Product Safety Labs

CA5712

CA5712 - Acute Oral Toxicity - Up-And-Down Procedure in Rats

Final Report

DATA REQUIREMENT(S): OECD 425 (2008)
EPA 870.1100 (2002)

AUTHOR(S): Jennifer Durando, BS

COMPLETION DATE: June 12, 2018

PERFORMING LABORATORY: Product Safety Labs
2394 US Highway 130
Dayton, NJ 08810 USA

LABORATORY PROJECT ID: Report Number: 47176
Study Number: 47176
Task Number: TK0257834

SPONSOR(S): Syngenta Crop Protection, LLC
410 Swing Road
Post Office Box 18300
Greensboro, NC 27419-8300 USA

STATEMENT OF DATA CONFIDENTIALITY CLAIMS

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GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT

This study meets the requirements of OECD Principles of GLP (as revised in 1997): ENV/MC/CHEM(98)17, OECD, Paris, 1998; U.S. EPA GLP (FIFRA): 40 CFR Part 160, 1989; Japanese Ministry of Agriculture, Forestry and Fisheries: No. 23-Syouan-5173, 2 February, 2012; and EC Directive 2004/10/EC, Official Journal of the European Union, L50/44, Feb. 20, 2004. Specific information related to the characterization of the test substance as received and tested is the responsibility of the study Sponsor (see Test Substance section).

I, the undersigned, declare that the methods, results and data contained in this report faithfully reflect the procedures used and raw data collected during the study.

Jennifer Durando, BS
Study Director, Product Safety Labs

06/12/2018
Date

Performing Laboratory: Product Safety Labs
2394 US Highway 130
Dayton, NJ 08810 USA

FLAGGING STATEMENT

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QUALITY ASSURANCE STATEMENT

The Product Safety Labs' Quality Assurance Unit has reviewed this final study report to assure the report accurately describes the methods and standard operating procedures, and that the reported results accurately reflect the raw data of the study.

QA activities for this study:

QA Activity	Performed By	Date Conducted	Date Findings Reported To Study Director And Management
Protocol review	A. Adamiec; M. Zakrzewski	Apr 13, 2017[1]; Mar 27, 2018	Apr 13, 2017; Mar 27, 2018
Critical phase inspection: *Sample preparation for Animal #3109*	A. Villagran	Feb 6, 2018	Feb 6, 2018
Raw data audit	M. Zakrzewski	Mar 27, 2018	Mar 27, 2018
Draft report review	M. Zakrzewski	Mar 27, 2018	Mar 27, 2018

Final report reviewed by:

Maryann Zakrzewski
Quality Assurance Auditor
Product Safety Labs

June 12, 2018
Date

[1] PSL's "generic" protocol used for this study was reviewed by the Quality Assurance group on this date.

GENERAL INFORMATION

Contributors

The following contributed to this report in the capacities indicated:

Name	Title
Jennifer Durando, BS	Study Director
William Masinja, MSc	Syngenta Study Monitor
Harry Maselli, ALAT	Primary Scientist
Cynthia Bodnar	Scientist
Stephanie Meade, BS	Scientist
Amber Norton, BS	Scientist
Mark Schooley	Scientist
Katherine Sibley, BS	Scientist
Matthew Sorber, BS	Scientist
Shannon Stevens, BS	Scientist

Study Dates

Study initiation date: December 13, 2017
Experimental start date: January 11, 2018
Experimental termination date: March 14, 2018

Deviations from the Guidelines

None

Amendment to Final Protocol

Protocol Section 10.C. GLP Compliance for JMAFF was updated to:

JMAFF GLP: Japanese Ministry of Agriculture, Forestry and Fisheries: No. 23-Syouan-5173, 2 February, 2012.

Deviations from the Final Protocol

None

Retention of Samples

The test substance is retained for at least 3 months following submission of the final report, unless otherwise specified by the Sponsor. All remaining test substance will be returned to the Sponsor or properly disposed. Records of sample disposition are maintained by Product Safety Labs (PSL).

Other

Information on care of the test system, equipment maintenance and calibration, storage, usage, and disposition of the test substance, and all other records that would demonstrate adherence to the protocol will be maintained. Facility records which are not specific to the subject study will be maintained by the testing facility and archived according to PSL SOP.

The original signed final report and electronic copies (in Microsoft Word and pdf) of the final report, including the signed QA and GLP Compliance pages will be sent to the Sponsor. A copy of the signed report, together with the protocol (P320.UDP SYN) and all raw data generated at PSL, is maintained in the PSL Archives in Notebook No. 47176: pages 1-55. PSL will maintain these records for a period of at least five years. After this time, the Sponsor will be offered the opportunity to take possession of the records or may request continued archiving by PSL.

