

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

MAR - 5 1993

BRIEFING MEMORANDUM

SUBJECT: Registration of SAN 582H / Frontier® Herbicide

FROM: Lawrence E. Culleen, Acting Director
Registration Division (H7505C)

TO: Douglas D. Campt, Director
Office of Pesticides Programs (H7501C)

BACKGROUND

On October 9, 1990 Sandoz Agro, Inc. submitted applications for registration of SAN 582H / Frontier® Herbicide as an end use herbicide and a technical manufacturing use product, and a pesticide petition (PP 0F3918) requesting that EPA establish tolerances for the residues of the herbicide, dimethenamid, 2-chloro-N-[(1-methyl-2-methoxy)ethyl]-N-(2,4-dimethyl-thien-3-yl)-acetamide in or on the raw agricultural commodities (RACs) corn forage, corn silage, corn grain and corn stover at 0.01 parts per million (ppm). Sandoz subsequently editorially amended PP 0F3918 to read corn grain, corn fodder, and corn forage at 0.01 ppm.

Frontier® Herbicide, a liquid emulsifiable concentrate containing 7.5 lb/gal active ingredient, is applied via aerial or broadcast ground application at 0.765 to 1.5 lbs ai/acre to field corn as a selective pre-emergence herbicide for control of most annual grasses, certain annual broadleaf weeds and sedges. Frontier® will directly compete against the currently registered chloroacetamide herbicides: Dual, metolachlor, and Lasso, alachlor.

Adequate chemistry, toxicological, ecological effects, and environmental fate data have been submitted and reviewed to support the conditional registration of dimethenamid for use as a preemergence herbicide in field corn. The terms of the conditional registration will require Sandoz Agro Inc. to submit a Dominant Lethal Study.

SCIENTIFIC FINDINGS

TOXICOLOGY BRANCH			CONCURRENCES			
YMBOL	HA 582H	177505C	75050	A7505C	H 1505C	
JRNAME	Shue	Culleen	adach	SAN 582H	Shue	
ATE	3/2/93	3/2/93	3/2/93	3/2/93	3/4/93	

PA Form 1320-1 (12-70)

*U.S.GPO:1989-624-485/10186

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Technical and formulated (Frontier® Herbicide) dimethenamid are classified in toxicity categories III [CAUTION] and II [WARNING], respectively, based on eye irritation. Frontier Herbicide is a skin sensitizer and bears the label statement: "May cause skin sensitization reactions in certain individuals".

Dimethenamid was negative in Ames Salmonella Gene Mutation, Mouse Micronucleus, and in vitro Cell Transformation studies. Dimethenamid was positive for mutagenicity in an unscheduled DNA Synthesis study and in an in vitro chromosome aberration study. Sandoz has agreed to perform an additional Dominant Lethal Study as a conditional requirement of registration.

Developmental toxicity studies in rat and rabbit demonstrated no effects on progeny below the maternal Lowest Effect Level (LEL). In rat the no observed effect levels (NOELs) for maternal and developmental toxicity were 50 mg/kg and 215 mg/kg, respectively. In rabbit, the NOELs for maternal and developmental toxicity were 37.5 and 75 mg/kg/day, respectively. In a two-generation rat reproduction study, the parental and reproductive NOEL was 36 mg/kg/day for males and 40 mg/kg/day for females.

In a 13-week rat dietary study the NOEL was 500 ppm (33.5 mg/kg/day for males and 40.1 mg/kg/day for females). In a 13-week dog dietary study the NOEL was 100 ppm (2.5 mg/kg/day). In a 21-day rabbit dermal study the NOEL is 50 mg/kg with mild irritant effect at all dose levels. In a 1-year dog chronic Feeding study the NOEL was 250 ppm (9.6 mg/kg/day) with a LEL = 1250 ppm (49 mg/kg/day) due to liver changes.

In the rat Chronic Feeding / Carcinogenicity study the NOEL was 100 ppm (5 mg/kg/day). There is limited evidence of carcinogenicity based on the occurrence of increased benign and/or malignant liver tumors in males and ovarian tubular adenomas in females at the 1500 ppm dose groups. In the mouse Carcinogenicity study there is no evidence of carcinogenicity under conditions of the study.

The Health Effects Division Carcinogenicity Peer Review Committee classified dimethenamid as a Group C - possible human carcinogen and recommended that for the purpose of risk characterization the Reference Dose (RfD) approach should be used for quantification for human risk.

CHEMISTRY BRANCH I - TOLERANCE SUPPORT

CBTS has reviewed the proposed uses and indicates that residues of the herbicide, dimethenamid, 2-chloro-N-[(1-methyl-2-methoxy)ethyl]-N-(2,4-dimethyl-thien-3-yl)-acetamide are not expected to exceed 0.01 parts per million (ppm) in corn grain, corn fodder, and corn forage. Secondary residues are not anticipated in meat, milk, poultry and eggs. An adequate analytical method is

available to enforce the proposed tolerances. The method has completed a successful Petition Method Validation in the Agency's Analytical Chemical Branch laboratories.

