

MICROBIO

Appendix D



CONTENTS

	Page
ABSTRACT	6
MATERIALS AND METHODS	7
I. GENERAL INFORMATION	7
II. TEST ARTICLE AND VEHICLE CONTROL	8
III. DESCRIPTION OF THE TEST SYSTEM	9
IV. EXPERIMENTAL DESIGN	10
V. EXPERIMENTAL PROCEDURES	11
A. Test Article Administration	11
B. Observation and Examination	11
C. Statistical Analysis	11
D. Data Retention	11
RESULTS AND DISCUSSION	12
I. Mortality	12
II. Clinical Observations	12
III. Body Weights	12
III. Gross Necropsy	12
CONCLUSION	12
COMMENTS AND/OR PROBLEMS	13
REFERENCES	13
 TABLES	
Table 1. Acute Oral Toxicity Study of Product Code MicrSoy-20 (MS-20) in Rats — Mortality, Clinical Signs and Gross Necropsy Findings	14
Table 2. Acute Oral Toxicity Study of Product Code MicrSoy-20 (MS-20) in Rats — Mean Body Weights	14
 FIGURE	
Figure 1. Acute Oral Toxicity Study of Product Code MicrSoy-20 (MS-20) in Rats — Mean Body Weight Growth Curves	15



APPENDICES

	Page
APPENDIX A	A-1
Test Article Information Sheet	A-3
APPENDIX B	B-1
Protocol (DV-PR-AC00139E)	B-3
Study Schedule	B-13
APPENDIX C	C-1
Records of Animal Room Temperature during Study Period	C-3
Records of Animal Room Relative Humidity during Study Period	C-7
Records of Animal Diet	C-11
Analysis Records of Animal Drinking Water	C-15
Analysis Records of Animal Diet	C-19
Laboratory Animal Quarantine Report	C-23
APPENDIX D	D-1
Individual Animal Data on Body Weights	D-3



ACUTE ORAL TOXICITY STUDY IN SD RATS PRODUCT CODE MICRISOY-20 (MS-20)

ABSTRACT

An acute oral toxicity study was conducted to evaluate the toxicity of "Product Code MicrSoy-20 (MS-20)" in Sprague-Dawley (SD) rats by gavage. Forty-eight rats were used and randomized into four groups, each consisting of six males and six females. The treatment rats were administered with Product Code MicrSoy-20 (MS-20) at dose levels of 5, 10 and 20 ml/kg (2.5, 5, 10 ml/kg twice at two hours apart), the control rats were administered with 20 ml/kg injection grade water (10 ml/kg twice at two hours apart). The dosing amount was adjusted basing on the individual body weight recorded prior to dosing. The rats were observed for 14 days. Examinations were conducted with respects to general demeanor, clinical signs, mortality, body weights/total body weight gains and necropsy findings. There was no mortality and clinical signs observed in treated and control rats. There were no differences in body weights and body weight gains among all treated and control rats. All rats showed no observable gross lesions at necropsy. In conclusion, Product Code MicrSoy-20 (MS-20) exerted no adverse toxic effects in SD rats at dose levels up to 20 ml/kg, which provided a safety margin of 240 over the recommended human dose basing on a conversion of body weight. The results of this study will be used for dosing selection for the repeated toxicity study and served as a reference of safety margin for human use.



MATERIALS AND METHODS

I. GENERAL INFORMATION

- A. DCB Study Code Number: AC00139
- B. Purpose and Objectives of Study: The purpose of this study was to evaluate the acute oral toxicity of "Product Code MicSoy-20 (MS-20)". The information will permit the dose range finding for the subsequent subacute oral toxicity study. This study was conducted in compliance with Good Laboratory Practice (GLP).
- C. Name of Sponsor: MICROBIO Co., Ltd.
Address: No. 81, Gauyang N. Rd., Lung Tan Shiang, Tao Yuan, Taiwan, R.O.C.
Representative: William Lu
- C. Testing Facility: General/Reproductive Toxicology Laboratory, Development Center for Biotechnology (DCB).
Address: 103, Lane 169, Kang-Ning St., Hsi-Chih City, Taipei County, Taiwan, R.O.C.
- E. Location of Study and Storage of Raw Data: This study was conducted in General/Reproductive Toxicology Laboratory, DCB and in animal room C-414. Raw data will be stored in the archives room.
- F. Personnel:
1. General/Reproductive toxicology unit
 - a. Study director: Juan Judy Liu, PhD, DVM
 - b. Associates: Tan-Fu Yuen, MS
Di-Sheng Wang, MS
Yu-Mai Chen, MS
 - c. Veterinary Histopathologist: Shin-Yung Hsu, DVM, PhD
 2. Collaborated units:
 - a. Chief of laboratory animal research division: Chou-Chu Hong, DVM, PhD, DACVM
 - b. Attending veterinarian: Tsung-Te Lin, DVM, MS



G. Schedule: Study Calendar (date/month/year)

1. Animal procurement: 3/10/2001
2. Quarantine and acclimation: 3/10/2001 to 11/10/2001
3. Date of dosing initiation: 12/10/2001
4. Date of study termination and necropsy: 26/10/2001

II. TEST ARTICLE AND VEHICLE CONTROL

A. Test Article

1. Name: Product Code MicrSoy-20 (MS-20)
2. Date of receipt: Oct. 5, 2001
3. Batch/Lot number: 20010209
4. DCB code: DV00199
5. Ingredients: MS-20 is a Chinese medicine. The components are very complicated. Until now, its effective components are still unable to determine
6. Other Characteristics: Dark brown liquid with prune juice odor
7. Solubility: Water-soluble
8. Amount Supplied: 22 bottles (180 ml/bottle)
9. Storage Conditions: Room temperature and protect from light
10. Expiration Date: Feb. 9, 2004

Statements:

1. The test article is a proprietary product of the sponsor, therefore the sponsor will be responsible for the requirements listed under "Test Article" of the GLP regulation (21 CFR §58.105, FDA).
2. The result and the report are generated by DCB for the test article submitted by the sponsor, and are intended for petition to government agency for product registration.

B. Vehicle Control

1. Name: Injection grade water
2. Source and manufacturer: Sin Tong Chemical Industrial Co., Ltd. Taiwan, ROC
3. Lot number: 4DS1287
4. Expiration date: June 12, 2002
5. Storage condition: Room temperature

D. Dosing Solutions: The undiluted solution of Product Code MicrSoy-20 (MS-20) was used to dose the animals. Three dosing levels at 5, 10 and 20 ml/kg as low, medium and high were chosen. The control rats were administered with 20 ml/kg of injection grade water to serve as vehicle control.



