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A RANGE-FINDING STUDY OF SC-19129 IN PREGNANT RABBITS

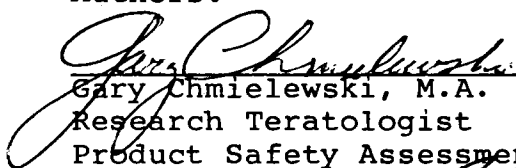
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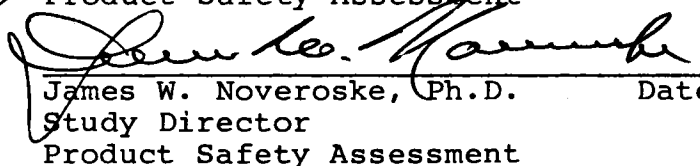
James W. Noveroske and Gary Chmielewski

Safety Assessment Project Number 2561

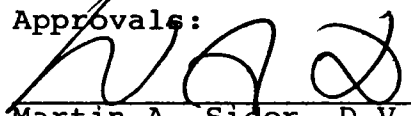
Department of Product Safety Assessment  
G. D. Searle & Co.  
Skokie, IL

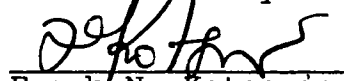
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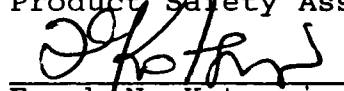
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 April 26, 1985  
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April 26, 1985

A RANGE-FINDING STUDY OF SC-19129 IN PREGNANT RABBITS

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DEPARTMENT OF PRODUCT SAFETY ASSESSMENT

G. D. Searle & Co., Skokie, IL

Title: A Range-Finding Study of SC-19129 in Pregnant Rabbits

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Author: James W. Noveroske and Gary Chmielewski

Study No.: S.A. 2561

Date: April 26, 1985

Type of Report: Final

Summary:

SC-19129, was administered twice daily by oral intubation to six female rabbits per group from Days 6 through 18 of gestation at dosage levels of 125, 250, 500, 750 and 1000 mg/kg/day. A control group received the vehicle, 0.5% methylcellulose and 0.1% polysorbate 80, in the same dosing regimen as the compound-treated groups.

No compound-related maternotoxic effects occurred at dosage levels of 125, 250 or 500 mg/kg/day. At 750 and 1000 mg/kg/day, there were clinical signs of low food intake and not eating; at 1000 mg/kg/day, there was also a slight but non-significant weight loss and two of six females died.

Examination of the reproductive status of females at Day 28 of gestation revealed no adverse effects on average numbers of implantations, resorptions, or live or dead fetuses per litter. A slight but significant reduction in average numbers of implantations and live fetuses per litter in females from the 250 and 750 mg/kg/day groups was considered unrelated to treatment since these effects were not seen at 500 and 1000 mg/kg/day.

S.A. 2561

## A RANGE-FINDING STUDY OF SC-19129 IN PREGNANT RABBITS

### INTRODUCTION

The study was conducted to determine potential toxic effects as evidenced by clinical signs, body weights, and fetal viability, and to provide a basis for dosage level selection in a teratology study.

### MATERIALS AND METHODS

Thirty-six female rabbits (New Zealand White strain, H.A.R.E., Hewitt, N.J.) approximately 4 months of age and weighing 3.06 to 4.13 kg, were divided into 6 groups of 6 rabbits each for this study.

Each rabbit was artificially inseminated (day 0 of gestation) with approximately six million motile spermatozoa contained in 0.25 ml of 0.9% physiological saline, and then injected intravenously via the marginal ear vein with 50 USP units of chorionic gonadotropin to help induce ovulation. The females were then assigned to treatment groups using a block design of random permutations, and given unique identification numbers using an ear tag. The rabbits were individually housed in stainless steel cages, and given approximately 150 g of Certified Purina Rabbit Chow #5322 per day and had free access to municipally supplied tap water throughout the study.

