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TOXICOLOGY RESEARCH CENTER

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REPUBLIC OF KOREA

Technical report: Laboratory Animal Science\*

Prepared for the Government of the Republic of Korea  
by the United Nations Industrial Development Organization,  
acting as executing agency for the United Nations Development Programme

Based on the work of Zenichi SATO,  
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## 1. Introduction

KRICT (the Korea Research Institute of Chemical Technology) Toxicology Research Center has been operating safety tests and laboratory animal production. Consequently, satisfactory results have been obtained. However, on the other hand, the results are only superficial, and they still have a long way to go towards being entirely satisfactory when the stability of the future is considered. Hence the instruction was given to the authority to complete the GLP of the world standard by April 1988, putting stress on indicating the bases of the experimental technique and system which is capable of the long-term safety tests and laboratory animal production with the higher quality which will be realized by checking the previous operation state and by establishing the future stable technique. At the same time, several points which should be paid attention to in future were also indicated.

Since the business has been managed without only big problem up to now, it is quite certain that the standard of the business will reach that of the world when the safety tests are operated according to SOPs of GLP and the production & provision of laboratory animals are operated under the production SOPs in future.

2. The Persons I met in Seoul

Oct. 26, 1987

Mr. Park Pyong Chol, UNDP project programmer

Nov. 25, 1987

Mr. Park Pyong Chol, UNDP project programmer

Persons I made contact with while I worked at KRICT

- 1) Jung Koo Roh, Ph.D., Director of Toxicology  
Research Center, KRICT
- 2) Sang Seop Han, Ph.D., Senior Research Scientist  
of Toxicology Research Center, KRICT

**3. EXPLANATORY NOTES**

**Abbreviation:**

**GLP: Good Laboratory Practices**

**KRICT: Korea Research Institute of Chemical  
Technology**

**SOPs: Standard operating procedures**

**SPF: Specific pathogen free**

**QAU: Quality assurance unit**

**QAM: Quality assurance manager**

**BS: Barrier system**

#### 4. Placement of the GLP Standard for Toxicity Test

Toxicology (50 items such as; acute toxicity test, long term test, subacute toxicity test, teratology test, etc.) is 1-2 year-long term experiments operated by many groups of people, using many types of animals and technology of various subjects such as pathology. Therefore, the main countries of the world indicate the test method in guidelines or law, which is called GLP. Korea has not placed GLP yet, however, KRICT is now planning to make KRICT GLP by studying the GLPs of USA, UK, and Japan. This time, the GLP standard was made, and minute SOPs will be made on each piece of work and test based on it.

The following are the items of the standard:

##### 1. General Provisions

1.1 Purpose

1.2 Scope

1.3 The definition of the terms

1.4 Confirmation of GLP tests

1.5 Inspection

1.6 The examination of sponsors, etc.

##### 2. Personnel

7 items, such as educational training or responsibility, are settled.

**3. Organization**

2 items of the standard of GLP organization, such as Research system and construction of units, are settled.

**4. Quality assurance unit**

Quality assurance unit should guarantee the quality of the tests. Any kind of data should be assured by this section to be admitted. 3 items are settled.

**5. Facilities**

Each testing facility shall be in an important place for operation. Special attention shall be paid to animal experiments as the largely effects the experimental reflexes.

**6. Equipment and Reagents**

5 items are settled for this important section which is related directly to the test.

**7. Test System**

5 items about living test system such as laboratory animals are settled.



8. Test and Control Articles

The accuracy of the test results depends entirely on how tests and control articles are treated. The articles should be treated scientifically so as to operate the experiment exactly. 5 items are settled.

9. SOPs

SOPs are to indicate the concrete method of various experimental technology and system control. 5 items are settled to make the Standard of SOPs.

10. Protocol and Conduct of the tests

Protocol should be very minutely made, as it precedes the experiment. 6 items are settled.

11. Operation of the experiment

8 items to be followed at the operation of experiment are settled.

