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

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM:

SUBJECT: Acute Studies Submitted in Support of a Registration

TO: Michael Mendelsohn
Product Manager (17)
Registration Division (TS-767C)

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Thru: Marcia van Gemert, Ph.D. M. van Gemert 9/9/88
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And

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Registrant: Griffin Corporation
Chemical: GX-071; N-ethyl perfluorooctanesulfonamide
Project: 8-0995
Caswell No.: 454E
Record No.: 225107

Action Requested: Reveiw of acute studies submitted in support of GX-071.

Comment: Griffin Corporation is requesting registration of GX-071, a technical of the toxicant N-ethyl perfluorooctanesulfonamide, for use in formulating end-use products in child-resistant bait stations for indoor cockroach control (per Note To Rick Tinsworth).

Seven acute oral, one acute dermal, primary dermal and eye irritation, a delayed contact hypersensitivity, and three mutagenicity studies were submitted on GX-071 in support of this request. These studies have been reviewed and the DER's are attached.

1) Acute oral LD_{50} in rats - UGA 002-2, dated April 21, 1986 (amended April 20, 1988). The combined LD_{50} was calculated as 543.48 mg/kg (607.14 mg/kg -males; 507.09 mg/kg-females). No target organ was identified.

2) Acute oral LD_{50} in rats - Project No. 86-1169, dated June 6, 1986 (amended April 20, 1988). The dose of 5000 mg/kg is above the LD_{50}. The liver and kidneys are the apparent target organs. Three males and four females died during the study.

3) Acute oral LD_{50} in rats - Project No. 85G-0037, dated October 31, 1985 (amended April 20, 1988). More than half of the animals died within 14 days of treatment with 5000 mg/kg.

4) Acute oral LD_{50} in rats - Project No. 85G-0034, dated September 30, 1985 (amended April 20, 1988). The LD_{50} for both sexes exceeded 817 mg/kg (HDT). No deaths or clinical signs of toxicity were observed.

5) Acute oral LD_{50} in rats - Project No. 86G-0031, dated October 23, 1986 (amended April 20, 1988). No LD_{50} was determined.

6) Acute oral LD_{50} in rats - UGA 003, dated November 20, 1985 (amended April 20, 1988). All animals died within 10 days following the administration of GX-071 at a dose level of 5 grams/kg (only dose tested).

7) Acute oral LD_{50} in rats - Project No. 86G-0001, dated February 6, 1986 (amended April 20, 1988). Only one animal died during the study. No LD_{50} was calculated. Under the conditions of the study, the LD_{50} for GX-071 would appear to be in excess of 6.0 grams/kg.

8) Single dose dermal toxicity in rabbits - Project No. 85G-0032, dated September 18, 1985 (amended March 21, 1988). The single dose dermal LD_{50} is greater than 2000 mg/kg (Tox. Category III).

9) Primary eye irritation in rabbits - Project No. 85G-0033, dated September 30, 1985 (amended March 21, 1988). GX-071 did not produce ocular irritation and was not considered an eye irritant.

10) Primary dermal irritation in rabbits - Project No. 85G-0031, dated September 26, 1985 (amended March 21, 1988). GX-071 was reported to be a potential mild skin irritant, based on a Primary Dermal Irritation Score of 0.13.

11) Delayed contact hypersensitivity in guinea pigs - SLS 3159.3, dated October 29, 1986 (amended March 24, 1988). No positive control was used in this study; therefore, the study is inadequate for use in the assessment of the potential of GX-071 to elicit a delayed contact hypersensitivity response in guinea pigs.

12) <u>In vitro</u> transformation of BALB/3T3 cells - Project No. 86G-0007, dated July 25, 1986 (amended March 21, 1988). Due to inadequacies in the study, this assay cannot be used to adequately assess the carcinogenic potential of GX-071 via its ability to transform BALB/3T3 cells <u>in vitro</u>.

13) <u>Salmonella</u>/mammalian activation gene mutation assay - Project No. 85G-0030, dated October 3, 1985 (amended March 21, 1988). The assay system was not responsive to the positive control chemicals under non-activated conditions and, therefore, the negative results observed with GX-071 cannot be interpreted.

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14) Sister chromatid exchange in Chinese hamster ovary cells - Project No. 86G-0002, dated July 25, 1986 (amended March 21, 1988). The study should be repeated using higher dose levels since the top dose did not result in at least a 50% reduction in the second mitosis (significant cell cycle delay).

The seven acute oral studies gave conflicting results (see Summary Table), which may be explained as due to the differences in the vehicle used and/or dosage regimen and/or volume administered. The test material, GX-071, is said to be insoluble in water, soluble in acetone and alcohol (neither of these was used in any of the studies), and its solubility in oil is less than 1%. The vehicles utilized in these acute oral studies were corn oil and soybean oil; one study utilized a gelatin suspension. The range of LD_{50} values obtained from the submitted studies is approximately 500 mg/kg to greater than 6.0 grams/kg. Using the lowest value obtained, GX-071 falls into Toxicity Category III. However, a question (raised by one of the study authors) regarding the availability of the test material for absorption, in light of GX-071's limited solubility, was not addressed. A more accurate expression of acute oral toxicity would probably have been determined if GX-071 had been tested in a vehicle in which it is soluble.

