

## FOSIE Third Plenary Meeting in Portugal: EC Concerted Action on Food Safety in Europe Establishes Conclusions on Risk Characterisation



Chairing the FOSIE Third Plenary Meeting, from left to right: Dr. Gunna Würtzen, Coca-Cola Nordic and Baltics (DK), Dr. Diane Benford, Food Standards Agency (UK), Drs. Ada Knaap, National Institute of Public Health and the Environment – RIVM (NL), Prof. Erik Dybing, Norwegian Institute of Public Health (N), and Prof. Bevan Moseley (UK).

The Third Plenary Meeting of the project Food Safety in Europe (FOSIE): The Risk Assessment of Chemicals in Food and Diet was organised by ILSI Europe in Lisbon, Portugal, 23–25 October 2002. This three-year programme is supported under the European Commission (EC) Fifth Framework Programme and has already resulted in a detailed report on the state of the art. The areas covered in this first report were: hazard identification by methods of animal-based toxicology; methods of *in vitro* toxicology; hazard characterisation of chemicals in food and diet: dose response, mechanisms and extrapolation issues; mathematical modelling and quantitative methods; assessment of intake from the diet and the contribution from

epidemiology (*Food and Chemical Toxicology*. 2002;40:137–427).

### The FOSIE programme

The FOSIE programme has been organised in Individual Theme Groups (ITGs A-G) for each area. At the Third Plenary Meeting, participants met in plenum with ITG G who had prepared an integrated report on characterisation and quantification of risk. In this, principles for hazard characterisation were combined with those for intake assessment. The ITGs form a collaborative multidisciplinary scientific network, primarily from Europe. The aim of the Third Plenary Meeting was to review, discuss and amend the integrated document prior to publication in a scientific journal.

(See FOSIE..., page 2)

## Announcement

### ILSI Europe Session on the Scientific Basis of Claims on Functional Foods, in the 9th European Nutrition Conference

1-4 October 2003, Rome, Italy

#### Background

Understanding the impact that changes in the food system have had on present and potential health of European people is a fantastic challenge that the 9th European Nutrition Conference would like to take. The conference has four major objectives:

- To assess nutrition-related health problems in Europe.
- To revise food patterns in Europe and their implications on health and the society.
- To evaluate different options in public health nutrition.
- To establish research needs in nutrition.

The conference will have plenary, parallel, and poster sessions on health and food and discuss science and applications. Scientists from different parts of Europe, as well as the various stakeholders in the European Food System, will be invited to contribute. Scientists involved in research projects funded under the EC Fifth Framework grant scheme will play a particular role.

#### ILSI Europe session

The ILSI Europe Functional Food Task Force will organise a session on the scientific basis of claims on functional foods. The session will cover the following topics:

- The rationale and scientific criteria for establishing health claims on functional foods.
- Claims for physical performance and fitness.
- Claims for mental state and performance.
- Overview of existing claims and regulatory frameworks in the EU and the world.

The session is scheduled for Thursday 2 October 2003, from 16.00 to 17.30 in Rome, Italy.

For further information, please consult the website: [www.fens2003.org](http://www.fens2003.org) ■



Pictured at the FOSIE dinner, from left to right: Prof. Ron Walker, University of Surrey (UK), Dr. Lutz Edler, German Cancer Research Center (D), and Dr. Juliane Kleiner, ILSI Europe (B).

(See FOSIE..., page 1)

### Plenary introduction

The third (and last) plenary meeting included partners in the Concerted Action and additional international experts were invited to ensure qualified discussion on all questions. Seventy-six participants attended the meeting and 22 countries were represented, in addition to the EU, Hungary and Poland, the meeting included experts from the USA, Canada, Russia, Australia, Singapore and Japan.

Prof. Erik Dybing, Norwegian Institute of Public Health (N), chaired the meeting. Introductory presentations were given in plenum. Dr. Juliane Kleiner presented an overview from ILSI Europe and the background of the FOSIE project, and Prof. Dybing presented the objectives of the workshop. Dr. Andrew Wadge, Food Standards Agency (UK), provided the risk manager's perspective and underlined the need for specific skills for risk communicators to ensure messages are understood by consumers. Dr. Maurice Smith, Unilever Research (NL), talked about "Setting the stage for risk characterisation (problem formulation, prior knowledge, basis for risk characterisation)" and described the risk characterisation process as concise,

clear logical steps, concluding with research needs that would support future developments.

