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INTARESE  
Integrated Assessment of Health Risks of Environmental Stressors in Europe

Integrated Project  
Thematic Priority

## D11 2<sup>nd</sup> Training Workshop

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**Internal Training Workshop**1<sup>st</sup> November 2006

Meeting Minutes

**Session 1 - The Assessment Methodology Purpose**

David Briggs opens the day and gives an overview of the program and the progress so far.

**WP1.1 - Integrated assessment framework Presentation and discussion of framework****Erik Lebret**

Erik explains how the INTARESE framework consists of several dimensions: the process (esp. issue framing), the full chain approach, the indicators and the appraisal rules. Within this area, it is important that everyone speaks a common language.

Presentation of results can greatly affect the perception of the risk. As an example, the presentation of the health risks potentially associated with electromagnetic fields illustrates how the same risk presented in different ways (compared to guideline values, policy aims, as absolute risk numbers, as relative risk numbers, as a monetary value, etc) can lead to different conclusions.

Several existing approaches, such as the Dutch Appraisal Framework, can be used to develop the INTARESE method. The framework should be a shared/common approach which could contain different methods. The same protocol can be used for different problems.

The *case studies* will help to further develop the framework. The case studies are the way to proceed and learn, but they are not the ultimate outcome of the project. That should be a framework that is specific enough to answer various policy questions, but also generalizable enough to be applicable to a variety of issues. The case studies are necessary to make the methods flexible and implementable in reality (because too often projects lead to methods which fail when used in reality).

**WP1.2 - Source-exposure Methodology for source-exposure analysis****Matti Jantunen**

Matti explained the use of empirical versus mechanistic models and that empirical models are data driven and results cannot be used outside the study area. He suggests using intake fractions (iF) to go from source to dose, because a strong feature of iF is the general applicability for different media. The use of iF is weak in local and short term situations, but is useful in general population and long term effect studies. iF can be used even when sources emit infrequently although for sources that emit with a low frequency other models should be applied. So, this general (simple) exposure model is, in principle, applicable for any source release, exposure pathway and route of entry. A general formula is given that could be used to calculate e.g. dose, and exposure.

$iF = \text{dilution} \times \text{temporal decay} \times \text{removal} \times \text{bioaccumulation} \times \text{intake}$

$\text{Dose} = \text{source emission} \times iF$

$\text{Exposure} = \text{source emission} \times \text{dilution} \times \text{temporal decay} \times \text{removal} \times \text{bioaccumulation}$

INTARESE is not going to recommend a specific model, but will link to advance models instead of having a default model for the user. The idea is that users can click on one of the parameters of the model and will be guided through the different options.

The question whether people in SP3 are skilled enough to operate these models was left for a later discussion. Since other models are more useful in other situations, the iF approach should be tuned with the methods developed in other SPs/WPs.



### Feedback from the Reviewers

The reviewers Prof. James Bridges and Prof. Stanislaw Tarkowski gave some considerations concerning the INTARESE project about 1) overall approach; 2) particular strengths; 3) areas where no time to understand sufficiently; 4) recommendations; 5) suggestions for further consideration; 6) issues for commission services.

1) *Overall approach* – INTARESE addresses a clear deficiency in current RA and decision making approaches. It is a very complex project with heavy demands making good use of available sources.

2) *Particular strengths* – High quality, broad disciplinary base, commitment. INTARESE has strong leadership. This project is largely meeting the agreed targets with impressive efforts to communicate. There is a common framework for activities of each WP and cross cutting to aid integration. The development of the toolbox is a primary deliverable. Another strength is the high quality and quantity of data available to date.

3) *Insufficient time to understand* – There was insufficient time for the reviewers to understand how INTARESE interacts with the Environmental Health Action Plan. How will mixed exposures be addressed? Furthermore, case histories are data rich, how will data poor case studies be dealt with?

4) *Recommendations* – It is important for INTARESE to speak a common language. Clear criteria for the adaptation/rejection of data should be used. Also clear criteria for the choice of case histories, chemicals, etc. There is a need to move resources within the project as the balance of priorities changes.

5) *Suggestions for further consideration* – Future case histories should not be chosen only on the basis of expertise but also I) added value approach; II) information/analysis sharing across SP; III) current as well as traditional issues. The means by which the cross cutting activities are embedded in the WP's require more strength. Another point of consideration is the linkage of INTARESE to the 6 and 7 programs.

