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TOXICOLOGY RESEARCH LABORATORY

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REPUBLIC OF KOREA

Technical report: Pathology*

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 William H. Butler
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Explanatory Notes

Abbreviations

KRICT - Korea Research Institute of Chemical Technology

GLP - Good Laboratory Practice

SOPS - Standard Operating Procedures

UNDP - United Nations Development Programme

Abstract

This mission forms part of the expert assistance provided for the KRICT Research centre in Pathology. It was undertaken between 12 October and 30 October 1987.

The main objective was to guide the staff of the Centre in the management of a pathological laboratory servicing a department of toxicology and to assist in the training of the personnel.

Particular emphasis was given to help the staff move towards conforming to GLP standards acceptable to Internationl Regulatory Agencies.

The staff were given guidance in the form of lectures, seminars, informal discussions. Recommendations were made on equipment and further training.

Introduction

This report covers a mission of 3 weeks, commincing 12 October 1987. This centre, established with UNDP aid and guidance, is intended to develop as the main facility for Contract Toxicology in the Republic of Korea. To achieve this goal it is necessary to develop expertise in toxicological pathology to a standard acceptable to Regulatory Authorities worldwide. This mission was aimed to provide advice, guidance and training which would further the development of the Research Centre and its staff.

The objectives of the mission were to work with the Director of the centre (Dr. Roh) and his staff (in particular Mr Ha) to provide assistance in the planning, operation of the histological laboratory and the histological assessment of tissues. In particular:

1. Train staff in the assessment of pathological changes and give an initial course of general pathology.
2. Advise on further training requirements.
3. Review the existing and planned equipment and advise on its suitability.
4. Advise on GLP compliance and assist in the preparation of SOPS.

These objectives were achieved through individual discussions, practical seminars and formal lectures as is described more fully later in this report.

Recommendations

1. Section of pathology must broaden its experience to include both acute and chronic studies.

2. Compliance with GLP and safety procedures should be a high priority objective for the centre.

3. The training programme to acquire pathological expertise should continue with existing staff. It is recognized that the acquisition of such expertise is dependant upon the accumulated individual expertise of the pathologists.

4. It is important that the scientific staff of the section of pathology are offered sufficient time to aquire this experience.

5. Continued training must be derived from

   a) Staff visiting laboratories actively engaged in toxicological pathology.

   b) When in-house studies are available i.e. 90 day and 2 year, external consultants must visit the laboratory to review the reports of KCRIT staff.

I. Objectives

The intention of the mission was to provide assistarce and advice which would develop the understanding and practical expertise required to enable the research centre to conduct pathological assessments of toxicological studies to internationally acceptable standards.

At present the Research Centre does not reach GLP or safety standards required by international Regulatory Authorities and some SOP's were lacking or inadequate.

Instruction was necessary for their construction a well as advice on safety procedures to be used.

II. Action

The general and specific objectives which were established were addressed by various actions which fell into a number of categories.

These are discussed under the following headings:

A. Informal discussions

B. Lectures

C. Seminars

D. Documentation

E. Equipment

F. Training Requirements

A. Informal Discussions

These contributions took place both on an ad hoc basis whenever staff had any specific questions to discuss and were concerned with individual diagnostic and technical problems. These discussions took place in conjunction with Dr K.P. Lee; UNIDO consultant.

During these discussions many points were raised:

1) The Toxicology laboratories should develop a Health and Safety Policy and Codes of Practice based on available guidelines.

2) The pathology section should have their own departmental safety manual.

3) There should be a separate room for tea and coffee. No smoking, eating or drinking should be allowed in laboratories.

4) According to GLP, there should be operating manuals for all equipment in plastic folders attached to each item of

equipment. A service record and maintenance checks for equipment should also be available.

5) All bottles containing chemicals (liquids or solids) should be labelled and marked with expiry dates. All shelves and drawers should be labelled.

6) Solvents need to be stored in solvent cabinets.

7) Personnel handling animals should be suitably protectively clothed. All post mortems or dissections of animals should be carried out in ventilated areas. The current facility is inadequate but I understand new laboratories will soon be available.

