#603

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

SUBJECT: Paranitrophenol, Fungicide for Leather. Resistration 40510-E and Section 18 Exemption

DATE: 13 JUN 1977

FROM: Reto Engler Ph.D.
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TO: Pm, Mr. A. Castillo
and Mr. D. Rodier
Special Registration Section

Recommendations:

I. TB can not be recommended for the registration of this compound.

1. There is no label provided.

2. Toxicology data is supplied in summary form, except for the patch and wear tests carried out by the Army.

3. The test submitted from the Army files pertain to human skin patch tests and wear tests (one of the wear tests is illegilbe because of faulty photocopy). These test generally show that treated leather applied directly to the skin causes some irritation where as the wear tests were negative. An exposure even in the wear test, however cannot be totally excluded.

4. In light of this, subacute and long term dermal toxicity tests as well as teratology tests must be submitted or initiated before registration can be considered. The summarized studies; oral LD_{50}, dermal ALD, skin irritation, skin sensitization, eye irritation, cataract study, 30-day oral study, 12 week skin painting and mutagenicity studies must be submitted for review in detail.

5. The whole submission is arranged hodge-podge. Toxicity data are filed under "Data Sheets". Nothing is filed in section "C". Toxicity and efficacy data are filed together.

We request a resubmission in a orderly fashion, containing the actual data on studies relevant to this registration.

II. Based on the summary data and the apparently accident free use of this chemical we recommend for a granting of a section 18 exemption. Any future such requests should be made contingent on the resubmission for registration as

specified under I. The treated leather items must only include those which result in no or casual (in frequent) direct skin contact.

Review:

The following toxicity data are submitted in summary.

Oral LD_{50} (rat)	300-600 mg/kg
Dermal "Average LD" rabbit	1.5 to 2.0 g/kg
Skin irritation	Draize score of 1.6
Skin sensitization	Not acceptable protocol
Eye irritation	Draize score 8.6
Cataract (chicks)	negative
i.p. mice LD_{50}	75-99 mg/kg
i.v. ALD dog	10 mg/kg
30 day oral (mice & rats)	toxic at 1/5 of LD_{50}
12 week skin painting	20% solution showed no papillomas
Lifetime studies	not done
Ames test (mutagenicity)	negative
Reproduction study	not done
Teratology	not done

Army tests:

1. August 21, 1944. PNP treated leather should not be used for leather coming into direct contact with skin.

2. August 9, 1944. Leather (0.45% PNP) applied to human skin twice within 2 weeks. Of 124 individuals only 2 showed a mild reaction. Based on this test PNP was approved for casual skin contact material.

3. November 20, 1944. Patch test on 149 humans. Two patches were applied within a 2 week interval. 2 cases of irritation and 2 cases of "sensitization" occured. PNP was judged to be unacceptable for any skin contrast (0.4% PNP).

4. PNP wearing test AE40-440 unreadable.

5. June 23, 1958. Wearing test 24 subjects (concentration not stated). Blood analysis and urinalysis suggested no detectable effect of PNP.

6. February 2, 1967, test with shoes which contained 1.4% instead of 0.7% PNP were carried out. A single and a repeated patch test as well as a wear test was performed. In the single patch test an increase in irritation as a result of overage was noted. In the wear test no adverse reaction were noted; it is speculated that probably socks afford sufficient protection. It is also stated that heavy sweating and not changing socks may result in dermatitis. The overtreated shoes were accepted by the Army on a one time basis.

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