SUBJECT: Cell W524 20% Emulsifiable Concentrate Fungicide

DATE: 2/26/75

FROM: TB

TO: Product Manager

Registration No. 279-EOON-2990

Registrant: FMC Corporation

Action Requested: Registration

Related Petitions: none

Established Tolerances: none

Formulation: Cell W524 20% Emulsifiable Concentrate Fungicide

Active Ingredient: 20.6% N, N-[1,4-Piperazinediylibis (2,2,2-Trichloroethylidene)] bis [formamide]

Inert Ingredients

Use: Control of powdery mildew on roses (greenhouse).

Application Date: 10 to 12 ounces per 100 gallons of water as a spray

Toxicity Data Summary:

<table>
<thead>
<tr>
<th>Toxicity Test</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Rat Oral LD50 (Tech)</td>
<td>&gt;6,000 mg/kg</td>
</tr>
<tr>
<td>Acute Rat Oral LD50 (Tech)</td>
<td>16,000 mg/kg</td>
</tr>
<tr>
<td>Acute Rat Oral LD50 (20% EC)</td>
<td>5,830 mg/kg</td>
</tr>
</tbody>
</table>

* Cleared under 40CFR 180.1001 (d), 121.2520 (c) (5) and 121.2505 (d)

INERT INGREDIENT INFORMATION IS NOT INCLUDED
Acute Rat Oral LD$_{50}$ (20% EC) 6,050 mg/kg
Acute Rat Oral LD$_{50}$ (20% EC) 6,600 mg/kg
Acute Mouse Oral LD$_{50}$ (tech) >6,000 mg/kg
Acute Mouse Oral LD$_{50}$ (20% formulation) >6,000 mg/kg
Acute Dog Oral LD$_{50}$ (Tech) >2,000 mg/kg
Acute Rabbit Dermal LD$_{50}$ (20% formulation) >770 mg/kg
Acute Rabbit Dermal LD$_{50}$ (Tech) >10,000 mg/kg
Acute Rabbit Dermal LD$_{50}$ (20% EC) 2,500 mg/kg
Acute Rabbit Eye Irritation (Tech) no irritation reported
Acute Rabbit Eye Irritation (20% EC) slight corneal opacity

Guinea Pig Sensitization (20% EC)

13 Week Rat Feeding (Tech) NEL <2500 ppm
13 Week Rat Feeding (Tech) NEL 500 ppm
13 Week Dog Feeding (Tech) NEL <2500 ppm
13 Week Dog Feeding (Tech) NEL 100 ppm
21 Day Rat Dermal (20% EC) concentrations of 0.5% and 1.5% of the 20% EC produced slight irritation.

2 Year Dog Feeding (Tech) NEL 100 ppm
2 Year Rat Feeding (Tech) NEL 625 ppm
3 Generation Rat Reproduction (Tech) not reviewed because study is in German.
Rat Teratogenic (Tech) no teratogenic effects at highest fed level of 1600 mg/kg

Application Method: Spray
Application Frequency: Every 7 to 10 days as necessary.

Background Information

On May 25, 1973 a temporary permit was issued as 279-EXP-50C for 110 gallons. In the C.L. Smith letter of 7/5/73, eye irritation
for the undiluted technical material and for the undiluted formulated product were requested.

A review of the toxicity data in connection with this temporary permit could not be located.

Toxicity Data

Structure: \[
\begin{array}{c}
\text{Cl}_3 \text{C-CH-NH=C=O} \\
\text{N} \\
\text{Cl}_3 \text{C-CH-NH-C=O}
\end{array}
\]

Synonym—Triforine

Acute Rat Oral LD_{50} (Tech)—E. Merch—Darmstadt—3/20/73

The material tested was identified as Triforine "W524" (Lot No. 6/70)

Five Wistar-AF/HAN-EMD-SPF rats of each sex were used per level of 8,000, 10,000, 12,800 and 16,000 mg/kg. Test material was administered as an aqueous suspension in demineralized, water and CMC.

Results: LD_{50} > greater than 16,000 mg/kg. No mortality occurred. Decreased activity was observed in all rats for 24 hours. This condition continued in the 12,800 and 16,000 mg/kg level for 48 hours.

