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

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Dantobrom
EPA Registration No. 38906-14

Dantobrom P
EPA File Symbol 38906-RL

Data Requirements for Use in Spas
and Swimming Pools

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Toxicology Branch/HED (TS-769)

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THRU: Jane E. Harris, Ph.D 8/28/85
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Toxicology Branch/HED (TS-769)

Registrant: Glyco, Inc.
Norwalk, CT 06856

Action Requested: Reassessment of Data Requirements for Dantobrom and Dantobrom P.

The Registrant has questioned the toxicology data requirements for their products for use in swimming pools and spas and has proposed to do the following studies on the organic moieties of the active materials:

1. Primary dermal irritation - dimethylhydantoin (DMH) and ethylmethylhydantoin (EMH).
2. Primary eye irritation - DMH and EMH.
3. Dermal sensitization - DMH and EMH.
4. Physiological disposition of DMH using radiolabeled DMH.

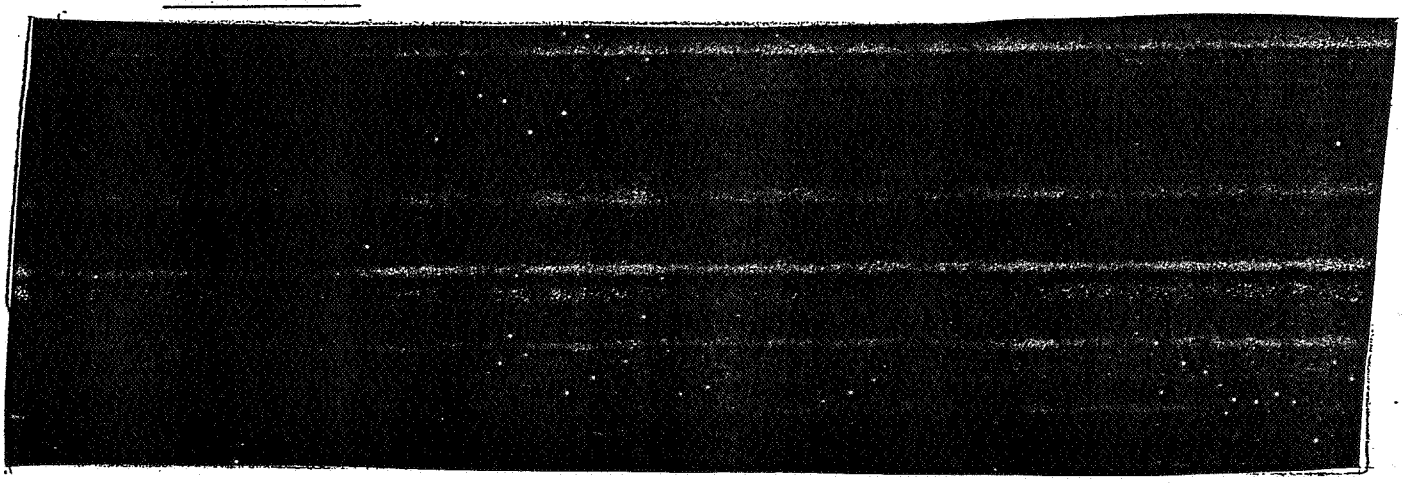
The composition of Dantobrom and Dantobrom P is as follows:

| | |
|---|---|
| 1-bromo-3 chloro-5,5 dimethylhydantoin ..... | 60.0% |
| 1,3 dichloro-5,5 dimethylhydantoin ..... | 27.4% |
| 1,3 dichloro-5 ethyl-5 methylhydantoin ..... | 10.6% |
| Inert ingredients ..... | 2.0% |

The Toxicology Consultant to the Registrant proposes that they not be required to perform three studies (the subchronic oral and the teratology studies) requested in the Toxicology Branch memorandum dated March 12, 1985. The consultant questions the need for these studies and references the Registrant's subchronic oral and teratology studies in support of Glycoserve, another of the Registrant's products which is used as a preservative in detergents.

The consultant argues that the Glycoserve study adequately demonstrates the subchronic oral toxicity of DMH, because the compound was administered at doses of up to 600 mg/kg/day, which was equivalent to 224 mg/kg of free DMH. He also argues that due to the structural similarities of EMH and DMH, the toxicity of both compounds should be similar, and therefore a separate subchronic study of EMH should not be necessary. Similarly, the consultant proposes that teratology studies be performed on EMH only.

Discussion



Glycoserve is registered as a preservative for use in detergents, used only at detergent manufacturing sites. It will never be found in the household. Only the manufacturers of the detergents will handle Glycoserve. The maximum concentration will be 1 percent of Glycoserve. Therefore, consumer exposure would be at a maximum of 1 percent in a detergent, before the detergent is diluted with water for use (Glyco memorandum dated June 7, 1984; Tox Chemical #273 AB).

The toxicology memorandum dated March 12, 1985, requested that subchronic oral and teratology studies be performed on the organic moieties contained in Dantobrom; 5,5-dimethylhydantoin and 5-ethyl,5-methylhydantoin. The use pattern of the compound (use in hot tubs, spas, and swimming pools) dictates extensive human exposure for prolonged periods of time; therefore, in addition to the requested studies, data required under 40 CFR 158.38 are: teratology studies in two species, a rat reproduction study, a chronic rodent study, a chronic nonrodent study, oncogenicity studies in two species, a 21-day dermal subchronic study, and a 90-day oral subchronic study.

Regarding the arguments made for the use of the Glycoserve data to determine the toxicity of DMH, Toxicology Branch is not aware of any available data to determine the equivalency of the two compounds, thus it does not seem possible to determine whether the products would be identical in terms of the DMH available to the test animals given the two compounds. It is also unclear whether the test animals given the two compounds would be exposed to similar hydrolysis or metabolic products. It is possible that the pharmacokinetic properties of Glycoserve may not be identical to DMH, possibly resulting in different maximum tolerated doses (MTD) to be tested in oncogenicity and teratology testing. It does not seem reasonable to extrapolate data from Glycoserve which is a mixture of chemicals to DMH, the main component of Dantabrom. For the reasons cited above, Toxicology Branch cannot accept the studies done on Glycoserve in lieu of data generated for DMH.

The acute dermal $LD_{50}$ study and the 72-hour absorption study referenced by the Registrant's consultant do not preclude the need for the 21-day dermal toxicity study required under 40 CFR 158.38.

Recommendations

Subdivision F of the Pesticide Assessment Guidelines §82-1 and §82-3 requires that toxicity testing be performed with the technical grade of each active ingredient. Toxicology Branch recognizes that it is most appropriate to test the organic moieties produced by dechlorination and debromination of Dantobrom in water. Considering the preponderance of DMH in the formulation (approximately 90 percent), and the close structural similarity between DMH and EMH, toxicology data on DMH might be adequate to determine the safety of the compound. The toxicology data required for registration of Dantobrom for use in spas and swimming pools are: teratology studies in two species, a rat reproduction study, a chronic rodent study, and chronic nonrodent study, oncogenicity

studies in two species, a 21-day dermal subchronic study, and a 90-day oral subchronic study. Also, a 90-day dermal toxicity study of DMH, instead of a subchronic oral and 21-day dermal toxicity study, would be acceptable to Toxicology Branch.