Any electronic raw data generated will be maintained on-site in accordance with GLP archiving procedures.

Performing laboratory test substance reference number

171123-1H

TABLE OF CONTENTS

1.0 EXECUTIVE SUMMARY

1.1 Study Design

An acute oral toxicity test was conducted with rats to determine the potential for CA5712 to produce toxicity from a single dose via the oral route.

Based on a limit dose of 2000 mg/kg, a Main Test was conducted using a default starting dose level of 175 mg/kg which was administered to one healthy female rat by oral gavage. Following the Up and Down procedure, fourteen additional animals were dosed at levels of 550 or 2000 mg/kg. Females were selected for the test because they are frequently more sensitive to the toxicity of test compounds than males. All animals were observed for mortality, signs of gross toxicity, and behavioral changes at least once daily for 14 days after dosing or until death occurred. Body weights were recorded prior to administration (initial) and again on Day 7 and Day 14 (terminal) following dosing or after death. Necropsies were performed on all animals.

1.2 Results

At 175 mg/kg dose level (1 animal); the animal survived exposure to the test substance, gained body weight, and appeared active and healthy during the study. There were no signs of gross toxicity, adverse clinical effects, or abnormal behavior. No gross abnormalities were noted for this animal when necropsied at the conclusion of the 14-day observation period.

At 550 mg/kg Dose Level (5 animals); all animals survived exposure to the test substance and gained body weight during the study. Following administration, two animals (animal nos. 3106 and 3111) were hypoactive and exhibited irregular respiration. However, the affected animals recovered by Day 1 and, along with the remaining three animals, appeared active and healthy for the remainder of the 14-day observation period. No gross abnormalities were noted for the animals when necropsied at the conclusion of the 14-day observation period.

At 2000 mg/kg Dose Level (9 animals); four animals died within two days of test substance administration (animal nos. 3105, 3107, 3110 and 3113). Prior to death, the animals exhibited irregular respiration, prone posture, reduced fecal volume, and/or ocular discharge. Following administration, the remaining five surviving animals were hypoactive and all animals exhibited irregular respiration, hunched or prone posture, piloerection, ataxia, and/or reduced fecal volume. However, the animals recovered by Day 4 and appeared active and healthy for the remainder of the 14-day observation period, gaining body weight over the course of the study. Gross necropsy of the deceased animals revealed distention of the stomach and intestines and discoloration of the lungs, liver, or stomach. No gross abnormalities were noted for any of the remaining animals when necropsied at the conclusion of the 14-day observation period.

1.3 Conclusion

Under the conditions of this study, the acute oral median lethal dose, LD_{50} of CA5712 is estimated to be 2000 mg/kg of body weight (based on the one dose with a partial response and an assumed sigma of 0.5) in female rats with a 95% PL[1] lower confidence interval of 1328 mg/kg. The upper confidence limit could not be calculated.

2.0 INTRODUCTION

2.1 Purpose

This study was conducted to provide information on potential health hazards from a short-term exposure to CA5712 by the oral route.

2.2 Regulatory Guidelines

The procedures as described in this protocol are based on the most recent version of the following testing guidelines:

- OECD Guidelines for the Testing of Chemicals, Test No. 425 (2008)
- U.S. EPA Health Effects Test Guidelines, OPPTS 870.1100 (2002)

2.3 Test Facility

This study was conducted at Product Safety Labs' test facility at 2394 US Highway 130, Dayton, New Jersey 08810. In the opinion of the Sponsor and the Study Director, this study did not unnecessarily duplicate any previous work.

3.0 MATERIALS AND METHODS

3.1 Test Substance

The test substance was identified as: CA5712
A#: CA5712
Batch ID 201701011

It was received on November 23, 2017, and was further identified with PSL Reference Number 171123-1H. The test substance was stored at room temperature. Documentation of the methods of synthesis, fabrication, or derivation of the test substance is retained by the Sponsor.

Characterization of the test substance was provided to PSL by the Sponsor (see Appendix 1):

[1] PL = Profile-likelihood based confidence interval

Composition: CA5712, 96.3% w/w

Physical Description: Off-white solid

pH: Not available.

Stability: Test substance was expected to be stable for the duration of testing.

