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DOG



CHILD-RESISTANT PACKAGING REVIEW
Technical Review Branch

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Reviewed by Rosalind L. Gross Rosalind L Gross 02/20/2007

EPA Reg. No. or File Symbol 80490-E

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EPA Petition or EUP No. _____

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Type Product(s) Insecticide

Data Accession No(s). MRID 469217-00, 469217-03 to 09

Product Mgr./Chemical Review Mgr/Contact Person RM 07(Hebert)
Division RD

Product Name(s) Promeris Spot On For Dogs

Company Name(s) Fort Dodge Animal Health

Submission Purpose Examine data for 8 CRP tests (test data for 4 pipette sizes) to ascertain if CRP is acceptable for 5 different pipette sizes of Dog Product and bracket data from EPA Reg. No. 80490-E Dog Product for 1.6ml Cat Product if possible

Active Ingredient(s), PC code, & % Amitraz 14.34%
Metaflumizone 14.34%

## Summary of Findings

**Note for all sizes based on product toxicity a child failure is access to one blister unit. CRP certification is acceptable. The results are as follows:**

- 0.67ml and 3.33ml sizes **do not meet CRP criteria** because they are not a pass of the child test, they are inconclusive according to the sequential test chart in 16 CFR 1700.20.

- 1.33ml and 6.66ml sizes **meet the CRP criteria**. The 6.66ml size is a marginal

pass and cannot be used for bracketing.

- 5.33ml size **does not meet the CRP criteria** as it cannot be bracketed using the 3.33ml and 6.66ml sizes because the two packages have different seals and are not the same package. Furthermore, the 3.33ml size did not meet CRP criteria at F=1 and the 6.66ml size was a marginal pass.

**The 1.6ml size of EPA Reg. No. 80490-G** may use bracketing from the 1.33 and 3.33ml size of EPA Reg. No. 80490-E. The results for the 1.33ml size of EPA Reg. No. 80490-E indicate the study is a pass of both the Senior Adult test in 16 CFR 1700.20 and child test according to the sequential chart in 16 CFR 1700.20. The results for the 3.33ml size of EPA Reg. No. 80490-E indicate the study is a pass of both the Senior Adult test in 16 CFR 1700.20 and child test according to the sequential chart in 16 CFR 1700.20, but **only if a child failure is equal to access to more than one blister. In the case of EPA Reg. No. 80490-G since CRP is voluntary a child failure is equal to access to 9 blisters. Therefore for the purposes of voluntary CRP for EPA Reg. No. 80490-G in the 1.6ml size the criteria for CRP have been met based on the 1.33ml and 3.33ml sizes of EPA Reg. No. 80490-E. The 0.8ml size of EPA Reg. No. 80490-G met all the criteria for CRP.**

**Note since the desiccant strip was not used in the test package if any human experience/epidemiological evidence indicates a problem once the product is in the marketplace, the Agency reserves the right to question the child resistance of the package involved for both EPA Reg. No. 80490-E and EPA Reg. No. 80490-G.**

## Company Data

A CRP certification, 4 Senior Adult Use Effectiveness (SAUE) Studies and 4 Child Resistant Effectiveness (CRE) Studies (MRID 467217-03 to 467217-09) were submitted. The studies were submitted as hard copy and electronically. A SAUE and a CRE study were done on the 0.67ml, 1.33ml, 3.33ml, and 6.66ml sizes of the Dog product.

### 0.67ml SAUE MRID 467217-04 and CRE MRID 467217-03

A SAUE (MRID 469217-04) was done using the 0.67ml pipette in the blister. The results were 1 senior failed to open the package in the one minute test period. The results were 99% SAUE.

The CRE (MRID 469217-03) was done using the 0.67ml pipette filled with water inside the blister. Each child was given 3 cards with 3 blisters each (9 blisters total) at the beginning of the test. A **blister failure** was defined as any breach into the unsealed/formed area of the package. A **child failure** was considered access to 9 blisters according to the **registrant**. The results indicate 1 child accessed 3 units, 1

child accessed 2 units and 6 children accessed one unit each. The results indicate 8 children accessed one or more units.

