UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

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JUL 21 1981

MEMORANDUM

SUBJECT: Registration of a New Chemical
for use in swimming pools as a sanitizer and algistat

TO: Douglas D. Campt
Director
Registration Division (TS-767)

ICI Americas, Inc. submitted an application on May 16, 1978, for the registration of Baquacil [poly(nexamethylene biquanide hydrochloride)] for use as a swimming pool sanitizer. This applcation was assigned the file symbol 10182-RO. On September 11, 1980, ICI Americas, Inc. also requested an additional use as an algistat.

In the reviews for the uses of Baquacil, the following summaries are given.

Toxicology Branch

The following data have been submitted, reviewed and accepted in support of Baquacil.

1. Acute oral LD_{50}-rat. Toxicity category III

2. Acute dermal LD_{50}-rat. Toxicity category III

3. Primary skin irritation-rat. Toxicity category III

4. Primary eye irritation-rabbit. Toxicity category I

5. Photcreaction patch test. Baquacil was found to be essentially non-irritating and did not induce sensitization when evaluated on 26 panelists.

6. Subacute dermal-rabbit. No signs of systemic toxicity or skin irritations and test animals gained weight at the same rate as the controls. No histopathological or hematological abnormalities were found.

7. Teratogenicity study-mouse. Marginal retardation of ossification appears to occur at each treatment level (10, 20, and 40 mg/kg). However, the material is not teratogenic. The NOEL for delayed

CONCURRENCES

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ossification did not appear to have been established; by the original test data; however, the company submitted additonal evidence including historical data. It was then determined that the NOEL for delayed ossification was 10 mg/kg/day.

8. Teratogenicity study-rabbit. No terata or abnormalities were seen in either the soft of skeletal tissues of the treated groups.

9. Teratogenicity study-rat. Teratologic NOEL is considered to be 1000 ppm Baquacil in the diet during gestation of the rat.

10. Three generation reproductive study-rat. Baquacil administered through three successive generations at dietary levels of 200, 550, and 1300 ppm did not produce any adverse compound. The NOEL for this reproduction study is 1300 ppm.

11. 90-day oral toxicity-rat. This study provided only supplementary information. The feeding levels were 2,500 and 5,000 ppm. A conclusive NOEL could not be established because organ weights and histopathology on all animals were incompletely reported; however, adverse effects were not noted. Since the NOEL is established at 200 ppm by the rat 2 year feeding study, further information from the 90-day study was not necessary.

12. 90-day oral toxicity -beagle dog. The NOEL for this study is 5,5000 ppm. Weight gain was affected at 11,000 ppm.

13. 80-week skin painting study-mouse. Baquacil was not found to be oncogenic.

14. Life time feeding study-mouse. No oncogenic effects found.

15. Long-term feeding study-rat. NOEL is considered to be 200 ppm of Baquacil in diet of rats.

16. 26-week toxicity study-beagle dog. Dosage levels of 1500 and 4500 ppm produced distinct dose-related hepatoxicity and nephrosis, while the low dose (500 ppm) showed no such effects. The middle and high dose animals also showed effects on liver function such as increased retention values for bromo sulfophthalein (BSP), and one female at the low dose also showed a BSP retention time increase at 22 weeks.

While this finding in one animal did not allow in unequivocal determintion of a NOEL at 500 ppm, it is of minor significance considering the otherwise negative findings at this level of the study, and the overall lifetime evaluation of the chemical in other species.

17. Absorption and excretion studies-rat. Concentration found in the liver 0.6 ppm, kidney 0.8 ppm, and heart 0.1 ppm. None could be found in the brain, and undetectable levels of Baquacil were found after three weeks of the return to normal diet.

18. Salmonella reverse mutation test. Baquacil was not found to be mutagenic in this test system.

19. Mammalian cell transformation test. No mutagenic activity found in this test system.

20. Subacute inhalation-rat. Showed severe nasal irritation, dysphea and reduction in weight gain at 26, 12.5 and 2.75 mg/m^3. No abnormalities found in blood taken for biochemical analysis. No NOEL was established.

Ecological Effect Branch

The 48-hour aquatic invertebrate study is scientifically sound and with an LC_{50} of 0.18 ppm Baquacil is highly toxic to Daphnia magna. The 96-hour fish study is scientifically sound with an LC_{50} of 4.4 ppm for rainbow trout and an LC_{50} of 0.91 ppm for bluegill sunfish. The 0.91 ppm of Baquacil is highly toxic to bluegill and the 4.4 ppm of Baquacil is moderately toxic to rainbow trout. These studies meet the guideline requirements for fish acute LC_{50}s.

Environmental Fate Branch:

Baquacil shows no evidence of hydrolysis or photodegradation and the level of N-nitrosamine observed in the biguanide products is less than 0.01 ppm. After one year only 10-20% of the activty was recovered in etholamine traps for sandy loam (pH 7.0), sandy loam (pH 6.6), and loam solid treated with 1, 10, and 100 kg/ha. Over 50% is bound and of the 50%, 33-40% appears to be polymeric in nature. Baquacil is resistant to microbial attack, and at concentrations of 40 mg/l and higher the sludge process is affected such that

respiration is inhibited, pH changes to a basic nature (5.5-6.0 to 7.5-8.0) which lends to nitrification, inhibition, and suspended solids accumulation. From 10-23% of the material may be discharged into the receiving aquatic environment over 25 days or 1% per day depending on the concentrations of suspended solids. No effects is observed on anaerobic sludge digestion from 56-250 mg/l concentrations of Baquacil. TLC analysis indicated very low mobility in calcareous clay loam, coarse sand, coarse sandy loam, and loam soils. 90-95% of the parent material remained in the top 5 cm of the soil. No activity was detected in the leachate. Baquacil adsorbs to sandy loam (pH 6.6), sandy loam (pH 8.0), calcareous clay loam and coarse sand readily, with equilibrium reached in 1-4 days. The leaching study, soil metabolism, and activated sludge study lend to the fact that Baquacil is strongly adsorbed and desorption would not be rapid.

Adverse Data Submission

On January 27, 1981, ICI Americas submitted two new guinea pig sensitization studies conducted on Baquacil. These studies indicated that 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%. In contrast, the photoreaction patch test with 5% PHMB using natural sunlight with human subjects (24 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, and therefore human skin senitization to Baquacil at the exposure level encountered in swimming pools is unlikely to occur.

Recommendation: Based on the data submitted, it is recommended that Baquacil for use as a sanitizer and algistat for swimming pools be registered under Section 3(c)(5) of the Act.

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Non Concur

Date JUL 27 1981

Keto Engler
Chief, Disinfectants Branch
Registration Division (TS-767)

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