Methods for Estimating Risk of Chemical Injury: Human and Non-human Biota and Ecosystems
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1 *Introduction, General Conclusions and Recommendations**

1.1 INTRODUCTION

This publication consists of two parts, a Joint Report expressing combined views of the Workshop participants and 28 individual contributions commissioned in advance. This is the introduction to the Joint Report. Two related but somewhat distinct methodological issues are discussed in the Report:

(1) adequacy of existing methods for quantitative estimation of risk of human injury associated with exposure to chemicals; and
(2) approaches to quantitative estimation of chemical injury in non-human biota and ecosystems.

Since the prediction of harm both to human health and to non-human biota requires a reliable assessment of exposure, procedures for quantitative estimation of exposure have also been reviewed and evaluated.

To date, estimations of exposure to chemicals have mainly been carried out as part of epidemiological investigations or in compliance with regulatory decisions aimed at human health protection. However, increasing attention is now being devoted to the effects of chemicals on non-human biota. Since many approaches and methods used in human exposure estimation are broadly applicable to non-human targets, an attempt has been made to deal with estimation and assessment of exposure for all types of organisms and populations.

Some judgment of the magnitude of risk enters explicitly or implicitly into all control decisions whether they involve regulatory or other protective measures. Various methods have been used to arrive at such judgments, the most common approach being the use of empirical safety factors. More recently the approach has been to estimate acceptable levels of risk. The advantages of quantitative estimation of risk have now been recognized. This approach has been used for some years in the evaluation of the effects of ionizing radiation, and similar procedures have been applied to chemical carcinogenesis. The application of these methods has in turn indicated changes in the protocols for testing of carcinogens which are necessary in order to obtain more suitable data for

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quantitative risk estimation. The extensive use of quantitative risk estimation in the evaluation of chemical carcinogenesis has not been matched in the study of other toxicological endpoints.

In analysing laboratory studies, the emphasis in this report has been placed on basic biological mechanisms and how knowledge of mechanisms of mutagenesis and carcinogenesis can be put to use in qualitative and quantitative risk assessment. Although the role of chemicals in producing heritable mutations is important, it has not been possible in the present study to accomplish more than to note this fact and call attention to the relationship between chemically induced mutations in test systems and cancer development in experimental animals.

The most relevant source of information for risk estimation in man is epidemiology, and much attention has been paid in the report to the evaluation of various epidemiological methods and their utility in quantitative estimation of risk, in particular cancer risk.

In the initial phases of the study the possibility of evaluating the existing methods for risk estimation in ecosystems was considered. However, it soon became apparent that a review and evaluation of methods that can provide quantitative information on chemical injuries in non-human biota was required first. Accordingly, the study has been restricted to the assessment of approaches for estimation of chemical injury to plants, animals and microorganisms, and their populations, communities and ecosystems. Most ecotoxicological tests are applicable either to individual organisms or to populations. Multispecies tests are now being developed to predict effects of chemicals on communities and on ecosystems In specific instances, large-scale field tests are necessary to forecast changes in the structure and function of communities and ecosystems, and to provide data for calibrating laboratory test systems. A promising approach to the intergration of ecotoxicological data is mathematical modelling which has also received some attention in the Joint Report.

Much confusion and misunderstanding has been caused by the lack of agreed definitions and terminology. Even such basic terms as exposure, environmental and biological monitoring and surveillance, risk and hazard, estimation and assessment may have a different meaning to scientists with different backgrounds and experience. Since the International Programme on Chemical Safety is now in the process of preparing a document on agreed terms, no attempt has been made to propose a consistent set of definitions. Nevertheless, definitions of some terms have been provided for the purpose of the present study. They are included in the relevant sections of the Joint Report.

1.2 GENERAL CONCLUSIONS

(1) Estimation and assessment of exposure to chemicals is an essential component of experimental studies, epidemiological inquiries and field surveys

of non-human biota. Lack or inadequacy of exposure data often limits the value of such studies.

(2) Environmental monitoring methods may not always yield information of direct relevance to the estimation of human exposure. An effort has been made recently to link environmental and biological monitoring in order to obtain a data base that could provide more adequate information for human exposure assessment.

(3) Methods for estimating exposure of non-human biota are not sufficiently developed, particularly as regards modelling and identification of chemical species involved.

(4) Risk estimation can be based on animal or human evidence of harmful effects associated with exposure to chemicals. At present, the results of short-term tests for carcinogenicity are generally regarded as providing only supportive information.

(5) Experiments with laboratory animals are usually conducted at high doses. The application of information obtained in laboratory studies requires both low-dose extrapolation by means of appropriate mathematical models and biological extrapolation to human beings. The degree of confidence in biological extrapolation depends on an understanding of mechanisms of toxic action in different species. This knowledge is still very limited.

(6) Quantitative risk estimation has been used mainly for carcinogenesis. In principle, the same methods are applicable to the estimation of risk of other harmful effects associated with exposure to chemicals. However, since different mechanisms of biological action are involved, different mathematical models are necessary for the estimation of risk. Due to these shortcomings, empirical methods such as the application of safety factors continue to be used when animal toxicological data are applied to human health hazard assessment.

(7) Chemical injury is usually due to a mixture of chemicals. It is important to bear this in mind when evaluating epidemiological data and ecotoxicological field studies.

(8) Most studies of chemical injury in non-human biota do not go beyond the population level. There has been some progress in methods for evaluating the impact of chemicals on ecosystems. Such evaluation requires integration of different kinds of information ranging from physical and chemical properties of pollutants to the effects on organisms at different trophic levels and ecosystem processes.

1.3 GENERAL RECOMMENDATIONS

(1) Better procedures should be developed for obtaining data on the amounts, uses and environmental releases of natural and man-made chemicals.

(2) The existing national and international environmental monitoring programmes should be reviewed and, where necessary, reoriented to provide better

data bases for estimating human exposure and exposure of non-human biota. Environmental monitoring programmes should be linked with programmes for personal monitoring and biological monitoring where appropriate. Further, there is a need for strict quality control procedures to ensure comparability of results obtained in different laboratories.

(3) An international inventory of existing banks of human and non-human biological material and of environmental samples should be made, and, if necessary, additional banks established. Such repositories of specimens from exposed and unexposed areas may be of great interest for historical monitoring and in epidemiology and ecotoxicological field studies, particularly of wildlife.

(4) From the viewpoint of risk estimation, the highest priority in toxicological research should be given to studies of mechanisms of mutagenesis, carcinogenesis and other toxic actions of chemicals. Also, quantitative aspects of toxicological research and epidemiological studies require increased emphasis.

(5) An effort should be made to develop and apply mathematical models for risk estimations that are appropriate for toxic effects and processes other than chemical carcinogenesis.

(6) In the past, quantitative risk estimation has received inadequate attention in ecotoxicological research. In the future, it should be accorded special emphasis.