The animal room was maintained at  $65^{\circ}\pm 5^{\circ}\text{F}$  temperature and 25% or greater relative humidity with a 12-hour light and 12-hour dark cycle. The study was started on February 5, 1985 and terminated on March 6, 1985.

SC-19129, N-L- $\beta$ -aspartyl-L-phenylalanine, 1-methylester, was given to 5 groups of 6 rabbits each for 13 consecutive days (Days 6 through 18 of gestation) at dosage levels of 125, 250, 500, 750 and 1000 mg/kg/day. SC-19129 was administered orally by gavage twice daily as a suspension of 0.5% methylcellulose (w/v) and 0.1% polysorbate 80 (v/v) in distilled water. The doses of SC-19129, Lot #84K-047-101, were prepared as fresh suspensions daily and the quantity (4 ml/kg) administered was based on the most recent body weight. The sixth group of rabbits served as controls and received the vehicle, 0.5% methylcellulose and 0.1% polysorbate 80 in distilled water, in the same volume as the compound-treated rabbits.

The identity, strength, purity, composition, and stability of the test article were determined before use. The results of the test article analyses are shown in Appendix B.

Body weights of the rabbits were recorded on Days 0, 6, 8, 10, 13, 16, 19, and 28 of gestation. The rabbits were examined daily for adverse clinical signs throughout the study, sacrificed by an overdose of an euthanizing agent injected via the marginal ear vein on Day 28 of gestation, and the uterus examined to obtain the numbers of corpora lutea, implantations, resorptions, and live or dead fetuses.

Maternal body weights and body weight changes were analyzed using a one-way analysis of variance, and if the ANOVA F-test was significant at the 5% level, Student's t-tests (using the pooled error variance from the one-way analysis of variance) of control versus the other dose groups were performed. A Bartlett-Box test for homogeneity

of variance was done. Numbers of corpora lutea were not analyzed or reported. The Kruskal-Wallis test was used to analyze the following variables: numbers of implantations, resorptions, and live and dead fetuses per litter. If significant at the 5% level, then the Mann-Whitney U test was used to compare the control to each compound-treated group. All t-tests were two-tailed and significance levels achieved have been reported for 5% for t-tests, Bartlett-Box tests and Mann-Whitney U tests.

The study was conducted at G. D. Searle & Co. and the final report, protocol, raw data, and supporting documents are on file at G. D. Searle & Co., Skokie, Illinois.

A list of the study professionals that participated in the study is as follows:

Laboratory Animal

Resources	J. Erickson
Analytical Coordinator	K. Pilipauskas
Biostatistics	A. Mackenthun
Teratology	G. Chmielewski
Product Development	
Analytical Department	J. Jiu

## RESULTS AND DISCUSSION

No compound-related deaths or clinical signs occurred at dosage levels of 125, 250 or 500 mg/kg/day. At 750 and 1000 mg/kg/day, two of six animals per group had clinical signs of low food intake or not eating for four or more days. The two animals of the 1000 mg/kg/day group died, while the two animals of the 750 mg/kg/day group recovered. In addition, one animal from the 250 mg/kg/day group aborted, but this was considered unrelated to treatment.

Average maternal body weight gain of rabbits given 125, 250, 500 or 750 mg/kg/day was unaffected (Tables 1 and 3). At 1000 mg/kg/day, there was a slight, but non-significant ( $p < 0.05$ ), loss in average body weight between Days 6 to 10 compared to that of the control group.

Examination of the reproductive status of females at Day 28 of gestation revealed no adverse effects of SC-19129 on average numbers of implantations, resorptions and live or dead fetuses per litter at 125, 250, 500, 750, and 1000 mg/kg/day. The slight but significant decrease ( $p > 0.05$ ) in average numbers of implantations and live fetuses per litter in the 250 and 750 mg/kg/day groups compared to that of the control group was considered unrelated to treatment since these effects were not seen at dosage levels of 500 and 1000 mg/kg/day.

