

US EPA ARCHIVE DOCUMENT



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

W. L. Lanning
SRPD

013026

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

17-DEC-1998

MEMORANDUM

SUBJECT: *MOLINATE* - Report of the FQPA Safety Factor Committee.

FROM: Brenda Tarplee, Executive Secretary
FQPA Safety Factor Committee
Health Effects Division (7509C)

THROUGH: Ed Zager, Chairman
FQPA Safety Factor Committee
Health Effects Division (7509C)

TO: Christine Olinger, Risk Assessor
Reregistration Action Branch 1
Health Effects Division (7509C)

PC Code: 041402

The Health Effects Division (HED) FQPA Safety Factor Committee met on October 30, 1998 to evaluate the hazard and exposure data for molinate and recommended that the FQPA safety factor (as required by Food Quality Protection Act of August 3, 1996) be retained in assessing the risks posed by this chemical.

I. HAZARD ASSESSMENT

1. Determination of Susceptibility

The Hazard Identification Assessment Review Committee (HIARC) determined that there was clear evidence of increased susceptibility in rat fetuses following *in utero* exposure to molinate in developmental toxicity study. Increased susceptibility was also demonstrated in the developmental neurotoxicity study in rats.

In the prenatal developmental toxicity study in rats, developmental toxicity manifested as an increase in runting occurred at a dose lower than that which caused maternal toxicity characterized as decreased body weight, body-weight gain, and food consumption, increased salivation and dehydration, and RBC cholinesterase inhibition.

In the developmental neurotoxicity study in rats, the NOAEL for developmental neurotoxicity was not achieved, based on a reduction in the startle amplitude in the auditory startle test at all dose levels. The maternal NOAEL is 6.9 mg/kg/day, based on decreased body weight/gain and food consumption at 26.1 mg/kg/day (LOAEL).

In the prenatal developmental toxicity studies in rabbits, developmental and maternal toxicity were observed at the same dose levels.

There was no evidence of increased susceptibility to offspring in the two-generation reproduction study in rats, since reproductive/offspring toxicity in pups (decreased brain, testes, spleen, cauda weights, delayed vaginal opening, microscopic lesions in ovary, increased incidence of sperm abnormality, decreased % pups born live, pup survival and litter size) were observed at the same dietary levels where maternal toxicity effects were observed (increased incidence of abnormal sperm, decreased cauda weight, microscopic lesions in adrenal and ovary) in the parental animals. (*Memorandum*: L. Taylor to W. Phang, dated October 30, 1998; HED Doc. No. 012944).

2. Adequacy of Toxicity Database

There are no data gaps for the assessment of the effects of molinate following *in utero* and/or postnatal exposure.

3. Neurotoxicity

Neurotoxic effects are consistent findings in studies on molinate. Molinate was positive in a delayed neurotoxicity study in the hen, and neurotoxic effects were observed in the rat following both acute and subchronic oral exposures. Evidence of neurotoxicity was also observed in the following studies:

2-year chronic toxicity study - rat
Carcinogenicity study - mouse
Chronic toxicity study - dog
Mechanistic study - rat
Range finding developmental studies - rat
Subchronic toxicity inhalation study - rat

Refer to the HIARC report on molinate for the details on findings (HED Doc. No. 012944).

II. EXPOSURE ASSESSMENT AND CHARACTERIZATION

1. Dietary (Food) Exposure Considerations

Molinate is applied early- to mid-season as a pre-plant, post-plant, and post-flood herbicide used on rice. The maximum seasonal rate is 9 lb ai/A in 2 or 3 applications. The parent compound, 4-hydroxy-molinate, and molinate acid are regulated and included in the risk assessment. No Codex MRLs have been established.

There are no monitoring data (FDA, PDP, etc) for molinate, however, fourteen field trials are available reflecting two formulations and four different application scenarios. Residues of molinate and its metabolites were found at less than the limit of quantitation for half of the field trials. Residues detected in six of the remaining trials were less than 0.25 ppm; and in one trial, residues of the hydroxy compound and the molinate acid were detected at 0.56 ppm and 0.12 ppm, respectively (LOQ for each analyte is 0.05 ppm). The metabolites are not considered to be any more toxic than the parent (the parent compound was not detected in any of the trials).

Residues of molinate are distributed throughout the plant with hay/straw exhibiting higher residues than grain. Meat and milk tolerances, however, are not required (Category 3, 40 CFR §180.6).

The HED Dietary Exposure Evaluation Model (DEEM) is used to assess the risk from acute and chronic dietary exposure to residues of molinate in food. The preliminary DEEM analyses, assuming tolerance level residues and 100% crop treated, indicate that refinements will be required for molinate. Additional refinements may include averaging of residues (since rice is a blended commodity), use of a processing factor (residues in polished rice are approximately one-third of raw grain), and incorporation of percent crop treated information.

2. Dietary (Drinking Water) Exposure Considerations

The environmental fate data base for molinate is complete. These data indicate the parent compound is persistent and is expected to reach surface water. This is supported by the available monitoring data.

Surface water monitoring data are available (for the parent) and will be used for risk assessment since there are no standard rice models for conducting drinking water exposure assessments. Data are available from the USGS, State of California, State of Arkansas, and other sources. Not all of these data represent locations where drinking water exposure is possible. Additionally, there is concern for the lack of characterization of these data for localities downstream of rice fields in the Southeast.

3. Residential Exposure Considerations

There are currently no registered residential uses of molinate, therefore, this type of exposure to infants and children is not expected.

III. SAFETY FACTOR RECOMMENDATION AND RATIONALE

1. FQPA Safety Factor Recommendation

The Committee recommended that the FQPA safety factor for protection of infants and children (as required by FQPA) be retained.

2. Rationale for Retaining the FQPA Safety Factor

The FQPA Safety Factor Committee recommended that the FQPA safety factor be retained due to:

- ▶ Increased susceptibility observed in the prenatal developmental toxicity study in rats.
- ▶ Increased susceptibility observed in the developmental neurotoxicity study in rats.
- ▶ Reproductive effects *were seen* in mice (anti-fertility study) and rats (sperm morphology study) following oral administration (although there was no evidence of increased susceptibility in the 2-generation reproduction study).
- ▶ Uncertainty associated with the lack of characterization for the surface water monitoring data used for drinking water exposure assessments.

3. Population Subgroups for Application of the Safety Factor

The Committee determined that the 10x FQPA safety factor is applicable for the following subpopulations:

Acute Dietary Assessment: The Committee determined that the FQPA Safety Factor should be retained (10x) for acute dietary risk assessment for All Populations which

include Infants and Children because the increased susceptibility was demonstrated in both the prenatal developmental toxicity and developmental neurotoxicity studies.

Chronic Dietary Assessment: The Committee determined that the FQPA Safety Factor should be retained (10x) for chronic dietary risk assessment for **All Populations which include Infants and Children** because of the concern for the severe reproductive effects seen following repeated oral exposures in studies with rats and mice.