**1.33ml** SAUE MRID 467217-06 and CRE MRID 467217-05

A SAUE (MRID 469217-06) was done using the 1.33ml pipette in the blister. The results were 100% SAUE.

The CRE (MRID 469217-05) was done using the 1.33ml pipette filled with water inside the blister. Each child was given 3 cards with 3 blisters each (9 blisters total) at the beginning of the test. A **blister failure** was defined as any breach into the unsealed/formed area of the package. A **child failure** was considered access to 5 blisters according to the **registrant**. The results indicate 1 child accessed 2 units and 2 children accessed one unit each. The results indicate 3 children accessed one or more units.

**3.33ml** SAUE MRID 467217-07and CRE MRID 467217-08

A SAUE (MRID 469217-07) was done using the 3.33ml pipette in the blister. The results were 100% SAUE.

The CRE (MRID 469217-08) was done using the 3.33ml pipette filled with water inside the blister. Each child was given 3 cards with 3 blisters each (9 blisters total) at the beginning of the test. A **blister failure** was defined as any breach into the unsealed/formed area of the package. A **child failure** was considered access to 2 blisters according to the **registrant**. The results indicate 8 children accessed one unit each.

**6.66ml** SAUE MRID 467217-09 and CRE MRID 467217-09

A SAUE (MRID 469217-09) was done using the 6.66ml pipette in the blister. The results were 100% SAUE.

The CRE (MRID 469217-09) was done using the 6.66ml pipette filled with water inside the blister. Each child was given 3 cards with 3 blisters each (9 blisters total) at the beginning of the test. A **blister failure** was defined as any breach into the unsealed/formed area of the package. A **child failure** was considered access to 1 blister according to the **registrant**. The results indicate 1 child accessed 9 units, 1 child accessed 3 units, 2 children accessed 2 units each and 1 child accessed 1 unit. The results indicate 5 children accessed one or more units.

**Packaging**

**The 0.67, 1.33, and 3.33ml packages** tested were a plastic pipette inside a gold plastic-aluminum blister with a **peelable seal**, ASTM D3475-06 type **VIIID(2)**. The pipettes were filled with water. The blister is the intended child-resistant package. Each

card contains 3 blisters each with a pipette. The instructions on the blister read "CUT AT DOTTED LINE" AND "FOLD AT LINE TEAR AT SLIT". These instructions allow a test subject to either use a tool or not. **In the marketplace each blister will contain a 10 x50 mm desiccant strip, but this was not included in the test packages.**

**The 6.66ml Senior adult package** tested was a plastic pipette inside a gold plastic-aluminum blister, with a **weldable seal** (per 2/14/07 email D. Chaleff, Fort Dodge Animal Health to R. Gross, EPA), and the **Child package** tested was a plastic pipette inside a blue plastic-aluminum blister, with a **weldable seal** (per 2/14/07 email D. Chaleff, Fort Dodge Animal Health to R. Gross, EPA). Both the Senior adult and Child package are ASTM D3475-06 type **VIIIF**. The blister is the intended child-resistant package. Each card contains 3 blisters each with a pipette. The instructions on the blister read "CUT AT DOTTED LINE". These instructions indicate a test subject should use a tool and the package does not have an internal tear notch as do the other sizes tested. **In the marketplace each blister will contain a 10 x50 mm desiccant strip, but this was not included in the test packages.**

