Molinate; CASRN 2212-67-1

Human health assessment information on a chemical substance is included in the IRIS database only after a comprehensive review of toxicity data, as outlined in the IRIS assessment development process. Sections I (Health Hazard Assessments for Noncarcinogenic Effects) and II (Carcinogenicity Assessment for Lifetime Exposure) present the conclusions that were reached during the assessment development process. Supporting information and explanations of the methods used to derive the values given in IRIS are provided in the guidance documents located on the IRIS website.

STATUS OF DATA FOR Molinate

File First On-Line 09/26/1988

<table>
<thead>
<tr>
<th>Category (section)</th>
<th>Assessment Available?</th>
<th>Last Revised</th>
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<tbody>
<tr>
<td>Oral RfD (I.A.)</td>
<td>yes</td>
<td>09/26/1988</td>
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<tr>
<td>Inhalation RfC (I.B.)</td>
<td>not evaluated</td>
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<tr>
<td>Carcinogenicity Assessment (II.)</td>
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I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

I.A. Reference Dose for Chronic Oral Exposure (RfD)

Substance Name — Molinate
CASRN — 2212-67-1
Primary Synonym — Ordram
Last Revised — 09/26/1988

The oral Reference Dose (RfD) is based on the assumption that thresholds exist for certain toxic effects such as cellular necrosis. It is expressed in units of mg/kg-day. In general, the RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. Please refer to the Background Document for an elaboration of these concepts. RfDs can also be derived for the noncarcinogenic health effects of
substances that are also carcinogens. Therefore, it is essential to refer to other sources of information concerning the carcinogenicity of this substance. If the U.S. EPA has evaluated this substance for potential human carcinogenicity, a summary of that evaluation will be contained in Section II of this file.

I.A.1. Oral RfD Summary

<table>
<thead>
<tr>
<th>Critical Effect</th>
<th>Experimental Doses*</th>
<th>UF</th>
<th>MF</th>
<th>RfD</th>
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<tbody>
<tr>
<td>Reproductive toxicity</td>
<td>NOEL: 0.2 mg/kg/day</td>
<td>100</td>
<td>1</td>
<td>2E-3 mg/kg/day</td>
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<tr>
<td>Rat Fertility Study</td>
<td>LEL: 4 mg/kg/day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(gavage)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stauffer Chemical Co., 1981</td>
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</table>

*Conversion Factors -- 1 ppm = 0.05 mg/kg/day (assumed rat food consumption)

I.A.2. Principal and Supporting Studies (Oral RfD)


Six groups of male Sprague-Dawley rats were administered technical grade molinate by corn oil gavage at 0, 0.2, 4, 12, 30, and 60 mg/kg/day. Samples were taken from each dose solution for concentration analysis and archival retention. There were no significant reductions in male or female fertility indices at 0.2 mg/kg/day, but there were considerable reductions including dose-related alterations in sperm morphology in both male and female indices at 4 mg/kg/day. The necropsy data for pregnant females indicated a significant reduction in the number of viable fetuses/litter as a result of matings in the 4 mg/kg/day group. An increase in the number of resorptions/litter as a result of matings of untreated females with males in the 4 mg/kg/day dose group was also observed. Based on the above effects, the NOEL and LEL are 0.2 and 4 mg/kg/day, respectively.
I.A.3. Uncertainty and Modifying Factors (Oral Rfd)

UF — An uncertainty factor of 100 was used to account for the inter- and intraspecies differences. An additional UF was not used to account for the lack of a long-term dog study since the 13-week studies showed that the dog is not likely to be more sensitive than the rat.

MF — None

I.A.4. Additional Studies/Comments (Oral Rfd)

Data Considered for Establishing the Rfd:

1. Fertility - rat: Principal study - see previous description; core grade supplementary
2. 3-Generation Reproduction - rat: NOEL=0.63 mg/kg/day (HDT); core grade minimum (Stauffe Chemical Co., 1977a)
3. 2-Year Feeding (oncogenic) - rat: Systemic NOEL=0.63 mg/kg/day; Systemic LEL=2 mg/kg/day (increase in organ weight); core grade minimum (Stauffe Chemical Co., 1977b)
4. 13-Week Feeding - dog: NOEL=22.5 mg/kg/day; LEL=45 mg/kg/day (increased thyroid weight); no core grade (Stauffe Chemical Co., 1964a)
5. 13-Week Feeding - rat: NOEL=8 mg/kg/day; LEL=16 mg/kg/day (ovarian vacuolation); no core grade (Stauffe Chemical Co., 1964b)

Data Gap(s): Chronic Dog Feeding Study, Rat Teratology Study, Rabbit Teratology Study

I.A.5. Confidence in the Oral Rfd

Study — Medium
Database — Low
Rfd — Low

The critical study is of fair quality and is given a medium confidence rating. Since the database on chronic toxicity is poor, the database is given a low confidence rating. Low confidence in the Rfd follows.

I.A.6. EPA Documentation and Review of the Oral Rfd

Source Document — This assessment is not presented in any existing U.S. EPA document.

Other EPA Documentation — Pesticide Registration Files

Verification Date — 03/23/1988

Screening-Level Literature Review Findings — A screening-level review conducted by an EPA contractor of the more recent toxicology literature pertinent to the RfD for Molinate conducted in November 2001 did not identify any critical new studies. IRIS users who know of important new studies may provide that information to the IRIS Hotline at hotline.iris@epa.gov or (202)566-1676.

I.A.7. EPA Contacts (Oral RfD)

Please contact the IRIS Hotline for all questions concerning this assessment or IRIS, in general, at (202)566-1676 (phone), (202)566-1749 (FAX) or hotline.iris@epa.gov (internet address).

I.B. Reference Concentration for Chronic Inhalation Exposure (RfC)

Substance Name — Molinate
CASRN — 2212-67-1
Primary Synonym — Ordram

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Molinate
CASRN — 2212-67-1
Primary Synonym — Ordram

This substance/agent has not undergone a complete evaluation and determination under US EPA's IRIS program for evidence of human carcinogenic potential.
III. [reserved]
IV. [reserved]
V. [reserved]

VI. Bibliography

Substance Name — Molinate
CASRN — 2212-67-1
Primary Synonym — Ordram

VI.A. Oral RfD References


VI.B. Inhalation RfC References

None

VI.C. Carcinogenicity Assessment References

None
VII. Revision History

Substance Name — Molinate
CASRN — 2212-67-1
Primary Synonym — Ordram

<table>
<thead>
<tr>
<th>Date</th>
<th>Section</th>
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<td>I.A.</td>
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<td>I.A.6.</td>
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VIII. Synonyms

Substance Name — Molinate
CASRN — 2212-67-1
Primary Synonym — Ordram
Last Revised — 09/26/1988

- 2212-67-1
- 1H-azepine-1-carbothioic acid, hexahydro-, S-ethyl ester
- ethyl 1-hexamethyleneiminecarbothiolate
- felan
- hydram
- jalan
- Molinate
- molmate
- Ordram
- R-4572
- S-aethyl-N-hexahydro-1H-azepinthiocarbamat
- S-ethyl hexahydro-1H-azepine-1-carbothioate
- S-ethyl 1-hexamethyleneiminothiocarbamate
- S-ethyl-N-hexamethylenethiocarbamate
- Stauffer R-4,572
- yalan
- yulan