8e

LUBRIZOL

Contains No CBI

8EHQ-0194-12819

THE LUBRIZOL CORPORATION
29400 LAKELAND BOULEVARD
WICKLIFFE, OHIO 44092-2298
TELEPHONE: 216/943-4200

CERTIFIED MAIL - R.R.R.

January 3, 1994

A

RECD
OFFICE OF POLLUTION
PREVENTION AND TOXICS
94 JAN 10 AM 7:42

Document Control Officer (TS-790)
Attn: Section 8(e) Coordinator
Information Management Division
Office of Toxic Substances
Environmental Protection Agency
401 M Street, S.W.
Washington, D.C. 20460

TO WHOM IT MAY CONCERN:

We are notifying the Environmental Protection Agency under Section 8(e) of the Toxic Substances Control Act of the preliminary results of a 28-day oral toxicology study in rats on zinc O, O' di-2-ethylhexyl dithiophosphate (CAS Registry Number 4259-15-8).

Lubrizol is participating in this study as a member of the Health, Regulatory and Environmental Task Group of the Petroleum Additives Panel of the Chemical Manufacturers Association. This study is being voluntarily conducted for the OECD SIDS Program. Other participants in the study are Chevron, Ethyl Petroleum, Exxon Chemical and Texaco Chemical.

We are including a copy of a preliminary report that was generated on December 16, 1993 by WIL Research Inc., the contract laboratory performing the study. Dose levels in the study were 10, 50, 125, 250 and 500 mg/kg. Some mortality was observed at 500 mg/kg during the in-life portion of the study. Animals were sacrificed on December 10 as scheduled. Gross pathological findings during necropsy were minimal.

The reportable finding at this stage of the study appears to be the statistically significant increase in absolute adrenal gland weight in males and relative adrenal weight in both sexes at 250 and 500 mg/kg. This finding would appear to be reportable under the April 2, 1992 guidance from EPA to Latham and Watkins for subacute/subchronic/chronic studies due to the apparent no effect level for this finding of 125 mg/kg.

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70 pgs.

Other observations made during the study were changes in fecal consistency and coloration at 125, 250 and 500 mg/kg, and rales were observed in males at 50, 125, 250 and 500 mg/kg and in females at 125, 250 and 500 mg/kg.

We will continue to keep EPA abreast of any new reportable findings in the study. A final report will be sent to EPA according to the voluntary agreement under the OECD SIDS Program. Questions on this study can be directed to Dr. Richard C. Kraska of my staff at 216-943-1200, extension 5167.

Sincerely yours,

THE LUBRIZOL CORPORATION

Donald I. Hoke, Ph.D.
Manager of Product Safety & Compliance

RCK:snd
8ECMAZDP.STD
Enclosures

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OFFICE OF POLLUTION
PREVENTION AND TOXICS
94 JAN 10 AM 7:42

DEC 23 1993

December 16, 1993

Carol Stack, Ph.D.
Manager, Petroleum Additives HERTG
Chemical Manufacturers Association
2501 M Street NW
Washington, D.C. 20037

For Distribution by CMA
CHEMSTAR DIVISION
From Carol Stack
Ref. No. OECD WORD Group-PA
Date 12/27/93

Ref) WIL-186002
(CMA No.: PA-5.0 RF/REP-WIL)

Dear Carol:

Presented is an interim progress report (unaudited draft form) for the study entitled "A 28-Day Oral (Gavage) Dose Range-Finding Toxicity Study of Zinc 0,0-Diethylhexyldithiophosphate (ZDDP) in Rats."

INTRODUCTION

Summarized data in draft form are provided in the attachment. This study was designed to evaluate the possible toxic effects of the test material when administered to rats for 28 days in order to establish dose levels for an OECD reproduction/developmental toxicity screening study (Guideline 421).

Execution of the technical aspects of the study were performed according to the following schedule:

FUNCTION	DATE OF EXECUTION
Receipt of Animals	10/28/93
Acclimation Period	10/28-11/11/93
Assignment of Animals to Treatment Groups	11/11/93
Test Material Administration	11/12-12/9/93
Necropsy	12/10/93

At this juncture, all technical events for the study have been completed in accordance with the original work plan.

METHODOLOGY

Thirty male and thirty female Sprague-Dawley Crl:CD®BR Rats were allocated to either one vehicle control group or to various dosage groups of ZDDP according to the following figure. The males and females were 72 and 79 days old respectively, at study initiation.

Group Number	Test Article	Dosage Level (mg/kg/day)	Dosage Concentration (mg/ml)	Dosage Volume (ml/kg)	Number of Animals Males	Number of Animals Females
1	Mazola® corn oil	0	0	5	5	5
2	ZDDP	10	2	5	5	5
3	ZDDP	50	10	5	5	5
4	ZDDP	125	25	5	5	5
5	ZDDP	250	50	5	5	5
6	ZDDP	500	100	5	5	5

Formulations of ZDDP were prepared by diluting the appropriate amount of test material (weight/volume) with Mazola® corn oil to achieve the appropriate concentration for each group. Test formulations were prepared assuming a purity of ZDDP of 100%. Periodically, aliquots of the test formulations were collected and forwarded to the Chevron Research and Technology Company for verification of homogeneity, stability and concentration. The formulations were stirred continuously during the administration procedure.

The appropriate test or control article was administered orally by gavage as a single daily dose for 28 successive days. Dosages were administered at a constant dosage volume of 5 ml/kg and adjusted based on the most recent body weight. During the study the following observations and examinations were performed on all rats:

Clinical Observations: Observations for mortality/moribundity performed twice daily. Detailed clinical observations recorded daily prior to treatment. Pharmacotoxic signs were recorded at approximately the time of dosing and between 1-and 2-hours post-administration.

Measurement of Body Weights: Study days -7 and 0 and every other day during treatment.

Measurement of Food Consumption: Weekly.

Necropsy: Study Day 28. Complete macroscopic examination performed including acquisition of selected organ weights (brain, liver, kidneys, heart, testes, epididymides, ovaries and adrenal glands).

All work product generated during the course of study will be maintained in the WIL Research Laboratories, Inc., Archives in compliance with regulatory requirements.

RESULTS:

The major test material-related effects are summarized in the following:

- Survival: Mortality: 3/5 males and 1/5 females at 500 mg/kg/day. All were attributed to test article related etiology; 1/5 Females died at 125 mg/kg/day - the cause of death could not be determined.

- Appearance and Behavior: Changes in fecal consistency (soft stool, diarrhea, mucoid feces) or discoloration of the feces and staining of various body surfaces were observed in the 125, 250 and 500 mg/kg/day groups generally in both sexes. Rales were also observed at dosages of 50 mg/kg/day and higher in the males and 125 mg/kg/day and higher in the females. Salivation was noted at the time of administration in the 50 (males only), 125, 250 and 500 mg/kg/day groups.

- Body Weights:
  - Males: Primary deficits in body weight gain occurred during study days 0-2 (250 and 500 mg/kg/day groups). Deficits in body weight gain continued for the 500 mg/kg/day males through day 12 of study. No effects were observed at dosages of 125 mg/kg/day and less.
  - Females: Body weight gain at dosages as high as 250 mg/kg/day was comparable to the control group during the study. At 500 mg/kg/day, transient effects on weight gain ($p<0.01$) occurred during study days 0-2.

- Food Intake:
  Males/Females: Slight inhibition (substatistical) of food intake (g/animal/day) occurred study week 0-1 at the 500 mg/kg/day level only. No other adverse effects were detected. Compensatory increases were noted during weeks 1-2 (females, $p<0.05$), 2-3 and 3-4 (females, $p<0.01$).

- Macroscopic Pathology and Organ Weight Data: Thickened gastric mucosa was noted in 1/2 males (500 mg/kg/day) and 1/5 and 2/4 females (250 and 500 mg/kg/day, respectively) at terminal necropsy. Absolute adrenal weights were elevated in the 250 and 500 mg/kg/day groups in both sexes; statistical significance occurred in the males only.

PRELIMINARY CONCLUSIONS:

- The 500 mg/kg/day dosage would exceed a maximum tolerated dose for the subsequent OECD guideline 421 reproduction/developmental toxicity screening study.

- Based on the results obtained to date, the NOAEL is considered to be 10 mg/kg/day.

- Histopathological evaluation of tissues is scheduled to be completed on January 30, 1994.

GENERAL CONSIDERATIONS:

To the best of my knowledge, there were no significant deviations from the protocol, and WIL Standard Operating Procedures which would effect the scientific integrity of the study.

Sincerely,

Mark D. Nemec, B.S.
Associate Director of Reproductive
and Developmental Toxicology

MDN/cll
Enclosure

TO: Carol Stack, Ph.D., Chemical Manufacturers Association, Washington, DC
FROM: Ian C. Lamb, Ph.D., WIL Research Laboratories, Inc.
DATE: December 21, 1993
FAX NO.: FAX'93-1099
RE) Project WIL-186002: A 28-Day Oral Dose Range-Finding Toxicity Study of ZDDP in Rats (CMA Project No. PA-5.0-RF/REP-WIL)

TOTAL PAGES THIS TRANSMISSION = 17

Please find attached the information you requested. If you have any questions please contact me.

Best Regards,
Ian C. Lamb
Ian Lamb, 12-21-93.

For Distribution by CMA
CHEMSTAR DIVISION
From Carol Stack
Ref. No. OECD 416-PA
Date 12/21/93

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PROJECT NO.:WIL-186002
SPONSOR:CMA
SPONSOR NO.:PA-5.ORF/REP-WIL

A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS
ORGAN WEIGHTS RELATIVE TO FINAL BODY WEIGHTS (GRAMS/100 GRAMS)

10:25 21-DEC-93 PAGE 1
WEEK 4

UNAUDITED DRAFT

		----- MALE -----					
GROUP:		0 MG/KG/DAY	10 MG/KG/DAY	50 MG/KG/DAY	125 MG/KG/DAY	250 MG/KG/DAY	500 MG/KG/DAY
FINAL BODY WT							
	MEAN	491.	490.	495.	477.	462.	453.
	S.D.	33.5	47.2	64.5	38.6	48.7	37.5
	N	5	5	5	5	5	2
BRAIN							
	MEAN	0.406	0.420	0.418	0.434	0.430	0.459
	S.D.	0.0363	0.0385	0.0587	0.0274	0.0375	0.0290
	N	5	5	5	5	5	2
LIVER							
	MEAN	4.055	4.047	4.113	4.018	4.304	4.420
	S.D.	0.1536	0.1673	0.2578	0.3136	0.4015	0.5544
	N	5	5	5	5	5	2
KIDNEYS							
	MEAN	0.716	0.761	0.764	0.705	0.747	0.742
	S.D.	0.0444	0.0191	0.0643	0.0591	0.0413	0.0990
	N	5	5	5	5	5	2
HEART							
	MEAN	0.331	0.347	0.319	0.324	0.304	0.293
	S.D.	0.0305	0.0392	0.0481	0.0107	0.0266	0.0339
	N	5	5	5	5	5	2

NONE SIGNIFICANTLY DIFFERENT USING DUNNETT'S TEST

DEC 21 '93 16:13 F-536 T-538 P-003 WIL RESEARCH 4192893650

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PROJECT NO.:WIL-186002
SPONSOR:CMA
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A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS
ORGAN WEIGHTS RELATIVE TO FINAL BODY WEIGHTS (GRAMS/100 GRAMS)

UNAUDITED DRAFT

		----- MALE -----					
	GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	50 MG/KG/DAY	125 MG/KG/DAY	250 MG/KG/DAY	500 MG/KG/DAY
TESTES							
	MEAN	0.688	0.759	0.757	0.759	0.786	0.869*
	S.D.	0.0550	0.0569	0.1109	0.0830	0.0545	0.0092
	N	5	5	5	5	5	2
EPIDIDYMIDES							
	MEAN	0.246	0.259	0.268	0.264	0.280	0.312
	S.D.	0.0277	0.0264	0.0403	0.0310	0.0263	0.0304
	N	5	5	5	5	5	2
ADRENAL GLANDS							
	MEAN	0.014	0.014	0.013	0.015	0.019*	0.023**
	S.D.	0.0033	0.0017	0.0029	0.0019	0.0023	0.0021
	N	5	5	5	5	5	2

* = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP 1 AT 0.05 LEVEL USING DUNNETT'S TEST
** = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP 1 AT 0.01 LEVEL USING DUNNETT'S TEST

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WIL RESEARCH
4192893650

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PROJECT NO.:WIL-186002 A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS 10:25 21-DEC-93 PAGE 3
SPONSOR:CMA ORGAN WEIGHTS RELATIVE TO FINAL BODY WEIGHTS (GRAMS/100 GRAMS) WEEK 4
SPONSOR NO.:PA-5.ORF/REP-WIL

----- F E M A L E -----

GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	50 MG/KG/DAY	125 MG/KG/DAY	250 MG/KG/DAY	500 MG/KG/DAY
FINAL BODY WT						
MEAN	294.	285.	293.	298.	300.	317.
S.D.	21.8	13.9	8.8	21.0	11.6	18.9
N	5	5	5	4	5	4
BRAIN						
MEAN	0.668	0.669	0.650	0.633	0.638	0.597*
S.D.	0.0450	0.0227	0.0261	0.0545	0.0333	0.0240
N	5	5	5	4	5	4
LIVER						
MEAN	4.044	3.923	3.877	3.737	4.176	4.503
S.D.	0.4046	0.2987	0.2244	0.4613	0.3874	0.2851
N	5	5	5	4	5	4
KIDNEYS						
MEAN	0.730	0.755	0.757	0.702	0.742	0.711
S.D.	0.0698	0.0361	0.0402	0.0655	0.0704	0.0549
N	5	5	5	4	5	4
HEART						
MEAN	0.363	0.387	0.367	0.342	0.327	0.324
S.D.	0.0106	0.0175	0.0240	0.0162	0.0305	0.0322
N	5	5	5	4	5	4

UNAUDITED DRAFT

* = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP 1 AT 0.05 LEVEL USING DUNNETT'S TEST

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PROJECT NO.:WIL-186002 A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS 10:25 21-DEC-93 PAGE 4
SPONSOR:CMA ORGAN WEIGHTS RELATIVE TO FINAL BODY WEIGHTS (GRAMS/100 GRAMS) WEEK 4
SPONSOR NO.:PA-5.0RF/REP-WIL

----- F E M A L E -----

GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	50 MG/KG/DAY	125 MG/KG/DAY	250 MG/KG/DAY	500 MG/KG/DAY
OVARIES						
MEAN	0.048	0.050	0.050	0.049	0.053	0.049
S.D.	0.0144	0.0048	0.0089	0.0026	0.0098	0.0049
N	5	5	5	4	5	4
ADRENAL GLANDS						
MEAN	0.032	0.031	0.031	0.031	0.037	0.035
S.D.	0.0028	0.0035	0.0028	0.0029	0.0047	0.0024
N	5	5	5	4	5	4

UNAUDITED DRAFT

NONE SIGNIFICANTLY DIFFERENT USING DUNNETT'S TEST

DEC 21 '93 16:14 F-536 T-538 P-006 WIL RESEARCH 4192893650

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PROJECT NO.:WIL-186002
SPONSOR:CMA
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A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS
ORGAN WEIGHTS RELATIVE TO FINAL BODY WEIGHTS (GRAMS/100 GRAMS)

UNAUDITED DRAFT

MALE GROUP: 0 MG/KG/DAY

ANIMAL	FBW(G)	BRAIN	LIVER	KIDNEYS	HEART	TESTES	EPIDIDYMIDES	ADRENAL GLANDS
18856	479.	0.436	4.134	0.645	0.378	0.729	0.263	0.015
18866	534.	0.356	4.034	0.755	0.324	0.609	0.228	0.016
18877	503.	0.378	4.270	0.720	0.318	0.652	0.272	0.012
18880	497.	0.425	3.873	0.751	0.340	0.712	0.207	0.017
18888	443.	0.433	3.964	0.707	0.296	0.736	0.262	0.009
MEAN	491.	0.406	4.055	0.716	0.331	0.688	0.246	0.014
S.D.	33.5	0.0363	0.1536	0.0444	0.0305	0.0550	0.0277	0.0033
N	5	5	5	5	5	5	5	5

