IV. MEETING REPORT OF THE INTERNATIONAL WORKSHOP ON APPROACHES TO INTEGRATED RISK ASSESSMENT

22-24 APRIL 2001

1. Background

For practical reasons, human health and environmental risk assessment methodologies have generally developed independently. However, with increased recognition of the need to more effectively protect both humans and the environment, an integrated, holistic approach to risk assessment that addresses real life situations of multichemical, multimedia, multiroute, and multispecies exposures is needed. It was recommended that IPCS convene a group of international scientific experts to develop approaches for integrated risk assessment.

In April 1998, IPCS convened an IPCS/OECD/EPA Scoping Meeting on Integrated Approaches to Human Health and Environmental Risk Assessment, in conjunction with a US EPA national symposium on "Extrapolation in Human Health and Ecological Risk Assessment". A number of potential activities/issues related to integrated risk assessment were identified at this scoping meeting. In November 1998, a follow-up planning meeting was convened by IPCS to further identify mechanisms and approaches for integrated risk assessment. That planning meeting agreed on a working definition of integrated risk assessment[1] developed a preliminary generic framework for integrated risk assessment, and proposed that a number of case studies be developed to evaluate the framework. IPCS convened a Framework Sub-Group meeting in July 1999 to review and revise the draft generic framework, and to develop criteria for identification of case studies and guidance for how the case studies would be developed. A meeting to further evaluate possible case study demonstrations of the generic framework was held in November 1999 and four case studies were chosen and their format/content finalized in July 2000. At the July 2000 meeting, plans were made to convene an international workshop to evaluate the framework and demonstrate the benefits of integration using the four case studies. That workshop was convened in Ispra, Italy in April 2001.

2. Goals of the Workshop

The overall goals of the workshop were to promote international understanding and acceptance of integrated risk assessment (IRA). Specific objectives of the meeting were:

1) to demonstrate and communicate the benefits of IRA to the international scientific community;

2) to evaluate a generic framework for IRA using case studies to test its strengths and weaknesses;

3) to identify what integration means with respect to conducting research to develop and support the IRA process;

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[1] Integrated risk assessment is a science-based approach that combines the processes of risk estimation for humans, biota, and natural resources in one assessment.

4) to identify how the IRA paradigm informs the environmental research agenda;

5) to facilitate the implementation and application of the paradigm of integrated risk assessment; and

6) to publish the results of the meeting in peer-reviewed scientific literature.

3. Overview of Generic Framework

Dr Glenn Suter, US EPA, provided an overview of the generic framework:

- Discussion issues: Terminology. Currently, US based terminology is used, but there is a need to incorporate OECD/IPCS harmonization project on terminology.
- Often in EU, the distinction between risk assessment and risk management is unclear. The risk assessor is also risk manager, which leads to differences in approaches.
- In some countries (EU) exposure assessment is already integrated. There still is need to focus more on characterization of effects and dose-response assessments.
- We need a common language, understanding, and harmonized methodologies for effective integration.
- Integration is not always possible; the issue must be defined at the problem formulation stage.

4. Presentation of Case Studies

Four case studies were described to illustrate how an integrated risk assessment could be conducted. Focused on selected stressors in the environment, these were:

- Persistent organic pollutants (POPs) in humans and wildlife (presented by Dr Peter Ross).
- Tributyltin and triphenyltin compounds in humans and wildlife (presented by Dr Jun Sekizawa).
- Organophosphorous compounds in the environment (presented by Dr Theo Vermeire).
- Ultraviolet radiation effects on amphibians, coral, humans, and oceanic primary productivity (presented by Dr Steven Hedtke).

5. Working Group "A" Discussions

Dr Munns provided instructions to workshop participants for the first set of working group deliberations. Participants, organized into four groups, were asked to identify the benefits and obstacles of integrated risk assessment as illustrated in the four case studies by considering the following questions:

- What aspects of human health and ecological risk assessments can be integrated to advantage?
- What are the benefits of integration?
- What are the barriers to integration?
- What do we loose by not integrating?

