EFFICACY REVIEW

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Product(s): Woodstream Bromethalin 0.01% Pellet

Date: April 11, 2007

EPA Reg No(s): 47629-RG

DP Bar code(s): D333299

Chemical Code: Bromethalin 112802

Formulation(s): Bromethalin 0.01% in a place pack

Purpose for Review: The purpose for this review is to determine if the Bromethalin place pack is efficacious against Norway rats and house mice and the laboratory data collected are acceptable for registration of the above named product.

MRID No(s):

46943503 Mills, B.G. August 18, 2006. Bromethalin Pellet 0618: Standard Mouse Block/Pellet Laboratory Test 1.210. LiphaTech, Inc. Laboratory Project Identification: 06038. 49pp.

46943504 Mills, B.G. August 18, 2006. Bromethalin Pellet 0618: Standard Norway Rat Block/Pellet Laboratory Test 1:209. LiphaTech, Inc. Laboratory Project Identification: 06037. 54pp.

Good Laboratory Practices: Yes

Branch Chief: Meredith Laws

Team Leader: John Hebert, Product Manager 07

IRB Reviewer: Geraldine R. McCann, Biologist

BACKGROUND: Woodstream, Inc. has applied for a new product registration for their Bromethalin pellets. There are no previous reviews in the jacket to consider. The data matrix mentions two place pack efficacy studies done by LiphaTech to demonstrate the palatability of a Bromadiolone pellet packet [MRID 42906201 (LiphaTech Project number 90158)and MRID 42906202 (LiphaTech Project number 91085). The material has not been documented as the packet material for this product anywhere, but the product manufacturer states the product will be sold as a place pack. The source of the studies (LiphaTech), show the place pack material to be the same in each of the previously mentioned studies and are requesting the information be “bridged” from the Bromadiolone place pack studies to the Bromethalin studies. This review will evaluate the results of the laboratory studies and determine if the data are acceptable.

REVIEW OF DATA:

46943503 Mills, B.G. August 18, 2006. Bromethalin Pellet 0618: Standard Mouse Block/Pellet Laboratory Test 1.210. LiphaTech, Inc. Laboratory Project Identification: 06038. 49pp. [redacted]

The standard OPP rat and mouse challenge diet formulated for this test was Manufactured August 3, 2006 (Lot #21506), and August 14, 2006 (Lot # 22606). The Toxic bait formulated for this test was dyed with the [redacted] and manufactured July 27, 2006 (Lot number 20806), analyzed on July 28, 2006, and August 30, 2006. The analysis of the toxic bait was very close in both instances: 93.32 mg/kg and 93.28 mg/kg.

The bait-exposure phase of the bioassay began on August 7, 2006, to August 9th, 2006, with Control animals being exposed to the OPP Rat and Mouse Challenge diet from August 7 to August 18, 2006. The mice were caged in single-sex groups of 5 mice per group and placed in solid-bottom, all metal cages designed to hold laboratory mice and having a bottom surface area of 2.15 ft^2. Tap water was provided the animals ad libitum via water bottles equipped attached to the front of the cages.

Two groups of 20 animals were used for this test: The test-group males (n=10) weighed 23.4 g to 28.2 g (mean = 25.65 g) at the start of the test, while the females (n=10) weighed 19.9 g to 22.3 g (mean = 20.8 g). The Control group males (n=10) weighed 22.2 g to 27.8 g (mean = 24.69 g) at the start of the test, while the Control group females (n=10) weighed 19.4 g to 21.6 (mean = 20.46 g). There was an average of 4.54 g difference in mean weights between the sexes of all test mice (control and tested groups), all well within the allowable weight range difference between sexes of 5 g. The actual temperature and humidity range were documented for this study between 19.1 C to 24.1 °C and 45.1% and 65.4 % relative humidity for this test. The protocol states the temperature should be between 20-25 °C, and humidity will be 50-55%.

The results for this trial are summarized in the Table below. All test-group males died within 1 to 5 days and the females died within 2 to 11 days of the onset of exposure to toxic bait. The 90% mortality criterion for an efficacy trial was met. No mortalities were reported for the control group.

