December 14, 2000

MEMORANDUM

SUBJECT: Molinate - Report of the Cancer Assessment Review Committee

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Executive Secretary  
Cancer Assessment Review Committee  
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The Cancer Assessment Review Committee met on November 1, 2000 to evaluate the carcinogenic potential of Molinate. Attached please find the Final Cancer Assessment Document.

cc: K. Dearfield  
R. Hill  
Y. Woo  
J. Pletcher
CANCER ASSESSMENT DOCUMENT

EVALUATION OF THE CARCINOGENIC POTENTIAL OF

MOLINATE (2nd Review)

P.C. Code: 041402

FINAL REPORT

14-DECEMBER-2000

CANCER ASSESSMENT REVIEW COMMITTEE
HEALTH EFFECTS DIVISION
OFFICE OF PESTICIDE PROGRAMS
COMMITTEE MEMBERS IN ATTENDANCE:

Karl Baetcke
William Burnam
Marion Copley
Kerry Dearfield
Vicki Dellarco
Virginia Dobozy
Richard Hill
Yiannakis Ioannou
Tim McMahon
Esther Rinde
Joyceyn Stewart
Clark Swentzel
Linda Taylor
Yin-Tak-Woo

NON-COMMITTEE MEMBERS IN ATTENDANCE

John M. Fletcher, Pathology Consultant
Lori Brunsman, Statistical Analysis

(Signature indicates concurrence with the assessment unless otherwise stated.)
DATA PRESENTATION:

Linda Taylor, Toxicologist

DOCUMENT PREPARATION:

Sanjivani Diwan, Executive Secretary

COMMITTEE MEMBERS IN ATTENDANCE:

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Les Broussard, Statistical Analysis

(Signature indicates concurrence with the pathology report and statistical analysis of data, respectively)
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EXECUTIVE SUMMARY

In the first review of molinate by the Cancer Peer Review Committee (CPRC; Document No. 009761, dated September 14, 1992), it was determined that 2-year dietary administration of molinate was associated with a statistically significant positive trend for kidney carcinomas, as well as combined adenomas/carcinomas and a significant increase by pairwise comparison of the control with 300 ppm dose group for combined kidney adenomas/carcinomas in male Crl:CD®(SD)BR rats. The evidence for increased incidence of benign interstitial cell tumors of the rat testes was considered equivocal. The Committee classified molinate as Group C - Possible Human Carcinogen - and recommended using the linear low dose extrapolation model (Q1*) based on the incidence of combined kidney tumors for quantification of potential human cancer risk. Molinate was not carcinogenic to female rats and male and female mice. The CPRC concluded that the doses tested in rats and mice were adequate to assess the carcinogenic potential of molinate.

As part of the reregistration process, the Cancer Assessment Review Committee (CARC) met on November 1, 2000 to reevaluate the carcinogenic potential of molinate in light of (1) the submission of the dominant lethal assay (as required by the CPRC); (2) a re-analysis of the kidney tumor data using the Peto analysis to account for the differential survival of the groups, and (3) upgraded UDS assay. The CARC also reviewed testicular tumor data to determine whether the proposed mechanism for reduced fertility might be applicable to testicular tumor formation.

In a 2-year chronic/carcinogenicity study, Crl:CD®(SD)BR rats [50 rats/sex/treatment group] were administered molinate [97.6%] at dietary levels of 0 ppm, 7 ppm [σ 0.3/σ 0.4 mg/kg/day], 40 ppm [σ 1.8/σ 2.0 mg/kg/day], and 300 ppm [σ 13/σ 15 mg/kg/day] for 24 months. A satellite group of rats [20 rats/sex] was administered molinate via the diet for 12 months at a dose level of 600 ppm [σ 29/σ 35 mg/kg/day] to evaluate pathology other than neoplasia. The CARC reaffirmed the CPRC’s earlier decision regarding the kidney and testicular tumors and based on the revised kidney tumor analysis concluded that 1) the administration of molinate was associated with significant positive trend for kidney adenomas, carcinomas and combined adenomas/carcinomas and a significant increase by pairwise comparison of controls with 300 ppm dose group for combined kidney adenomas/carcinomas; 2) the kidney tumors were not associated with alpha-2µ-globulin; 3) the incidence of kidney tumors exceeded the range for the historical controls range (adenomas: 0%-3.3%; carcinomas: 0%-3.3%), and 4) this tumor type is considered rare in male rats. Additionally, the CARC reaffirmed the CPRC’s conclusion that the evidence for testicular interstitial cell tumors was equivocal because: 1) there was no statistically significant increase by trend test or pairwise comparison, although the number of these tumors in the high-dose males was more than double the number in the control group; 2) the incidence was outside the historical control range (0%-6.7%); 3) tumors at all dose levels exceeded this range (low 13%, mid 12%, high 15% vs 6.7% in concurrent control); and 4) an incompletely reported 1980 Japanese study which also showed an increase in testicular tumors, provided additional support. The Committee determined that although the proposed mechanism for reduced male
fertility [decreased testosterone biosynthesis] might be applicable to testicular tumor formation, the histopathological lesions observed in the testes [degeneration and atrophy] do not appear to be compatible with tumor formation. Nevertheless, they raise a major concern regarding the reproductive effects of molinate.

