MEMORANDUM:

SUBJECT: Registration #s: 11678-1,-2,-8,-9,-14,-40: Captan, miscellaneous toxicity data for review.

Tox. Chem. No.: 159
Accession No.: 252584, 252585

TO: H. Jacoby (PM 21)
Registration Division (TS-767C)

FROM: Marion P. Copley, D.V.M.
Section VI, Toxicology Branch
Hazard Evaluation Division (TS-769C)

THRU: Jane Harris, Ph.D., Section Head
Section VI, Toxicology Branch
Hazard Evaluation Division (TS-769C)
and
Theodore M. Farber, Ph.D., Branch Chief
Toxicology Branch
Hazard Evaluation Division (TS-769C)

Makhteshim Agan (america) Inc. has submitted a mouse acute oral and rat acute intraperitoneal (I.P.) study for review. The oral study is core-guideline, and the I.P. study is acceptable.

A Registration Standard is being prepared for Captan and a Special Review is currently underway.
DATA EVALUATION REPORT

STUDY TYPE: Acute Oral - Mouse

ACCESSION NUMBER: 252584

TEST MATERIAL: Captan

STUDY NUMBER: E.H./P., 1-1-106-83

SPONSOR: Makhteshim - Agan (America) Inc.

TESTING FACILITY: Pharmatox, Landkreis Hannover, Germany

TITLE OF REPORT: Acute Toxicological Study of Captan after Oral Application to the Mouse

AUTHORS: S. Dickhaus, E. Heisler

REPORT ISSUED: June 1983

CONCLUSION

Toxicity Category: III

Classification: Core-guideline

Combined LD50 14 day = 2110 (1901 - 2342) mg/kg
Slope = 1.22 (1.14 - 1.31)

MATERIALS: 1. Captan, white powder, 92.7 %
2. CFI-mice, Winkelmann, Paderborn strain, 26-28 g.

METHODS: Mice were fasted for 2 hours before dosing. Test material was administered orally by gavage in 1% methylcellulose. Animals were observed after treatment for deaths and toxic signs. The mice were weighed on days 0 and 14. Gross necropsy was performed on all animals that died on study and on all survivors which were sacrificed on day 14. Doses given and lethality are presented in the table under results.

RESULTS:

<table>
<thead>
<tr>
<th>Dose (mg/kg)</th>
<th>Males deaths/dosed</th>
<th>Females deaths/dosed</th>
<th>Combined deaths/dosed</th>
<th>Body weight (g) day 0</th>
<th>Body weight (g) day 14</th>
</tr>
</thead>
<tbody>
<tr>
<td>1500</td>
<td>0/5</td>
<td>0/5</td>
<td>0/10</td>
<td>26.8</td>
<td>27.6</td>
</tr>
<tr>
<td>1890</td>
<td>1/5</td>
<td>1/5</td>
<td>2/10</td>
<td>26.8</td>
<td>25.8</td>
</tr>
<tr>
<td>2380</td>
<td>4/5</td>
<td>3/5</td>
<td>9/10</td>
<td>26.6</td>
<td>24.0</td>
</tr>
<tr>
<td>3000</td>
<td>5/5</td>
<td>5/5</td>
<td>10/10</td>
<td>27.0</td>
<td>---</td>
</tr>
</tbody>
</table>
Clinical signs of toxicity included writhing, increased respiration rate, convulsions, tremors and staggering (observed in all treatment groups). Decreased body weight gain was dose related. Most of the deaths were within 24 hr. Gross necropsy showed: G.I. tract - hyperemia kidneys - lighter than normal livers - swollen

There was no mention of when clinical signs subsided.
STUDY TYPE: Acute Intraperitoneal - Rats  TOX. CHEM. NO.: 159

ACCESSION NUMBER: 252585

TEST MATERIAL: Captan

STUDY NUMBER: E.H./P., 1-4-107-83

SPONSOR: Makhteshim - Agan (America) Inc.

TESTING FACILITY: Pharmatox, Landkeis Hannover, Germany

TITLE OF REPORT: Acute Toxicological Study of Captan after Intraperitoneal Application to the Rat

AUTHORS: S. Dickhous, E. Heisler

REPORT ISSUED: August 1983

CONCLUSION

Toxicity Category: N.A.

Classification: acceptable

LD₅₀ (males) = 39.5 (35.3 - 44.2) mg/kg
Slope = 1.26 (1.18 - 1.35)
LD₅₀ (females) = 34.8 (31.1 - 39.0) mg/kg
Slope = 1.24 (1.15 - 1.34)

MATERIALS: 1. Captan, white powder, 92.7%
2. SPF, Wistar rats (strain Winkelmann, Paderborn), mean weights were: 200 g - males, 180 g - females.

METHODS: Test material was administered to rats by intraperitoneal injection in 1% methylcellulose. Animals were observed after treatment for deaths and toxic signs. The rats were weighed on days 0 and 14. Gross necropsy was performed on all animals that died on study and on all survivors which were sacrificed on day 14. Doses given and lethality are presented in the table under results.

RESULTS:

<table>
<thead>
<tr>
<th>Dose (mg/kg)</th>
<th>Males deaths/dosed</th>
<th>Females deaths/dosed</th>
<th>Males Body weight (g)</th>
<th>Females Body weight (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>0/10</td>
<td>0/10</td>
<td>day 0 201.6</td>
<td>day 0 182.7</td>
</tr>
<tr>
<td>30</td>
<td>1/10</td>
<td>2/10</td>
<td>day 14 239.2</td>
<td>day 14 197.8</td>
</tr>
<tr>
<td>40</td>
<td>5/10</td>
<td>7/10</td>
<td>day 0 200.2</td>
<td>day 0 193.3</td>
</tr>
<tr>
<td>50</td>
<td>9/10</td>
<td>10/10</td>
<td>day 14 237.7</td>
<td>day 14 183.3</td>
</tr>
</tbody>
</table>

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Clinical signs of toxicity initially included writhing (rapid onset), tonic-clonic convulsions, staggering, gasping and incoordination followed by sedation and coma. Decreased body weight gain was dose related. Reduced food and water consumption were also noted in the weekly reports for all groups. Most of the deaths were within 24 hr.

Gross necropsy showed: G.I. tract - hyperemia (acute deaths) livers - patchy pattern and increased organ weight (no numbers given) at the terminal sacrifice

There was no mention of when clinical signs subsided.