III. DESCRIPTION OF THE TEST SYSTEM

- A. Species: Rats
- B. Strain: Crl:CD(SD)fSPF
- C. Source: National Laboratory Animal Breeding & Research Center, National Science Council, Taipei, Taiwan.
- D. Age at Initiation of Study: Approximately 6 weeks old, with body weight range of 172 to 191 g for males and 133 to 147 g for females.
- E. Quarantine (SOP: DCB-DV-AC00032) and Acclimation: After 7 days of quarantine in room C-431, rats were moved to room C-414 for 2 days of acclimation prior to use. All suitable rats were accepted to this study.
- F. Method of Identification (SOP: DCB-DV-TE00446): Rats were identified with a unique number by ear notch and cage tags.
- G. Method of Caging: The rats were housed two per cage in a stainless steel wire mesh cage. Each cage was labeled with the animal number, study number, test article code, dose level, species and sex.
- H. Environmental Conditions:
 - 1. Housing: Each suspended stainless steel cage contains 2 rats. The cages have wire mesh bottoms that allow urine and fecal material to fall through onto the tray containing absorbent wooded chips.
 - a. Temperature (SOP: DCB-DV-AC00023): maintained at $21 \pm 2^{\circ}\text{C}$.
 - b. Humidity (SOP: DCB-DV-AC00023): maintained at $50 \pm 20\%$ relative humidity.
 - c. Light Cycle (SOP: DCB-DV-AC00023): 12 hours light and 12 hours dark, automatic.
 - 2. Diet (SOP: DCB-DV-AC00025): Laboratory Autoclavable Rodent Diet 5010 (PMI[®] Feeds Inc., St. Louis, MO) was supplied *ad libitum* throughout the study period (SOP: DCB-DV-AC00025). The dates of manufacturing were 9/8/2001 & 16/8/2001 (See Appendix C).
 - 3. Water (SOP: DCB-DV-AC00026): Tap water was supplied *ad libitum* via water bottles attached to the cages.
 - 4. Contaminants: Results of the PMI[®] feeds and the DCB water supply assays were reviewed and determined that any contaminants covered by those assays were at concentrations which were not affecting the results of the present study (See Appendix C).
- I. IACUC Approved Protocol Number: 2001-TP-010-a.



IV. EXPERIMENTAL DESIGN

- A. Treatment Groups: Four groups of rats, each consisting of 6 males and 6 females (24 males and 24 females in total) were used. The control group was administered with the injection grade water. The remaining three groups were administered with MS-20 at low (5 ml/kg), medium (10 ml/kg) or high dose (20 ml/kg), respectively.
- B. Randomization (SOP: DCB-DV-TE00462): The rats were divided into weight classes with weight variation not exceeding $\pm 20\%$ of the mean body weight. The rats were then randomized and assigned into 4 groups using the computerized Laboratory Integration Management System (Computer Service Center, DCB).
- C. Test Article Administration
1. Rationales for dose levels selection:
 - a. The recommended daily human dose is 1-5 ml; for a 60-kg subject, therefore, the maximal recommended daily dose is 0.083 ml/kg, approximately.
 - b. To achieve a bigger safety margin, the rats were dosed twice in this study.
 - c. The dose levels (5, 10 and 20 ml/kg) of test article selected in this study provided a safety margin of 60, 120 and 240 over the recommended human dose, basing on the conversion of body weights. A corresponding safety margin of 9.4, 18.8 and 37.6 were also provided, respectively, basing on a conversion of surface area.

2. Dose levels:

Group no., dose levels, dosing solutions, dosing volumes and animal no. in this acute oral toxicity study are presented as below:

Group No.	Dose Levels (ml/kg)	Dosing Solutions	Dosing volumes (ml/kg)	Animal No. M/F
1	0	injection grade water	10 × 2	6M, 6F
2	5	MS-20	2.5 × 2	6M, 6F
3	10	MS-20	5 × 2	6M, 6F
4	20	MS-20	10 × 2	6M, 6F

3. Dosing process: Oral gavage was conducted according to SOP: DCB-DV-TE00447.



V. EXPERIMENTAL PROCEDURES

- A. Test Article Administration (SOP: DCB-DV-TE00447): Test article solutions at 2.5, 5 and 10 ml/kg or injection grade water (10 ml/kg) were administered twice at two hours apart to 6 rats of each sexes by gavage. A suitable size of disposable plastic syringe with a ball tipped dosing needle of 16 gauge in diameter and 80 mm in length was used for each dosing group. The rats were fasted overnight before and till the end of dosing. The volume administered was adjusted on the basis of individual body weight recorded before dosing. The dosing day was defined as SD1 (Study Day 1). The body weights range on SD1 was 172-191 g for males and 133-147 g for females.
- B. Observation and Examination
1. Animal observations (SOP: DCB-DV-TE00469): The rats were observed for mortality and clinical signs at approximate 1, 2, 3 and 4 hours after the second dosing. During the following days, the animals were observed twice daily (before 10:00 AM and after 3:00 PM, at least six hours apart) on working days and once daily on weekends for 14 days. Any mortality, moribundity and clinical signs were recorded and documented.
 2. Body weight (SOP: DCB-DV-TE00450): Rats were weighed before dosing (SD1), weekly thereafter (SD8) and on the day of necropsy (SD15).
 3. Gross necropsy (SOP: DCB-DV-TE00449): Gross necropsies were performed on all rats that survived at the termination of the study (SD15). The survivors were euthanized by i.p. injection with an overdose of sodium pentobarbital solution (SOP: DCB-DV-TE00424) and necropsied in a randomized order.
- C. Statistical Analysis: Results were expressed as mean \pm standard deviation (SD). Comparisons of all data collected on body weights for each dose and sex were performed using ANOVA and Dunnett's test (SigmaStatTM, V2.03, 1997). $P < 0.05$ is used as the criterion of significance.
- D. Data Retention: All raw data, documentation, records, protocols and final reports generated as a result of this study will be inventoried and archived by the Quality Assurance Unit at archives room at Drug Safety Building of DCB. The retention duration of these records will be in accordance with the relevant regulations.



RESULTS AND DISCUSSION

I. Mortality

A summary of the mortality in rats is presented in Table 1. There was no mortality observed in control and Product Code MicrSoy-20 (MS-20) treated rats during the 14-day study period.

II. Clinical Observations

A summary of clinical observations in rats is presented in Table 1. There was no clinical sign observed in Product Code MicrSoy-20 (MS-20) treated rats and control rats during the 14-day study period.

III. Body Weights

A summary of the mean body weights and mean body weight gains in rats are presented in Table 2. The mean body weight growth curves are shown in Figure 1. Individual animal data are presented in Appendix D. There were no differences in body weights as well as body weight gains observed between Product Code MicrSoy-20 (MS-20) treated and control rats.

IV. Gross Necropsy

A summary of gross observations is presented in Table 1. There was no gross lesion observed in Product Code MicrSoy-20 (MS-20) treated and controls rats at necropsy.

CONCLUSION

There were no mortality and any clinical signs were observed in rats treated with Product Code MicrSoy-20 (MS-20) via oral route at dose levels of 5, 10 and 20 ml/kg, followed by 14 days of observation. There were no differences in body weights as well as body weight gains observed between Product Code MicrSoy-20 (MS-20) treated and control rats. At necropsy, all rats showed no observable gross lesions. In conclusion, Product Code MicrSoy-20 (MS-20) exerted no adverse toxic effects in SD rats at dose levels up to 20 ml/kg, which provided a safety margin of 240 over the recommended human dose basing on a conversion of body weight. The results of this study will be used for dosing selection for repeated toxicity study and served as a reference of safety margin for human use.



COMMENTS AND/OR PROBLEMS

To the best of our knowledge, there were no deviations from the study protocol that would affect the integrity of this study. No problems were encountered during the study that would adversely affect the study results or interpretation.

REFERENCES

1. OECD Guideline for the Testing of Chemicals # 401: Acute Oral Toxicity, 1987.
2. Derelanko, M. J. and Hollinger, M. A. (1995) CRC Handbook of Toxicology. CRC press, USA.
3. Guideline for the Nonclinical Pharmacology/Toxicology Studies for Medicinal Products Application, DOH, ROC, 3rd ed., 2000.