The CARC also discussed the adequacy of the dose levels tested. Based on the opinion of the majority of the members, the Committee concluded that the dosing in the rat study was adequate and not excessive.

In accordance with the EPA Draft Guidelines for Carcinogen Risk Assessment (July 19, 1999), the CARC classified the data for molinate into the category "Suggestive evidence for carcinogenicity but not sufficient to assess human carcinogenic potential" based on the limited evidence of kidney tumors in male rats'. The Committee further concluded that quantification of carcinogenic risk is not required.
I. INTRODUCTION

On September 14, 1992, the Health Effects Division’s Cancer Peer Review Committee (CPRC) evaluated the carcinogenic potential of molinate (CPRC, 1992; Doc. No. 009761). The CPRC determined that the 2-year dietary administration of molinate was associated with a statistically significant positive trend for kidney carcinomas, as well as combined adenomas/carcinomas and a significant increase by pairwise comparison of controls with 300 ppm dose group for combined kidney adenomas/carcinomas in male Crl:CD®(SD)BR rats. The Committee classified molinate as Group C - Possible Human Carcinogen - and recommended that a linear low dose extrapolation model \( (Q_1^*) \) be used for quantification of potential human cancer risk.

On November 1, 2000, the Cancer Assessment Review Committee (CARC) reevaluated the carcinogenic potential of molinate as part of the reregistration process because additional information/data had become available since 1992 CPRC meeting.

The material available for CARC to review consisted of (1) the original CPRC data package [HED Document No. 009761], including summaries of the available studies and the Qualitative Risk Assessment; (2) the previous Cancer Peer Review Document [HED Document No. 009761]; (3) the Data Evaluation Records (DERs) for the rat and mouse studies; (4) the Quantitative Risk Assessments [original and revised]; (5) a newly-generated table showing the incidence of nephropathy in the male rat; (6) the DER for the dominant lethal assay in rodents [HED Document No. 013017; requested by the CPRC]; (7) Male Kidney Tumor Rates and Peto’s Prevalence Test results; and (8) HED Mechanism of Toxicity SARC memo [for fertility effects].

Although the mechanistic data were submitted to address the reproductive/fertility effects of molinate in the rodent, since the incidences of testicular tumors were slightly increased in the rat study, the Committee also re-evaluated this tumor type in light of these data.

A. EVALUATION OF CARCINOGENICITY EVIDENCE, REVIEW OF ADDITIONAL DATA

a. Evaluation of Carcinogenicity Evidence

1. Rat Chronic Toxicity/Carcinogenicity Study

Table 2. Original Analysis of Male Kidney Tumor Rates* and Exact Trend Test and Fisher's exact Test Results (p values)

<table>
<thead>
<tr>
<th></th>
<th>Dose (ppm)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>7</td>
<td>40</td>
<td>300</td>
</tr>
<tr>
<td>Cortical Adenomas (%)</td>
<td>0/57</td>
<td>0/46</td>
<td>0/49</td>
<td>2/48</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>p=</td>
<td>0.057</td>
<td>1.000</td>
<td>1.000</td>
<td>0.207</td>
</tr>
<tr>
<td>Carcinomas (%)</td>
<td>0/57</td>
<td>0/46</td>
<td>0/49</td>
<td>3/48</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>p=</td>
<td>0.013*</td>
<td>1.000</td>
<td>1.000</td>
<td>0.092</td>
</tr>
<tr>
<td>Combined (%)</td>
<td>0/57</td>
<td>0/46</td>
<td>0/49</td>
<td>5/48</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>p=</td>
<td>0.001**</td>
<td>1.000</td>
<td>1.000</td>
<td>0.018*</td>
</tr>
</tbody>
</table>

*Number of tumor-bearing animals/Number of animals examined, excluding those that died before week 55.