6) *Issues for commission services* – A rather similar set of activities is needed for impacts on the environment. Exclusion of any consideration of food is not sensible for areas such as agricultural use, dioxin exposure etc. Flexibility in terms of how resources are used within the project is essential. Commission needs to be productive in linking related projects. Stan made the comment that it is important to have suggestions from INTARESE what other projects should contribute to INTARESE. Same conclusion from which areas it is important to know about projects and have some information. David mentioned that it is good to know about projects that have an interest in food since INTARESE has little expertise on foods.

### WP1.3 - Exposure-effect Methodology for exposure-health effect analysis

#### Gerard Hoek

Gerard presented the aim of WP1.3 (Develop general methods to use exposure – response functions and that can be applied to all kind of exposures that SP3 is dealing with) and what has been done so far in the work package. The content of a first draft manuscript was presented: 1. Methods for using exposure response functions were identified and 2. reviewed 3. Key problems were identified and possible solutions were given. At last a suggested methodology (if possible a systematic review + meta-analysis, if needed supplied with expert judgment) was identified.

Next Gerard elaborated a little bit on the use of exposure – response functions in Health Impact Assessments (HIA's). A HIA describes the whole chain of source – emission – concentration – exposure – internal dose – biological effective dose and biological effect. Problems with HIA's may be transparency of the approaches chosen, lack of a systematic approach, limited data in all parts of the source – effect chain and poor integration between disciplines. A wrong way to derive exposure – response functions is to use the IMBY principle (In My Back Yard) i.e. only your own results, or to use the so called 'best study' (which deals the best with your desired results), or to use the 'most significant' study. Best ways for deriving an exposure response function (ERF) are using existing, up-to-date, ERF's published by accepted organizations (like WHO), or in absence of such ERF's doing a systematic review (including a meta-analyses) of the literature. If there is a lack of published literature, consultation of an expert panel might be an option.

For the future a refinement of this approach is foreseen and the proposed focus is on assessing the possibility to integrate epi – tox study results, with a detailed characterization of the uncertainties in the derived exposure – response function.

### WP1.4 - Risk Characterisation Methodology for risk characterization

#### Jouni Tuomisto

Due to time constraints, Jouni focused on the 'INTARESE general method' and did not go into detail about other aspects of his WP.



The general approach should contain different aspects of different existing approaches. Based on what is currently available at KTL, USTUTT, the INTARESE 'car' could contain the following elements:

- an engine: the causal modelling (USTUTT)
- the causal chain (USTUTT)
- understanding of the impacts (RIVM)
- use of existing knowledge/ previous assessments (KTL, Pyrkilo)
- ways to steer the work and resolve disputes (KTL, Pyrkilo)
- stakeholder communication (KTL, Pyrkilo)

### **WP1.5 – Cross-cutting issues Managing uncertainty: sources, analysis methods etc.**

#### **Marco Martuzzi**

Marco showed an example to address the different issues in this WP like environmental justice/ethics (e.g. small minority of highly exposed children potentially subject to very large attributable risks), vulnerable group (children, others?), and uncertainty (assume causality, what model, no cost-effective measure possible, what is the question?).

#### **Martin Kraye von Krauss**

An overview of what is and why assess uncertainty was given by Martin Kraye. He explained that uncertainty is any departure from the unachievable ideal of complete determinism and given by a three dimensional concept of location, level and nature. Location of uncertainty (1<sup>st</sup> dimension) refers to the location of which the uncertainty manifests itself in the model. The level of uncertainty (2<sup>nd</sup> dimension) on a scale is represented by perfect knowledge, statistical uncertainty (known outcomes and probabilities), scenario uncertainty (known outcomes and unknown probabilities), recognized ignorance (unknown outcomes and probabilities), and finally total ignorance. Uncertainties are assessed to make different perspectives transparent and to help focus attention on the process through which decisions are made. At the end of his presentation Martin gave some implications for INTARESE. He underlined the enormous potential within the project: innovative risk assessment methods, key elements of a broader 'risk appraisal', and inclusion of stakeholders and concrete applications in case studies. On the other hand, however, some risks within INTARESE: few social scientists, few handshakes between partners, danger that we fall into the trap of producing ever more elegant and sophisticated quantitative assessments of risk and uncertainty, but fail to address the needs of our stakeholders. Finally, the take home message Martin gave was that uncertainty in RA is a concept reaching beyond the notions of statistics. Managing uncertainty is about assessment and governance improving the assessment of uncertainty and adapting decision-making processes.

## **Session 2 - Implications for Implementation**

David introduced the purposes of the afternoon session and asked everybody to consider everything you heard and to ask yourself what does it mean. For SP3 it is important to consider the implications for your WP and to give some clear messages back to SP1 to help them how to help you better. For SP2 the question is more what do you see in terms of data looking at problems or opportunities. Alena's interpretation for SP2 achievement was more in terms of what do we expect of the data, baseline criteria and how far can you go in applying methodology.