12. Reporting of the experiment results

5 items about the responsibility, approval, guarantee, and the contents are settled.

**13. Storage of Records and Data**

Some of the records and data should be kept over 5 years or permanently. 4 items are settled.

**14. Additional Rules**

The operation day for KRICT GLP is settled.

14 sections consisting of 105 items of standard rules to make GLP are settled as above. The standard of SOPs, which controls technical field such as laboratory animals, pathology, biochemical etc, and System, Management and personnel control, is made according to the above rules. KRICT has already started to make the SOPs.

5. Placement of the SOPs of production and provision of  
the laboratory animals

Test results cannot be guaranteed without high quality laboratory animals. KRICT's laboratory animals have been produced based on this principle, and SPF mice and rats have been produced for one and half year.

- a. Productivity has reached a high level.
- b. As for the quality control, there have been no particular problems such as illness or infectious disease.
- c. The present production or management is operated under the elementary SOPs, and basically, the operation has successfully produced and provided the high quality laboratory animals by now. To provide higher quality laboratory animals under more stabilized production, the standard to make new SOPs are indicated. Although GLP standard does not restrain the animal production, many parts are referred to.

**SOPs for Production and Provision**

**1. General Rules**

**2. Detailed Rules**

- (1) Control of raw materials 2 items
- (2) Control of environmental & sanitary conditions  
3 items
- (3) Control of mass-production of mice & rats  
8 items
- (4) Control of breeding and supply of mice & rats  
6 items
- (5) Breeding control 9 items
- (6) Quality control 2 items
- (7) Maintenance of equipment 6 items
- (8) Maintenance of safety 4 items
- (9) Records & Reports 9 items
- (10) Additional data 10 items

The above 10 sections consisted of 51 items of  
Standard rules shall be used to make the concrete  
SOPs.

6. Management, Checking of Facilities and SOPs

Indication

The air-condition for the BS facilities under operation at present are controlled by two full-time machine controllers and engineers. These facilities are very well kept with daily, weekly, and monthly checks according to SOPs. The control system is considered to be of first class, as there is no trouble in the checked figures shown in the following list. However, considering the superannuation of the facilities in future, I advised that further attention on the maintenance shall be needed.

<u>Item</u>	<u>Target value</u>	<u>Found vlaue</u>	<u>Judgment</u>
Temperature	20 - 26 °C	23 -25 °C	Complies
Humidity	40 - 60 %	45 - 55 %	Complies
Frequency of ventilations	10 - 15 times/hr	<15 times/hr	Complies
Rate of air stream	13 - 18 cm/sec	12 -15 cm/sec	Complies
Odor	20 ppm ammonium	(not examined because no animals were housed)	
Noise	60 dB	40.0 - 46.5 dB	Complies

### 7. Cages and Other Equipment

Mice & rats have been the only animals used until now. However, as it is considered that the types of animals will gradually be increased towards dogs, rabbits, monkeys or cats, the cages or other equipment should be of international standard, considering the GLP. Particularly, the cages for the long-term experiments should have both the reasonable comfortability for the animals and scientific standard.

The reasons which decide the cage size scientifically should be kept on record. The following list is referred to world wide, which I advised should be referred to the test production of cages in KRICT Toxicology (for the animals at the pressing need).

