

CHILD-RESISTANT PACKAGING REVIEW
 Technical Review Branch

IN 05/05/2011 OUT 06/20/2011

RD, TRB, Reviewed by Rosalind L. Gross *Rosalind L. Gross* 06/20/2011

EPA Reg. No. or File Symbol 65331-1

DP Barcode 389427

Decision # 447933

EPA Petition or EUP No. _____

Date Division Received 04/19/2011

Type Product(s) Insecticide (flea product)

Data Accession No(s). 48454801 and 48454802

Product Mgr./Chemical Review Mgr/Contact Person RM 10
 Division RD

Product Name(s) Frontline Spray Treatment

Company Name(s) Merial Ltd.

Submission Purpose Review of CRP studies and leakage study to determine if they are adequate to support CRP certification for MeadWestvaco Calmar trigger sprayer, the Mixor HP, with a 250ml and 500ml bottle.

Active Ingredient(s), PC code, & % Fipronil 0.29%

Summary of Findings

All the requirements for CRP have been met.

The CRP certification dated April 18, 2011 for EPA Registration No. 65331-1 is acceptable. There were **5 child failures** for the Child-Resistance Effectiveness (CRE) study (MRID 48454801 1365-098) - 45 month old male (opened the package), 46 month old female and 48 month old female (visible drops of water), a 44 month old male and a 51 month old male (indeterminate results). **The 5 child failures for the CRE (MRID 48454801 1365-098) are a pass of the child test according to the sequential test in 16 CFR 1700.20.** The Senior Adult Use Effectiveness (SAUE)

results were 97%. **The study is a pass of the Senior Adult test in 16 CFR 1700.20 and the effectiveness specifications in 16 CFR 1700.15(b).** For the leakage test ten 500ml sample bottles were tested and none of them indicated any leakage on any of the 10 bottles and trigger sprayers throughout the test. **Note** the instructions given to the seniors during testing (see package description section), which are on the April 18, 2011 label, must be the instructions on the final accepted label.

Should any human experience/epidemiological evidence indicate a problem once the product is in the marketplace, the Agency reserves the right to reexamine this data comprehensively and to question the child resistance of the package involved.

Package Description

The package is a MeadWestvaco Calmar, Inc. Mixor HP ASTM Type IXB (1). The package consists of a plastic one-piece continuously-threaded closure and a trigger sprayer pump. The trigger sprayer closure is permanently attached to the container by continuous threading and engagement of matching ratchets on the closure and the two sets of ratchets on the container. The trigger's square shaped nozzle has 4 positions, two off positions indicated by the symbol " X " that are located 180⁰ apart and two spray positions indicated by a spray pattern that are also located 180⁰ apart. The trigger sprayer is operated by pressing and holding down the rectangular tab, rotating the nozzle from the off position to the spraying position, and then squeezing the trigger. The tab does not lock into the cutout on the nozzle in the spray position, allowing the nozzle to be moved from the spray position to the off position without pressing the tab. Once in the off position, the nozzle is locked into place by means of the rectangular tab located on the trigger shroud that locks into a square cutout on the nozzle.

The Mixor HP trigger sprayer is used with both a 250ml and a 500ml bottle. Only one Child-Resistance Effectiveness (CRE) test and Senior Adult Use Effectiveness (SAUE) test are required as both the 250ml and 500ml bottle have the same neck finish. The directions given to the seniors for the SAUE test, which match the directions on the label submitted 4-18-2011, are

Directions provided to senior panelists:



Toxicity

The toxic or harmful amount of Fipronil for an 11.4 kg child is 2.5mg/kg times 11.4kg, which equals 28.5mg.

Company Data

The CRE test was done on a 250ml bottle with a MeadWestvaco Calmar, Inc. Mixor HP trigger sprayer. The test package was filled with water, the package was opened, sprayed, and closed 25 times prior to testing, and the pump was primed. Before and after the CRE the package was weighed. The children were given the primed trigger sprayer packages. **The results of the test indicated a 45 month old male opened the package after the demonstration by turning the nozzle with his teeth and then spraying the package 4 times.**

The weight loss associated with the 50 packages from the CRE indicated from 0 to 2.21g¹ loss per package (June 8, 2011 addendum S1 and June 13, 2011² Supplement from Perritt Labs). Discussions on June 7, 8, and 10, 2011 with Karen Mardis, Merial and Richard Ward, Perritt Labs (June 10, 2011) occurred to determine what these weight loss values mean in terms of a child failure.