## COMPLIANCE STATEMENT

Although this is a range-finding study and not within the scope of Good Laboratory Practice regulations, the laboratory phase was conducted with the intention of complying with the GLP regulations. One known deviation occurred as follows:

1. Animal room temperature level fell below protocol specified limits on March 4-5, 1985 for approximately a 9 hour period.

However, this deviation did not affect the quality or integrity of the study and this report accurately reflects the data obtained during the performance of the study.



TABLE 1

## A RANGE-FINDING STUDY OF SC-19129 IN PREGNANT RABBITS

## Maternal Body Weights

	Control	(mg/kg/day)				
		125	250	500	750	1000
Average Body Weight (Kg)						
Day 0	3.66	3.79	3.49	3.66	3.51	3.53
Day 6	3.67	3.79	3.55	3.71	3.54	3.52
Day 8	3.66	3.79	3.57	3.72	3.53	3.48
Day 10	3.70	3.83	3.62	3.73	3.57	3.37
Day 13	3.75	3.84	3.65	3.76	3.56	3.50
Day 16	3.83	3.90	3.74	3.85	3.58	3.65
Day 19	3.87	3.94	3.74	3.88	3.56	3.68
Day 28	4.06	4.07	3.79	4.09	3.70	3.89
Change						
Days 0-6	0.00	0.00	+0.06	+0.05	+0.03	-0.01
Days 6-19	+0.20	+0.15	+0.19	+0.16	+0.02	+0.13
Days 19-28	+0.20	+0.13	+0.14	+0.22	+0.14	+0.21
Days 0-28	+0.40	+0.28	+0.37	+0.43	+0.19	+0.35

TABLE 2  
A RANGE-FINDING STUDY OF SC-19129 IN PREGNANT RABBITS  
Reproductive Status of Females at Sacrifice

		(mg/kg/day)				
	Control	125	250	500	750	1000
Females						
Total No.	6	6	6	6	6	6
No. Live Pregnant	6	5	5	4	6	4
No. Live Not Pregnant	0	1	0	2	0	0
No. Died Pregnant	0	0	0	0	0	2
No. Aborted	0	0	1	0	0	0
Implantations						
Total No.	54	40	27	32	32	38
No./Pregnant Female	9.0	8.0	5.4*	8.0	5.3*	9.5
Resorptions						
Total No.	5	5	9	2	7	6
No./Pregnant Female	0.8	1.0	1.8	0.5	1.2	1.5
Fetuses						
Total No.	49	35	18	30	25	32
No. Live	48	34	18	30	25	32
No. Dead	1	1	0	0	0	0
No. Live/Pregnant Female	8.0	6.8	3.6*	7.5	4.2*	8.0
No. Dead/Pregnant Female	0.2	0.2	0.0	0.0	0.0	0.0

\*Significantly different ( $p > 0.05$ ) from control

TABLE 3

## A RANGE-FINDING STUDY OF SC-19129 IN PREGNANT RABBITS

## Individual Female Body Weights (kg)

## Control Group

Female	Reproductive Status	Gestation Day							
		0	6	8	10	13	16	19	28
85-185	Pregnant	3.50	3.55	3.54	3.56	3.62	3.70	3.78	3.99
85-186	Pregnant	3.87	3.80	3.93	4.00	4.01	4.12	4.18	4.26
85-187	Pregnant	3.70	3.61	3.65	3.69	3.74	3.83	3.85	4.09
85-188	Pregnant	3.39	3.53	3.44	3.48	3.57	3.64	3.69	3.95
85-189	Pregnant	3.82	3.71	3.70	3.72	3.78	3.85	3.84	4.03
85-190	Pregnant	3.69	3.78	3.70	3.76	3.78	3.86	3.88	4.06

TABLE 3 (Cont.)