### **A. Parallel sessions: case studies (how to implement the methodology)**

#### **Water and Chemicals**

MarK Nieuwenhuijsen (IC) opens the session and explains that the purpose of the parallel session is to discuss the issues and problems encountered thus far. The session starts with household chemicals and a short introduction on this topic from Emilie Vermande (AFSSET)

Main items for **household chemicals** are:

- Integration of WP 3.4 (Water) and WP 3.5 (Household chemicals) in SP1 is desired, but not specified how;
- Data collection and data gaps → how to deal with missing data, confidentiality;
- Development of methodology and by whom (within WP 3.5 or from elsewhere);
- Uncertainties.



The approach of intake fractions explained by Matti Jantunen is not completely clear to everyone. Some people think that it will not be suitable for household chemicals because the focus is more on environmental stressors. Others think that the intake fraction model is applicable but the approach should be simplified. In WP3.5 aggregate exposure to multiple sources is of more interest so it remains questionable whether intake fraction model can be used. There are some reasons why the intake fraction model may not be useful:

- Global rather than specific;
- Lack of data;
- Most importantly: Fate of the chemicals is unknown. For instance in perfuming substances like limonene where the chemical reaction with ozone turned out to be most relevant. In short: formation of byproducts is very important!

The focus for household chemicals is on exposure and mainly on the complexity of exposure.

Marc introduces issues observed in WP3.4 on **water**:

- Disinfections in water, e.g. nitrates;
- Specific issue on time frames → health effects can not always be linked to exposures due to lag times, for instance with cancers (chronic exposure);
- Dose response is not always linear as observed in endocrine disrupting chemicals;
- Complex mixtures are observed in water, which may change significantly over time due to changing sources, developments/innovations;
- Generally work is performed with concentrations rather than with sources. These sources are also hard to describe because sometimes unknown;
- Terminology used.

### **Climate, Land and Waste**

First important issues for all three areas were assessed and thereafter discussed.

#### **Climate**

- Knowledge present about concentration response function;
- Sensitivity analyses;
- Involvement stakeholders not yet for climate;
- Not one dose-response function for different countries but groups or regions in Europe.

#### **Land**

- Dose-response;
- Combined exposure;
- Uncertainty;
- How to run the risk assessment for stakeholders.

#### **Waste**

- Role of stakeholders, stakeholders means interest. Profound implications will influence results;
- Exposure modeling is very recent business for waste and therefore difficult to find the appropriate data;
- Dose-response relationship. Assess whether there is a (causal) association. More guidance having done systematic review, what to do with conflicting evidence;
- Risk characterization part needs to be elaborated, more to understand

Some general issues coming out of this parallel session presented by Francesco Forastiere (ASL) during the feedback session:

- Involvement of stakeholder;
- Framework needs to be adapted - large gaps;
- Source-dose - in many cases sources are more important;
- Exposure-response – need to consider situations where hazard identification is still an issue and how to deal with complex exposures;
- Risk characterization – need more examples, more explicit about monetary evaluation;
- SP1-SP3 stable relationship, need to organize topical workshops;
- Criteria for case histories need development (variability, policy issues, technology issues, time frame, local value, generalizability).



### Transport and Housing

The session started with questions to WP1.2 and WP1.3. WP1.2 intends to provide tools such as exposure modeling tools and web based questionnaires which will help the user where and how to give input data. The tool will provide links to specific models to help the user but no default model will be given. WP1.3 will provide a document with the steps that need to be taken to perform the HIA. No default exposure-response functions (ERF) will be given, but a method to select the ERF that suits the case best. Next to the document an assistant will be provided to help the user with the application of the model.

A short overview of the ideas of WP3.1 Transport (Irene van Kamp) and WP3.2 Housing (Paul Wilkinson) is given. WP3.1 will focus on *road* transport and WP3.2 will focus on energy efficiency (temperature difference, ventilation, external emissions and cost issues). Since the methods of SP1 are in draft available the suggestion is made to workout a case in a modular form without worrying about the actual input. E.g. choose a 'normal' ERF for the 1<sup>st</sup> pass assessment, perform the HIA, see if the method works and if it does, go back and use a proper ERF as input. General conclusion is that WP3.1 and WP3.2 will provide a sketch of a HIA, and will put this on the website for SP1 to give recommendations and guidance.

## B. Parallel sessions: monitoring and surveillance

### Environmental monitoring

WP2.1 investigated data availability for network data and assessed the quality and comparability. A substantial amount of sites was classified as not comparable. However, when performing an HIA for a local situation the comparability between countries may not be a big issue and local data will be helpful. WP2.1 has a report available on the website.