## Toxicity

The dog product (EPA Reg. No. 80490-E) based on a toxicity review 12/29/2004, D311471, Decision 351841 indicates an oral $LD_{50}$ of >500 and <5000mg/kg and an inhalation $LC_{50}$ of >0.57 and <2.32mg/L, both of which are toxicity triggers requiring CRP. A Confidential Statement of Formula10/20/2004 indicates a product density of 1.025-1.067g/ml. A worst case calculation of **an oral $LD_{50}$** of 500mg/kg means a **toxic or harmful amount for an 11.4kg child** would be **5700mg** = 5.7g divided by 1.067g/ml = **5.34ml**. The inhalation $LC_{50}$ toxicity trigger is worse than the oral $LD_{50}$ trigger and CRP is supposed to protect against the worst trigger. CRP for the worst case calculation of **an inhalation $LC_{50}$** of 0.57mg/L means **a toxic or harmful amount for an 11.4kg child** would be **50.2mg** = 4.4mg/kg X 11.4kg = 50.2mg divided by 1.067g/ml = **0.047ml**. Note the data for **an inhalation $LC_{50}$** of 0.57mg/L **showed significant signs of toxicity**. Since the pipette is a liquid and based on its method of application there is a possibility of oral and inhalation exposure. **This means for purposes of CRP calculations a toxic or harmful amount for an 11.4kg child is access to 1 pipette of the dog product (EPA Reg. No. 80490-E).**

**The cat product (EPA Reg. No. 80490-G) is not subject to CRP based on acute toxicity criteria in 40 CFR 157.22. This product is in voluntary CRP**. The toxicity data for this product indicate a worst case **acute oral $LD_{50}$ of 5g/kg,** which for an **11.4kg child represents a toxic or harmful amount of 57g**. With a product density of 1.11g/ml represents **51.35ml**. 51.35ml represents 39 pipettes @ 1.33ml, 33 pipettes @ 1.6ml, and 16 pipettes @ 3.33ml. Therefore for the purposes of **CRP testing a child failure will represent access to 9 units/blisters.**

## Discussion and Conclusion

A CRP certification, 4 SAUE Studies and 4CRE Studies (MRID 467217-03 to

467217-09) were submitted. The studies were submitted as hard copy and electronically. A SAUE and a CRE study were done on the 0.67ml, 1.33ml, 3.33ml, and 6.66ml sizes of the Dog product.

**The CRP certification was acceptable. Note based on product toxicity a child failure is access to one pipette regardless of number of ml in a pipette from 0.67 – 6.66ml for the dog product (EPA Reg. No. 80490-E).**

**0.67ml** SAUE MRID 467217-04 and CRE MRID 467217-03

A SAUE (MRID 469217-04) was done using the 0.67ml pipette in the blister. A senior adult failure was defined as any senior unable to open the package in the first five minute test period that passed the screening test or unable to open the package in the one minute test period. The results were 1 senior failed to open the package in the one minute test period. **The results were 99% SAUE. The study is a pass of the Senior Adult test in 16 CFR 1700.20.**

The CRE (MRID 469217-03) was done using the 0.67ml pipette filled with water inside the blister. Each child was given 3 cards with 3 blisters each (9 blisters total) at the beginning of the test. A **blister failure** was defined as any breach into the unsealed/formed area of the package. A **child failure** was considered access to 9 blisters according to the **registrant**. **The Agency defines a child failure as access to 1 blister.** The results indicate 1 child accessed 3 units, 1 child accessed 2 units and 6 children accessed one unit each. Specifically, one 45 month old male in the second 5 minute test period accessed 3 units, one 45 month old male in the second 5 minute test period accessed 2 units, one 42 month old male in the second 5 minute test period accessed 1 unit, one 44 month old female in the second 5 minute test period accessed 1 unit, one 45 month old female in the second 5 minute test period accessed 1 unit, one 47 month old female in the second 5 minute test period accessed 1 unit, one 49 month old male in the first 5 minute test period accessed 1 unit, and one 50 month old male in the second 5 minute test period accessed 1 unit. **The results indicate 8 children accessed one or more units. This study is not a pass of the child test, it is inconclusive according to the sequential test chart in 16 CFR 1700.20. The sequential test chart in 16 CFR 1700.20 indicates another 50 children need to be tested to ascertain whether or not the package is child-resistant.**