Acute Rat Dermal LD_{50} (Tech)—E. Merch—Darmstadt 3/20/73

The material tested was identified as Triforine. Five Wistar-AF/HAN-EMD-SPF Rats of each sex were tested at the level of 10 gms/kg. The test material was diluted 1:1 with demineralized water. The test site was a 6x6 cm shaved area on each rat. Length of exposure was 24 hours. The treatment site was covered with tinfoil. All rats were checked and weighed daily.

Results: LD_{50} > 10 gm/kg. Two deaths occurred which were not considered compound related. Other findings were unremarkable.

Acute Rabbit Eye Irritation—(Tech)—E. Merch—Darmstadt 3/20/73

The material tested was identified as Triforine.
Exactly 0.1 gm of Triforine was instilled into the eyes of three male New Zealand rabbits. The eyes were examined daily for seven days. The Draize scoring method was used.

Results—no irritation was observed.

Acute Rat Oral LD$_{50}$ (20% EC) E. Merck-Darmstadt.

Only a summary was provided for this 14 day study.
Results LD$_{50}$=5830 mg/kg

Acute Rat Oral LD$_{50}$ (Tech)—CH Boehringer Sohn—11/16/71

Only a summary was provided.

Results: LD$_{50}$=greater than 6000 mg/kg—no clinical symptoms reported.

Acute Mouse Oral LD$_{50}$ (Tech)—C.H. Boehringer Sohn 11/16/71

Only a summary was provided.

Results: LD$_{50}$=greater than 6000 mg/kg—no clinical symptoms.

Acute Dog Oral LD$_{50}$ (Tech) C.H. Boehringer Sohn 11/16/71

Only a summary was provided.

Results: LD$_{50}$=greater than 2000 mg/kg. Dose produced emetic effect.

Acute Rat Intraperitoneal LD$_{50}$ (Tech) E.H. Boehringer Sohn 11/16/71.

Only a summary was provided.

Results: LD$_{50}$=greater than 6000 mg/kg—no clinical symptoms.

Acute Rat Oral LD$_{50}$ (20% w/v formulation) C.H. Boehringer Sohn 11/16/71

Only a summary was provided.

Results: LD$_{50}$=6050 mg/kg.
Acute Mouse Oral \text{LD}_{50} (20\% \text{w/v formulation}) \text{C.H.} \text{Boehringer Sohn} 11/16/71.

Only a summary was provided.

Results: \text{LD}_{50} \text{greater than 6000 mg/kg}

\underline{Acute Rabbit Dermal \text{LD}_{50}} (20\% \text{w/v formulation}) \text{C.H.} \text{Boehringer Sohn} 11/16/71.

Only a summary was provided.

Results: \text{LD}_{50} \text{greater than 770 mg/kg.}

\underline{Acute Rabbit Dermal Irritation (20\% \text{w/v formulation}) \text{C.H.} \text{Boehringer Sohn} 11/16/71.}

The test material was tested undiluted or diluted 1 to 1 with water. Only a summary was provided.

Results: Moderate to severe reversible erythema was reported with both test material concentrations.

\underline{Acute Rabbit Eye Irritation (20\% \text{w/v}) \text{C.H.} \text{Boehringer}}

Material tested was 1\% dilution of the 20\% \text{w/v} formulation. Only a summary was provided.

Results: no irritation was reported.

\underline{Acute Rat Oral \text{LD}_{50} (20\% \text{formulation}) \text{E.} \text{Merck-Darmstadt 3/29/73}}

The material tested was identified as Triforine EC 20\% "W534 EC 20\%" "CA70203" (Lot No. 040/121) emulsion concentrate.

Five Wistar-AF/HAN-EMD-SPF rats of each sex were tested per level in a dosage range from 4,000 to 10,000 mg/kg. The 20\% formulation was diluted in demineralized water (20 gms in 100 ml.) Observation period was 14 days.

