the substance is used it will cause adverse effects in humans or ecological systems. The Hershberger Bioassay (OPPTS 890.1400) is used as an *in vivo* screening assay for androgen agonists, androgen antagonists, and 5α-reductase inhibitors and is one of four in vivo mammalian assays in the EDSP Tier 1 battery of assays.

1.2 Purpose

The purpose of this assay is to screen four test substances selected by the National Toxicology Program for androgen agonist/antagonist activity and 5α-reductase inhibition properties using a castrated rat model (OPPTS 890.1400).

1.3 Regulatory Compliance

This study will be conducted in accordance with Good Laboratory Practice regulations as promulgated by the United States Environmental Protection Agency's (U.S. EPA) Good Laboratory Practice (GLP) Regulations (40 CFR Part 160), the Endocrine Disruptor Screening Program Test Guideline OPPTS 890.1400: Hershberger Bioassay (U.S. EPA), OECD Guideline 441 Hershberger Bioassay in Rats: A Short-term Screening Assay for (Anti) Androgenic Properties (adopted 7 September 2009) and ILS SOP's. The study protocol will be reviewed by the ILS Quality Assurance (QA) Unit before final approval by the Sponsor. All changes to the study protocol will be approved by the Sponsor.

Flutamide and testosterone propionate will not be analyzed as stated in 40 CFR 160.105(b) of the U.S. EPA GLP requirements, a positive response in the test system following administration will be evident following statistical analysis of the tissue weights.

A QA inspection of critical phases will be conducted to assure the quality and integrity of the study results and conformance to the study protocol. An audit of the final report will be conducted to determine consistency between reported information and raw data. An appropriate QA statement will be included in the final report.

ILS Project No.N135 – Study No.:232; The Hershberger Bioassay (OPPTS 890.1400); Oxybenzone, Octylmethoxycinnamate, Octylsalate, Octocrylene

1.4 Sponsor

National Institutes of Environmental Health
P.O. Box 12233
Research Triangle Park, NC27709
[redacted]
Contract Office Technical Representative
NTP, NIEHS

NTP Investigator

[redacted]
Telephone No.:
Facsimile No.:
E-mail:

1.5 Testing Facility

Integrated Laboratory Systems, Inc. (ILS)

Shipping Address:	601 Keystone Park Drive, Suite 100 Durham, NC27713
Mailing Address:	P.O. Box 13501 Research Triangle Park, NC27709

Study Director

[redacted]
Telephone No.:
Facsimile No.:
E-mail:

1.6 Study Dates

Animal Arrival Dates:	May 23, 2011, June 6, 2011
Experimental Start Date:	May 30, 2011
Experimental Termination Date:	June 24, 2011

TEST SUBSTANCES, REFERENCE SUBSTANCES, VEHICLE

2.1 Test Substance: 2-Hydroxy-4-Methozybenzophenone (Oxybenzone)

CAS No.	131-57-7
Source:	Ivy Fine Chemicals Corporation
Lot/Batch No.:	20100801
ILS Repository No.:	11-29

ILS Project No.N135 – Study No.:232; The Hershberger Bioassay (OPPTS 890.1400); Oxybenzone, Octylmethoxycinnamate, Octylsalate, Octocrylene

Formula:	$C_{14}H_{12}O_3$
Description:	Light yellow powder
Purity:	99.9%
Expiration Date:	01 August 2012
Storage	
Test Substance:	Room Temperature
Dose Formulation:	Room Temperature
Stability	
Dose Formulation:	Stable in corn oil for 42 days

2.2 Test Substance: 2-Ethylhexyl p-methoxycinnamate (Octylmethoxycinnamate)

CAS No.	5466-77-3
Source:	Acros Organics
Lot/Batch No.:	A0293319
ILS Repository No.:	11-32
Formula:	$C_{18}H_{26}O_3$
Description:	Clear colorless liquid
Purity:	99.8%
Expiration Date:	04 July 2011
Storage	
Test Substance:	Room Temperature
Dose Formulation:	Between 1-10°C, protected from light
Stability	
Dose Formulation:	Stable in corn oil for 42 days

