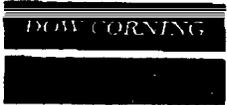


CODING FORMS FOR SRC INDEXING

Microfiche No.	OTS0559773		
New Doc ID	88990000245	Old Doc ID	8EHQ-0899-14526
Date Produced	11/05/98	Date Received	08/10/99
		TSCA Section	8E
Submitting Organization	DOW CORNING CORP		
Contractor			
Document Title	INITIAL SUBMISSION: ACUTE ORAL TOXICITY STUDY OF MSO-2 IN RATS. WITH COVER LETTER DATED 8/4/1999		
Chemical Category	2,8,9-TRIOXA-5-AZA-1-SILABICYCLO(3.3.3)UNDECANE, 1-METHYL-		

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



8EHQ-99-14526

Re: TSCA Section 8(e) Notification of Substantial Risk:
2,8,9-Trioxa-5-aza-1-silabicyclo[3.3.3]undecane, 1-methyl-3,7-bis-
[(2-propenyloxy)methyl]- (CASRN 225504-94-9)

Dear Sir:

In accordance with the provisions of Section 8(e) of the Toxic Substances Control Act (TSCA), as interpreted in the Statement of Interpretation and Enforcement Policy (40 FR 11110, March 16, 1978), Dow Corning is submitting a Notification of Substantial Risk concerning a final report which we recently obtained from our Japanese joint venture, Dow Corning Toray Silicone Company, Ltd. This acute toxicity study was conducted by a contract toxicology laboratory in Japan on a chemical substance currently in research and development at Dow Corning Toray Silicone.

Test Material:

225504-94-9 2,8,9-Trioxa-5-aza-1-silabicyclo[3.3.3]undecane, 1-methyl-3,7-bis-
bis[(2-propenyloxy)methyl]-

Manufacturer:

Dow Corning Corporation
2200 West Salzburg Road
Midland, Michigan 48686-0994

Contain NO CBI

Recently Obtained Study:

Acute Oral Toxicity Study of MSO-2 in Rats (MSDS)

Dow Corning Corporation
1999-10000-47290
November 5, 1998

25230

Dow Corning Corporation
Midland, Michigan 48686-0994
Phone: (517) 496-4000



88990000245

Summary:**Findings**

An acute oral toxicity study was conducted in male and female Crj:CD (SD) IGS rats at the oral dose limit of 2,000 mg/kg body weight following O.E.C.D. Guideline 401.

No mortalities were observed. Clinical observations included salivation, decreased spontaneous locomotion, decreased respiratory rate, ptosis and clonic convulsions in both sexes. Staggering gait was observed in females. Salivation was observed immediately after administration to 30 minutes-1 hou. after treatment. Staggering gait was observed 5 minutes to 2 hours after treatment. Decreased spontaneous locomotion was observed 5 minutes to 6 hours after treatment. Decreased respiratory rate and ptosis were observed 10 minutes to 4-6 hours after treatment. Clonic convulsion was observed at 3 to 4 hours after treatment. All clinical signs disappeared by 1 day after administration; no further abnormalities were observed in either sex.

Discussion

The duration of the clinical observations is not clearly stated in the report; these neurotoxic effects may well have been transient in nature. The study also was conducted using relatively young animals (five weeks old, 98-115 grams body weight) which could have exhibited increased sensitivity: EPA testing guidelines call for use of 8-12 weeks old test animals (greater than 200 grams body weight). Finally, the test material is a research and development chemical substance and currently is not manufactured or processed for commercial purposes. Consequently, at this time, we believe that the results of this study are not indicative of a substantial risk to human health or the environment. Nevertheless, we are reporting these findings to EPA to ensure our compliance with both the letter and the spirit of TSCA Section 8(e).

Actions:

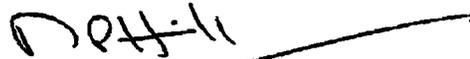
Dow Corning will notify EPA of any further relevant information that may be developed concerning this material.

For purposes of TSCA Section 8(e) notification, the general CONFIDENTIAL designation on the attached health and safety study is waived by Dow Corning.

A 05.