## A RANGE-FINDING STUDY OF SC-19129 IN PREGNANT RABBITS

Individual Female Body Weights (kg)

125 mg/kg Group

Female	Reproductive Status	Gestation Day							
		0	6	8	10	13	16	19	28
85-191	Not Pregnant	3.68	3.66	3.75	3.73	3.79	3.85	3.90	4.03
85-192	Pregnant	4.00	4.02	4.04	4.11	3.96	3.99	4.10	4.12
85-193	Pregnant	3.66	3.76	3.78	3.80	3.86	3.93	3.96	4.17
85-194	Pregnant	3.52	3.53	3.43	3.53	3.52	3.59	3.60	3.65
85-195	Pregnant	3.95	3.87	3.90	3.92	4.01	4.09	4.16	4.41
85-196	Pregnant	3.80	3.78	3.80	3.81	3.83	3.90	3.87	4.00

TABLE 3 (Cont.)

## A RANGE-FINDING STUDY OF SC-19129 IN PREGNANT RABBITS

## Individual Female Body Weights (kg)

## 250 mg/kg Group

Female	Reproductive Status	Gestation Day							
		0	6	8	10	13	16	19	28
85-197	Pregnant	3.56	3.61	3.65	3.72	3.69	3.81	3.83	4.03
85-198	Pregnant	3.48	3.55	3.59	3.66	3.68	3.78	3.62	3.59
85-199	Pregnant	3.70	3.73	3.76	3.84	3.83	3.92	3.96	4.19
85-200	Pregnant	3.11	3.10	3.11	3.11	3.18	3.19	3.22	3.42
85-201	Pregnant	3.88	3.92	3.95	3.97	4.06	4.21	4.24	-- <sup>a</sup>
85-202	Pregnant	3.23	3.41	3.39	3.44	3.45	3.53	3.59	3.71

--<sup>a</sup> Animal Aborted

TABLE 3 (Cont.)

## A RANGE-FINDING STUDY OF SC-19129 IN PREGNANT RABBITS

Individual Female Body Weights (kg)

500 mg/kg Group

Female	Reproductive Status	Gestation Day							
		0	6	8	10	13	16	19	28
85-203	Not Pregnant	3.12	3.24	3.32	3.38	3.43	3.47	3.45	3.51
85-204	Pregnant	3.48	3.61	3.65	3.69	3.76	3.87	3.90	4.13
85-205	Not Pregnant	3.06	3.15	3.13	3.13	3.15	3.16	3.14	3.31
85-206	Pregnant	4.08	4.01	4.01	3.97	3.93	3.89	3.88	4.09
85-207	Pregnant	3.67	3.72	3.74	3.75	3.84	4.02	4.04	4.28
85-208	Pregnant	3.43	3.52	3.48	3.51	3.51	3.63	3.68	3.88

TABLE 3 (Cont.)

## A RANGE-FINDING STUDY OF SC-19129 IN PREGNANT RABBITS

Individual Female Body Weights (kg)

750 mg/kg Group

Female	Reproductive Status	Gestation Day							
		0	6	8	10	13	16	19	28
85-209	Pregnant	4.13	4.12	4.14	4.16	4.14	4.17	4.24	4.40
85-210	Pregnant	3.46	3.53	3.55	3.54	3.46	3.28	3.23	3.29
85-211	Pregnant	3.33	3.39	3.42	3.49	3.55	3.63	3.64	3.81
85-212	Pregnant	3.11	3.14	3.12	3.17	3.28	3.38	3.43	3.54
85-213	Pregnant	3.96	3.82	3.81	3.80	3.83	3.85	3.77	3.96
85-214	Pregnant	3.07	3.26	3.16	3.23	3.12	3.15	3.07	3.22

TABLE 3 (Cont.)