For the SAUE test the seniors were provided with a 250ml bottle with a MeadWestvaco Calmar, Inc. Mixor HP trigger sprayer. The test package was filled with water, there were pictorial symbols on the package nozzle, and written directions were provided. The Seniors were asked to open the trigger sprayer, spray it until water was seen (note water spraying was not timed), and close the trigger sprayer properly. A properly resecured determination was made on the package used for the 1 minute test period by pressing the trigger to see if it sprayed, and a visual examination of the

¹ June 8, 2011 addendum S1 to 1365-098 corrected weight loss reporting from milligrams to grams.

² June 13, 2011 Supplement to 1365-098 explains weight loss values and their meaning in terms of child failure.

nozzle to confirm it was in the "X" closed position. The results of the study were 97% SAUE.

For the leakage test ten 500ml sample bottles were filled with placebo of the same density as the finished product. These bottles had the Mixor HP trigger sprayer attached with the same TIP as would be used in normal manufacturing operations. All 10 bottles were sprayed until empty. Examination of the trigger sprayer and bottle throughout the test was done to determine if any leakage occurred. The results indicate no leakage on any of the 10 bottles and trigger sprayers throughout the test.

Analysis of Data and Conclusion

Failure

For the purposes of CRP testing a **child failure** is access to any amount of product by any method. For instance, full or partial activation of the trigger, opening the trigger sprayer, remove sprayer from the bottle, leakage, etc.

A Senior Adult Use Effectiveness failure is an inability to open the package during the 5 minute test period, an inability to open and properly resecure the package during the 1 minute test period, or during either the 5 minute or 1 minute test period - access to the contents through an incorrect method (e.g. remove sprayer from bottle), leakage, or any unusual failures. Properly resecured was determined by pressing the trigger to see if it sprayed, and a visual examination of the nozzle to confirm it was in the "X" closed position.

Child-Resistance Effectiveness Test (MRID 48454801 1365-098)

The CRE test was done on a 250ml bottle with a MeadWestvaco Calmar, Inc. Mixor HP trigger sprayer. The test package was filled with water, the package was opened, sprayed, and closed 25 times prior to testing, and the pump was primed. Before and after the CRE the package was weighed. The children were given the primed trigger sprayer packages. **The results of the test indicated a 45 month old male opened the package after the demonstration by turning the nozzle with his teeth and then spraying the package 4 times. Note** leakage on the package was reported as a comment and not considered a child failure in the report.

The weight loss associated with the 50 packages from the CRE indicated from 0 to 2.21g³ loss per package (June 8, 2011 addendum S1 and June 13, 2011⁴ Supplement from Perritt Labs). Discussions on June 7,8, and 10, 2011 with Karen

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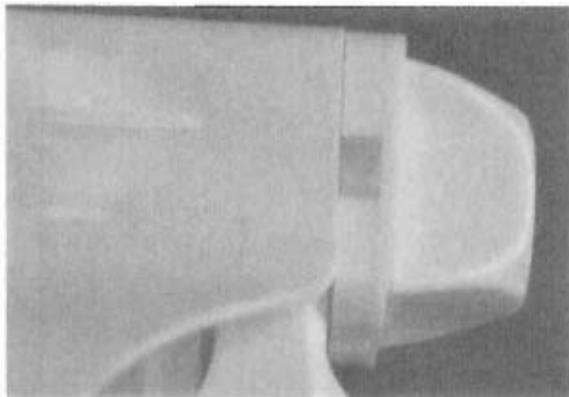
Mardis, Merial and Richard Ward, Perritt Labs (June 10, 2011) occurred to determine what these weight loss values mean in terms of a child failure. The results of these discussions are as follows:

- 2.21g weight loss was associated with the 45 month old male child failure, who sprayed the package 4 times.
- 30 packages had a recorded weight loss of 0.1g or less, which is attributed to ambient loss and/or weighing condition differences from one day to the next.
- 15 packages had a recorded weight loss of 0.11g - 0.46g, which is attributed to having the nozzle in the closed position and pulling the trigger to spray. This action may allow water in or on the trigger sprayer mechanism. The trigger sprayer mechanism is under the shroud and detection of water by the tester or access to water by the children during testing is difficult. The water is assumed to have evaporated before the post test weighing thus the weight loss. This possible release of water is **not considered a failure** because it was not detected by a tester, there was no record of visible drops of water, there was no record of water on the children, no record of breakage of the shroud or other parts, no record of access to water by the proper method of spraying, no record of water on the bottle, no record of any other access to the water.
- 5 packages had a recorded weight loss of 0.7g – 2.21g, which are amounts that would be expected to travel beyond the trigger sprayer mechanism and shroud onto the bottle surface where detection of water by the tester or access to water by the children during testing is possible.
 - a. Package 29 with a weight loss 0.7g is a 44 month old male and package 49 with a weight loss 0.77g is a 51 month old male both have no record of visible drops of water, there was no record of water on the children, no record of breakage of the shroud or other parts, no record of access to water by the proper method of spraying, no record of water on the bottle, no record of any other access to the water. However, the amount of water involved is sufficient to call these results indeterminate. Consequently, these **two children will be considered child failures**.
 - b. Package 44 with a weight loss 2.21g is a 45 month old male, who opened the package and was reported as a failure in the CRE (see above). Package 1 with a weight loss 0.98g is a 46 month old female and package 33 with a weight loss 0.95g is a 48 month old female **both have recorded CRE observations of visible drops of water. These children (46 and 48 month old females) were not reported as failures of the CRE, but under the definition of a child failure (see above) they are considered as child failures**.

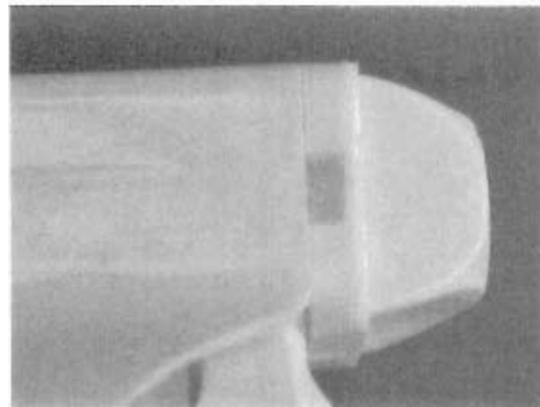
In conclusion there were **5 child failures** for the CRE (MRID 48454801 1365-098) - 45 month old male (opened the package), 46 month old female and 48 month old female (visible drops of water), a 44 month old male and a 51 month old male (indeterminate results). **The 5 child failures for the CRE (MRID 48454801 1365-098) are a pass of the child test according to the sequential test in 16 CFR 1700.20.**

Senior Adult Use Effectiveness Test (MRID 48454801 1365-098)

For the SAUE test the seniors were provided with a 250ml bottle with a MeadWestvaco Calmar, Inc. Mixor HP trigger sprayer. The test package was filled with water, there were pictorial symbols on the package nozzle, and written directions (as noted in the Package Description section above) were provided. The pictorial symbols on the test package nozzle were:



Spray pattern



"X" symbol

The Seniors were asked to open the trigger sprayer, spray it until water was seen (note water spraying (to ensure primed trigger) was not timed), and close the trigger sprayer properly. A properly resecured determination was made on the package used for the 1 minute test period by pressing the trigger to see if it sprayed, and a visual examination of the nozzle to confirm it was in the "X" closed position. The results of the study were 97% SAUE. **The study is a pass of the Senior Adult test in 16 CFR 1700.20 and the effectiveness specifications in 16 CFR 1700.15(b).**

Leakage Test (MRID 48454802 SD-AQL-016 v1)

Ten 500ml sample bottles were filled with placebo of the same density as the finished product. These bottles had the Mixor HP trigger sprayer attached with the same TIP as would be used in normal manufacturing operations. All 10 bottles were sprayed until empty. Examination of the trigger sprayer and bottle throughout the test was done to determine if any leakage occurred. The results indicate no leakage on any of the 10 bottles and trigger sprayers throughout the test.

Conclusion

All the requirements for CRP have been met.

The CRP certification dated April 18, 2011 for EPA Registration No. 65331-1 is acceptable. There were **5 child failures** for the CRE (MRID 48454801 1365-098) - 45 month old male (opened the package), 46 month old female and 48 month old female (visible drops of water), a 44 month old male and a 51 month old male (indeterminate results). **The 5 child failures for the CRE (MRID 48454801 1365-098) are a pass of the child test according to the sequential test in 16 CFR 1700.20.** The SAUE results were 97%. **The study is a pass of the Senior Adult test in 16 CFR 1700.20 and the effectiveness specifications in 16 CFR 1700.15(b).** For the leakage test ten 500ml sample bottles were tested and none of them indicated any leakage on any of the 10 bottles and trigger sprayers throughout the test. **Note the instructions given to the seniors during testing (see package description section), which are on the April 18, 2011 label, must be the instructions on the final accepted label.**

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