8) A general safety committee should be formed for the toxicology laboratories. It should consist of a Chairman and one safety representative from each Department. Before major experiments with hazardous chemicals are performed, safety aspects relating to experimental conduct should be identified and any decisions adhered to. The safety representative in each department should check on any safety features which need attending to and a six-monthly audit performed.

9) For general GLP purposes a line management chart is required so that personnel can identify immediate supervisors in case of absence or crisis.

B. Lectures

A series of lectures was given to up to 6 scientific staff. Comprehension appeared to be high but was greatly assisted by the presence of Dr K.P. Lee. The material was presented informally with discussion.

Titles and summaries of lectures were as follows:

1) 14 October. Introduction to Pathology.

Acute injury. The histological features of acute injury were described using various chemical agents as model toxins.

2) 15 October. Mechanisms of acute injury.

The correlation between morphological changes and biochemical mechanisms was disscussed.

3) 16 October. Correlation between histology, clinical chemistry and haematology in toxicity studies.

Examples were given of various types of toxicological injury and the correlation with other parameters. The difficulties of making such assessments are discussed.

4) 19 October. Three separate seminar subjects were given:

a) Neurotoxicity. The major types of both central and peripheral neurotoxicity were discribed.

b) Toxicologcal aspects of enzyme induction. The common types of pathlogical change caused by inducers of mixed function oxidase enzymes are discussed.

c) Testicular toxicity. Specific testicular toxins were demonstrated and the methods of assessement of such damage.

5) 20 October. Spontaneous disease - non neoplastic.

A review of spontaneous disease in rodents was given discussing problems of diagnosis.

6) 20 October. Spontaneous disease - neoplastic.

A review of spontaneous neoplasm - mainly rats and mice was given discussing problems of diagnosis.

7) 21 October. Neoplasia - Human.

As a background to neoplasia in toxicology the presentation of neoplasia in man was discussed.

8) 22 October. Neoplasia - Aetiology.

The toxicological basis for disease in man was described.

9) 22 October. Preneoplasia -

The basis of the concepts of preneoplasia was discussed with the implications for toxicology.

10) 23 October. Liver neoplasia - rat.

The specific example of rat liver neoplasia was discussed with special reference to the toxicological problems of assessment.

11) 26 October. Liver neoplasia - mouse.

The problems of diagnosis and interpretation of mouse tumour were described.

12) 28 October. Kidney neoplasia.

The mechanism and significance of renal tumours were discussed.

13) 28 October. Bladder neoplasia.

The toxicologl significance of bladder tumours in rats were compared with man.

Training

The group attending the summaries and slide sessions consisted of Mr Ha, a veterinary graduate, and up to 5 science graduates. Clearly the science graduates had little previous exposure to pathology but all appeared eager to learn.

It is only possible to learn diagnosis pathology by hands on experience guided by a pathologist of greater experience. Inevitally this is a slow process of aquisition.

I would most strongly recommend that Mr Ha spends time in another laboratory of comparable size allowing as much assimilation as possible. Following such training, at a time when KRICT has its own material from long term studies, a consultant pathologist should visit the laboratory.

During the visit he should check the diagnosis and be in a position to explain the differing diagnosis. This exercise should be undertaken before any report is issued by KRICT.

Technical training. There is little or no trained technical personnel. One technican was in place who had some previous experience of hospital pathology. It will be essential for Mr Ha to train the technical staff. In order to achieve this level of expertise Mr Ha, while working in other laboratories, should pay particular attention to technical expertise.

C. Seminars/Demonstrations

Practical seminars and demonstrations were held in the laboratories during which histological slides of specific lesions were examined and discussed.

D. Documentation

Standard operating procedures were discussed as well as guidelines for the different countries.

E. Equipment

A review of existing equipment was undertaken. Some recommendations for safety were made and additional apparatus suggested. The photomicroscope with T.V. was brought into use. Photographs were obtained of the sections used for teaching.

Conclusion

KRICT has made a most encouraging start in developing its expertise in toxicological pathology. With a continued training programme for dedicated staff the required standards should be reached. This will require continued supervision for some time so that any reports will be internationally acceptable.

Attention to detail is essential in particular in all aspects of laboratory management with regard to GLP.