The Minimum Space Necessary for Laboratory Animals

Animal Type	Weight	Breeding Method	Floor Surface/		Height	
			in <sup>2</sup>	cm <sup>2</sup>	in	cm
Mouse	<10	Cage	6.0	38.71	5	12.70
	10-15	Cage	8.0	51.62	5	12.70
	15-25	Cage	12.0	77.42	5	12.20
	>25	Cage	15.0	96.78	5	12.70
Rat	<100	Cage	17.0	109.68	7	17.78
	100-200	Cage	23.0	148.40	7	17.78
	200-300	Cage	29.0	187.11	7	17.78
	300-400	Cage	40.0	258.08	7	17.78
	400-500	Cage	60.0	387.12	7	17.78
	>500	Cage	70.0	451.64	7	17.78
Guinea pig	≤ 350	Cage	60.0	387.12	7	17.78
	>350	Cage	101.0	651.65	7	17.78
	<u>kg</u>		<u>ft<sup>2</sup></u>	<u>m<sup>2</sup></u>		
Rabbits	<2	Cage	1.5	0.14	14	35.56
	2-4	Cage	3.0	0.28	14	35.56
	4-5.4	Cage	4.0	0.37	14	35.56
	>5.4	Cage	5.0	0.46	14	35.56
Dogs	<15	Fence/Motor corridor	8.0	0.74		
	15-30	Fence/Motor corridor	12.1	1.12		
	>30	Fence/Motor corridor	24.0	2.23		
	<15	Cage	8.0	0.74	32	81.28
	15-30	Cage	12.1	1.12	36	91.44
	>30	Cage	c		c	

## 8. Indication of the Problems

### 8.1 Operation of Toxicity test based on the GLP standards

Many tests have been operated in spite of a few experimental items. However, a lot of them were of tests not following GLP standard, and from now on, it is necessary to study GLP thoroughly to change the system from now-GLP to GLP-fit test. No operation out of SOPs should be done. However, the staff should be scientific and positive in reporting and adjusting the SOPs if a better method is found. There is a tendency with excellent SOPs that the staff do not try to perform any other but the settled items. Or, some among the GLP standard test operators tend to want to leave the section because of the misunderstanding of GLP. This phenomenon is seen particularly among the high-level researchers, so that the education of those people should be of importance.



## 8.2 Neccessity of the early arrangement of the laboratory animal science research room

Although the SPF animal production has been satisfactory, it is considered to be urgently neccessary to arrange the quality control, prevention of infectious diseases, test results analyses etc. for the laboratory animal science research room, since both the production of SPF animals and the number of animals out of SPF shall increase in future. The laboratory should be arranged so that the reseach of bacteria, virus, protozoa, and parasites.

## 8.3 The neighbouring problems of the GLP facilities and those of other science sections

Toxicity testing demands a long-term experiment, and the whole period of time is considered to have an effect on the experiment. Therefore, the neighbouring problems are to be avoided as much as possible. However, a research building which seems to effect the test is built in neighbouring area. As there is a reason to compromise with this location, what should be done in future is to solue the matter by using leading wires, doors, air-conditions on scientific ground.

#### 8.4 The problems of collecting information

KRICT TOXICOLOGY has to operate entrust experiments and research from all over the world. And the method is different dependig on the purpose of the test of the trustee and the supervising government authorities of the trustee's country (Japan: the Ministry of Public Welfare, the Ministry of Agriculture and Fcrestry, the Ministry of Labor, the Ministry of International Trade and Industry, U.S.A.: FDA, EPA, OECD etc.) Moreover, there is an occational adjustment of the experimental method in each country, and large adjustments such as prohibition of accute toxicity could be possible. Therefore, it is neccessary to acquire the information systematically from all over the world at any time. KRICT Toxicology Center as an international experiment operator, also has the responsibility to provide more information to the sponsors. At present, although there is comparatively a lot of information concerning chemical substances, there seems not to be enough information about medical supplies. It is expected that a information collecting system will be established in future.

8.5 The problems of establishing kind treatment towards laboratory animals, and morals cocerned with this

KRICT Toxicology Center uses a lot of laboratory animals, the living reagents, for the wide range of test items. So, it is important to keep in mind the importance of life and how to lessen the sacrifice of the animals. The animals under the operation are forced to feel pain, and most of them die. Therefore it is neccessary to research throughly how to lesser the pain and provide them with easier living conditions while they are undergoing operations, or, when they die, if we should give them euthanasia so long as the experimental result will not be harmed. Also, the development of experimental methods without animals should be considered as an important research subject to the people who are in charge of animal experiments.

All the above mentioned should mean that all staff need to have higher education and morals.