UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

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NOV 12 1991

MEMORANDUM

OFFICE OF PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: Technical Difenzoquat (Avenge; AC 84,777): Evaluation of a Teratology Study with Rats

Case No.: 0223
Record No.: 267783
HED Project No.: 0-1675
Tox. Chem. No.: 363A

FROM: Krystyna K. Locke, Toxicologist
Section I, Toxicology Branch I (IRS) Krystyna K. Locke 10/29/90
Health Effects Division (H7509C)

TO: Terri Stowe PM/RM Team No. 74
Reregistration Branch
Special Review/Reregistration Division (H7508C)

THRU: Roger Gardner, Section Head Roger Gardner 12-19-90 KZR 11/7/91
Section I, Toxicology Branch I (IRS)
Health Effects Division (H7509C)

Toxicology Branch/HED has completed an evaluation of the following Study:

An Oral Developmental Toxicity (Embryo-Fetal Toxicity/Teratogenicity) Study with AC 84,777 in Rats; Argus Research Laboratories, Inc.; Study No.: 101-008; Sponsor's Study No.: 971-89-146; March 22, 1990.
MRID No.: 41521203.

This study meets the December 24, 1989 acceptance criteria for 83-3 Teratology Study and was classified as Core Guideline. Maternal and developmental NOELs and LOELs were as follows:

Maternal NOEL: 60 mg/kg
Maternal LOEL: 120 mg/kg (Recurrent excessive salivation and decreased body weight gain and food consumption during the dosing period).

Developmental Toxicity NOEL: 120 mg/kg

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Developmental
Toxicity LOEL: 240 mg/kg (Slightly decreased body weights of male and female fetuses)

Difenzoquat was administered by gavage at dose levels of 30, 60, 120 and 240 mg/kg of body weight/day. The control group received deionized water which was a vehicle for Difenzoquat.

This study ~~is~~ WAS well planned, conducted and reported. A detailed evaluation (DER) is attached.

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GUIDELINE: 83-3

Primary Review by:
Krystyna K. Locke, Review Section I, Toxicology Branch I/HED K.K. Locke 10/29/90

Secondary Review by: Roger Gardner Roger Gardner 12-19-90
Section Head, Review Section I, Toxicology Branch I/HED

DATA EVALUATION RECORD

Study Type: Teratology - Developmental Toxicity
Species: Rat
Guideline: 83-3

EPA Identification No.s: EPA MRID (Accession) No. 41521203
EPA ID No. 241-239; Case No. 0223
ERA Record No. 267783
EPA Shaughnessy No. 106401
Caswell No. 363A
HED Project No. 01675

Test Material: Difenzoquat (Technical)

Synonyms: Avenge, AC 84,777

Sponsor: American Cyanamid Company, Agricultural Research Division, Princeton, New Jersey.

Study Number(s): 101-008 (testing laboratory's) and
971-89-146 (sponsor's)

Testing Facility: Argus Research Laboratories, Inc., Perkasie, PA

Title of Report: An Oral Developmental Toxicity (Embryo-Fetal Toxicity/Teratogenicity) Study with AC 84,777 in Rats.

Author(s): Elizabeth A. Lochry

Report Issued: March 22, 1990

Conclusions:

Charles River rats were treated with Technical Difenzoquat during gestation days 6 through 15 and were sacrificed on gestation day 20. The nominal doses of Difenzoquat, administered by gavage, were 0, 30, 60, 120 and 240 mg/kg of body weight/day. The analytical concentrations of dosing solutions ranged from 98 to 102% of the nominal concentrations. The dose levels used were based on the results of a preliminary study. Maternal and developmental NOELs and LOELs were as follows:

Maternal NOEL = 60 mg/kg
Maternal LOEL = 120 mg/kg (Excessive salivation and decreased body weight gain and food consumption during the dosing period).

Developmental Toxicity NOEL = 120 mg/kg
Developmental Toxicity LOEL = 240 mg/kg (Slight decreased body weights of male and female fetuses).

Classification of Study: Core Guideline

The study is well planned, conducted and reported, and meets the December 24, 1999 acceptance criteria for 83-3 Teratology Study.

A. Materials

A copy of the "Materials and Methods" section from the investigator's report is appended (Attachment I).