**1.33ml** SAUE MRID 467217-06 and CRE MRID 467217-05

A SAUE (MRID 469217-06) was done using the 1.33ml pipette in the blister. A senior adult failure was defined as any senior unable to open the package in the first five minute test period that passed the screening test or unable to open the package in the one minute test period. **The results were 100% SAUE. The study is a pass of the Senior Adult test in 16 CFR 1700.20.**

The CRE (MRID 469217-05) was done using the 1.33ml pipette filled with water inside the blister. Each child was given 3 cards with 3 blisters each (9 blisters total) at

the beginning of the test. A **blister failure** was defined as any breach into the unsealed/formed area of the package. A **child failure** was considered access to 5 blisters according to the **registrant**. **The Agency defines a child failure as access to 1 blister.** The results indicate 1 child accessed 2 units and 2 children accessed one unit each. Specifically, one 47 month old male in the first 5 minute test period accessed 2 units, one 46 month old female in the second 5 minute test period accessed 1 unit, and one 50 month old female in the second 5 minute test period accessed 1unit. **The results indicate 3 children accessed one or more units. This study is a pass of the child test according to the sequential test chart in 16 CFR 1700.20.**

**3.33ml** SAUE MRID 467217-07and CRE MRID 467217-08

A SAUE (MRID 469217-07) was done using the 3.33ml pipette in the blister. A senior adult failure was defined as any senior unable to open the package in the first five minute test period that passed the screening test or unable to open the package in the one minute test period. **The results were 100% SAUE. The study is a pass of the Senior Adult test in 16 CFR 1700.20.**

The CRE (MRID 469217-08) was done using the 3.33ml pipette filled with water inside the blister. Each child was given 3 cards with 3 blisters each (9 blisters total) at the beginning of the test. A **blister failure** was defined as any breach into the unsealed/formed area of the package. A **child failure** was considered access to 2 blisters according to the **registrant**. **The Agency defines a child failure as access to 1 blister. The results indicate 8 children accessed one unit each.** Specifically, one 44 month old female in the first 5 minute test period accessed 1 unit, one 44 month old female in the second 5 minute test period accessed 1 unit, one 45 month old female in the second 5 minute test period accessed 1 unit, one 46 month old female in the first 5 minute test period accessed 1 unit, one 48 month old female in the second 5 minute test period accessed 1 unit, one 49 month old male in the first 5 minute test period accessed 1 unit, and two 51month old females in the second 5 minute test period each accessed 1 unit. **This study is not a pass of the child test, it is inconclusive according to the sequential test chart in 16 CFR 1700.20. The sequential test chart in 16 CFR 1700.20 indicates another 50 children need to be tested to ascertain whether or not the package is child-resistant.**

**5.33ml extrapolation** SAUE and CRE

The 3.33ml and 6.66ml sizes of EPA Reg. No. 80490-E were used to bracket the 5.33ml size of EPA Reg. No. 80490-E. However, **the bracket is based on the fact that both package sizes used are the same package with the same type of seal and that the SAUE and CRE results are not marginal.** The rationale for bracketing is that if 2 package sizes have a high pass then any size of the same package between them should also meet the requirements of CRP. **Any differences** in the 2 packages tested could alter this and **eliminate the possibility of bracketing**. **Marginal data** for either or both the SAUE and CRE of either package means that potential exists for the next size package to not meet the SAUE and CRE requirements and **eliminates the**