Table 1. Acute Oral Toxicity Study of Product Code MicrSoy-20 (MS-20) in Rats — Mortality (N/N), Clinical Signs and Gross Necropsy Findings

Sex	Dose (ml/kg)	Mortality	Clinical Signs	Gross Necropsy Findings
Male	0 (Control)	0/6	NOA	NOL
	5	0/6	NOA	NOL
	10	0/6	NOA	NOL
	20	0/6	NOA	NOL
Female	0 (Control)	0/6	NOA	NOL
	5	0/6	NOA	NOL
	10	0/6	NOA	NOL
	20	0/6	NOA	NOL

N/N = Number of rats found dead / Number of rats observed

NOA = No observable abnormality

NOL = No observable lesions

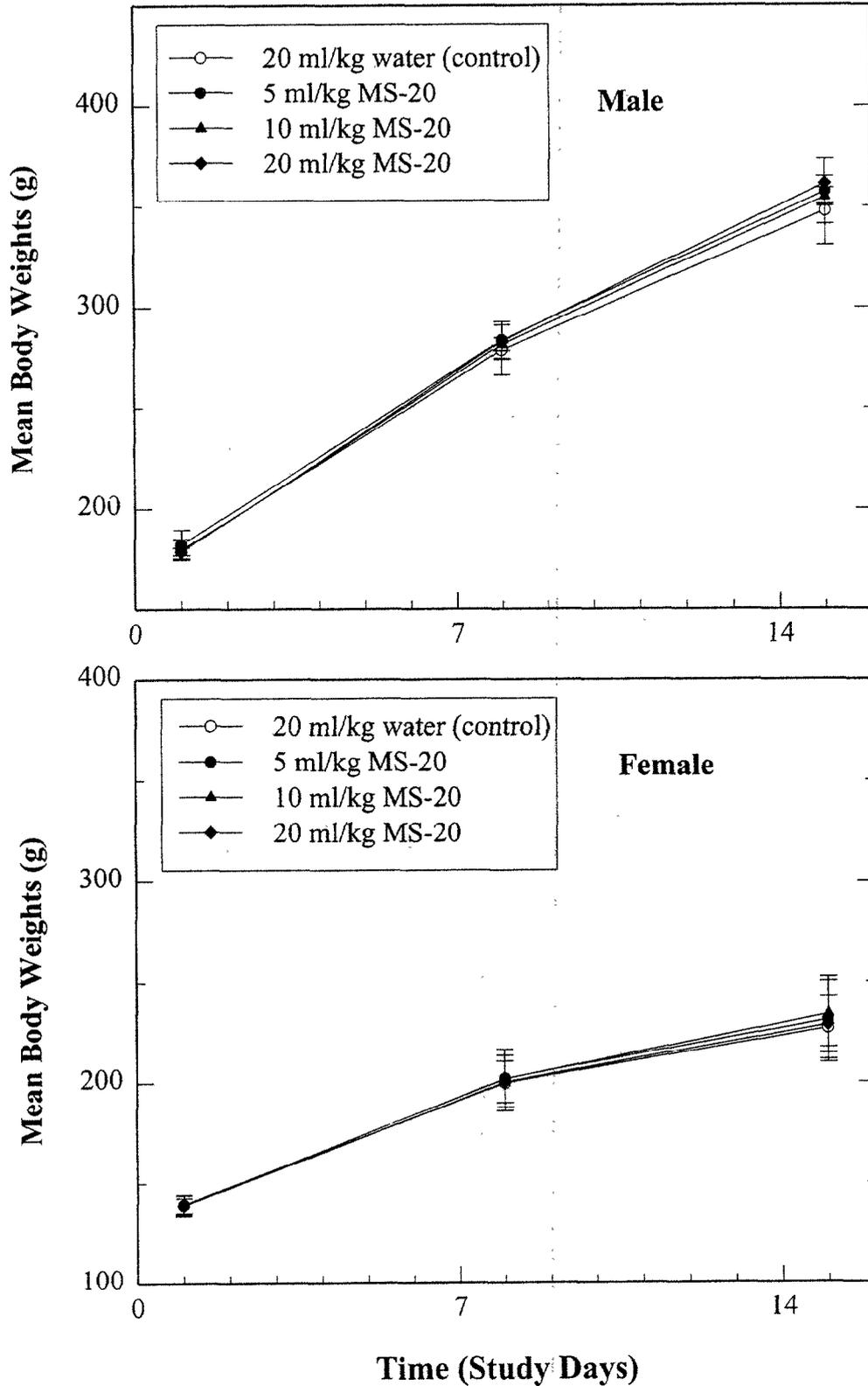
Control: Injection grade water

Table 2. Acute Oral Toxicity Study of Product Code MicrSoy-20 (MS-20) in Rats — Mean Body Weights (Mean ± SD, N=6)

Sex	Dose (ml/kg)	Mean Body Weights (g)			Weight Gains (g)
		Initial (SD1)	SD 8	Final (SD15)	(On SD15)
Male	0 (Control)	179.8±5.2	278.7±12.6	347.7±17.1	167.8±13.9
	5	182.3±7.4	283.7±9.2	357.2±16.2	174.8±17.3
	10	178.8±4.3	281.5±7.8	354.5±11.0	175.7±10.7
	20	178.7±3.3	283.0±9.1	361.3±10.4	182.7±11.8
Female	0 (Control)	139.3±4.8	199.7±13.7	226.8±15.6	87.5±12.3
	5	139.2±5.4	202.0±14.3	231.0±21.3	91.8±18.9
	10	139.7±4.6	201.7±11.7	233.7±16.5	94.0±15.3
	20	139.0±3.7	200.3±10.3	228.5±14.3	89.5±15.7

Control: Injection grade water

Fig 1. Acute Oral Toxicity Study of Product Code MicrSoy-20 (MS-20) in Rats
— Mean Body Weight Growth Curves



Appendix A (附件一)

Test Article Information Sheet

試驗物質資料表

S
A
T
I
(



Test Article Information Sheet

DV00199

DV-QA00033E

Sponsor : MICROBIO Co., Ltd.Address : No.81 Gaiyang N. Rd., Lung tan Shiang, Tao Yuan, TaiwanTelephone : 886-3-4710888 Fax : 886-3-4710288Delivery Date : 10 / 05 / 2001 (MM/DD/YY)Category : Health Food Herb Medicine Drugs Cleanser Medical Devices
 Cosmetics Pesticides Others : _____1. Sample Name : Product code MicrSoy-20(MS-20)

2. a. Ingredients :

MS-20 is a Chinese medicine. The components are very complicated. Until now, its effective components are still unable to determine.

b. Purity : _____

3. Batch / Lot No. : 20010209

4. Physical Appearance :

a. Powder Liquid Others : _____b. Odor : No Yes : Prune Juicec. Color : Dark-brown5. How Supplied (Amount / Pack) : 180 ml/Bottle6. Amount Supplied : 22 Bottle



Test Article Information Sheet

DV00199

2/2

7. Solubility (Approx. ___ g/L)
H2O Souble, DMSO, Other Solvents

8. Storage

a. Storage Temperature: [X] Room Temperature [] Refrigeration [] Frozen

b. Other Environment Condition: [] Desiccation [X] Protect from Light

[] Others:

c. Expiration Date: 02/ 09/ 2004 (MM / DD / YY)

9. Treatment of Residual Samples

[X] Retrieved by the Sponsor

[] Managed by DCB with Extra Fees

[] Disposed by DCB with Waste Disposal Method Provided:

10. Handling Precautions and Others

Directions: To drink 1~5c.c. daily by dilution with 100c.c. water before breakfast. It's not suggested to drink water in 10 minutes after MS-20. After 10 minutes later, we suggest you to drink water as usual. Before dilution, the product can be stored at room temperature after opening, but please use the product immediately after dilution.