*First cortical adenoma observed at week 106, dose 300 ppm.

First carcinoma observed at week 92, dose 300 ppm.

Note: Significance of trend denoted at control.

Significance of pair-wise comparison with control denoted at dose level.

If *, then p < 0.05. If **, then p < 0.01.
3. **Non-neoplastic Kidney Lesions**

The non-neoplastic lesions of the kidney which were not discussed in the earlier CPRC document were evaluated by the CARC. The incidence of nephropathy in male rats, listed in Table 3 below, was evaluated by the CARC to examine the non-neoplastic changes that preceded the kidney tumor formation. It was determined that the incidence of nephropathy in male rats was comparable among the groups.

<table>
<thead>
<tr>
<th>Table 3. Nephropathy Incidence in Male Rats</th>
</tr>
</thead>
<tbody>
<tr>
<td>interval/grade/group</td>
</tr>
<tr>
<td>-----------------------</td>
</tr>
<tr>
<td>13-24 weeks n=</td>
</tr>
<tr>
<td>grade 1&amp;2</td>
</tr>
<tr>
<td>grade 3</td>
</tr>
<tr>
<td>grade 4&amp;5</td>
</tr>
<tr>
<td>total</td>
</tr>
<tr>
<td>12-month sacrifice n=</td>
</tr>
<tr>
<td>grade 1&amp;2</td>
</tr>
<tr>
<td>grade 3</td>
</tr>
<tr>
<td>grade 4&amp;5</td>
</tr>
<tr>
<td>total</td>
</tr>
<tr>
<td>all n=</td>
</tr>
<tr>
<td>grade 3</td>
</tr>
<tr>
<td>total</td>
</tr>
</tbody>
</table>

* a [%]; {}% total incidence

**Testicular tumors.** Although there was no statistically-significant increase in interstitial cell tumors of the testes, the CPRC noted that the number of these tumors in the high-dose males was more than double the number in the control group [Table 3, page 7 of CPRC document]. The historical control incidence was reported as ranging from 0% to 6.7% [mean 2.98%]. In the rat study, the incidence of the interstitial cell tumor of the testes at all dose levels exceeded this range [low 13%, mid 12%, high 15% vs 6.7% in concurrent control]. The evidence of testicular tumors was supported by the findings in a 1980 Japanese study. Although the raw data were not retained, this study revealed an increased incidence of interstitial cell tumors at dose levels of 100 ppm and 200 ppm [page 9 of CPRC document].

Molinate is reported to decrease testosterone biosynthesis. According to the registrant, Zeneca Corporation, the proposed mode of toxicity for reproductive effects of molinate involves interference with production of testosterone which requires the production of molinate sulfoxide and is dependent on the enzyme cholesterol ester hydrolase. The Registrant also argued that the reproductive toxicity to the rat is induced by a mechanism that is specific to rodents and that this
mechanism is not relevant to humans. The data were presented to the Mechanism of Toxicity
SARC (MTSARC, 2000; HED Doc # 014033). The CARC Committee discussed the mode of
action data and determined that decreased testosterone biosynthesis is a biologically plausible
mechanism for the induction of testicular tumors. However, it was noted that testicular
degeneration and atrophy rather than hyperplasia and hypertrophy were observed at 300 ppm in
the long-term study in rats and there was no evidence of cell proliferation leading to hyperplasia
of the testes following molinate exposure. These histopathological lesions do not appear to be
compatible with tumor formation. In addition, there were no data on LH levels which would
have provided evidence for the stimulation of Leydig cells. CARC reaffirmed the CPRC’s
conclusion that the evidence for testicular tumors was equivocal.

