



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

CASWELL FILE

NOV 30 1987

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

Subject: Section 18 for Harmony on Wheat and Barley

To: Robert Forrest, PM-41
Registration Division, TS-767C

From: Marcia van Gemert, Ph.D.
Head, Section III
Toxicology Branch, HED

M. van Gemert 11/30/87

Thru: Theodore M. Farber, Ph.D.
Chief, Toxicology Branch, HED

*W. Farber
11/30/87*

Chemical: Harmony, DPX-M6316

Project No: 8-0195

Caswell No: 573S

Firm: Dupont

The State of Virginia has requested a Section 18 for use of Harmony on wheat and barley to control wild garlic. In the last Section 18 from Virginia (memo dated Feb. 2, 1987) for use of Harmony on wheat and barley numerous submitted studies on Harmony were cited. Two studies have been reviewed since that memo, a teratology study in rabbits, and a 2-generation reproduction study in rats. These studies are summarized below.

1. Teratology study in rabbits: Study # MR- 7108-001 dated april 10, 1985 from Haskell Laboratories. The NOEL and LOEL for maternal toxicity are approximately 158 and 511 mg/kg/day (these are the reported doses received by animals in the 200 and 650 mg/kg/day groups, respectively) based on mild reductions in maternal body weight gain at 511 mg/kg/day. Although the fetotoxic potential of the test material could not be ruled out (based on slight, nonsignificant decreases in fetal body weights at 511 mg/kg/day and on mild, nonsignificant increases in fetal and litter incidences of subcutaneous hemorrhages in all groups exposed to the test material), the noted effects were of negligible biological importance. Therefore the NOEL for developmental toxicity was greater than 511 mg/kg/day, the highest dose tested.

2. Two-generation reproduction study in rats, Study # 432-85, dated Dec. 3, 1985. Haskell Laboratories. The LELs for parental

reproductive or developmental toxicity of INM-6316 in rats could not be established since no toxic effects were demonstrated at any of the dose levels tested, (i.e., 25, 500 and 2500 ppm). Therefore, the NOEL for this study was greater than 2500 ppm, the highest dose level tested.

Recommendations:

If further work is conducted, it is recommended that:

1. the reproductive/developmental toxicity of the test material be tested at higher dose levels, levels that would produce parental or other toxicity.
2. More animals/sex/group be assigned to the study to provide at least 20 pregnant females per group.
3. Individual and summarized data be presented for food consumption, gestation lengths, precoital intervals, and the numbers of breeding pairs with evidence of copulation be given.

Core classification: supplementary

Company responses to the original toxicology reviews and new data on the triazine amine plant metabolite have recently been submitted and are presently under review. The original PADI was 0.005 mg/kg/day based on a NOEL of 10 mg/kg/day from the 90-day rat subchronic feeding study with a safety factor of 2000.

Theoretically, RCB is now handling all TMRCs of new chemicals and this action should be deferred to them for handling. However, the state of Virginia is asking for exactly the same tolerance as they did last year, and therefore the same numbers used last year should apply. The toxicology picture at this moment has not changed since last year.