FBW = FINAL BODY WEIGHT

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PROJECT NO.:WIL-186002
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SPONSOR NO.:PA-5.ORF/REP-WIL

A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS
ORGAN WEIGHTS RELATIVE TO FINAL BODY WEIGHTS (GRAMS/100 GRAMS)

MALE GROUP: 10 MG/KG/DAY

UNAUDITED DRAFT

ANIMAL	FBW(G)	BRAIN	LIVER	KIDNEYS	HEART	TESTES	EPIDIDYMIDES	ADRENAL GLANDS
18855	424.	0.479	3.903	0.745	0.370	0.835	0.288	0.015
18863	491.	0.420	3.900	0.739	0.403	0.725	0.285	0.015
18873	555.	0.373	4.294	0.760	0.306	0.726	0.247	0.011
18874	477.	0.405	4.130	0.784	0.323	0.805	0.249	0.013
18889	503.	0.423	4.006	0.775	0.332	0.706	0.227	0.014
MEAN	490.	0.420	4.047	0.761	0.347	0.759	0.259	0.014
S.D.	47.2	0.0385	0.1673	0.0191	0.0392	0.0569	0.0264	0.0017
N	5	5	5	5	5	5	5	5

FBW = FINAL BODY WEIGHT

DEC 21 '93 16:14 F-536 T-538 P-008 WIL RESEARCH 4192893650

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PROJECT NO.:WIL-186002 A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS 10:07 21-DEC-93 PAGE 3
SPONSOR:CHA ORGAN WEIGHTS RELATIVE TO FINAL BODY WEIGHTS (GRAMS/100 GRAMS) WEEK 4
SPONSOR NO.:PA-5.ORF/REP-WIL

MALE GROUP: 50 MG/KG/DAY

UNAUDITED DRAFT

ANIMAL	FBW(G)	BRAIN	LIVER	KIDNEYS	HEART	TESTES	EPIDID YMIDES	ADRENAL GLANDS
18851	475.	0.436	3.851	0.834	0.375	0.739	0.282	0.013
18868	518.	0.382	4.160	0.676	0.272	0.705	0.253	0.010
18870	395.	0.511	3.841	0.820	0.367	0.949	0.332	0.017
18872	567.	0.363	4.321	0.741	0.284	0.665	0.236	0.010
18883	518.	0.396	4.392	0.749	0.299	0.728	0.237	0.014
MEAN	495.	0.418	4.113	0.764	0.319	0.757	0.268	0.013
S.D.	64.5	0.0587	0.2578	0.0643	0.0481	0.1109	0.0403	0.0029
N	5	5	5	5	5	5	5	5

FBW = FINAL BODY WEIGHT

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PROJECT NO.:WIL-186002
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A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS
ORGAN WEIGHTS RELATIVE TO FINAL BODY WEIGHTS (GRAMS/100 GRAMS)

MALE GROUP: 125 MG/KG/DAY

UNAUDITED DRAFT

ANIMAL	FBW(G)	BRAIN	LIVER	KIDNEYS	HEART	TESTES	EPIDIDYMIDES	ADRENAL GLANDS
18853	434.	0.445	4.180	0.689	0.313	0.839	0.302	0.014
18857	449.	0.465	3.470	0.650	0.323	0.757	0.265	0.018
18867	524.	0.393	4.055	0.655	0.324	0.739	0.263	0.013
18871	509.	0.422	4.143	0.749	0.320	0.633	0.216	0.015
18881	468.	0.444	4.241	0.784	0.342	0.829	0.274	0.010
MEAN	477.	0.434	4.018	0.705	0.324	0.759	0.264	0.015
S.D.	38.6	0.0274	0.3136	0.0591	0.0107	0.0830	0.0310	0.0019
N	5	5	5	5	5	5	5	5

FBW = FINAL BODY WEIGHT

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PROJECT NO.:WIL-186002
SPONSOR:CMA
SPONSOR NO.:PA-5.ORF/REP-WIL

A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS
ORGAN WEIGHTS RELATIVE TO FINAL BODY WEIGHTS (GRAMS/100 GRAMS)

MALE GROUP: 250 MG/KG/DAY

UNAUDITED DRAFT

ANIMAL	FBW(G)	BRAIN	LIVER	KIDNEYS	HEART	TESTES	EPIDIDYMIDES	ADRENAL GLANDS
18862	506.	0.395	4.138	0.713	0.292	0.696	0.235	0.019
18875	430.	0.447	4.314	0.702	0.288	0.819	0.284	0.019
18879	426.	0.460	3.756	0.789	0.279	0.782	0.293	0.021
18887	523.	0.384	4.841	0.742	0.315	0.795	0.285	0.015
18890	423.	0.463	4.473	0.790	0.345	0.837	0.303	0.020
MEAN	462.	0.430	4.304	0.747	0.304	0.786	0.280	0.019
S.D.	48.7	0.0375	0.4015	0.0413	0.0266	0.0545	0.0263	0.0023
N	5	5	5	5	5	5	5	5

FBW = FINAL BODY WEIGHT

SPONSOR COPY

PROJECT NO.:WIL-186002
SPONSOR:CMA
SPONSOR NO.:PA-5.ORF/REP-WIL

A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS
ORGAN WEIGHTS RELATIVE TO FINAL BODY WEIGHTS (GRAMS/100 GRAMS)

MALE GROUP: 500 MG/KG/DAY

UNAUDITED DRAFT

ANIMAL	FBW(G)	BRAIN	LIVER	KIDNEYS	HEART	TESTES	EPIDID YMIDES	ADRENAL GLANDS
18876	479.	0.438	4.812	0.672	0.269	0.875	0.290	0.021
18884	426.	0.479	4.028	0.812	0.317	0.862	0.333	0.024
MEAN	453.	0.459	4.420	0.742	0.293	0.869	0.312	0.023
S.D.	37.5	0.0290	0.5544	0.0990	0.0339	0.0092	0.0304	0.0021
N	2	2	2	2	2	2	2	2

FBW = FINAL BODY WEIGHT

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PROJECT NO.:WIL-186002
SPONSOR:CMA
SPONSOR NO.:PA-5.ORF/REP-WIL

A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS
ORGAN WEIGHTS RELATIVE TO FINAL BODY WEIGHTS (GRAMS/100 GRAMS)

FEMALE GROUP: 0 MG/KG/DAY

UNAUDITED DRAFT

ANIMAL	FBW(G)	BRAIN	LIVER	KIDNEYS	HEART	OVARIES	ADRENAL GLANDS
18894	282.	0.688	4.128	0.833	0.376	0.049	0.035
18898	298.	0.664	3.953	0.715	0.352	0.052	0.032
18918	328.	0.625	4.680	0.686	0.354	0.027	0.029
18921	290.	0.628	3.866	0.655	0.372	0.045	0.029
18927	270.	0.733	3.593	0.763	0.363	0.067	0.034
MEAN	294.	0.668	4.044	0.730	0.363	0.048	0.032
S.D.	21.8	0.0450	0.4046	0.0698	0.0106	0.0144	0.0028
N	5	5	5	5	5	5	5

FBW = FINAL BODY WEIGHT

DEC 21 '93 16:16 F-536 T-538 P-013 WIL RESEARCH 4192893650

FEMALE GROUP: 10 MG/KG/DAY

UNAUDITED DRAFT

ANIMAL	FBW(G)	BRAIN	LIVER	KIDNEYS	HEART	OVARIES	ADRENAL GLANDS
18905	293.	0.659	3.788	0.720	0.382	0.052	0.031
18906	270.	0.670	3.926	0.789	0.374	0.051	0.028
18910	304.	0.651	4.438	0.776	0.372	0.048	0.027
18917	274.	0.708	3.741	0.712	0.391	0.044	0.035
18923	284.	0.658	3.722	0.778	0.415	0.057	0.034
MEAN	285.	0.669	3.923	0.755	0.387	0.050	0.031
S.D.	13.9	0.0227	0.2987	0.0361	0.0175	0.0048	0.0035
N	5	5	5	5	5	5	5

FBW = FINAL BODY WEIGHT

DEC 21 '93 16:16 F-536 T-538 P-014 WIL RESEARCH 4192893658

PROJECT NO.:WIL-186002
SPONSOR:CMA
SPONSOR NO.:PA-5.ORF/REP-WIL

A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS
ORGAN WEIGHTS RELATIVE TO FINAL BODY WEIGHTS (GRAMS/100 GRAMS)

FEMALE GROUP: 50 MG/KG/DAY

UNAUDITED DRAFT

ANIMAL	FBW(G)	BRAIN	LIVER	KIDNEYS	HEART	OVARIES	ADRENAL GLANDS
18895	305.	0.662	3.639	0.728	0.370	0.046	0.032
18896	295.	0.678	4.122	0.786	0.325	0.043	0.027
18909	297.	0.623	4.027	0.731	0.377	0.059	0.034
18919	285.	0.621	3.958	0.726	0.379	0.061	0.029
18925	284.	0.665	3.641	0.813	0.384	0.043	0.032
MEAN	293.	0.650	3.877	0.757	0.367	0.050	0.031
S.D.	8.8	0.0261	0.2244	0.0402	0.0240	0.0089	0.0028
N	5	5	5	5	5	5	5

FBW = FINAL BODY WEIGHT

DEC 21 '93 16:16 F-536 T-538 P-015 WIL RESEARCH 4192893650

SPONSOR COPY

PROJECT NO.:WIL-186002 A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS 10:07 21-DEC-93 PAGE 10
SPONSOR:CMA ORGAN WEIGHTS RELATIVE TO FINAL BODY WEIGHTS (GRAMS/100 GRAMS) WEEK 4
SPONSOR NO.:PA-5.ORF/REP-WIL

FEMALE GROUP: 125 MG/KG/DAY

UNAUDITED DRAFT

ANIMAL	FBW(G)	BRAIN	LIVER	KIDNEYS	HEART	OVARIES	ADRENAL GLANDS
18892	327.	0.581	4.199	0.725	0.321	0.049	0.032
18903	278.	0.669	4.043	0.777	0.360	0.051	0.034
18913	289.	0.689	3.488	0.696	0.339	0.050	0.031
18929	298.	0.591	3.218	0.611	0.346	0.045	0.027
MEAN	298.	0.633	3.737	0.702	0.342	0.049	0.031
S.D.	21.0	0.0545	0.4613	0.0695	0.0162	0.0026	0.0029
N	4	4	4	4	4	4	4

FBW = FINAL BODY WEIGHT

DEC 21 '93 16:16 F-536 T-538 P-016 . WIL RESEARCH 4192893650

FEMALE GROUP: 250 MG/KG/DAY

UNAUDITED DRAFT

ANIMAL	FBW(G)	BRAIN	LIVER	KIDNEYS	HEART	OVARIES	ADRENAL GLANDS
18893	297.	0.593	4.354	0.808	0.343	0.061	0.038
18901	294.	0.677	4.061	0.656	0.310	0.048	0.031
18911	291.	0.656	4.522	0.821	0.313	0.042	0.036
18912	297.	0.616	3.552	0.724	0.296	0.050	0.036
18928	320.	0.647	4.391	0.703	0.372	0.066	0.044
MEAN	300.	0.638	4.176	0.742	0.327	0.053	0.037
S.D.	11.6	0.0333	0.3874	0.0704	0.0305	0.0098	0.0047
N	5	5	5	5	5	5	5

FBW = FINAL BODY WEIGHT

DEC 21 '93 16:16 F-536 T-538 P-017 WIL RESEARCH 4192893650

PROJECT NO.:WIL-186002
SPONSOR:CMA
SPONSOR NO.:PA-5.ORF/REP-WIL

A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS
ORGAN WEIGHTS RELATIVE TO FINAL BODY WEIGHTS (GRAMS/100 GRAMS)

FEMALE GROUP: 500 MG/KG/DAY

UNAUDITED DRAFT

ANIMAL	FBW(G)	BRAIN	LIVER	KIDNEYS	HEART	OVARIES	ADRENAL GLANDS
18891	330.	0.570	4.421	0.633	0.282	0.049	0.033
18899	317.	0.599	4.666	0.751	0.350	0.043	0.037
18904	330.	0.591	4.785	0.748	0.348	0.048	0.032
18922	290.	0.628	4.141	0.710	0.314	0.055	0.036
MEAN	317.	0.597	4.503	0.711	0.324	0.049	0.035
S.D.	18.9	0.0240	0.2851	0.0549	0.0322	0.0049	0.0024
N	4	4	4	4	4	4	4

FBW = FINAL BODY WEIGHT

PROJECT NO.:WIL-186002
SPONSOR:CMA
SPONSOR NO.:PA-5.ORF/REP-WIL

A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS
ORGAN WEIGHTS (GRAMS) - SUMMARY OF MEANS

UNAUDITED DRAFT

		MALE					
	GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	50 MG/KG/DAY	125 MG/KG/DAY	250 MG/KG/DAY	500 MG/KG/DAY
BRAIN	MEAN	1.98	2.04	2.04	2.06	1.97	2.07
	S.D.	0.106	0.073	0.036	0.081	0.036	0.042
	N	5	5	5	5	5	2
LIVER	MEAN	19.93	19.88	20.45	19.18	19.95	20.11
	S.D.	1.665	2.614	3.723	2.368	3.480	4.165
	N	5	5	5	5	5	2
KIDNEYS	MEAN	3.52	3.73	3.76	3.36	3.44	3.34
	S.D.	0.403	0.389	0.383	0.398	0.322	0.170
	N	5	5	5	5	5	2
HEART	MEAN	1.63	1.69	1.56	1.55	1.40	1.32
	S.D.	0.193	0.174	0.146	0.139	0.188	0.042
	N	5	5	5	5	5	2
TESTES	MEAN	3.36	3.70	3.69	3.60	3.61	3.93*
	S.D.	0.139	0.221	0.112	0.290	0.317	0.368
	N	5	5	5	5	5	2

* = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP 1 AT 0.05 LEVEL USING DUNNETT'S TEST

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A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS
ORGAN WEIGHTS (GRAMS) - SUMMARY OF MEANS

UNAUDITED DRAFT

GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	50 MG/KG/DAY	125 MG/KG/DAY	250 MG/KG/DAY	500 MG/KG/DAY
			----- M A L E -----			
EPIDIDYMIDES						
MEAN	1.21	1.26	1.31	1.25	1.29	1.41
S.D.	0.126	0.115	0.045	0.109	0.119	0.021
N	5	5	5	5	5	2
ADRENAL GLANDS						
MEAN	0.0676	0.0668	0.0628	0.0728	0.0858*	0.1020**
S.D.	0.01763	0.00603	0.00783	0.00716	0.00605	0.00148
N	5	5	5	5	5	2

* = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP 1 AT 0.05 LEVEL USING DUNNETT'S TEST
** = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP 1 AT 0.01 LEVEL USING DUNNETT'S TEST

UNAUDITED DRAFT

	GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	50 MG/KG/DAY	125 MG/KG/DAY	250 MG/KG/DAY	500 MG/KG/DAY
		----- F E M A L E -----					
BRAIN							
	MEAN	1.95	1.91	1.91	1.88	1.91	1.89
	S.D.	0.085	0.067	0.105	0.095	0.123	0.054
	N	5	5	5	4	5	4
LIVER							
	MEAN	11.94	11.20	11.37	11.16	12.53	14.30
	S.D.	2.079	1.315	0.727	1.848	1.336	1.611
	N	5	5	5	4	5	4
KIDNEYS							
	MEAN	2.14	2.15	2.22	2.09	2.22	2.25
	S.D.	0.173	0.150	0.104	0.233	0.194	0.206
	N	5	5	5	4	5	4
HEART							
	MEAN	1.07	1.10	1.08	1.02	0.98	1.03
	S.D.	0.065	0.065	0.068	0.031	0.128	0.123
	N	5	5	5	4	5	4
OVARIES							
	MEAN	0.1378	0.1440	0.1480	0.1449	0.1608	0.1534
	S.D.	0.03448	0.01658	0.02519	0.01085	0.03524	0.01229
	N	5	5	5	4	5	4

