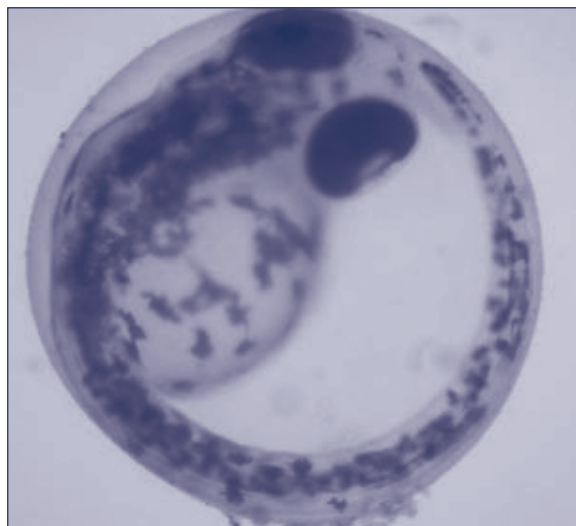




## Integrated Risk Assessment: Trendy Slogan or Conceptual Breakthrough?

### Endocrine disruptors provide a perfect test case

There are serious concerns about the incoherent approaches used in the risk assessment of chemicals. Ecological risk assessment has evolved largely in isolation from the framework applied to human risk assessment, and approaches can vary considerably depending on the effect profile of chemicals and the settings in which they occur. Known carcinogens are treated differently from other chemicals and the methods used, in e.g. occupational hygiene, are incompatible with those employed for environmental pollutants. Most methods follow a chemical-by-chemical assessment and largely ignore the effect of mixtures.



Zebra fish embryo, *Danio rerio* (30 h stage) studied as part of the SENSPESTI project to demonstrate whether cholinergic pesticides act as endocrine disruptors. Image: Carla Falugi.

Motivated by these concerns, an international expert group under the umbrella of the joint WHO/ UNEP/ILO International Programme on Chemical Safety (IPCS) published a paper, *Integrated Risk Assessment*<sup>1</sup>, which sets out to promote acceptance of an *integrated, holistic approach to risk assessment*. The paper outlines a generic framework that addresses real life situations of multichemical, multimedia, multiroute, and multispecies exposures. The vision is to integrate ecological and human health risk assessment, with the aim to provide more coherent inputs to decision-making processes.

### Common Concerns

In principle, the European Commission shares these concerns. In its communication on *A European Environment and Health Strategy*<sup>2</sup> of June 2003, the term *integrated approach* was adopted as a key element of future action. However, the scope for *integration* is even broader than in the WHO paper. It is meant to imply *integration of information* on the state of the environment and human health, *integrating research* on environment and health topics, *integration of environment and health concerns into other Community policies*, *integrated understanding of the cycle of pollutants* to identify the most efficient ways of exposure prevention, *integrated intervention* taking account of cost-effectiveness, ethical issues and questions of feasibility, as well as *integration of stakeholders* to ensure efficient implementation of the strategy. As part of the European strategy, an array of research projects has been embodied in the 5<sup>th</sup> and the 6<sup>th</sup> EU RTD Framework Programmes, outlined in the first CREDO newsletter by Tuomo Karjalainen and Kirsi Haavisto. These projects are expected to deliver the knowledge and the tools necessary for tackling all these complex issues properly. CREDO is viewed as being an integral part of this direct research support to policy.

*Integrated risk assessment* is a concept under construction. The term denotes a consensus on shortcomings of existing procedures and a common vision to achieve something that is better than the status quo by combining different lines of evidence. However, the road-map is far from being clear.

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*Commonalities* in pollutant sources, exposure routes, and some mechanisms of adverse effects provide a starting point for describing human health risk and ecological threats in an integrated manner. This is what the WHO paper propagates. *Differences* in toxicokinetics, toxicodynamics, assessment endpoints and protection goals of course provide a constant source of counterarguments. Thus, to reach a balanced judgement it is necessary to clarify where human and ecological risk assessment can really benefit from each other and where integration may only produce a counter-productive increase in complexity, time and costs.

The WHO expert group has highlighted benefits and obstacles of its holistic view by means of four explorative case studies on risks of persistent organic pollutants, organotin, organophosphorous pesticides and UV radiation. The experts concluded that much more in-depth research is needed with the aim to develop internationally accepted guidance on integrated risk assessment. In this context, work carried out in the CREDO cluster may have pilot character. There is no other field of research where the willingness and the need to co-operate across traditional borders between disciplines is greater than in the arena of endocrine disruption.