Recertification Date: End of June 2019

3.2 Experimental Design

3.2.1 Animals

Species/Strain: Rat/Sprague-Dawley derived, albino.

Number of Animals: 15

Sex: Female, nulliparous and non-pregnant

Age/Body Weight: Young adult (8-12 weeks)/164-200 grams at experimental start.

Source: Received from SAGE® Labs on January 3, 17 and February 14, 2018.

Justification of Test System and Route of Exposure: The rat was the system of choice because, historically, it has been the preferred and most commonly used species for acute oral toxicity tests. The oral route of administration was used because human exposure may occur via this route.

3.2.2 Husbandry

Housing: The animals were singly housed in suspended stainless steel caging, which conforms to the size recommendations in the most recent *Guide for the Care and Use of Laboratory Animals* (Natl. Res. Council, 2011). Enrichment (e.g., toy) was placed in each cage. Litter paper was placed beneath the cage and was changed at least three times per week.

Animal Room Temperature: 19-26ºC. Temperature was above the targeted upper limit for one day during the study.

Animal Room Relative Humidity: 38-62%

Animal Room Air Changes: 12/hour. Airflow measurements are evaluated regularly and the records are kept on file at PSL.

Photoperiod: 12-hour light/dark cycle

Acclimation Period: 6-29 days

3.2.3 Food and feeding

Food: Envigo Teklad Global 16% Protein Rodent Diet® #2016. The diet was available *ad libitum*, except during fasting.

Water: Filtered tap water was supplied *ad libitum*.

Contaminants: There were no known contaminants reasonably expected to be found in the food or water at levels which would have interfered with the results of this study. Analyses of the food and water are conducted regularly and the records are kept on file at PSL.

3.2.4 Identification

Cage: Each cage was identified with a cage card indicating at least the study number and identification and sex of the animal.

Animal: A number was allocated to each rat on receipt and a stainless steel ear tag bearing this number was attached to the rat. This number, together with a sequential animal number assigned to study number 47176, constituted unique identification. Only the sequential animal number is presented in this report.

3.3 Selection of Animals

Prior to each dosing, experimentally naive rats were fasted overnight by removing the feed from their cages. During the fasting period, the rats were examined for health and weighed. Fifteen healthy, naive female rats (not previously tested) were selected for test.

3.4 Preparation of Test Substance

The test substance, as received, was a solid. The test substance was prepared as a w/v mixture in distilled water. Each preparation was mixed well prior to use.

3.4.1 Dose calculations

Individual doses were calculated based on the initial body weights using a constant dose volume of 10 mL/kg. All doses were administered volumetrically at 10 mL/kg.

3.4.2 Dosing

The prepared test substance was administered to the stomach using a stainless steel ball-tipped gavage needle attached to an appropriate syringe. Following administration, each animal was returned to its designated cage. Feed was replaced approximately 3-4 hours after dosing.

Individual animals were dosed as follows:

Main Test

Dosing Sequence	Animal No.	Dose Level (mg/kg)	Short-Term Outcome	Long-Term Outcome
1	3101	175	S	S
2	3102	550	S	S
3	3103	2000	S	S
4	3104	2000	S	S
5	3105	2000	D	D
6	3106	550	S	S
7	3107	2000	D	D
8	3108	550	S	S
9	3109	2000	S	S
10	3110	2000	D	D
11	3111	550	S	S
12	3112	2000	S	S
13	3113	2000	D	D
14	3114	550	S	S
15	3115	2000	S	S

S – Survival D – Death

The test substance was administered in sequence to the animals as described above. The decision to proceed with the next animal was based on the survival of the previous animal following dosing. Dose progressions and stopping criteria were determined using the statistical program described in Section 3.8.

3.5 Cage-Side Observations

The animals were observed for mortality, signs of gross toxicity, and behavioral changes approximately 30 minutes post-dosing, during the first several hours post-dosing and at least once daily thereafter for 14 days after dosing or until death occurred. Observations included gross evaluation of skin and fur, eyes and mucous membranes, respiratory, circulatory, autonomic and central nervous systems, somatomotor activity and behavior pattern. Particular attention was directed to observation of tremors, convulsions, salivation, diarrhea, and coma.

3.6 Body Weights

Individual body weights of the animals were recorded prior to test substance administration (initial) and again on Day 7 and Day 14 (terminal) following dosing or after death.

3.7 Necropsy

Surviving rats were euthanized on Day 14 via CO_2 inhalation. Gross necropsies were performed on all deceased and euthanized animals. Tissues and organs of the thoracic and abdominal cavities were examined.

