World Health Organization

Second Meeting of the

# WHO CHEMICAL RISK ASSESSMENT NETWORK

20-22 June 2017
PARMA, ITALY


Hosted by

efsa
European Food Safety Authority

## ACKNOWLEDGEMENTS

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## Introduction

The WHO Chemical Risk Assessment Network ("the Network") is a voluntary collaborative initiative whose overall goal is to improve chemical risk assessment globally through facilitating sustainable interaction between institutions on chemical risk assessment issues and activities. The Network was established at the end of 2013 and now includes 85 institutions engaged in chemical risk assessment activities from 45 countries. The institutions in the Network consist of government departments, academia, WHO Collaborating Centres and professional societies. The Network held its first meeting in October 2014 in Paris, France (*http://www.who.int/entity/ipcs/network/meeting2014/en/index.html*) at which a number of initial Network activities were identified.

The second meeting of the Network took place from 20-22 June 2017 in Parma, Italy, hosted by the European Food Safety Authority (EFSA). The meeting was attended by 74 representatives from 63 Network institutions in 39 countries. The goal of the meeting was to review progress made since the first Network meeting in 2014 and to identify new activities and opportunities for collaboration.


## Welcome Address

Hans Verhagen, Head of EFSA's Risk Assessment and Scientific Assistance Department, welcomed attendees on behalf of EFSA. He introduced EFSA's mission, goals and values, noting that EFSA collaborates with approximately 1,500 European experts from governments, academic institutions and food safety agencies. He noted the multidisciplinary nature of EFSA's work, the high rate of change driven by new scientific knowledge, new risks and the ever increasing availability of data, combined with greater expectations for transparency and engagement. He emphasized the need to encourage consistency through harmonization of methods and through international collaboration.

## Meeting Arrangements

The agenda adopted by the meeting had been developed by the WHO/IPCS Secretariat, assisted by the Network Coordinating Group and informed by surveys completed by Network Participants. The meeting was arranged as a mixture of keynote lectures, plenary sessions and breakout group discussions over 2½ days. Posters describing the work of each institution were also displayed in the open area of the venue throughout the meeting and participants were able to consult the posters and informally network with other attendees during the meal and refreshment breaks. Attendees also received a USB key with the meeting presentations and documents, and also two page descriptions of the main Network activities which were intended to be shared with colleagues (these are reproduced as appendices in this report). The meeting was co-chaired by Raquel Duarte-Davidson of Public Health England and Chris Weis of NIEHS, USA.

# Risk Communication

*Summary of keynote presentation by Lucia de Luca, EFSA communication specialist, delivered 20 June 2017.*

**Lucia de Luca**, a communications specialist working at EFSA, delivered a keynote presentation titled "Risk Communication". The presentation covered why risk communication was an important part of risk assessment, the changing demands for communication of information as more sources of information become available and the key elements required to successfully bridge the gap between scientific knowledge and the information needs of stakeholders.


Lucia de Luca set out how an effective risk assessor also needs to be an effective risk communicator, and how failing to engage with the communications aspects of chemical risk assessment can lead to loss of credibility and failure to induce the desired outcome.

It was set out how risk communication has changed in recent years, from a one-way process of evidence being delivered by experts towards more of a conversation with the audience. The increasing challenges with time are that problems have become complex, with more data available and more sources of information (not always reliable). Yet at the same time there is much greater demand from audiences for more information, much more quickly, with greater transparency and reflecting uncertainties in a way which the (non-expert) audience can relate to.

If there is a demand for information, that demand will be filled by someone – how can we ensure that it is the message of the chemical risk assessor which comes across?

The key to building the bridge between scientists and the non-expert audience (which may include the risk managers and other stakeholders) is to understand the audience's perception, present information in a way the audience can relate to and to work to promote and disseminate a consistent message across all channels.

However, this will only be successful if there is trust, and trust needs to be built up in advance, by engaging with others, building relationships over time with key stakeholders so that you will be perceived as a trusted source of information when there are important messages to be delivered. This will include anticipating issues before they arise rather than always reacting afterwards.

It had to be recognised that audiences will not consider facts in isolation, but that culture, traditions etc. will affect how facts are perceived. People will perceive different risks in different ways, often being more concerned with unfamiliar risks and risks outside of their control than with familiar risks, regardless of which risk presents the greater threat of harm.

It is also necessary to consider new ways to present information (including via social media). Scientific issues become more complex but people will relate to complex information if it is presented clearly as concepts which they can understand, and the use of videos and infographics becomes increasingly important, whereas some traditional communication routes such as press releases become less effective.

Taking a multi-actor approach (coordinating communications between risk assessors, risk managers and stakeholders), building relationships over time to develop trust and presenting consistent messages in a clear and transparent way were identified as the keys to successful risk communication.

# Establishing the credibility of predictive toxicology approaches for regulatory safety assessment

*Summary of keynote presentation by Professor Maurice Whelan, European Commission's Joint Research Centre (JRC), delivered 21 June 2017.*

**Maurice Whelan**, a scientist at the European Commission's Joint Research Centre, delivered a keynote presentation titled "Establishing the credibility of predictive toxicology approaches for regulatory safety assessment".

Maurice Whelan described the role of the JRC and specifically the European Union Reference Laboratory for Alternatives to Animal Testing (EURL ECVAM) in assisting the EU to refine hazard and risk evaluation of chemicals. This was not just by developing and validating new methods and *in vitro* assays to directly replace animal tests, but through alternative testing strategies which were not necessarily directly linked only to predicting apical effects.

The new approaches were based on understanding mechanisms behind adverse health effects (biological perturbations), and bringing together multiple pieces of evidence to reach conclusions on mode of action information in an integrated weight-of-evidence approach. This approach moved the mode of action information to the centre of the decision process as essential information, rather than as optional additional information. It also brought together experimental work, computational methods and read-across principles as key information rather than each having separate roles.

In the EU, the development of alternative approaches had benefited from some key driving forces such as the ban in the EU on animal testing for cosmetics, significant research efforts (e.g. SEURAT-1), developments in concepts like Adverse Outcome Pathways (AOPs) and the desire to use read-across to fill information gaps in EU REACH.

The challenges for adoption of new approaches by decision-makers were highlighted. One challenge was achieving credibility, which requires sharing knowledge and understanding in a transparent way. The development of Integrated Approaches to Testing and Assessment (IATA) aimed to set out the approach which was taken in a clear and transparent way, and development of new reporting templates was needed to help to achieve this. Another challenge was characterizing the uncertainties in a systematic way. It was noted that conventional approaches also have many sources of uncertainty, but since they were more familiar they were more often accepted.

The concept of validation for new approaches was discussed. "Validation" meant different things to different people, and was more complex when applied to a combination of approaches. There was no clear benchmark for comparison since traditional "standard" toxicity tests were not necessarily 'validated' in any defined sense, and did not exist for all endpoints in any case. It could not be assumed that the animal tests were doing a good job – for example cases of skin allergy were still increasing in the human population.

A structured framework to present the evidence about mechanisms in a way that can be used in decision-making was needed, and AOPs were such a framework which needed to be widely shared and built upon to increase credibility (e.g. the AOP Knowledge Base led by OECD in collaboration with partners).

Follow-up discussion highlighted the fact that different regulatory sectors had different needs, and that the research community did not necessarily focus on regulatory needs. It was important to work with regulators and with risk managers, legislators and policy makers to ensure effective translation of research into regulatory use. Case studies would have an important role.

It was noted that as countries developed their regulatory systems, they could first adopt the protection goals they needed and then adopt the required methods, rather than necessarily replicate traditional approaches which had been used elsewhere.

# From Paris to Parma

*This session presented some activities which had been undertaken through the Network since the first meeting in 2014.*

**Virunya Bhat** (WHO Collaborating Centre on Water and Indoor Air Quality and Food Safety at NSF International) presented the outcome of the Network project on Chemical-Specific Adjustment Factors (CSAF).This project reviewed the use of CSAF since the publication of a guidance document by WHO in 2005. She described that many CSAF have been derived, or have been attempted, by regulators and in academic research and that they have most frequently focused on interspecies differences in toxicokinetics, often based on PBPK modelling. The results of the review have been published in a journal article.