NONE SIGNIFICANTLY DIFFERENT USING DUNNETT'S TEST

SPONSOR COPY

A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS

ORGAN WEIGHTS (GRAMS) - SUMMARY OF MEANS

UNAUDITED DRAFT

GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	50 MG/KG/DAY	125 MG/KG/DAY	250 MG/KG/DAY	500 MG/KG/DAY
----- F E M A L E -----						
ADRENAL GLANDS						
MEAN	0.0924	0.0888	0.0904	0.0920	0.1112	0.1087
S.D.	0.00553	0.00901	0.00946	0.01032	0.01926	0.00629
N	5	5	5	4	5	4

NONE SIGNIFICANTLY DIFFERENT USING DUNNETT'S TEST

SPONSOR COPY

PROJECT NO.:WIL-186002
SPONSOR:CMA
SPONSOR NO.:PA-5.ORF/REP-WIL

A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS
ORGAN WEIGHTS RELATIVE TO BRAIN WEIGHTS (GRAMS/100 GRAMS)

UNAUDITED DRAFT

		----- MALE -----					
	GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	50 MG/KG/DAY	125 MG/KG/DAY	250 MG/KG/DAY	500 MG/KG/DAY
BRAIN							
	MEAN	1.98	2.04	2.04	2.06	1.97	2.07
	S.D.	0.106	0.073	0.036	0.081	0.036	0.042
	N	5	5	5	5	5	2
LIVER							
	MEAN	1007.697	972.565	1004.405	930.432	1010.896	969.398
	S.D.	114.4179	124.0205	181.0827	109.1472	162.1312	181.3319
	N	5	5	5	5	5	2
KIDNEYS							
	MEAN	178.055	182.525	184.324	162.958	174.533	161.471
	S.D.	24.7745	18.3285	16.4[illegible]	15.8303	13.2460	11.5082
	N	5	5	5	5	5	2
HEART							
	MEAN	82.038	82.756	76.550	75.021	71.175	63.803*
	S.D.	8.6789	7.6806	5.9958	5.3182	8.5293	3.3566
	N	5	5	5	5	5	2
TESTES							
	MEAN	169.647	181.503	181.293	175.090	183.362	189.713
	S.D.	2.3185	14.3608	6.6245	17.8330	14.1434	13.8749
	N	5	5	5	5	5	2

* = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP 1 AT 0.05 LEVEL USING DUNNETT'S TEST

SPONSOR COPY

A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS
ORGAN WEIGHTS RELATIVE TO BRAIN WEIGHTS (GRAMS/100 GRAMS)

GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	50 MG/KG/DAY	125 MG/KG/DAY	250 MG/KG/DAY	500 MG/KG/DAY
	----- MALE -----					
EPIDIDYMIDES						
MEAN	61.167	61.885	64.159	60.901	65.251	67.899
S.D.	8.4085	5.6700	2.3933	7.0119	5.4081	2.4169
N	5	5	5	5	5	2
ADRENAL GLANDS						
MEAN	3.399	3.268	3.082	3.524	4.353*	4.927**
S.D.	0.8559	0.2604	0.3666	0.3369	0.2970	0.1725
N	5	5	5	5	5	2

UNAUDITED DRAFT

* = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP 1 AT 0.05 LEVEL USING DUNNETT'S TEST
** = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP 1 AT 0.01 LEVEL USING DUNNETT'S TEST

SPONSOR COPY

PROJECT NO.:WIL-186002 | A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS | 12:44 14-DEC-93 PAGE 3

SPONSOR:CMA | ORGAN WEIGHTS RELATIVE TO BRAIN WEIGHTS (GRAMS/100 GRAMS) | WEEK 4

SPONSOR NO.:PA-5.0RF/REP-WIL

		----- FEMALE -----					
	GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	50 MG/KG/DAY	125 MG/KG/DAY	250 MG/KG/DAY	500 MG/KG/DAY
BRAIN							
	MEAN	1.95	1.91	1.91	1.88	1.91	1.89
	S.D.	0.085	0.067	0.105	0.095	0.123	0.054
	N	5	5	5	4	5	4
LIVER							
	MEAN	609.913	587.134	597.674	594.588	655.782	756.030*
	S.D.	92.2580	56.9007	47.2692	94.3638	65.6684	65.9061
	N	5	5	5	4	5	4
KIDNEYS							
	MEAN	109.380	112.979	116.474	111.320	116.932	119.072
	S.D.	6.9805	8.0073	4.3981	11.1374	15.0901	8.0226
	N	5	5	5	4	5	4
HEART							
	MEAN	54.618	57.832	56.634	54.199	51.381	54.216
	S.D.	3.7062	3.1497	5.2578	3.8536	5.8582	5.1846
	N	5	5	5	4	5	4
OVARIES							
	MEAN	7.075	7.565	7.826	7.720	8.417	8.136
	S.D.	1.7827	0.9252	1.6884	0.5157	1.7615	0.7511
	N	5	5	5	4	5	4

UNAUDITED DRAFT

* = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP 1 AT 0.05 LEVEL USING DUNNETT'S TEST

SPONSOR COPY

PROJECT NO.:WIL-186002
SPONSOR:CMA
SPONSOR NO.:PA-5.ORF/REP-WIL

A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS
ORGAN WEIGHTS RELATIVE TO BRAIN WEIGHTS (GRAMS/100 GRAMS)

	----- F E M A L E -----					
GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	50 MG/KG/DAY	125 MG/KG/DAY	250 MG/KG/DAY	500 MG/KG/DAY
ADRENAL GLANDS						
MEAN	4.730	4.657	4.753	4.898	5.821*	5.762*
S.D.	0.2011	0.4571	0.5279	0.4968	0.9064	0.3205
N	5	5	5	5	5	4

UNAUDITED DRAFT

* = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP 1 AT 0.05 LEVEL USING DUNNETT'S TEST

SPONSOR COPY

PROJECT NO.:WIL-186002 A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS 11:58 14-DEC-93 PAGE 1

SPONSOR:CMA SUMMARY OF SURVIVAL AND DISPOSITION

SPONSOR NO.:PA-5.ORF/REP-WIL

MALES

GROUP :	1					2					3					4					5					6				
WEEK	LIVE	FD	EM	EE	SE	LIVE	FD	EM	EE	SE	LIVE	FD	EM	EE	SE	LIVE	FD	EM	EE	SE	LIVE	FD	EM	EE	SE	LIVE	FD	EM	EE	SE
0	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0	4	1	0	0	0
1	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0	3	1	0	0	0
2	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0	2	1	0	0	0
3	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0	2	0	0	0	0
4	0	0	0	0	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0	2

UNAUDITED DRAFT

WEEK = WEEK OF STUDY FD = FOUND DEAD EM = EUTHANIZED MORIBUND EE = EUTHANIZED IN EXTREMIS SE = SCHEDULED EUTHANIZATION

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 50 MG/KG/DAY 4- 125 MG/KG/DAY 5- 250 MG/KG/DAY 6- 500 MG/KG/DAY

PROJECT NO.:WIL-186002
SPONSOR:CMA
SPONSOR NO.:PA-5.ORF/REP-WIL

A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS
SUMMARY OF SURVIVAL AND DISPOSITION

FEMALES

GROUP :	1					2					3					4					5					6				
WEEK	LIVE	FD	EM	EE	SE	LIVE	FD	EM	EE	SE	LIVE	FD	EM	EE	SE	LIVE	FD	EM	EE	SE	LIVE	FD	EM	EE	SE	LIVE	FD	EM	EE	SE
0	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0
1	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0	4	1	0	0	0	5	0	0	0	0	5	0	0	0	0
2	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0	4	0	0	0	0	5	0	0	0	0	4	1	0	0	0
3	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0	4	0	0	0	0	5	0	0	0	0	4	0	0	0	0
4	0	0	0	0	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0	4	0	0	0	0	5	0	0	0	0	4

UNAUDITED DRAFT

WEEK = WEEK OF STUDY FD = FOUND DEAD EM = EUTHANIZED MORIBUND EE = EUTHANIZED IN EXTREMIS SE = SCHEDULED EUTHANIZATION

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 50 MG/KG/DAY 4- 125 MG/KG/DAY 5- 250 MG/KG/DAY 6- 500 MG/KG/DAY

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PROJECT NO.:WIL-186C02 A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS 11:58 14-DEC-93 PAGE 1

SPONSOR:CMA SUMMARY OF SURVIVAL AND DISPOSITION

SPONSOR NO.:PA-5.ORF/REP-WIL

MALES

GROUP :	1					2					3					4					5					6				
WEEK	LIVE	FD	EM	EE	SE	LIVE	FD	EM	EE	SE	LIVE	FD	EM	EE	SE	LIVE	FD	EM	EE	SE	LIVE	FD	EM	EE	SE	LIVE	FD	EM	EE	SE
0	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0	4	1	0	0	0
1	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0	3	1	0	0	0
2	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0	2	1	0	0	0
3	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0	2	0	0	0	0
4	0	0	0	0	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0	2

UNAUDITED DRAFT

WEEK = WEEK OF STUDY FD = FOUND DEAD EM = EUTHANIZED MORIBUND EE = EUTHANIZED IN EXTREMIS SE = SCHEDULED EUTHANIZATION

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 50 MG/KG/DAY 4- 125 MG/KG/DAY 5- 250 MG/KG/DAY 6- 500 MG/KG/DAY

SPONSOR COPY

PROJECT NO.:WIL-186002
SPONSOR:CMA
SPONSOR NO.:PA-5.ORF/REP-WIL

A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS
SUMMARY OF SURVIVAL AND DISPOSITION

FEMALES

GROUP :	1					2					3					4					5					6				
WEEK	LIVE	FD	EM	EE	SE	LIVE	FD	EM	EE	SE	LIVE	FD	EM	EE	SE	LIVE	FD	EM	EE	SE	LIVE	FD	EM	EE	SE	LIVE	FD	EM	EE	SE
0	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0
1	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0	4	1	0	0	0	5	0	0	0	0	5	0	0	0	0
2	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0	4	0	0	0	0	5	0	0	0	0	4	1	0	0	0
3	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0	4	0	0	0	0	5	0	0	0	0	4	0	0	0	0
4	0	0	0	0	5	0	0	0	0	5	0	0	0	0	5	0	0	0	0	4	0	0	0	0	5	0	0	0	0	4

UNAUDITED DRAFT

WEEK = WEEK OF STUDY FD = FOUND DEAD EM = EUTHANIZED MORIBUND EE = EUTHANIZED IN EXTREMIS SE = SCHEDULED EUTHANIZATION

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 50 MG/KG/DAY 4- 125 MG/KG/DAY 5- 250 MG/KG/DAY 6- 500 MG/KG/DAY

SPONSOR COPY

PROJECT NO.:WIL-186002 A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS 12:27 14-DEC-93 PAGE 1

SPONSOR:CMA SUMMARY OF CLINICAL FINDINGS: TOTAL OCCURRENCE/NO. OF ANIMALS

SPONSOR NO.:PA-5.ORF/REP-WIL

----- M A L E -----

TABLE RANGE: 11-12-93 TO 12-10-93

GROUP:	1	2	3	4	5	6
-NO SIGNIFICANT CLINICAL OBSERVATIONS	58/ 5	87/ 5	123/ 5	89/ 5	50/ 5	11/ 5
-FOUND DEAD	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	3/ 3
-SCHEDULED EUTHANIZATION	5/ 5	5/ 5	5/ 5	5/ 5	5/ 5	2/ 2
-HYPOACTIVE	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-ANIMAL COOL TO THE TOUCH	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-HAIR LOSS BASE OF TAIL	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	37/ 3
-HUNCHED APPEARANCE	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	5/ 3
-LESION BASE OF TAIL	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	23/ 3
-DRIED CLEAR MATTING UROGENITAL AREA	0/ 0	1/ 1	0/ 0	1/ 1	0/ 0	0/ 0
-RIGHT FOERLIMB APPEARS RED IN COLOR	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-LEFT FORELIMB APPEARS RED IN COLOR	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-RIGHT FOREPAW APPEARS SWOLLEN	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-LEFT FOREPAW APPEARS SWOLLEN	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-EXTREMITIES APPEAR PALE IN COLOR	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-DRIED RED MATERIAL PREPUCE AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-HAIR LOSS VENTRAL THORACIC AREA	0/ 0	0/ 0	0/ 0	0/ 0	2/ 1	0/ 0
-SCABBING BASE OF TAIL	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-HAIR LOSS RIGHT FORELIMB	41/ 2	26/ 1	0/ 0	37/ 2	19/ 1	0/ 0
-HAIR LOSS LEFT FORELIMB	37/ 3	26/ 1	0/ 0	26/ 2	4/ 1	0/ 0
-SCABBING RIGHT FORELIMB	16/ 2	6/ 1	0/ 0	12/ 1	0/ 0	0/ 0
-SCABBING LEFT FORELIMB	6/ 2	11/ 1	0/ 0	1/ 1	0/ 0	0/ 0
-WET TAN MATTING ANOGENITAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1	11/ 5
-WET YELLOW STAINING VENTRAL ABDOMINAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 50 MG/KG/DAY 4- 125 MG/KG/DAY 5- 250 MG/KG/DAY 6- 500 MG/KG/DAY

UNAUDITED DRAFT

PROJECT NO.:WIL-186002
SPONSOR:CMA
SPONSOR NO.:PA-5.ORF/REP-WIL

A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS
SUMMARY OF CLINICAL FINDINGS: TOTAL OCCURRENCE/NO. OF ANIMALS

----- M A L E -----

TABLE RANGE: 11-12-93 TO 12-10-93

GROUP:	1	2	3	4	5	6
-WET YELLOW STAINING UROGENITAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	3/ 2
-WET YELLOW STAINING ANOGENITAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	2/ 2
-DRIED BROWN STAINING RIGHT FORELIMB	55/ 3	2/ 1	0/ 0	7/ 1	0/ 0	4/ 2
-DRIED BROWN STAINING LEFT FORELIMB	51/ 3	2/ 1	0/ 0	0/ 0	0/ 0	4/ 2
-DRIED TAN MATTING ANOGENITAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	6/ 3	11/ 5
-DRIED TAN MATTING UROGENITAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	3/ 3
-DRIED BROWN MATERIAL PROXIMAL END OF TAIL	0/ 0	0/ 0	0/ 0	0/ 0	3/ 1	19/ 5
-DRIED BROWN STAINING VENTRAL NECK	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	2/ 1
-DRIED BROWN STAINING VENTRAL THORACIC AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	3/ 2
-DRIED BROWN STAINING ANOGENITAL AREA	5/ 1	1/ 1	0/ 0	1/ 1	0/ 0	4/ 2
-DRIED BROWN STAINING VENTRAL ABDOMINAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	2/ 2
-DRIED BROWN MATERIAL ENTIRE LENGTH OF TAIL	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1	10/ 3
-DRIED TAN STAINING PROXIMAL END OF TAIL	0/ 0	0/ 0	0/ 0	0/ 0	6/ 2	6/ 3
-RALES	0/ 0	0/ 0	4/ 3	8/ 1	2/ 2	4/ 2
-LABORED RESPIRATION	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	2/ 2
-DRIED RED MATERIAL AROUND NOSE	1/ 1	8/ 3	7/ 2	4/ 2	4/ 3	11/ 4
-DRIED TAN STAINING AROUND NOSE	0/ 0	0/ 0	0/ 0	0/ 0	2/ 1	5/ 4
-DRIED BROWN MATTING AROUND NOSE	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	6/ 3
-AREA AROUND NOSE APPEARS RED IN COLOR	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-WET RED MATERIAL AROUND NOSE	1/ 1	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0
-RED NASAL DISCHARGE	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0	0/ 0
-DRIED RED STAINING AROUND NOSE	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-SCABBING RIGHT EAR	31/ 5	2/ 1	9/ 3	11/ 2	2/ 1	1/ 1

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 50 MG/KG/DAY 4- 125 MG/KG/DAY 5- 250 MG/KG/DAY 6- 500 MG/KG/DAY