Prof. Andrew Renwick, University of Southampton (UK), presented an overview of the concept of risk characterisation. It is an iterative process in which additional information would indicate re-evaluation. He underlined the importance of data on the extent and nature of exposure. Such information is needed for clarification on whether the hazard is

relevant to exposed persons. He also gave examples of the difficulties in communicating about risk because of the complexity of the data. A future task is the development of a mechanism for providing meaningful advice about uncertain outcomes. The presentation included the different approaches for threshold effects and non-threshold effects and indicated possibilities for future harmonisation by including probabilistic modelling.

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### The joint FAO/WHO project

The joint FAO/WHO project on updating the principles and methods for risk assessment of chemicals in food was presented by Dr. Samuel Page, World Health Organization (CH). This programme was established to provide mechanisms/rationales for harmonisation, to the extent possible, in view of processes developed by JECFA, JMPR and other scientific groups. It will build on previous work by IPCS, OECD, FOSIE, other ILSI projects, EC and national scientific risk assessment.

Dr. Achim Boenke, European Commission DG Research (EU), described the provisions for food quality and safety research under the Sixth Framework Programme, which includes epidemiology of food-related diseases and allergies, impact of food on health, safer and environmentally friendly production methods, impact of animal feed on human health and environmental health risk.

Finally, Dr. Angelika Tritscher, Nestlé (CH), provided information about the work programme for the meeting. The working groups were asked to review, discuss and amend the risk characterisation process from the perspective of the defined categories: (a) low-molecular weight chemicals,

(b) micronutrients and nutritional supplements, (c) macronutrients, and (d) whole foods. Novel foods should be included in one of these groups as appropriate.

### Montecarlo project

The final session included a presentation by Prof. Michael Gibney, Institute of European Food Studies (IRL), on the outcome of the EC Shared-Cost Project "Montecarlo". Within the Montecarlo project, seven organisations from five EU countries have developed conceptual models and databases for probabilistic

modelling of food chemical intake.

Actual data have been compiled on food intake and concentrations of chemicals in the food that were entered

into models to validate the modelling. The project will be completed by the end of January 2003, but a follow-up study funded by the Irish government will include development of a commercial product.

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### Conclusions

The last plenary session discussed the working group recommendations. The working groups were commended for their excellent work, commitment and enthusiasm for reporting back to plenum on both overall views for the structure of the final report and on more technical details. Their reports were compiled by ITG G and presented by Prof. Robert Kroes, IRAS-Utrecht University (NL), president of ILSI Europe and chair for ITG G.

The final report on risk characterisation has been submitted to *Food and Chemical Toxicology* for publication in January 2003. Other future publication opportunities include placement of the report on various websites on the Internet, including the ILSI Europe homepage. The previous FOSIE publication, *Food and Chemical Toxicology*, 2002;40:137–427, will also be available on Internet to allow potential readers easy access to the complete information.

The third FOSIE meeting concluded with a presentation by Dr. Boenke, who spoke about more information on food safety research under the Sixth Framework Programme, for which funding has been greatly increased in

comparison to previous programmes. The research will be addressed by end users such as the European Food Safety Authority. In this respect, he encouraged participants to build on the foundation established by FOSIE. ■



*Enjoying the FOSIE dinner in Lisbon, Dr. Andrew Renwick, University of Southampton (UK) (left) and Dr. Bette Meek, Health and Welfare Canada (CDN) (right).*

## Announcement

### ILSI Europe Session on Risk Assessment in Food at EUROTOX

28 September–1 October 2003, Florence, Italy

#### Background

EUROTOX is the association of European toxicologists and European toxicological societies. The purpose of EUROTOX and its annual congresses is to further develop the research and knowledge of toxicology at academic, industry, and government levels and to promote European research in the field of toxicology worldwide.

#### ILSI Europe session

The ILSI Europe Risk Assessment of Chemicals in Food and the Novel Food Task Forces will support a session on risk assessment in food at the EUROTOX 2003 conference, to be held on 28 September–1 October 2003 in Florence, Italy. The general principles for risk assessment for foods will be presented in three presentations on hazard identification/characterisation, on exposure assessment, and on risk characterisation.