3.8 Statistical Analysis

Statistical analysis was performed for the calculation of the mean density value for dosing. In addition, the *Acute Oral Toxicity (Guideline 425) Statistical Program* (Westat 2001) was used for all data analyses including: dose progression selections, stopping criteria determinations and/or LD_{50} and confidence limit calculations.

4.0 RESULTS AND DISCUSSION

Individual body weights, doses, and mortalities are presented in Table 1. Individual cage-side and necropsy observations are presented in Tables 2 and 3, respectively. The Certificate of Analysis and PSL's GLP Qualification Letter are presented in Appendices 1 and 2, respectively.

4.1 Clinical Observations

175 mg/kg Dose Level (1 animal)

The animal survived test substance administration. There were no signs of gross toxicity, adverse clinical effects, or abnormal behavior.

550 mg/kg Dose Level (5 animals)

All animals survived exposure to the test substance. Following administration, two animals (animal nos. 3106 and 3111) were hypoactive and exhibited irregular respiration. However, the affected animals recovered by Day 1 and, along with the remaining three animals, appeared active and healthy for the remainder of the 14-day observation period.

2000 mg/kg Dose Level (9 animals)

Four animals (animal nos. 3105, 3107, 3110 and 3113) died within two days of test substance administration. Prior to death, the animals exhibited irregular respiration, prone posture, reduced fecal volume, and/or ocular discharge. Following administration, the remaining five surviving animals were hypoactive and all animals exhibited irregular respiration, hunched or prone posture, piloerection, ataxia, and/or reduced fecal volume. However, the animals

recovered by Day 4 and appeared active and healthy for the remainder of the 14-day observation period.

4.2 Bodyweight

175 mg/kg Dose Level (1 animal)

The animal gained body weight during the study, there were no treatment related changes in the body weights.

550 mg/kg Dose Level (5 animals)

All animals gained body weight during the study, there were no treatment related changes in the body weights.

2000 mg/kg Dose Level (9 animals)

The five surviving animals gained body weight during the study, there were no treatment related changes in the body weights of these animals.

4.3 Necropsy

175 mg/kg Dose Level (1 animal)

No gross abnormalities were noted for the animal when necropsied at the conclusion of the 14-day observation period.

550 mg/kg Dose Level (5 animals)

No gross abnormalities were noted for any of the animals when necropsied at the conclusion of the 14-day observation period.

2000 mg/kg Dose Level (9 animals)

Gross necropsy of the deceased animals revealed distention of the stomach and intestines and discoloration of the lungs, liver, or stomach. No gross abnormalities were noted for any of the remaining animals when necropsied at the conclusion of the 14-day observation period.

5.0 CONCLUSIONS

Under the conditions of this study, the acute oral median lethal dose, LD_{50} of CA5712 is estimated to be 2000 mg/kg of body weight (based on the one dose with a partial response and an assumed sigma of 0.5) in female rats with a 95% PL[1] lower confidence interval of 1328 mg/kg. The upper confidence limit could not be calculated.

[1] PL = Profile-likelihood based confidence interval

6.0 REFERENCES

National Research Council. (2011). *Guide for the Care and Use of Laboratory Animals (8th ed.)*. Washington, DC: The National Academies Press.

TABLES SECTION

TABLE 1 Individual Body Weights, Doses, and Mortalities

Animal No.	Sex	Dose Level (mg/kg)	Body Weight (g)					Dose[1] mL	Mortalities	
			Day 0 Weight	Day 7 Weight	Gain*	Day 14 Weight	Gain*		Day	Weight (g)
3101	F	175	169	201	32	210	41	1.69	E	-
3102	F	550	179	227	48	233	54	1.79	E	-
3106	F		183	219	36	234	51	1.83	E	-
3108	F		199	224	25	233	34	1.99	E	-
3111	F		186	209	23	223	37	1.86	E	-
3114	F		169	198	29	212	43	1.69	E	-
3103	F	2000	179	208	29	236	57	1.79	E	-
3104	F		186	210	24	231	45	1.86	E	-
3105	F		200	-	-	-	-	2.00	1	199
3107	F		179	-	-	-	-	1.79	1	177
3109	F		196	230	34	243	47	1.96	E	-
3110	F		180	-	-	-	-	1.80	2	166
3112	F		200	211	11	242	42	2.00	E	-
3113	F		164	-	-	-	-	1.64	2	159
3115	F		189	227	38	234	45	1.89	E	-

E - Euthanized via CO_2 inhalation after weighing on Day 14
* - Body weight gain from Day 0.
F - Female

[1] The test substance was administered as a w/v suspension in distilled water using a constant dose volume of 10 mL/kg of body weight (constant volume).

