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Contractor	CENTRE INFL DE TOXICOLOGIE		
Document Title	INITIAL SUBMISSION: T-AMYL PEROXYETHYL-2-HEXANOATE, SKIN SENSITIZATION TEST IN GUINEA-PIGS (MAXIMIZATION METHOD OF MAGNUSSON, B. & KLIGMAN, A.M., W/CVR LTR DATED 102999 (SANITIZED)		
Chemical Category	HEXANEPEROXOIC ACID, 3,4,4-TRIMETHYL-,1,1-DIMETHYLETHYL *, *		

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COMPANY SANITIZED

October 29, 1999

Document Control Officer
Attn: Section 8(e) Coordinator
TS-790
EPA/OPPT
401 M Street, SW
Washington, DC 20460

MR 26051

8EHQ-99-14577
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Re: TSCA Section 8(e) Notification

Dear Sir/Madam:

Akzo Nobel Chemicals Inc. (ANCI) is submitting to the EPA this notification in accordance with TSCA Section 8(e) and EPA's Statement of Interpretation and Enforcement Policy 43, Fed. Reg. 1110 (March 16, 1978).

Skin sensitization studies (Magnusson and Kligman method) in guinea pigs were conducted with Hexaneperoxoic acid, 3,4,4-trimethyl-, 1,1-dimethylethyl ester (CAS# 13122-18-4) and Hexaneperoxoic acid, 2-ethyl-, 1,1-dimethylpropyl ester (CAS#686-31-7). Application of CAS# 13122-18-4 resulted in 53% of the sensitized animals with very slight erythema and 42% of the sensitized animals with well-defined erythema. Application of CAS# 686-31-7 resulted in 40% of the sensitized animals with very slight erythema and 45% of the sensitized animals with well-defined erythema.

ANCI is also seeking guidance on EPA policy concerning future 8(e) submissions of skin sensitization studies. Assuming potential or actual human exposure to the test substance, please clarify the significant risk reporting threshold for percentage of animals sensitized with respect to the severity of the reaction. That is, should animals with skin scores of 1 be considered positive responders?

As you will notice in the attached reports, the French laboratory that conducted the study on these substances did not count animals with a skin score of 1 as positive responders.

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Akzo Nobel Chemicals
300 South Riverside Pkwy
Cincinnati, Ohio 45202-4127
Tel: (513) 506-7501
Fax: (513) 506-7580

In skin sensitization studies, the severity of the response can be expressed as the percentage of animals that show a positive response. In the attached reports, we considered that all treatment animals showing a positive skin score should be counted as positive because all negative control animals showed a zero score. We would very much appreciate your guidance in this matter.

The attachments to this TSCA 8(e) notification contain Confidential Business Information (CBI), and therefore we have circled in red all CBI on the attachments that are marked "Confidential". We have also included a sanitized copy of the attachments.

Sincerely,



Edwin C. Bisinger Jr., M.S., DABT
Product Regulatory Manager

Telephone: 312-906-7639
Telefax: 312-906-7749
e-mail: edwin.c.bisinger@akzo-nobel.com

SUMMARY

At the request of _____, the potential of the test substance t-AMYL PEROXYETHYL-2-HEXANOATE (batch No. 616-9809-715 (19/09/98)) to induce delayed contact hypersensitivity was evaluated in guinea-pigs according to the maximization method of Magnusson and Kligman and to OECD (No. 406, 17th July 1992) and EC (92/69/EEC, B.6, 31st July 1992) guidelines. The study was conducted in compliance with the principles of Good Laboratory Practice Regulations.

Methods

Thirty guinea-pigs were allocated to two groups: a control group 1 (five males and five females) and a treated group 2 (ten males and ten females).

On day 1, intradermal injections of Freund's complete adjuvant mixed with the test substance (treated group) or the vehicle (control group) were performed in the interscapular region.

On day 7, the same region received a topical application of sodium lauryl sulfate in vaseline (10%, w/w) in order to induce local irritation.

On day 8, the test substance (treated group) or the vehicle (control group) was applied to the same test site which was then covered by an occlusive dressing for 48 hours.

On day 22, after a rest period of 12 days, all animals of the treated and control groups were challenged by a cutaneous application of the test substance to the right flank. The left flank served as control and received the vehicle only. Test substance and vehicle were maintained under an occlusive dressing for 24 hours.

Skin reactions were evaluated approximately 24 and 48 hours after removal of the dressing.

Test substance concentrations were as follows:

Induction (treated group)

- intradermal injections: t-AMYL PEROXYETHYL-2-HEXANOATE (_____ at the concentration of 5% (w/w) in corn oil,
- topical application: t-AMYL PEROXYETHYL-2-HEXANOATE undiluted.

Challenge (all groups)

- topical application: t-AMYL PEROXYETHYL-2-HEXANOATE (_____ undiluted.

At the end of the study, animals were killed without examination of internal organs. No skin samples were taken from the challenge application sites.

The sensitivity of the guinea-pigs in CIT experimental conditions was checked with a positive sensitizer, 2,4-Dinitro Chlorobenzene (DNCB). During the induction period, the reference substance DNCB was applied at the concentrations of 0.1% (w/w) (day 1) and 1% (w/w) (day 8) in corn oil. For the challenge application, the reference substance DNCB was applied at the concentration of 1% (w/w) in corn oil.