

CODING FORMS FOR SRC INDEXING

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|--------------------------------|--|----------------------|------------------|
| Microfiche No. | OTS0574095 | | |
| New Doc ID | 88010000027S | Old Doc ID | 8EHQ-1100-14815S |
| Date Produced | 10/30/00 | Date Received | 11/03/00 |
| | | TSCA Section | 8E |
| Submitting Organization | FMC CORP | | |
| Contractor | FMC TOXICOLOGY LAB | | |
| Document Title | INITIAL SUBMISSION: TSCA HLTH & SFTY STUDY CVR SHT REPORTING RAT 90-DAY FEEDING STUDY OF [], BENZIMIDAZOYL HETEROCYCLE, DATED 10/30/2000 (SANITIZED) | | |
| Chemical Category | BENZIMIDAZOYL HETEROCYCLE (CONFIDENTIAL) | | |

**INITIAL
SUB-
MISSION**

TSCA HEALTH & SAFETY STUDY COVER SHEET - revised 6/25/96

TSCA CBI STATUS:

CHECK IF THIS PAGE CONTAINS CONFIDENTIAL BUSINESS INFORMATION (CBI)

Clearly mark the confidential information with bracketing and check the box in the appropriate section... Submit a sanitized cover sheet with CBI deleted.

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| 1.0 SUBMISSION TYPE <i>Contains CBI</i> <input type="checkbox"/> 8(d) <input checked="" type="checkbox"/> 8(e) <input type="checkbox"/> FYI <input type="checkbox"/> 4 <input type="checkbox"/> OTHER: Specify _____ <input checked="" type="checkbox"/> Initial Submission <input type="checkbox"/> Follow-up Submission <input type="checkbox"/> Final Report Submission Previous EPA Submission Number or Title if update or follow-up: _____ Docket Number, if any: # _____ <input type="checkbox"/> continuation sheet attached | | | | | | | | |
|--|---|-----------------------------|------------|------|----------|--|--|--|
| 2.1 SUMMARY/ABSTRACT ATTACHED (may be required for 8(e); optional for §4, 8(d) & FYI) <input checked="" type="checkbox"/> YES <input type="checkbox"/> NO | 2.2 SUBMITTER TRACKING NUMBER OR INTERNAL ID 00-139 | 2.3 FOR EPA USE ONLY | | | | | | |
| 3.0 CHEMICAL/TEST SUBSTANCE IDENTITY <i>Contains CBI</i> <i>Reported Chemical Name (specify nomenclature if other than CAS name):</i> CAS# _____ Purity <u>N.A.</u> % <input checked="" type="checkbox"/> Single Ingredient <input checked="" type="checkbox"/> Commercial/Tech Grade <input type="checkbox"/> Mixture Trade Name: _____ Common Name: <u>benzimidazolyl heterocycle</u> <table border="1"> <thead> <tr> <th>CAS Number</th> <th>NAME</th> <th>% WEIGHT</th> </tr> </thead> <tbody> <tr> <td></td> <td></td> <td></td> </tr> </tbody> </table> Other chemical(s) present in tested mixture _____ <input type="checkbox"/> continuation sheet attached | | | CAS Number | NAME | % WEIGHT | | | |
| CAS Number | NAME | % WEIGHT | | | | | | |
| | | | | | | | | |
| 4.0 REPORT/STUDY TITLE <i>Contains CBI</i> Rat 90-Day Feeding Study Company Sanitized | | | | | | | | |
| 5.1 STUDY/TSCATS INDEXING TERMS [CHECK ONE] HEALTH EFFECTS (HE): <input checked="" type="checkbox"/> ENVIRONMENTAL EFFECTS (EE): _____ ENVIRONMENTAL FATE (EF): _____ | | | | | | | | |
| 5.2 STUDY/TSCATS INDEXING TERMS (see instructions for 4 digit codes) STUDY SUBJECT ROUTE OF VEHICLE OF TYPE: <u>STOX</u> ORGANISM (HE, EE only): <u>RATS</u> EXPOSURE (HE only): <u>ORAL</u> EXPOSURE (HE only): <u>FOOD</u> Other: _____ Other: _____ Other: _____ Other: _____ | | | | | | | | |
| 6.0 REPORT/STUDY INFORMATION <i>Contains CBI</i> <input checked="" type="checkbox"/> Study is GLP Laboratory: <u>FMC Toxicology Laboratory</u> Report/Study Date: <u>on-going</u> Source of Data/Study Sponsor (if different than submitter): _____ Number of pages: _____ <input type="checkbox"/> continuation sheet attached | | | | | | | | |
| 7.0 SUBMITTER INFORMATION <i>Contains CBI</i> Submitter: <u>Linda M. Clark</u> Title: <u>Product Reg. Affairs</u> Phone: <u>(215) 299-6133</u> Company Name: <u>FMC Corporation</u> Company Address: <u>1735 Market Street</u> <u>Philadelphia, PA 19103</u> Submitter Address (if different): _____ Technical Contact: <u>Jane McCarty</u> Phone: <u>(609) 951-3662</u> <input type="checkbox"/> continuation sheet attached | | | | | | | | |
| 8.0 ADDITIONAL/OPTIONAL STUDY COMMENTS <i>Contains CBI</i> <input type="checkbox"/> continuation sheet attached | | | | | | | | |