Based on examples, an explanation of how these principles may be applied will be given for the various food situations, e.g. novel, whole foods, GMOs, and botanical preparations.

The presentations will reflect the findings of the EC Concerted Action on Food Safety in Europe (FOSIE) and the outcome of two ILSI Europe workshops on "Safety Assessment of Novel Foods and Concepts to Determine Their Safety in Use" (November 2002, Barcelona) and "Principles for the Safety Assessment of Botanicals and Botanical Preparations in Foods and Food Supplements" (May 2002, Marseille).

*For further information, please consult the website [www.eurotox.com](http://www.eurotox.com)* ■

# “Safety Assessment of Novel Foods and Concepts to Determine their Safety in Use” Discussed at Workshop in Barcelona

The safety of traditional foods and food ingredients and foods subjected to traditional processing technologies is usually assumed on the basis of historical safety practices. Where materials or technologies are introduced for the first time into the food chain, assurance of their safety in use must be derived by other means. Regulatory frameworks exist to ensure that novel foods and processes undergo an assessment before they enter the market place for the first time but, because of the nature of novel foods and ingredients, assessment of their safety in use often requires special consideration.

A draft guidance paper prepared by an expert group established under the auspices of the ILSI Europe Novel Food Task Force provided the basis for discussion at an ILSI Europe Workshop on the Safety Assessment of Novel Foods and Concepts to Determine Their Safety in Use held in Barcelona, Spain, 20-22 November 2002. More than 50 scientists from the fields of food technology, nutrition and toxicology participated. The workshop was chaired by Dr. Marianna Schauzu from the German Federal Institute of Risk Assessment (D) and co-chaired by Dr. Gareth Edwards, RHM Technology (UK). The aim of the workshop was to examine and provide the basis for further refinement of the principles elaborated in the draft guidance paper.

## Opening session

Following a brief opening session, the concepts discussed in the draft guidance paper were outlined to the workshop participants in a series of

presentations by members of the ILSI Europe Novel Food Expert Group. Dr. Andrew Cockburn, Monsanto (UK), made an introductory presentation on the concept of safety. He pointed out that the history of the human food supply has been one of continuous innovation with the introduction of “novel” food sources and production practices extending back over many millennia. Historically, attainment of an assurance of safety has been largely

through the pragmatic process of trial and error. In modern times, assurance of safety in general is sought through a formalised, science-based process of risk assessment. In the case of novel foods, this has led to categorisation by classes which lend

themselves to different methodological strategies, all of which nevertheless require a multidisciplinary approach.

The starting point in the risk assessment process is one that recognises that, while zero risk is unattainable, food should be safe and wholesome. The fact that traditional methods of testing as applied to simple chemicals have limitations which make them inappropriate to the testing of whole foods and complex mixtures has led to a comparative approach in which the objective is to ensure that a novel food is at least as safe and nutritious as the traditional foods it replaces. All the elements of a conventional risk assessment (hazard identification, hazard characterisation, exposure assessment and risk characterisation) must be

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addressed, but this should be done holistically, which gives full weight to compositional and historical considerations as well as the results of toxicological and nutritional studies, possible human studies and circumstances of use to arrive at a reasonable certainty that no harm will result under anticipated conditions of consumption.

## Presentations

Dr. Gunhild Kozianowski, Südzucker AG Mannheim/Ochsenfurt (D), described how primary evaluation and pre-test considerations contribute to the determination of safety in use of novel foods and Prof. Dietrich Knorr, Berlin University of Food Technology (D), presented the same in relation to novel processes.

Much of the information required during the primary evaluation and pre-test consideration may be readily available in the public domain while other information may need to be sourced by specific pre-test study. A detailed characterisation of the history and composition of novel foods and foods to which novel processes have been applied, together with an analysis of anticipated human exposure and a knowledge of their biochemical properties in relation to human digestive and metabolic processes allow the determination of an initial level of concern or presumption of safety.

A well-conducted primary evaluation on the basis of comprehensive pre-test considerations will allow a case-by-case-oriented determination of the necessary safety studies and of the composition of the material appropriate for such studies. Thus, it may reduce the reliance on, and the need for, toxicological testing. It

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Chairing the Novel Food workshop in Barcelona, Dr. Gareth Edwards, RHM Technology Ltd. (UK) and Dr. Marianna Schauzu, Federal Institute of Risk Assessment (D).

also allows the identification of data gaps for further research and it provides the basis for a definition (specification) of the material ultimately to be approved for marketing.