*[see Appendix 3 – Chemical-Specific Adjustment Factors (CSAF) in chemical risk assessment]*

**Janine Ezendam** (WHO Collaborating Centre for Immunotoxicology and Allergic Hypersensitivity at RIVM) presented an ongoing Network activity to publish guidance on the methods available to assess the risks presented by engineered nanomaterials to the immune system. The increasing use of nanomaterials in occupational settings and in consumer products was noted. There is a potential for immunotoxic effects, but the current methods available to assess exposure and to identify immunotoxic effects from nanomaterials are not necessarily fit for purpose. An international group of experts had drafted a document intended for the Environmental Health Criteria series, and Network Participants were invited to provide peer review comments.

*[see Appendix 4 – Immunotoxicity associated with exposure to nanomaterials]*

**Jules de Kom** (Ministry of Health, Suriname) described the activities which had taken place since the 2014 Network meeting which had involved institutions in developing countries. The 2014 meeting had asked for capacity building activities specific to developing countries. A meeting of a sub-Network of developing country institutions was held in December 2015 in Bangkok, Thailand at which a number of potential projects had been identified. Since 2014 there has been increased involvement of developing country institutions in Network meetings (increasing from 9 in 2014 to more than 20 at the current meeting). There have been 13 training fellowships provided to Network Participants and two rounds of in-country training, both through the Chulabhorn Research Institute in Thailand. Further training fellowships and in-country training events were also planned for later in 2017. The electronic distance learning tool (eDLT) also continued to be promoted for use in capacity building. Jules also reported back from a meeting held the previous day at which the institutions from developing countries had agreed that the training courses made available so far were useful, requested more information be shared on tools which could be used in countries with limited resources and requested a coordination mechanism to assist with implementing Network projects.

The **WHO Secretariat** also provided information to the meeting on the levels of participation in Network activities since the 2014 Network meeting (40 institutions had participated in at least one activity, 18 institutions had participated in multiple activities) and also details of the scientific conferences and meetings at which the Network had been promoted.

## Capacity Building Strategy

A draft capacity building strategy for the Network was introduced by the WHO Secretariat. The draft strategy aimed to increase chemical risk assessment capacity in Network Participants, particularly in developing countries, and was intended to be the basis of capacity-building projects for the next 3 years. The strategy, its four proposed themes and possible actions under those themes were discussed in an interactive group session (world café format). The four themes were 1) promoting best chemical risk assessment practices, 2) developing human resources, 3) identifying technical resources and 4) identifying future risk assessment needs.

The following conclusions were reached.

- For promoting best chemical risk assessment practices the elements in the strategy were supported but it was noted that country-specific context was very important and that need assessments (for both developing and for developed countries) would be needed before specific plans were taken forward, and a community of practice approach should also be considered. Cross-discipline work was considered to be important, e.g. developing case studies for the same substance but across different matrices such as air, soil and water to show the differences in approach.
- For providing training the need to identify and respond to the needs of the target audience was emphasised, and also how to ensure acceptable quality standards. There was also a need to define what a successful outcome meant. It was noted that many institutions now make webinars available.
- For technical resources it was identified that a large number of substances of concern (and settings of concern) could be identified across countries, and also that a large number of toolkits, models and laboratories were available. A role for WHO in potentially providing directories of laboratories (by region) and the toolkits and models available was identified, distinguishing between those with costs for access and those freely available.
- For future risk assessment needs, the potential economic benefits from innovation and controlling associated risks as an incentive to invest in capacity building were highlighted. A large number of technical areas (e.g. computational skills) and resources (e.g. poisons centres) were identified as likely to be important for future risk assessment needs.
- More broadly, it was noted that mechanisms for greater interaction and sharing information were not set out in the strategy. A need for a collaborative workspace or even a social media type of platform for the Network was identified.

As part of the Capacity Building Strategy Discussion, Attendees worked in Groups to brainstorm ideas.

PANEL DISCUSSION

## Combined exposures and chemical mixtures

*This session discussed different aspects of the topic of combined exposures.*

The existing WHO tiered Framework was described by Bette Meek (University of Ottawa). The Network coordinating forum on this topic where several Network institutions share their experiences and identify areas for potential collaboration was described by Djien Liem (EFSA). A project being developed by the WHO European Office relating to chemicals in indoor air was described by WHO EURO staff member Irina Zastenskaya, and Jacob van Klaveren (RIVM) presented an introduction to the European Union project "EuroMix" which aims to develop test strategies for chemical mixtures. Titus Maswabi (University of Botswana) provided a developing country perspective on the difficulties of assessing the risks from combined exposures with only limited resources available. He noted the desire of scientists in developing countries to work alongside the developed countries to address this issue since developing countries were not exempt from exposures to mixtures of chemicals.

*[see Appendix 5 – Combined Exposures]*


**A new WHO publication**

"Chemical mixtures in source water and drinking-water"- was launched with a presentation by Bette Meek. The document, developed to support the WHO Guidelines on Drinking-Water Quality, is an example of the use of the tiered WHO framework for combined exposures, includes some case studies and provides practical recommendations to prioritise mixtures of chemicals for risk assessment and risk management.

PANEL DISCUSSION

## Human Biomonitoring – the role of the Network

Daam Settachan (WHO Collaborating Centre for Capacity Building and Research in Environmental Health Science and Toxicology at the Chulabhorn Research Institute) described a Network meeting on this topic held in 2016. Kathy Hughes (Existing Substances Risk Assessment Program, Health Canada) described the biomonitoring activities of Health Canada where they have several ongoing population health surveys which are used to inform risk assessment and risk management under their National Chemicals Management Plan and within their regulatory system for pesticides (to obtain additional information on non-occupational exposures). Andrea Richarz (EC Joint Research Centre) described the European Commission's IPCheM information platform for providing access to chemical occurrence data in Europe. Meeting participants also described biomonitoring initiatives in other countries, and it was indicated that there is interest in biomonitoring activities in both developed and developing countries. A particular concern of participants was in the ethical issues associated with starting biomonitoring activities, and there was interest in the recently published guidance on ethical issues from WHO.

PLENARY PRESENTATION

## Benchmark Dose (BMD)

The concept of the benchmark dose (BMD) was presented by Bernard Bottex of EFSA, and the development of technical guidance over time was described. A recent workshop in which EFSA and WHO collaborated concluded that there was broad agreement internationally with most aspects of BMD practice (e.g. transparent reporting, use of model averaging over single model analysis) but still some areas of diverse practice between countries and between agencies. There was a need for training and promotion of best practices, user friendly tools (e.g. the EFSA web-based tool) and improvements to toxicity testing to better suit BMD analyses.

EFSA and WHO proposed to initiate a "Community of Practice" for BMD modelling to share examples of BMD, including between institutions in the Network. This should assist harmonization of practice. This proposal was supported by Network Participants.

PLENARY PRESENTATION

## Systematic Review

Paul Whaley of Lancaster University presented an introduction to systematic review methods and gave examples of how methods developed in clinical medicine were being adapted for use in some chemical risk assessments. The value of systematic methods and when they should be used was described. It was noted that a group of authors from Network Institutions are developing a WHO publication on systematic review in chemical risk assessment as a high level framework to facilitate wider understanding and use of these methods. Webinars on this topic would continue to be delivered to Network Participants.

*[see Appendix 6 – Systematic Review in Chemical Risk Assessment]*

PLENARY PRESENTATION

## Introduction to Emerging Risks

Theo Vermeire of RIVM introduced this topic, giving examples of how new materials and new uses of chemicals can give rise to new risks in the occupational and consumer product sectors. A possible Network activity to identify new risks, e.g. by sharing expertise from existing surveillance schemes to evaluate and prioritize risks was described. Meeting participants noted that countries at all levels of resources could experience new risks, but what was considered a "new" risk could vary between countries – and experience from countries which had already managed a risk could be transferred to countries where the risk was new.

PLENARY PRESENTATION

## Interplay of WHO tools and methodologies for chemical risk assessment

Bette Meek of the University of Ottawa presented an overview of WHO work on chemical risk assessment methodologies over time, and developments more broadly in how risk assessments are conducted. Trends towards greater use of tiered approaches, focussed problem formulation, refined testing strategies and greater transparency were noted. The greater use of mechanistic information and using data or PBPK modelling to replace default values were now possible, but there were challenges in getting regulatory uptake. An overview of recent WHO tools and frameworks was presented (Mode of Action, Combined Exposures, CSAF, characterizing PBPK models, characterizing uncertainty). The challenge of informing regulators about developments within the scientific research community was highlighted. Meeting participants were invited to discuss what further guidance or communication materials were needed to facilitate uptake of new methodologies. During the discussion it was noted that the term "New Approach Methodologies" or NAMs was often applied to novel approaches which had been developed in recent years.[1] These new methodologies were by and large not covered by the existing IPCS guidance documents. Consideration could be given either to updating the existing documents (where applicable), or creating an additional IPCS document dedicated to the use of these methods in chemical risk assessment. It was suggested that a mapping and "application guide" showing how tools can be integrated to increase efficiency and reduce uncertainties/address variability in assessments could facilitate uptake of the tools.