Test Compound: Purity: 99.4%
Description: White crystalline solid, soluble in water.
Lot No.: AC 6027-118
Contaminant: CBI appendix was not submitted, but analytical data are available from the sponsor.

Vehicle: R.O. deionized water, obtained by passing local water through a reverse osmosis membrane, and analyzed monthly for possible bacterial contamination and annually for possible chemical contamination. Results of analyses were submitted.

Test Animal(s): Species: Rat
Strain: Charles River Crl:CD®(SD)BR, males and females.
Source: Charles River Laboratories, Inc., Portage, Michigan, (females)
Charles River Laboratories, Inc., St. Constant, Canada (males).
Age (at receipt): 71 days (females) and 73 days (males)
Weight: Females: 180-228 g on the day following arrival and 215-259 g on day 0 of presumed gestation.
Males: 213-336 g on the day following arrival and 505-874 g at the initiation of the cohabitation period.

B. Study Design

This study was designed to assess the developmental toxicity potential of AC 34,777 (Difenzoquat; Avenge) when administered by gavage to female rats on gestation days 6 through 15, inclusive.

Mating:

Following a two-week acclimation period, healthy virgin female rats were placed into cohabitation with breeder male rats (one female was paired with one male rat). Female rats with spermatozoa observed in a vaginal lavage or a copulatory plug observed in situ were considered to be at day 0 of presumed gestation and assigned to individual housing. Day 0 of presumed gestation occurred during the four-day period, on September 26 through September 29, 1989. The male rats were used only for the purpose of breeding, were not administered the test substance and were not considered by the testing laboratory to be part of the Test System.

Group Arrangement:

Test Group	Dose Level (mg/kg/day*)	Number Assigned
I	0 (Vehicle)	25
II	30	25
III	60	25
IV	120	25
V	240	25

*Based on nominal concentrations of Difenzoquat in dosing solutions and adjusted for purity. The analytical concentrations of Difenzoquat in solutions used for dosing of groups II, III, IV and V averaged 98, 102, 100 and 102 % of nominal concentrations, respectively.

The above dose levels, selected by the sponsor, were based on the results of a pilot study (Argus Research Laboratories, Inc., Protocol No. 101-008P, 10/25/89; Sponsor's Study No. 971-89-145).

Dosing:

All doses were in a volume of 5 ml/kg of body weight/day. Dosing was based on daily body weights obtained for each female just before intubation. Dosing solutions were prepared weekly during the treatment period and were stored refrigerated, protected from light. All dosing solutions were analyzed for the concentration of Difenzoquat, but no reference is made to the analyses for stability.

Observations

The animals were checked for mortality or abnormal condition from the initiation of dosing to the termination of the study.

Dams were sacrificed on day 20* of gestation. Examinations at sacrifice consisted of 1) gross necropsy; 2) excising and weighing the intact gravid uterus; 3) examination of thoracic and abdominal cavities for gross lesions; 4) preserving of tissues with gross lesions in neutral 10% formalin for possible future histopathological evaluation; and 5) examination of the abdomen for pregnancy, number and placement of implantations, early and late resorptions, live and dead fetuses and number of corpora lutea. Dead fetuses and late resorptions were differentiated by the degree of autolysis present; marked to extreme autolysis indicated that the fetus was a late resorption.

The fetuses were examined in the following manner:

Each fetus was weighed, sexed and examined for external alterations. Live fetuses were sacrificed by immersion in the appropriate fixative. Approximately one-half of the fetuses in each litter were fixed in Bouin's solution and examined for soft tissue alterations using a variation of Wilson's sectioning technique[5]. The remaining fetuses in each litter were eviscerated, cleared, stained with alizarin red S[6] and examined for skeletal alterations.

Historical control data were provided to allow comparison with concurrent controls. A full report on the pilot study was also provided.

Statistical analysis

Statistical analysis methods employed are detailed in Attachment I, pages 25 and 26.

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*One 60 mg/kg/day dosage group rat and one 240 mg/kg/day dosage group rat were inadvertently sacrificed on day 19 rather than on day 20 of gestation. Cesarean-sectioning and litter data for these dams/litters were excluded from statistical analyses; but were included in the appropriate tables of individual data. All fetuses appeared normal for their gestational ages at gross external, soft tissue and/or skeletal examination of both litters.

