

CHILD-RESISTANT PACKAGING REVIEW  
Technical Review Branch

IN 09/07/2010 OUT 11/01/2010

Reviewed by Rosalind L. Gross  
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11/01/2010

EPA Reg. No. or File Symbol 65331-1

DP Barcode D381900

Decision No. 438540

EPA Petition or EUP No. \_\_\_\_\_

Date Division Received \_\_\_\_\_

Submission Dated 08/13/2010

Type Product(s) Insecticide

Data Accession No(s). 481946-00 & 481946-01

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

Product Name(s) Frontline Spray Treatment

Company Name(s) Merial Limited

Submission Purpose Review CR Protocol Trigger Sprayer Information

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

**Summary of Findings**

**The proposed approach is unacceptable because examination of the registrant's samples of the MeadWestvaco Calmar, Inc. Mixer HP trigger sprayer has caused concern regarding potential exposure to the product from a resecured package. There are concerns regarding whether or not a primed package is "properly resecured". For example could activation of the trigger in the closed position lead to drops coming out of the trigger nozzle? Additionally, there are concerns regarding whether a primed package once resecured and the trigger activated would spray product at its next**

opening without activation of the trigger. The SAUE data examined in 2004 involved tests done on **empty bottles**, which would **not have demonstrated whether or not a primed package is “properly resecured”**. Therefore, the Agency is requesting both SAUE and CRE testing for this package in accordance with 16 CFR 1700.20. Some recommendations regarding the Senior Adult Use Effectiveness (SAUE) and Child-Resistant Effectiveness (CRE) are made in the Analysis of Information and Conclusion section of this review.

Note the registrant will need to submit a **CRP certification** for their product with the test data per 40 CFR Part 157 and **revised labeling with the directions for opening and properly reclosing the package used in the Senior Adult Use Effectiveness Test. The CRP certification must be signed by the registrant.** The directions for opening and properly reclosing the package on the label, any package insert and/or outer packaging **must be identical** to those used in the Senior Adult Use Effectiveness Test.

### **Company Submission**

The registrant submitted a protocol testing request for a MeadWestvaco Calmar, Inc. Mixer HP trigger sprayer ASTM Type IXB (1). The same size neck finish Mixer HP trigger sprayer would be used for both a 250 and 500ml spray bottle. Once assembled the Mixer HP trigger sprayer would be permanently attached to the container neck finish by continuous threading and engagement of matching ratchets in the closure and two sets of ratchets on the container neck finish. The registrant provided samples of the MeadWestvaco Calmar, Inc. Mixer HP trigger sprayer. A leakage test similar to MRID 448277-01 will be performed.

The Mixer HP trigger sprayer would not be tested for the Senior Adult Effectiveness (SAUE) test based on Agency correspondence (January 22, 2004) indicating the MeadWestvaco Calmar, Inc. Mixer HP trigger sprayer CRP test data had been reviewed and with certain additional evidence could be used. The Mixer HP trigger sprayer would be tested with placebo (purified water) filled samples for the Child-Resistant Effectiveness (CRE) test. The samples used for the CRE test will have the trigger sprayer primed. The CRE test would be conducted per 16 CFR 1700.20. Should the package not pass the CRE test the registrant **requests the package be treated as a unit dose package with a failure defined as access to 28.5mg of fipronil** (equivalent to 26 activations of the trigger at 1.3ml (product) per activation and a product density of 854mg/ml).

### **Package**

The package is a MeadWestvaco Calmar, Inc. Mixer HP trigger sprayer ASTM Type IXB (1) according to the registrant. Note the Mixer MP trigger sprayer appears to be

similar, but is manufactured in Europe, whereas the Mixor HP trigger sprayer is manufacturer in the United States. The registrant should specify in all submissions which trigger sprayer is being used and tested. The trigger sprayer closure is a **28mm/400** (per the manufacturer's internet listing) and it is "**permanently**" attached by continuous threading and engagement of matching ratchets in the closure and two sets of ratchets 180° apart on the container neck finish. The trigger nozzle has 4 positions, two off positions indicated by the symbol "X" that are 180° apart and a spray and stream position that are 180° apart. The package is opened by pressing and holding down a rectangular tab on the trigger shroud and rotating the nozzle to the spray/stream position and activating the trigger. The package is properly reclosed by rotating the nozzle until the tab on the trigger shroud is locked into place, which means the tab is in the square cutout on the trigger nozzle.