ILS Project No.N135 – Study No.:232; The Hershberger Bioassay (OPPTS 890.1400); Oxybenzone, Octylmethoxycinnamate, Octylsalate, Octocrylene

2.3 Test Substance: Octyl Salicylate (Octylsalate)

CAS No.	118-60-5
Source:	Sigma-Aldrich
Lot/Batch No.:	44698PJ
ILS Repository No.:	11-30
Formula:	$C_{15}H_{22}O_3$
Description:	Colorless liquid
Purity:	99.6%
Storage	
Test Substance:	Room Temperature
Dose Formulation:	Between 1-10°C, protected from light
Stability	
Dose Formulation:	Stable in corn oil for 42 days

2.4 Test Substance: 2-Ethylhexyl 2-Cyano-3,3-Diphenylacrylate (Octocrylene)

CAS No.	6197-30-4
Source:	Sigma-Aldrich
Lot/Batch No.:	01697MJ
ILS Repository No.:	11-31
Formula:	$C_{24}H_{27}NO_2$
Description:	Yellow viscous liquid
Purity:	99.2%
Storage	
Test Substance:	Room Temperature

ILS Project No.N135 – Study No.:232; The Hershberger Bioassay (OPPTS 890.1400); Oxybenzone, Octylmethoxycinnamate, Octylsalate, Octocrylene

Dose Formulation:	Between 1-10°C, protected from light

Stability

Dose Formulation:	Stable in corn oil for 42 days

2.5 Reference Substance: Testosterone Propionate (Androgen agonist)

CAS No.	57-85-2
Source:	Sigma-Aldrich Company (St. Louis, MO)
Lot/Batch No.:	048K1328
ILS Repository No.:	09-26
Formula:	$C_{22}H_{32}O_3$
Description:	White to off-white powder
Purity:	100.2%
Dose Formulation:	Testosterone propionate will be prepared at ILS in corn oil once at a dose level of 0.08 mg/mL and dispensed into vials to be used daily during the study.

Storage:

Reference Substance:	Room temperature, away from light
Dose Formulation:	Between 1-10°C

2.6 Reference Substance: Flutamide (Androgen antagonist)

CAS No.	13311-84-7
Source:	Sigma-Aldrich Company (St. Louis, MO)
Lot/Batch No.:	107K1293
ILS Repository No.:	11-77
Formula:	$C_{11}H_{11}F_3N_2O_3$
Description:	Yellow powder

ILS Project No.N135 – Study No.:232; The Hershberger Bioassay (OPPTS 890.1400); Oxybenzone, Octylmethoxycinnamate, Octylsalate, Octocrylene

Purity:	>99%
Dose Formulation:	Flutamide will be prepared at ILS in corn oil once at a dose level of 0.6 mg/mL and dispensed into vials to be used daily during the study.
Storage:	
Reference Substance:	Room temperature, away from light
Dose Formulation:	Between 1-10°C
Stability:	
Dose Formulation:	Flutamide in corn oil stored between 1-10°C was demonstrated to be stable for 42 days (Graves, 2001).

2.7 Vehicle: Corn Oil

CAS No.:	8001-30-7
Source:	MP Biomedicals, LLC (Solon, OH)
Lot/Batch No.:	7862K
ILS Repository No.:	11-94
Formula:	$C_{27}H_{50}O_6$
Description:	Yellow oil
Storage:	
Vehicle:	Room Temperature

2.8 Archive Samples

A ~1 g sample of the test substances, a ~1 mg sample reference substances (Flutamide Lot 107K1293 and testosterone propionate Lot 048K1328), and 1 mL of the vehicle and dose formulations will be stored at room temperature until acceptance of the final report; after acceptance of the report by the Sponsor archival samples will be discarded.