Undiluted product has a high acidity of pH around 3.8

MS-20 has two packages which are 180ml/Bottle and 30ml/Bottle

Product Chemist:

Jason Liu

10/5/2004 (Signature) (MM/DD/YY)

Sponsor Representative:

William Liu

10/5/2004 (Signature) (MM/DD/YY)

Appendix B (附件二)

Protocol (DV-PR-AC00139E)

試驗計畫書

Study Schedule

試驗進度表

fast.

0.1,

Protocol (DV-PR-AC00139E)

試驗計畫書



財團法人生物技術開發中心
DEVELOPMENT CENTER FOR BIOTECHNOLOGY

SERIAL NO:	DV-PR-AC00139E
PROJECT CODE:	DV-TA00199
PAGE	1 OF 7

ACUTE ORAL TOXICITY STUDY IN SD RATS PRODUCT CODE MICRSOY-20 (MS-20)

PROTOCOL

DEVELOPMENT CENTER FOR BIOTECHNOLOGY
DRUG DEVELOPMENT DIVISION



Signature Page

Study Director:

Jiuan Judy Liu Oct 19, 2001
Jiuan Judy Liu, PhD, DVM

Investigators:

Di-Sheng Wang, MS

Tan-Fu Yuen, MS

Yu-Mai Chen, MS

Quality Assurance Officer:

Wen-Jing Chen Oct. 19, 2001
Wen-Jing Chen, MS

Facility Manager:

Jiuan Judy Liu Oct 19, 2001
Jiuan Judy Liu, PhD, DVM

Sponsor's Representative:

Jaceta Wu for William Lu Oct. 11, 2001
William Lu



ACUTE ORAL TOXICITY STUDY IN SD RATS PRODUCT CODE MICRISOY-20 (MS-20)

I. PURPOSE

The purpose of this study is to evaluate the acute oral toxicity of "Product Code MicrSoy-20 (MS-20)" and to determine the 14-day median lethal dose (LD₅₀) of the test article. The information will permit the determination of a suitable dose range for the subsequent subacute oral toxicity study. This study will be conducted with inspections for compliance with Good Laboratory Practice (GLP).

II. TESTING FACILITY

- A. Name: General / Reproductive Toxicology Laboratory, Drug Development Division, Development Center for Biotechnology
- B. Address: 103, Lane 169, Kang-Ning St., Hsi-Chih City, Taipei County, 221, Taiwan, R.O.C.

III. SPONSOR

- A. Name: MICROBIO Co., Ltd.
- B. Address: No. 81, Gauyang N. Rd., Lung Tan Shiang, Tao Yuan, Taiwan, R.O.C.
- C. Representative: William Lu

IV. TEST ARTICLE (To be supplied by the sponsor prior to study initiation)

- A. Name: Product Code MicrSoy-20 (MS-20)
- B. Received Date: Oct. 5, 2001
- C. Batch/Lot Number: 20010209
- D. DCB Code: DV00199
- E. Ingredients: MS-20 is a Chinese medicine. The components are very complicated. Until now, its effective components are still unable to determine.
- F. Other Characteristics: Dark brown liquid with prune juice odor
- G. Solubility: Water-soluble
- H. Amount Supplied: 22 bottles (180 ml/bottle)
- I. Storage Conditions: Room temperature and protect from light



- J. Expiration Date: Feb. 9, 2004
- K. Vehicle Control: Injection grade water

Statement:

The test article is a proprietary product of the sponsor, therefore the sponsor will be responsible for the requirements listed under "Test Article" of the GLP regulation (21CFR §58.105, FDA).

V. STUDY SCHEDULE

- A. Proposed Animal Dosing Date: Oct. 12, 2001
- B. Proposed Gross Necropsy Date: Oct. 26, 2001

VI. TEST SYSTEM

- A. Species: Rats
- B. Strain: Crl:CD(SD)fSPF
- C. Source: National Laboratory Animal Breeding & Research Center, National Science Council, Taipei, Taiwan
- D. Age at Initiation of Study: Approximately 6 weeks old
- E. Method of Identification: Rats will be identified by ear notch (SOP: DCB-DV-TE00446) and cage tags.
- F. Number on Study: Six males and Six females per control and dose group; 24 males and 24 females in total.
- G. Justification for Selection: The Sprague-Dawley (SD) rat is chosen as rodent species since it is widely accepted by Health Authorities as an appropriate experimental model, with documented susceptibility to a wide range of toxic substances.
- H. IACUC Approved Protocol Number: 2001-TP-010-a

VII. EXPERIMENTAL DESIGN

- A. Test Animals
 - 1. Quarantine and acclimatization

The rats will be housed in an AAALAC accredited animal facility with a controlled environment of $21 \pm 2^\circ\text{C}$ and $50 \pm 20\%$ relative humidity, in a 12-hr/12-hr light/dark cycle with light on at 6:00 AM and off at 6:00 PM (SOP:

DCB-DV-AC00023). The rats will be housed two per cage in stainless steel wire mesh cages. They will be quarantined (SOP: DCB-DV-AC00032) and acclimated for at least 6 days prior to use. The unsuitable rats will be excluded from this study.

2. Diet and water supply

Laboratory Autoclavable Rodent Diet 5010 (PMI® Feeds Inc., St. Louis, MO) and tap water will be supplied *ad libitum* throughout the study (SOPs: DCB-DV-AC00025, DCB-DV-AC00026).

3. Randomization (SOP: DCB-DV-TE00462)

Computerized LIMS system (Computer Service Center, DCB) will be used for randomization and dose groups assignment. The rats will be divided into weight classes, then randomly assigned into each group (six males and six females per group). The weight variation of the animals to be used should not exceed $\pm 20\%$ of the mean body weight.

B. Experimental Design

1. Dose levels

Group no., dose levels, dosing solutions, dosing volumes and animal no. in this acute oral toxicity study are presented as below:

Group No.	Dose Levels (ml/kg)	Dosing Solutions	Dosing volumes (ml/kg)	Animal No. M/F
1	0	injection grade water	10 × 2	6M, 6F
2	5	MS-20	2.5 × 2	6M, 6F
3	10	MS-20	5 × 2	6M, 6F
4	20	MS-20	10 × 2	6M, 6F

2. Rationales for dose levels selection:

- a. The recommended daily human dose is 1-5 ml; for a 60-kg subject, therefore, the maximal recommended daily dose estimated is 0.083 ml/kg approximately.
- b. To achieve a bigger dose volume, the rats will be dosed twice in this study.
- c. The dose levels (5, 10 and 20 ml/kg) of test article selected in this study will provide a safety margin of 60, 120 and 240 over the recommended human



dose, basing on the conversion of body weights. A corresponding safety margin of 9.4, 18.8 and 37.6 will also be provided, respectively, basing on a conversion of surface area.

