2-27-81

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

FEB 27 1981

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Baquacil; EPA Reg.#10182-RO; Additional Data
CASWELL#676 Accession#244217

FROM: William Dykstra, Toxicologist
Toxicology Branch, HED (TS-769) WHD FDC 2/10/81

TO: A.E. Castillo (32)
Registration Division (TS-767) WDB

Recommendations:

1) The results of the two newly submitted skin sensitization studies demonstrate that under different experimental conditions, PHMB can be a moderate sensitizer to guinea pig skin.

In both test cases the concentration of PHMB was well above the Baquacil swimming pool use level of 0.001% PHMB.

In contrast, the photo-reaction patch test with 5% PHMB using natural sunlight with human subjects (25 panelists) provides human data which were suggestive of the fact that no human skin sensitization occurred under the conditions of the experiment. Toxicology Branch believes that the negative results of the human study should supersede the positive results of the guinea pig studies.

Therefore, Toxicology Branch concludes that human skin sensitization to Baquacil at the exposure level encounte. in swimming pools is unlikely to occur.

However, additional precautionary labeling may be added to the 20% Baquacil concentrate in order to keep skin contact to a minimum, thereby avoiding any potential human skin sensitization from contact with the concentrate. The additional need for precautionary labeling to protect human skin from the concentrate is found in the submitted skin irritation study (Exhibit D).

Review:

1. Exhibit A: Report No. CRL/T/1423; Vantocil IB; Skin Sensitization Studies (ICI Ltd.; Organics; CTL Ref. 400156/001; July 18, 1980)

Test Sample:

Vantocil IB (BX 791/2 (ADGM 1021) was supplied as a clear liquid, with a shelf-life in excess of two years.

Magnusson and Kligman Study:

Vantocil IB was used as a 1% (w/v) aqueous solution in the induction phase and was used as supplied for topical application and challenge.

Buehler Study:

Vantocil IB was used as a 10% (w/v) aqueous solution for topical induction applications and challenge. 20%, 10%, and 1% (w/v) aqueous solutions were used for rechallenge.

Results:

Magnusson and Kligman Study:

Challenge of test and control guinea pigs resulted in signs of mild to moderate erythema in 14 out of 20 test animals and mild erythema in 1 out of 8 controls at 24 hours. At 48 hours mild to moderate erythema was present in 15 out of 20 test animals and mild erythema was still present in one control animal. Although one control showed signs of skin irritation, the test material should be considered as having caused skin sensitization under the conditions of this study.

Buehler Study:

Challenge of test and control guinea pigs resulted in signs of faint erythema in 6 out of 10 test animals at 24 hours, but there were no signs of erythema in any of the control animals. Rechallenge with a 20% solution of the test material resulted in faint to moderate erythema in 8 out of 9 test animals and faint erythema in 3 out of 10 controls (one test animal did not receive the 20% challenge application). Rechallenge with a 10% solution resulted in faint erythema in 3 out of 10 test animals but not in controls, and rechallenge with a 1% solution did not cause an erythematous response in either test or control animals.

In conclusion, a 10% solution of the test material, is a moderate sensitizer to guinea pig skin under the conditions of this study. The lack of a response with a 1% solution at rechallenge is suggestive of a challenge dose-response relationship with this material.

Conclusion:

Vantocil IB was a skin sensitizer in guinea pigs under the conditions of the two studies.

Classification: Core-Minimum Data

2. Exhibit B. Skin Sensitization Tests on PHMB (20% in water) and Antibacterial 9073 (25% in water) (ICI, Ltd.; Report No. TR/684, 1/6/69)

Reviewed in memo of 6/15/78 from William Dykstra to Libby Zink.

Classification: Inadequate Study

(a) At least 10 applications of the test material is required before challenge to assess allergic response.

3. Exhibit C: Photo-reaction Patch Test using Natural Sunlight (Hilltop Research, Project No. 76-165-72; June 10, 1976)

Reviewed in memo of 6/15/78 from William Dykstra and Libby Zink.

Conclusion: Baquacil SB and Vancide TH were not skin senitizers in humans.

Classification: Core-Minimum Data

4. Exhibit D: Report No. CTL/T/1409; Vantocil P; Skin Irritation Study (ICI, Ltd.; CTL Ref. Y00156/002; February 21, 1980).

0.5 ml of test material was applied to intact and abraded skin sites on the fur clipped trunks of six NZW rabbits under an impervious cuff for 24 hr.

Observation and evaluation at 24 and 72 hours after treatment.

Results: P.I. = 2.6; moderate irritant to intact skin and severe irritant to abraded skin. Well defined to moderate erythema was observed in each animal at each skin site at 24 hr. This had subsided slightly at 72 hours. Slight to moderate edema was observed in all animals except one (where there was no edema). In addition, it was noted that the abrasions in each animal appeared blanched and thickened with scabbing for up to ten days following the original application.

These observations were restricted to the abraded skin sites although a few sites of intact skin although a few sites of intact skin showed similar signs. However, the signs of blanching on the intact skin were thought to be associated with areas of clipper damage. By day 21, there were signs of scabbing and healing at the site of the abrasions.

In a separate study, three male rabbits were treated with the test material as described in the methods section. Histopathological examination of intact and abraded skin sites indicated moderate to marked acute inflammation characterized by epidermal acanthosis and a polymorphonuclear cell infiltrate in the superficial corium. There were also areas of focal necrosis extending slightly into the corium.

The necrotic and inflammatory foci appeared to be perifollicular in location.

Classification: Core-Minimum Data; TOX Category II: WARNING

TS-769:th:TOX/HED:WDYKSTRA:2-6-81:#2