2.9 Dose Formulation Analysis

Dose formulations will be prepared at ILS and analyzed at Midwest Research Institute and Battelle Memorial Institute in accordance with GLP regulations as promulgated by

ILS Project No.N135 – Study No.:232; The Hershberger Bioassay (OPPTS 890.1400); Oxybenzone, Octylmethoxycinnamate, Octylsalate, Octocrylene

the U.S. EPA GLP Regulations (40 CFR Part 160). Three samples (top, middle, and bottom) of the test substance formulations will be analyzed in duplicate for concentration and homogeneity. Concentration results will be acceptable if the mean concentration is within 10% of the target concentration. Homogeneity results will be acceptable if the coefficient of variation is ≤5%. Samples will be shipped overnight to the following addresses for analysis prior to administration:

Octylmethoxycinnamate:
Midwest Research Institute
[redacted]
Program: NTP Chemistry Support
425 Volker Boulevard
Kansas City, MO 64110-2299

Oxybenzone, Octylsalate and Octocrylene:
Battelle Memorial Institute
[redacted]
TOXBC Test Article Custodian
651 W. Fifth Avenue
Columbus, OH 43201-2693

EXPERIMENTAL DESIGN

One hundred and four castrated male Sprague-Dawley rats will be allocated to one of thirteen designated dose groups. To evaluate the test substance for agonist properties, animals will be administered one of two dose levels, or the vehicle control. To evaluate for antagonist properties animals will be administered one of three dose levels of the test substance and co-administered testosterone propionate (0.4 mg/kg, agonist). A vehicle control group will be administered corn oil and testosterone propionate (0.4 mg/kg) and serve as the positive control for the agonist group and the negative control for the antagonist group. Flutamide will be administered orally to animals that are co-administered with 0.4 mg/kg testosterone propionate and serve as a positive antagonist control. Animals will be dosed for 10 consecutive days via oral gavage (test substances and flutamide) and subcutaneous injection (testosterone propionate) based upon daily body weights. Approximately twenty-four hours following the final dose administration, the animals will be humanely euthanized; the glans penis, ventral prostate, levator ani plus bulbocavernous muscle, Cowper's glands, and seminal vesicles with coagulating gland and fluid will be excised and weights recorded. Changes in androgen dependent tissue weights will be evaluated to determine the ability of the test substances to act as an androgen agonist/antagonist or 5α-reductase inhibitor.

ILS Project No.N135 – Study No.:232; The Hershberger Bioassay (OPPTS 890.1400); Oxybenzone, Octylmethoxycinnamate, Octylsalate, Octocrylene

3.1 Test System

Species:	Rats, *Rattus norvegicus*
Strain:	Sprague-Dawley Crl:CD®(SD) IGS
Source:	Charles River Laboratories International, Inc. (Raleigh, NC)
Number/Sex:	208/Castrated males. Surgical manipulation performed by Charles River Laboratories International, Inc.
Acclimation:	Animals will be allowed to recover from the surgical manipulation for at least five days at Charles River Laboratories International, Inc. The animals will then be acclimated to ILS for at least seven days in the room where the study will occur.
Age at administration:	Postnatal Day (PND) 58/59 (Study 1), 59/60 (Study 2) Note: PND 0 is the day of birth
Weight at administration:	275-425 grams
Identification:	Each animal will be uniquely identified by ear punch prior to the start of the study. Until the animals are ear punched, they will be identified by the temporary numbers located on the animal's cage.
Justification:	Animal model used is in accordance with OPPTS 890.1400: Hershberger Bioassay (U.S. EPA).

3.2 Animal Husbandry

All procedures are in compliance with the Animal Welfare Act Regulations, 9 CFR 1-4 and animals will be handled and treated according to the *Guide for the Care and Use of Laboratory Animals* (ILAR, 1996).

ILS Project No.N135 – Study No.:232; The Hershberger Bioassay (OPPTS 890.1400); Oxybenzone, Octylmethoxycinnamate, Octylsalate, Octocrylene

