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DATA EVALUATION RECORD

This is a supplement to the original DER (Tox. Doc. No. 008798) for the rat developmental toxicity study on difenzoquat (MRID 41521203). It also provides information for the change of the NOAEL for developmental toxicity.

STUDY TYPE: Prenatal Developmental Study in Rats; OPPTS 870.3700 [§83-3 (*a*)]

P.C. CODE: 106401 MRID NO.:41521203

TEST MATERIAL (PURITY): Difenzoquat (99.4% purity)

SYNONYMS: AC 84,777

CITATION: Lochry, EA (1990) An oral developmental toxicity (embryo-fetal toxicity/ teratogenicity) study with AC 84,777 in rats. Argus Research Laboratories Inc., Perkasie, PA. Study No. 101-008 (Testing Lab) or 971-89-146 (sponsor) March 22, 1990. MRID No. 41521203. Unpublished.

SPONSOR: American Cyanamid Co., Ag. Res. Division, Princeton, NJ.

EXECUTIVE SUMMARY: In a developmental toxicity study (MRID 41521203), presumed pregnant female Charles River Crl:CD (SD)BR rats (25/dose group) were administered difenzoquat by gavage at dose levels of 30, 60, 120, and 240 mg/kg/day. A vehicle control group (25 presumed pregnant females) was given deionized water. The test animals were dosed from gestation day (GD) 6 through 15 and were sacrificed on GD 20.

Maternal: Under the conditions of this study, difenzoquat did not produce treatment-related death at any dose levels. There were no abortions or early deliveries. The number of corpora lutea, implants, resorptions, and live fetuses were comparable to those of the controls. Treatment- related effects were seen in the 120 and 240 mg/kg groups. An increase in the incidence of excessive salivation was seen in 120 (18/25), and 240 mg/kg dams (19/25); the salivation in these groups was long-lasting, recurrent and statistically significant ($p<0.01$). One dam in the 240 mg/kg group also showed signs of decreased motor activity, head-tilt and tremor. At 120 and 240 mg/kg, difenzoquat produced a dose related reduction in food consumption and body weight gains (83% and 84% of the control, respectively) during the treatment period (GD 6-16). **Based on these findings, the maternal LOAEL was 120 mg/kg, and NOAEL was 60 mg/kg.**

Developmental toxicity: Under the testing conditions, difenzoquat, at any dose levels, did not produce fetal death. Fetal body weights were comparable among the test groups. There were no treatment-related visceral or skeletal alterations, or malformation. **The NOAEL for developmental toxicity was 240 mg/kg (HDT).** It should be noted that in the previous DER (Tox. Doc. No. 008798), the developmental LOAEL was established at 240 mg/kg/kg based on decreased in fetal weight. After re-evaluation of the data, it was found that the mean fetal weights were comparable among groups (Table III), and the decrease was marginal and not statistically significant (Table III).

This study was classified as **acceptable/guideline** and **satisfies** the requirements for a rat developmental toxicity study ((§83-3 (a))

Table I. Mean Maternal Body Weight Gains (gm)[a]

	Dose (mg/kg/day)				
	0	30	60	120	240
Predosing (GD 0-6)	30.1±12.8	35.3± 7.6	33.5± 5.0	30.4± 6.0	29.6± 7.1
GD 6-16	54.7±15.3	52.4± 9.8	50.7± 9.7	45.2 ± 7.8*	46.0±10.7
GD 16-20	58.9± 6.7	60.8± 6.7	58.0± 9.2	61.4± 9.6	63.1± 8.4
GD 0-20	143.7±14.1	148.6±17.9	142.6±17.0	137.0±16.0	138.3±14.9
Corrected Body weight Gains+	65.3±10.6	70.5±13.6	67.1±12.8	59.9± 9.0	60.2±15.5

a: Data excerpted from Table 4 (p-46) of the report (MRID 41521203)
+: Corrected body weight gain = (body weight gain) - (gravid uterus weight)
Supplemental information to Table 1 of the DER (Tox. Doc. No.008798)
*: $p<0.05$ GD = gestation day

Table II. Feed Consumption (gm of food/kg bwt/day)[a]

	Dose (mg/kg/day)				
	0	30	60	120	240
Predosing					

GD 0-6	85.7±7.8	90.1±9.6	89.0±6.0	87.6±4.5	89.9±7.2
GD 6-16	82.9±5.2	79.7±4.0	79.6±4.1*	77.8±4.0*	74.4±5.2**
GD 16-20	76.5±4.2	75.9±5.5	76.0±4.1	75.9±5.0	75.5±4.3
Entire gestation period	78.5±3.0	78.0±4.1	77.9±3.0	76.8±2.6	76.2±3.6

a: Data excerpted from Table 5 (p-48) of the report (MRID 41521203).
Supplemental information to Table II of the DER (Tox. Doc. No. 008798).
*: p<0.05; **: p<0.01
GD = gestation day

Table III Mean Fetal Body Weight

	Dose (mg/kg/day)				
	0	30	60	120	240
Mean fetal body weights(gam)	3.50±0.21	3.48±0.19	3.43±0.19	3.53±0.24	3.39±0.29

Data excerpted from Table III of the report (MRID 41521203) (p. 50).