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TOXICOLOGY RESEARCH LABORATORY

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REPUBLIC OF KOREA

Technical report: Reproductive Toxicology*

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 Hiroaki Kawanishi
consultant in reproductive toxicology

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United Nations Industrial Development Organization
Vienna

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1. Introduction

This is the report of consultation for reproductive toxicology study, especially teratology study for experimental animals, in Toxicology Research Center, Life Science Division, Korea Reserach Institute of Chemical Technology (KRICT). Because the technique of detection for fetal malformation can be shown by Dr. S.H.Kim,D.V.M.,M.Sc., group leader of Special Toxicity Team, who learned it at The Imamichi Institute for Animal Reproduction(IIAR), present consultation was focused on the another subjects regarding reproductive toxicity study.

Consultant : Hiroaki Kawanishi,D.V.M.,M.Sc.

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Period : June 13,1988 to June 25,1988

Object : Special Toxicity group(group leader, Sung Hoon Kim,D.V.M.,M.Sc.)
Toxicology Research center
Life Science Division
Korean Institute of Chemical Technology (KRICT)

Subjects : Self checking system for data and documents
Practical role of Quality Assurance Unit(QAU)
Diagnosis of fetal malformation
Importance of background data
Learning behavior
Taking photograph of soft X-ray
How to decide dosing level
Preparation of final report

2. Self checking system for data and documents

The importance of self checking, not by QAU, was stressed for performing study precisely at first. The data form and document sheet should be prepared so as to the personnel attended the proper study can check easily their data by themselves. For example, when the volume of dosing solusion based on body weight data and the data sheet of body weight and dosing is independent, body weights should be posted to the dosing sheet. And volume will be calculated using the body weight data. When these data is procedured by off line, there are two factors which allow mistake. So, these data must be checked before

dosing. If miscalculation was found out after dosing, reliability of the study will be poor.

At this standpoint, " check sheets" used in IIAR were shown as practical example. A part of data sheets which were designated in Standard Operation Procedure(SOP) of KRICT was revieved and some sheets were pointed out to be reformed.

3. Practical role of Quality Assurance Unit(QAU)

The role and duty of QAU are described in Good Laboratory Practice(GLP) regulations of Food and Drug Agency(FDA) ,USA and of Health and Welfare Department, Japan. That is, QAU has to report the idea lead by results delivered from checking in accordance with QAU program for management. Management has to deal with suitable disposal for study performance after QAU reporting if necessary. Regarding these standpoints, some cases were discussed in practically using the sheet of IIAR. Representative of QAU, KRICT, Mr. C.C.Shin, stated that he promoted his mutual understand for QA operations by this simulations.

4. Importance of background data.

Historical reproductive data accumulated in IIAR was shown in slide photograph and variation ranges of two rat strains were compared. The importance of background data for the evaluation of effect of test articles was stressed with some examples. Two actual cases of reproductive toxicity studies carried out in IIAR which were dose related changes within normal range and dose unrelated changes out of normal range, were discussed if test article affected reproductive function. These demonstrations seemed to be good material to comprehend the importance of background data.

5. Diagnosis of fetal malformations

Some spontaneous or chemical induced fetal malformations were shown in slide photograph. Terminology, degree of anomalies and frequencies of each malformations presented there were discussed.

6. Learning test

Guidelines require to examine the learning ability of F_1 offspring from dams treated with test article. Water T-maze performance is one of the most popular method. Simulation of learning test were performed using multiple water T-maze. Number of errors were counted and consumed time was measured. Errors were distinguished to three types, selecting error,inzone error and backing error, and were counted totally. S.H.Kim, J.I.Park, C.Y.Kim and J.S.Ahn attended to

swimming test. Everyone experienced animal handling, recording the swimming tract and time measuring, and S.H.Kim and C.Y.Kim learned how to distinguish errors to three types.

7. Taking Soft X-ray photograph

Skeletal examination by soft X-ray photograph is simple method to detect major skeletal malformation without sacrifice in adult rat. S.H.Kim anf C.Y.Kim learned how to take soft-X ray photograph and determined suitable condition for taking good photograph.

8. How to decide dosing level

Some standpopints to set up dose level was discussed. The dose level of reproductive toxicity tests should be decided based upon the data of range finding test in principal, although another study can present informations in some times. S.H.Kim was given exercises for dose setting. He understood basically, but seemed to be confused a little. Another exercises to reinforce to make sense for deciding dose level will be necessary.

9. Preparation of final report

Although the final report of toxicology study should be described as the paper of natural science, some additional pages should be described. That is, Statement of management, Title and Purpose of the study, Organization which performed study, Each date of examinations on the study initiation to final report, Personnel name in charge, Signiture of scientists who evaluated the sudy, and Certification of QAU. Furthermore, Environmental monitoring records of animal room, Analyses records of food and water for components and contaminants and Qualification of test article should be prepared as attachements. Actual example of IIAR was shown and explained.

10. General impression and recommendation

At the present situation, the system of study administration according to GLP regulations is already established and staffs are trained basically. Barrier sustained animal room for special pathogen free rat is functionning and Standard Operation Procedures(SOPs) have been prepared. The potentiality of this laboratory will grow up if only experiences will accumulate.

Following subjects are recommended.

1)To set up some studies to keep scientists busy by academical training.

Some studies which include same examination items as real study should be carried out with or without any chemical compound. This should be useful

for not only staff training but accumulation of background data.Furtheremore, if histopathological examination of malformed fetuses induced known teratogen will be carried out, it should be benefit to develop to judge teratogenicity for scientists.

2)Education of scientist for statistical analysis for study evaluation.

3)Subscription of journals

Teratology

Congenital Anomalies

Toxicology Abstracts

Japanese Journal of Toxicology Science

Agenda of Consultation (attachment)

Date	Time	Agenda	Personnel
June 13(M)	PM 7:15	Arrive on Daejeon, Korea	
14(Tu)	AM	Laboratory tour guided by Dr. Roh, Director of Toxicology Research Center	
	PM	Short talking with Mr. S. H. Kim, about present situalion of his laboratory Making of consultation schedule	S.H.Kim
15(W)	AM	Review of SOP and data sheets	S.H.Kim
	PM	Meeting with C.C.Shin,Representative of QAU	C.C.Shin S.H.Kim
16(Th)	AM	Meeting with Dr.C.S.Ha,Pathologist, Introduction of the checking system for making pathological specimens	C.S.Ha S.H.Kim
	PM	Discussion to determine dose level	S.H.Kim
17(F)	AM	Diagnosis of fetal malformation	S.H.Kim
	PM	Introduction of backgrounf data of IIAR	J.I.Park C.Y.Kim
20(M)	AM	Simulation of multiple water T-maze test	S.H.Kim
	PM	Data calculation of T-maze test Introduction of checking system of IIAR and final report	J.I.Park C.Y.Kim J.S.Ahn S.S.Han Kim Shin
21(Tu)	AM	Practise of taking photograph using soft-X ray	S.H.Kim
	PM	Determination of suitable condition for taking good photograph	C.Y.Kim
22(W)	AM	(continue)	
	PM	Discussion for making dose level(again)	S.H.Kim
23(Th)		Summarize of consultation Inspection of KGLP committee	
24(F)	AM	Talking about evaluation for test article	S.H.Kim
	PM	Slide seminar	
25(S)		Daejeon~Seoul~Tokyo	