Housing (pre-allocation):	1 per cage
Housing (post-allocation):	2 per cage
Cage Type:	polycarbonate
Cage Size:	23 cm wide by 44 cm long (1012 cm^2 area) and 21 cm high
Bedding:	Absorbent heat-treated hardwood bedding (Northeastern Bedding Corp., Warrensburg, NY)
Cage Changes:	Twice per week
Diet:	Teklad Global 16% Protein Rodent Diet (Teklad Diets, Madison WI) *ad libitum* Autoclaved Purina 5L79 Rat and Mouse diet *ad libitum* given at Charles River Laboratories International, Inc. prior to shipment. A copy of the diet composition will be included in the raw data.
Analysis:	The manufacturer's analytical results will be included in the raw data and reviewed prior to animal arrival to ensure the genistein equivalent content of genistein plus daidzein does not exceed 350 µg/g (Owens et al., 2003).
Archival:	A sample of the diet (~200 g) will be retained and stored between 0 and -30°C until acceptance of the final report.
Water:	Reverse osmosis treated tap water (City of Durham, NC) *ad libitum*
Supplied:	Glass water bottles with stainless steel sipper tube
Analysis:	The results of the current annual comprehensive chemical analyses of water from National Testing Laboratories, Inc. (Cleveland, OH) will be reviewed prior to initiation of the study and will be included in the raw data.
Water Bottle Changes:	Once per week

ILS Project No.N135 – Study No.:232; The Hershberger Bioassay (OPPTS 890.1400); Oxybenzone, Octylmethoxycinnamate, Octylsalate, Octocrylene

Animal Room Conditions:

Temperature:	19-25°C
Humidity	30-70%
Lighting:	12/12 hour light/dark cycle

Enrichment: None

3.3 Allocation

The animals will be assigned to a dose group using a procedure that stratifies animals across groups by body weight such that mean body weight of each group is not statistically different from any other group using analysis of variance (ANOVA) (Statistical Analysis System version 9.1, SAS Institute, Cary, NC). Only clinically healthy animals and animals that have completed preputial separation (PPS) will be used for allocation.

3.4 Group Designation

Study 1

Table 1. Androgen Agonist

Group Number	Animal Identification	Test Substance/Controls	Dose Level (mg/kg/day)
1	01-08	Corn Oil Control	0
2	09-16	Oxybenzone	320
3	17-24	Oxybenzone	1000
4	25-32	Octylmethoxycinnamate	320
5	33-40	Octylmethoxycinnamate	1000

ILS Project No.N135 – Study No.:232; The Hershberger Bioassay (OPPTS 890.1400); Oxybenzone, Octylmethoxycinnamate, Octylsalate, Octocrylene

Table 2. Androgen Antagonist

Group Number	Animal Identification	Test Substance/Controls	Dose Level (mg/kg/day)
6*	41-48	Corn Oil Control + Testosterone Propionate	0 + 0.4
7	49-56	Oxybenzone+ Testosterone Propionate	100 + 0.4
8	57-64	Oxybenzone+ Testosterone Propionate	320 + 0.4
9	65-72	Oxybenzone+ Testosterone Propionate	1000 + 0.4
10	73-80	Octylmethoxycinnamate + Testosterone Propionate	100 + 0.4
11	81-88	Octylmethoxycinnamate + Testosterone Propionate	320 + 0.4
12	89-96	Octylmethoxycinnamate + Testosterone Propionate	1000 + 0.4
13	97-104	Flutamide + Testosterone Propionate	3.0 + 0.4

*Group will serve as the negative control for the androgen antagonist assay.

ILS Project No.N135 – Study No.:232; The Hershberger Bioassay (OPPTS 890.1400); Oxybenzone, Octylmethoxycinnamate, Octylsalate, Octocrylene

Study 2

Table 3. Androgen Agonist

Group Number	Animal Identification	Test Substance/Controls	Dose Level (mg/kg/day)
1	105-112	Corn Oil Control	0
2	113-120	Octylsalate	235
3	121-128	Octylsalate	750
4	129-136	Octocrylene	320
5	137-144	Octocrylene	1000

ILS Project No.N135 – Study No.:232; The Hershberger Bioassay (OPPTS 890.1400); Oxybenzone, Octylmethoxycinnamate, Octylsalate, Octocrylene

Table 4. Androgen Antagonist

Group Number	Animal Identification	Test Substance/Controls	Dose Level (mg/kg/day)
6*	145-152	Corn Oil Control + Testosterone Propionate	0 + 0.4
7	153-160	Octylsalate+ Testosterone Propionate	75 + 0.4
8	161-168	Octylsalate+ Testosterone Propionate	235 + 0.4
9	169-176	Octylsalate+ Testosterone Propionate	750 + 0.4
10	177-184	Octocrylene+ Testosterone Propionate	100 + 0.4
11	185-192	Octocrylene+ Testosterone Propionate	320 + 0.4
12	193-200	Octocrylene+ Testosterone Propionate	1000 + 0.4
13	201-208	Flutamide + Testosterone Propionate	3.0 + 0.4

*Group will serve as the negative control for the androgen antagonist assay.