There is no other consortium providing a better assembly of the critical mass needed to achieve the ambitious goal of an integrated assessment. Moreover, CREDO cluster projects address important aspects of integration, e.g. the assessment of *combined effects* that may be expected to result from simultaneous exposure to multiple endocrine disruptors via multiple routes. Thus, endocrine disruptors provide a perfect test case for the pros and cons of the concept of integrated risk assessment. If it is really a conceptual breakthrough and not just a trendy slogan, this should be demonstrable for endocrine disrupting agents.

CREDO projects are expected to come up with some well-founded conclusions on whether and how effects of single and combined endocrine disruptors should be considered in an integrated risk assessment scheme for wildlife and humans. To achieve this goal, a structured approach to the issue should be outlined at an early stage. The CREDO cluster workshop on risk assessment<sup>3</sup> this March in Mallorca (31.03.04 - 01.04.04) should provide an opportunity to work on this topic in a productive atmosphere.

*Dr Andreas Kortenkamp, cluster coordinator*  
School of Pharmacy, University of London, UK

*Dr Michael Faust*  
Faust & Backhaus Environmental Consulting, Bremen,  
Germany

<sup>1</sup> Integrated Risk Assessment, report prepared for the WHO/UNEP/ILO International Programme on Chemical Safety, 2001, [www.who.int/pcs/emerg\\_site/integr\\_ra/ira\\_report.htm](http://www.who.int/pcs/emerg_site/integr_ra/ira_report.htm).

<sup>2</sup> A European Environment and Health Strategy, communication from the Commission to the Council, the European Parliament and the European Economic and Social Committee. COM (2003) 338 final, Brussels.

<sup>3</sup> See page 3 of this Newsletter for more information.

## Meeting report: International symposium on environmental endocrine disruptors

3-5<sup>th</sup> December 2003, Sendai, Japan

Since 1998, international symposia supported by the Ministry of the Environment, Government of Japan have encouraged researchers in and outside of Japan to share information on the initiatives being taken in dealing with endocrine disrupter (ED) related issues. A central objective of the 6<sup>th</sup> symposium was to discuss ED research needs and future directions through international co-operation.

With a programme open to the public that was also attended by press and TV, speakers provided an introduction to the current state of the ED issue from the standpoint of government, researchers, industry and educators. Endocrine disrupting chemicals are generally preferred in Japan to be called *environmental hormones*. In *Current Strategies against Environmental Endocrine Disruptors by the Ministry of the Environment, Government of Japan*, there are four pillars of the Japanese 'Strategic Programmes on Environmental Endocrine Disruptors' (SPEED '98): environmental monitoring; experimental research; risk assessment and work to strengthen international networks. Future themes to be promoted are environmental monitoring; technical development; international initiatives; risk communication as well as a review of the SPEED '98. In *The Role of Politics in ED Issues*, politicians discussed how politics has been involved in the issue of EDs and what will be expected of governments in the future. Emphasis was placed on risk communication to the public and the need to communicate the results of research to the public.

The two day programme for experts opened with an introduction to the current status of *Overseas Initiatives* in Europe and the USA, followed by sessions on *Basic Science, Wildlife, Exposure and Human Health*. Session 6, *Causal Criteria for Assessing EDs*, gave an overview of the criteria of temporality, strength of association, consistency, biological plausibility and evidence of recovery as used in the IPCS Global Assessment of the State-of-the-Science of Endocrine Disruptors. Debating use of causal criteria for assessing ED chemicals in the form of human and wildlife case studies, benefits of the causal framework were seen to be in focusing on hypothesis testing, providing objective criteria and helping in identification of research needs. However, uncertainties exist over scientific judgment and the weight of individual criteria. Further information on the presentations, including abstracts, is available at

[www.env.go.jp/chemi/end/sympo2003.html](http://www.env.go.jp/chemi/end/sympo2003.html)

## Multi-organic risk assessment of endocrine disrupters

31<sup>st</sup> March - 1<sup>st</sup> April 2004, Mallorca, Spain

Endocrine disrupting chemicals (EDCs) act not only on the reproductive system but also in a variety of other organs and tissues. There are several mechanisms by which EDCs can exert their effects. These include steroid receptor-mediated events in both reproductive and non-reproductive tissues. However, many effects of EDCs, such as disruption of steroidogenesis, can be traced to mechanisms independent of receptor activation. These and other issues must be considered when shaping integrated risk assessment strategies.