TABLE 2 Individual Cage-Side Observations

Animal Number	Animal Sex	Dose Level (mg/kg)	Observation	Day of Observation (x=observation is present)																		
				0(20 mins)	0(26 mins)	0(0.5 hr)	0(3 hrs)	0(3.5 hrs)	1	2	3	4	5	6	7	8	9	10	11	12	13	14
3101	F	175	Active and healthy			x	x		x	x	x	x	x	x	x	x	x	x	x	x	x	x
3102	F	550	Active and healthy			x	x		x	x	x	x	x	x	x	x	x	x	x	x	x	x
3103	F	2000	Irregular respiration	x		x		x														
			Prone	x		x		x														
			Reduced fecal volume						x													
			Active and healthy							x	x	x	x	x	x	x	x	x	x	x	x	x
3104	F	2000	Active and healthy			x				x	x	x	x	x	x	x	x	x	x	x	x	x
			Irregular respiration				x															
			Hypoactivity				x															
			Hunched posture				x															
			Reduced fecal volume						x													
3105	F	2000	Irregular respiration		x	x	x															
			Prone		x	x	x															
			Dead						x													

TABLE 2 Individual Cage-Side Observations (Continued)

Animal Number	Animal Sex	Dose Level (mg/kg)	Observation	Day of Observation (x=observation is present)																
				0(0.5 hr)	0(3 hrs)	0(3.5 hrs)	1	2	3	4	5	6	7	8	9	10	11	12	13	14
3106	F	550	Irregular respiration	x																
			Hypoactivity	x																
			Active and healthy		x		x	x	x	x	x	x	x	x	x	x	x	x	x	x
3107	F	2000	Irregular respiration	x	x															
			Prone	x	x															
			Dead				x													
3108	F	550	Active and healthy	x		x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
3109	F	2000	Irregular respiration	x	x															
			Hypoactivity	x	x															
			Hunched posture		x															
			Reduced fecal volume				x													
			Active and healthy					x	x	x	x	x	x	x	x	x	x	x	x	x

TABLE 2 Individual Cage-Side Observations (Continued)

Animal Number	Animal Sex	Dose Level (mg/kg)	Observation	Day of Observation (x=observation is present)																
				0(0.5 hr)	0(3 hrs)	0(3.5 hrs)	1	2	3	4	5	6	7	8	9	10	11	12	13	14
3110	F	2000	Irregular respiration	x		x	x													
			Prone	x		x	x													
			Reduced fecal volume				x													
			Dead					x												
3111	F	550	Active and healthy	x			x	x	x	x	x	x	x	x	x	x	x	x	x	x
			Irregular respiration		x															
			Hypoactivity		x															
3112	F	2000	Irregular respiration	x	x		x	x	x											
			Prone	x			x													
			Ataxia		x															
			Reduced fecal volume				x	x												
			Hypoactivity					x												
			Active and healthy							x	x	x	x	x	x	x	x	x	x	x

TABLE 2 Individual Cage-Side Observations (Continued)

Animal Number	Animal Sex	Dose Level (mg/kg)	Observation	Color	Location	Day of Observation (x=observation is present)																			
						0(0.5 hr)	0(3 hrs)	0(3.5 hrs)	0(4 hrs)	1	2	3	4	5	6	7	8	9	10	11	12	13	14
3113	F	2000	Irregular respiration			x	x			x													
			Prone			x	x			x													
			Ocular discharge	Clear	Bilateral					x													
			Dead								x												
3114	F	550	Active and healthy			x			x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
3115	F	2000	Active and healthy			x						x	x	x	x	x	x	x	x	x	x	x	x
			Irregular respiration					x		x	x												
			Piloerection					x		x													
			Hypoactivity					x															
			Hunched posture					x															

TABLE 3 Individual Necropsy Observations

Animal Number	Animal Sex	Dose Level (mg/kg)	Organ / Tissue	Grade	Observation	Modifier	Color	Location
3101	F	175	All tissues and organs		No gross abnormalities			
3102	F	550	All tissues and organs		No gross abnormalities			
3103	F	2000	All tissues and organs		No gross abnormalities			
3104	F	2000	All tissues and organs		No gross abnormalities			
3105	F	2000	Stomach	Moderate	Distention			
			Liver		Discoloration	Dark	Red	Around edges
3106	F	550	All tissues and organs		No gross abnormalities			
3107	F	2000	Stomach	Moderate	Distention			
			Intestines	Moderate	Distention			
3108	F	550	All tissues and organs		No gross abnormalities			