3.5 Dose Administration

The test substances, flutamide dose formulations, and the vehicle control dose formulations will be administered by oral gavage at a dosing volume of 5 mL/kg body weight. Testosterone propionate dose formulations will be administered by subcutaneous injection into the dorsoscapular region at a dosing volume of 0.5 mL/kg body weight. In co-administered animals, oral gavage will precede subcutaneous injections.

The dose formulations will be administered on a staggered start for 10 consecutive days in Study 1 (PND 58/59 through PND 67/68). The first four animals from each group will be dosed beginning on PND 58, and the second four animals from each group will begin on PND 59. The dose formulations will be administered on a staggered start for 10

consecutive days in Study 2 (PND 59/60 through PND 68/69). The first four animals from each group will be dosed beginning on PND 59, and the second four animals from each group will begin on PND 60. In both studies, dosing will occur 24 hours (± 2 hours) from the previous dose. Dose volume will be determined on individual animal daily body weight. The dosing sequence will be stratified across dosing groups; one animal from each group and then repeated until all animals are dosed.

3.5.1 Justification of Route of Administration

Selection of the route of administration is in accordance with OPPTS 890.1400: Hershberger Bioassay (U.S. EPA, 2009).

3.5.2 Justification of Dose Levels

Selection of the dose levels for each test article was based on the LD_{50} and OPPTS 890.1400 guidelines which specifies to "select doses that ensure animal survival and that are without significant toxicity or distress to the animals after ten consecutive days of chemical administration…". The guideline further specifies that "In general, the highest dose should not cause a reduction in the final body weight of the animals greater than 10% of control weight." Octylsalate dose was selected based upon data obtained from a uterotrophic study performed by ILS where body weight loss of ~10% was observed after 3 consecutive days of dosing. All other test articles showed <5% body weight loss after 3 days of dosing.

3.5.3 Disposal of Dose Formulations

Dose formulations will be disposed of as hazardous material following dosing each day.

3.6 In-Life Animal Observations

Mortality/Moribundity:	Twice daily on weekdays, once daily on weekends/holidays
Clinical Observations:	Observed within 2 days of arrival, again for allocation of animals to study groups, daily prior to dose administration, and prior to euthanasia. If adverse clinical signs are seen additional observations may be recorded.
Body Weights:	Collected within 2 days of arrival, again for allocation of animals to study groups, daily prior to dose administration, and prior to euthanasia.

3.7 Termination

Moribunds/Unscheduled:	Tissue collection will not be performed on accidental deaths, moribund, or animals found dead during the acclimation period.

ILS Project No.N135 – Study No.:232; The Hershberger Bioassay (OPPTS 890.1400); Oxybenzone, Octylmethoxycinnamate, Octylsalate, Octocrylene

	Beginning on the first day of dose administration, any animals found moribund or dead will be necropsied under the supervision of a pathologist and cause of death will be determined and recorded if possible. Moribund animals will be euthanized by carbon dioxide (CO_2) inhalation and death confirmed by cervical dislocation.
Scheduled:	Twenty four hours (± 2 hours) after the final dose administration, animals will be humanely euthanized by CO_2 asphyxiation with death confirmed by cervical dislocation; euthanasia will occur in the same order as they were dosed.
Tissue Collection:	Gross observations of the tissues that are being excised for tissue weights will be recorded.
Tissue Weights:	The following tissues will be excised, trimmed of excess adhering tissue and fat, weighed, and weights recorded to the nearest 0.0001 g. 1. Ventral Prostate 2. Seminal vesicles with coagulating gland with fluid 3. Levator ani plus bulbocavernous muscle complex 4. Cowper's glands (weighed as a pair) 5. Glans penis

3.8 Statistical Analysis

Descriptive statistics (mean, standard deviation, number per group) will be calculated using MS Excel. Final body weight, body weight gain, and tissue weights will be analyzed using Statistical Analysis System version 9.1 (SAS Institute, Cary, NC). Studentized residual plots will be used to detect possible outliers and Levene's test will be used to assess homogeneity of variance. If the data is heterogeneous, then appropriate transformation will be performed and the data will be re-analyzed to assess homogeneity.