3. Test article administration (SOP: DCB-DV-TE00447)

Test article solution (MS-20) at respective volumes of 2.5, 5 and 10 ml/kg or injection grade water (10 ml/kg) will be administered to 6 rats each sex twice (at two hours apart) by gavage. A suitable size of disposable plastic syringe with a ball tipped dosing needle of 16 gauge in diameter and 80 mm in length will be used for each dosing group. The rats will be fasted overnight till the end of dosing. The volume administered (2.5, 5, 10 ml/kg) will be adjusted on the basis of individual body weight recorded before dosing. The rats can be replaced if death occurred within 1-2 hours after dosing and is confirmed by gross necropsy as a gavage accident. The dosing day is defined as SD1 (Study Day 1).

4. Reason for selection of route

The oral route is the route expected to be used in human.

VIII. OBSERVATION AND EXAMINATION

A. Observations of Animals (SOP: DCB-DV-TE00469)

The rats will be observed for mortality and clinical signs at approximate 1, 2, 3 and 4 hours after the second dosing. During the following days, the animals will be observed twice daily (before 10:00 AM and after 3:00 PM, at least six hours apart) on working days and once daily on weekends for 14 days. Any mortality, moribundity and clinical signs will be recorded and documented.

B. Body Weight (SOP: DCB-DV-TE00450)

Body weight will be recorded on all animals prior to the start of dosing (SD1) and then at weekly interval (SD8) up to the end of the study period (SD15).

C. Gross Necropsy (SOP: DCB-DV-TE00449)

Gross necropsies will be performed on found dead, moribund sacrificed animals and on all surviving rats at the end of study (SD15). The surviving rats will be euthanized by i.p. injection of overdosed sodium pentobarbital solution (SOP: DCB-DV-TE00424) and necropsied in a randomized order.



IX. STATISTICAL ANALYSIS

Results will be expressed as mean and standard deviation ($M \pm SD$). Comparisons of all data collected on body weights for each dose and sex will be performed using ANOVA and Dunnett's test (SigmaStat™, V2.03, 1997). $P < 0.05$ will be used as the criterion of significance. Should mortality occur, the median lethal dose (LD_{50}) values with 95% confidence intervals (95% CI) will be graphically interpolated, using the log/probit regression method (Minitab Release 10, 1994).

X. RECORDS RETENTION

All raw data, documentation, records, protocols and final reports generated as a result of this study will be inventoried and archived by the Quality Assurance Unit at DCB's archives located in Drug Safety Building. Those records will be retained in accordance with the periods regulated in the relevant regulations.

XI. REGULATORY REQUIREMENTS

This study will be performed in compliance with (1) Good Laboratory Practice for Nonclinical Laboratory Studies (21 CFR 58), FDA, U.S.A., 1987; (2) Good Laboratory Practice for Nonclinical Laboratory Studies, Department of Health, R.O.C., 3rd ed., 2000; (3) General Requirements for the Competence of Calibration and Testing Laboratories (ISO/IEC Guide 25), ISO/IEC, 3rd ed., 1990; (4) Specific Criteria for Biological Testing, Chinese National Laboratories Accreditation, R.O.C., 2nd ed., 2000.

XII. REFERENCES

1. OECD Guideline for the Testing of Chemicals # 401: Acute Oral Toxicity, 1987.
2. Derelanko, M. J. and Hollinger, M. A. (1995) CRC Handbook of Toxicology. CRC press, USA.
3. Guideline for the Nonclinical Pharmacology/Toxicology Studies for Medicinal Products Application, DOH, ROC, 3rd ed., 2000.

Study Schedule

試驗進度表

試驗進度表 Study Schedule

DV-OA00045A

Laboratory: General/Reproductive Toxicology Test Article No.: DV00199

Study No.: AC00139(E) Project Code: DV-TA00199

Study Director: Juan July Liu Oct 9 / 2001 QA Officer: Jim-Jin Chen Oct 9 / 2001

Page 1 of 1

DATE	WK	PROGRESS	QAU INSP.	REMARK
Oct. 11, 2001	Thu	Body weight recording Pre-study clinical observation Animal randomization and groupings Fasting overnight before dosing		
Oct. 12, 2001	Fri	Body weight recording (SD1) Test article administration via gavage Clinical observation	<i>Jim-Min Liu</i> <i>Oct. 12, 2001</i>	
Oct. 13, 2001	Sat	Clinical observation		
Oct. 14, 2001	Sun	Clinical observation		
Oct. 15, 2001	Mon	Clinical observation		
Oct. 16, 2001	Tue	Clinical observation		
Oct. 17, 2001	Wed	Clinical observation		
Oct. 18, 2001	Thu	Clinical observation		
Oct. 19, 2001	Fri	Body weight recording (SD8) Clinical observation		
Oct. 20, 2001	Sat	Clinical observation		
Oct. 21, 2001	Sun	Clinical observation		
Oct. 22, 2001	Mon	Clinical observation		
Oct. 23, 2001	Tue	Clinical observation		
Oct. 24, 2001	Wed	Clinical observation		
Oct. 25, 2001	Thu	Clinical observation		
Oct. 26, 2001	Fri	Clinical observation Body weight recording Study termination (SD15) Necropsy/gross observations	<i>Jim-Min Liu</i> <i>Oct. 26, 2001</i>	

Appendix C (附件三)

- Records of Animal Room Temperature during Study Period
動物飼育室溫度紀錄統計表
- Records of Animal Room Relative Humidity during Study Period
動物飼育室相對溼度紀錄統計表
- Record of Animal Diet
動物飼料紀錄
- Analysis Records of Animal Drinking Water
水質分析報表
- Analysis Records of Animal Diet
動物飼料分析報表
- Laboratory Animal Quarantine Report
試驗動物檢疫報告

Records of Animal Room Temperature during Study Period
動物飼育室溫度紀錄統計表

Vertical text on the left edge of the page, possibly a page number or header, appearing as a series of characters.



動物飼育室溫度紀錄統計表
Records of Animal Room Temperature during Study Period

飼育室編號
 Animal Room No.: C 414

試驗期間
 Study Period: Oct. 12 ~ Oct. 26, 200

日期 Date	溫度 (Temperature, °C)		
	平均值±標準差 Mean ± SD	當日最高 Maximum	當日最低 Minimum
10/12/2001	20.8 ± 0.2	21.0	20.5
10/13/2001	20.9 ± 0.2	21.1	20.5
10/14/2001	20.8 ± 0.2	21.0	20.5
10/15/2001	20.9 ± 0.2	21.1	20.5
10/16/2001	20.7 ± 0.2	21.0	20.5
10/17/2001	20.8 ± 0.2	21.1	20.5
10/18/2001	20.9 ± 0.2	21.1	20.5
10/19/2001	20.8 ± 0.2	21.0	20.5
10/20/2001	20.8 ± 0.2	21.0	20.5
10/21/2001	20.8 ± 0.2	21.0	20.5
10/22/2001	20.7 ± 0.2	21.0	20.5
10/23/2001	20.8 ± 0.2	21.0	20.5
10/24/2001	20.8 ± 0.2	21.0	20.4
10/25/2001	20.9 ± 0.2	21.1	20.6
10/26/2001	20.8 ± 0.2	21.1	20.4