*[see Appendix 7 – Mode of Action]*

1 Examples include novel (high-throughput) in vitro tests, in silico (computational) methods, "omics" techniques and concepts such as adverse outcome pathways (AOPs) within defined approaches such as Integrated Approaches to Testing and Assessment (IATA).


## Network operation and membership renewal

Betsy Galluzzo of MDB Inc. (supporting the WHO Secretariat through funding from NIEHS) presented the results of a survey of participants on how the Network was operating and whether or not and how their organization was benefitting from participating in the Network.

Most participants felt that they had benefitted from the Network and had shared Network information with their colleagues. Suggestions were made for what information should appear in the broadcast emails and Newsletters, and easier access to information on ongoing Network activities was requested. There was strong support for participating in regular training webinars.

The process for renewal of Network participation was explained by the WHO Secretariat. It was explained that the Network Terms of Reference set out an initial participation period of 4 years, and the first renewals would become due from January 2018. The renewal process would be similar to the initial application, with a form requesting details of areas of work undertaken by the institution, and also details of engagement with the Network. Renewals would be subject to review by WHO management, which would take account of the new 'Framework of engagement with non-State actors' (FENSA) which had been put in place by WHO. The renewal period would be 2 years. It was noted that this relatively short renewal period would present a work burden for Network Participants and a longer renewal period was requested.

# GROUP DISCUSSIONS

## Network activities

Potential Network activities were discussed in breakout groups, with the discussions divided according to the following four themes, each of which was supported by a background "thought-starter" paper:

1. Emerging Risks;
2. Interplay of Existing Methodologies;
3. New Science in Chemical Risk Assessment;
4. Prioritizing Chemicals and Settings of Concern for Risk Assessment.

Notes from the report back of these group discussions are presented in Appendix 8. Based on the outcome of the discussions, proposals for next steps for Network activities were presented to the meeting by the WHO Secretariat – see Next Steps next page.

## Network activities - Next Steps

*The WHO Secretariat summarised the plans for future activities which had received general support during the meeting as follows, and indicated that another meeting of the Network would take place within 3 years.*

| TOPIC | PROPOSED ACTIVITIES |
|---|---|
| Emerging risks | A workshop should be convened to identify priorities, map available systems and scope how a Network activity could be formulated. |
| Capacity Building | New training activities should be implemented in line with the new capacity building strategy, building on the successful training activities already undertaken and including providing access to information on training opportunities and hosting webinars for the Network. |
| Tools for prioritization of chemicals and settings of concern | Information on available tools should be collected, especially exposure assessment tools. A mechanism for sharing the results of using these tools should be explored. The ultimate objective would be to develop a user-friendly online tool, to test the tool in case studies and then offer training on the use of the tool and a platform to share the results. |
| New and alternative methods | Not a separate activity in itself, but as with other methodologies WHO would seek to raise awareness and share experiences to promote harmonized approaches, and develop training and case studies to help integrate the use of new methods along with existing methods. Incorporating new methods should be considered if IPCS guidance is updated. |
| Existing methods | Guidance on the existing methodologies which have been addressed by IPCS activities should be developed – for all levels of need. In addition to mapping the guidance available, decision-trees and protocols were needed for when to apply different methods, along with a platform for sharing assessments. Settings such as contaminated sites should be addressed as well as single substance assessments. |
| Human biomonitoring | WHO should keep the Network informed about developments in biomonitoring, and in particular on the ethical aspects for which WHO guidance was being developed. |
| Benchmark Dose (BMD) | WHO with Network members including EFSA should establish a Community of Practice on the use of benchmark dose modelling, to share assessments and provide a forum to resolve problem issues. The aim would be to achieve greater transparency and harmonization, to build capacity and to increase regulatory acceptance. |
| Immunotoxicity of nanomaterials | The Network will be invited to contribute to the peer review of this document before it is finalized for publication in the Environmental Health Criteria series. |
| Systematic review methods | The framework on systematic review in chemical risk assessment should be completed and further training webinars should be offered to the Network. Later, Network institutions could be invited to share experiences of using systematic review methods. |
| Other risk assessment methodology work | The Network coordinating fora for Mode of Action and for Combined Exposures should continue. The WHO Chemical Risk Assessment Toolkit should be enhanced and promoted as the basis for methodology work where possible. For example, case studies could be published alongside digital versions of the Toolkit. |
| International chemicals management policy | The Network has a potential role in international chemicals policy, e.g. the implementation of SAICM and the relevant Sustainable Development Goals (SDGs). The Network will contribute to the implementation of the WHO Road Map to enhance health sector engagement in SAICM.[2] |
| Fund raising | The Network should facilitate fund raising by Network institutions through assisting the development of joint funding proposals with increased chances of success for collaborative Network activities. |
| Collaborative working | A collaborative workspace should be developed for the Network to share information, share assessments and offer opportunities for more frequent interactions. Such a platform should help to build an enabling environment to take Network activities forward. |

2 http://www.who.int/ipcs/saicm/roadmap/en/

Meeting Document #1

20-22 June 2017

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## Second Meeting of the

# WHO CHEMICAL RISK ASSESSMENT NETWORK

## Agenda

| Time | Monday 19 June 2017 |
|---|---|
| | Training events and meeting for Network institutions from developing countries – see separate agenda |

| Time | Tuesday 20 June 2017 |
|---|---|
| **09:00 – 09:40** | Opening of meeting and welcome address;<br>Introduction and meeting goals from the WHO Secretariat |
| **09:40 – 10:30** | Keynote Presentation (Lucia de Luca, EFSA, Italy; "Risk Communication") |
| **10:30 – 11:00** | Refreshment break |
| **11:00 – 12:30** | From Paris to Parma: Presentation of Network activities 2014 to 2017 |
| **12:30 – 14:00** | Lunch break and 1st networking session based on institution posters |
| **14:00 – 14:30** | Capacity Building Strategy for the Network – Introduction |
| **14:30 – 16:00** | Discussion of Capacity Building Strategy – interactive group format (refreshment break at mid-point) |
| **16:00 – 17:00** | Thematic discussion of Combined Exposures and Chemical Mixtures |
| **17:00 – 17:50** | Challenges and Opportunities for Collaboration in Chemical Risk Assessment – moderated discussion |
| **17:50 – 18:00** | Outline of programme for Day 2 |

| Time | Wednesday 21 June 2017 |
|---|---|
| **09:00 – 10:00** | Keynote Presentation ( Maurice Whelan, Joint Research Centre, Italy; "Establishing the credibility of predictive toxicology approaches for regulatory safety assessment") |
| **10:00 – 10:30** | Follow up from group discussions on Capacity Building Strategy |
| **10:30 – 11:00** | Refreshment break |
| **11:00 – 12:00** | Human Biomonitoring – the role of the Network |
| **12:00 – 12:30** | Proposal for a Benchmark Dose (BMD) Community of Practice |
| **12:30 – 13:30** | Lunch break and 2nd networking session based on institution posters |
| **13:30 – 14:00** | Systematic Review in Chemical Risk Assessment |
| **14:00 – 14:20** | Introduction to Emerging Risks |
| **14:20 – 14:40** | Interplay of WHO tools and methodologies for Chemical Risk Assessment |
| **14:40 – 14:50** | Introduction to group discussion session on Network activities |
| **14:50 – 15:20** | Refreshment break |
| **15:20 – 17:30** | Group discussions on Network activities under four themes<br>1) Emerging risks; 2) Interplay of existing methodologies; 3) New science in chemical risk assessment; 4) Prioritizing chemicals and settings of concern for risk assessment |

| Time | Thursday 22 June 2017 |
|---|---|
| **9:00 – 10:30** | Report back from group discussions on Network activities |
| **10:30 – 11:00** | Refreshment break |
| **11:00 – 11:30** | Review of how the Network is operating |
| **11:30 – 12:10** | Membership renewal and administrative aspects |
| **12:10 – 12:40** | Next steps and proposals for future promotion of the Network |
| **12:40 – 13:00** | Wrap up and closing remarks |
| **13:00** | Close of meeting |