4. Adequacy of Dosing for Determining Carcinogenic Potential

The CPRC concluded that the highest dose [300 ppm] tested was adequate for the assessment of
carcinogenic potential. Survival was not adversely affected by treatment. In fact, fewer high-dose
rats died than in the control and other dose groups [both sexes]. Neurological signs [adducted
hindlimbs, ataxia, atrophied hindlimb, atrophied sacral region, atrophied thigh], which were
noted late in the study (during the 21st month), were observed at the high-dose level in both
sexes, although the males were affected more than the females. Decreased body weight, body-
weight gain, and food consumption were observed at the 300 ppm [BW 88% σ/87% Φ of control
at 54 weeks; 92% σ/95% Φ of control at 12 weeks]/BWG σ 85%/Φ 83% of control for 0-13
week interval; σ 79% and Φ 70% overall]. The decrease in body weight in males was observed
throughout the study, but the decrease in females at the 300 ppm dose level was not observed
until the =12 weeks due probably to the fact that this group weighed =6% more than the control
group initially.

The CARC revisited the issue of adequacy of dosing. There was a split decision among CARC
members (6 vs 9). Six members considered that the high-dose was excessive based on: 1) decrease in body weight and body weight gains (15% in a 90-day subchronic study and an
overall 20% decrease in the combined chronic/carcinogenicity study); 2) RBC cholinesterase
inhibition in some animals; and 3) presence of neurological clinical signs and decreased absolute
brain weight. Some members felt that these effects may have compromised the health of the
animals. The remaining 9 members considered that the dosing was adequate and not excessive
because: 1) the body weight decreases were accompanied by decrease in food consumption; 2)
survival was not adversely affected; in fact, survival at the highest dose was enhanced in both
sexes and 3) RBC ChE inhibition, late occurrence of neurological signs and histopathological
changes noted above were not considered to result in significant adverse consequences in these
animals. Based on the opinion of the majority of the members, the Committee concluded that the
dosing was adequate.

b. Mutagenicity

The data are discussed on pages 12-13 of CPRC document. The CPRC recommended that a
rodent dominant lethal study be performed because of the indicated activity for three endpoints in
the mouse lymphoma assays with activation, the observed germ cell interaction of molinate, and
the positive response in a published mouse bone marrow micronucleus test (page 13 of CPRC
document). Additionally, the CPRC suggested that a sister chromatid exchange assay in germ
cells or a UDS assay in germ cells be performed to fulfill the guideline requirement since the
available UDS assay was classified Unacceptable (page 13 of CPRC document).

Subsequent to the CPRC assessment, additional information on the UDS assay [regarding
cytotoxicity, hepatocyte viability, concentrations tested, number of cells for which net grain
counts were determined, and selection of areas for cytoplasmic grain counts] was submitted.
Upon review, it was concluded that molinate did not induce unscheduled DNA synthesis. The
study was upgraded to acceptable and satisfies the guideline requirement for Unscheduled DNA
Synthesis in Mammalian Cells in Culture [OPPTS 870.5550].

Additionally, the results of a dominant lethal assay were submitted. The study is acceptable and
satisfies the guideline requirement for a Dominant Lethal assay [OPPTS 870.5450]. The CARC
determined that molinate did not induce germ cell mutations.

c. **Structure-Activity Correlations**

There were no data on additional chemicals for consideration, but one of the Committee member
pointed out that triallate, an S-chloroallyl thiocarbamate, may be metabolically activated to
chlorinated genotoxic reactive intermediates which are not applicable to molinate. Therefore,
triaallate may not be a good structural analog for molinate as indicated in the CPRC document.

II. COMMITTEE'S ASSESSMENT OF THE WEIGHT-OF-THE-EVIDENCE

1. **Carcinogenicity**

The CARC reaffirmed the previous assessment by the CPRC regarding the kidney and testicular
tumors in male rats (CPRC, Document No.011437). The Committee concluded that molinate
was carcinogenic to male rats but not carcinogenic to female rats and male and female mice
based on the following weight-of-the-evidence:

a. Revised statistical analysis indicated that the administration of molinate was associated
with a statistically significant positive trend for kidney adenomas, carcinomas, as well as
combined adenomas/carcinomas and a significant increase by pairwise comparison of the
control with 300 ppm dose group for combined kidney adenomas/carcinomas in male
Crl:CD®(SD)BR rats. The increased incidence of kidney tumors in the male rat at the
high-dose level exceeded the available historical control data for both adenomas and
carcinomas (range for both: 0%-3.3%). The tumors occurred late in life, with first tumor
occurring at 92 weeks. The kidney tumors in male rats are considered to be rare tumors. The possible mode of action via α-2μ-globulin accumulation in the kidney was not demonstrated following molinate exposure. There was no increase in tumors in female Crl:CD®(SD)BR rats.