[5]Wilson, J.G. (1965). Methods for administering agents and detecting malformations in experimental animals. Teratology: Principles and Techniques (Wilson, J.G. and Warkany, J., eds). University of Chicago Press, pp. 262-277.

[6]Modifcation of method of Staples, R.E. and Schnell, V.L. (1963). Refinement in rapid clearing technique in the KOH-alizarin red S method for fetal bone. Stain Technol. 39:61-63.

Compliance

A signed Statement of No Data Confidentiality Claims was provided.

A signed Statement of Compliance with EPA GLP's was provided.

A signed Quality Assurance Statement was provided.

C. Results

Maternal Toxicity

Chromodacryorrhea occurred in two rats from the control group. Excessive salivation was observed in 6 rats (24%) from the 60 mg/kg group, in 18 rats (72%) from the 120 mg/kg group and in 19 rats (76%) from the 240 mg/kg group. In the last two groups, this salivation was long-lasting, recurrent and statistically significant ($p < 0.01$), whereas only transient, single occurrences (and statistically insignificant) of excessive salivation were observed in the 60 mg/kg group. One rat in the 240 mg/kg group also had decreased motor activity, head-tilt and tremors, and another rat in the same group had red urine. Nothing remarkable was observed in the 30 mg/kg group.

Mortality

Treatment-related deaths did not occur. One rat in each of the 60, 120, and 240 mg/kg groups was found dead on gestation days 10, 15 and 8, respectively. Based on necropsy findings, these deaths were attributed to intubation accidents. The rat in the 60 mg/kg group was not pregnant, whereas the remaining two rats were pregnant.

Clinical Observations

Body Weight

The investigators supplied the following data:

Table I: Mean Maternal Body Weight Gains (grams)[a]

Group	I	II	III	IV	V
Difenzoquat[b]	0	30	60	120	240
Predosing Period (Days 0-6)	30.1	35.3	33.5	30.4	29.6

Dosing Period (Days 6-16)	54.7	52.4	50.7	45.2*	46.0
Postdosing Period (Days 16-20)	58.9	60.8	58.8	61.4	63.0
Entire Gestation Period (Days 0-20)	143.7	148.6	142.6	137.0	138.3
Corrected Body Weight Gains[c]	65.3	70.5	67.1	59.9	60.2

[a]Data extracted from Argus Research Laboratories Protocol No. 101-008, Table 4, page 46. Rats found dead during the study and those sacrificed inadvertently on gestation day 19 rather than 20 (one in each 60 and 240 mg/kg group) were excluded from Table 4.

[b]Mg/kg of body weight/day.

[c]Corrected body weight gains for entire gestation period = body weight gain for entire gestation period minus gravid uterus weight.

*Significantly different from the vehicle control (Group I) value; $p \leq 0.05$.

Difenzoquat reduced maternal body weight gains only in the 120 and 240 mg/kg groups, and only during the dosing period. Maternal body weight gains for these respective groups averaged 82.6% and 84.1% of the control group value for the entire dosing period. The absence of statistical significance for the 240 mg/kg group was attributed by the testing laboratory to the large standard deviation that occurred for this group, 46.0 ± 10.7 g vs 45.2 ± 7.8 g (120 mg/kg group). Mean gravid uterine weights were similar among the five test groups.

Food Consumption

The investigators supplied the following data:

Table II: Mean Maternal Food Consumption (g/kg b.w./day)[a]

Group	I	II	III	IV	V
Predosing Period (Days 0-6)	85.7	90.1	89.0	87.6	89.9
Dosing Period (Days 6-16)	82.9	79.7*	79.6*	77.8*	74.4**
Postdosing Period (Days 16-20)	76.5	75.9	76.0	75.9	75.5
Entire Gestation Period (Days 0-20)	78.5	78.0	77.9	76.8	76.2

[a]Data extracted from Argus Research Laboratories Protocol No. 101-008, Table 5, page 48. Rats found dead during the study and those sacrificed inadvertently on gestation day 19 rather than 20 (one in each 60 and 240 mg/kg group) were excluded from Table 5.

Significantly different from the vehicle control (Group I) value: * $p \leq 0.05$ and ** $p \leq 0.01$.

