UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

Office of Chemical Safety and Pollution Prevention

CHILD RESISTANT PACKAGING REVIEW

November 14, 2011

MEMORANDUM

Subject:	Name of Pesticide Products:	LC-2010-1 Fipronil for Cats -1 LC-2010-2 Fipronil for Dogs - 2 LC-2010-3 Fipronil and S-Methoprene for Cats - 3 LC-2010-4 Fipronil and S-Methoprene for Dogs - 4
	Product Type:	Insecticide (flea, tick and lice product)
	EPA Reg. Nos:	86230-1, -2, -3, -4
	DP Barcodes:	D393688, D393696, D393698, D393700
	Decision Nos.:	452790, 452791, 452793, 452794
	MRID:	48570601
	Action Code:	R340
	PC Codes:	129121 Fipronil 105402 S-Methoprene
From:	Breann Hanson, Biologist B Hanson Technical Review Branch (TRB) Registration Division (RD; 7505P)	
Through:	Rosalind Gross, Ph.D. RLG TRB RD; 7505P	
To:	Bonaventure Akinlosotu, RM Team 10 Insecticide Branch RD; 7505P	
Applicant:	LoradoChem Inc.	

FORMULATIONS FROM LABEL:

EPA Reg. No. 86230-1

Active Ingredient:		% by wt
129121	Fipronil	9.7

EPA Reg. No. 86230-2

Active Ingredient:		% by wt
129121	Fipronil	9.7

EPA Reg. No. 86230-3

Active Ingredients:		% by wt
129121	Fipronil	9.8
105402	S-Methoprene	11.8

EPA Reg. No. 86230-4

Active Ingredients:		% by wt
129121	Fipronil	9.8
105402	S-Methoprene	11.8

ACTION REQUESTED: The Risk Manager requests: "For your review: MRID 48570601, CRP data to support amendment "to add a new site to manufacture the 3-pipette size tube". N/B: Same data pkg for [all 4 Laredo products; 86230-1, -2, -3, and -4]. Also submits CSF for review."

BACKGROUND: LoradoChem Inc. (herein the "registrant") has submitted a request to amend their existing registrations for LC-2010-1 Fipronil for Cats, EPA Reg. No.: 86230-1, LC-2010-2 Fipronil for Dogs, EPA Reg. No.: 86230-2, LC-2010-3 Fipronil and S-Methoprene for Cats, EPA Reg. No.: 86230-3, and LC-2010-4 Fipronil and S-Methoprene for Dogs, EPA Reg. No.: 86230-4; the registrant is proposing to add a manufacturing site (Klocke Verpackungs-Service, Weringarten, Germany) for producing the 3-blister packs for all 5 previously approved pipette sizes (0.017 fl. oz for cat products; 0.023, 0.045, 0.91, and 0.136 fl. oz. for dog products). The pipettes are purple for the Fipronil only products, EPA Reg. No. 86230-1 and EPA Reg. No. 86230-2; the pipettes are teal for the for the Fipronil and S-Methoprene products, EPA Reg. No. 86230-3 and EPA Reg. No. 86230-4. The currently registered and previously evaluated pipette colors and sizes were manufactured at Cipla, India.

In a teleconference between the registrant and EPA (date 15/MAR/2011), it was explained to EPA that the new site is manufacturing the products using the same formulations with the same processes previously approved; however, the pipette that contains the finished product will have to change because of a difference in the filling equipment at the additional supplier. The only difference is the material used on the back of the pipettes. EPA requested that additional data on the "new" pipette be submitted, as well as information on the blisters, in order to confirm that there would be no change to CRP.

Included with the data packages was a report (MRID 48570601) compiled by Great Lakes Marketing containing information to achieve approval for the additional site of manufacture with the "new" pipette. As mentioned in a letter to EPA (dated 4/AUG/2011) from the registrant, although "the Master label

shows the product potentially being offered in a 3-pipette, 6-pipette, and single presentation, it is understood that this application only supports the 3-pipette package from this manufacturing location."

In order to confirm that there were no changes to CRP with the "new" pipette, the registrant has submitted two studies; both a senior panel (Study No.: GLM 11234) and child panel (Study No.: GLM 11210) were conducted with the pipette color and size that previously gave the poorest, worst-case results. It was agreed that these two studies would support all the applications in all the sizes currently approved. The studies were completed in the "Self-Certification" format.

DATA ON "NEW" MANUFACUTRING SITE:

Pipettes:

The package consists of a pipette containing the product inside a blister. There are 3 blisters connected to each other per card; the blister is the child-resistance feature. Within MRID 48570601 the registrant provided detailed diagrams and pictures illustrating that there are no changes to the size or shape of the pipettes at the Klocke manufacturing site.

