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CODING FORMS FOR SRC INDEXING

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Date Produced	05/06/99	Date Received	10/12/99
		TSCA Section	8E
Submitting Organization	BAYER CORP		
Contractor	BAYER AG, TOXICOLOGY		
Document Title	INITIAL SUBMISSION: SXX 0665, SUBACUTE TOXICITY STUDY IN THE BEAGLE DOG, WITH TSCA HLTH & SFTY STUDY CVR SHT DATED 100799		
Chemical Category	2-(1-CHLORCYCLOPROPYL)-1-(2-CHLORPHENYL)-3-(1,2,4-TRIAZOL-*		

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TSCA HEALTH & SAFETY STUDY COVER SHEET

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 (i.e. Contains CBI). Submit a sanitized cover sheet with CBI deleted. Mark the sanitized copy, "Public Display Copy" in the heading.

1.0 SUBMISSION TYPE - Contains CBI <input type="checkbox"/> 8(d) <input checked="" type="checkbox"/> 8(e) <input type="checkbox"/> FYI <input type="checkbox"/> 4 <input type="checkbox"/> OTHER: Specify _____ XX- 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 Cert# P 917006934 99-2-71 1	2.3 FOR EPA USE ONLY
3.0 CHEMICAL/TEST SUBSTANCE IDENTITY - Contains CBI <i>Reported Chemical Name (specify nomenclature if other than CAS name):</i> CAS# 120983-64-4 2-(1-Chlorocyclopropyl)-1-(2-chlorophenyl) - 3-(1,2,4-triazol-1-yl)propan-2-ol Purity _____ % <input type="checkbox"/> Single Ingredient <input checked="" type="checkbox"/> Commercial/Tech Grade <input type="checkbox"/> Mixture Trade Name: SXX 0665 Common Name: _____		
4.0 REPORT/STUDY TITLE - Contains CBI Subacute Toxicity Study in Beagle Dog - T2034799 <input type="checkbox"/> Continuation sheet attached		 1999 OCT 12 AM 11:38 RECEIVED DPPT CBI/C
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 EXPOSURE (HE only): _____ VEHICLE OF EXPOSURE (HE only): _____ TYPE: <u>STOX</u> ORGANISM (HE, EE only): <u>DOGS</u> EXPOSURE (HE only): _____ Other: _____ Other: _____ Other: _____ Other: _____		
6.0 REPORT/STUDY INFORMATION <input type="checkbox"/> Contains CBI - Study is GLP Laboratory: <u>Bayer Ag - Department of Tox, Wuppertal, Germany</u> Report/Study Date: 5/6/99 Source of Data/Study Sponsor (if different than submitter) _____ Number of pages: 202 <input type="checkbox"/> continuation sheet attached		
7.0 SUBMITTER INFORMATION <input type="checkbox"/> Contains CBI Submitter: <u>Donald W. Lamb, Ph.D.</u> Title: <u>V. P. Prod. Safety & Reg. Affs.</u> Phone: <u>412-777-7431</u> Company Name: <u>Bayer Corporation</u> Company Address: <u>100 Bayer Road</u> <u>Pittsburgh, PA 15205-9741</u> Submitter Address (if different): _____ Technical Contact: <u>Donald W. Lamb, Ph.D.</u> Phone: <u>(412)777-7431</u> <input type="checkbox"/> continuation sheet attached		
8.0 ADDITIONAL/OPTIONAL STUDY COMMENTS <input type="checkbox"/> Contains CBI SXX 0665 is a metabolite of toxicological concern for a compound (JAU 6476) which is under development as a fungicide. <input type="checkbox"/> continuation sheet attached		

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Submitter Signature: Donald W Lamb Date: 10/7/99

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9.0 CONTINUATION SHEET
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CONTINUED FROM COVER SHEET SECTION # 2.1

TSCA 8(e) Evaluation:

SXX 0665 is a compound which was under development as a potential fungicide, but development of this compound was ceased due to the toxicity profile of the compound. A related fungicide, JAU 6476 is presently under development, and it has been shown that JAU 6476 breaks down to SXX 0665, upon drying, after application to plants/seeds, and upon administration to test animals. (Note: The extent of breakdown varies considerably based on the plant/seed to which JAU 6476 is applied). However, as JAU 6476 has fungicide properties, and the development of JAU 6476 as a fungicide is not based on the conversion of JAU 6476 to SXX 0665, JAU 6476 is not considered to be a delivery system for applying SXX 0665 to plants/seeds. Therefore, although SXX 0665 does have fungicide activity and may be of toxicological concern for evaluating risk assessment and in determining RFD values for JAU 6476, SXX 0665 is strictly a metabolite of JAU 6476 and is not a compound which is being developed for commercial use. Thus, SXX 0665 is not regulated by TSCA 8(e) however, (as SXX 0665 is a metabolite of toxicological concern for a compound (i.e., JAU 6476) which is under development as a fungicide) this study contains data that triggers reporting (i.e., in the mid- and high-dose groups there was a decrease in bone marrow cellularity which was associated with a slight decrease in the red cell count, HB, and HCT), thus the submitting.

Abstract

SXX 0665 was administered orally to Beagle dogs (2 males and 2 females per dose group) at doses of 10, 100/5000, or 1000 ppm in the feed over a period of up to 39 days.

The dose for group II was increased from 100 to 5000 ppm on day 26, because no overt toxicity had been observed.

Mortality was unaffected by treatment with SXX 0665. At necropsy, three of the four dogs in the 100/5000 ppm group were judged as skinny.

Daily observations revealed no signs of test item related toxicity. Feed consumption was not affected in any dose group until the dose was increased in the 100 ppm group. After the dose was increased in this group, the feed intake was strikingly reduced and body weight was decreased. Oculotoxic effects from the test item were not observed.

For hematological investigations, a slight decrease was observed for the red cell count, HB, and HCT in the 1000 ppm dose group, and questionable changes were observed in the 100/5000 ppm dose group. Despite the low incidence of this finding (2 of 4 females in each dose group), an effect on the bone marrow can not be completely excluded because histopathological investigations showed additional evidence for such an effect (i.e., a reduced cellularity of the bone marrow was observed in 2 of 4 animals, each, in the 1000 and 100/5000 ppm groups).

Clinical chemistry investigations showed a moderate increase in alkaline phosphatase (APH) in the 1000 and 100/5000 ppm groups, with no concomitant change in other liver parameters. An increase of APH often occurs as a consequence or in connection with enzyme induction, which was seen in both dose groups.

Urinalysis did not reveal findings indicating test article related effects.

Liver cytoplasmic changes were seen in the 100/5000 ppm dose group, which are most likely due to a loss of glycogen storage.

In summary, the NOEL for this study was 10 ppm of SXX 0665.

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