Final body weight, body weight gain, and tissue weights will be analyzed using one way analysis of variance. Corn oil plus testosterone propionate will be utilized as the control group for androgen antagonist activity (corn oil control is utilized as control for androgen agonist activity).

3.9 Performance Criteria

The study should be evaluated if 1) three or more of the ten possible individual CV's in the negative control and high dose group exceed the maximum allowable CV's designated for androgenic and anti-androgenic effects listed in Table 5, or 2) if at least two of the target tissues' p values fall between 0.05 and 0.10 when compared to the negative control.

ILS Project No.N135 – Study No.:232; The Hershberger Bioassay (OPPTS 890.1400); Oxybenzone, Octylmethoxycinnamate, Octylsalate, Octocrylene

Table 5. Maximum Coefficients of Variation

Tissue	Androgen Agonist	Androgen Antagonist
Glans Penis	22%	17%
Cowper's Glands	55%	35%
LABC	30%	20%
Ventral Prostate	45%	40%
Seminal Vesicles	40%	40%

Source: U.S. EPA (2009)

REPORT

The report will include all items in the study protocol as well as a comprehensive presentation of all data collected in the study.

RECORD RETENTION

All original data [including the original signed study protocol and all amendments (if any), test substance information, animal receipt records, animal caretaker records, observations, body weight records, clinical observations, etc.] and the original final report will be maintained by ILS for 5 years following finalization of the study report. At that time, sponsor will be contacted for appropriate disposition of study data.

REFERENCES

Institute of Laboratory Animal Resources.(1996). *Guide for the Care and Use of Laboratory Animals.* National Academy Press, Washington, DC.

Owens, W., Ashby, J., Odum, J., and Onyon, L. (2003). The OECD Program to Validate the Rat Uterotrophic Bioassay. Phase 2: Dietary Phytoestrogen Analyses. 111: 1559-1567.

U.S. EPA (Environmental Protection Agency). (2009). Endocrine Disruptor Screening Program Test Guidelines. OPPTS 890.1400: Hershberger Bioassay. EPA 740-C-09-008. Office of Prevention, Pesticides and Toxic Substances, U.S. EPA, Washington, DC.

KEY PERSONNEL

Study Director:
Study Toxicologist:
Toxicology Study Manager:
Animal Facility Operations Manager:
Necropsy Manager:
Facility Veterinarian:
Health and Safety Manager:

Appendix VIII:

Amendments, Deviations, and Notes to File

Integrated Laboratory Systems, Inc.

Protocol Amendment

ILS Project No.-Study No.: N135-232

Protocol Amendment No.: 1

Section Amended: 1.3

Amendment Made: Flutamide will not be analyzed as stated in 40 CFR 160.113 (a) (1).

Reason for Amendment: Incorrect section of 40 CFR 160 was listed.

Section Amended: 3.4

Amendment Made: Group numbers in study 2 are being changed from 1-13 to 14-26.

Reason for Amendment: Group numbers are being amended for clarification purposes so the group numbers in study 1 are different than study 2.

[redacted]

Chief, Toxicology Branch
National Toxicology Program, NIEHS

6/16/11
Date

[redacted]

Contract Office Technical Representative
National Toxicology Program, NIEHS

6/16/11
Date

[redacted]

Study Director
Investigative Toxicology Division
Integrated Laboratory Systems, Inc.

6/16/11
Date

Page 1 of 2

[redacted]
Study Toxicologist
Investigative Toxicology Division
Integrated Laboratory Systems, Inc.

6-20-11
Date

Integrated Laboratory Systems, Inc.

Protocol Amendment

ILS Project No.-Study No.: N135-232

Protocol Amendment No.: 2

Section Amended: 3.8

Amendment Made: SAS Version 9.2 will be used to statistically analyze data as of 20 June 2011.

