

CODING FORMS FOR SRC INDEXING

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		TSCA Section	SE
Submitting Organization	BAYER CORP		
Contractor	BAYER AG TOXICOLOGY		
Document Title	INITIAL SUBMISSION: TSCA HLTH & SFTY STUDY CVR SHT RE REVIEW OF TEST SUBSTANCE PILOT STUDY ON DEVELOPMENTAL TOXICITY IN RATS AFTER ORAL ADMINISTRATION, DATED 1/15/01 (SANITIZED)		
Chemical Category	ACYLPYRROLIDINONE (CONFIDENTIAL)		

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TSCA HEALTH & SAFETY STUDY COVER SHEET

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1.0 SUBMISSION TYPE 8(d) <input checked="" type="checkbox"/> XX 8(e) <input type="checkbox"/> FYI <input type="checkbox"/> 4 OTHER: Specify _____ XX- Initial Submission - Follow-up Submission Final Report Submission Previous EPA Submission Number or Title if update or follow-up: _____ Docket Number, if any: # _____ continuation sheet attached		
2.1 SUMMARY/ABSTRACT ATTACHED (may be required for 8(e); optional for §4, 8(d) & FYI) X- YES NO	2.2 SUBMITTER TRACKING NUMBER OR INTERNAL ID 71064575129203377814 01-2-01	2.3 FOR EPA USE ONLY
3.0 CHEMICAL/TEST SUBSTANCE IDENTITY Reported Chemical Name (specify nomenclature if other than CAS name): Acylpyrrolidinone CAS# N/A Purity ___% X- Single Ingredient Commercial/Tech Grade Mixture Trade Name: _____ Common Name: AMS 21601 CAS Number NAME % WEIGHT Other chemical(s) present in tested mixture continuation sheet attached		
4.0 REPORT/STUDY TITLE Review of Test Substance Pilot Study on Developmental Toxicity in Rats After Oral Administration continuation sheet attached		
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: DTOX ORGANISM (HE, EE only) RATS EXPOSURE (HE only): _____ EXPOSURE (HE only): _____ Other: _____ Other: _____		
6.0 REPORT/STUDY INFORMATION Study is GLP Laboratory Bayer AG Toxicology Report/Study Date: 1/11/01 Source of Data/Study Sponsor (if different than submitter) _____ Number of pages _____ continuation sheet attached		
7.0 SUBMITTER INFORMATION Donald W. Lamb VP, Product Safety & Regulatory Affairs Phone: 412-777-7431 Bayer Corporation - 100 Bayer Road, Pittsburgh, PA. 15205 Submitter Address (if different): _____ Technical Contact: Same as above Phone: () _____ continuation sheet attached		
8.0 ADDITIONAL/OPTIONAL STUDY COMMENTS This compound is _____ continuation sheet attached		

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Submitter Signature: Donald W. Lamb Date: 01/15/01

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9.0 CONTINUATION SHEET
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Submitter Tracking Number/Internal ID

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01-2-01

TSCA 8(e) Review

Results are being reported based on the marginal increase in post implantation loss in the high-dose group (1000 mg/kg), which was above the recent historical control data, and the marginal increase in common malformations in the high-dose group reported in this pilot developmental toxicity study in rats.

7 inseminated female Wistar rats each were daily treated orally by gavage with the test substance in 0.5% aqueous carboxymethylcellulose from day 6 to day 19 p.c. with doses of 0, 100, 300 and 1000 mg/kg body weight (bw)/day (dose volume 10 ml/kg bw). The fetuses were delivered by cesarean section on day 20 p.c. Investigations were performed on general tolerance of the test compound by the females as well as on its effect on intrauterine development.

There were no treatment related maternal findings at a dose level up to and including 300 mg/kg bw/day. In the 1000 mg/kg dose group feed intake was transiently slightly reduced after start of treatment (days 6-9 p.c.). Reduced amount of and light colored (most possibly related to the high amount of white test substance given) feces were as well transiently observed during treatment. Further on body weight loss occurred intermittently in the 1000 mg/kg group, resulting in slightly reduced body weight gain during the treatment and gestation period and slightly decreased corrected body weight gain. Necropsy revealed no treatment related findings.

With respect to intrauterine development gestation rate, litter size, fetal sex distribution, fetal weight, and placental weight and appearance were not affected by treatment up to and including 1000 mg/kg. Postimplantation loss was marginally increased at the 1000 mg/kg dose level. Since incidence lay above the range of recent historical control data, toxicological relevance could not be completely for this finding. However, final evaluation of postimplantation loss was not possible due to the low number of females in this dose group (4 litters available for evaluation).

External, visceral and skeletal evaluation of fetuses revealed no meaningful effects, except of a marginally increased number of fetuses and litters with common malformations at the 1000 mg/kg dose level (atrial septal defect, anophthalmia, dysplastic scapulae; altogether 4 fetuses in 2 litters affected, 3 fetuses originated from the same litter). Toxicological relevance was not assumed for marginally increased incidence of common malformations, since all findings were different in type and dose relationship was not evident for the individual types of malformation. However, final evaluation was not possible due to the low number of females in this dose group.

Summarizing all findings, maternal effects were evident at the 1000 mg/kg dose level (decreased feed intake, reduced amount of and light colored feces, body weight loss and impaired body weight development). Final evaluation of marginally increased postimplantation loss and incidence of common malformations at the 1000 mg/kg dose level was not possible, due to the low number of females in this dose group.