TOLERANCE ASSESSMENT

The dimethenamid Reference Dose (RfD) was established at 0.05 mg/kg/day based on the rat chronic feeding study. Tolerances established for dimethenamid on corn grain and feed raw agricultural commodities are at the analytical limit of quantification of 0.01 ppm. Dietary exposure to dimethenamid was evaluated under the Dietary Risk Evaluation System. The Theoretical Maximum Residue Concentration is 0.007% of the Reference Dose.

PRODUCT CHEMISTRY

The inert ingredients in the formulation are cleared for use. All product chemistry data requirements have been satisfied.

ENVIRONMENTAL FATE AND GROUNDWATER BRANCH

Dimethenamid is stable to hydrolysis and the primary means of dissipation for dimethenamid applied on the soil surface is by photolysis and once below the soil surface by microbial metabolism. Depending on the soil characteristics dimethenamid has the potential to be moderate to highly mobile material. Although dimethenamid has the potential to be highly mobile, this was not demonstrated in any of the four field dissipation studies in which dimethenamid and oxalamide (the primary degradate) were not detected below the 20-30 cm soil segments. Dimethenamid has a rapid to moderately rapid dissipation rate with reported half-lives ranging from 8 days (Missouri and North Carolina) to 43 days (Minnesota) in the four terrestrial field dissipation studies.

Dimethenamid appears to have low potential to bioaccumulate. Dimethenamid and its degradates have a low potential to accumulate in rotational crops.

Based on available information dimethenamid could result in groundwater contamination under normal use. Dimethenamid has the potential to be highly mobile although it was not detected below 20-30 cm in field dissipation studies. Dimethenamid demonstrated physical characteristics of persistence and mobility that are in the range associated with known leachers. Therefore, the following Groundwater Advisory must appear on Frontier® Herbicide labels:

Groundwater Advisory

Dimethenamid has properties that may result in groundwater contamination. Application in areas where soils are permeable and groundwater is near the surface

or in coarse soils, could result in groundwater contamination.

Other Environmental Hazard Statements

Following application and during rainfall events that cause runoff, dimethenamid may reach surface water bodies including streams, rivers and reservoirs.

Care must be taken when using this product to prevent back siphoning into wells, spills, or improper disposal of excess pesticide, spray mixtures or rinsates.

Check valves or anti-siphoning devices must be used on all mixing equipment.

ECOLOGICAL EFFECTS BRANCH

Dimethenamid was shown to be practically non-toxic to avian species, moderately toxic to coldwater and warmwater fishes, slightly toxic to aquatic invertebrates, and practically non-toxic to honey bees. Frontier® Herbicide is highly toxic to some non-target plants.

Based on the toxicity data, dimethenamid will cause minimal risk to mammalian, avian, and aquatic fish and invertebrate life. Non-target plants or endangered plants adjacent to the treatment area will be at risk. The following environmental hazard precautionary statements are required to appear on the Frontier® Herbicide label to mitigate the risk:

Environmental Hazard Statements

Do not apply when weather conditions favor drift from treatment areas (gusty winds, high temperatures, drought, low relative humidity, and when a temperature inversion exists). Do not apply directly to water, or to areas where surface water is present or to intertidal areas below the mean high-water mark. Do not contaminate water when disposing of equipment washwaters or rinsate.

Sandoz argued against adding a statement that drift would result in damage to sensitive plants adjacent to the treatment area for equity reasons since their competitors do not bear this statement and the ongoing drift studies will show that the concentration of herbicide off site will be less than the effect level. Also, Frontier® is not a contact herbicide but effects germination of plants. Therefore, this statement is not required to appear on the label, at this time. This decision will be reassessed once the drift data are submitted and reviewed.

PUBLIC INTEREST FINDING

BEAD determined that dimethenamid will not fill a need that is not currently being met with other registered pesticides or that the benefits from use of dimethenamid will exceed those of the existing alternatives. However, dimethenamid is likely to capture a portion of the current alachlor and metolachlor market. Because the application rate of dimethenamid is approximately half of these other product, successful market penetration would result in decrease in total pounds of herbicide use in corn. Also, successful competition could lower herbicide prices to farmers.

SUMMARY OF DATA GAPS

1. A Dominant Lethal Study is due two years after the date of the conditional registration.

2. Sandoz Agro Inc. is a participant in the EPA sanctioned NACA Spray Drift Task Force to develop a generic data base for spray drift data requirements. Product specific testing requirements are reserved pending completion and review of the generic data base.

RECOMMENDATION

I recommend that you concur with the Section 3(c)(7)(C) registrations of dimethenamid. The condition for registration shall require that Sandoz Agro, Inc. submit to the Agency a Dominant Lethal Study within the time frame specified in the registration notice.

CONCUR: _____

DO NOT CONCUR: _____

DATE: _____