### Analysis of Information and Conclusion

#### Leakage Test

The leakage test described by the registrant as being similar to that done for MRID 448277-01 would be acceptable, to demonstrate no leakage for the life of the product. The leakage test should involve the use of 10 samples, 500ml each filled with placebo of the same density as the actual product. Each sample should be sprayed until empty. The amount of leakage of each sample should be reported. The 500ml size is the worst case scenario and would also cover the 250ml size.

#### Senior Adult Use Effectiveness (SAUE) Test and Child-Resistant Effectiveness (CRE) Test

Examination of the registrant's samples of the MeadWestvaco Calmar, Inc. Mixor HP trigger sprayer has caused concern regarding potential exposure to the product from a resecured package. There are concerns regarding whether or not a primed package is "properly resecured". For example could activation of the trigger in the closed position lead to drops coming out of the trigger nozzle? Additionally, there are concerns regarding whether a primed package once resecured and the trigger activated would spray product at its next opening without activating the trigger. The SAUE data examined in 2004 involved tests done on **empty bottles**, which would not have demonstrated whether or not a primed package is "properly resecured". Therefore, the Agency is requesting both SAUE and CRE testing for this package in accordance with 16 CFR 1700.20. Note the test packages used for both SAUE and CRE testing should contain placebo and be primed.

For the SAUE and CRE testing either the 250ml or the 500ml size may be used provided they both have the same size neck finish. Testing the package (trigger sprayer and bottle) in terms of whether the seniors can open and properly reclose the

trigger sprayer is acceptable provided the trigger sprayer once assembled is permanently attached to the container neck finish. **If this is not true then the protocol should be modified and the Agency contacted, accordingly.**

### **SAUE**

The **definition of open** is push the tab on the trigger shroud, rotating the nozzle to the spray position, and activating the trigger once. The **definition of properly resecured** includes turning the trigger nozzle so the tab on the trigger shroud is locked into place, which means the tab is in the square cutout on the trigger nozzle, a primed trigger sprayer will not dispense any product upon activation, and a visual examination of the package does not reveal any unusual failures. **A senior failure** will be a senior unable to open the package during the first 5 minute test period or unable to open and properly resecure the package in the 1 minute test period. **A senior failure also includes** access to the contents through an incorrect mechanism e.g. removal of the trigger sprayer from the bottle (regardless of whether or not the trigger sprayer is put back on the bottle), leakage, and any unusual failures. Note the final report should include the definitions of open, properly resecure, and senior failure. It is recommended that the the SAUE should include having the test clock stopped and the tester asking the subject to please spray the trigger sprayer into a container until water is seen and then stop spraying. Then the tester should say please close the package properly. [This is similar to 16 CFR 1700.20(a)(3) Test Instructions for Senior Test numbers 7 and 10 regarding emptying the pills from a package.] The rationale for this instruction, which is **not part of the opening or properly resealing directions**, is to ensure the trigger is primed and dispensing product in order to determine if it is properly resecured. **Whatever set of directions are used for the SAUE passing data should be a part of the final report** submitted to the Agency. Further, this set of **directions must be the same in all locations associated with the retail package** e.g. the bottle label, package insert, and outer package.

### **CRE**

**A trigger sprayer is a multiple use package and not a single use/unit dose package. A trigger sprayer does not meet the definition of unit packaging in 40 CFR 157.21(g).** Consequently, per 16 CFR 1700.20 a child failure is any child who opens the package or gains access to any amount of its contents.

The **definition of a child failure** will include pushing the tab on the trigger shroud, rotating the nozzle and activating the trigger; using teeth to turn the nozzle and spray product; access to any amount of product by any means (e.g. activation of trigger resulting in release of any amount of product regardless of nozzle position, removal of trigger sprayer from bottle, leakage, chew hole in bottle, etc.). Once a child has activated the trigger sprayer once (which is a failure) the total number of activations up

to a maximum of ten will be recorded. This is to facilitate any future discussions Merial may wish to have should the package not pass the CRE test. However, the Agency maintains that a trigger sprayer is a multiple use package and not a single use/unit dose package. A trigger sprayer does not meet the definition of unit packaging in 40 CFR 157.21(g).

Note the registrant will need to submit a CRP certification for their product with the test data per 40 CFR Part 157 and revised labeling with the directions for opening and properly reclosing the package used in the Senior Adult Use Effectiveness Test. **The CRP certification must be signed by the registrant.** The directions for opening and properly reclosing the package on the label, any package insert and/or outer packaging **must be identical** to those used in the Senior Adult Use Effectiveness Test.