In a *Thermoplastic Pipette Manufacturing Comparison* it is noted that at the Cipla facility;

> "...the fill line is a vertical fill machine that utilizes heat to form the base of 6 pipettes per stroke into a cavity mold, the top film is sealed to the base at the neck and sides..., the pipettes are injections filled through the bottom and then the bottom of the pipette is sealed."

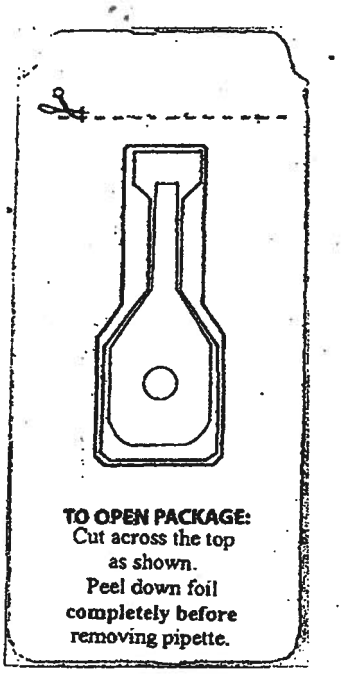
At the Klocke facility;

> "...[they] utilize a horizontal fill line to create identical pipettes. In this process the pipette bases are created through heating the film into a horizontal mold (10 pipettes per stroke), the formed pipette bases are injection filled..., the top film is then laid over the base and heat sealed."

The additional adult study submitted (Study No. 11234) confirms (see below) the ability of the study participants to access the pipettes produced at the new facility.

Blisters:

The blister, which is the child-resistant feature, is opened by the directions on the back of the blister. These directions indicate: to cut across the top of the blister along a dotted line with a scissors icon; peel down the foil on the back of the blister completely; and then remove the pipette. See diagram, below.



These are the same directions noted in the previous reviews for 86230-1, -2, -3 and -4; there are NO changes in the directions for use.

In *Thermoplastic Blister (Plantine) Manufacturing Comparison* it is noted that although the equipment at each facility is customized, the principle process steps used in creation and sealing of the blister packages is the same.

The additional studies submitted (Study Nos.: GLM 11234 and GLM 11210) confirm (see below) that there are no changes to the CRP feature/blister between the two manufacturing facilities.

GLM 11234: Senior Panel Self-Certification

At the beginning of each test period, the adult received 1 blister card; each blister card contained 3 purple, 0.136 fl oz. pipettes filled with placebo. The test subjects were to open one blister during a 5 minute test period and another blister during a one minute test period.

An SAUE failure was the inability to access one pipette in the prescribed test time of 5 minutes for the first package or 1 minute for the second package, breaking or cutting the pipette that has the potential to release the contents in the prescribed test time of 5 minutes for the first package or 1 minute for the second package, or accessing any amount of placebo (water) while opening the blister in the prescribed test time of 5 minutes for the first package or 1 minute for the second package.

Data Analysis: Senior ages, gender distributions, age allocations, as well as test site and tester requirements all adhered to the senior testing regulations set forth in 16 CFR 1700.20. There were 4 senior failures. This corresponds to a 96% success rate. The self-certification for Study No. GLM 11234 is acceptable; the study is considered as "passing" the senior test according to 16 CFR 1700.20.

GLM 11210: Child Panel Self-Certification

The study involved giving each child 1 blister card; each blister card contained 3 purple, 0.017 fl. oz. pipettes filled with placebo.

A unit failure for the child test was defined as access to the pipette or any partial or complete access to the placebo (water).

Data Analysis: Child ages, gender distributions, age allocations, as well as test site and tester requirements all adhered to the child testing regulations set forth in 16 CFR 1700.20. There were no child failures. The self-certification for Study No. GLM 11210 is acceptable; the study is considered as "passing" the child test according to the sequential test chart in 16 CFR 1700.20.

COMMENTS AND RECOMMENDATIONS:

As noted in the previous TRB reviews for EPA Reg. No. 86230-1, -2, -3 and -4, all senior and child CRP requirements were met for all pipette colors and sizes produced at Cipla, India. As the two self-certifications submitted by the registrant and reviewed above indicate, the pipette and blister produced at the new manufacturing site in Germany are adequate to cover all senior and child CRP requirements. EPA has no objection to allowing assembly of EPA Reg. No. 86230-1, -2, -3 and -4 at the additional manufacturing site.