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

OFFICE OF  
PREVENTION, PESTICIDES  
AND  
TOXIC SUBSTANCES

MEMORANDUM

June 12, 1998

SUBJECT: Review of Bitrex Test and Volume of a Swallow for Maxforce Gel Applicators - RBF 5

FROM: Rosalind L. Gross, Chemist  
Technical Review Branch

A handwritten signature in cursive script, appearing to read "R L Gross".

TO: Susan T. Lewis, Chief  
Insecticides Branch

Summary:

In conclusion, the registrant's data is reasonable. The average volume of a swallow was 6.62 g and the concept of less product from a syringe than a cup are both consistent with the literature (Watson et. al.). However, it would have been preferable if the children had taken multiple swallows (e.g. 5) of the cheese spread rather than one swallow per subject to calculate the average amount of a swallow. A Bitrex taste test on children to determine the maximum number of swallows ingested would have been informative.

Company Data:

An abridged version of two studies in MRID 44353403 were reviewed. These two studies are: an October 29, 1994 Peryam and Kroll study of 20 ppm Bitrex with adults; and an August 7, 1997 Great Lakes Marketing Associates, Inc. study on 42 to 51 month old children regarding the volume of a swallow for Maxforce Gel Applicators.

The results of the Peryam and Kroll study involved 50 panelists tested with 5 samples each of a control and a test sample with 20 ppm Bitrex. The panelists rated the control and test samples on a tolerability scale and a food action scale. The results indicate that the 20 ppm Bitrex made ingestion intolerable and the test sample likely to be consumed only if there were no other food choice.

The August 7, 1997 Great Lakes Marketing Associates, Inc. study on the volume of a swallow for Maxforce Gel Applicators involved 68 children 42 to 51 month old, nine of whom were excluded for failure to participate in the study. The children were asked to take one swallow from a 3 ounce cup of water followed by one swallow of a commercial cheese spread from a 12, 30, 60 g syringe or an applicator. At most 16 children tested any one of the 4 devices with the cheese spread. The results indicate the mean for one swallow of water from a 3 ounce cup was 6.62 g and the average amount of one swallow of cheese spread ingested from the four devices was 0.378 g, with the maximum amount being 2.0 g from the applicator.

The registrant concludes that 20 ppm Bitrex would limit the child to only one swallow of RBF 5 and that this one swallow (average amount 0.378 g) would represent an MOE of 152 based on a NOAEL 0.5 mg/kg. The registrant implies RBF 5 is the consistency of cheese spread. Since the NOAEL is 2.5 mg/kg per the May 21, 1998 Toxicology Hazard Assessment, the MOE is 760.

#### Analysis of Data and Conclusion:

Watson, W.A. et. Al. American J. Of Emergency Medicine 1983, 3: 278, "The Volume of a Swallow: Correlation of Deglutition with Patient and Container Parameters" tested 95 children between 2 and 18 years old. Each subject was asked to take 5 swallows from 4 containers to calculate the average volume of a swallow per container. The average volume of a swallow from a 5 ounce cup (diameter 6.5 cm) for children 24 to 42 months old was  $3.8 \pm 2.4$  ml, which is consistent with the  $4.6 \pm 1.9$  ml for children 15 to 42 months old by Jones, DV, Work, CE, Am J. Dis. Child. 1961, 102:173, "Volume of a Swallow". The average volume of a swallow from a 4 ounce prescription bottle (diameter 1.5 cm) for children 24 to 42 months old was  $1.24 \pm 0.5$  ml. The smaller average volume of a swallow from a 4 ounce prescription bottle suggests it may be safer in terms of reducing the amount of an ingestion than a larger diameter cup according to Watson et. al.

A review of the Consumer Product Safety Commission (CPSC) "Final Report Study of Aversive Agents", which was sent to Congress November 18, 1992 indicates that Bitrex is added to a product at between 20 and 50 ppm as an aversive agent and that acute toxicity from Bitrex does not occur at these levels. The CPSC Final Report cited a number of studies testing the efficacy of denatonium benzoate (Bitrex) as a deterrent to ingestion of liquid products. One study done by Procter and Gamble Company involved testing children between 18 and 47 months old with a dishwashing liquid containing 11.4 ppm Bitrex. The majority of the children ingested less than one swallow, and none of the children ingested more than three swallows. An accidental ingestion of one to two swallows of a thumb sucking deterrent (15 ml total) by a 21 month old child was reported by a Poison Control Center to the CPSC. The CPSC notes despite the aforementioned information there is "no direct evidence that denatonium benzoate or any other possible aversive agent is effective at limiting ingestions.....in the home.....".

In conclusion, the registrant's data is reasonable. The average volume of a swallow was 6.62 g and the concept of less product from a syringe than a cup are both consistent with the literature (Watson et. al.). However, it would have been preferable if the children had taken multiple swallows (e.g. 5) of the cheese spread rather than one swallow per subject to calculate the average amount of a swallow. A Bitrex taste test on children to determine the maximum number of swallows ingested would have been informative.