Meeting Document #3

20-22 June 2017

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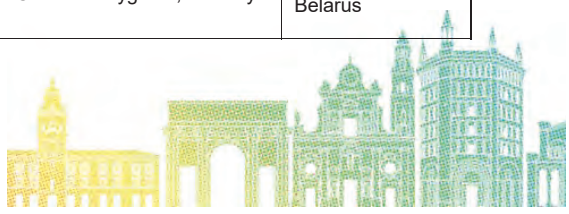
Second Meeting of the

# WHO CHEMICAL RISK ASSESSMENT NETWORK

**List of Meeting Participants**

| First name | Family / Last name | Network Participant | Country |
|---|---|---|---|
| Sam | Adu-Kumi | Environmental Protection Agency | Ghana |
| Ismayil N. | Afandiyev | Azerbaijan Medical University | Azerbaijan |
| Biljana | Antonijevic | Toxicological Risk Assessment Centre, Faculty of Pharmacy, University of Belgrade | Serbia |
| Tina | Bahadori | United States Environmental Protection Agency (EPA) | United States |
| Virunya | Bhat | WHO Collaborating Centre on Water and Indoor Air Quality and Food Safety at NSF International | United States |
| Kok Meng | Chan | Malaysian Society of Toxicology | Malaysia |
| Maya | Corminboeuf | Federal Office of Public Health | Switzerland |
| Pavel | Čupr | Research Centre for Toxic Compounds in the Environment (RECETOX) | Czech Republic |
| Amaia | de Ariño | ELIKA - Basque Foundation for Agrofood Safety | Spain |
| Jules | De Kom | Ministry of Health | Suriname |
| Hammadi | Dekhil | ANCSEP - National Agency of Sanitary and Environmental Control of Products | Tunisia |
| Lennart | Dock | Swedish Chemicals Agency (KEMI) | Sweden |
| Alena | Drazdova | Scientific Practical Centre of Hygiene, Ministry of Health | Belarus |



| First name | Family / Last name | Network Participant | Country |
|---|---|---|---|
| Raquel | Duarte- Davidson | Public Health England | United Kingdom |
| Janine | Ezendam | WHO Collaborating Centre for Immunotoxicology and Allergic Hypersensitivity | Netherlands |
| Elaine | Faustman | Institute for Risk Analysis and Risk Communication (IRARC), University of Washington | United States |
| Mary | Gulumian | WHO Collaborating Centre for Occupational Health at the National Institute for Occupational Health (NIOH) | South Africa |
| Ziva | Hamama | Public Health Services, Ministry of Health | Israel |
| Annika | Hanberg | Institute of Environmental Medicine, Karolinska Institutet | Sweden |
| Frank | Hearl | National Institute for Occupational Safety and Health | United States |
| Matthias | Herzler | BfR - German Federal Institute for Risk Assessment | Germany |
| Akihiko | Hirose | Biological Safety and Research Center, National Institute of Health Sciences | Japan |
| Kathy | Hughes | Existing Substances Risk Assessment Program, Health Canada | Canada |
| Myung-Sil | Hwang | National Institute of Food and Drug Safety Evaluation | Republic of Korea |
| Lívia Emi | Inumaru | ANVISA - Brazilian National Health Surveillance Agency | Brazil |
| Homa | Kashani | Institute for Environmental Research, Teheran University of Medical Sciences | Iran |
| Dinara | Kenessary | Human Health Risk Assessment Laboratory, Kazakh National Medical University | Kazakhstan |
| Hyun-Kyung | Kim | National Institute of Food and Drug Safety Evaluation | Republic of Korea |
| Djien | Liem | European Food Safety Authority (EFSA) | Italy |
| Ligia | Lindner Schreiner | ANVISA - Brazilian National Health Surveillance Agency | Brazil |
| Stefan | Mandic- Rajcevic | WHO Collaborating Centre for Occupational Health, International Centre for Rural Health | Italy |
| Samwel | Manyele | Government Chemist Laboratory Agency | United Republic of Tanzania |
| Carine | Marks | Tygerberg Poison Information Centre | South Africa |
| Titus Motswadi | Maswabi | Department of Environmental Health, University of Botswana | Botswana |

| First name | Family / Last name | Network Participant | Country |
|---|---|---|---|
| Bette | Meek | Institute of Population Health, University of Ottawa | Canada |
| Francesca | Metruccio | International Centre for Pesticides and Health Risk Prevention (ICPS) | Italy |
| Chung Sik | Min | National Institute of Food and Drug Safety Evaluation | Republic of Korea |
| Angelo | Moretto | International Centre for Pesticides and Health Risk Prevention (ICPS) | Italy |
| Akiyoshi | Nishikawa | Biological Safety and Research Center, National Institute of Health Sciences | Japan |
| Mattias | Öberg | Swedish Toxicology Sciences Research Center (Swetox) | Sweden |
| Kumiko | Ogawa | Biological Safety and Research Center, National Institute of Health Sciences | Japan |
| Kyi Lwin Oo | | Occupational and Environmental Health Division, Department of Health, Ministry of Health | Myanmar |
| Jean-Nicolas | Ormsby | ANSES - French Agency for Food, Environmental and Occupational Health & Safety | France |
| Lucija | Perharic | National Institute of Public Health | Slovenia |
| Ravichandran | | Regional Occupational Health Centre-Southern (ICMR), Bangalore | India |
| Federico | Rubino | WHO Collaborating Centre for Occupational Health, International Centre for Rural Health | Italy |
| Mathuros | Ruchirawat | WHO Collaborating Centre for Capacity Building and Research in Environmental Health Science and Toxicology at the Chulabhorn Research Institute (CRI) | Thailand |
| Clemens | Ruepert | WHO Collaborating Centre for Occupational and Environmental Epidemiology and Toxicology at IRET | Costa Rica |
| Hans | Sanderson | Aarhus University - Department of Environmental Science | Denmark |
| Tiina | Santonen | WHO Collaborating Centre for Occupational Health, Finnish Institute of Occupational Health | Finland |
| Jutamaad | Satayavivad | WHO Collaborating Centre for Capacity Building and Research in Environmental Health Science and Toxicology at the Chulabhorn Research Institute (CRI) | Thailand |
| Tamar | Schlekat | Society of Environmental Toxicology and Chemistry (SETAC) | United States |
| Golebaone | Senai | Environmental and Occupational Health Division, Chemical Management Unit, Ministry of Health | Botswana |

| First name | Family / Last name | Network Participant | Country |
|---|---|---|---|
| Daam | Settachan | WHO Collaborating Centre for Capacity Building and Research in Environmental Health Science and Toxicology at the Chulabhorn Research Institute (CRI) | Thailand |
| Nalinee | Sripaung | WHO Collaborating Centre for Occupational Health of the Bureau of Occupational and Environmental Diseases | Thailand |
| Inoka | Suraweera | Environmental and Occupational Health Directorate, Ministry of Health | Sri Lanka |
| Gheorghii | Turcanu | National Center of Public Health | Moldova |
| Mathieu | Valcke | Institut national de santé publique du Québec | Canada |
| Jakob | Van Klaveren | National Institute for Public Health and the Environment (RIVM) | Netherlands |
| Theo | Vermeire | National Institute for Public Health and the Environment (RIVM) | Netherlands |
| Angelique | Vickers | Pesticides Control Authority | Jamaica |
| Rachid | Wahabi | Environmental Health Department, Ministry of Health | Morocco |
| Karma | Wangdi | Department of Public Health of the Ministry of Health | Bhutan |
| Christopher | Weis | WHO Collaborating Centre for Environmental Health Sciences at the National Institute of Environmental Health Sciences (NIEHS) | United States |
| Paul | Whaley | Lancaster Environment Centre, Lancaster University | United Kingdom |
| Martin | Wilks | Swiss Centre for Applied Human Toxicology | Switzerland |
| Kunihiko | Yamazaki | Environmental Health Department, Ministry of the Environment | Japan |
| Ahmed- Chaouki | Zerouala | ANSES - French Agency for Food, Environmental and Occupational Health & Safety | France |
| Johanna | Zilliacus | Institute of Environmental Medicine, Karolinska Institutet | Sweden |