The objective of this international workshop organised by the EURISKED consortium is to integrate and disseminate state of the art knowledge relevant to the risk assessment of EDCs. Speakers from Europe and the US will exchange the latest results and review the evidence for a suspected common mode of action. The programme includes sessions on:

- Integrated Risk Assessment and the EU policy context (Session I)
- From humans to wildlife - Are there common modes of action for endocrine active chemicals? (Sessions II and III)
- Are there multi-organic effects of endocrine disrupters? (Session IV)
- Panel discussion with speakers (Session V) and poster sessions

Around 100 participants including representatives from the cluster and other EU funded projects, industry, delegates from the EU and chemical risk assessment experts from international organizations are expected to attend the workshop at the Hotel Barceló Albatros. Discussion of the latest results and cooperative research between partners within the cluster but also with scientists not belonging to the cluster, including industrial partners, are therefore the ultimate objectives of this workshop. Dissemination of workshop results will be through publication of proceedings in "*Toxicology*". The full programme and registration forms can be found on the EURISKED web site at

[www.eurisked.org/events.htm](http://www.eurisked.org/events.htm)

## Ecological relevance of chemically induced endocrine disruption in wildlife

5-7<sup>th</sup> July 2004, University of Exeter, United Kingdom

Human toxicology studies focus on the protection of the individual, but in ecotoxicology wildlife protection is directed principally at the population level. Nevertheless, assessments of chemical effects in wildlife are conducted at biochemical (biomarker), tissue and individual organism levels. Furthermore, most laboratory studies on chemical effects have been done on single chemicals, but wildlife is often exposed to complex mixtures that potentially have interactive effects. A wide range of endpoints for effects of endocrine active substances in wildlife species have been identified, but their ecological relevance are not yet fully understood. A major challenge for studies into endocrine disruption in wildlife is to better harmonise lab-based studies on chemicals and the endpoints used with effects occurring in wildlife populations.

The cluster workshop organised by COMPREDO and to be held at Exeter University, UK, will provide a forum for the dissemination, and discussion of, the most recent data on the ecological relevance of chemically induced endocrine disruption in wildlife. The principal aims of the workshop are as follows:

- To critically review the current international status of endocrine disruption in wildlife populations (Session I).
- To critically review the current inventory of endpoints used in biological effect monitoring studies and laboratory toxicity testing for endocrine disrupting chemicals and to identify appropriate endpoints for the assessment of wildlife population-level effects (Sessions II and III).
- To provide guidance and to suggest appropriate methods for the toxicity assessment of interactive effects of endocrine disrupters in complex mixtures (Session IV).
- To assess methods for risk assessment for endocrine disrupters and to identify future requirements for risk assessment strategies (Session V).

Attending the cluster workshop will be representatives from the four core CREDO projects, Environment Protection Agencies, Industry, the European Commission, NGOs and UK Government. There will also be key researchers in this field attending from Japan, and the US. Exeter University is located in the Southwest of England and is set in beautiful surroundings. Excursions will be run to provide those attending with the opportunity to get out and see some of the local wildlife too! Further details, including registration requirements are located at

[www.ex.ac.uk/emfb/workshop/](http://www.ex.ac.uk/emfb/workshop/)

## CREDO coordination

For further information and to be kept informed of developments within CREDO please contact:

Dr Andreas Kortenkamp  
andreas.kortenkamp@ulsop.ac.uk  
Tel/fax: +44 20 7753 5908

Dr Ragnor Pedersen  
ragnor.pedersen@ulsop.ac.uk  
Tel/fax: +44 20 7753 5811

Centre for Toxicology  
The School of Pharmacy  
University of London  
29-39 Brunswick Square  
London WC1N 1AX  
United Kingdom

### [www.credocluster.info](http://www.credocluster.info)

Contact at the European Commission:

Dr Tuomo Karjalainen  
Tuomo.Karjalainen@cec.eu.int

Dr Kirsi Haavisto  
Kirsi.Haavisto@cec.eu.int

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