Results: \text{LD}_{50} = 6,600 mg/kg. Toxic signs included a decrease in the activity of all animals, pilo erection and tremors at 5,600 mg/kg and higher, prone positions were observed among the animals at levels of 7,200 mg/kg and higher.
Acute Rat Dermal LD₅₀ (20% formulation) - E. Merch-Darmstadt 3/29/73

The material tested was identified as Triforine EC 20% "W524 EC 20%" "CA 70203" (Lot No. 040/121) emulsion concentrate.

Five Wistar-AF/HAN-EMD-SPF rats of each sex were used per level of 1,000, 1,563, 3,125 and 5,000 mg/kg. Length of exposure was 24 hours after which the test site was washed with water.

Results - LD₅₀ = 2500 mg/kg - no signs of irritation were evident.

Acute Rabbit Eye Irritation (20% formulation) E. Merch-Darmstadt 3/29/73.

The material tested was identified as Triforine EC 20% "W524 EC 20%" "CA70203" (Lot No. 040/121) emulsion concentrate.

Exactly 0.1 ml of the test material was instilled into the conjunctival sac of the left eye of nine rabbits. The post treatment care included 3 rabbits' eyes not washed 3 washed after 2 seconds and 3 washed after 4 seconds.

Results - The unwashed eyes showed moderate irritation in the conjunctiva and slight corneal opacity over the entire eye which persisted during the entire 14 day observation period.

The 2 and 4 second washed eyes produced very slight irritation only during the first two days. All eyes were completely normal by day three.

Percutaneous Sensitization in Guinea Pig (20% formulation) E. Merch Darmstadt 3/29/73.

The material tested was identified as Triforine EC 20% "W524 EC 20%" "CA70203" (Lot No. 040/121) emulsion concentrate.

Test schedule is as follows:

<table>
<thead>
<tr>
<th>Trial Group I</th>
<th>Triforine EC 20% undiluted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial Group II</td>
<td>Triforine EC 20% as 1.25% aqueous dilution (concentration intended for usage)</td>
</tr>
<tr>
<td>Comparative Group</td>
<td>Dinitrochlorobenzene as 2% solution in ether</td>
</tr>
<tr>
<td>Control Group I</td>
<td>Demineralized water</td>
</tr>
<tr>
<td>Control Group II</td>
<td>No treatment</td>
</tr>
</tbody>
</table>

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The test animals were treated five times weekly over a two week consecutive period for a total of ten applications. The comparative group received treatment for five days only. The animals were rested for 14 days prior to a final challenge application at 1/10 the treatment concentration.

Results—Definite dermal irritation was observed during the 14 day treatment period. No sensitization was observed when the challenge dose was applied.

21 Day Rat Dermal (20% formulation) Lab for Pharm and Toxicology April 4, 1972.

The material tested was identified as W-524 20% EC, Lot 1

Twenty Sprague Dawley rats of each sex were tested at final concentration of 0.5 and 1.5% of the 20% emulsion concentrate. These concentrations were applied to test sites covering about 1/10 of the body surface. Half the test sites were abraded. Length of exposure was four hours a day, seven days a week for 21 days. Fifty percent of the animals were sacrificed at 21 days. The remaining 50% were held for a 21 day recovery period.

Observations and tests for effects included mortality, assessment of skin reaction by the Draize method, behavior weekly body weights, the following hematology at 0 and 3 weeks:

- hemoglobin
- erythrocytes
- differential blood count
- thrombocytes
- osmotic resistance of RBC
- hematocrit
- prothrombin time
- reticulocytes

The following clinical chemistry after three weeks:

- SGOT
- SGPT
- liver function
- cellulose acetate electrophoresis
- inorganic phosphorus
- ChE
- glucose
- BUN
- total bilirubin
- total protein
- calcium
- sodium-potassium
- CO₂

Urinalysis at 0 and 3 weeks, terminal eye examination, terminal hearing test and teeth examination.
Terminal studies included macroscopic examination of all animals; absolute weights of the heart, liver, lungs, kidneys, adrenals, thymus, hypophysis, gonades, thyroid and brain; histological examination of the aforesaid organs from 5 males and 5 females of the 1.5% test level irradiated skin which were sacrificed after the 3 week exposure period.