**Non-governmental organizations in Official Relations with WHO**

| First name | Family / Last name | Network Participant | Country |
|---|---|---|---|
| Emanuela | Corsini | International Union of Toxicology (IUTOX) | Italy |

**Observers**

| First name | Family / Last name | Organization | Country |
|---|---|---|---|
| George | Fotakis | European Chemicals Agency (ECHA) | Finland |
| Takahiro | Hasegawa | Organisation for Economic Co- operation and Development (OECD) | France |
| Andrea | Richarz | European Commission Joint Research Centre | Italy |
| Maurice | Whelan | European Commission Joint Research Centre | Italy |

**Secretariat**

| First name | Family / Last name | Organization | Country |
|---|---|---|---|
| Richard | Brown | World Health Organization HQ | Switzerland |
| Betsy | Galluzzo | MDB Inc. | United States |
| Kersten | Gutschmidt | World Health Organization HQ | Switzerland |
| Kurt | Straif | International Agency for Research on Cancer (IARC) | France |
| Philippe | Verger | World Health Organization HQ | Switzerland |
| Carolyn | Vickers | World Health Organization HQ | Switzerland |
| Irina | Zastenskaya | WHO European Centre for Environment and Health | Germany |

World Health Organization

## Review of the application of

# CHEMICAL-SPECIFIC ADJUSTMENT FACTORS (CSAF) IN CHEMICAL RISK ASSESSMENT

### What is a Chemical-Specific Adjustment Factor?

*When conducting quantitative risk assessments for environmental chemicals, a chemical-specific adjustment factor (CSAF) can be applied instead of more traditional, default uncertainty factors that are not based on chemical-specific data. CSAF methodology incorporates quantitative data on interspecies (i.e., animal to human) differences or human variability in either toxicokinetics or toxicodynamics (i.e., mode of action), which results in more informative, precise and confident human health risk estimates.*

### Project Description

This review was undertaken by a group of experts from institutions who participate in the WHO Chemical Risk Assessment Network. The CSAF Working Group identified and summarized CSAF examples that have been published since the 2005 WHO/IPCS Guidance on this topic. The review included CSAF that have been adopted by regulatory agencies, CSAF evaluated but not adopted (and the underlying reasons), and proposed CSAF not originating from a regulatory agency. More than 100 CSAF were identified illustrating the utility and evolution of CSAF in regulatory decisions. Challenges in CSAF development related to the adequacy of, or confidence in, the supporting data, including verification or validation of physiologically-based pharmacokinetic (PBPK) models. The analysis also identified issues related to adequacy of CSAF documentation, such as inconsistent definition and often limited and/or inconsistent reporting, of both supporting data and/or risk assessment context. Based on this analysis, recommendations for standardized terminology, documentation and relevant interdisciplinary research and engagement are included in the manuscript to facilitate the continuing evolution of CSAF development and guidance.

## Why is it important to Risk Assessment?

CSAF methodology promotes the use of chemical-specific toxicokinetic or toxicodynamic data to address interspecies differences and human variability when quantifying human health hazards from environmental chemical exposures. Compared to the use of traditional default or categorical uncertainty factors, CSAF methodology allows the risk assessment community and society as a whole to benefit from reduced uncertainty, increased confidence, and more accurate reflections of potential health risks associated with environmental chemical exposures.

## What can it be applied to/How can it be useful to me?

Whether you develop human health risk assessments or are a regulator that reviews risk assessments submitted for regulatory consideration, CSAF methodology helps reduce uncertainty and increase confidence in the risk assessment conclusions and potential regulatory decisions that may result. More specifically, the results of this CSAF project can help risk assessors and regulators determine what types of toxicokinetics and toxicodynamics data have been useful for CSAF derivation, how much data are adequate, and how to describe or report the data to facilitate interpretation. Notably, more than 100 CSAF examples are tabulated with respect to chemical of interest, CSAF subfactor(s) derived, CSAF subfactor value(s), regulatory context, and dose metric(s). Also included are examples and the underlying reasons when CSAF were considered but not adopted by regulatory agencies.

## Related Trainings

Scientific sessions on this topic were presented at the Society of Toxicology Annual Meeting in March 2017 in Baltimore, MD, USA and at the EUROTOX Annual Meeting in September 2016 in Seville, Spain.

## Additional Resources


- VS Bhat, B (M.E.) Meek, M Valcke, JC English, AR Boobis, and RJ Brown. Evolution of Chemical-Specific Adjustment Factors (CSAF) based on Recent International Experience; Increasing Utility and Facilitating Regulatory Acceptance. Critical Reviews in Toxicology. Bhat et al (2017) Critical Reviews in Toxicology vol. 47, Issue 9, pages 729-749.
- WHO/IPCS (International Programme on Chemical Safety). 2005. Chemical-Specific Adjustment Factors (CSAF) for Interspecies differences and human variability: Guidance Document for the Use of Data in Dose/Concentration-Response Assessment. (IPCS harmonization project document no. 2). WHO/IPCS/01.4, 1-96. Geneva, Switzerland. http://www.inchem.org/documents/harmproj/harmproj/harmproj2.pdf
- U.S. Environmental Protection Agency. 2014. Guidance for Applying Quantitative Data to Develop Data-Derived Extrapolation Factors for Interspecies and Intraspecies Extrapolation. Risk Assessment Forum. EPA/100/R-14/002F. Washington DC 20460.


### CONTACT INFORMATION


The CSAF Working Group lead is Virunya Bhat, Principal Toxicologist at NSF International, Michigan, USA, a World Health Organization Collaborating Center on Water and Indoor Air Quality and Food Safety. Contact via the WHO Secretariat at: ipcsmail@who.int.


World Health Organization

# IMMUNOTOXICITY ASSOCIATED WITH EXPOSURE TO NANOMATERIALS

## Why a project on Immunotoxicity Associated with Exposure to Nanomaterials?

*Nanoparticles interact with components of the immune system, more than with any other organ system in the body. At the same time, while there are many methods available for assessing the immunotoxicity of chemicals, the most appropriate approach for testing the toxicity to the immune system brought about by exposure to nanomaterials remains to be assessed.*

## Project Description

The objective of this project is to present the current state of the science of testing nanomaterials for immune system toxicity, and to design strategies for assessing the risk for immune-mediated health effects. The output will be a WHO publication in the Environmental Health Criteria series titled "***Principals and methods to assess the risk of immunotoxicity associated with exposure to nanomaterials***".

A group of subject matter experts was selected by WHO to draft the text of this publication. Up until 21 July 2017 the draft document is available for public and peer review on the WHO/IPCS web site at *www.who.int/ipcs* and Network Participants are invited to provide comments on the draft text. Following the comment period WHO will convene an expert meeting to finalize the publication, taking into account the comments received.

Following publication, presentations on the topic will be presented at Network meetings and scientific conferences. A webinar on the topic may also be offered to Network Participants.

## Why is it important to Risk Assessment?

Interaction of nanoparticles with the immune system has the potential to cause various consequences. This could include immune suppression - leading to reduced resistance to infections and neoplasms. Alternatively, inflammatory responses may be induced – leading to diseases associated with inflammation such as lung fibrosis, colitis, stimulation of respiratory allergy and allergic asthma, and facilitation of tumor formation. Despite the potential consequences, these potential effects of nanomaterials are not often tested for risk assessment purposes within regulatory frameworks, because it is not clear how best to achieve this. Appropriate testing strategies are needed which can be incorporated into regulatory frameworks in order to fill this gap in the risk assessment process

## What can it be applied to/How can it be useful to me?

When the publication is available it can be used to further the development of testing strategies and regulatory testing schemes can be updated to extend the scope for testing for potential harmful effects of nanomaterials on the immune system.