Additionally, participants were asked to 1) consider how integrated risk assessment can facilitate more timely and responsive regulatory decisions, 2) can help to identify emerging risk issues, and 3) can improve the cost effectiveness of assessments.

Summaries of each of the four Working Group "A" discussions were:

A-1. Persistent organic pollutants

What aspects can be integrated?

- several aspects of ecological and health risk assessments can be integrated
- exposure and effect each can be integrated
- integration goes beyond using "more data" or "packaging existing data"

Benefits

- comprehensive data sets
- reduce uncertainty
- better understanding of mechanism of action
- greater knowledge of environmental chemistry
- reduced cost

Obstacles

- institutional barriers
- scientific/cultural barriers
- differences in terminology/language
- initial cost may be higher

What do we lose?

- base decisions on limited data
- may miss low dose, chronic effects
- may overlook other endpoints (e.g., look for immune problems in Inuits based on observations in seals.
- initial cost may be higher

Predictive risk assessment?

- example - polybrominated diphenyl ethers
- concerns based on knowledge of PCBs, from both environmental media, wildlife, and humans
- global exposures are increasing in some regions
- limited data sets indicate similar mechanisms of action and dose-response relationships
- concluded that current environmental levels may result in potentially adverse effects

A-2. Organotins

What aspects can be integrated?

- sources/transport/pathways of exposure
- mechanisms of action and outcomes

Benefits

- exploit all available data
- improves cross-species extrapolation
- reduces changes of overlooking critical effects
- identification of critical issues
- identifies data gaps
- may serve as "early warnings" for other organisms

Obstacles

- difficult to overcome traditions
- lack of scientific expertise
- ecological and health assessments usually performed by difference experts
- legislative frameworks may be too rigid
- perception that integration is a complex process
- limited availability of data
- inadequate communication of risks

What do we lose?

- do not lose anything, so why not integrate
- critical effects may be overlooked
- integration will eventually result in speedier, more cost-effective regulatory decisions

Research needs

- better data on mechanisms of action
- better tools to use research data

Special issue

- where do economic, psycho-social, and cultural effects fit in?

A-3. Organophosphorous pesticides (OPs)

What aspects can be integrated?

- exposure (similar pathways occur in different species)
- effects acting via similar modes of action; however, caution must be exercised since acetylcholinesterase inhibition will differ for different OPs and different species

Benefits

- better understanding of effects of different levels of acetylcholinesterase inhibition in different species
- more thorough understanding of risks and risk trade-offs
- assist in identifying emerging new risks
- help identify targeted research needs

Obstacles
- institutional/language
- lack of training/decision making experience
- legal mandates
- funding

What do we lose?
- Integration is not always needed. It depends upon issues of concern raised in the problem formulation stage.

A-4. UV radiation

What aspects can be integrated?
- UV exposure assessment is common to both human health and ecological risk assessment
- molecular mechanisms of DNA damage is common to all species; divergence in modes of action result in different endpoints
- can compare different endpoints in different populations

Benefits
- common ground of comparison of data
- opportunity to detect critical pathways across species
- strengthens association of exposure/effects in one species if also observed in other species
- wider use of available data
- improves knowledge on links between molecular events and endpoints

Obstacles
- eco and human health research have different levels of sophistication and uncertainty
- focusing on common causal relationships may lead to oversimplification

What do we lose?
- all the benefits

6. Working Group "B" Discussions

Dr Munns provided instructions to workshop participants for the second set of working group deliberations. Participants, organized into three groups, were asked to identify what is needed to facilitate implementation of integrated risk assessment by considering the following questions:

- What research is needed to conduct integrated risk assessments?
- How will the integrated risk assessment paradigm inform the international research agenda?
- What mechanisms can be employed to facilitate implementation of the paradigm?