Results—Slight dermal irritation was evident at three weeks among both test and controls. All other parameters investigated were unremarkable.

Observations were completely negative after the 3 week recovery period.

13 Week Rat Feeding—Tech—C.H. Boehringer Sohn Ingelheim 4/22/71

The material tested was identified as W524, Lot III.

Fifteen SPF rats (62 days old) of each sex were tested per level of 0, 2,500, and 7,000 ppm and 25 rats of each sex at 20,000 ppm. Ten rats of each sex from the 20,000 ppm were allowed a 6 week recovery period after the 13 week test period to ascertain the reversibility of toxic damage.

Observations and tests for effects, included weekly body weights, mortality, food consumption, physical condition, behavior and the following laboratory determinations at 0, 6, and 13 and 18 weeks:

<table>
<thead>
<tr>
<th>RBC</th>
<th>reticulocytes</th>
</tr>
</thead>
<tbody>
<tr>
<td>hematocrit</td>
<td>thrombocytes</td>
</tr>
<tr>
<td>hemoglobin</td>
<td>coagulation time</td>
</tr>
<tr>
<td>MCV</td>
<td>leukocyte</td>
</tr>
<tr>
<td>MCH</td>
<td>differential blood count</td>
</tr>
<tr>
<td>MCHC</td>
<td>glucose in serum</td>
</tr>
<tr>
<td>SGPT</td>
<td>potassium</td>
</tr>
<tr>
<td>BUN</td>
<td>cholesterol in serum</td>
</tr>
<tr>
<td>AP</td>
<td>urinalysis</td>
</tr>
</tbody>
</table>

Terminal studies included absolute weights of the following organs;

8
heart
lungs
thymus
thyroid
liver
kidney
spleen
prostate
gonads
adrenals
pituitary gland
brain
salivary gland

and histopathologic examination of the aforesaid and the following organs:

pancreas
stomach
small intestine
colon
mesenteric lymph node
bladder
uterus
aorta
trachea
esophagus
skeletal muscle
optic nerve

Histology was done by Dr. T. Tilo

Results: One female of the 20,000 ppm level died on day 47. Due to autolysis. The cause of death could not be determined.

The sixth week hematological results revealed slight to significant decreases in the absolute number of RBC, hematocrit and hemoglobin values among all test animals, especially the females. The results at 13 weeks showed major recovery of all parameters toward normal. However the values still reflect abnormal conditions. The results at 18 weeks revealed complete recovery. Elevated cholesterol in serum was evident at 13 weeks in all test females. This condition was not evident in the recovery group rats. The absolute liver weights of the test animals revealed a slight dose dependent increase. This finding was not found in the recovery group rats.

The histopathological examination revealed a dose dependent siderosis of the liver, spleen and kidney. Some cases were also reported in the myocardial fibers and in the lungs. Siderosis was also evident among the recovery group rats.

A no effect level cannot be established for this study.

13 Week Rat Feeding (Tech)-C.H. Boehringer Sohn Ingelheim/Rhiem 5/16/71

The test material was identified as W524, Lot III.
Fifteen SPF rats of each sex (73 days old) were tested per level of 0, 100 and 500 ppm.

Observation and tests for effects included weekly body weights, mortality, food consumption, physical condition, behavior, and the following laboratory determinations at 0, 6, and 13 weeks:

- RBC: thrombocytes
- hematocrit: coagulation time
- hemoglobin: leukocytes
- MCV: differential blood count
- MCH: glucose in serum
- MCHC: SSPT
- reticulocytes: potassium in serum
- BUN: cholesterol in serum
- AP

Terminal studies included absolute weights of the following organs:

- heart: prostate
- lungs: gonads
- thymus: adrenals
- thyroid: pituitary gland
- liver: brain
- kidneys: salivary gland
- spleen

and histopathological examination of the aforesaid and following organs from ten rats of each sex per treatment level:

- pancreas: skeletal muscle
- stomach: esophagus
- small intestine: trachea
- colon: aorta
- mesenteric lymph node: optic nerve
- bladder
- uterus

Histology was done by Dr. T. Tilov, Hematology was done by Dr. I. Wei Be.