Maternal food consumption, reported as absolute (g/rat/day) and relative (g/kg of body weight/day), was similar among the five test groups during the predosing and postdosing periods. During the dosing period, absolute and relative food consumption values were significantly lower ($p \leq 0.01$) for the 120 and 240 mg/kg groups, as compared with the control group values. Relative food consumption decreases for these respective groups averaged 93.8% and 89.7% of the control group value for the entire dosing period. The corresponding absolute food consumption decreases were 91.6% and 87.8% of the control group value. These decreases were most pronounced during the first three days (gestation days 6 to 9) and last four days (gestation days 12 to 16) of the dosing period.

Significant decreases ($p \leq 0.05$ to $p \leq 0.01$) in mean absolute and relative food consumption values occurred also at several intervals during the dosing period in the 30 and 60 mg/kg groups.

However, these decreases were generally dose-independent and very small. Relative food consumption decreases for these respective groups averaged 96.1% ($p \leq 0.05$) and 96.0% ($p \leq 0.05$) of the control group value for the entire dosing period. The corresponding absolute food consumption decreases were 96.6% and 95.3% of the control value, and were statistically insignificant.

Gross Pathological Observations

The investigators supplied the following data: 1) Summary of necropsy findings; and 2) Individual observations at scheduled and unscheduled sacrifices. At scheduled sacrifice, slight, moderate or marked dilation of the pelvis of one of both kidneys occurred in 2, 3, 2, 1 and 2 pregnant rats from the control, 30, 60, 120 and 240 mg/kg groups, respectively. One rat from the 240 mg/kg group, which had moderate dilation of the pelvis of both kidneys, had also tan, hard, granular substance in the pelvis of one kidney and a thick-walled urinary bladder containing a stone-like, off-white mass. Based on the currently observed incidence, as well as the submitted historical control data, none of these lesions were attributed to treatment.

No gross lesions were found in the nonsurviving rat from the 60 mg/kg group. Red areas on the apical lobe of the lungs was the only lesion observed in the nonsurvivor from the 120 mg/kg group. The nonsurviving rat in the 240 mg/kg group had distended lungs and white frothy liquid in the trachea.

Cesarean Section Observations

Table III: Cesarean Section Observations[a]

Difenzoquat (mg/kg/day)	0	30	60	120	240
#Animals Assigned	25	25	25	25	25
#Animals Mated	25	25	25	25	25
Prenancy Rate (%)	96	92	96	100	100
Maternal Wastage					
#Died	0	0	1	1	1
#Died/ pregnant	0	0	0	1	1

#Non pregnant	0	0	1	0	0
#Aborted	0	0	0	0	0
#Pre-mature Delivery	0	0	0	0	0
Total Corpora Lutea	408	393	396	427	414
Corpora Lutea/Dam	17.0	17.1	17.2	17.8	18.0
Total Implantations	348	340	331	350	345
Implantations/Dam	14.5	14.8	14.4	14.6	15.0
Total Live Fetuses	329	318	314	329	326
Live Fetuses/Dam	13.7	13.8	13.6	13.7	14.2
Total Resorptions	19	23	18	21	18
Early	19	22	18	20	17
Late	0	1	0	1	1
Resorptions/Dam	0.8	1.0	0.8	0.9	0.8
Total Dead Fetuses	0	0	0	0	0
Dead Fetuses/Dam	0	0	0	0	0
Mean Fetal Weight (gm)	3.50	3.48	3.43	3.53	3.39

Preimplantation Loss (%)	14.7	13.4	16.3	18.0	16.7
Postimplantation Loss (%)	5.5	6.8	5.5	6.2	5.3
Sex Ratio (% Males)	50.4	51.6	48.7	50.1	46.3

[a]Data extracted from Argus Research Laboratories Protocol No. 101-008, Tables 6 and 7, pages 49 and 50. Rats found dead during the study and those sacrificed inadvertently on gestation day 19 rather than 20 (one in each 60 and 240 mg/kg group) were excluded by the testing laboratory from the Cesarean section observation data.

Cesarean section observations were based on the 24, 23, 23, 24 and 23 pregnant rats that were sacrificed on gestation day 20 in the control, 30, 60 120 and 240 mg/kg groups, respectively. Difenzoquat, at all levels tested, had no effect on any of the above parameters examined. Slight decreases in the mean fetal weights, in the 240 mg/kg group, were not statistically significant and did not appear to be biologically remarkable. The mean fetal weights (percent of control values) were: 96.9 (males and females), 96.4 (males) and 97.9 (females).