## A RANGE-FINDING STUDY OF SC-19129 IN PREGNANT RABBITS

Individual Female Body Weights (kg)

1000 mg/kg Group

Female	Reproductive Status	Gestation Day							
		0	6	8	10	13	16	19	28
85-215	Pregnant	3.60	3.67	3.71	3.71	3.82	3.90	3.99	4.20
85-216	Pregnant	3.54	3.55	3.51	3.49	3.52	3.53	3.52	3.79
85-217	Pregnant	3.46	3.42	3.38	3.39	3.44	3.53	3.57	3.72
85-218	Pregnant	3.58	3.56	3.54	3.50	3.62	3.64	3.65	3.86
85-219	Pregnant	3.84	3.77	3.72	3.42	3.11	-- <sup>a</sup>	--	--
85-220	Pregnant	3.13	3.15	3.05	2.73	--	--	--	--

--<sup>a</sup> Animal Died



TABLE 4

## A RANGE-FINDING STUDY OF SC-19129 IN PREGNANT RABBITS

## Individual Fetal Data

## Control Group

Animal Number	Reproductive Status	Number of			
		Implant- ations	Resorp- tions	Live Fetuses	Dead Fetuses
85-185	Pregnant	8	0	8	0
85-186	Pregnant	8	1	6	1
85-187	Pregnant	8	0	8	0
85-188	Pregnant	9	0	9	0
85-189	Pregnant	11	1	10	0
85-190	Pregnant	10	3	7	0

TABLE 4 (Cont.)

## A RANGE-FINDING STUDY OF SC-19129 IN PREGNANT RABBITS

## Individual Fetal Data

125 mg/kg/day Group

Animal Number	Reproductive Status	Number of			
		Implant- ations	Resorp- tions	Live Fetuses	Dead Fetuses
85-191	Not Pregnant	0	0	0	0
85-192	Pregnant	4	0	4	0
85-193	Pregnant	9	1	8	0
85-194	Pregnant	9	2	7	0
85-195	Pregnant	11	2	8	1
85-196	Pregnant	7	0	7	0

TABLE 4 (Cont.)

## A RANGE-FINDING STUDY OF SC-19129 IN PREGNANT RABBITS

## Individual Fetal Data

250 mg/kg/day Group

Animal Number	Reproductive Status	Number of			
		Implant- ations	Resorp- tions	Live Fetuses	Dead Fetuses
85-197	Pregnant	6	1	5	0
85-198	Pregnant	7	7	0	0
85-199	Pregnant	8	0	8	0
85-200	Pregnant	3	0	3	0
85-201	Pregnant	A N I M A L   A B O R T E D			
85-202	Pregnant	3	1	2	0

TABLE 4 (Cont.)

## A RANGE-FINDING STUDY OF SC-19129 IN PREGNANT RABBITS

## Individual Fetal Data

500 mg/kg/day Group

Animal Number	Reproductive Status	Number of			
		Implant- ations	Resorp- tions	Live Fetuses	Dead Fetuses
85-203	Not Pregnant	0	0	0	0
85-204	Pregnant	9	1	8	0
85-205	Not Pregnant	0	0	0	0
85-206	Pregnant	7	0	7	0
85-207	Pregnant	9	0	9	0
85-208	Pregnant	7	1	6	0

TABLE 4 (Cont.)

## A RANGE-FINDING STUDY OF SC-19129 IN PREGNANT RABBITS

## Individual Fetal Data

750 mg/kg/day Group

Animal Number	Reproductive Status	Number of			
		Implant- ations	Resorp- tions	Live Fetuses	Dead Fetuses
85-209	Pregnant	9	1	8	0
85-210	Pregnant	6	6	0	0
85-211	Pregnant	4	0	4	0
85-212	Pregnant	5	0	5	0
85-213	Pregnant	7	0	7	0
85-214	Pregnant	1	0	1	0

TABLE 4 (Cont.)

## A RANGE-FINDING STUDY OF SC-19129 IN PREGNANT RABBITS

## Individual Fetal Data

1000 mg/kg/day Group

Animal Number	Reproductive Status	Number of			
		Implant- ations	Resorp- tions	Live Fetuses	Dead Fetuses
85-215	Pregnant	10	2	8	0
85-216	Pregnant	8	1	7	0
85-217	Pregnant	12	3	9	0
85-218	Pregnant	8	0	8	0
85-219	Pregnant	A N I M A L   D I E D			
85-220	Pregnant	A N I M A L   D I E D			

## PROTOCOL

1. Study Title: A Range-Finding Study of SC-19129 in Pregnant Rabbits

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2. Study Sponsor: G. D. Searle & Co.