Records of Animal Room Relative Humidity during Study Period

動物飼育室相對溼度紀錄統計表

動物飼育室相對溼度紀錄統計表
Records of Animal Room Relative Humidity during Study Period

飼育室編號
Animal Room No.: C 414

試驗期間
Study Period: Oct. 12~Oct. 26, 2001

日期 Date	溼度 (Relative Humidity ; %)		
	平均值±標準差 Mean ± SD	當日最高 Maximum	當日最低 Minimum
10/12/2001	56.3 ± 2.5	61.7	52.7
10/13/2001	55.3 ± 3.1	61.5	49.6
10/14/2001	55.8 ± 2.5	60.6	52.0
10/15/2001	55.1 ± 2.9	60.5	51.5
10/16/2001	56.9 ± 2.8	61.3	52.8
10/17/2001	55.7 ± 2.9	60.9	51.7
10/18/2001	54.7 ± 2.0	59.7	52.5
10/19/2001	55.6 ± 2.4	60.9	52.0
10/20/2001	56.0 ± 2.1	59.4	52.5
10/21/2001	59.3 ± 4.2	64.2	54.0
10/22/2001	58.5 ± 3.1	64.9	50.2
10/23/2001	56.2 ± 2.8	60.5	52.1
10/24/2001	56.6 ± 3.3	65.2	52.4
10/25/2001	55.5 ± 5.0	66.8	47.2
10/26/2001	56.4 ± 7.2	88.0*	51.2

* : The relative humidity of the animal room was above the normal range temporarily due to the malfunction of the cooling tower, however the daily average was in normal range.



Record of Animal Diet

動物飼料紀錄

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
61
62
63
64
65
66
67
68
69
70
71
72
73
74
75
76
77
78
79
80
81
82
83
84
85
86
87
88
89
90
91
92
93
94
95
96
97
98
99
100

Record of Animal Diet

1. Experiment Date : From Oct. 12, 2001 to Oct. 26, 2001.
2. Room Number : Room 414.
3. Animal Feed Production Company : PMI. Feeds , Inc.
 - a. Product Name : Laboratory Autoclavable Rodent Diet 5010
 - b. Production Date : Aug. 9, 2001/Aug. 16, 2001
 - c. Bag Serials Number :
Aug. 9 , 2001: 0386, 0394.
Aug.16, 2001: 0341, 0345, 0361, 0490.

Prepared by:Wen-Bing Liu Oct. 19, 2001

Analysis Records of Animal Drinking Water

水質分析報表

C-16

各淨水場清水平均水質

資料來源：臺北自來水事業處水質中心

時間：90年1至10月

※註：ND表示低於偵測極限

0.02mg/L；錳0.008mg/L；鉛：0.00088mg/L；三鹵甲烷包括(三氯甲烷=0.00012mg/L；一溴二氯甲烷=0.00007mg/L；二溴一氯甲烷=0.00008mg/L；三溴甲烷=0.00005mg/L)

檢驗項目	水質標準	單位\場別	直潭淨水場	長興*淨水場	公館淨水場	雙溪淨水場			陽明	
						雙溪水 源	士林水 源	三角埔	頂北投 取水口	大屯水 源
水溫	---	°c	22.2	21.6	21.9	22.2	20	24	21.9	19.1
濁度	<2	NTU	0.19	0.18	0.23	0.13	0.61	0.18	0.34	0.3
色度	<5	UNIT	1	1	1	1	1	1	1	---
總鹼度	---	mg/L	20	21	19	25	64	57	31	---
pH值	6.0-8.5	---	7	7	7	7.1	6.7	6.9	7.5	7.5
氯鹽	<250	mg/L	6.15	6.31	6.23	10.65	14.32	31.07	15.08	---
硫酸鹽	<250	mg/L	8.4	9.24	8.87	16.48	17.05	51.75	29.54	---
氨氮	<0.1	mg/L	ND	ND	ND	ND	ND	ND	ND	ND
硝酸亞氮	<0.1	mg/L	ND	ND	ND	ND	ND	ND	ND	---
硝酸氮	<10	mg/L	0.58	0.6	0.58	0.72	3.43	1.14	0.9	---
溶解固形物	<6(X)	mg/L	52	58	59	89	159	242	166	144
氟鹽	<0.8	mg/L	0.07	0.07	0.07	0.07	0.07	0.11	0.08	---
游離氯	0.2-1.0	mg/L	0.59	0.57	0.56	0.58	0.5	0.41	0.56	0.62
總硬度	<400	mg/L	27.6	29.4	29.5	43.7	81.8	125.1	96.3	---
鈣	---	mg/L	6.7	7.4	7.9	10.8	20.4	34.4	26.5	---
鎂	---	mg/L	2.7	2.8	2.4	5	7.7	9.8	7.6	---
鐵	<0.3	mg/L	0.08	ND	ND	ND	ND	ND	ND	---
錳	<0.05	mg/L	ND	ND	ND	ND	ND	ND	ND	---
總菌落數	<100	CFU/mL	<1	8	<1	<1	<1	<1	7	<1
大腸桿菌群	<6	CFU/100mL	<1	<1	<1	<1	<1	<1	<1	<1
總有機碳	---	mg/L	0.37	0.36	0.38	0.56	0.33	0.27	0.51	0.32
三鹵甲烷	<0.1	mg/L	0.0041	0.0055	0.0052	0.0137	ND	0.0002	0.0048	---
鉛	<0.05	mg/L	ND	ND	ND	ND	ND	ND	ND	---
鋁	---	mg/L	0.342	0.07	0.049	0.063	0.085	0.021	0.132	---

*：為本實驗室用水採樣標準

Analysis Records of Animal Diet

動物飼料分析報表



Lab Diet

The Guarantee of Consistency

PMI Feeds, Inc. guarantees that Lab Diets are the same diets and formulation that you may currently be using in your study. In fact, in order for you to maintain total dietary control of your experiment for now and in the future, Lab Diets, the Richmond standard, are the only diets you should use.

We, the undersign, guarantee that Lab Diets conform in every manner to your current Laboratory feed.

Damon C. Shelton, Ph.D.
Lab Animal Diet Consultant

Daniel T. Hopkins, Ph.D.
Director, Technical Services

William C. Sadler, Ph.D.
General Manager,
Specialty Businesses



Laboratory Autoclavable Rodent Diet

5010

Chemical Composition¹

Nutrients²

Protein %.....	23.5
Arginine %.....	1.40
Cystine %.....	0.34
Glycine %.....	1.20
Histidine %.....	0.58
Isoleucine %.....	1.24
Leucine %.....	1.87
Lysine %.....	1.42
Methionine %.....	0.49
Phenylalanine %.....	1.08
Tyrosine %.....	0.64
Threonine %.....	0.94
Tryptophan %.....	0.29
Valine %.....	1.22
Serine %.....	1.23
Aspartic Acid %.....	2.68
Glutamic Acid %.....	5.02
Alanine %.....	1.49
Proline %.....	1.73
Taurine %.....	0.03
Fat (ether extract) %.....	5.1
Fat (acid hydrolysis) %.....	6.2
Cholesterol, ppm.....	275
Unsaturated Acid %.....	1.82
Unsaturated Acid %.....	0.12
Arachidonic Acid %.....	<0.01
Omega-3 Fatty Acids %.....	0.42
Total Saturated Fatty Acids %.....	1.40
Total Monounsaturated Fatty Acids %.....	1.52
Fiber (Crude) %.....	3.9
Neutral Detergent Fiber % ³	12.7
Acid Detergent Fiber % ³	4.5
Nitrogen-Free Extract (by difference) % ...	50.3
Starch %.....	36.2
Glucose %.....	0.26
Fructose %.....	0.30
Sucrose %.....	1.02
Lactose %.....	0
Total Digestible Nutrients %.....	76.0
Gross Energy, kcal/gm.....	4.06
Physiological Fuel Value ⁴ , kcal/gm.....	3.41
Metabolizable Energy, kcal/gm.....	3.17