If you have any questions concerning this study, please contact Dr. Thomas Barfknecht, Product Toxicologist, Product Safety Group, HERA Americas, at 517-496-5728 or at the address provided herein. If you require further general information regarding this submission, please contact Dr. Rhys G. Daniels, Senior Regulatory Compliance Specialist, Regulatory Compliance Group, HERA Americas, at 517-496-4222 or at the address provided herein.

Sincerely,



Michael P. Hill
Americas Vice President and Corporate Director
Health and Environmental Sciences
(517) 496-4057

PGD99108

A16-0327

1988-1000-47290

CONFIDENTIAL

Receipt No.	F-1979
Report No.	D-5483

FINAL REPORT

Hira Research Laboratories
Chemical Biotesting Center
Chemicals Inspection & Testing Institute
Japan

TITLE

Acute Oral Toxicity Study of MSO-2 in Rats (MSDS)

SPONSOR

Dow Corning Toray Silicone Co., Ltd.
2-2, Chigusa-kaigan, Ichihara-shi, Chiba 299-0108, Japan

Contain NO CBI**SUMMARY**

Acute oral toxicity study of MSO-2 was conducted in 5 of each male and female C₃H/CD (SD) IGS rats aged 5 weeks.

No animals were died for dosing of the test substance.

In clinical signs of the 2,000 mg/kg group, salivation, decreased spontaneous locomotion, decreased respiratory rate, ptosis and clonic convulsion were observed in both sexes, staggering gait was observed in females. Salivation was observed immediately after administration to 30 min. or 1 h after administration. Staggering gait was observed at 5 min. to 2 h after administration. Decreased spontaneous locomotion was observed at 5 min. to 6 h after administration. Decreased respiratory rate and ptosis were observed at 10 min. to 4 or 6 h after administration. Clonic convulsion was observed at 3 or 4 h after administration. These all findings disappeared by 1 day after administration, and no abnormalities were observed in both sexes since then.

Although the body weights in the female 2,000 mg/kg group had a tendency to suppress at 1 day after administration, these normally increased since the 3 day after administration. No abnormalities observed with regard to body weight in males.

No abnormalities were noted with regard to necropsy in both sexes.

In conclusion, the LD₅₀ value of MSO-2 for mus was estimated to be more than 2,000 mg/kg in both sexes.

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PAGE 3/10

A16-0327

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AUTHOR

Study Director:

Signed in original November 5, 1998
Takayuki Koga, Senior Laboratory Animal Technician

APPROVAL

Management:

Signed in original November 5, 1998
Yoshifumi Fujino, M.S.

A 08

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A16-0327

I, the undersigned, hereby declare that this report provides correct English translation of the final report (Study Code A16-0327, issued on November 5, 1998).

Ryuichiro Mizuguchi

Ryuichiro Mizuguchi, B.S.
Hita Research Laboratories
Chemical Bioretesting Center
Chemicals Inspection &
Testing Institute, Japan

July 1, 1999

Date

Study Code: A16-0327
Test Substance Code: HR3860
Sponsor Code: T-070

TESTING FACILITY

Hita Research Laboratories, Chemical Biotesting Center
Chemicals Inspection & Testing Institute, Japan
822, 3-chome, Ishi-machi, Hita, Oita 877-0061, Japan

PURPOSE OF STUDY

The purpose of this study was to assess the single dose oral toxicity of the test substance both qualitatively and quantitatively.

TESTING METHOD

This study was conducted in conformity with the "Acute oral toxicity, 401 in OECD Guidelines for Testing of Chemicals" (February 24, 1987) excluding simultaneous dosing for both sexes.

PERIOD OF STUDY

Commencement of Study: September 22, 1998
Completion of Study: November 5, 1998

PERSONS CONCERNED WITH STUDY

Study Staff: Satoru Chogi, B.S.
Junior Laboratory Animal Technician

Staff, Animal Management: Hatsune Ehara,
Junior Laboratory Animal Technician
Takayuki Koga,
Senior Laboratory Animal Technician

LOCATION AND PERIOD FOR RETENTION OF RAW DATA AND SPECIMENS

All the records related to the study shall be retained in the archives at Hita Research Laboratories, CITI, for 5 years after completion of the study. Disposition of the retained records after termination of the retention period requires the sponsor's prior consent.