Developmental Toxicity

Table IV: External Examinations[a]

Difenzoquat (mg/kg/day)	0	30	60	120	240
#Pups examined	329	318	314	329	326
#Pups affected	1[b]	0	0	0	0
Fetal incidence (%)	0.3	0	0	0	0
#Litters examined	24	23	23	24	23
#Litters affected	1	0	0	0	0
Litter incidence (%)	4.2	0	0	0	0

[a]Data extracted from Argus Research Laboratories Protocol No. 101-008, Table 9, page 52. Litters from the rats sacrificed inadvertantly on gestation day 19 rather than 20 (one in each 60 and 240 mg/kg groups) were excluded from the above data.

[b]One control group fetus had a thread-like tail. No other gross external alterations were observed in this and other groups.

Table IV: Visceral Examinations[a]

Difenzoquat (mg/kg/day)	0	30	60	120	240
#Pups examined	159	153	152	156	158
#Pups affected	1[b]	1[b]	0	1[b]	0
Fetal incidence (%)	0.6	0.6	0	0.6	0
#Litters examined	24	23	23	24	23
#Litters affected	1	1	0	1	0
Litter incidence (%)	4.2	4.3	0	4.2	0

[a]Data extracted from Argus Research Laboratories Protoool No. 101-008, Table 10, page 53. Litters from the rats sacrificed inadvertantly on gestation day 19 rather than 20 (one in each 60 and 240 mg/kg groups) were excluded from the above data.

[b]Slight or moderate dilation of the pelvis of one or both kidneys was observed in these fetuses. No other soft tissue alterations occurred in this and other groups.

Table IV: Skeletal Examinations[a]

Difenzoquat (mg/kg/day)	0	30	60	120	240
#Pups examined	170	165	162	173	167
#Pups affected	8	6	8	2	6
Fetal incidence (%)	4.7	3.6	4.9	1.1	3.6
#Litters examined	24	23	23	24	23
#Litters affected	4	3	5	1	3
Litter incidence (%)	16.7	13.0	21.7	4.2	13.0
Ribs (Wavy, cervical or incompletely ossified)[b]					
Fetal incidence: N (%)	1 (0.6)	1 (0.6)	5 (3.1)	0	1 (0.6)
Litter incidence: N (%)	1 (4.2)	1 (4.3)	4 (17.4)	0	1 (4.3)
Vertebrae (Bifid centrum or delayed ossification)[b]					
Fetal incidence:	3 (1.8)	2 (1.2)	0	0	0
Litter incidence: N (%)	3 (12.5)	1 (4.3)	0	0	0

Sternal Centers and Pelvis (Incomplete ossification and/or non-ossification)[b]					
Fetal incidence: N (%)	4 (2.3)	3 (1.8)	3 (1.8)	2 (1.1)	5 (3.0)
Litter incidence: N (%)	3 (12.5)	3 (13.0)	3 (13.0)	1 (4.2)	3 (13.0)

[a]Data extracted from Argus Research Laboratories Protocol No. 101-008, Table 11, pages 54-56 and the summary of the results section, pages 35 and 36. Litters from the rats saorificed inadvertently on gestation day 19 rather than 20 (one in each 60 anbd 240 mg/kg groups) were excluded from the above data.

[b]See Attachment II of this review for details on skeletal alterations.

D. Discussion/Conclusions

a. Maternal Toxicity:

The following effects were observed in the 120 and 240 mg/kg groups: 1)long-lasting, recurrent and statistically significant ($p < 0.01$) excessive salivation; and 2) Decreased body weight gain end food consumption during the dosing period. Decreased motor activity, head-tilt and tremors were noted in one rat from the 240 mg/kg group and red urine in another rat from the same group.

b. Developmental Toxicity:

i. Deaths/Resorptions:

There were no dead fetuses in any group. Total resorptions, 0.8 - 1.0/dam, were very similar in all groups.

ii. Altered Growth:

Difenzoquat had no effect on growth (body weights) of the fetuses in the 30, 60 and 120 mg/kg groups. A slight decrease in the mean fetal weights (96.9% of the control value), in the 240 mg/kg group, was not statistically signficant and did not appear to be biologically significant.