The information provided by the study is summarized in the table below:

Table 1. Tabulated Data from the LTI# 06038 Standard Mouse Test by B.G. Mills with Bromadiolone (Lot # 20806)

Pretest Weights		Bait Consumption and Mortality		
Sex (n)	**Ave. Wt (g)**	**OPP Diet Cons. (g)**	**Toxic Bait Cons. (g)**	**Total Bait Consumed (g)**
M (10)	25.65	135.7	25.6	161.3

Inert ingredient information may be entitled to confidential treatment

F (10)	20.8		Percent **Toxic Bait** Consumed **15.87%**
Total (20)	Group Difference 4.85	**100% Mortality**	

469749-02 Mills, B.G. August 18, 2006. Bromethalin Pellet 0618: Standard Norway Rat Block/Pellet Laboratory Test 1:209. Liphatech, Inc.. Laboratory Project Identification: 06037. 54pp. [redacted]

The bait for this test was the same as for the previous test: the standard OPP rat and mouse challenge diet formulated for this test was Manufactured August 3, 2006 (Lot #21506), and August 14, 2006 (Lot # 22606). The Toxic bait formulated for this test was dyed with the [redacted] and manufactured July 27, 2006 (Lot number 20806), analyzed on July 28, 2006, and August 30, 2006. The analysis of the toxic bait was very close in both instances: 93.32 mg/kg and 93.28 mg/kg.

The bait-exposure phase of the bioassay began on August 7, 2006, to August 9th, 2006, with Control animals being exposed to the OPP Rat and Mouse Challenge diet from August 7 to August 18, 2006. The Norway rats were caged in single-caged in screen bottom all-metal cages designed to hold laboratory rats and having a bottom surface area of 500 to 2000 cm^2. Tap water was provided the animals ad libitum via water bottles equipped attached to the front of the cages.

Two groups of 20 animals were used for this test: The test-group males (n=10) weighed 251.1 g to 281.2 g (mean = 263.32 g) at the start of the test, while the females (n=10) weighed 206.0 g to 251.0 g (mean = 227.64 g). The Control group males (n=10) weighed 219.1 g to 276.3 g (mean = 258.08 g) at the start of the test, while the Control group females (n=10) weighed 157.0 g to 245.6 (mean = 217.05 g). There was an average of 38.36 g difference in mean weights between the sexes of all test rats (control and tested groups), all well within the allowable weight range difference between sexes of 50 g. The actual temperature and humidity range were documented for this study between and noted in the first study Deviation. Two deviations were noted for this study. The first deviation concerns the temperature and relative humidity: "On page 3 of the protocol (Section 5.1) it is stated that temperature and relative humidity during the study will be between 20 to 25°C, and 50-55% rH, respectively. The actual range was 16.9-25.0°C and 47.3-94.2% relative humidity for the pre-test holding period, and 18.4-23.5°C and 46.8-63.4% relative humidity for the test period. The mean temperature, 20.6°C and 20.1 °C for the pre-test and test periods respectively, was within the range of 20-25°C. The mean relative humidity, 59.3% rH and 53.3% rH for the pre-test and test periods, respectively, was slightly higher than the range of 50-55% rH in the case of the pre-test period and within the range in the case of the test period." The justification stated: "These conditions are what actually occurred in the test room and did not affect the outcome of the study."

The second deviation states: "On page 3 of the protocol (Section 3.1) it is stated that this test will be conducted with a two-day bait exposure period. The test substance was removed from test animal cages after forty-two hours of bait exposure." The justification

stated: "The test substance was removed when the test animals appeared to be moribund and were no longer exhibiting any activity, including the consumption of test substance."

The results for this trial are summarized in the Table below. All test-group rats died within 2 to 3 days of the onset of exposure to toxic bait. The 90% mortality criterion for an efficacy trial was met. No mortalities were reported for the control group.

The information provided by the study is summarized in the table below:

The test results are summarized below:

Table 1. Tabulated Data from the LTI# 06037 Standard Rat Acute Block/Pellet Test by B.G. Mills with Bromadiolone (Lot # 20806)

Pretest Weights		**Bait Consumption and Mortality**		
Sex (n)	**Ave. Wt (g)**	**OPP Diet Cons. (g)**	**Toxic Bait Cons. (g)**	**Total Bait Consumed (g)**
M (10)	263.32	199.3	169.3	368.8
F (10)	227.64	**100% Mortality**	Percent **Toxic Bait** Consumed **45.96%**	
Total (20)	Group Difference 35.68			

Efficacy Comments

1. Please submit all raw data and SOP's when mentioning their use in future studies.

2. The laboratory tests are for loose bait (pellets) and the product is a place pack. Woodstream has established the place pack materials being used for their product are the same as those used in the Bromadiolone studies cited.

3. The efficacy indicates the product may be more suited to rats than to mice for palatability because of the efficacy results 15.87% for mice compared to 45.96% for rats (see tables above). Both tests resulted in 100% mortality within the allotted time frame and are both considered acceptable tests.

Conclusion(s) The Woodstream studies conducted by LiphaTech MRIDs 46943503 and 46943504 are acceptable. The place pack material stated to be used in the LiphaTech studies has been accepted as that material proposed for use with the Bromethalin pelleted product shown to be acceptable in the above named studies.