The idea of WP2.1 is to provide background network data and *help* finding the local data. WP2.1 can help with comparing the quality and comparability of data gathered in different countries. The data that is evaluated will be put on the website, meaning not the data itself, but its availability. A useful suggestion is to link persons from WP2.1 who are involved in specific data (e.g. air pollution data) to the relevant WP in SP3 (e.g. WP3.1 transport).

David Briggs stressed that the job of SP2 is to assess what's needed for SP3 and sample the quality of that data instead of combining datasets over Europe.

### Biomonitoring

During this session chaired by Greet Schoeters (VITO) those present brainstormed about how biomonitoring data can be used for SP1 (assessment methodology), requirements to biomonitoring data and biomonitoring databases as well as limitations and gaps. Provided that good reference data from a EU wide biomonitoring network are available, biomonitoring data can be a very powerful tool for exposure and dose assessment (WP1.2 source-exposure). Biomarkers of exposure are real estimates of dose and can be used as dose estimates in dose-response functions (WP1.3 exposure-response). In addition, biomarker studies may give information on vulnerable subpopulations (WP1.5 cross cutting issues). Addressing mixtures, biomarkers may be a unique tool to measure effects of mixtures e.g. presence of pollutants with the same mode of action. However, this potential is not fully explored yet and in the coming years a lot is to be expected from biomarkers based on 'omics'. In reference to limitations *high quality data* of validated biomarkers are preferred but are not always available. *Time scale* is important (when to measure) and *kinetics of biomarkers* should be taken into consideration. Some other issues are *ethics* (how to communicate the results need attention) and *communication* (participants should be invited and informed which is very intensive but on the other hand raises also public awareness). A general remark is that biomarkers will be further developed, validated and used in the near future. The planned EU wide pilot project for human biomonitoring will offer (initially for a limited set of selected biomarkers of exposure) harmonized data for Europe. Although these data and biomarkers are not yet available, INTARESE should look at the future, anticipate on the availability of this new information and include it in the risk assessment framework concept that is under development. The following WP's from SP3 have expressed the need for obtaining biomarker data: waste, household chemicals, and transport.

### Health



Key issue: what do we need the data for in INTARESE?:

1. data gives background knowledge as reference
2. gives opportunities to do reality check of model outcomes
3. after interventions: evaluation of policy results (HIA)
4. calculate absolute numbers e.g. attributable deaths due to heat

We don't use data in INTARESE to calculate exposure-response relations. INTARESE will use existing relations only.

SP2 has to seek guidance from SP3 in data needs. Recommendations are welcome on yearly or daily data (what is available, what is best to use?)

Not only concentrate on morbidity and mortality data. Also e.g. medication use, surveys.

Overview of all available data in Europe from surveys would be very welcome. Also information on life-expectancy and macro-socio economic information would be useful.

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### **Implications on user needs**

Loredana Ghinea (Cefic) discussed the implications of earlier sessions for user perspective asking two questions 1) how does this match user needs and 2) what message can we take back to users? Concerning the first question it is of the utmost importance to speak a common language and know the differences in perspective of research and policy. The expectation is that INTARESE will create a framework for assessing complex issues considering all aspects involved and implications of specific decisions. The challenge for INTARESE is to clearly define the scope of integrated assessment and to deal with the need for simple messages and the reality of complex facts. An important message is that there will be different levels of satisfaction depending on what user you are. Finally, users' feedback is important as it will be the reality check.

### **Implications on toolbox design**

The main goals of SP4 are:

- To develop a toolbox for integrated assessment
- Provision of data, models, assessment methods, visualization and reporting techniques

Currently, the work in SP4 is confined to WP4.1 (active in first 12 months), which defines the functionality and designs the structure of the *integrated assessment toolbox* on the basis of the needs of users, available data, models and current technical capabilities.

Several meetings have been held, and a '*demonstrator*' has been developed and presented. This demonstrator is a *web-based tool* showing some potential of the toolbox. This toolbox will not be ready for SP3 WPs to use in their assessments, but input of SP3 work can be used in (further) development of the toolbox.

The deadline for the Consortium Requirements document (month 12) is too early (user needs etc need to be defined), so this deadline has been postponed to month 15. In the next phase, WP4.2 will take over and will start making the actual toolbox. A first version should be ready in month 30.

A remaining question: *how to get people to use the toolbox?* (esp outside INTARESE)

### **Summary and conclusions**

David thanks everybody for their presence and contribution to a fruitful meeting. Over the next few months there is a need for topical workshops in which we try to address some specific questions.