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Submitter Signature: Linda M. Clark Date: 10/30/00

9.0 CONTINUATION SHEET

TSCA CBI STATUS:

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Clearly mark the confidential information with bracketing and check the box in the appropriate section ("Contains CBI").
Submit a sanitized cover sheet with CBI deleted. Mark the sanitized copy, "Public Display Copy" in the heading.

Submitter Tracking Number/Internal ID

00-139

CONTINUED FROM COVER SHEET SECTION # 2.1*Contains CBI*

This study is being submitted under TSCA 8(e) due to death and significant histopathology findings demonstrating evidence of severe and prolonged incapacitation at a dose level of 600 ppm.

Groups of ten rats per sex were administered _____ in the diet for 90 days. This chemical is _____ still in the Research & Development phase. The dose levels were 0, 20, 60, 200 and 600 ppm. Clinical observations were recorded daily; body weights and food consumption were recorded weekly. At the time of the final sacrifice, blood was collected for hematology and clinical chemistry determinations. Selected tissues were weighed. All tissues from the control groups and the livers, spleen and kidneys from the remaining groups were examined microscopically for lesions. Because there was high mortality in the 600 ppm group, tissues from the 200 ppm group were examined as well as tissues with findings in the high dose animals.

Mortality/sacrifice for humane reasons at 600 ppm included all of the males and 8 of 10 females. Treatment related clinical signs of toxicity were noted only in the 600 ppm group and included decreased feces, pallor, unthriftiness and abdominal gripping. There were significant decreases in body weight gains compared to the controls in both the 600 ppm males and females and the 200 ppm males (during weeks 1-5 only). Decreased liver, thymus and adrenal weights were noted in the 600 ppm females that survived to termination. Increased spleen weights were correlated with the microscopic finding of hematopoietic cell proliferation in the 600 ppm females and were judged to be an adaptive response to the chemical. Biologically significant effects on hematology parameters included decreased MCV and MCH and increased nucleated red blood cells at 600 ppm in females and decreased hemoglobin and MCV and MCH at 200 ppm in males. Clinical chemistry findings in 600 ppm females included increased total bilirubin and decreased globulin levels, likely due to lymphoid depletion (in the lymph nodes, spleen and thymus). The histopathology findings confirmed the liver toxicity with necrosis, hepatocyte vacuolation and hematopoietic cell proliferation at 600 ppm in male and female rats. Other histopathology findings at 600 ppm include: kidneys – tubular epithelium necrosis; bone marrow – granulocytic hyperplasia; lungs – subacute inflammation; and thrombosis in the heart.