Minerals

Ash %.....	7.2
Calcium %.....	1.00
Phosphorus (total) %.....	0.67
Phosphorus (non-phytate) %.....	0.43
Potassium %.....	0.92
Magnesium %.....	0.22
Sulfur %.....	0.24
Sodium %.....	0.28
Chlorine %.....	0.39
Fluorine, ppm.....	35.0
Iron, ppm.....	181.0
Zinc, ppm.....	124.3
Manganese, ppm.....	115.0
Copper, ppm.....	19.6
Cobalt, ppm.....	0.41
Iodine, ppm.....	1.19
Chromium, ppm.....	1.95
Selenium, ppm.....	0.32

Vitamins

Carotene, ppm.....	4.5
Vitamin K (total), ppm.....	3.4
Menadione (added), ppm.....	2.9
Thiamin, ppm.....	80.7
Riboflavin, ppm.....	8.0
Niacin (available), ppm.....	100.0
Niacin (total), ppm.....	128.1
Pantothenic Acid, ppm.....	25.4
Choline, ppm.....	2200
Folic Acid, ppm.....	6.0
Pyridoxine, ppm.....	16.5
Biotin, ppm.....	0.35
B ₁₂ , mcg/kg.....	33.0
Vitamin A, IU/gm.....	44.1
Vitamin D ₃ (added), IU/gm.....	4.4
Vitamin E, IU/kg.....	66.1
Ascorbic Acid, mg/gm.....	—

¹ Product Code

² Based on the latest ingredient analysis information. Since nutrient composition of natural ingredients varies, analysis will differ accordingly.

³ Nutrients expressed as percent of ration except where otherwise indicated. Moisture content is assumed to be 10.0% for the purpose of calculations.

⁴ NDF = approximately cellulose, hemicellulose and lignin.

⁵ ADF = approximately cellulose and lignin.

⁶ Physiological Fuel Value (kcal/gm) = Sum of decimal fractions of protein, fat and carbohydrate (use Nitrogen Free Extract) x 4.34 kcal/gm respectively.

Laboratory Animal Quarantine Report

試驗動物檢疫報告

實驗動物檢疫報告
Laboratory Animal Quarantine Report

DV-AC00032B

動物來源 (Animal Source): 研所初級中區 (NLABRC)

P.I.: Dr. Juan Tudy Liu

IACUC Protocol No.: _____ Project Code: _____ Study No.: _____

接收日期 Received Date	品種/品系 Species/Strain	性別/數量 No./Sex	檢疫期 Quarantine Period*	通過日期 Release Date**
Oct. 3, 2001	Rat / SD	♂ / 1	Oct 2 - Oct. 9, 2001	Oct. 9, 2001
"	"	♂ / 1	"	"

備註 (Remarks): 研所 10/025

*: 檢疫項目及結果皆存放於動物房檔案室。

The documents and results of the quarantine are kept at the archive of the Laboratory Animal resource Division (LARD).

** : 通過檢疫後，才轉移到飼育室。

The animals are moved to the designated animal rooms after passing the quarantine procedures.

Juan Tudy Liu

Attending Veterinarian

Oct. 9, 2001

Date

Appendix D (附件四)

Individual Animal Data on Body Weights

個別試驗動物體重數據

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
61
62
63
64
65
66
67
68
69
70
71
72
73
74
75
76
77
78
79
80
81
82
83
84
85
86
87
88
89
90
91
92
93
94
95
96
97
98
99
100



Individual Animal Data on Body Weights

個別試驗動物體重數據

Acute Oral Toxicity Study in SD Rats - Product Code MicrSoy-20 (MS-20)

大鼠口服急性毒性測試-代號 MicrSoy-20 (MS-20)

Individual Animal Data of Body Weights

個別試驗動物體重數據

Project Code: DV-TA00199 Study No.: AC00139

Species/Strain: Rats/SD Sex: Male

組別	動物編號	劑量 (Dose)	Body Weight (g)		
Group	Animal ID	ml/kg	SD 1	SD 8	SD 15
1	1010251054	0	175	270	337
	1010251056	0	181	267	328
	1010251052	0	177	278	343
	1010251060	0	176	269	341
	1010251073	0	181	291	365
	1010251075	0	189	297	372
	N		6	6	6
	Mean		179.8	278.7	347.7
	SD		5.2	12.6	17.1
	SEM		2.1	5.1	7.0
2	1010251064	5	179	281	360
	1010251080	5	172	269	339
	1010251074	5	178	288	364
	1010251078	5	184	296	383
	1010251059	5	190	288	356
	1010251068	5	191	280	341
	N		6	6	6
	Mean		182.3	283.7	357.2
	SD		7.4	9.2	16.2
	SEM		3.0	3.8	6.6
3	1010251051	10	176	269	336
	1010251062	10	173	277	351
	1010251053	10	185	280	352
	1010251066	10	177	289	367
	1010251067	10	181	285	358
	1010251076	10	181	289	363
	N		6	6	6
	Mean		178.8	281.5	354.5
	SD		4.3	7.8	11.0
	SEM		1.8	3.2	4.5

Prepared by: Yu-Mai Ok Nov 7, 2001

Checked by: Di-Sheng Wang Nov-19, 2001

Acute Oral Toxicity Study in SD Rats - Product Code MicrSoy-20 (MS-20)

大鼠口服急性毒性測試-代號 MicrSoy-20 (MS-20)

Individual Animal Data of Body Weights

個別試驗動物體重數據

Project Code: DV-TA00199 Study No.: AC00139

Species/Strain: Rats/SD Sex: Male

組別	動物編號	劑量 (Dose)	Body Weight (g)		
Group	Animal ID	ml/kg	SD 1	SD 8	SD 15
4	1010251063	20	175	287	372
	1010251065	20	177	287	362
	1010251061	20	176	282	367
	1010251079	20	180	271	345
	1010251069	20	184	296	369
	1010251070	20	180	275	353
	N		6	6	6
	Mean		178.7	283.0	361.3
	SD		3.3	9.1	10.4
	SEM		1.4	3.7	4.2

Prepared by: Yu-Mai Chen Nov. 7, 2001

Checked by: Di-Sheng Wang Nov. 19, 2001

Acute Oral Toxicity Study in SD Rats - Product Code MicrSoy-20 (MS-20)

大鼠口服急性毒性測試 - 代號 MicrSoy-20 (MS-20)