## Additional Resources

Existing resources for immunotoxicity testing:

- Harmonization Project Document No. 10: Guidance for immunotoxicity risk assessment for chemicals *http://www.who.int/entity/ipcs/methods/harmonization/areas/guidance_immunotoxicity.pdf?ua=1*
- EHC 180 on “Principles and Methods for Assessing Direct Immunotoxicity Associated with Exposure to Chemicals” *http://www.inchem.org/documents/ehc/ehc/ehc180.htm*
- EHC 212 on “Principles and Methods for Assessing Allergic Hypersensitization Associated with Exposure to Chemicals” *http://www.inchem.org/documents/ehc/ehc/ehc212.htm*
- EHC 236 on “Principles and Methods for Assessing Autoimmunity Associated with Exposure to Chemicals” *http://www.who.int/entity/ipcs/publications/ehc/ehc236.pdf?ua=1*

**CONTACT INFORMATION**

WHO Collaborating Centre for Immunotoxicology and Allergic Hypersensitivity, at the National Institute of Public Health and the Environment (RIVM), Bilthoven, the Netherlands. Contact via the WHO Secretariat at: ipcsmail@who.int

World Health Organization

# NETWORK COORDINATING GROUP ON COMBINED EXPOSURES

## What are Combined Exposures?

*In the risk assessment of chemicals, the classical approach is to assess the potential health risks of exposure to* single *chemicals through inhalation of air, dermal contact or ingestion of food. The principles and methods are well described in comprehensive guidance documents such as the Environmental Health Criteria 240 (WHO, 2009). An internationally harmonised approach for risk assessment of exposures to multiple chemicals via multiple routes (referred to as 'combined exposures'), however, is still in development, particularly because of the complexity of the problem formulation, the huge number of chemicals involved, and the toxicological profiles and exposure patterns of these chemicals in humans and species present in the environment. Developing a harmonized method for risk assessment of combined exposure to multiple chemicals has been identified as a key priority area by many risk assessment organisations and a number of collaborative research activities have been launched to support this development.*

## Network Activities

The creation of the Network Coordinating Group on Combined Exposures was decided at the first meeting of WHO's Chemical Risk Assessment Network in 2014 in Paris. The first meeting took place with 10 representatives of 9 different organisations (ANSES, BfR, ECETOC, ECHA, EFSA, OECD, University of Ottawa, USEPA and WHO) in September 2015 to discuss the terms of reference and to brainstorm about activities it could develop in relation to the Network needs. It was agreed that the group would start identifying other major groups active in this area, and by collating factsheets with summary information on combined exposure activities of participants to be shared with the wider WHO Chemical Risk Assessment Network. This would form a good starting point to seek out similarities or opportunities for cooperation between Group members and to identify a work plan that would provide added value to already ongoing activities.

At the meeting in March 2016, JRC and RIVM joined the group and a start was made to enable the participants to monitor the progress in ongoing case studies, reviews of methods, development of guidance documents and to follow the activities in the EUROMIX project[1] in which many active organisations are participating.

In the meeting of July 2016, EFSA and RIVM provided a report on a jointly organised workshop in May 2016 aimed at sharing information and to highlight innovations on toxicity testing for chemical mixtures. In addition, JRC provided some explanation about the outcome of its review of regulatory approaches and published combined exposure case studies.

1 Further details see https://www.euromixproject.eu/

At the November 2016 meeting, Professor Alan Boobis reported from discussions in the EUROMIX project on international harmonisation (workshops for risk assessors, risk managers and stakeholders in 2016-2017) and on aggregated exposure assessment (dermal, inhalation and food routes).

## Why is it important to Risk Assessment?

Through the years, faster and more sensitive technology has become available to identify the relevant constituents of a mixture to which humans are exposed. Besides, huge amounts of toxicity data can nowadays be generated using high-throughput *in vitro* systems and *in silico* systems. The current activities in the area of combined exposures will benefit from the application of such modern technology to generate new scientific knowledge, models and tools to predict the potential health risks of exposure to multiple chemicals via different routes with more accuracy, precision and certainty.

## How can it be useful to me?

It is clear that different sets of data, inconsistencies in the way we interpret chemical occurrence and toxicological data, may lead to different risk assessment outcomes which can be confusing for the risk manager, for stakeholders and the public at large. International cooperation is needed to achieve synergy by merging data and knowledge, by validating models and tools and by implementing a consistent and harmonized approach in our risk assessments.

## Additional Resources


- Bopp S, Berggren E, Kienzler A, van der Linden S, Worth A (2015). Scientific methodologies for the combined effects of chemicals – a survey and literature review; EUR 27471 EN; doi:10.2788/093511. *http://publications.jrc.ec.europa.eu/repository/bitstream/JRC97522/jrc_tech_rep_sci%20meth%20for%20mix_final.pdf*
- EFSA (European Food Safety Authority) (2013). International Framework Dealing with Human Risk Assessment of Combined Exposure to Multiple Chemicals. EFSA Journal 2013;11(7):3313, 69 pp. doi:10.2903/j.efsa.2013.3313 *https://www.efsa.europa.eu/en/efsajournal/pub/3313*
- EFSA Panel on Plant Protection Products and their Residues (PPR) (2014). Scientific Opinion on the identification of pesticides to be included in cumulative assessment groups on the basis of their toxicological profile (2014 update). EFSA Journal 2013;11(7):3293, 131 pp. doi:10.2903/j.efsa.2013.3293 *https://www.efsa.europa.eu/en/efsajournal/pub/3293*
- EuroMix. A tiered strategy for risk assessment of mixtures of multiple chemicals *https://www.euromixproject.eu/*
- Meek ME, Boobis AR, Crofton KM, Heinemeyer G, Raaij MV and Vickers C (2011). Risk assessment of combined exposure to multiple chemicals, A WHO/IPCS framework. Regulatory Toxicology and Pharmacology, 60, Supp 2, S1-S14. *http://www.sciencedirect.com/science/article/pii/S0273230011000638.*
- OECD (2011). WHO OECD ILSI/HESI International Workshop on Risk Assessment of Combined Exposures to Multiple Chemicals, Workshop Report. *http://www.oecd.org/officialdocuments/displaydocumentpdf/?cote=env/jm/mono%282011%2910&doclanguage=en* .
- SC (Scientific Committee on Consumer Safety Scientific Committee on Health and Environmental Risks and Scientific Committee on Emerging and Newly Identified Health Risks) (2011). Toxicity and Assessment of Chemical Mixtures. *http://ec.europa.eu/health/scientific_committees/environmental_risks/docs/scher_o_155.pdf.*
- US- EPA (U.S. Environmental Protection Agency) (2003). Framework for cumulative risk assessment. EPA/630/P-02/001F May 2003. *https://www.epa.gov/risk/framework-cumulative-risk-assessment*
- WHO: IPCS Workstream on the assessment of combined exposures to multiple chemicals, multiple project reports available at: *http://www.who.int/ipcs/methods/harmonization/areas/aggregate/en/.*



**CONTACT INFORMATION**

Contact via the WHO Secretariat at: ipcsmail@who.int


World Health Organization

# SYSTEMATIC REVIEW IN CHEMICAL RISK ASSESSMENT

## What is a systematic review?

Systematic review methods are a set of formal techniques and processes for identifying, appraising and aggregating existing evidence as it relates to answering a research question, intended to minimize risk of bias in synthesizing evidence, and maximize the usefulness and transparency of the results of the effort spent in conducting the systematic review.

## Project Description

The WHO Network Systematic Review Working Group is developing a systematic review framework on chemical risk assessment. This framework is intended to describe the critical components of a systematic review in a concise format, along with the advantages of using systematic review methods and when to consider using a systematic review to address a problem in chemical risk assessment.

The purpose is to provide guidance to chemical risk assessors who are not currently familiar with systematic review methods via a high-level overview without being prescriptive or endorsing any existing published systematic review method.

## Why is it important to Risk Assessment?

Challenges for toxicology practice and recent controversies about health risks posed by chemical substances have prompted the development of new approaches to apply systematic review principles to the field of toxicology and environmental health sciences. Systematic reviews support evidence-based decision-making in a timely, efficient, credible, and transparent manner. Due to the rigor of the methods used, well-conducted systematic reviews can provide high quality summaries of what existing evidence says in answer to questions about health risks from chemicals, with minimum risk that the answer will be biased. They allow decision makers and other stakeholders to see the evidence trail leading to the answer and provide insight into why there might be differences in opinion as to what that answer is.

## What can it be applied to/How can it be useful to me?

Systematic reviews can be helpful to use in the decision-making processes around cases of conflicting evidence or high uncertainty around a topic, sensitive topics of stakeholder concern, issues of critical health or environmental effects, or questions around significant economic consequences of regulatory action.

Several considerations must be deliberated before embarking on a systematic review, including the availability of time and resources to conduct the review, the necessary expertise necessary to conduct the review, and the acceptability of the review method and conclusions to decision makers and other stakeholders.