UNAUDITED DRAFT

PROJECT NO.:WIL-186002
SPONSOR:CMA
SPONSOR NO.:PA-5.0RF/REP-WIL

A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS
SUMMARY OF CLINICAL FINDINGS: TOTAL OCCURRENCE/NO. OF ANIMALS

----- M A L E -----

TABLE RANGE: 11-12-93 TO 12-10-93

GROUP:	1	2	3	4	5	6
-RIGHT EAR APPEARS RED AND SWOLLEN	1/ 1	0/ 0	4/ 1	0/ 0	0/ 0	4/ 1
-MUCOID DIARRHEA	0/ 0	0/ 0	0/ 0	2/ 2	17/ 4	26/ 5
-SOFT STOOL	0/ 0	0/ 0	0/ 0	0/ 0	32/ 5	11/ 4
-DIARRHEA	0/ 0	0/ 0	0/ 0	0/ 0	11/ 3	4/ 3
-MUCOID DIARRHEA APPEARS YELLOW IN COLOR	0/ 0	0/ 0	0/ 0	0/ 0	12/ 4	32/ 5
-DECREASED DEFECATION	0/ 0	0/ 0	1/ 1	0/ 0	0/ 0	3/ 2
-FECES APPEAR SMALL IN SIZE	0/ 0	0/ 0	1/ 1	0/ 0	0/ 0	0/ 0
-YELLOW MUCOID FECES WITH APPARENT WHITE MATERIAL	0/ 0	0/ 0	0/ 0	1/ 1	1/ 1	4/ 4
-MUCOID FECES	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	2/ 1
-WET TAN MATTING UROGENITAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	5/ 3
-UNKEMPT APPEARANCE	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	9/ 3
-DRIED BROWN STAINING UROGENITAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	2/ 2
-WET CLEAR MATTING ANOGENITAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	8/ 4
-DRIED TAN MATTING VENTRAL NECK	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	9/ 4
-DRIED TAN MATTING VENTRAL THORACIC AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	8/ 3
-DRIED TAN MATTING RIGHT FOERELIMB	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1	9/ 4
-DRIED TAN MATTING LEFT FORELIMB	1/ 1	0/ 0	0/ 0	0/ 0	0/ 0	9/ 4
-DRIED TAN MATTING VENTRAL ABDOMINAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	11/ 4
-WET YELLOW MATERIAL PROXIMAL END OF TAIL	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	3/ 2
-DRIED CLEAR MATTING VENTRAL NECK	0/ 0	0/ 0	1/ 1	2/ 2	1/ 1	1/ 1
-DRIED CLEAR MATTING VENTRAL THORACIC AREA	0/ 0	0/ 0	1/ 1	1/ 1	1/ 1	1/ 1
-DRIED CLEAR MATTING RIGHT FORELIMB	0/ 0	0/ 0	1/ 1	1/ 1	1/ 1	1/ 1
-DRIED CLEAR MATTING LEFT FORELIMB	0/ 0	0/ 0	1/ 1	1/ 1	1/ 1	1/ 1

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 50 MG/KG/DAY 4- 125 MG/KG/DAY 5- 250 MG/KG/DAY 6- 500 MG/KG/DAY

UNAUDITED DRAFT

SPONSOR COPY

A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS
SUMMARY OF CLINICAL FINDINGS: TOTAL OCCURRENCE/NO. OF ANIMALS

----- M A L E -----

TABLE RANGE: 11-12-93 TO 12-10-93

GROUP:	1	2	3	4	5	6
-HAIR LOSS VENTRAL ABDOMINAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	19/ 1	0/ 0
-DRIED CLEAR MATTING AROUND MOUTH	0/ 0	0/ 0	1/ 1	1/ 1	0/ 0	0/ 0
-DRIED RED STAINING AROUND MOUTH	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-WET TAN STAINING AROUND MOUTH	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0
-DRIED TAN STAINING AROUND MOUTH	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	2/ 1
-DRIED BROWN MATTING AROUND MOUTH	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	9/ 4
-TEETH LONG, TRIMMED	0/ 0	3/ 1	0/ 0	0/ 0	4/ 1	0/ 0
-UPPER INCISORS MALALIGNED	0/ 0	24/ 1	0/ 0	0/ 0	20/ 1	0/ 0
-AREA AROUND MOUTH APPEARS RED IN COLOR	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	3/ 2
-AREA AROUND MOUTH APPEARS SWOLLEN	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-DRIED CLEAR MATTING ANOGENITAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0
-WET RED MATERIAL PREPUCE AREA	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0	2/ 1
-DRIED RED STAINING DISTAL END OF TAIL	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-DRIED CLEAR MATTING VENTRAL ABDOMINAL AREA	0/ 0	0/ 0	1/ 1	1/ 1	0/ 0	0/ 0

UNAUDITED DRAFT

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 50 MG/KG/DAY 4- 125 MG/KG/DAY 5- 250 MG/KG/DAY 6- 500 MG/KG/DAY

PROJECT NO.:WIL-186002
SPONSOR:CMA
SPONSOR NO.:PA-5.ORF/REP-WIL

A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS
SUMMARY OF CLINICAL FINDINGS: TOTAL OCCURRENCE/NO. OF ANIMALS

----- F E M A L E -----

TABLE RANGE: 11-12-93 TO 12-10-93

GROUP:	1	2	3	4	5	6
-NO SIGNIFICANT CLINICAL OBSERVATIONS	116/ 5	130/ 5	137/ 5	62/ 5	78/ 5	14/ 5
-FOUND DEAD	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0	1/ 1
-SCHEDULED EUTHANIZATION	5/ 5	5/ 5	5/ 5	4/ 4	5/ 5	4/ 4
-AGGRESSIVE	0/ 0	0/ 0	0/ 0	0/ 0	2/ 1	0/ 0
-VOCALIZED	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0
-HYPOACTIVE	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0	0/ 0
-ANIMAL COOL TO THE TOUCH	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0	0/ 0
-HAIR LOSS BASE OF TAIL	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	34/ 4
-HUNCHED APPEARANCE	0/ 0	0/ 0	0/ 0	2/ 1	1/ 1	3/ 2
-LESION BASE OF TAIL	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	11/ 3
-HAIR LOSS LEFT HINDLIMB	0/ 0	0/ 0	0/ 0	18/ 1	13/ 1	4/ 2
-HAIR LOSS LEFT LATERAL ABDOMINAL AREA	0/ 0	0/ 0	0/ 0	18/ 1	3/ 1	0/ 0
-EXTREMITIES APPEAR PALE IN COLOR	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0	0/ 0
-HAIR LOSS UROGENITAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	43/ 4
-HAIR LOSS ANOGENITAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	25/ 4
-HAIR LOSS RIGHT HINDLIMB	0/ 0	0/ 0	0/ 0	13/ 1	13/ 1	17/ 2
-DRIED CLEAR MATTING RIGHT HINDLIMB	1/ 1	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0
-HAIR LOSS VENTRAL THORACIC AREA	0/ 0	0/ 0	0/ 0	0/ 0	16/ 1	0/ 0
-SCABBING BASE OF TAIL	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	8/ 4
-HAIR LOSS RIGHT LATERAL ABDOMINAL AREA	0/ 0	0/ 0	0/ 0	15/ 1	3/ 1	0/ 0
-HAIR LOSS RIGHT FORELIMB	15/ 2	0/ 0	0/ 0	42/ 3	23/ 3	15/ 1
-HAIR LOSS LEFT FORELIMB	20/ 1	0/ 0	0/ 0	12/ 3	19/ 2	17/ 2
-SCABBING RIGHT FORELIMB	2/ 1	0/ 0	0/ 0	0/ 0	2/ 1	0/ 0

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 50 MG/KG/DAY 4- 125 MG/KG/DAY 5- 250 MG/KG/DAY 6- 500 MG/KG/DAY

UNAUDITED DRAFT

----- F E M A L E -----

TABLE RANGE: 11-12-93 TO 12-10-93

GROUP:	1	2	3	4	5	6
-SCABBING LEFT FORELIMB	6/ 1	0/ 0	0/ 0	0/ 0	0/ 0	4/ 3
-WET TAN MATTING ANOGENITAL AREA	0/ 0	0/ 0	0/ 0	1/ 1	1/ 1	10/ 4
-DRIED RED STAINING RIGHT FORELIMB	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0	3/ 2
-DRIED RED STAINING LEFT FORELIMB	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0	3/ 2
-WET YELLOW STAINING UROGENITAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1	1/ 1
-WET YELLOW STAINING ANOGENITAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-WET YELLOW STAINING LEFT FORELIMB	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0
-DRIED BROWN STAINING RIGHT FORELIMB	7/ 1	0/ 0	0/ 0	16/ 2	7/ 1	1/ 1
-DRIED BROWN STAINING LEFT FORELIMB	12/ 1	0/ 0	0/ 0	12/ 2	0/ 0	2/ 1
-DRIED TAN MATTING ANOGENITAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	3/ 2	12/ 5
-DRIED TAN MATTING UROGENITAL AREA	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0	4/ 2
-DRIED BROWN MATERIAL PROXIMAL END OF TAIL	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	6/ 3
-DRIED BROWN STAINING VENTRAL NECK	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	2/ 2
-DRIED BROWN STAINING ANOGENITAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	17/ 5
-DRIED BROWN STAINING VENTRAL ABDOMINAL AREA	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0	3/ 3
-DRIED BROWN MATERIAL ENTIRE LENGTH OF TAIL	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	2/ 2
-DRIED TAN STAINING PROXIMAL END OF TAIL	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1	4/ 3
-RALES	0/ 0	0/ 0	0/ 0	7/ 2	5/ 2	2/ 1
-LABORED RESPIRATION	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0	0/ 0
-DRIED RED MATERIAL AROUND NOSE	1/ 1	1/ 1	0/ 0	1/ 1	0/ 0	13/ 4
-DRIED TAN STAINING AROUND NOSE	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0	2/ 2
-DRIED BROWN MATTING AROUND NOSE	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0	1/ 1
-LACRIMATION RIGHT EYE	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0	0/ 0

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 50 MG/KG/DAY 4- 125 MG/KG/DAY 5- 250 MG/KG/DAY 6- 500 MG/KG/DAY

UNAUDITED DRAFT

----- F E M A L E -----

TABLE RANGE: 11-12-93 TO 12-10-93

GROUP:	1	2	3	4	5	6
-LACRIMATION LEFT EYE	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0	0/ 0
-DRIED RED MATERIAL AROUND RIGHT EYE	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-DRIED RED STAINING AROUND NOSE	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-SCABBING RIGHT EAR	3/ 1	13/ 4	4/ 1	0/ 0	0/ 0	0/ 0
-RIGHT EAR APPEARS RED AND SWOLLEN	0/ 0	2/ 1	0/ 0	0/ 0	0/ 0	0/ 0
-BROWN NASAL DISCHARGE	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0	0/ 0
-DRIED BROWN MATERIAL AROUND RIGHT EYE	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0
-HAIR LOSS AROUND RIGHT EYE	0/ 0	0/ 0	0/ 0	0/ 0	12/ 1	0/ 0
-MUCOID DIARRHEA	0/ 0	0/ 0	0/ 0	0/ 0	4/ 2	22/ 5
-SOFT STOOL	0/ 0	0/ 0	0/ 0	0/ 0	5/ 4	21/ 5
-DIARRHEA	0/ 0	0/ 0	0/ 0	0/ 0	3/ 2	7/ 4
-MUCOID DIARRHEA APPEARS YELLOW IN COLOR	0/ 0	0/ 0	0/ 0	2/ 2	7/ 3	34/ 5
-DECREASED DEFECATION	0/ 0	0/ 0	0/ 0	2/ 1	3/ 1	1/ 1
-FECES APPEAR SMALL IN SIZE	0/ 0	1/ 1	0/ 0	5/ 1	0/ 0	0/ 0
-YELLOW MUCOID FECES WITH APPARENT WHITE MATERIAL	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1	2/ 2
-MUCOID DIARRHEA WITH APPARENT WHITE MATERIAL	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-WET TAN MATTING UROGENITAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	5/ 3
-UNKEMPT APPEARANCE	0/ 0	0/ 0	0/ 0	2/ 1	2/ 1	10/ 2
-DRIED BROWN STAINING UROGENITAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	2/ 2
-WET CLEAR MATTING ANOGENITAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0
-WET CLEAR MATTING VENTRAL NECK	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	2/ 2
-WET CLEAR MATTING RIGHT FORELIMB	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-DRIED TAN MATTING VENTRAL NECK	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 50 MG/KG/DAY 4- 125 MG/KG/DAY 5- 250 MG/KG/DAY 6- 500 MG/KG/DAY

UNAUDITED DRAFT

SPONSOR COPY

A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS
SUMMARY OF CLINICAL FINDINGS: TOTAL OCCURRENCE/NO. OF ANIMALS

----- F E M A L E -----

TABLE RANGE: 11-12-93 TO 12-10-93

GROUP:	1	2	3	4	5	6
-DRIED TAN MATTING VENTRAL THORACIC AREA	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1	1/ 1
-DRIED TAN MATTING RIGHT FOERELIMB	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0
-DRIED TAN MATTING LEFT FORELIMB	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0
-DRIED TAN MATTING VENTRAL ABDOMINAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	5/ 4
-SCABBING VENTRAL NECK	0/ 0	0/ 0	1/ 1	0/ 0	0/ 0	0/ 0
-DRIED CLEAR MATTING VENTRAL NECK	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0
-DRIED CLEAR MATTING VENTRAL THORACIC AREA	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0
-DRIED CLEAR MATTING RIGHT FORELIMB	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0
-DRIED CLEAR MATTING LEFT FORELIMB	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0
-HAIR LOSS VENTRAL ABDOMINAL AREA	0/ 0	0/ 0	0/ 0	2/ 1	20/ 1	0/ 0
-DRIED CLEAR MATTING AROUND MOUTH	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0
-DRIED RED STAINING AROUND MOUTH	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	4/ 3
-DRIED TAN STAINING AROUND MOUTH	0/ 0	0/ 0	0/ 0	2/ 2	1/ 1	4/ 4
-DRIED BROWN MATTING AROUND MOUTH	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0	1/ 1
-SCABBING AROUND MOUTH	0/ 0	2/ 1	3/ 2	0/ 0	0/ 0	0/ 0
-DRIED RED MATERIAL AROUND MOUTH	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	2/ 1
-DRIED CLEAR MATTING ANOGENITAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0
-DRIED CLEAR MATTING VENTRAL ABDOMINAL AREA	1/ 1	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0
-HAIR LOSS RIGHT LATERAL NECK	0/ 0	0/ 0	0/ 0	2/ 1	0/ 0	0/ 0
-SCABBING RIGHT LATERAL NECK	0/ 0	0/ 0	0/ 0	4/ 1	0/ 0	0/ 0

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 50 MG/KG/DAY 4- 125 MG/KG/DAY 5- 250 MG/KG/DAY 6- 500 MG/KG/DAY

UNAUDITED DRAFT

SPONSOR COPY

PROJECT NO.:WIL-186002
SPONSOR:CMA
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A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS
SUMMARY OF CLINICAL FINDINGS: TOTAL OCCURRENCE/NO. OF ANIMALS

----- M A L E -----

TABLE RANGE: 11-12-93 TO 12-09-93

GROUP:	1	2	3	4	5	6
AT TIME OF DOSING						
-AGGRESSIVE	0/ 0	0/ 0	0/ 0	1/ 1	4/ 2	8/ 3
-VOCALIZED	0/ 0	0/ 0	0/ 0	0/ 0	3/ 2	2/ 2
-ANIMAL COOL TO THE TOUCH	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-SHALLOW RESPIRATION	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-WET TAN MATTING AROUND NOSE	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-WET CLEAR MATTING VENTRAL THORACIC AREA	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0	0/ 0
-WET CLEAR MATTING RIGHT FORELIMB	0/ 0	0/ 0	0/ 0	1/ 1	1/ 1	1/ 1
-WET CLEAR MATTING LEFT FORELIMB	0/ 0	0/ 0	0/ 0	1/ 1	1/ 1	1/ 1
-WET TAN MATTING RIGHT FORELIMB	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-WET TAN MATTING LEFT FORELIMB	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-WET TAN STAINING AROUND MOUTH	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0	1/ 1
-SALIVATION	0/ 0	0/ 0	4/ 3	5/ 4	7/ 5	4/ 2

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 50 MG/KG/DAY 4- 125 MG/KG/DAY 5- 250 MG/KG/DAY 6- 500 MG/KG/DAY