Individual Animal Data of Body Weights

個別試驗動物體重數據

Project Code: DV-TA00199 Study No.: AC00139

Species/Strain: Rats/SD Sex: Female

組別	動物編號	劑量 (Dose)	Body Weight (g)		
Group	Animal ID	ml/kg	SD 1	SD 8	SD 15
1	1010250061	0	135	187	205
	1010250071	0	133	184	215
	1010250056	0	141	193	220
	1010250060	0	139	215	239
	1010250052	0	142	204	241
	1010250054	0	146	215	241
	N			6	6
	Mean		139.3	199.7	226.8
	SD		4.8	13.7	15.6
	SEM		1.9	5.6	6.4
2	1010250051	5	133	185	207
	1010250065	5	135	194	233
	1010250068	5	136	191	213
	1010250070	5	141	223	267
	1010250062	5	143	210	228
	1010250067	5	147	209	238
	N			6	6
	Mean		139.2	202.0	231.0
	SD		5.4	14.3	21.3
	SEM		2.2	5.9	8.7
3	1010250057	10	138	193	222
	1010250069	10	134	193	232
	1010250073	10	136	200	229
	1010250077	10	140	196	232
	1010250072	10	145	204	221
	1010250074	10	145	224	266
	N			6	6
	Mean		139.7	201.7	233.7
	SD		4.6	11.7	16.5
	SEM		1.9	4.8	6.8

Prepared by: Yi-Mei Chen, Nov. 7, 2001

Checked by: Di-Sheng Wang, Nov 19, 2001

Acute Oral Toxicity Study in SD Rats - Product Code MicrSoy-20 (MS-20)

大鼠口服急性毒性測試 - 代號 MicrSoy-20 (MS-20)

Individual Animal Data of Body Weights

個別試驗動物體重數據

Project Code: DV-TA00199 Study No.: AC00139

Species/Strain: Rats/SD Sex: Female

組別	動物編號	劑量 (Dose)	Body Weight (g)		
Group	Animal ID	ml/kg	SD 1	SD 8	SD 15
4	1010250058	20	138	186	222
	1010250059	20	137	202	240
	1010250063	20	135	203	243
	1010250076	20	137	194	222
	1010250055	20	145	217	238
	1010250066	20	142	200	206
	N		6	6	6
	Mean		139.0	200.3	228.5
	SD		3.7	10.3	14.3
	SEM		1.5	4.2	5.8

Prepared by: Ju-Mei Chen Nov. 7, 2001

Checked by: Di-Sheng Wang Nov. 19, 2001

Acute Oral Toxicity Study in SD Rats - Product Code MicrSoy-20 (MS-20)

大鼠口服急性毒性測試 - 代號 MicrSoy-20 (MS-20)

Individual Animal Data of Body Weight Gains

個別試驗動物體重變化數據

Project Code: DV-TA00199 Study No.: AC00139

Species/Strain: Rats/SD Sex: Male

組別	動物編號	劑量 (Dose)	Body Weight (g)		
Group	Animal ID	ml/kg	SD 1	SD (8-1)	SD (15 -1)
1	1010251054	0	175	95	162
	1010251056	0	181	86	147
	1010251052	0	177	101	166
	1010251060	0	176	93	165
	1010251073	0	181	110	184
	1010251075	0	189	108	183
	N			6	6
	Mean		179.8	98.8	167.8
	SD		5.2	9.2	13.9
	SEM		2.1	3.8	5.7
2	1010251064	5	179	102	181
	1010251080	5	172	97	167
	1010251074	5	178	110	186
	1010251078	5	184	112	199
	1010251059	5	190	98	166
	1010251068	5	191	89	150
	N			6	6
	Mean		182.3	101.3	174.8
	SD		7.4	8.6	17.3
	SEM		3.0	3.5	7.1
3	1010251051	10	176	93	160
	1010251062	10	173	104	178
	1010251053	10	185	95	167
	1010251066	10	177	112	190
	1010251067	10	181	104	177
	1010251076	10	181	108	182
	N			6	6
	Mean		178.8	102.7	175.7
	SD		4.3	7.4	10.7
	SEM		1.8	3.0	4.4

Prepared by: Ju-Mai Che Nov 7, 2001

Checked by: Di-Sheng Wang Nov. 19, 2001

Acute Oral Toxicity Study in SD Rats - Product Code MicrSoy-20 (MS-20)

大鼠口服急性毒性測試 - 代號 MicrSoy-20 (MS-20)

Individual Animal Data of Body Weight Gains

個別試驗動物體重變化數據

Project Code: DV-TA00199 Study No.: AC00139

Species/Strain: Rats/SD Sex: Male

組別	動物編號	劑量 (Dose)	Body Weight (g)		
Group	Animal ID	ml/kg	SD 1	SD (8-1)	SD (15 -1)
4	1010251063	20	175	112	197
	1010251065	20	177	110	185
	1010251061	20	176	106	191
	1010251079	20	180	91	165
	1010251069	20	184	112	185
	1010251070	20	180	95	173
	N		6	6	6
	Mean		178.7	104.3	182.7
	SD		3.3	9.1	11.8
	SEM		1.3	3.7	4.8

Prepared by: Ji-Lin Chen Nov 7, 2001

Checked by: Di-Sheng Wang Nov. 19, 2001

Acute Oral Toxicity Study in SD Rats - Product Code MicrSoy-20 (MS-20)

大鼠口服急性毒性測試 - 代號 MicrSoy-20 (MS-20)

Individual Animal Data of Body Weight Gains

個別試驗動物體重變化數據

Project Code: DV-TA00199 Study No.: AC00139

Species/Strain: Rats/SD Sex: Female

組別	動物編號	劑量 (Dose)	Body Weight (g)		
Group	Animal ID	ml/kg	SD 1	SD (8-1)	SD (15-1)
1	1010250061	0	135	52	70
	1010250071	0	133	51	82
	1010250056	0	141	52	79
	1010250060	0	139	76	100
	1010250052	0	142	62	99
	1010250054	0	146	69	95
	N			6	6
	Mean		139.3	60.3	87.5
	SD		4.8	10.5	12.3
	SEM		1.9	4.3	5.0
2	1010250051	5	133	52	74
	1010250065	5	135	59	98
	1010250068	5	136	55	77
	1010250070	5	141	82	126
	1010250062	5	143	67	85
	1010250067	5	147	62	91
	N			6	6
	Mean		139.2	62.8	91.8
	SD		5.4	10.8	18.9
	SEM		2.2	4.4	7.7
3	1010250057	10	138	55	84
	1010250069	10	134	59	98
	1010250073	10	136	64	93
	1010250077	10	140	56	92
	1010250072	10	145	59	76
	1010250074	10	145	79	121
	N			6	6
	Mean		139.7	62.0	94.0
	SD		4.6	8.9	15.3
	SEM		1.9	3.6	6.3

Prepared by: Ju-Mai Chen Nov. 7, 2001

Checked by: Di-Sheng Wang Nov. 19, 2001

Acute Oral Toxicity Study in SD Rats - Product Code MicrSoy-20 (MS-20)

大鼠口服急性毒性測試 - 代號 MicrSoy-20 (MS-20)

Individual Animal Data of Body Weight Gains

個別試驗動物體重變化數據

Project Code: DV-TA00199 Study No.: AC00139

Species/Strain: Rats/SD Sex: Female

組別	動物編號	劑量 (Dose)	Body Weight (g)		
Group	Animal ID	ml/kg	SD 1	SD (8-1)	SD (15 -1)
4	1010250058	20	138	48	84
	1010250059	20	137	65	103
	1010250063	20	135	68	108
	1010250076	20	137	57	85
	1010250055	20	145	72	93
	1010250066	20	142	58	64
	N		6	6	6
	Mean		139.0	61.3	89.5
	SD		3.7	8.7	15.7
	SEM		1.5	3.6	6.4

Prepared by: Ju-Mai Chen, Nov 7, 2001

Checked by: Di-Shing Wang, Nov 19, 2001