Reason for Amendment: A new version of SAS was received and installed.

[redacted]

6/28/11
Date

Chief, Toxicology Branch
National Toxicology Program, NIEHS

[redacted]

6/29/11
Date

Contract Office Technical Representative
National Toxicology Program, NIEHS

[redacted]

6/20/11
Date

Study Director
Investigative Toxicology Division
Integrated Laboratory Systems, Inc.

[redacted]

6/20/11
Date

Study Toxicologist
Investigative Toxicology Division
Integrated Laboratory Systems, Inc.

Page 1 of 1

Integrated Laboratory Systems, Inc.

Protocol Amendment

ILS Project No.-Study No.: N135-232

Protocol Amendment No.: 3

Section Amended: 3.8

Amendment Made: Evaluation of all five tissue weights by multivariate analysis will be performed on antagonist assay data.

Reason for Amendment: Statistical analyses suggested by Hershberger Bioassay Guidelines (OPPTS 890.1400) when one of five tissue weights is statistically significant as compared to controls. Sponsor requested analysis when tissue weights are marginally significant (p=0.05-0.10) as compared to controls.

[redacted]
Chief, Toxicology Branch
National Toxicology Program, NIEHS

9/22/11
Date

[redacted]
Contract Office Technical Representative
National Toxicology Program, NIEHS

9/22/11
Date

[redacted]
Study Director
Investigative Toxicology Division
Integrated Laboratory Systems, Inc.

9/30/11
Date

[redacted]
Study Toxicologist
Investigative Toxicology Division
Integrated Laboratory Systems, Inc.

10/5/11
Date

Page 1 of 1

Integrated Laboratory Systems, Inc.

Protocol Amendment

ILS Project No.-Study No.: N135-232

Protocol Amendment No.: 4

Section Amended: Record Retention

Amendment Made: All original data [including the original signed study protocol and all amendments (if any), test substance information, animal receipt records, animal caretaker records, observations, body weight records, clinical observations, etc.] and the original final report will be transferred to the National Toxicology Program Archives following finalization of the study report.
NTP Archives
[redacted]
615 Davis Drive, Suite 300
Durham, NC 27713

Reason for Amendment: Change in disposition of original data.

[redacted]
Chief, Toxicology Branch
National Toxicology Program, NIEHS
1/4/12
Date

[redacted]
Contract Office Technical Representative
National Toxicology Program, NIEHS
1/4/12
Date

[redacted]
Study Director
Investigative Toxicology Division
Integrated Laboratory Systems, Inc.
1/4/12
Date

[redacted]
Study Toxicologist
Investigative Toxicology Division
Integrated Laboratory Systems, Inc.

Page 1 of 1

Integrated Laboratory Systems, Inc.

Protocol Deviation 1

ILS Project No.-Study No.: N135-232

Protocol Section Deviated from:	3.2
Nature of Deviation:	The recorded temperature was out of the specified protocol range 19-25°C on 07-10, and 20-22 June 2011 and and was recorded at either 26 or 27°C at the afternoon room check.
Reason for Deviation:	Due to low outside humidity this time of year and the number of air changes required per hour (between 10 and 15) the temperature was slightly elevated in the afternoon.
Corrective Action:	Mechanical changes to the HVAC system and assessment of software to better understand room temperature changes are under evaluation to correct this problem.
Impact on Study:	Clinical observations and daily mortality/moribundity checks did not show any adverse effects related to the slightly higher temperature reading.
Protocol Section Deviated from:	3.5
Nature of Deviation:	The following animal was not dosed in a group stratified sequence per the study protocol.

Animal ID	Date
18	31 May 2011

Reason for Deviation:	It appears to be incorrect recording of the actual time dosed.
Corrective Action:	Staff was verbally reminded to accurately document the dosing form.
Impact on Study:	None. Dosing out of sequence does not impact the outcome of the study. Each animal was administered the correct dose volume.

Protocol Section Deviated from:	3.5
Nature of Deviation:	The actual time dosed for animal number 100 in dose group 13 (positive control) was not recorded on 30 May 2011.
Reason for Deviation:	Technician oversight.
Corrective Action:	Staff was verbally reminded to accurately document the dosing form with the correct time of dose administration.
Impact on Study:	None. The animal responded appropriately to the administration of Flutamide and Testosterone Propionate at the time of necropsy.