With regard to the mutagenicity studies submitted, the choice of studies provided fulfills the requirement for a battery of tests, since they address the three required categories of genetic effects; i.e., gene mutations; structural chromosomal aberrations; and other mechanisms of mutagenicity. Since all three of the submitted mutagenicity studies will have to be repeated (see above), the Registrant may choose to perform the same or different tests to provide data addressing these three categories.

Since the technical grade of GX-071 and the manufacturing use product are the same thing (as per our conversation on September 9, 1988), separate toxicity studies on the TGAI and the MP are not required. It is to be noted that toxicity data comparable to the toxicity data submitted on GX-071 will be required for an end-use product.

The request for registration of GX-071 for use in bait station roach traps for use in the home is not supported by the available toxicity data, since all of the mutagenicity studies and the delayed contact hypersensitivity study are inadequate.

CONCLUSION

The request for registration of GX-071 is not supported by adequate toxicity data. None of the mutagenicity studies is adequate. The delayed contact hypersensitivity study is also inadequate, based on the lack of a positive control. Additionally, one acute oral LD_{50} study (MRID # 406126-20) is classified as supplementary, pending submission of the body-weight data.

ACUTE ORAL TOXICITY SUMMARY TABLE FOR GX-071

Laboratory - Toxikon 9/30/85 MRID No. 406126-05
Vehicle - Corn oil
Dose Regimen - Single dose, 1.5 ml total
Species/Supplier - Sprague-Dawley rat/Charles River
LD_{50}: 817 mg/kg

Dose level (mg/kg)	Mortality Males	Females	Total
817	0/5	0/5	0/10
495	0/5	0/5	0/10
300	0/5	0/5	0/10

Laboratory - University of Georiga 4/21/86 MRID No. 406126-02
Vehicle - Soybean oil
Dose Regimen - Triple-divided, 1.5 hours apart, 2 ml/portion
Species/Supplier - Sprague-Dawley rat/Harlan
LD_{50}: 543 mg/kg (472-762)

Dose level (mg/kg)	Mortality Males	Females	Total
600	2/5	4/5	6/10
500	2/5	2/5	4/10
400	1/5	1/5	2/10
300	0/5	0/5	0/10

Laboratory - Toxikon 10/23/86 MRID No. 406126-06
Vehicle - Soybean oil
Dose Regimen - Triple-divided, 1.5 hours apart, 2 ml/portion
Species/Supplier - Sprague-Dawley rat/Charles River
LD_{50}: unable to calculate

Dose level (mg/kg)	Mortality Males	Females	Total
6000	4/5	1/5	5/10
2000	2/5	3/5	5/10
500	4/5	2/5	6/10
500	1/5	2/5	3/10
200	0/5	0/5	0/10
60	1/5	0/5	1/10

ACUTE ORAL TOXICITY SUMMARY TABLE FRO GX-071
(cont'd)

Laboratory - University of Georgia 11/20/85 MRID No. 40626-07
Vehicle - Soybean oil
Dose Regimen - Double-divided, 2.0 hours apart, total volume 4 ml
Species/Supplier - Sprague-Dawley rat/Harlan
LD_{50}: unable to calculate

	Mortality		
Dose level (mg/kg)	Males	Females	Total
5000	5/5	5/5	10/10

Laboratory - Toxikon 6/6/86 MRID No. 406126-03
Vehicle - Soybean oil
Dose Regimen - Triple-divided, 1.5 hours apart, 2 ml/portion
Species/Supplier - Sprague-Dawley rat/Charles River
LD_{50}: unable to calculate

	Mortality		
Dose level (mg/kg)	Males	Females	Total
5000	3/5	4/5	7/10

Laboratory - Toxikon 10/31/85 MRID No. 406126-04
Vehicle - Corn oil
Dose Regimen - Double-divided, 4.0 hours apart, total 5 ml
Species/Supplier - Sprague-Dawley rat/Charles River
LD_{50}: unable to calculate

	Mortality		
Dose level (mg/kg)	Males	Females	Total
5000	2/5	4/5	6/10

Laboratory - Toxikon 2/6/86 MRID No. 406126-20
Vehicle - Gelatin suspension
Dose Regimen - Single dose hardened gelatin
Species/Supplier - Sprague-Dawley rat/Charles River
LD_{50}: unable to calculate

	Mortality		
Dose level (mg/kg)	Males	Females	Total
6000	0/5	1/5	1/10
3000	0/5	0/5	0/10
1500	0/5	0/5	0/10