## Additional Resources


- Rooney AA, et. al. How credible are the study results? Evaluating and applying internal validity tools to literature-based assessments of environmental health hazards. *Environ Int.* 2016 Jul-Aug;92-93:617-29. doi: 10.1016/j.envint.2016.01.005. PubMed PMID: 26857180; PubMed Central PMCID: PMC4902751.
- Whaley P, et. al. Implementing systematic review techniques in chemical risk assessment: Challenges, opportunities and recommendations. *Environ Int.* 2016 Jul-Aug;92-93:556-64. doi: 10.1016/j.envint.2015.11.002. PubMed PMID: 26687863; PubMed Central PMCID: PMC4881816.
- Vandenberg LN, et. al. A proposed framework for the systematic review and integrated assessment (SYRINA) of endocrine disrupting chemicals. *Environ Health.* 2016 Jul 14;15(1):74. doi: 10.1186/s12940-016-0156-6. PubMed PMID: 27412149; PubMed Central PMCID: PMC4944316.
- Sheehan MC, Lam J. Use of Systematic Review and Meta-Analysis in Environmental Health Epidemiology: a Systematic Review and Comparison with Guidelines. *Curr Environ Health Rep.* 2015 Sep;2(3):272-83. doi: 10.1007/s40572-015-0062-z. Review. PubMed PMID: 26231504; PubMed Central PMCID: PMC4513215.


## Related Trainings/Tools

- HAWC, *Health Assessment Workspace Collaborative:* an online tool for literature screening, data extraction, and visualization. (*https://hawcproject.org/; https://github.com/shapiromatron/hawc; http://hawc.readthedocs.io/en/latest/* )
- Science in Risk Assessment and Policy (SciRAP) reliability criteria: a web-based reporting and evaluation resource developed to facilitate and increase the use of academic toxicity and ecotoxicity studies in regulatory assessment of chemicals. (*http://scirap.org/)*
- DistillerSR: Systematic review management software (*https://www.evidencepartners.com/products/distillersr-systematic-review-software/)*

### CONTACT INFORMATION


The Systematic Review Framework Working Group is lead by Christopher P. Weis, PhD, DABT, Toxicology Liaison and Senior Advisor at the WHO Collaborating Center at the National Institutes of Health/National Institute of Environmental Health Science, USA. Contact via the WHO Secretariat at: ipcsmail@who.int.


World Health Organization

# NETWORK COORDINATING GROUP ON MODE OF ACTION

## What is Mode of Action?

*Mode of action is a biologically plausible series of key events leading to an effect*

*WHO/IPCS has developed the Mode of Action Human Relevance Framework. The framework is based on the premise that any human health effect caused by exposure to an exogenous substance can be described by a series of causally linked biochemical or biological key events that result in a pathological or other disease outcome.*

*The Framework is a tool for Weight of Evidence analysis.*

## Network Activities

In 2001 the WHO/IPCS Conceptual Framework for Evaluating an (animal) Mode of Action for Chemical Carcinogenesis was published. This framework provided a generic approach to the principles commonly used for evaluating mode of action.

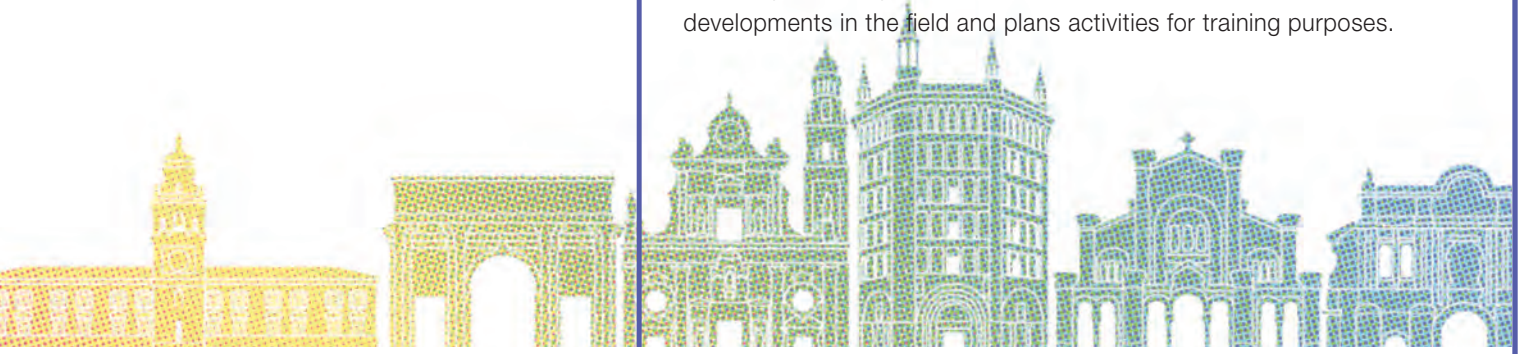
In 2006 the Harmonization Project completed work to extend the 2001 Framework to address the issue of human relevance. The WHO/IPCS "***Framework for Analysing the Relevance of a Cancer Mode of Action for Humans***", along with three case studies, was published in a Special Issue of Critical Reviews in Toxicology: Volume 36 (10).

Following development of the "***Framework for Analysing the Relevance of a Cancer Mode of Action for Humans***", WHO/IPCS decided to consider whether the framework for cancer could be applied to other end-points/modes of action.

Both the cancer and non-cancer frameworks have also been published in the Harmonization Project Series. In 2013 the WHO/IPCS frameworks were consolidated and updated, and published as "***New developments in the evolution and application of the WHO/IPCS framework on mode of action/species concordance analysis***".

The Mode of action Framework analysis templates have also be published at: *http://echa.europa.eu/documents/10162/13552/whoipcs_templates_for_mode_of_action_analysis_en.docx*

WHO/IPCS continues work on Mode of Action with representatives from Regulatory Agencies and Academia that follows-up developments in the field and plans activities for training purposes.



## Why is it important to Risk Assessment?

Mode of action analysis facilitates harmonization of risk assessment. Harmonization in this context refers to a biologically consistent approach to risk assessment for all endpoints, for which exploration of biological linkages is critical to ensuring maximal utility of relevant information.

Principles and concepts of mode of action analysis can be applied throughout human health risk assessment, with the extent of the analysis being tailored to the issue under consideration. Critical to this more tailored consideration of appropriate testing and assessment strategies is formal, transparent consultation with risk managers, with public accountability, where possible, for the relevant extent of resource investment to address the problem at hand (i.e., problem formulation).

## How can it be useful to me?

Mode of action analysis can used for hazard and risk assessment processes including qualitative and quantitative human relevance and variability (e.g., effects at various life stages and within susceptible subgroups), dose–response extrapolation and potential for combined effects of chemicals.

It can also be used to decide on hypothesis-based targeted testing or application of non-test methods to meet the objectives specified in problem formulation, including efficient grouping of chemicals and consideration of read-across, (Q)SAR modeling or appropriate testing within a category approach to fill data needs.

Mode of action can further inform research priorities relevant to the development of new test and non-test methods, biomarkers and expert systems that feed back to the risk assessment and therapeutic intervention strategies (for intoxication).

## Additional Resources


- WHO Mode of Action web page: *http://www.who.int/ipcs/methods/harmonization/areas/cancer/en/*
- Boobis, A. *et al* (2008). IPCS Framework for analyzing the relevance of a cancer mode of action for humans. Critical Reviews in Toxicology 36, (10). *http://www.tandfonline.com/doi/abs/10.1080/10408440600977677*
- Meek, M.E *et al* (2013). New developments in the evolution and application of the WHO/IPCS framework on mode of action/species concordance analysis. Journal of Applied Toxicology 34, (1), 1-18. *http://onlinelibrary.wiley.com/wol1/doi/10.1002/jat.2949/full*


**CONTACT INFORMATION**


Contact via the WHO Secretariat at: ipcsmail@who.int


# Appendix 8: Conclusions from the group discussions on Network activities

## 1. Emerging Risks

- The role of the Network should be to facilitate interaction between the diverse range of existing schemes and mechanisms
  - *Across different sectors (e.g. occupational, consumer)*
  - *Across different departments*
- There was a need to be clear about emergency/acute versus ongoing risks
  - *Poisons centres capture acute events*
  - *Low level signals are harder to capture*
  - *Incident coding systems are not used in developing countries*
- Need to establish priorities / where there is interest, and where there is scope to share best practices
  - *Surveillance versus Reactive systems versus Predictive systems*
- In principle the Network could play a role in interpretation of signals
  - *Avoid duplicating existing systems*
- Priorities should be:
  - *To hold a workshop of interested organizations*
  - *Map existing systems and determine priorities*
  - *Collect and share examples of best practices*

### Plenary discussion:

- Role of IHR (International Health Regulations)
  - *Focussed on acute events, but the requirement to have surveillance systems in place (as IHR-mandated core capacities) could increase capacity for surveillance of all types of event*
- There is more scope for poisons centres to work together between regions (WHO Network could have a role here)
- More poisons centres could be recruited to the Network.