3. Facility: G. D. Searle & Co., 4901 Searle  
Parkway, Skokie, Illinois 60077.

4. Proposed Dates:

A. Initiate Breeding: February 5, 1985

B. Initiate Dosing: February 11, 1985

C. Initiate Day 28 Sacrifice: March 5, 1985

5. Purpose: To determine potential toxic effects as evidenced by clinical signs, body weights, and fetal viability, and to provide a basis for dosage level selection in a Teratology study.

6. Overview of Study Design:

<u>Group</u>	<u>Treatment</u>	<u>Dosage Level (mg/kg/day)</u>	<u>Number of Females/Group</u>
1	Control	0	6
2	SC-19129	125	6
3	SC-19129	250	6
4	SC-19129	500	6
5	SC-19129	750	6
6	SC-19129	1000	6

7. Laboratory Procedures: This is an exploratory/range-finding study and is not within the scope of Good Laboratory Practice Regulations.

8. Proposed Clinical Use:

9. Test Article:

- A. Chemical Name: N-L- $\beta$ -aspartyl-L-phenylalanine, 1-methylester.
- B. Formulation: The appropriate amount of test article will be suspended in 0.5% methylcellulose (w/v), 0.1% polysorbate 80 (v/v) in distilled water.
- C. Administration:
1. Route: Orally by gavage.
  2. Frequency: One half dose, twice daily.
  3. Duration: The females will be dosed from day 6 through day 18 of gestation. The quantity of control vehicle or test article suspensions will be based on the most recent body weight.
  4. Volume: Both the control vehicle and test article suspensions will be given at 4 ml/kg.
- D. Analysis
1. Test Article
    - a. Identity, strength, purity and composition: Will be determined before use.
    - b. Stability: Will be reported if available.
  2. Test Article Carrier Mixture:
    - a. Stability: Will be reported if available.
- E. Storage
1. Test Article: Will be stored in a well-closed, light-resistant container at controlled room temperature.
  2. Test article carrier mixture: Will be prepared fresh daily.
- F. Estimated Test Article Requirements: 1200g



10. Study Design Conditions:

- A. Animals: 36 virgin female rabbits of the New Zealand White strain (H.A.R.E., Hewitt, N.J.) will be used in this study. The rabbit is widely used as the non-rodent species for teratogenic studies, and a vast amount of historical control data is available. The rabbits will be approximately 4 months of age and weigh approximately 3 to 5 kg at the start of the study. The rabbits will be allowed approximately 1 month acclimatization prior to the start of the study.
- B. Husbandry and Diet: Rabbits will be individually housed in stainless steel cages during the study. The rabbits will be given approximately 150 g of Certified Purina Rabbit Chow #5322 per day and have free access to municipally supplied tap water throughout the study. No special analyses of feed and water will be performed since no contaminants known to be capable of interfering with the study are reasonably expected to be present. Animal room temperature will be  $65^{\circ} + 5^{\circ}\text{F}$  and relative humidity will be 25% or greater; Both parameters will be monitored. A 12-hour light/12-hour dark cycle will be used throughout the study.
- C. Breeding Procedure: Female rabbits will be artificially inseminated (day 0 of gestation) with semen from breeder colony males of the same strain and source. Each female will then receive 50 USP units of a chorionic gonadotropin intravenously via the marginal ear vein to help induce ovulation. The females will then be assigned to treatment groups by using a block design of random permutations and be given their unique identification numbers using ear tags.

11. Maternal Observations:

- A. Clinical Signs: Animals checked at least once a day and all remarkable signs observed will be recorded.
- B. Mortality: Any rabbits that die will be examined internally to verify reproductive status and to possibly determine cause of death.
- C. Body Weight: Females will be weighed on gestation days 0, 6, 8, 10, 13, 16, 19, and 28.