b. In male Crl:CD®(SD)BR rats, the incidence of testicular interstitial cell tumor exceeded the historical control incidences (range: 0%-6.7%), and the increase was observed at all dose levels but no-dose response was seen. The Committee also noted that the increase in tumor incidence was only marginal and the tumors occurred late in life, with first tumor occurring in high-dose males at 77 weeks. Although the evidence for interstitial testicular cell tumors is equivocal [no increase in trend or pair-wise comparisons], the evidence that the testes is a target organ and increase in testicular tumors in an incompletely reported Japanese study added support to the presumption that the testicular tumors may have been compound related.

The CARC, therefore, reviewed the testicular tumor data in light of the mechanistic data which demonstrated that molinate interferes with testosterone biosynthesis. The Committee determined that although this mechanism is biologically plausible for the induction of testicular tumor following molinate exposure, testicular degeneration and atrophy rather than hyperplasia and hypertrophy were observed in the long-term study in rats. These histopathological lesions do not appear to be compatible with tumor formation. Therefore, the submitted data do not provide compelling evidence for the proposed mode of action for testicular tumors. Nevertheless, they raise a major concern regarding the reproductive effects of molinate.

The CARC determined that the dosing in the rat study was adequate and not excessive to assess the carcinogenic potential of molinate based on 1) longer survival in both sexes of the high-dose rats; 2) decrease in body weight gain and food consumption; and 3) neurological and histopathological changes were not considered significantly adverse.

c. There was no compound-related increase in tumors observed in male or female mice up to dietary concentrations of 2000 ppm. The dose levels were considered adequate to determine the carcinogenic potential of the test material.

2. Mutagenicity

Based on the available data, the CARC concluded that there was a low concern for the mutagenicity of molinate.
1. Experimental Design

In a 2-year chronic toxicity/carcinogenicity study in rats, CrI:CD®(SD)BR rats [50 rats/sex/treatment group] were administered Molinate [97.6%] via the diet at dose levels of 0 ppm, 7 ppm [♂♂ 0.3/♀ 0.4 mg/kg/day], 40 ppm [♂♂ 1.8/♀ 2.0 mg/kg/day], and 300 ppm [♂♂ 13/♀ 15 mg/kg/day] for 24 months. A satellite group of rats [20 rats/sex] was administered Molinate via the diet for 12 months at a dose level of 600 ppm [♂ 29/♀ 35 mg/kg/day] to evaluate pathology other than neoplasia. An additional 20 rats/sex of the control group and 10 rats/sex/group of the treated rats were sacrificed at 12 months.

2. Discussion of Tumor Data

Kidney tumors. As discussed in the CPRC document [HED Document No. 009761, page 4], male rats displayed a statistically-significant positive trend for kidney carcinomas and combined adenomas/carcinomas and a significant increase by pair-wise comparison of controls with the 300 ppm group for combined kidney adenomas/carcinomas (Table 2 of this document). Data from a 10-day special study indicated that the kidney tumors were not associated with alpha-2-microglobulin accumulation. The CPRC determined that the kidney tumors were present at numbers above the mean and range for the historical controls (adenoma: mean: 0.93%, range: 0% - 3.3%; carcinoma: mean 0.56%, range: 0% - 3.3%); and this tumor type is considered rare in male rats.

Reanalysis of the kidney tumor data using the Peto Prevalence Test (Brunsman, 1999; Table 1) showed a statistically significant positive trend for kidney adenomas, which was not indicated by the previous analysis using the Exact Trend Test and Fisher's Exact Test (Table 2). Additionally, other p values were slightly changed from the previous analysis. The CARC reaffirmed the CPRC's conclusion that there was a statistically significant positive trend for kidney carcinomas and combined adenomas/carcinomas and a statistically significant increase by pairwise comparison of the 300 ppm dose group with the controls for combined adenomas/carcinomas. The Committee also determined that there was a significant (p<0.01) positive trend for kidney cortical adenomas in male rats.
Table 1. Reanalysis of Male Kidney Tumor Rates* and Peto’s Prevalence Test Results (p values)