1999 - 10000 - 47290

MATERIALS

1. TEST SUBSTANCE (INFORMATION PROVIDED BY THE SPONSOR)

1.1 Name

3,7-bis(2-propenoxymethyl)-1-methyl-2,8,9-trioxa-5-aza-1-silabicyclo[3.3.3]undecane

(3,7-bis(allyloxymethyl)-1-methylsilatrane)

Abbreviation: MSO-2

CAS No.: —

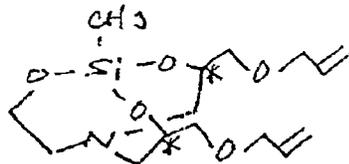
1.2 Lot No.

98062

1.3 Supplier

Dow Corning Toray Silicone Co., Ltd.

1.4 Structural Formula



A mixture of three diastereomers

*: Optically active substance

(Molecular formula: $C_{15}H_{27}NO_5Si$)

1.5 Purity (GC)

97.9 w/w%

1.6 Name and Concentration of Impurities (GC)

Methanol 0.1 w/w%

Methyltrimethoxysilane 0.1 w/w%

Allylglycidyl ether 1.9 w/w%

1.7 Physicochemical Properties

Appearance at Ordinary Temperature: Light yellow liquid

Molecular Weight: 329.46

Stability: hydrolyzed (not rapidly)

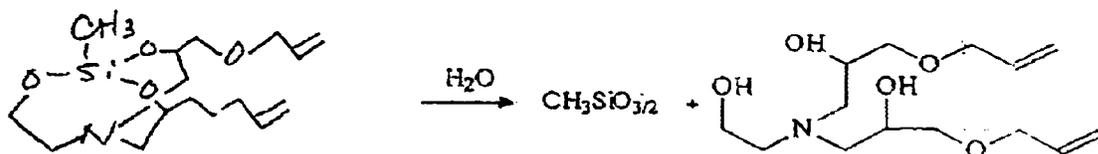
Melting Point: —

Boiling Point: >150°C/5 torr

Vapor Pressure: —

Partition Coefficient: —

Hydrolysis:



Solubility: Oil soluble

Degree of Solubility: Water: slightly soluble

DMSO: >50 mg/ml (measured at our laboratory)

Acetone: freely soluble

Others: —

1.8 Storage Conditions

The test substance was stored at room temperature.

2. ANIMALS

Specific pathogen free Crj: CD (SD) IGS rats were obtained from Charles River Japan, Inc. (Hino Breeding Center, 735, Shimokomatsuki, Hino-cho, Game-gun, Shiga 529-1633, Japan) and were quarantined and acclimatized. Healthy animals with favorable weight gains were assigned to groups using body weight-stratified randomization. Their body weights ranged 107.1–115.1 g in males and 97.7–102.5 g in females, and they were 5 weeks of age in both sexes at the dosing. The animals were identified by painting on the tail with oily ink.

METHODS

1. PREPARATION OF THE TEST SUBSTANCE

1.1 Vehicle

Olive oil (Lot No. 001RYA, Fujimi Pharmaceutical Co., Ltd.)

1.2 Preparation

Test substance was weighed accurately and dissolved in olive oil with continuous agitation to make 20w/v% solution. This solution was prepared with concentration correction by purity of test substance (97.9w/w%).

1.3 Time of Preparation

Test preparation was made on the day of use.

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2 DOSING

2.1 Administration method

All animals were fasted overnight before administration and 3-4 hours after administration. The administration was performed in the morning using a Nelaton catheter (Terumo Corporation) and a syringe (Terumo Corporation) by a single oral gavage.

2.2 Doses

The doses were set as follows:

Group	Dose (mg/kg)	Volume (ml/kg)	Concentration (%)	Number of animals	
				Male (Animal No.)	Female (Animal No.)
Vehicle control	0	10	0	5 (1-5)	5 (1-5)
High dose	2,000	10	20	5 (6-10)	5 (6-10)

3. OBSERVATIONS AND EXAMINATIONS

3.1 Mortality

Mortality was recorded everyday for 14 days.