Results: The toxicity data resulting from the parameters investigated revealed no significant difference between test and control values.
The no effect level for this study is 500 ppm.

13 Week Dog Feeding (Tech)-C.H. Boehringer Sohn Ingelheim/Rhinem
2/5/71

The test material was identified as W524, Lot III.

Four pure bred 8 month old beagle dogs were used per level of 0, 3,500, 10,000, 30,000 and 30,000 ppm. Animals from one of the two levels of 30,000 ppm were held for a recovery period of 6 weeks after completion of the 13 week test schedule.

Observations and tests for effects included mortality, weekly body weights, daily food consumption, physical conditions, behavior and the following laboratory determinations at 0, 6, and 13 weeks:

- hemoglobin
- WBC
- RBC
- differential blood count
- hemocrit
- reticulocytes
- prothrombin time
- glucose
- blood
- SGPT
- SGOT
- sedimentation rate
- AP
- creatinine in serum
- cholesterol
- urea-N in serum
- sodium
- total bilirubin in serum
- potassium
- chloride
- CO₂
- calcium
- total protein

Urinalysis and a ophthalmological examination.

Terminal studies included absolute weights of the following organs:

- heart
- prostate
- lung
- testis
- liver
- adrenals
- kidneys
- pituitary gland
- spleen
- thyroid
- brain

and histopathological examination of the aforesaid and following organs:

- parotid
- ileum
- tongue
- colon transversum
- arcus aortae
- colon sigmoideum
esophagus  gallbladder
stomach  bladder
duodenum  thymus
jejunum  pancreas
cervical lymph node  eyes
mesenteric lymph node  optic nerve
skeletal  muscle
spinal medulla  peripheral nerve
bone marrow  trachea
skin

Histology was done by Dr. J.V. Sandersleven University of Munich.

Results: The 6 week hematology studies revealed moderately reduced RBC values for the 10,000 and 30,000 ppm levels; moderately reduced hematocrit values for all the levels; Slight to moderate reduction in hemoglobin for all test levels and a slight to significant increase in reticulocyte counts at all test levels.

The 13 week clinical findings revealed a slight to moderate increase in alkaline phosphatase and bilirubin at the 10,000 and 30,000 ppm levels and slight to moderate increase in cholesterol at 30,000 ppm.

The 30,000 ppm animals examined after the 6 week recovery were normal with respect to the clinical studies.

Organ weights revealed a slight to moderate dose dependent increase in the absolute liver and spleen weights of all test animals.

Fine drop-like fathy infiltration of individual liver cells was evident in three 3500 ppm animals and in four 30,000 ppm animals. Siderosis of the Kupffer's cells was evident in six animals of the 3500 ppm level and all the animals of the higher dosage levels.

A no-effect level can not be established for this study.

13 Week Dog Feeding (Tech)-Laboratorium fur Pharmakologie und Toxicologie-Hamburg  3/31/71

The material tested was identified as W-524 Charge T-3/70.
Four 8-10 month old pure bred Beagle dogs were tested per level of 0, 100, 600, and 3500 ppm.

Observations and tests for effects included opthalmic examination, mortality, behavior, food consumption; weekly body weights, clinical chemistry and the following hematology at 0, 4, 8, and 11th week:

- hemoglobin
- erythrocyte
- differential count
- hematocrit
- thrombocytes
- reticulocytes
- prothrombin time
- blood clotting time
- BSR
- osmotic resistance of RBC
- CO₂
- sodium
- potassium
- chloride

- SGPT
- liver function
- cholesterol
- glucose
- BUN
- SGOT
- SAP
- bilirubin
- protein
- celluloseacetate-electrophoresis
- uric acid
- creatinine

Final examinations included urinalysis and absolute weights of the following organs:

- heart
- trachea
- stomach
- lungs
- esophagus
- jejunum
- kidney
- lymph node
- colon
- thymus
- skeletal muscle
- parotis
- gonades
- spinal cord
- urinary bladder
- brain
- skin

- prostate/uterus
- liver
- aorta
- duodenum
- spleen
- pancreas
- ileum
- adenal
- peripheral nerve
- rectum
- pituitary
- tongue
- eye
- thyroid
- gall bladder
- bone marrow
The liver, kidney, spleen and bone marrow were histologically examined.