TABLE 3 Individual Necropsy Observations (Continued)

Animal Number	Animal Sex	Dose Level (mg/kg)	Organ / Tissue	Grade	Observation	Modifier
3109	F	2000	All tissues and organs		No gross abnormalities	
3110	F	2000	Stomach	Slight	Distention	
3111	F	550	All tissues and organs		No gross abnormalities	
3112	F	2000	All tissues and organs		No gross abnormalities	
3113	F	2000	Stomach	Extreme	Discoloration	Dark
			Intestines	Slight	Distention	
			Lungs	Moderate	Discoloration	Dark
			Liver	Moderate	Discoloration	Pale
3114	F	550	All tissues and organs		No gross abnormalities	
3115	F	2000	All tissues and organs		No gross abnormalities	

APPENDICES SECTION

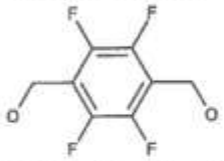
APPENDIX 1 Certificate of Analysis

syngenta

Syngenta Crop Protection AG
GLP Testing Facility WMU
Analytical Development & Product Chemistry
Breitenloh 5
4333 Münchwilen, Switzerland

Certificate of Analysis

CA5712 tech.



201701011 - Purity: 96.3 %

Batch Identification	**201701011**
Other Batch ID	986404
Product Code	**CA5712 tech.**
Other Product Code(s)	CA5712A
ISO Common Name	---
CA Reg. No.	92339-07-6
CA Index Name	2,3,5,6-Tetrafluoro-1,4-benzenedimethanol
IUPAC Name	---
Molecular formula	$C_8 H_6 F_4 O_2$
Molecular mass	210.1
Chemical Analysis	
– **Identity of CA5712***	**confirmed**
– **Content of CA5712***	**96.3 % w/w**
Methodology used for Characterization / Recertification	NMR, GC, Karl Fischer titration
Physical Analysis	
– **Appearance***	**off-white solid**
Stability:	
– **Storage Temperature**	**< 30°C**
– **Recertification Date**	**End of June 2019**

If stored under the conditions given above, this test substance can be considered stable until the recertification date is reached.
This Certificate of Analysis summarizes data which originates either from a single study or from several individual studies. Tests marked with an asterisk (*) have been conducted in compliance with GLP.
Raw data, documentation, study plans, any amendments to study plans and reports pertaining to this/these study/studies are stored under the study number(s) referenced below within the archives of the GLP Testing Facility WMU at Syngenta Crop Protection AG, Switzerland.

Study number of batch characterization: CHMU170333
Study number(s) of batch recertification:

Authorization: 26-Jun-17

Dr. Karine Heintz
Analytical Development & Product Chemistry

APPENDIX 2 GLP Qualification

Product Safety Labs

Good Laboratory Practice Qualification

Product Safety Labs
2394 US Highway 130
Dayton, NJ 08810
USA

Product Safety Labs subscribes to the principles of the Good Laboratory Practice Standards and the respective Quality Systems as defined in the following:

US FDA GLP; 21 CFR Part 58
US EPA FIFRA GLP; 40 CFR Part 160
US EPA TSCA GLP; 40 CFR Part 792

Which are compatible with:
OECD GLP; EC Directive 2004/10/EC
JMAFF GLP; Ref. No.11-Nousan-6283

As a contract research organization, we are mandated to comply with the Good Laboratory Practices (GLP) as contracted by the Sponsor. The United States Food and Drug Administration (FDA) and the United States Environmental Protection Agency (EPA) do not "certify" laboratories as GLP compliant. These agencies conduct periodic inspections to monitor laboratories for compliance with Good Laboratory Practice standards. GLP compliance is study specific and driven by the requirements of individual study protocols, which are approved by the Sponsor, and signed by the Study Director. The GLP Compliance Statement is provided within individual study reports attesting to the regulatory status of the work performed.

Dan Merkel, BS, MBA
President

Rhonda S. Krick, BS
Director, Quality Assurance

Inspectional History			
EPA		FDA	
July	1988	August	2005
January	1990	October	2009
February	1990	August	2013
September	1993	September	2016
January	1995		
July	1997		
September	1997		
October	2000		
July	2001		
March	2005		
January	2007		
January	2011		
August	2014		

Issued: 01/12/2017

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