3.2 Clinical Sign

General condition was recorded frequently until 6 h after administration, then at least once a day from day 1 to day 14.

3.3 Body Weight

Body weights were measured immediately before administration, day 1, day 3, day 7 and day 14.

3.4 Necropsy

All animals were necropsied after euthanasia by exsanguination under ether anesthesia at 14 days after administration.

4. STATISTICAL ANALYSIS

The mean body weight and the standard deviation were calculated in each group for both sexes.

RESULTS

1. MORTALITY (TABLE 1)

No animals were died in both sexes.

2. CLINICAL SIGNS (TABLE 2, ADDENDUM 1)

2.1 Male

Vehicle control group: Mucous stool was observed in 3 animals at 2 to 3 h after administration.

2,000 mg/kg group: Salivation was observed in 2 animals immediately after administration to 30 min. after administration. Decreased spontaneous locomotion was observed in all animals at 5 min. to 6 h after administration. Decreased respiratory rate was observed in 4 animals at 10 min. to 4 h after administration. Ptosis was observed in 4 animals at 10 min. to 4 h after administration. Clonic convulsion was observed in 3 animals at 3 h after administration. These findings disappeared by 1 day after administration.

2.2 Female

Vehicle control group: Mucous stool was observed in 3 animals at 1 to 3 h after administration.

2,000 mg/kg group: Salivation was observed in all animals immediately after administration to 1 h after administration. Staggering gait was observed in 3 animals at 5 min. to 2 h after administration. Decreased spontaneous locomotion was observed in all animals at 5 min. to 6 h after administration. Decreased respiratory rate was observed in all animals at 10 min. to 6 h after administration. Ptosis was observed in all animals at 10 min. to 6 h after administration. Clonic convulsion was observed in 2 animals at 3 to 4 h after administration. These findings disappeared by 1 day after administration.

3. BODY WEIGHT CHANGE (TABLE 3)

Male: Body weights were normally increased through out the observation period.

Female: Although the body weights in the 2,000 mg/kg group had a tendency to suppress at 1 day after administration, these normally increased since the 3 day after administration.

4. NECROPSY (TABLE 4)

No abnormalities were noted in both sexes.

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DISCUSSION

The acute oral toxicity of MSO-2 was examined in Crj: CD (SD) rats. The dose level was set at 2,000 mg/kg and observations were carried out for 14 days after administration.

No animals were died for dosing of the test substance.

In clinical signs of the 2,000 mg/kg group, salivation, decreased spontaneous locomotion, decreased respiratory rate, ptosis and clonic convulsion were observed in both sexes, staggering gait was observed in females. Salivation was observed immediately after administration to 30 min. or 1 h after administration. Staggering gait was observed at 5 min. to 2 h after administration. Decreased spontaneous locomotion was observed at 5 min. to 6 h after administration. Decreased respiratory rate and ptosis were observed at 10 min. to 4 or 6 h after administration. Clonic convulsion was observed at 3 or 4 h after administration. Although it was considered that salivation appeared owing to irritation of test substance because it appeared sporadically from immediately after administration, it was also undeniable that there is effect of administration of test substance because of appearance of related nerves symptoms and the time appeared salivation. These all findings disappeared by 1 day after administration, and no abnormalities were observed in both sexes since then.

Although the body weights in the female 2,000 mg/kg group had a tendency to suppress at 1 day after administration, these normally increased since the 3 day after administration. No abnormalities observed with regard to body weight in the male 2,000 mg/kg group.

No abnormalities were noted with regard to necropsy in both sexes.

In conclusion, the acute oral toxicity of MSO-2 for rats was considered to be comparatively weak, and the LD₅₀ value was estimated to be more than 2,000 mg/kg in both sexes.

Table 1 Acute oral toxicity study of HR3860 in rats

Mortality		Number of deaths on day														LD ₅₀ (mg/kg)	
Sex	Exp. group (mg/kg)	0	1	2	3	4	5	6	7	8	9	10	11	12	13		14
		0' 5 10 30(min) 1 2 3 4 5 6(h)															
Male	Vehicle control																0/5*
	2,000																0/5
																	> 2,000
Female	Vehicle control																0/5
	2,000																0/5
																	> 2,000

* Immediately after administration.

