

TSCA HEALTH & SAFETY STUDY COVER SHEET

TSCA CBI STATUS: NONE

**BEHQ-0103-15254**

<b>1.0 SUBMISSION TYPE</b> <input type="checkbox"/> 8(d) <b>XX 8(e)</b> <input type="checkbox"/> FYI <input type="checkbox"/> 4 <input type="checkbox"/> OTHER: Specify _____ <b>XX-</b> Initial Submission    - 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					
<b>2.1 SUMMARY/ABSTRACT ATTACHED</b> (may be required for 8(e): optional for §4, 8(d) & FYI) X- YES <input type="checkbox"/> NO	<b>2.2 SUBMITTER TRACKING NUMBER OR INTERNAL ID</b> 7106 4575 1292 0338 1545 02-2-25	<b>2.3 FOR EPA USE ONLY</b> <div style="text-align: right; font-size: small;">                     2003 JAN 19 AM 9:49                      RECEIVED                      OPPT NCIC                 </div>			
<b>3.0 CHEMICAL/TEST SUBSTANCE IDENTITY</b> Reported Chemical Name (specify nomenclature if other than CAS name): CAS#:    N/A Purity ___% X- Single Ingredient <input type="checkbox"/> Commercial/Tech Grade <input type="checkbox"/> Mixture    Trade Name <u>AE0317309</u> Common Name:    Triketone <div style="text-align: center; font-size: large; font-weight: bold;">Contain NO CBI</div> <table style="width:100%; border: none;"> <tr> <td style="width:33%;"><u>CAS Number</u></td> <td style="width:33%;"><u>NAME</u></td> <td style="width:33%;"><u>% WEIGHT</u></td> </tr> </table> Other chemical(s) present in tested mixture _____ <input type="checkbox"/> continuation sheet attached			<u>CAS Number</u>	<u>NAME</u>	<u>% WEIGHT</u>
<u>CAS Number</u>	<u>NAME</u>	<u>% WEIGHT</u>			
<b>4.0 REPORT/STUDY TITLE</b> Summary results of 90-Day Toxicity Study in the Rat by Dietary Administration <input type="checkbox"/> continuation sheet attached					
<b>5.1 STUDY/TSCATS INDEXING TERMS</b> [CHECK ONE] HEALTH EFFECTS (HE): <u>X</u> ENVIRONMENTAL EFFECTS (EE): _____    ENVIRONMENTAL FATE (EF): _____					
<b>5.2 STUDY/TSCATS INDEXING TERMS</b> (see instructions for 4 digit codes) STUDY    SUBJECT    ROUTE OF    VEHICLE OF TYPE: TOX    ORGANISM (HE, EE) <u>RATS</u> EXPOSURE (HE only): _____    EXPOSURE (HE only) _____ Other: _____    Other: _____    Other: _____					
<b>6.0 REPORT/STUDY INFORMATION</b> <input type="checkbox"/> Study is GLP Laboratory <u>Bayer Toxicology</u> Report/Study Date : <u>12/5/02</u> Source of Data/Study Sponsor (if different than submitter) _____    Number of pages <u>-</u> <input type="checkbox"/> continuation sheet attached					
<b>7.0 SUBMITTER INFORMATION</b> Janet M. Mostowy, Ph.D. VP, Product Safety & Regulatory Affairs    Phone:    412-777-3490 Bayer Corporation - 100 Bayer Road, Pittsburgh, PA. 15205 Technical Contact: <u>SAME AS ABOVE</u> Phone: ( ) _____ <input type="checkbox"/> continuation sheet attached					
<b>8.0 ADDITIONAL/OPTIONAL STUDY COMMENTS</b> This compound is an experimental herbicide. <input type="checkbox"/> continuation sheet attached <div style="text-align: right;">   <b>BEHQ-03-15254</b> </div>					

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Submitter Signature: [Signature]    Date: 12/18/02

  
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## 9.0 CONTINUATION SHEET

Submitter Tracking Number/Internal ID

7106 4575 1292 0338 1545  
02-2-25

### Continuation of 2.1

#### **TSCA 8(e) Evaluation**

Although the MTD was exceeded in this study at doses of 7,000 and 12,000 ppm, based on the findings listed below, this study results are being reported.

Toxicological findings of significance for adverse effects reporting which occurred in the 7000 and 12,000 ppm dose groups were: death, corneal lesions, pelvic dilatation, urinary epithelial hyperplasia, interstitial fibrosis of the urinary tract, and thyroid hyperplasia. Also, one female in the 1000 ppm dose group had a white area on the cornea and thyroid hyperplasia was observed in males in this dose group.