Since many of the independent discussions led to similar conclusions and recommendations, the outcomes of all three working groups were combined as:

A. What research is needed to facilitate the implementation of integrated risk assessment?

All the working groups found it difficult and challenging to separate research needs for risk assessment generally from those specific to integrate risk assessment. The following specific needs were identified:

- Exposure assessment and exposure models need to be developed from multiple sources and pathways for both health and wildlife. There needs to be better harmonisation of exposure monitoring and improved environmental and human health surveillance methods as well as access to monitoring data.
- There is a need for improved PB/PK modeling as a tool for combining data sets from different species, and for improving interspecies extrapolation.
- Effects assessment research focusing on common endpoints across phyla/species is needed.
- Effects assessment research focusing on understanding mechanisms of action at the molecular, cellular, organismic and population levels is needed. Examples included: gene array methods for species variance; common biomarkers across species.
- There is a need for improved risk communication methods and common risk measures for both problem formulation and ultimate risk management decisions (also taking into account psychosocial, cultural, and economic factors).
- Develop more effective methods of cost/benefit analysis and demonstrate the benefits of integrated risk assessment.

B. What mechanisms/action can be taken to facilitate the implementation of the IRA paradigm?

- Removal of non-scientific barriers including institutional/political/cultural.
- Removal of language/terminology barriers.
- Communicate to the international/scientific and risk assessment community the advantages of IRA *via* publications, conferences, etc. Scientific advisory committees can also be used to promote integration.
- Promote funding for targeted research of integrated risk assessment.
- Promote integration in educational institutions.
- Publish proceedings of this conference and completed case studies in peer-reviewed scientific literature.
- Develop a "real-life" case study that can be used in a practical situation, demonstrating the advantages of integrated risk assessment.
- Develop a guidance document on conducting integrated risk assessment.
- Develop a website which serves as a clearinghouse for information on integrated risk assessment.

7. Overview of Long-term Research Initiative (LRI)

Dr Rob Taalman, CEFIC, provided an overview of the Long-term Research Initiative (LRI). LRI sponsors global, generic research aimed at improving risk assessment methodologies and is a joint venture of CEFIC, ACC, and JCIA. Examples of activities which will provide better data for use in integrated risk assessment include:

- New test methods for persistence of chemicals in marine and soil environments.
- Conduct tests to determine whether freshwater data can be used as a surrogate for the marine environment.
- Establish database of workplace and consumer exposure.
- Develop an electronic platform with a complete set of risk models for both humans and the environment.
- For developing countries with limited resources, IRA will be a very valuable tool.
- Creation of closer, integrated work among human health and ecological scientists and analysts is needed. More integrated, cooperative work would not alone lead to short-term gains but to a more holistic view in general. A deeper, daily, working integration would greatly increase the chance of serendipitous recognition of problems for which evidence in any one sector is limited, but when all data are considered together, cause for concern may become evident.

8. Next Steps

Based on the recommendations of the Workshop, the following activities were identified to meet the objectives of the integrated risk assessment project:

- Revise generic framework based upon written/oral comments; including issues related to terminology.
- Revise case studies based upon discussions during Working Group "A". Focus should be on benefits, using the format of the case study on OPs as a prototype.
- Publish framework, case studies, and meeting procedures both as an internal WHO document and in the peer-reviewed scientific literature (potential journals include: Human and Experimental Toxicology; Journal of Risk Analysis; and Human and Ecological Risk Assessment).
- Develop an Executive Summary of the Workshop Proceedings and publish widely in journals, newsletters, and at scientific meetings.
- Develop an "integrated risk assessment" on an issue of high political visibility to demonstrate benefits.

9. General Discussions/Concluding Remarks

Dr Kröes and Dr Reiter closed the workshop with the following observations:

- Implementation of integrated risk assessment should be an evolutionary (not a revolutionary) process. Integrated, cooperative work will not only lead to short-term gains but to a more holistic view in general.
- Implementation can occur at three levels: 1) improved scientific data; 2) putting it into practice; and 3) acceptance at governmental levels.