## 2. Interplay of Existing Methodologies

- There is a need to inform people about what methodologies are available
  - *Map out what is available*
- Guidance needed on when to conduct a risk assessment
  - *Use already existing assessments?*
    - Create an indexed library of completed assessments to demonstrate the tools in use – "real practice" rather than "best practice"
  - *Does exposure data exist to allow an assessment?*
  - *Is the situation serious enough to move directly to risk management?*
- Need assistance to convince decision-makers that risk assessments are needed
  - *Assistance to communicate the economic benefits*
    - Government – to compare risks and costs
    - Companies - to demonstrate the benefit to the bottom line
- Promote the WHO Risk Assessment Toolkit
  - *Training to use the Toolkit*
  - *Flow diagrams or decision trees help*
  - *Share case studies*
  - *Share protocols (more novel approach)*
- Create a project to develop guidance to help risk assessors at different levels of need

### Plenary discussion:

- A library of completed assessments will tend to cover single substance assessments rather than situations such as contaminated sites where local conditions are important
  - *E.g. OECD eChemPortal is a search portal for single substance assessments*
- Countries could share assessments, but do not necessarily have time to provide translations.
- Guidance from KEMI on chemicals management aimed at developing countries will become available through UN Environment

## 3. New Science in Chemical Risk Assessment

- Exposure data is a significant data gap
  - *Opportunities for the Network to share data/aggregate data*
- Guidance on methodologies will need to be revised to reflect new science, or supplementary guidance will be needed
- Use case studies to make use of new methods attractive to risk assessors
  - *May need different case studies aimed at developing and developed countries*
- Network can create awareness of new science, and validate use of the new methods with capacity building based on case studies
- There are new opportunities for bioinformatics for example in epidemiological studies
- A challenge for training is the huge range in people's knowledge of new methods, can you teach new methods without understanding risk assessment basics first

- *At what point do "new" methods become part of basic understanding?*

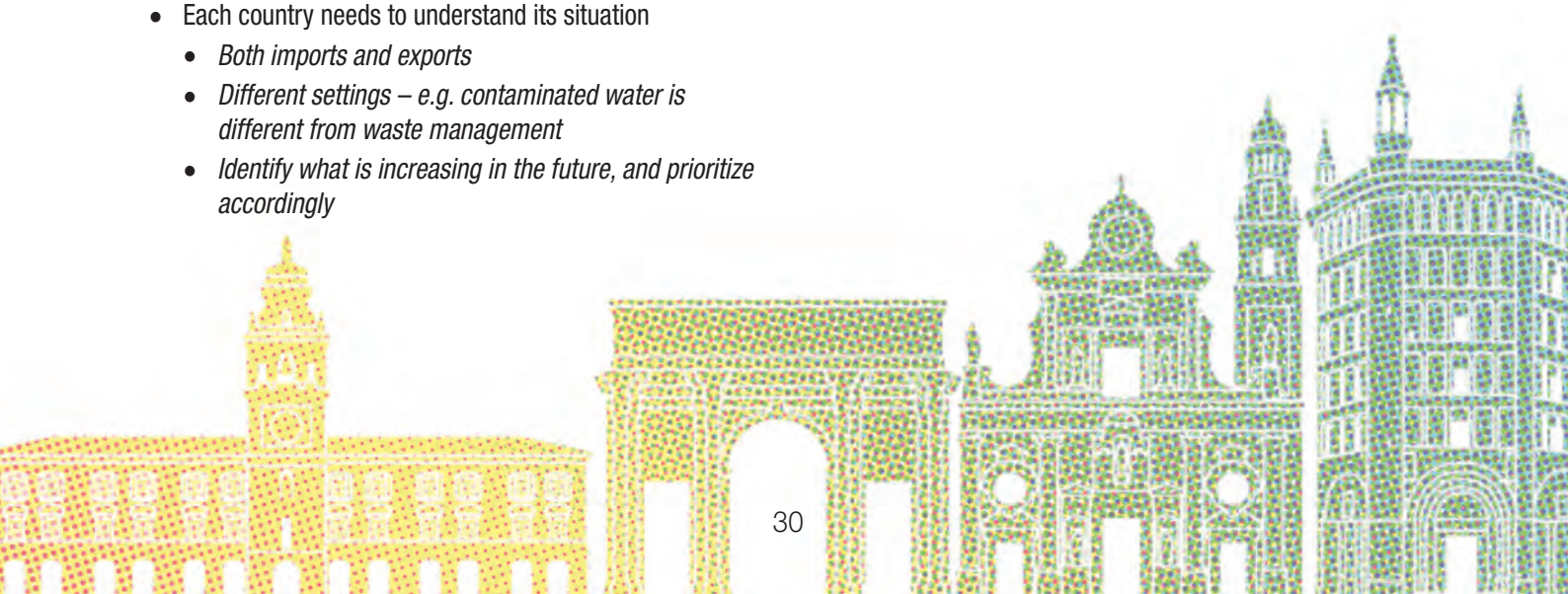
- OECD publications tend to be ahead of WHO publications for featuring alternative approaches – there is ongoing need to review and update WHO guidance
- New methods need to be standardized and in some way "validated" before gaining regulatory acceptance, but could address endpoints which are not easily addressed by traditional toxicology
  - *Many see new methods currently as complimentary approaches rather than replacements*
- Need to build stakeholder consensus
  - *Depends on understanding what information is needed*
  - *Affordability (not everything has to be gold standard)*
  - *Languages remain a barrier to gaining acceptance*
- Potential for the Network to:-
  - *develop a platform to share experiences (positive and negative experiences)*
  - *assist in getting agreement on terminology*
  - *provide pragmatic guidance*
  - *develop training e.g. university curricula tailored to answer the needs of regulators*

## 4. Prioritizing Chemicals and Settings of Concern for Risk Assessment

- There are some commonalities, but many country-specific and site-specific issues for communities
  - *common examples of chemicals of concern across many countries*
  - *likewise common settings of concern (e.g. mining, oil and gas, poor planning of cities)*
- Clear need for prioritization tools, and tools need to be tiered because countries are at different levels of development
- Tools should be user-friendly, rapid
  - *Provide training on the tools*
  - *Include within the WHO Risk Assessment Tookit?*
- Share the results of using the prioritization tools
- Each country needs to understand its situation
  - *Both imports and exports*
  - *Different settings – e.g. contaminated water is different from waste management*
  - *Identify what is increasing in the future, and prioritize accordingly*
- Online tools which are generic and which allow direct entry of data and as much automation as possible are more likely to be used than guidance documents
  - *Unless tools are rapid and easy to use at the lower tiers they will not be used*
    - A full risk assessment is not always necessary
- There is much more scope for refinement on exposure side rather than on toxicology side
  - *Tools to link emissions to exposure would be much less resource intensive than setting up biomonitoring programmes*
- Important to get participation and acceptance from affected populations and all stakeholders in order to get the approach accepted by society
- There is scope for sharing between countries of tools which can be applied across common problem chemicals
- Approaches to identifying common chemicals of concern should ideally be prospective as well, not just retrospective.

## Overall Plenary discussion

- All of the proposed areas for activities start with a need for prioritization, and require tiered approaches
- All tools need to be accompanied by training
  - *Case studies accompanied by step-by-step guides*
- To be effective the Network needs:
  - *A platform to share information and work collaboratively*
    - Use new technologies, shared facilities
    - Organize a centralized library of materials (virtual)
  - *Communities of Practice to share experiences*
  - *Champions to lead activities rather than rely on the Secretariat*
- The Network could act as vehicle to support fund raising for projects
  - *Projects need to be specific and show a clear benefit*



## FOR MORE INFORMATION

http://www.who.int/ipcs/network/en/ • ipcsmail@who.int