UNAUDITED DRAFT

PROJECT NO.:WIL-186002
SPONSOR:CMA
SPONSOR NO.:PA-5.ORF/REP-WIL

A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS
SUMMARY OF CLINICAL FINDINGS: TOTAL OCCURRENCE/NO. OF ANIMALS

----- F E M A L E -----

TABLE RANGE: 11-12-93 TO 12-09-93

GROUP:	1	2	3	4	5	6
AT TIME OF DOSING						
-AGGRESSIVE	0/ 0	2/ 2	0/ 0	8/ 3	22/ 5	11/ 3
-VOCALIZED	0/ 0	0/ 0	0/ 0	3/ 1	14/ 3	0/ 0
-EXCESSIVE CHEWING	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0	0/ 0
-RALES	0/ 0	0/ 0	0/ 0	1/ 1	1/ 1	0/ 0
-SHALLOW RESPIRATION	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0	0/ 0
-WET RED MATERIAL AROUND NOSE	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-CLEAR NASAL DISCHARGE	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0
-SALIVATION	0/ 0	1/ 1	1/ 1	11/ 3	27/ 5	23/ 5
-ORAL CAVITY APPEARS OBSTRUCTED BY THICK BROWN MATERIAL	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0	0/ 0
-WET BROWN MATTING AROUND MOUTH	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1	1/ 1
-WET RED MATERIAL IN ORAL CAVITY	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0

UNAUDITED DRAFT

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 50 MG/KG/DAY 4- 125 MG/KG/DAY 5- 250 MG/KG/DAY 6- 500 MG/KG/DAY

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PROJECT NO.:WIL-1860C2 A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS 12:30 14-DEC-93 PAGE 1

SPONSOR:CMA SUMMARY OF CLINICAL FINDINGS: TOTAL OCCURRENCE/NO. OF ANIMALS

SPONSOR NO.:PA-5.ORF/REP-WIL

----- M A L E -----

TABLE RANGE: 11-12-93 TO 12-09-93

GROUP:	1	2	3	4	5	6
1-HOUR POST-DOSE						
-VOCALIZED	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-ANIMAL COOL TO THE TOUCH	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-HAIR LOSS BASE OF TAIL	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	5/ 3
-HUNCHED APPEARANCE	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	5/ 2
-LESION BASE OF TAIL	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	12/ 3
-RIGHT FOERLIMB APPEARS RED IN COLOR	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-LEFT FORELIMB APPEARS RED IN COLOR	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-EXTREMITIES APPEAR PALE IN COLOR	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-DRIED BROWN MATERIAL ANOGENITAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-VENTRAL NECK APPEARS RED IN COLOR	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-WET TAN MATTING ANOGENITAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	6/ 4
-WET YELLOW STAINING VENTRAL NECK AREA	0/ 0	0/ 0	1/ 1	1/ 1	0/ 0	2/ 2
-WET YELLOW STAINING VENTRAL THORACIC AREA	0/ 0	0/ 0	1/ 1	1/ 1	1/ 1	2/ 2
-WET YELLOW STAINING VENTRAL ABDOMINAL AREA	0/ 0	0/ 0	1/ 1	1/ 1	1/ 1	0/ 0
-WET YELLOW STAINING UROGENITAL AREA	0/ 0	0/ 0	1/ 1	3/ 3	6/ 2	1/ 1
-WET YELLOW STAINING ANOGENITAL AREA	0/ 0	0/ 0	1/ 1	3/ 3	3/ 2	1/ 1
-WET YELLOW STAINING RIGHT FORELIMB	0/ 0	0/ 0	1/ 1	0/ 0	0/ 0	2/ 2
-WET YELLOW STAINING LEFT FORELIMB	0/ 0	0/ 0	1/ 1	0/ 0	0/ 0	2/ 2
-DRIED BROWN STAINING RIGHT FORELIMB	0/ 0	0/ 0	0/ 0	1/ 1	2/ 2	1/ 1
-DRIED BROWN STAINING LEFT FORELIMB	0/ 0	0/ 0	0/ 0	1/ 1	2/ 2	1/ 1
-DRIED TAN MATTING ANOGENITAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	2/ 2	6/ 3
-DRIED TAN MATTING UROGENITAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	6/ 3
-DRIED BROWN MATERIAL PROXIMAL END OF TAIL	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1	5/ 3

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 50 MG/KG/DAY 4- 125 MG/KG/DAY 5- 250 MG/KG/DAY 6- 500 MG/KG/DAY

UNAUDITED DRAFT

30

SPONSOR COPY

PROJECT NO.:WIL-186002
SPONSOR:CMA
SPONSOR NO.:PA-5.ORF/REP-WIL

A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS
SUMMARY OF CLINICAL FINDINGS: TOTAL OCCURRENCE/NO. OF ANIMALS

----- M A L E -----

TABLE RANGE: 11-12-93 TO 12-09-93

GROUP:	1	2	3	4	5	6
1-HOUR POST-DOSE						
-DRIED BROWN STAINING VENTRAL NECK	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-DRIED BROWN STAINING VENTRAL THORACIC AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-DRIED BROWN STAINING ANOGENITAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	3/ 3
-DRIED BROWN STAINING VENTRAL ABDOMINAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	2/ 2
-DRIED BROWN MATERIAL ENTIRE LENGTH OF TAIL	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	3/ 3
-DRIED TAN STAINING PROXIMAL END OF TAIL	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0
-RALES	0/ 0	1/ 1	6/ 4	5/ 2	4/ 2	5/ 3
-LABORED RESPIRATION	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-DRIED RED MATERIAL AROUND NOSE	0/ 0	0/ 0	2/ 2	5/ 3	6/ 3	5/ 3
-DRIED TAN STAINING AROUND NOSE	0/ 0	0/ 0	0/ 0	0/ 0	11/ 4	6/ 4
-DRIED BROWN MATTING AROUND NOSE	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-WET CLEAR MATTING AROUND NOSE	0/ 0	0/ 0	1/ 1	4/ 2	3/ 3	2/ 2
-WET TAN MATTING AROUND NOSE	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	3/ 3
-WET RED MATERIAL AROUND NOSE	1/ 1	0/ 0	0/ 0	1/ 1	1/ 1	0/ 0
-RED NASAL DISCHARGE	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0
-DRIED CLEAR MATTING AROUND NOSE	0/ 0	0/ 0	0/ 0	0/ 0	2/ 1	1/ 1
-MUCOID DIARRHEA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-SOFT STOOL	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	3/ 1
-DIARRHEA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	2/ 2
-MUCOID DIARRHEA APPEARS YELLOW IN COLOR	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	2/ 2
-YELLOW MUCOID FECES WITH APPARENT WHITE MATERIAL	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-WET TAN MATTING UROGENITAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	3/ 2
-UNKEMPT APPEARANCE	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	7/ 3

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 50 MG/KG/DAY 4- 125 MG/KG/DAY 5- 250 MG/KG/DAY 6- 500 MG/KG/DAY

UNAUDITED DRAFT

SPONSOR COPY

PROJECT NO.:WIL-186002
SPONSOR:CMA
SPONSOR NO.:PA-5.ORF/REP-WIL

A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS
SUMMARY OF CLINICAL FINDINGS: TOTAL OCCURRENCE/NO. OF ANIMALS

----- M A L E -----

TABLE RANGE: 11-12-93 TO 12-09-93

GROUP:	1	2	3	4	5	6
1-HOUR POST-DOSE						
-VOCALIZED	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-ANIMAL COOL TO THE TOUCH	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-HAIR LOSS BASE OF TAIL	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	5/ 3
-HUNCHED APPEARANCE	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	5/ 2
-LESION BASE OF TAIL	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	12/ 3
-RIGHT FOERLIMB APPEARS RED IN COLOR	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-LEFT FORELIMB APPEARS RED IN COLOR	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-EXTREMITIES APPEAR PALE IN COLOR	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-DRIED BROWN MATERIAL ANOGENITAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-VENTRAL NECK APPEARS RED IN COLOR	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-WET TAN MATTING ANOGENITAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	6/ 4
-WET YELLOW STAINING VENTRAL NECK AREA	0/ 0	0/ 0	1/ 1	1/ 1	0/ 0	2/ 2
-WET YELLOW STAINING VENTRAL THORACIC AREA	0/ 0	0/ 0	1/ 1	1/ 1	1/ 1	2/ 2
-WET YELLOW STAINING VENTRAL ABDOMINAL AREA	0/ 0	0/ 0	1/ 1	1/ 1	1/ 1	0/ 0
-WET YELLOW STAINING UROGENITAL AREA	0/ 0	0/ 0	1/ 1	3/ 3	6/ 2	1/ 1
-WET YELLOW STAINING ANOGENITAL AREA	0/ 0	0/ 0	1/ 1	3/ 3	3/ 2	1/ 1
-WET YELLOW STAINING RIGHT FORELIMB	0/ 0	0/ 0	1/ 1	0/ 0	0/ 0	2/ 2
-WET YELLOW STAINING LEFT FORELIMB	0/ 0	0/ 0	1/ 1	0/ 0	0/ 0	2/ 2
-DRIED BROWN STAINING RIGHT FORELIMB	0/ 0	0/ 0	0/ 0	1/ 1	2/ 2	1/ 1
-DRIED BROWN STAINING LEFT FORELIMB	0/ 0	0/ 0	0/ 0	1/ 1	2/ 2	1/ 1
-DRIED TAN MATTING ANOGENITAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	2/ 2	6/ 3
-DRIED TAN MATTING UROGENITAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	6/ 3
-DRIED BROWN MATERIAL PROXIMAL END OF TAIL	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1	5/ 3

UNAUDITED DRAFT

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 50 MG/KG/DAY 4- 125 MG/KG/DAY 5- 250 MG/KG/DAY 6- 500 MG/KG/DAY

PROJECT NO.:WIL-186002
SPONSOR:CKA
SPONSOR NO.:PA-5.0RF/REP-WIL

SPONSOR COPY

A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS
SUMMARY OF CLINICAL FINDINGS: TOTAL OCCURRENCE/NO. OF ANIMALS

----- M A L E -----

TABLE RANGE: 11-12-93 TO 12-09-93

GROUP:	1	2	3	4	5	6
1-HOUR POST-DOSE						
-DRIED BROWN STAINING VENTRAL NECK	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-DRIED BROWN STAINING VENTRAL THORACIC AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-DRIED BROWN STAINING ANOGENITAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	3/ 3
-DRIED BROWN STAINING VENTRAL ABDOMINAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	2/ 2
-DRIED BROWN MATERIAL ENTIRE LENGTH OF TAIL	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	3/ 3
-DRIED TAN STAINING PROXIMAL END OF TAIL	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0
-RALES	0/ 0	1/ 1	6/ 4	5/ 2	4/ 2	5/ 3
-LABORED RESPIRATION	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-DRIED RED MATERIAL AROUND NOSE	0/ 0	0/ 0	2/ 2	5/ 3	6/ 3	5/ 3
-DRIED TAN STAINING AROUND NOSE	0/ 0	0/ 0	0/ 0	0/ 0	11/ 4	6/ 4
-DRIED BROWN MATTING AROUND NOSE	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-WET CLEAR MATTING AROUND NOSE	0/ 0	0/ 0	1/ 1	4/ 2	3/ 3	2/ 2
-WET TAN MATTING AROUND NOSE	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	3/ 3
-WET RED MATERIAL AROUND NOSE	1/ 1	0/ 0	0/ 0	1/ 1	1/ 1	0/ 0
-RED NASAL DISCHARGE	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0
-DRIED CLEAR MATTING AROUND NOSE	0/ 0	0/ 0	0/ 0	0/ 0	2/ 1	1/ 1
-MUCOID DIARRHEA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-SOFT STOOL	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	3/ 1
-DIARRHEA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	2/ 2
-MUCOID DIARRHEA APPEARS YELLOW IN COLOR	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	2/ 2
-YELLOW MUCOID FECES WITH APPARENT WHITE MATERIAL	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-WET TAN MATTING UROGENITAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	3/ 2
-UNKEMPT APPEARANCE	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	7/ 3

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 50 MG/KG/DAY 4- 125 MG/KG/DAY 5- 250 MG/KG/DAY 6- 500 MG/KG/DAY

UNAUDITED DRAFT

SPONSOR COPY

PROJECT NO.:WIL-186002
SPONSOR:CMA
SPONSOR NO.:PA-5.ORF/REP-WIL

A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS
SUMMARY OF CLINICAL FINDINGS: TOTAL OCCURRENCE/NO. OF ANIMALS

----- M A L E -----

TABLE RANGE: 11-12-93 TO 12-09-93

GROUP:	1	2	3	4	5	6
1-HOUR POST-DOSE						
-WET CLEAR MATTING ANOGENITAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	5/ 3
-WET CLEAR MATTING VENTRAL NECK	0/ 0	1/ 1	1/ 1	1/ 1	2/ 2	3/ 2
-WET CLEAR MATTING VENTRAL THORACIC AREA	0/ 0	1/ 1	1/ 1	1/ 1	1/ 1	2/ 2
-WET CLEAR MATTING RIGHT FORELIMB	0/ 0	1/ 1	1/ 1	2/ 1	3/ 2	7/ 3
-WET CLEAR MATTING LEFT FORELIMB	0/ 0	1/ 1	1/ 1	2/ 1	3/ 2	7/ 3
-WET CLEAR MATTING VENTRAL ABDOMINAL AREA	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0	1/ 1
-WET TAN MATTING VENTRAL NECK	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0	5/ 3
-WET TAN MATTING VENTRAL THORACIC AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	5/ 3
-WET TAN MATTING RIGHT FORELIMB	0/ 0	0/ 0	0/ 0	1/ 1	3/ 1	7/ 4
-WET TAN MATTING LEFT FORELIMB	0/ 0	0/ 0	0/ 0	1/ 1	3/ 1	6/ 4
-WET TAN MATTING VENTRAL ABDOMINAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	3/ 2
-DRIED TAN MATTING VENTRAL NECK	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	2/ 2
-DRIED TAN MATTING VENTRAL THORACIC AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	3/ 2
-DRIED TAN MATTING RIGHT FOERELIMB	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	3/ 3
-DRIED TAN MATTING LEFT FORELIMB	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	3/ 3
-DRIED TAN MATTING VENTRAL ABDOMINAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	4/ 2
-WET YELLOW MATERIAL PROXIMAL END OF TAIL	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-DRIED CLEAR MATTING VENTRAL NECK	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0	1/ 1
-DRIED CLEAR MATTING VENTRAL THORACIC AREA	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0	1/ 1
-DRIED CLEAR MATTING RIGHT FORELIMB	0/ 0	0/ 0	0/ 0	1/ 1	1/ 1	4/ 2
-DRIED CLEAR MATTING LEFT FORELIMB	0/ 0	0/ 0	0/ 0	1/ 1	1/ 1	4/ 2
-DRIED CLEAR MATTING AROUND MOUTH	0/ 0	0/ 0	0/ 0	0/ 0	5/ 2	6/ 3
-DRIED RED STAINING AROUND MOUTH	0/ 0	0/ 0	1/ 1	2/ 2	2/ 2	0/ 0

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 50 MG/KG/DAY 4- 125 MG/KG/DAY 5- 250 MG/KG/DAY 6- 500 MG/KG/DAY

UNAUDITED DRAFT

SPONSOR COPY

A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS

SUMMARY OF CLINICAL FINDINGS: TOTAL OCCURRENCE/NO. OF ANIMALS

----- M A L E -----

TABLE RANGE: 11-12-93 TO 12-09-93

GROUP:	1	2	3	4	5	6
1-HOUR POST-DOSE						
-WET CLEAR MATTING AROUND MOUTH	1/ 1	1/ 1	4/ 4	5/ 3	8/ 4	13/ 3
-WET TAN STAINING AROUND MOUTH	0/ 0	0/ 0	2/ 1	0/ 0	6/ 3	1/ 1
-WET YELLOW STAINING AROUND MOUTH	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	5/ 4
-DRIED TAN STAINING AROUND MOUTH	0/ 0	0/ 0	4/ 4	18/ 5	23/ 5	7/ 4
-SALIVATION	0/ 0	0/ 0	0/ 0	9/ 3	15/ 2	13/ 3
-DRIED BROWN MATTING AROUND MOUTH	0/ 0	0/ 0	1/ 1	4/ 2	1/ 1	3/ 3
-WET TAN MATTING AROUND MOUTH	0/ 0	0/ 0	1/ 1	1/ 1	1/ 1	8/ 4
-AREA AROUND MOUTH APPEARS RED IN COLOR	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	2/ 2
-AREA AROUND MOUTH APPEARS SWOLLEN	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-WET RED STAINING AROUND MOUTH	0/ 0	0/ 0	1/ 1	0/ 0	0/ 0	0/ 0
-APPARENT MECHANICAL INJURY TO LEFT HINDPAW	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1