iii. Developmental Anomalies:

Treatment-related anomalies (alterations) did not occur. The incidence of visceral alterations (dilated kidney pelvis) and/or skeletal alterations (mostly incomplete ossification of ribs, vertebrae, sternal centers and pelvis) was either similar in all five test groups or was higher in the control and the 30 and 60 mg/kg groups than in the 120 and 240 mg/kg groups.

iv. Malformations:

Treatment-related malformations did not occur. The only malformations observed were a thread-like tail in one fetus from the control group and wavy ribs (one or more) in the fetuses from the following groups: One in each the 30 and 240 mg/kg groups, and two in the 60 mg/kg group.

E. Study Deficiencies:

Data on the stability of dosing solutions were not submitted. However, according to the Registration Standard prepared by Residue Chemistry Branch (currently Dietary Exposure Branch) in 1988, Difenzoquat is very stable at wide range of temperatures, as follows: 1) Aqueous solution was stable for > 24 months at 25° C; 2) Aqueous solutions could be stored indefinitely at 50° C; and 3) Only 2.2% loss of active ingredient occurred during 160 hours of incubation at 120° C.

No reason was given why female rats used in this study were obtained from Charles River Laboratories in Portage, Michigan, and males from Charles River Laboratories in St. Constant, Canada.

F. Core Classification: Guideline

Maternal NOEL = 60 mg/kg
Maternal LOEL = 120 mg/kg (Excessive salivation, and decreased body weight gain and food consumption during the dosing period).

Developmental Toxicity NOEL = 120 mg/kg

Developmental Toxicity LOEL = 240 mg/kg (Slightly decreased body weights of male and female fetuses).

G. Risk Assessment: (If a concern is suggested by the results of this study, a margin of safety should be estimated for both dietary and occupational exposures).

No concern is suggested.

Attachment I

Page _____ is not included in this copy.

Pages __19__ through __37__ are not included in this copy.

The material not included contains the following type of information:

__ _ __ Identity of product inert ingredients.

__ _ __ Identity of product impurities.

__ _ __ Description of the product manufacturing process.

__ _ __ Description of quality control procedures.

__ _ __ Identity of the source of product ingredients.

_____ Sales or other commercial/financial information.

_____ A draft product label.

_____ The product confidential statement of formula.

_____ Information about a pending registration action.

__X__ FIFRA registration data.

__ _ __ The document is a duplicate of page(s) _____.

_____ The document is not responsive to the request.

__ _ __ Internal deliberative information.

_____ Attorney-Client work product.

__ _ __ Claimed Confidential by submitter upon submission to the Agency.

MRID No.: 41521203

Study No.: 101-008 (Testing Laboratory's)
- 971-89-146 (Sponsor's)

Study Date: 3/22/90

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Subdivision F
Guideline Ref. No. 83-3
December 24, 1989

83-3 Teratology Studies (Rat)

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. ✓ Technical form of the active ingredient tested.
2. ✓ At least 20 pregnant animals/dose group for mice, rats or hamsters are available. At least 12 pregnant animals/dose group for rabbits are available (three test groups and control group).
3. ✓ At the high dose, overt maternal effects such as slight weight loss are reported (or a limit dose is given, 1,000 mg/kg).
4.* ✓ At the low dose, no developmental toxicity is reported.
5. ✓ Dosing duration is at least during the period of major organogenesis, but may extend up to one day prior to term.
6.* ✓ Analysis for test material ~~stability, homogeneity, and~~ concentration in dosing medium ●
7. ✓ Individual daily observations.
8. ✓ Individual body weights.
9. ✓ Individual food consumption.
10. ✓ Necropsy on all animals
11. ✓ Individual uterine examination including number of fetal deaths, early and late resorptions and numbers of viable fetuses per sex.
12. ✓ All ovaries examined to determine number of corpora lutea.
13. ✓ Individual litter weights and/or individual fetal weights per sex/litter.
14. ✓ Individual fetus external examination.
15. ✓ Individual fetus skeletal examination for 1/3 to 1/2 of each litter for rodents and all for all rabbits.
16. ✓ Individual fetus soft tissue examination.

● Stability data of aqueous solutions are available in Difenzoquat Registration Standard (DEB chapter)

Criteria marked with a * are supplemental and may not be required for every study.