D. Food Consumption: Estimated for all females throughout the study.

12. Caesarean Section:

On day 28 of gestation, all females will be sacrificed with an overdose of a euthanizing agent. The uterus will be exposed and the numbers of corpora lutea, implantations, resorptions, and live or dead fetuses recorded.

13. Statistical Procedures:

The mean values and standard deviations of each variable will be determined. Maternal body weights and body weight changes will be analyzed by a one-way analysis of variance, Student's t-tests (using the pooled error variance from the one-way analysis of variance) of control vs. the other dose groups (if the F ratio among treatments is significant at the 5% level), and the Bartlett-Box test for homogeneity of variance. All t-tests will be two-tailed. The Kruskal-Wallis test will be used to analyze the following variables: numbers of implantations, resorptions, and live or dead fetuses per litter. If significant at the 5% level, then the Mann-Whitney U test will be used to compare each compound-treated group to the control group. Significance levels achieved will be reported for 5% for t-tests, Mann-Whitney U tests and Bartlett-Box test.

14. Archiving of Materials:

All raw data, supporting documents, protocol, specimens, and the final report will be transferred to the R&D Central File.

15. Protocol Approval

A. J. W. Noveroske, Ph.D.  
Study Director  
Product Safety Assessment:

J. W. Noveroske 1/18/85  
Date

B. F. N. Kotsonis, Ph.D.  
Diplomate, A.B.T.  
Director, Toxicology  
Product Safety Assessment:

F. N. Kotsonis 1/18/85  
Date

C. F. E. Kohn, Ph.D.  
Senior Director,  
Product Safety Assessment:

F. E. Kohn 1/22/85  
Date

APPENDIX B

R&D PRODUCT DEVELOPMENT FUNCTION  
REPORT REVIEW AND RELEASE

Page 1 of 3

DEPARTMENT: Product Development Analytical

DOCUMENT NUMBER: F-321-034-09

TITLE OF REPORT: SC-19129

TYPE OF REPORT: Analytical Summary in Support of Product Safety  
Assessment Study Number 2561

AUTHOR(S):	DATE	REVIEWER(S):	DATE
<u></u>	<u>25-March '85</u>	<u>Samuel J. Sweney</u>	<u>4-4-85</u>
_____	_____	_____	_____
_____	_____	_____	_____

TECHNICAL WRITER:

Michele Newcomb Michele Newcomb

APPROVAL:	DATE
<u></u>	<u>25-March '85</u>
_____	_____

APPROVAL FOR RELEASE:

<u></u>	<u>4/4/85</u>	<u>Larry Hansen</u>	<u>4/5/85</u>
R. Baum, Director	Date	L. Hansen,	Date
Analytical Development		Senior Director	
		Product Development	

NORTH AMERICAN PRECLINICAL RESEARCH AND DEVELOPMENT  
SEARLE PHARMACEUTICALS AND CONSUMER PRODUCTS  
SKOKIE, ILLINOIS

S.A. 2561

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Subject: SC-19129

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Summary Number: F-321-034-09

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Applicable to SA Study Number: 2561

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Test Article Characterization and Stability

Lot 84K-047-101 was analyzed using the release methods of testing, released against the current specifications (NS-S84-015-A), and given a re-evaluation period of one year prior to use in this study.

Table 1

Lot Designation	84K-047-101
Analysis Report #	84N1058, 84N1007
Completion Date	10/16/84
Identity (HPLC)	Conforms to Standard
Assay BY HPLC (on dried basis)	100.0% n = 3 s = 0.2
Water	9.8%

These results and all other results, coupled with the use of Lot 84K-047-101 within its re-evaluation period indicate that Lot 84K-047-101 of SC-19129 was suitable for use in this study.

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Subject: SC-19129

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Summary Number: F-321-034-09

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Applicable to SA Study Number: 2561

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GLP Compliance Statement

To the best of our knowledge, the support activities provided by the Product Development Analytical Department for this study were conducted in compliance with the Good Laboratory Practices Regulations, as set forth in part 58, 21 CFR.

S.A. 2561

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