Results: The hematology data revealed a moderate reduction in the hemoglobin, erythrocyte and hematocrit values for the 3500 ppm test level. Siderosis was evident in the liver, spleen and bone marrow of the 600 and 3500 ppm animals. The effect appears dose dependant, with a slight effect at 600 ppm and a moderate effect at 3500 ppm.

The no-effect level for this study is 100 ppm.

Pathology was done by Dr. W. Dantewill.

Rat Teratogenic (Tech)—Laboratorium Fur Pharmakologie und Toxikologie, Hamburg 4/14/72

The material tested was identified as W-524 Lot 1.

Twenty female Sprague-Dawley rats weighing between 201 and 257 grams were used per level of 0, 100, 400, 800, and 1600 mg/kg. A deministration of test material was done daily from day 6 to 15 of gestation. The pregnant females sacrificed one day before parturition (day 20).

Observations and tests for effects included mortality, behavior, appearance, daily food consumption daily, body weight, number of fetuses, fetal sex, fetal viability, number of resorption sites, fetal weight, fetal malformations, fetal retardations, macroscopic examination of fetus, and fetal skeletal examination.

Results—There was a significant reduction in the number of fetuses and a corresponding increase (39%) in the number of resorptions at the 1600 mg/kg level.

No abnormalities were observed amongst the fetuses. The variation rate (strain according to Dauson) was increased at the 1600 mg/kg.

No teratogenic effects were reported.

2 Year Dog Feeding (Tech)—C.H. Boehringer Sohn-3/20/74

The material tested was identified as W524—XX Lot T 3/70, 22.7.71.
Four ten month old pedigree beagles of each sex were used per level of 0, 10, 40, 100, ppm 1000 ppm. Test diet was available seven days a week.

Observations and tests for effects included mortality, weekly body weights, food consumption, behavior, hematology and clinical chemistry included the following tests in weeks 0, 6, 13, 26, 52, 78 and 104:

<table>
<thead>
<tr>
<th>Test</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>RBC</td>
<td>bone marrow</td>
</tr>
<tr>
<td>hematocrit</td>
<td>glucose</td>
</tr>
<tr>
<td>hemoglobin</td>
<td>SGPT</td>
</tr>
<tr>
<td>MCV</td>
<td>SGOT</td>
</tr>
<tr>
<td>MCH</td>
<td>creatinine</td>
</tr>
<tr>
<td>MCHC</td>
<td>urea-N in the serum</td>
</tr>
<tr>
<td>reticulocytes</td>
<td>SAP</td>
</tr>
<tr>
<td>thrombocytes</td>
<td>bilirubin</td>
</tr>
<tr>
<td>prothrombin time</td>
<td>cholesterol</td>
</tr>
<tr>
<td>blood sedimentation rate</td>
<td>WBC</td>
</tr>
<tr>
<td>sodium</td>
<td>osmotic resistance</td>
</tr>
<tr>
<td>potassium in the serum</td>
<td>siderocytes</td>
</tr>
<tr>
<td>chloride in the serum</td>
<td>iron in the serum</td>
</tr>
<tr>
<td>calcium in the serum</td>
<td>serum electrophoresis</td>
</tr>
<tr>
<td>CO₂ in the serum</td>
<td>urinanalysis</td>
</tr>
<tr>
<td>protein in the serum</td>
<td></td>
</tr>
</tbody>
</table>

The fungus of the eyes of all animals were examined at weeks 0, 13, 26, 52, 78 and 104.