[redacted]

7/27/11
Date

Study Director
Investigative Toxicology Division
Integrated Laboratory Systems, Inc.

Integrated Laboratory Systems, Inc.

Protocol Deviation 2

ILS Project No.-Study No.:	N135-232
Protocol Section Deviated from:	3.7
Nature of Deviation:	Tissues were collected and weighed for animals 05 (found dead) and 86 (humane sacrifice).
Reason for Deviation:	Tissues collected at discretion of study director for informational purposes only.
Corrective Action:	None.
Impact on Study:	None because the tissue weights were not used in statistical analyses or data evaluation.

[redacted]

8-8-11
Date

Study Director
Investigative Toxicology Division
Integrated Laboratory Systems, Inc.

Integrated Laboratory Systems, Inc.

SOP Deviation

ILS Project No.-Study No.:	N135-232
SOP No.-Mod. No. Deviated:	1064-3

SOP Section Deviated:	II, B, 5
Nature of Deviation:	Staff did not list the weight set used on 14 June 2011 to check the accuracy of the top-loading balance.
Reason for Deviation:	Research assistant oversight.
Corrective Action:	Research assistant was reminded to include the weight set used when checking the accuracy of the balance.
Impact on Study:	There is no scientific impact on the study since the balance was checked for accuracy.

[redacted]

7·27·11
Date

Study Director, ILS, Inc.

Integrated Laboratory Systems, Inc.

SOP Deviation

ILS Project No.-Study No.:	N135-232
SOP No.-Mod. No. Deviated:	788-0

SOP Section Deviated:	II, 6
Nature of Deviation:	Prosector did not document appropriate end time for animals 27, 52, or 82.
Reason for Deviation:	Prosector oversight.
Corrective Action:	Prosectors were reminded to include necropsy end time.
Impact on Study:	There is no scientific impact on the study since the start time on these animals were recorded, and the end time on the next animal was recorded and within the study protocol guidelines.

[redacted]

7/20/11
Date

Study Director, ILS, ~~Inc.~~

Integrated Laboratory Systems, Inc.

SOP Deviation

ILS Project No.-Study No.: N135-232

SOP No.-Mod. No. Deviated: 718-10

SOP Section Deviated:	II-A-1
Nature of Deviation:	Supervisor was not notified that temperature was out of range (27°C) on 08 June 2011.
Reason for Deviation:	Oversight by technician that the temperature range for this study is 19-25°C, and not 18-26°C as stated in the ILS SOP.
Corrective Action:	Technician was reminded that the study protocol states the correct temperature range is 19-25°C, and if it is out of range the supervisor must be contacted by the end of the next business day.
Impact on Study:	Clinical observations and daily mortality/moribundity checks did not show any adverse effects related to the slightly higher temperature reading.

[redacted] 7-26-11

Study Director, ILS, Inc. Date

Integrated Laboratory Systems, Inc.

SOP Deviation

ILS Project No.-Study No.:	N135-232
SOP No.-Mod. No. Deviated:	722-13

SOP Section Deviated:	II, H
Nature of Deviation:	Staff did not initial the husbandry activities form on 20 June 2011.
Reason for Deviation:	Husbandry oversight.
Corrective Action:	Husbandry staff was reminded to include initials and date.
Impact on Study:	There is no scientific impact on the study since the changes were made and documented.

[redacted]

Study Director, ILS, Inc.

7/26/11

Date

Integrated Laboratory Systems, Inc.

Note to File

ILS Project No.-Study No.: N135-232

Note to File: 1

This study was conducted in blocks as study 1 and study 2. The animals for study 1 arrived on 23 May 2011 and were housed in room 419. Animals for study 2 arrived on 06 June 2011 and were housed in room 402. They were housed in different rooms throughout the assay and therefore have separate study related forms (i.e. daily room monitoring, animal husbandry, feed use forms, etc.) from these days.

[redacted]

8-8-11

Date

Study Director, ILS, Inc.