<table>
<thead>
<tr>
<th>Dose (ppm)</th>
<th>0</th>
<th>7</th>
<th>40</th>
<th>300</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortical Adenomas (%)</td>
<td>0/17</td>
<td>0/15</td>
<td>0/19</td>
<td>2*28</td>
</tr>
<tr>
<td></td>
<td>(0)</td>
<td>(0)</td>
<td>(0)</td>
<td>(7)</td>
</tr>
<tr>
<td>p=</td>
<td>0.028*</td>
<td>-</td>
<td>-</td>
<td>0.132</td>
</tr>
<tr>
<td>Carcinomas (%)</td>
<td>0/32</td>
<td>0/30</td>
<td>0/29</td>
<td>3*44</td>
</tr>
<tr>
<td></td>
<td>(0)</td>
<td>(0)</td>
<td>(0)</td>
<td>(7)</td>
</tr>
<tr>
<td>p=</td>
<td>0.005**</td>
<td>-</td>
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<td>0.061</td>
</tr>
<tr>
<td>Combined (%)</td>
<td>0/32</td>
<td>0/30</td>
<td>0/29</td>
<td>5*44</td>
</tr>
<tr>
<td></td>
<td>(0)</td>
<td>(0)</td>
<td>(0)</td>
<td>(11)</td>
</tr>
<tr>
<td>p=</td>
<td>0.001**</td>
<td>-</td>
<td>-</td>
<td>0.027*</td>
</tr>
</tbody>
</table>

*Number of tumor-bearing animals/Number of animals examined, excluding those that died or were sacrificed before observation of the first tumor.

*First cortical adenoma observed at week 106, dose 300 ppm, in a final sacrifice animal.

*First carcinoma observed at week 92, dose 300 ppm.

Note: Significance of trend denoted at control.

Significance of pair-wise comparison with control denoted at dose level.

If *, then p < 0.05. If **, then p < 0.01.
3. **Structure-Activity Relationship**

   - Although thiobencarb has not been classified by IHE with respect to its carcinogenic potential, a dose-related increase in testicular interstitial cell tumors in male rats was observed. Additionally, thiobencarb was not mutagenic in *Salmonella* and human lymphocyte assays but was mutagenic in mouse micronucleus assay [see pages 14-16 of CPRC document for mutagenicity of other related compounds].

III. **CLASSIFICATION OF CARCINOGENIC POTENTIAL**

In accordance with the EPA *Draft Guidelines for Carcinogen Risk Assessment* (July 19, 1999), the Committee classified the data for molinate into the category "suggestive evidence for carcinogenicity but not sufficient to assess human carcinogenic potential" based on the following weight-of-the-evidence considerations:

1. Exposure to molinate resulted in a marginal increase in the incidence of tumors of the kidneys (adenomas, carcinomas, and combined adenomas/carcinomas) in male rats only. The evidence for testicular tumors in male rats was equivocal. There was no evidence of an increased incidence of tumors in female rats or in male and female mice. The evidence was limited to one sex of one species only.

2. Molinate was found to have a low mutagenicity concern.

3. The structurally related compound, thiobencarb also produced testicular tumors in male rats.

IV. **QUANTIFICATION OF CARCINOGENIC POTENTIAL**

Not required.
MOLINATE  Cancer Assessment Document  Final Report

VII. BIBLIOGRAPHY

Brunsmann, L. (1999) Revised Molinate Quantitative Risk Assessment (Q_{1*}) Based on Charles River Crl:CD(SD) BR Rat Dietary Study Using mg/kg b.w.^{345} /day Cross Species Scaling Factor. Memorandum from Lori Brunsmann, Science Analysis Branch to Virginia Dobozy, Reregistration Branch1, Health Effects Division, Office of Pesticide Program, dated Nov. 18, 1999. [Analysis of tumor data by Peto Prevalence Test was dated 7/19/2000]


MTSARC (2000) Assessment of Molinate by the Mechanism of Toxicity SARC. Memorandum from Linda Taylor, Reregistration Branch 1, Health effects Division to Wilhelmina Livingston, reregistration Branch, SRRD, Office of Pesticide Program. HED Doc # 014033 dated 3/8/00