Terminal studies included organ weights of the:

<table>
<thead>
<tr>
<th>Organ</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>heart</td>
<td>prostate</td>
</tr>
<tr>
<td>lungs</td>
<td>testes</td>
</tr>
<tr>
<td>liver</td>
<td>adrenals</td>
</tr>
<tr>
<td>kidney</td>
<td>pituitary</td>
</tr>
<tr>
<td>spleen</td>
<td>thyroid</td>
</tr>
<tr>
<td>brain</td>
<td></td>
</tr>
</tbody>
</table>

Histological examination was conducted on the aforesaid organs and the following organs:
tongue  skeletal muscle
gl. mandibularis  peripheral nerve
arcus aortae  eyes with optic nerve
esophagus  spinal medulla
stomach  bone marrow
duodenum  trachea
jejunum  skin
ileum  injection sites
colon  mammary
 gall-bladder  brain stem
bladder  pons
thymus  cerebellum
pancreas  medulla oblongata
cervical lymph node  intestinal lymph node
optic chiasm

Results: Little or no variation was detected in the body weights, food consumption, clinical signs, clinical chemistry, ophthalmoscopy, ophthalmic histology, autopsy findings, organ weights and routine hematology.

Bone marrow analysis revealed a shift of the granulopoietic-erythropoietic in 5 of 8 animals at the 1000 ppm level.

One 100 ppm level animal died due to bronchopneumonia.

The histological findings revealed a significant increase in the iron content of the Kupffer cells in the liver of the 1000 ppm animals. An increase in the iron content of bone marrow was established in 2 of 8 animals of the 1000 ppm level.

No effect level for this study is 100 ppm.

2 Year Rat Feeding (Tech) – C.H. Boehringer Sohn Ingelheim – June/74

The test material was identified as W524-XX Lot T 3/70.

Thirty five to fifty young SPF rats of each sex were tested per level of 0, 25, 125, 625, and 3125 ppm.

Observations and tests for effects included mortality, weekly body weights, weekly food consumption, physical condition, behavior and the following hematological and clinical chemistry determinations from 15 animals of each at 0, 6, 13, 52, 78, and 104 weeks:
RBC
hematocrit
hemoglobin
MCV
MCH
MCHC
reticulocytes
thrombocytes
WBC

glucose in serum
SGPT
BUN
SAP
potassium in serum
cholesterol in serum
urinalysis
congluation time
differential blood count

Terminal studies included absolute weights of the:

heart
lung
thymus
thyroid
liver
kidneys
spleen

prostate
gonads
adrenals
pituitary gland
brain
salivary gland

The aforesaid organs and the following organs were examined histologically from 15 animals of each level:

pancreas
stomach
small intestine
colon
mesenteric lymph node
urinary bladder
n. ischiadicus

uterus
aorta
trachea
esophagus
skeletal muscle
brain
eyes β optic nerve

Results-The mortality, urinalysis, body weights, food consumption and water consumption results of the control animals were comparable to the test values.

The six week hematology studies revealed a slight reduction in the RBC among the 3125 ppm males and a significant increase in the reticulocyte count for sexes of the 3125 ppm level. By 104 weeks, these values had returned to within an normal range. The only adverse finding was a slight reduction in the hemocrit value. Siderin deposits appear evenly distributed among both test and control animals.
Other parameters investigated revealed variations within the biological normal range.

The only finding considered to be compound induced is the slight anemia occurring among the 3125 ppm level animals during the 6th week investigation period. This judgement is supported by prior similar findings.

The no effect level is 625 ppm.

Three Generation Rat Reproduction

This study was written in German, Translation by the company is necessary prior to its review.

Conclusion: These toxicity data reveal the 20% EC formulation to be relatively low in oral and dermal toxicity. The eye irritation study with the undiluted 20% EC formulation produced slight corneal opacity which persisted for 14 days. This finding requires the use of the signal word "Danger" on the front panel and the precautionary wording as follows:

1) Causes eye damage
2) Do not get in eyes
3) Wear goggles or face shield
4) First Aid
   In case of contact immediately flush eyes with plenty of water for at least 15 minutes. Call a physician.

No inhalation toxicity information was available for review. According to the Guidelines such acute information is required on both the active ingredients and formulation as sold.

TB objects to the registration of this formulation.

Robert Coberly, Biologist
Toxicology Branch
Registration Div.

cc: Branch Reading File

RCoberly:ir: 2/18/75
Initial G.E. Whitmore 5/1/77