#### **Abstract**

The test substance, a herbicide of the triketone family, (batch no. Y2235; yellow crystals, 97.4% purity) was administered continuously via the diet to separate groups of Wistar rats (10/sex/group) at concentrations of 2, 30, 1000, 7000 and 12,000 ppm (equating to 0.13, 1.96, 66.0, 454 and 829 mg/kg/day in males and 0.15, 2.32, 77, 537 and 956 mg/kg/day in females) for at least 90 days. A similarly constituted group of 10 males and 10 females received untreated diet and acted as a control. Clinical signs were recorded daily, body weight and food consumption were measured weekly. A detailed physical examination was performed once during the acclimatization phase and weekly throughout the study. In addition, grasping righting, corneal, pupillary, auditory startle and head shaking reflexes were examined once during the acclimatization phase and during Week 11-12. Ophthalmological examinations were performed on all animals during the acclimatization phase and on all animals in study groups during Weeks 2, 4, 8 and 12. The week before necropsy a blood sample was collected from the retro orbital venous plexus of each animal for hematology and clinical chemistry determinations. Urine samples were collected overnight before necropsy from all animals. All animals were necropsied, selected organs weighed (from animals serving to terminal sacrifice) and a range of tissues were taken, fixed and examined microscopically.

The Maximum Tolerated Dose (MTD) was exceeded at both 12000 and 7000 ppm as 6 males and 1 female at 12000 ppm and 2 males at 7000 ppm were found dead or killed for humane reasons. On Day 72, it was decided to kill the surviving males at these doses.

At 12000 and 7000 ppm, yellow (intensive) colored urine was noted in a large number of the animals of both sexes and during an extended period. It was associated on a few occasions with soiled ano/uro genital area. A few other clinical signs were also treatment-related but noted on lesser occasions and more often before premature sacrifice or death: few or no feces, labored or noisy respiration, increased salivation, wasted, piloerection, general pallor, reduced motor activity, cold to touch and hunched posture. In both dose groups, body weight changes and food consumption were adversely affected.

'Snowflake' corneal lesions were noted in 5/20 and 3/20 animals at 12000 and 7000 ppm, more often associated with neovascularization of cornea. No treatment-related effects were noted at the neurotoxicity assessment. No relevant variations were observed in any hematological parameters.

Higher cholesterol was noted in females at 12000 ppm and in both sexes at 7000 ppm. Higher triglycerides was also noted in males at 7000 ppm.

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#### **ABSTRACT cont.**

Urinalysis revealed tendencies towards lower pH values, higher ketone levels and higher urinary volumes in females at 12000 ppm. Tendencies toward lower pH values and higher ketone levels were observed in both sexes at 7000 ppm with less crystals in males (but higher potential for calculi in the bladder).

At 12000 ppm, the autopsy revealed similar abnormalities in the urinary tract and all of them associated with the presence of yellow calculi. At final sacrifice, calculi were also observed macroscopically in 4/9 females. At 7000 ppm and final sacrifice, treatment-related changes were found within the organs of the urinary system, the liver and in the thyroid gland. Changes in the urinary system (kidney/urinary bladder/ureters) were associated with the presence of calculi and were found in 5/9 and 6/10 females. They included higher kidney weights, pelvic dilatation (unilateral or bilateral), urinary epithelial hyperplasia, inflammation and interstitial fibrosis of the urinary tract.

In the liver, mean absolute and/or relative liver weights in males and females were increased. A slight to moderate diffuse centrilobular hepatocellular hypertrophy was observed in 6/7 males and 1/10 females. A periportal vacuolation was found in 8/10 females. In the thyroid gland, there was a slight to mild diffuse follicular cell hyperplasia in 2/7 males, associated with a diffuse loss of colloid in 5/7 males.

At 1000 ppm, no marked effects were noted on body weight or food consumption. Colored urine was also noted for all males on a few days and one female presented a white area on the cornea. Higher cholesterol and triglycerides was noted in males. Tendencies towards lower pH values and higher ketone levels were observed in both sexes at 1000 ppm with less crystals in males. Mean liver weights in males and mean relative liver weights in females were increased. This finding was associated with a slight to moderate diffuse centrilobular hepatocellular hypertrophy in 9/10 males. In the thyroid gland, there was a slight to mild diffuse follicular cell hyperplasia in 5/10 males, associated with a diffuse loss of colloid in 9/10 males.

No treatment-related effects were noted at 2 or 30 ppm. The NOAEL in the Wistar rat when administered the test substance in the diet over a 90-day period was 30 ppm (equivalent to 1.96 mg/kg/day in males and 2.32 mg/kg/day in females).