UNAUDITED DRAFT

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 50 MG/KG/DAY 4- 125 MG/KG/DAY 5- 250 MG/KG/DAY 6- 500 MG/KG/DAY

PROJECT NO.:WIL-186002
SPONSOR:CMA
SPONSOR NO.:PA-5.ORF/REP-WIL

A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS
SUMMARY OF CLINICAL FINDINGS: TOTAL OCCURRENCE/NO. OF ANIMALS

----- F E M A L E -----

TABLE RANGE: 11-12-93 TO 12-09-93

GROUP:	1	2	3	4	5	6
1-HOUR POST-DOSE						
-VOCALIZED	0/ 0	0/ 0	0/ 0	0/ 0	4/ 1	0/ 0
-HYPOACTIVE	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0	0/ 0
-HAIR LOSS BASE OF TAIL	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	8/ 2
-HUNCHED APPEARANCE	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1	1/ 1
-LESION BASE OF TAIL	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	8/ 2
-HAIR LOSS UROGENITAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-SCABBING BASE OF TAIL	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-WET TAN MATTING ANOGENITAL AREA	0/ 0	0/ 0	0/ 0	1/ 1	2/ 2	13/ 4
-DRIED RED STAINING RIGHT FORELIMB	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0	2/ 2
-DRIED RED STAINING LEFT FORELIMB	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0	2/ 2
-WET YELLOW STAINING UROGENITAL AREA	0/ 0	0/ 0	0/ 0	1/ 1	1/ 1	0/ 0
-WET YELLOW STAINING ANOGENITAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-DRIED BROWN STAINING RIGHT FORELIMB	0/ 0	0/ 0	0/ 0	4/ 2	2/ 2	3/ 2
-DRIED BROWN STAINING LEFT FORELIMB	0/ 0	0/ 0	0/ 0	4/ 2	2/ 2	3/ 2
-DRIED TAN MATTING ANOGENITAL AREA	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0	6/ 3
-DRIED TAN MATTING UROGENITAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	3/ 2
-DRIED BROWN MATERIAL PROXIMAL END OF TAIL	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-DRIED BROWN STAINING VENTRAL NECK	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-DRIED BROWN STAINING ANOGENITAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	2/ 2
-DRIED BROWN STAINING VENTRAL ABDOMINAL AREA	0/ 0	0/ 0	0/ 0	2/ 2	0/ 0	1/ 1
-DRIED BROWN MATERIAL ENTIRE LENGTH OF TAIL	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	2/ 2
-DRIED TAN STAINING PROXIMAL END OF TAIL	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-RALES	0/ 0	0/ 0	0/ 0	9/ 2	6/ 2	1/ 1

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 50 MG/KG/DAY 4- 125 MG/KG/DAY 5- 250 MG/KG/DAY 6- 500 MG/KG/DAY

UNAUDITED DRAFT

SPONSOR COPY

A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS
SUMMARY OF CLINICAL FINDINGS: TOTAL OCCURRENCE/NO. OF ANIMALS

----- F E M A L E -----

TABLE RANGE: 11-12-93 TO 12-09-93

GROUP:	1	2	3	4	5	6
1-HOUR POST-DOSE						
-LABORED RESPIRATION	0/ 0	0/ 0	0/ 0	1/ 1	1/ 1	0/ 0
-DRIED RED MATERIAL AROUND NOSE	0/ 0	1/ 1	0/ 0	3/ 2	0/ 0	9/ 3
-DRIED TAN STAINING AROUND NOSE	0/ 0	0/ 0	0/ 0	3/ 1	4/ 2	8/ 3
-DRIED BROWN MATTING AROUND NOSE	0/ 0	0/ 0	0/ 0	5/ 3	0/ 0	1/ 1
-WET CLEAR MATTING AROUND NOSE	0/ 0	0/ 0	0/ 0	0/ 0	2/ 2	2/ 2
-WET TAN MATTING AROUND NOSE	0/ 0	0/ 0	0/ 0	0/ 0	3/ 2	1/ 1
-LACRIMATION RIGHT EYE	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0	1/ 1
-LACRIMATION LEFT EYE	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0	1/ 1
-WET RED MATERIAL AROUND NOSE	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0
-RED NASAL DISCHARGE	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0	0/ 0
-DRIED RED MATERIAL AROUND RIGHT EYE	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0	2/ 1
-DRIED RED STAINING AROUND NOSE	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1	1/ 1
-WET RED STAINING AROUND NOSE	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0	0/ 0
-WET BROWN MATTING AROUND NOSE	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0
-MUCOID DIARRHEA	0/ 0	0/ 0	0/ 0	2/ 2	2/ 2	4/ 3
-MUCOID DIARRHEA APPEARS YELLOW IN COLOR	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0	4/ 4
-WET TAN MATTING UROGENITAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1	8/ 4
-UNKEMPT APPEARANCE	0/ 0	0/ 0	0/ 0	1/ 1	2/ 1	2/ 1
-WET CLEAR MATTING ANOGENITAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	2/ 2	0/ 0
-WET CLEAR MATTING VENTRAL NECK	0/ 0	1/ 1	0/ 0	0/ 0	3/ 2	0/ 0
-WET CLEAR MATTING VENTRAL THORACIC AREA	0/ 0	0/ 0	0/ 0	0/ 0	3/ 2	0/ 0
-WET CLEAR MATTING RIGHT FORELIMB	0/ 0	1/ 1	1/ 1	0/ 0	4/ 2	0/ 0
-WET CLEAR MATTING LEFT FORELIMB	0/ 0	1/ 1	1/ 1	0/ 0	4/ 2	0/ 0

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 50 MG/KG/DAY 4- 125 MG/KG/DAY 5- 250 MG/KG/DAY 6- 500 MG/KG/DAY

UNAUDITED DRAFT

----- F E M A L E -----

TABLE RANGE: 11-12-93 TO 12-09-93

GROUP:	1	2	3	4	5	6
1-HOUR POST-DOSE						
-WET CLEAR MATTING VENTRAL ABDOMINAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0
-WET TAN MATTING VENTRAL NECK	0/ 0	0/ 0	0/ 0	0/ 0	3/ 2	1/ 1
-WET TAN MATTING VENTRAL THORACIC AREA	0/ 0	0/ 0	0/ 0	0/ 0	2/ 2	1/ 1
-WET TAN MATTING RIGHT FORELIMB	0/ 0	0/ 0	0/ 0	0/ 0	7/ 5	1/ 1
-WET TAN MATTING LEFT FORELIMB	0/ 0	0/ 0	0/ 0	0/ 0	7/ 5	1/ 1
-WET TAN MATTING VENTRAL ABDOMINAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	3/ 3
-DRIED TAN MATTING VENTRAL NECK	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0	0/ 0
-DRIED TAN MATTING RIGHT FOERELIMB	0/ 0	0/ 0	0/ 0	3/ 2	1/ 1	4/ 3
-DRIED TAN MATTING LEFT FORELIMB	0/ 0	0/ 0	0/ 0	3/ 2	1/ 1	4/ 3
-DRIED TAN MATTING VENTRAL ABDOMINAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	2/ 2
-DRIED CLEAR MATTING VENTRAL NECK	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0
-DRIED CLEAR MATTING VENTRAL THORACIC AREA	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0
-DRIED CLEAR MATTING RIGHT FORELIMB	0/ 0	0/ 0	0/ 0	1/ 1	1/ 1	2/ 2
-DRIED CLEAR MATTING LEFT FORELIMB	0/ 0	0/ 0	0/ 0	1/ 1	1/ 1	2/ 2
-DRIED CLEAR MATTING AROUND MOUTH	0/ 0	0/ 0	1/ 1	2/ 1	1/ 1	8/ 4
-DRIED RED STAINING AROUND MOUTH	0/ 0	0/ 0	0/ 0	5/ 2	0/ 0	2/ 2
-WET CLEAR MATTING AROUND MOUTH	0/ 0	0/ 0	1/ 1	0/ 0	7/ 4	4/ 3
-WET TAN STAINING AROUND MOUTH	0/ 0	0/ 0	0/ 0	2/ 1	2/ 2	1/ 1
-DRIED TAN STAINING AROUND MOUTH	0/ 0	0/ 0	0/ 0	27/ 4	18/ 4	31/ 5
-SALIVATION	0/ 0	0/ 0	0/ 0	0/ 0	6/ 2	2/ 2
-DRIED BROWN MATTING AROUND MOUTH	0/ 0	0/ 0	0/ 0	8/ 4	1/ 1	8/ 4
-WET TAN MATTING AROUND MOUTH	0/ 0	0/ 0	1/ 1	4/ 4	5/ 3	8/ 3
-ORAL CAVITY APPEARS OBSTRUCTED BY THICK BROWN MATERIAL	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0	0/ 0

UNAUDITED DRAFT

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 50 MG/KG/DAY 4- 125 MG/KG/DAY 5- 250 MG/KG/DAY 6- 500 MG/KG/DAY

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A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS
SUMMARY OF CLINICAL FINDINGS: TOTAL OCCURRENCE/NO. OF ANIMALS

----- F E M A L E -----

TABLE RANGE: 11-12-93 TO 12-09-93

GROUP:	1	2	3	4	5	6
1-HOUR POST-DOSE						
-DRIED RED MATERIAL AROUND MOUTH	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-WET BROWN MATTING AROUND MOUTH	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0
-WET RED STAINING AROUND MOUTH	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0	0/ 0

UNAUDITED DRAFT

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 50 MG/KG/DAY 4- 125 MG/KG/DAY 5- 250 MG/KG/DAY 6- 500 MG/KG/DAY

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PROJECT NO.:WIL-186002
SPONSOR:CMA
SPONSOR NO.:PA-5.ORF/REP-WIL

A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS
SUMMARY OF CLINICAL FINDINGS: TOTAL OCCURRENCE/NO. OF ANIMALS

----- M A L E -----

TABLE RANGE: 11-12-93 TO 12-09-93

GROUP:	1	2	3	4	5	6
2-HOURS POST-DOSE						
-WET TAN MATTING ANOGENITAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	4/ 4
-WET YELLOW STAINING VENTRAL NECK AREA	0/ 0	0/ 0	1/ 1	0/ 0	0/ 0	0/ 0
-WET YELLOW STAINING VENTRAL THORACIC AREA	0/ 0	0/ 0	1/ 1	0/ 0	0/ 0	0/ 0
-WET YELLOW STAINING VENTRAL ABDOMINAL AREA	0/ 0	0/ 0	1/ 1	0/ 0	0/ 0	0/ 0
-WET YELLOW STAINING UROGENITAL AREA	0/ 0	0/ 0	1/ 1	0/ 0	0/ 0	0/ 0
-WET YELLOW STAINING ANOGENITAL AREA	0/ 0	0/ 0	1/ 1	0/ 0	0/ 0	0/ 0
-WET YELLOW STAINING RIGHT FORELIMB	0/ 0	0/ 0	1/ 1	0/ 0	0/ 0	0/ 0
-WET YELLOW STAINING LEFT FORELIMB	0/ 0	0/ 0	1/ 1	0/ 0	0/ 0	0/ 0
-RALES	0/ 0	0/ 0	1/ 1	1/ 1	0/ 0	1/ 1
-WET CLEAR MATTING AROUND NOSE	0/ 0	0/ 0	0/ 0	1/ 1	1/ 1	1/ 1
-LACRIMATION RIGHT EYE	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-LACRIMATION LEFT EYE	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-RED NASAL DISCHARGE	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0	0/ 0
-PTOSIS RIGHT EYE	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-PTOSIS LEFT EYE	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-MUCOID DIARRHEA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	4/ 3
-WET TAN MATTING UROGENITAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-UNKEMPT APPEARANCE	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-WET CLEAR MATTING VENTRAL NECK	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-WET CLEAR MATTING RIGHT FORELIMB	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0	1/ 1
-WET CLEAR MATTING LEFT FORELIMB	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0	1/ 1
-WET TAN MATTING VENTRAL NECK	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-WET TAN MATTING RIGHT FORELIMB	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	2/ 2

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 50 MG/KG/DAY 4- 125 MG/KG/DAY 5- 250 MG/KG/DAY 6- 500 MG/KG/DAY

UNAUDITED DRAFT

PROJECT NO.:WIL-186002
SPONSOR:CMA
SPONSOR NO.:PA-5.ORF/REP-WIL

A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS
SUMMARY OF CLINICAL FINDINGS: TOTAL OCCURRENCE/NO. OF ANIMALS

----- M A L E -----

TABLE RANGE: 11-12-93 TO 12-09-93

GROUP:	1	2	3	4	5	6
2-HOURS POST-DOSE						
-WET TAN MATTING LEFT FORELIMB	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	2/ 2
-WET TAN MATTING VENTRAL ABDOMINAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-DRIED RED STAINING AROUND MOUTH	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0
-WET CLEAR MATTING AROUND MOUTH	0/ 0	0/ 0	2/ 2	0/ 0	1/ 1	1/ 1
-SALIVATION	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0	1/ 1
-DRIED BROWN MATTING AROUND MOUTH	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0
-WET TAN MATTING AROUND MOUTH	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 50 MG/KG/DAY 4- 125 MG/KG/DAY 5- 250 MG/KG/DAY 6- 500 MG/KG/DAY

UNAUDITED DRAFT

----- F E M A L E -----

TABLE RANGE: 11-12-93 TO 12-09-93

GROUP:	1	2	3	4	5	6
2-HOURS POST-DOSE						
-WET TAN MATTING ANOGENITAL AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	3/ 2
-RALES	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0	1/ 1
-WET CLEAR MATTING AROUND NOSE	0/ 0	1/ 1	0/ 0	0/ 0	0/ 0	0/ 0
-WET TAN MATTING AROUND NOSE	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-WET RED STAINING AROUND NOSE	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0	0/ 0
-MUCOID DIARRHEA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	3/ 2
-WET CLEAR MATTING VENTRAL NECK	0/ 0	1/ 1	0/ 0	0/ 0	0/ 0	0/ 0
-WET CLEAR MATTING VENTRAL THORACIC AREA	0/ 0	1/ 1	0/ 0	0/ 0	0/ 0	0/ 0
-WET CLEAR MATTING RIGHT FORELIMB	0/ 0	1/ 1	0/ 0	0/ 0	0/ 0	0/ 0
-WET CLEAR MATTING LEFT FORELIMB	0/ 0	1/ 1	0/ 0	0/ 0	0/ 0	0/ 0
-WET TAN MATTING VENTRAL NECK	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-WET TAN MATTING VENTRAL THORACIC AREA	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-WET TAN MATTING RIGHT FORELIMB	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-WET TAN MATTING LEFT FORELIMB	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-DRIED TAN MATTING VENTRAL NECK	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-DRIED CLEAR MATTING AROUND MOUTH	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-WET CLEAR MATTING AROUND MOUTH	0/ 0	1/ 1	0/ 0	0/ 0	0/ 0	0/ 0
-DRIED TAN STAINING AROUND MOUTH	0/ 0	0/ 0	0/ 0	2/ 2	1/ 1	2/ 2
-SALIVATION	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1	0/ 0
-DRIED BROWN MATTING AROUND MOUTH	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1
-WET TAN MATTING AROUND MOUTH	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	1/ 1

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 50 MG/KG/DAY 4- 125 MG/KG/DAY 5- 250 MG/KG/DAY 6- 500 MG/KG/DAY

UNAUDITED DRAFT

SPONSOR COPY

PROJECT NO.:WIL-186002
SPONSOR:CMA
SPONSOR NO.:PA-5.0RF/REP-WIL

A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS
BODY WEIGHTS (GRAMS) - SUMMARY OF MEANS

	GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	50 MG/KG/DAY	125 MG/KG/DAY	250 MG/KG/DAY	500 MG/KG/DAY
		----- M A L E -----					
DAY 0							
	MEAN	374.	383.	381.	376.	386.	384.
	S.D.	25.5	19.5	20.1	29.7	14.0	19.8
	N	5	5	5	5	5	5
2							
	MEAN	393.	397.	398.	395.	398.	381.
	S.D.	23.1	24.3	23.4	27.7	20.2	22.4
	N	5	5	5	5	5	5
4							
	MEAN	392.	398.	381.	399.	395.	361.
	S.D.	22.5	27.1	30.8	28.3	17.3	34.9
	N	5	5	5	5	5	5
6							
	MEAN	403.	409.	396.	412.	405.	352.
	S.D.	19.7	29.8	41.5	27.5	20.7	63.3
	N	5	5	5	5	5	5
8							
	MEAN	414.	422.	411.	421.	415.	368.
	S.D.	24.4	32.0	42.1	22.4	27.9	76.3
	N	5	5	5	5	5	4

NONE SIGNIFICANTLY DIFFERENT USING DUNNETT'S TEST

UNAUDITED DRAFT

UNAUDITED DRAFT

		MALE					
	GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	50 MG/KG/DAY	125 MG/KG/DAY	250 MG/KG/DAY	500 MG/KG/DAY
DAY 10							
	MEAN	421.	424.	421.	429.	419.	409.
	S.D.	25.7	31.9	43.3	23.4	27.9	27.4
	N	5	5	5	5	5	3
12							
	MEAN	428.	430.	430.	431.	425.	383.
	S.D.	26.0	30.4	43.7	22.8	30.4	62.7
	N	5	5	5	5	5	3
14							
	MEAN	430.	[illegible]	435.	438.	424.	427.
	S.D.	26.6	34.1	42.5	24.2	31.1	9.9
	N	5	5	5	5	5	2
16							
	MEAN	440.	442.	448.	448.	433.	442.
	S.D.	29.3	33.3	48.9	25.9	33.8	5.7
	N	5	5	5	5	5	2
18							
	MEAN	450.	454.	460.	457.	440.	445.
	S.D.	31.9	38.7	50.0	23.8	36.1	7.8
	N	5	5	5	5	5	2

NONE SIGNIFICANTLY DIFFERENT USING DUNNETT'S TEST

SPONSOR COPY

A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS

BODY WEIGHTS (GRAMS) - SUMMARY OF MEANS

	GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	50 MG/KG/DAY	125 MG/KG/DAY	250 MG/KG/DAY	500 MG/KG/DAY
		-----	-----	M A L E	-----	-----	-----
DAY 20							
	MEAN	451.	455.	457.	448.	431.	450.
	S.D.	31.4	41.2	43.4	28.8	38.7	12.7
	N	5	5	5	5	5	2
22							
	MEAN	466.	466.	470.	467.	448.	457.
	S.D.	33.6	43.2	52.4	29.9	44.1	7.1
	N	5	5	5	5	5	2
24							
	MEAN	470.	471.	479.	468.	449.	463.
	S.D.	33.9	[illegible]	52.5	29.3	43.4	7.1
	N	5	5	5	5	5	2
26							
	MEAN	480.	480.	489.	469.	457.	475.
	S.D.	33.5	46.6	54.3	44.9	46.3	4.2
	N	5	5	5	5	5	2
28							
	MEAN	491.	490.	495.	477.	462.	453.
	S.D.	33.5	47.2	64.5	38.6	48.7	37.5
	N	5	5	5	5	5	2

NONE SIGNIFICANTLY DIFFERENT USING DUNNETT'S TEST

UNAUDITED DRAFT

UNAUDITED DRAFT

----- F E M A L E -----

	GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	50 MG/KG/DAY	125 MG/KG/DAY	250 MG/KG/DAY	500 MG/KG/DAY
DAY 0							
	MEAN	254.	252.	255.	252.	256.	253.
	S.D.	10.8	11.6	9.7	9.6	10.8	10.0
	N	5	5	5	5	5	5
2							
	MEAN	264.	258.	264.	260.	268.	240.**
	S.D.	8.2	9.2	9.3	6.6	12.9	15.8
	N	5	5	5	5	5	5
4							
	MEAN	262.	258.	263.	259.	263.	243.*
	S.D.	10.1	11.3	11.1	6.0	10.0	16.0
	N	5	5	5	5	5	5
6							
	MEAN	268.	261.	268.	257.	267.	263.
	S.D.	8.7	8.5	13.1	15.4	22.2	14.5
	N	5	5	5	5	5	5
8							
	MEAN	273.	264.	271.	264.	270.	275.
	S.D.	13.0	13.5	7.4	5.9	20.8	10.9
	N	5	5	5	4	5	5

* = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP 1 AT 0.05 LEVEL USING DUNNETT'S TEST
** = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP 1 AT 0.01 LEVEL USING DUNNETT'S TEST

SPONSOR COPY

A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS

BODY WEIGHTS (GRAMS) - SUMMARY OF MEANS

	GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	50 MG/KG/DAY	125 MG/KG/DAY	250 MG/KG/DAY	500 MG/KG/DAY
		----- F E M A L E -----					
DAY 10							
	MEAN	272.	264.	273.	268.	280.	276.
	S.D.	8.2	9.6	12.5	16.5	20.0	13.2
	N	5	5	5	4	5	5
12							
	MEAN	273.	266.	275.	267.	280.	278.
	S.D.	14.6	9.4	9.9	8.8	14.9	10.2
	N	5	5	5	4	5	5
14							
	MEAN	274.	267.	276.	271.	284.	271.
	S.D.	7.4	9.7	10.5	15.9	17.9	34.4
	N	5	5	5	4	5	5
16							
	MEAN	276.	271.	279.	280.	279.	292.
	S.D.	13.1	14.0	8.6	22.2	18.6	8.8
	N	5	5	5	4	5	4
18							
	MEAN	283.	274.	283.	286.	290.	297.
	S.D.	11.4	6.7	12.3	23.6	13.5	12.7
	N	5	5	5	4	5	4

NONE SIGNIFICANTLY DIFFERENT USING DUNNETT'S TEST

UNAUDITED DRAFT

UNAUDITED DRAFT

		----- F E M A L E -----					
	GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	50 MG/KG/DAY	125 MG/KG/DAY	250 MG/KG/DAY	500 MG/KG/DAY
DAY 20							
	MEAN	280.	273.	283.	286.	284.	297.
	S.D.	12.6	12.3	9.4	25.7	16.5	13.6
	N	5	5	5	4	5	4
22							
	MEAN	287.	277.	291.	293.	290.	306.
	S.D.	12.9	7.7	12.2	26.9	12.2	11.7
	N	5	5	5	4	5	4
24							
	MEAN	285.	280.	288.	292.	288.	303.
	S.D.	15.5	11.8	10.3	31.3	12.2	15.0
	N	5	5	5	4	5	4
26							
	MEAN	289.	283.	290.	294.	296.	308.
	S.D.	18.5	7.3	15.0	17.4	9.9	19.7
	N	5	5	5	4	5	4
28							
	MEAN	294.	285.	293.	298.	300.	317.
	S.D.	21.8	13.9	8.8	21.0	11.6	18.9
	N	5	5	5	4	5	4

NONE SIGNIFICANTLY DIFFERENT USING DUNNETT'S TEST

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SPONSOR:CMA
SPONSOR NO.:PA-5.ORF/REP-WIL

SPONSOR COPY

A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS

BODY WEIGHT GAINS (GRAMS) - SUMMARY OF MEANS

		----- MALE -----					
	GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	50 MG/KG/DAY	125 MG/KG/DAY	250 MG/KG/DAY	500 MG/KG/DAY
DAY 0 TO 2							
	MEAN	20.	14.	17.	19.	11.	-3.**
	S.D.	12.1	8.2	5.5	5.3	7.0	9.9
	N	5	5	5	5	5	5
2 TO 4							
	MEAN	-1.	0.	-17.	4.	-3.	-20.
	S.D.	5.3	5.8	20.7	2.3	4.4	19.2
	N	5	5	5	5	5	5
4 TO 6							
	MEAN	11.	11.	15.	14.	10.	-9.
	S.D.	7.3	4.3	2.7	0.8	5.5	32.9
	N	5	5	5	5	5	5
6 TO 8							
	MEAN	11.	13.	15.	9.	9.	-5.
	S.D.	6.1	3.7	4.3	12.4	8.2	27.0
	N	5	5	5	5	5	4
8 TO 10							
	MEAN	7.	3.	10.	8.	4.	4.
	S.D.	7.1	4.2	3.0	3.5	7.5	10.7
	N	5	5	5	5	5	3

** = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP 1 AT 0.01 LEVEL USING DUNNETT'S TEST

UNAUDITED DRAFT

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	----- M A L E -----					
GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	50 MG/KG/DAY	125 MG/KG/DAY	250 MG/KG/DAY	500 MG/KG/DAY
DAY 10 TO 12						
MEAN	7.	6.	9.	2.	6.	-26.*
S.D.	8.0	5.1	3.5	9.7	4.8	36.5
N	5	5	5	5	5	3
12 TO 14						
MEAN	2.	1.	5.	6.	-1.	8.
S.D.	6.6	4.9	4.0	4.9	1.7	12.0
N	5	5	5	5	5	2
14 TO 16						
MEAN	11.	10.	13.	10.	9.	15.
S.D.	3.9	2.5	4.6	3.2	4.7	4.2
N	5	5	5	5	5	2
16 TO 18						
MEAN	9.	11.	12.	9.	7.	3.
S.D.	6.0	6.5	4.1	3.4	4.8	13.4
N	5	5	5	5	5	2
18 TO 20						
MEAN	1.	1.	-3.	-9.	-9.	6.
S.D.	2.2	5.0	11.8	18.4	17.9	20.5
N	5	5	5	5	5	2

UNAUDITED DRAFT

* = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP 1 AT 0.05 LEVEL USING DUNNETT'S TEST

SPONSOR COPY

A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS

BODY WEIGHT GAINS (GRAMS) - SUMMARY OF MEANS

GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	50 MG/KG/DAY	125 MG/KG/DAY	250 MG/KG/DAY	500 MG/KG/DAY
	----- M A L E -----					
DAY 20 TO 22						
MEAN	14.	12.	13.	19.	17.	7.
S.D.	5.9	2.5	13.7	3.0	11.4	19.8
N	5	5	5	5	5	2
22 TO 24						
MEAN	5.	5.	9.	1.	1.	6.
S.D.	2.6	3.7	4.0	3.8	5.9	14.1
N	5	5	5	5	5	2
24 TO 26						
MEAN	9.	9.	10.	2.	8.	12.
S.D.	2.7	5.0	4.6	25.4	3.9	2.8
N	5	5	5	5	5	2
26 TO 28						
MEAN	12.	10.	6.	7.	4.	-23.*
S.D.	1.9	1.9	14.4	11.5	2.9	41.7
N	5	5	5	5	5	2

UNAUDITED DRAFT

* = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP 1 AT 0.05 LEVEL USING DUNNETT'S TEST

PROJECT NO.:WIL-186002
SPONSOR:CMA
SPONSOR NO.:PA-5.0RF/REP-WIL

A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS
BODY WEIGHT GAINS (GRAMS) - SUMMARY OF MEANS

		----- F E M A L E -----					
	GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	50 MG/KG/DAY	125 MG/KG/DAY	250 MG/KG/DAY	500 MG/KG/DAY
DAY 0 TO 2							
	MEAN	9.	6.	9.	8.	12.	-13.**
	S.D.	3.8	4.7	10.7	11.0	4.9	13.0
	N	5	5	5	5	5	5
2 TO 4							
	MEAN	-2.	0.	0.	-1.	-5.	3.
	S.D.	3.5	5.0	7.4	6.0	4.3	13.1
	N	5	5	5	5	5	5
4 TO 6							
	MEAN	6.	3.	4.	-1.	4.	20.
	S.D.	5.5	4.2	8.0	18.0	14.8	7.4
	N	5	5	5	5	5	5
6 TO 8							
	MEAN	5.	4.	4.	1.	3.	12.
	S.D.	7.6	5.5	8.0	8.4	3.9	7.0
	N	5	5	5	4	5	5
8 TO 10							
	MEAN	-1.	-1.	2.	4.	10.	1.
	S.D.	8.6	5.4	8.9	14.9	5.7	5.4
	N	5	5	5	4	5	5

** = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP 1 AT 0.01 LEVEL USING DUNNETT'S TEST

UNAUDITED DRAFT

SPONSOR COPY

A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS

BODY WEIGHT GAINS (GRAMS) - SUMMARY OF MEANS

UNAUDITED DRAFT

	----- F E M A L E -----					
GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	50 MG/KG/DAY	125 MG/KG/DAY	250 MG/KG/DAY	500 MG/KG/DAY
DAY 10 TO 12						
MEAN	1.	3.	2.	-2.	-1.	3.
S.D.	9.4	6.0	7.5	7.9	6.2	10.8
N	5	5	5	4	5	5
12 TO 14						
MEAN	1.	1.	0.	5.	4.	-7.
S.D.	8.8	5.2	5	7.4	5.8	25.7
N	5	5	5	4	5	5
14 TO 16						
MEAN	2.	4.	3.	9.	-5.	6.
S.D.	9.1	5.9	7.3	8.3	7.7	9.4
N	5	5	5	4	5	4
16 TO 18						
MEAN	7.	3.	5.	6.	11.	5.
S.D.	3.7	9.1	5.7	5.1	8.3	9.1
N	5	5	5	4	5	4
18 TO 20						
MEAN	-3.	0.	-1.	0.	-6.	1.
S.D.	4.5	8.8	7.8	6.8	3.8	8.0
N	5	5	5	4	5	4

NONE SIGNIFICANTLY DIFFERENT USING DUNNETT'S TEST

5.

	----- F E M A L E -----					
GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	50 MG/KG/DAY	125 MG/KG/DAY	250 MG/KG/DAY	500 MG/KG/DAY
DAY 20 TO 22						
MEAN	7.	4.	8.	7.	6.	9.
S.D.	3.6	8.4	6.5	5.1	5.6	4.8
N	5	5	5	4	5	4
22 TO 24						
MEAN	-3.	2.	-2.	-1.	-2.	-3.
S.D.	4.9	3.5	6.3	4.5	2.7	7.8
N	5	5	5	4	5	4
24 TO 26						
MEAN	4.	3.	2.	2.	8.	5.
S.D.	6.3	6.4	8.5	14.2	5.0	7.2
N	5	5	5	4	5	4
26 TO 28						
MEAN	5.	2.	3.	5.	4.	9.
S.D.	3.7	8.5	7.3	5.4	3.6	9.6
N	5	5	5	4	5	4

UNAUDITED DRAFT

NONE SIGNIFICANTLY DIFFERENT USING DUNNETT'S TEST

5.