Number of dead animals / Number of animals.

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Table 2. Acute oral toxicity study of HR3860 in rats

Summary of clinical signs

Signs	Male		Female	
	Vehicle control	2,000 1a ^{b)}	Vehicle control	2,000 1a
Signs		5	5	5
Abnormalities detected	2		2	
Salivation		2		5
Staggering gait				3
Decreased spontaneous locomotion		5		5
Decreased respiratory rate		4		5
Proxi.		4		5
Clonic convulsion		3		2
Mucous stool	3		3	

a) 1a, terminal autopsy.

b) Number of animals examined.

Table 3-1 Acute oral toxicity study of HR3860 in rats
Summary of body weights(g): Male

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Dose (mg/kg)	Animal No.	0	1	3	7	14 (day)
Vehicle control	1	107.1	123.9	144.8	184.7	248.6
	2	113.0	133.7	151.7	187.3	251.2
	3	113.5	133.2	153.2	193.5	244.6
	4	109.8	128.2	148.9	192.3	247.7
	5	115.1	135.4	158.2	198.5	266.9
	Mean	111.7	130.9	151.4	191.3	251.8
±S.D.	± 3.2	± 4.7	± 5.0	± 5.4	± 8.8	
2,000	6	109.9	126.3	143.1	187.4	257.4
	7	114.8	129.6	154.9	206.4	240.9
	8	111.5	127.0	148.1	187.8	249.9
	9	112.7	127.1	148.3	187.8	247.3
	10	111.5	127.6	149.0	181.0	241.2
	Mean	112.1	127.5	148.7	190.1	247.3
±S.D.	± 1.8	± 1.3	± 4.2	± 9.6	± 6.8	

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Table 3-2 Acute oral toxicity study of HRS860 in rats
Summary of body weights(g): Female

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Dose (mg/kg)	Animal No.	0	1	3	7	14 (day)
Vehicle control	1	99.8	116.1	126.5	146.6	157.7
	2	100.7	114.1	133.6	154.2	189.0
	3	97.7	111.1	135.3	161.2	180.0
	4	101.6	120.0	141.5	171.0	200.0
	5	100.9	117.2	136.1	159.1	179.8
	Mean	100.1	115.7	134.6	158.4	183.3
	tS.D.	± 1.5	± 3.5	± 5.4	± 9.0	± 12.0
2,000	6	99.2	107.4	125.9	151.0	182.1
	7	102.5	112.2	136.0	158.2	180.9
	8	99.3	104.7	124.0	149.6	180.4
	9	100.0	110.7	128.6	156.0	180.4
	10	101.6	112.2	134.1	162.1	203.2
	Mean	100.5	109.4	129.7	155.4	185.2
	tS.D.	± 1.6	± 3.3	± 5.2	± 5.1	± 9.5

Table 4 Acute oral toxicity study of HR3860 in rats
 Summary of macroscopic examinations

Findings	Male		Female	
	Vehicle control]	2,000	Vehicle control	2,000 (mg/kg)
	ta ¹⁾	1a	1a	1a
	5 ^{b)}	5	5	5
No abnormalities detected	5	5	5	5

¹⁾ ta, terminal autopsy.

^{b)} Number of animals examined.

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Appendum 1-2. Acute oral toxicity study of HBR 3360 in rats

Clinical signs of individual animals

Exp. group (mg/kg)	2,000																								
	0					1					2				3				4				5		
Signs	Sex	0*	5	10	30(mic)	1	2	3	4	5	6	7	8	9	10	11	12	13	14 (day)						
No abnormalities detected	Male	6,7,9 ^{a)} 10	6,9			6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10					
	Female	6,7,8, 9				6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10				
Salivation	Male	8	8	7,8	7,8																				
	Female	10	10	6,7,8, 9,10	6,7,8, 9,10																				
Staggering gait	Male																								
	Female	6	6,9	6,7	6,7																				
Decreased spontaneous locomotion	Male	7,8,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10				
	Female	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10			
Decreased respiratory rate	Male	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10			
	Female	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10			
Pilois	Male	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10			
	Female	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10	6,7,8, 9,10			

a) Exposed only after administration.

b) Animal number.