**possibility of bracketing.**

The results for the **3.33ml** size of EPA Reg. No. 80490-E indicate the study is a pass of the Senior Adult test in 16 CFR 1700.20. A child failure is defined as access to one blister for the 3.33ml size. This study is **not a pass of the child test,** it is inconclusive according to the sequential test chart in 16 CFR 1700.20. The sequential test chart in 16 CFR 1700.20 indicates another 50 children need to be tested to ascertain whether or not the package is child-resistant. The results for the **6.66ml** size of EPA Reg. No. 80490-E indicate the study is a pass of the Senior Adult test in 16 CFR 1700.20. A child failure is defined as access to one blister for the 6.66ml size. This study is a pass of the **child test, but it is a marginal pass. The 3.33ml size has a peelable seal and is ASTM D3475-06 type VIIID(2) whereas the 6.66ml size has a weldable seal and is ASTM D3475-06 type VIIIF, which means they are not the same package. Therefore, the 5.33ml size cannot be bracketed from the 3.33ml and 6.66ml size and must be tested to ascertain whether or not it meets the conditions of the CRP regulations.**

**6.66ml** SAUE MRID 467217-09 and CRE MRID 467217-09

A SAUE (MRID 469217-09) was done using the 6.66ml pipette in the blister. A senior adult failure was defined as any senior unable to open the package in the first five minute test period that passed the screening test or unable to open the package in the one minute test period. **The results were 100% SAUE. The study is a pass of the Senior Adult test in 16 CFR 1700.20.**

The CRE (MRID 469217-09) was done using the 6.66ml pipette filled with water inside the blister. Each child was given 3 cards with 3 blisters each (9 blisters total) at the beginning of the test. A **blister failure** was defined as any breach into the unsealed/formed area of the package. A **child failure** was considered access to 1 blister according to the **registrant. The Agency defines a child failure as access to 1 blister.** The results indicate 1 child accessed 9 units, 1 child accessed 3 units, 2 children accessed 2 units each and 1 child accessed 1 unit. Specifically, one 43 month old male in the first 5 minute test period accessed 9 units, one 42 month old male in the first 5 minute test period accessed 3 units, one 46 month old male in the second 5 minute test period accessed 2 units, one 48 month old male in the second 5 minute test period accessed 2 units, one 42 month old male in the first 5 minute test period accessed 1 unit. **The results indicate 5 children accessed one or more units. This study is a pass of the child test according to the sequential test chart in 16 CFR 1700.20. However, it is a marginal pass and may not be used for bracketing purposes.**

**1.6ml size EPA Reg. No. 80490-G (cat) extrapolation** SAUE and CRE

The **1.6ml size of EPA Reg. No. 80490-G (cat) was conditionally** considered to have met the criteria for CRP **based on the evaluation and acceptance of CRP test data for the 1.33ml and 3.33ml sizes of EPA Reg. No. 80490-E (dog).** The

1.33ml and 3.33ml sizes of EPA Reg. No. 80490-E were used to bracket the 1.6ml size of EPA Reg. No. 80490-G. The results for the 1.33ml size of EPA Reg. No. 80490-E indicate the study is a pass of both the Senior Adult test in 16 CFR 1700.20 and child test according to the sequential chart in 16 CFR 1700.20. The child test pass for the 1.33ml size is based on a child failure is equal to access to one blister (results were three children accessed one or more units). The results for the 3.33ml size of EPA Reg. No. 80490-E indicate the study is a pass of both the Senior Adult test in 16 CFR 1700.20 and child test according to the sequential chart in 16 CFR 1700.20, but **only if a child failure is equal to access to more than one blister. In the case of EPA Reg. No. 80490-G since CRP is voluntary a child failure is equal to access to 9 blisters. Therefore for the purposes of voluntary CRP for EPA Reg. No. 80490-G in the 1.6ml size the criteria for CRP have been met based on the 1.33ml and 3.33ml sizes of EPA Reg. No. 80490-E. The 0.8ml size of EPA Reg. No. 80490-G met all the criteria for CRP**.

**Note since the desiccant strip was not used in the test package if any human experience/epidemiological evidence indicates a problem once the product is in the marketplace, the Agency reserves the right to question the child resistance of the package involved for both EPA Reg. No. 80490-E and EPA Reg. No. 80490-G.**