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TOXICOLOGY RESEARCH LABORATORY

DP/ROK/82/028/11-63

REPUBLIC OF KOREA

Technical Report: General 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 Geoffrey Conybeare,
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EXPLANATORY NOTES

Abbreviations:

ECG:	Electrocardiogram
KRICT:	Korea Research Institute of Chemical Technology
GLP:	Good Laboratory Practice
SOPS:	Standard Operating Procedures
UNDP:	United Nations Development Programme
QAU:	Quality Assurance Unit

ABSTRACT

This mission forms part of the expert assistance provided for the KRICT Toxicology Research Center in General Toxicology as job DP/ROK/82/028/11-63. It was undertaken between 8 March and 7 April 1988.

The main objective was to prepare, initiate and review the data from a toxicity study as well as instruct the staff at the centre in the practical aspects of running animal experiments.

The staff were given guidance in the form of seminars, informal discussions, demonstrations and practical training sessions.

A complete experiment which was urgently required, was prepared, initiated and executed to GLP standards.

Recommendations were made for subsequent studies from the data generated and guidance was given in the preparation of the report.

CONTENTS

I

INTRODUCTION

This report covers a mission of one month, commencing 8th March to 7th April 1988, during which 23 days were spent at the KRICT Toxicology Research Centre. This Centre, established with UNDP aid and guidance, is intended to develop as the facility for Contract Toxicology in the Republic of Korea. To achieve this goal it is necessary to develop expertise in general toxicology to standards acceptable to Regulatory Authorities Worldwide. This mission aimed to provide practical advice, guidance and training which would further the development of the Research Centre and its staff.

The objective of the mission was to work closely with the staff of the Centre and to provide assistance in the training, operation and administration of animal experiments and specifically to set up, intiate and perform an animal experiment on one of the new KRICT compounds. Assistance was given in interpreting the data, preparation of the final report and recommendations were given for subsequent animal experiments.

II

RECOMMENDATIONS

1) The Centre is well aware of its need to comply with GLP. However the Centre must intiate, with the utmost urgency, the checking for compliance and enforcement of SOPs by the QAU. Many SOPs have now been translated into Korean and it can not be emphasised enough that without compliance to GLP the Centre cannot be accepted by International Regulatory Agencies. A consultant should carry out a full QA audit later in 1988, when all the SOPs are complete and the work load established. This could be undertaken by Mr. George B Leslie or any Senior QAU manager from a pharmaceutical / contract laboratory. This audit will expose any weaknesses or areas still not in compliance with GLP.

2) The already successful training programme set up to advance the standards of the of the staff must continue. Both internally, with formal technical training and practical expertise, and externally, in the form of visiting consultants and fellowsh for staff to train abroad.

3) Metabolic and pharmokinetic data are essential to the design of toxicology studie At present these are performed by the understaffed Department of Pharmacology Screening and co-ordination between this and the Department of Toxicology should be established. A visit by a consultant in the field of metabolism and pharmokinetics would stream-line the system as neither department, I believe, are clear about what types of studies are essential.

4) Although the new facility is occupied and almost complete, the purchase of certain necessary equipment is still required, especially for the conduct of dog experiments.

5) Recommendations on data collection, particularly on the chronic and oncogenicity studies, were implemented before my departure from the Centre. However, at the end of the oncogenicity study, I believe, they will require some help in clinical examination necropsy and data collection from geriatric rats.

III

OBJECTIVES

The intension of this mission was to provide advise and assistance which would develop the understanding and practical expertise required to enable the Research Centre to conduct general toxicological studies to internationally accepted standards.

The Toxicology Department of KRICT has advanced rapidly since my last visit. However, there are still some areas in general toxicology that have yet to be developed. The most urgent is dog toxicology. (With rodent and dog studies it is then possible to test new drugs in man.)

Although the facility still lacks some basic equipment, the main contribution was to set up, execute and advise in the reporting of an urgently required sighting study in the dog.

Work on rodents seems to be well underway and the Centre just needs to expand its expertise into more varied routes of administrations and some help will be required at the end of the oncogenicity study.

IV

ACTIONS

Due to the nature of the mission the objectives which were established were addressed under two categories :

A. General

B. Specific

A. General Objectives

i. Informal Discussions

These took place on an ad hoc basis whenever staff had any specific questions to discuss. Some time was spent in various laboratories and animal facilities looking at procedures and making suggestions where appropriate.

ii. Formal Discussions

These were prearranged meetings involving members of staff.

Topics included :

1) Data collection from chronic and oncogenicity studies.

2) Preparation and issueing of protocols.

3) Dose level determination and stratagies for future studies.

4) Review of current data from the dog sighting study.

5) Drug solubility problems.

6) Diet analysis.

7) Review several reports and correct the English grammer

iii. Seminars

These were given to the toxicology staff as follows:

1) The effects of under and over nutrition in long term studies on survival, tumour incidence and ageing disease in laboratory rodents.

2) Investigation and eradication of congenintal cataracts in a mouse colony.

Joint video and poster sessions were given with Mr.C.B. Leslies covering the following subjects :

Rodent : handling, sexing, drug administration, necropsy, and clinical responses to certain drugs. Blood collection in rodents and intravenous infusion techniques in the dog.

B. Specific Objective

To set up and run a Sighting Study in Dogs.

This included :

1) Preparation of the dog accomodation.

2) Location and collection of suitable dog food.

3) Location and collection of dogs.

4) Location, collection and administration of pre-test medication e.g. anti-parasitic drugs.

5) Preparation and issueing of a protocol.

6) Liason with the Pharmacology Screening Department for serum drug level determinatio

7) Training staff for blood collection, urine collection by bladder catheterization, data recording etc.

8) Monitoring and directing the Dog Sighting Study.

9) Demonstration and training of staff in dog necropsy procedure.

10) Reviewing data at the end of the study for inclusion in the final report and recommendations for future studies.

This work load was greatly eased by Mr. Shin, who has just returned from a 3 month training fellowship in Japan where he studied dog toxicology.

V

RESULT

The staff at the Centre have greatly improved their stills and toxicological methods. This is most apparent in the rat studies where they should further improve and extend the type of work undertaken. They have opted for Japaness SOPs and are progressing towards GLP compliance. They have adapted well to improving methodology and show great enthusiasm to improving their skills.

VI

CONCLUSIONS

The Toxicology Research Centre has already acheived a great deal but still more needs to be dore.

The major priority must be to fully comply with GLP standards. Without this the Centre cannot acheive its aim of conducting studies under contract for clients who wish to market their products outside Korea.

Dog studies have now been intiated and further development and purchasing of equipment must proceed as fast as possible.

Staff training must continue in the form of consulting experts and overseas fellowships.

However, the attitudes of the Director and the enthusiasm of the staff speak for themselves in the acheivements already made and they should ensure the successful progress of the Centre.