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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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MEMORANDUM

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

SUBJECT: Polyhexamethyl Biguanide: Review the Proposed Use in Apparel

TO: Adam Heyward
Product Manager, Team # 34
Regulatory Management Branch II (RMB II)
Antimicrobials Division (AD)

FROM: Jonathan C. Chen, Ph.D. *Jonathan Chen* 12/26/00
Toxicologist, RASSB / AD

THRU: Allen Vaughan *Allen W. Vaughan*
Team Leader, Team Three 12-28-00
RASSB / AD

And

Norm Cook *Norm Cook*
Chief 01/02/01
RASSB / AD

DP BARCODE: D269684

P.C. CODE: 111801

REGISTRANT : Avecia Inc.
1405 Foulk road
P.O. Box 15457
Wilmington, Delaware 19850-5457

Introduction

The company (Avecia Inc.), has proposed to amend the Vantocil IB (20%PHMB aqueous solution) labeling to include items of apparel among the types of articles that can be treated. According to the Technical Information Bulletin Provide by the registrant, when using Vantocil IB in cellulosic materials and textiles, Vantocil IB is diluted and applied to give 0.025 - 5.0% on the dry weight of the substrate. Application is by conventional means such as padding, spraying, soaking or exhaustion. The following are examples of the products suitable for antimicrobial finishing: bedding, upholstery, carpet, curtains, wall coverings, mops, dishcloths, yarns, cords, and toweling. In the previous submission, shirts, underwear, sportswear, hosiery, sweatshirts, uniforms, wipes, tissues, dressings, bandages, incontinence pads, diapers, and feminine hygiene products are also included in the example product lists. The RASSB was asked to review this application based on the toxicology information for PHMB.

Background

In 1996, Zeneca AG products requested the registration of Vantocil IB to be added to cellulosic textiles, and textile spin finishes. Because PHMB is a human skin sensitizer, the Agency concluded that the requested registration by Zeneca AG products could not be toxicologically supported. It is not possible to predict whether a threshold level exists for this kind of effect and subsequent immunologic reaction (skin sensitization or possibly other toxic manifestations). In addition, the Agency indicated that there were no chronic toxicity studies (dog and mouse), carcinogenicity studies (rat and mouse), reproduction study (rat) and dermal penetration study (rat) to evaluate the chronic exposure scenarios. After the submission of the one rat multi-generation study (MRID 43617401), one 1-year dog oral toxicity study (MRID 43620501), one 2-year rat chronic toxicity and carcinogenicity (MRID 44059301), one 2-year mice oncogenicity (MRID 44074201), and two unacceptable in-vitro dermal penetration studies, the registrant (Avecia Inc.), has asked the Agency to amend the Vantocil IB labeling to include the cellulosic materials and textiles (items of apparel) among the types of articles that can be treated.

Discussion

PHMB is a skin sensitizer, as shown in both human skin patch study (MRID 00127871) and guinea pig dermal sensitization studies (MRIDs 42674201 and 00053468). No threshold can be established for the skin sensitization effects. Therefore, for a sensitized individual, very low doses can trigger the allergic reaction. It is difficult to predict the subsequent immunologic reaction (may vary from skin reaction or other toxic system effects) resulting from use of the treated products. With the potential long term exposure to some of the fabric materials, both initiation and subsequent sensitization may happen. Especially, some individuals with immature immune systems (like babies) or individuals with impaired immune systems (like AIDS patients) are also among the potential exposed population. On December 18, 2000, the Human Identification Assessment Review Committee (HIARC) evaluated the submitted toxicological studies, and agreed with the Agency's previous conclusion that skin sensitization is still an issue for the current registration. In addition, through chronic dermal exposure, 20% PHMB in aqueous solution appeared to induce hemangiosarcoma in the mouse painting study (MRID 00104796). The same types of cancer were noticed in both newly submitted 2-year rat oral chronic toxicity and carcinogenicity study (MRID 44059301) and 2-year oral mice oncogenicity study (MRID 44074201).

Conclusions

The requested registration cannot be toxicologically supported, because:

- (1). PHMB was demonstrated to be a human skin sensitizer; and
- (2). With the concern of long term chronic exposure, PHMB may cause cancer through the dermal exposure route.