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PROJECT NO.:WIL-186002
SPONSOR:CMA
SPONSOR NO.:PA-5.ORF/REP-WIL

A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS
WEEKLY FOOD CONSUMPTION (GRAMS/ANIMAL/DAY) - SUMMARY OF MEANS

		----- MALE -----					
	GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	50 MG/KG/DAY	125 MG/KG/DAY	250 MG/KG/DAY	500 MG/KG/DAY
WEEK	0 TO 1						
	MEAN	25.	25.	22.	27.	25.	20.
	S.D.	2.6	2.5	5.0	2.7	2.9	7.3
	N	5	5	5	5	5	4
	1 TO 2						
	MEAN	23.	23.	24.	25.	24.	29.
	S.D.	2.8	2.2	4.0	1.9	4.2	1.4
	N	5	5	5	5	5	2
	2 TO 3						
	MEAN	24.	23.	23.	24.	25.	31.
	S.D.	1.7	2.1	3.5	3.6	5.7	0.7
	N	5	5	5	5	5	2
	3 TO 4						
	MEAN	24.	23.	25.	25.	26.	31.
	S.D.	1.5	2.2	5.4	4.8	3.8	0.7
	N	5	5	5	5	5	2

NONE SIGNIFICANTLY DIFFERENT USING DUNNETT'S TEST

UNAUDITED DRAFT

PROJECT NO.:WIL-186002
SPONSOR:CMA
SPONSOR NO.:PA-5.0RF/REP-WIL

A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS
WEEKLY FOOD CONSUMPTION (GRAMS/ANIMAL/DAY) - SUMMARY OF MEANS

UNAUDITED DRAFT

----- F E M A L E -----

GROUP:	0 MG/KG/DAY	10 MG/KG/DAY	50 MG/KG/DAY	125 MG/KG/DAY	250 MG/KG/DAY	500 MG/KG/DAY
WEEK 0 TO 1						
MEAN	17.	17.	18.	17.	17.	15.
S.D.	0.5	1.5	1.4	2.2	3.3	2.8
N	5	5	5	4	5	5
1 TO 2						
MEAN	16.	16.	17.	17.	19.	19.*
S.D.	0.5	1.1	1.1	2.9	1.5	1.3
N	5	5	5	4	5	5
2 TO 3						
MEAN	17.	17.	18.	19.	19.	20.
S.D.	1.6	1.8	0.8	2.8	2.7	1.7
N	5	5	5	4	5	4
3 TO 4						
MEAN	17.	16.	18.	18.	19.	22.**
S.D.	2.2	0.5	1.0	1.5	1.8	2.1
N	5	4	5	4	5	4

* = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP 1 AT 0.05 LEVEL USING DUNNETT'S TEST
** = SIGNIFICANTLY DIFFERENT FROM CONTROL GROUP 1 AT 0.01 LEVEL USING DUNNETT'S TEST

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PROJECT NO.:WIL-186002
SPONSOR:CIA
SPONSOR NO.:PA-5.ORF/REP-WIL

A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS
GROSS NECROPSY OBSERVATIONS INCIDENCE SUMMARY

FOUND DEAD OR EUTHANIZED MORIBUND OR IN EXTREMIS

	MALE						FEMALE					
GROUP:	1	2	3	4	5	6	1	2	3	4	5	6
NUMBER OF ANIMALS IN DOSE GROUP	5	5	5	5	5	5	5	5	5	5	5	5
NUMBER OF ANIMALS FOUND DEAD OR EUTHANIZED MORIBUND/IN EXTREMIS	0	0	0	0	0	3	0	0	0	1	0	1
ADRENAL GLANDS												
-REDDENED	0	0	0	0	0	3	0	0	0	0	0	1
CECUM												
-DISTENDED	0	0	0	0	0	2	0	0	0	0	0	0
-YELLOW CONTENTS	0	0	0	0	0	3	0	0	0	1	0	1
COLON												
-DISTENDED	0	0	0	0	0	1	0	0	0	0	0	0
-YELLOW CONTENTS	0	0	0	0	0	3	0	0	0	0	0	1
DUODENUM												
-DISTENDED	0	0	0	0	0	1	0	0	0	0	0	0
-YELLOW CONTENTS	0	0	0	0	0	0	0	0	0	0	0	1
ILEUM												
-YELLOW CONTENTS	0	0	0	0	0	3	0	0	0	0	0	1
-DISTENDED	0	0	0	0	0	1	0	0	0	0	0	0
JEJUNUM												
-YELLOW CONTENTS	0	0	0	0	0	2	0	0	0	0	0	1
-DISTENDED	0	0	0	0	0	1	0	0	0	0	0	0
KIDNEYS												
-REDDENED	0	0	0	0	0	3	0	0	0	0	0	0

UNAUDITED DRAFT

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 50 MG/KG/DAY 4- 125 MG/KG/DAY 5- 250 MG/KG/DAY 6- 500 MG/KG/DAY

FOUND DEAD OR EUTHANIZED MORIBUND OR IN EXTREMIS

	MALE						FEMALE					
GROUP:	1	2	3	4	5	6	1	2	3	4	5	6
NUMBER OF ANIMALS IN DOSE GROUP	5	5	5	5	5	5	5	5	5	5	5	5
NUMBER OF ANIMALS FOUND DEAD OR EUTHANIZED MORIBUND/IN EXTREMIS	0	0	0	0	0	3	0	0	0	1	0	1
KIDNEYS - CONTINUED												
-REDDENED CORTICO-MEDULLARY JUNCTION	0	0	0	0	0	0	0	0	0	0	0	1
LYMPH NODE, ME.												
-REDDENED	0	0	0	0	0	1	0	0	0	0	0	0
LUNGS												
-DARK RED	0	0	0	0	0	1	0	0	0	0	0	0
-DARK RED AREA(S)	0	0	0	0	0	0	0	0	0	1	0	0
RECTUM												
-YELLOW CONTENTS	0	0	0	0	0	1	0	0	0	0	0	0
PITUITARY												
-REDDENED	0	0	0	0	0	3	0	0	0	1	0	1
STOMACH												
-DISTENDED	0	0	0	0	0	2	0	0	0	0	0	0
-DARK RED CONTENTS	0	0	0	0	0	1	0	0	0	0	0	0
-DARK RED AREA(S)	0	0	0	0	0	1	0	0	0	0	0	0
-REDDENED MUCOSA	0	0	0	0	0	1	0	0	0	0	0	0
EXTERNAL SURFACE												
-YELLOW MATTING	0	0	0	0	0	3	0	0	0	1	0	1
-RED MATTING	0	0	0	0	0	2	0	0	0	1	0	1
-BROWN MATTING	0	0	0	0	0	1	0	0	0	0	0	1

UNAUDITED DRAFT

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 50 MG/KG/DAY 4- 125 MG/KG/DAY 5- 250 MG/KG/DAY 6- 500 MG/KG/DAY

FOUND DEAD OR EUTHANIZED MORIBUND OR IN EXTREMIS

	MALE						FEMALE					
GROUP:	1	2	3	4	5	6	1	2	3	4	5	6
NUMBER OF ANIMALS IN DOSE GROUP	5	5	5	5	5	5	5	5	5	5	5	5
NUMBER OF ANIMALS FOUND DEAD OR EUTHANIZED MORIBUND/IN EXTREMIS	0	0	0	0	0	3	0	0	0	1	0	1
EXTERNAL SURFACE - CONTINUED												
TONGUE												
-EDEMATOUS AREA(S)	0	0	0	0	0	0	0	0	0	1	0	0
ABDOMINAL CAVITY												
-EMACIATED	0	0	0	0	0	1	0	0	0	0	0	0

UNAUDITED DRAFT

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 50 MG/KG/DAY 4- 125 MG/KG/DAY 5- 250 MG/KG/DAY 6- 500 MG/KG/DAY

SPONSOR COPY

PROJECT NO.:WIL-186002
SPONSOR:CMA
SPONSOR NO.:PA-5.ORF/REP-WIL

A 28-DAY ORAL DOSE RANGE-FINDING TOXICITY STUDY OF ZDDP IN RATS
GROSS NECROPSY OBSERVATIONS INCIDENCE SUMMARY

SCHEDULED NECROPSY

	MALE						FEMALE					
GROUP:	1	2	3	4	5	6	1	2	3	4	5	6
NUMBER OF ANIMALS IN DOSE GROUP	5	5	5	5	5	5	5	5	5	5	5	5
NUMBER OF ANIMALS EXAMINED	5	5	5	5	5	2	5	5	5	4	5	4
KIDNEYS												
-DILATED PELVIS	0	1	0	0	0	0	0	0	0	0	0	0
LYMPH NODE, ME.												
-ENLARGED	0	0	0	0	0	0	0	0	0	0	1	0
SPLEEN												
-ACCESSORY	1	0	0	0	0	0	0	0	0	0	0	0
STOMACH												
-REDDENED MUCOSA	0	0	0	0	0	0	0	0	0	1	0	0
-THICKENED	0	0	0	0	0	1	0	0	0	0	1	2
-YELLOW CONTENTS	0	0	0	0	0	0	0	0	0	0	1	0
THYMUS GLAND												
-HEMORRHAGIC	0	0	0	0	0	0	0	0	0	1	0	0
EXTERNAL SURFACE												
-SCABBING	1	0	0	0	0	0	0	1	0	0	0	0
-INCISOR(S)- MALALIGNED	0	1	0	0	0	0	0	0	0	0	0	0
-HAIR LOSS	0	1	0	0	0	0	0	0	0	1	1	0
-SWOLLEN	0	0	0	0	0	0	0	1	0	0	0	0
LYMPH NODE												
-ILIAC- ENLARGED	1	0	0	0	0	0	0	0	0	0	0	0

UNAUDITED DRAFT

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 50 MG/KG/DAY 4- 125 MG/KG/DAY 5- 250 MG/KG/DAY 6- 500 MG/KG/DAY

6.

SCHEDULED NECROPSY

	MALE						FEMALE					
GROUP:	1	2	3	4	5	6	1	2	3	4	5	6
NUMBER OF ANIMALS IN DOSE GROUP	5	5	5	5	5	5	5	5	5	5	5	5
NUMBER OF ANIMALS EXAMINED	5	5	5	5	5	2	5	5	5	4	5	4
LYMPH NODE - CONTINUED												
-CERVICAL- ENLARGED	1	1	1	2	0	0	1	2	0	0	2	1
-CERVICAL- REDDENED	0	0	0	0	0	0	0	1	0	0	0	1

1- 0 MG/KG/DAY 2- 10 MG/KG/DAY 3- 50 MG/KG/DAY 4- 125 MG/KG/DAY 5- 250 MG/KG/DAY 6- 500 MG/KG/DAY

UNAUDITED DRAFT

Contains No CBI

70

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

Donald I. Hoke, Ph.D.
Corporate Director
Product Safety & Compliance
The Lubrizol Corporation
29400 Lakeland Blvd.
Wickliffe, Ohio 44092-2298

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

DEC 08 1994

EPA acknowledges the receipt of information submitted by your organization under Section 8(e) of the Toxic Substances Control Act (TSCA). For your reference, copies of the first page(s) of your submission(s) are enclosed and display the TSCA §8(e) Document Control Number (e.g., 8EHQ-00-0000) assigned by EPA to your submission(s). Please cite the assigned 8(e) number when submitting follow-up or supplemental information and refer to the reverse side of this page for "EPA Information Requests".

All TSCA 8(e) submissions are placed in the public files unless confidentiality is claimed according to the procedures outlined in Part X of EPA's TSCA §8(e) policy statement (43 FR 11110, March 16, 1978). Confidential submissions received pursuant to the TSCA §8(e) Compliance Audit Program (CAP) should already contain information supporting confidentiality claims. This information is required and should be submitted if not done so previously. To substantiate claims, submit responses to the questions in the enclosure "Support Information for Confidentiality Claims". This same enclosure is used to support confidentiality claims for non-CAP submissions.

Please address any further correspondence with the Agency related to this TSCA 8(e) submission to:

Document Processing Center (7407)
Attn: TSCA Section 8(e) Coordinator
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
Washington, D.C. 20460-0001

EPA looks forward to continued cooperation with your organization in its ongoing efforts to evaluate and manage potential risks posed by chemicals to health and the environment.

Sincerely,

Terry R. O'Bryan

Terry R. O'Bryan
Risk Analysis Branch

Enclosure

12819 A

Recycled/Recyclable
Printed with Soy/Canola [illegible]
contains at least 50% [illegible]

Triage of 8(e) Submissions

Date sent to triage: DEC 14 1994

NON-CAP CAP

Submission number: 12819A

TSCA Inventory: Y N D

Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

ECO AQUATO

Group 2 - Ernie Falke (1 copy total)

ATOX SBTOX SEN w/NEUR

Group 3 - Elizabeth Margosches (1 copy each)

STOX CTOX EPI RTOX GTOX

STOX/ONCO CTOX/ONCO IMMUNO CYTO NEUR

Other (FATE, EXPO, MET, etc.):

Notes:

THIS IS THE ORIGINAL 8(e) SUBMISSION; PLEASE REFILE AFTER TRIAGE DATABASE ENTRY

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entire document: 0 1 2 pages 1,2 pages 1,2,5,6

Notes:

Contractor reviewer : PJL Date: 11/1/94

CECATS\TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA: Submission # 8EHQ 0194 - 12819 SEQ. A

TYPE: (INT) SUPP FLWP

SUBMITTER NAME: Lubrizol Corporation

INFORMATION REQUESTED: FLW P DATE:

0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:

(0639) REFER TO CHEMICAL SCREENING
0678 CAP NOTICE

VOLUNTARY ACTIONS

(0401) NO ACTION REPORTED
0402 STUDIES PLANNED/UNDERWAY
0403 NOTIFICATION OF WORKERS/USERS
0404 LABEL/MSDS CHANGES
0405 PROCESS/HANDLING CHANGES
0406 APP/USE DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

SUB. DATE: 01/03/94 OTS DATE: 01/10/94 CSRAD DATE: 05/19/94

CHEMICAL NAME:

CAS#: 4259-15-8

INFORMATION TYPE:		P F C
0201	ONCO (HUMAN)	01 02 04
0202	ONCO (ANIMAL)	01 02 04
0203	CELL TRANS (IN VITRO)	01 02 04
0204	MUTA (IN VITRO)	01 02 04
0205	MUTA (IN VIVO)	01 02 04
0206	REPRO/TERATO (HUMAN)	01 02 04
0207	REPRO/TERATO (ANIMAL)	01 02 04
0208	NEURO (HUMAN)	01 02 04
0209	NEURO (ANIMAL)	01 02 04
0210	ACUTE TOX. (HUMAN)	01 02 04
0211	CHR. TOX. (HUMAN)	01 02 04
0212	ACUTE TOX. (ANIMAL)	01 02 04
(0213)	SUB ACUTE TOX (ANIMAL)	01 02 04
0214	SUB CHRONIC TOX (ANIMAL)	01 02 04
0215	CHRONIC TOX (ANIMAL)	01 02 04

INFORMATION TYPE:		P F C
0216	EPI/CLIN	01 02 04
0217	HUMAN EXPOS (PROD CONTAM)	01 02 04
0218	HUMAN EXPOS (ACCIDENTAL)	01 02 04
0219	HUMAN EXPOS (MONITORING)	01 02 04
0220	ECO/AQUA TOX	01 02 04
0221	ENV. OCCC/REL/FATE	01 02 04
0222	EMER INCI OF ENV CONTAM	01 02 04
0223	RESPONSE REQEST DELAY	01 02 04
0224	PROD/COMP/CHEM ID	01 02 04
0225	REPORTING RATIONALE	01 02 04
0226	CONFIDENTIAL	01 02 04
0227	ALLERG (HUMAN)	01 02 04
0228	ALLERG (ANIMAL)	01 02 04
0239	METAB/PHARMACO (ANIMAL)	01 02 04
0240	METAB/PHARMACO (HUMAN)	01 02 04

INFORMATION TYPE:		P F C
0241	IMMUNO (ANIMAL)	01 02 04
0242	IMMUNO (HUMAN)	01 02 04
0243	CHEM/PHYS PROP	01 02 04
0244	CLASTO (IN VITRO)	01 02 04
0245	CLASTO (ANIMAL)	01 02 04
0246	CLASTO (HUMAN)	01 02 04
0247	DNA DAM/REPAIR	01 02 04
0248	PROD/USE/PROC	01 02 04
0251	MSDS	01 02 04
0299	OTHER	01 02 04

TRIAGE DATA:

NON-CBI INVENTORY: (YES) / NO / IN TERMINI

ONGOING REVIEW: YES (DROP/REFER) / NO (CONTINUE) / REFER

SPECIES: RAT

TOXICOLOGICAL CONCERN: (LOW) / MED / HIGH

USE:

PRODUCTION:

COMMENTS: Non-Cap

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8(e)-12819A >

<TOX CONCERN>

L >

<COMMENT>

SUBACUTE ORAL TOXICITY IN RATS IS OF LOW CONCERN. DOSAGE (28 DAYS) AND MORTALITY DATA ARE AS FOLLOWS: 10 MG/KG/DAY (0/5 M, 0/5 F), 50 MG/KG/DAY (0/5 M, 0/5 F), 125 MG/KG/DAY (0/5 M, 1/5 F), 250 MG/KG/DAY (0/5 M, 0/5 F), OR 500 MG/KG/DAY (3/5 M, 1/5 F). CLINICAL SIGNS INCLUDED SALIVATION, RALES, AND CHANGES IN FECAL CONSISTENCY. GROSS PATHOLOGICAL SIGNS INCLUDED THICKENED GASTRIC MUCOSA, INCREASED ADRENAL WEIGHTS (AT THE TWO HIGHEST DOSE LEVELS), AND, IN DECEDENTS, REDDENED AND DISTENDED AREAS IN THE GASTROINTESTINAL TRACT. THE NOAEL FOR ALL SIGNS WAS 10 MG/KG/DAY.
$$$$ -CPSS- 0406951403