Dr. Irène Perrin, Nestlé (CH), presented the issues to be addressed by toxicological testing in the safety assessment of novel foods. The potential complexity and levels of ingestion of novel foods by humans lead to special considerations in terms of study design, the appropriate form of the material to be tested and the setting of test levels. The limitations imposed on conventional toxicological

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testing methodology by these considerations require careful use of pre-test considerations during the design of the testing programme to ensure that the information generated will be relevant to the product as marketed and used. Commonly, a 90-day feeding study may provide an adequate basis for a testing programme with further, targeted studies

depending on the level of concern from the pre-test considerations or biological effects observed but it will often be neither possible nor appropriate to aim at achieving a high safety margin with the intention of establishing an ADI. Ultimately, the results of any animal tests require careful interpretation in order to distinguish true toxicity from physiological adaptive or nutritional effects.

### **Animal studies on novel foods**

The nutritional considerations for the diets used in animal studies on novel foods were described by Dr. Morten Poulsen, Danish Veterinary and Food Administration (DK). In most cases, the aim will be to incorporate novel foods into the test animal diet at the highest level possible but this must be done without compromising the diet's nutritional adequacy.

To achieve this, detailed knowledge of the composition of the novel food will be required, including information on the type, content and bioavailability of micro- and macronutrients, and the presence of anti-nutritional factors and contaminants. The choice of type of diet may depend on the characteristics of the novel food to be tested and the ease with which test and control diets can be formulated to ensure nutritional

adequacy and comparability. Control and test diets should be formulated and manufactured individually.

Practical considerations include the desirability of establishing protocols and procedures for constructing diets that cover the specification of raw materials, the analysis of feed samples before use and the method of mixing the novel food into the diet. Finally, careful attention must be given to the stability of the diet during storage and feeding. Generally, it is not possible to be prescriptive about the detailed formulation and use of diets in animal studies – these must be determined on a case-by-case basis in the light of knowledge about the characteristics of the novel food to be tested.

### **Human studies**

Dr. Paul Hepburn, Unilever (UK), described how human studies contributing to the safety assessment of novel foods fall into two main categories: those conducted pre-launch and those conducted post-launch. Those performed pre-launch could be further categorised into controlled human studies and test marketing.

Although human studies should never replace other elements of a safety assessment programme, they can, among other things, provide confirmation of safety previously assessed by other means, demonstrate the nutritional quality of novel foods and confirm the validity of predictions relating to consumer usage patterns and intake. In these ways human studies provide a valuable, though not essential, element in the safety assurance process.

In describing how information generated during the investigations outlined by the previous speakers might be integrated to provide an assessment of safety in use, Dr. Edwards contrasted the characteristics of foods with those of chemicals for which traditional approaches to safety assessment have been developed. Differences in the inherent toxic potency, level of exposure and likelihood of nutritional effects generally mean that traditional approaches to

(See SAFETY..., page 6)



Participants at the Barcelona workshop, from left to right, front row: Dr. John Howlett, rapporteur (UK), Mrs. Irène Perrin, rapporteur, Nestec Ltd. (CH), and second row: Dr. John O'Brien, Groupe Danone (F), Prof. Ron Walker, University of Surrey (UK), and Dr. Gerrit Speijers, National Institute of Public Health and the Environment – RIVM (NL).

(See SAFETY..., page 5)

attaining assurance of safety in use cannot be applied to novel foods without modification. Furthermore the diverse nature of novel foods as a class requires that different approaches be

*differences in the inherent toxic potency, level of exposure and likelihood of nutritional effects generally mean that traditional approaches to attaining assurance of safety in use cannot be applied to novel foods without modification*

adopted for different categories of novel foods. Overall, the aim should be to establish a reasonable certainty of no harm through consideration of all available data, including comparisons with traditional counterparts where possible, and from the outcome that the highest identifiable safe level from any toxicological or human studies exceeds the estimated daily intake by consumers.

### Future possibilities

Dr. Ad Peijnenburg, RIKILT-DLO (NL), completed the presentation of the draft guidance document by outlining future possibilities for the application of newly developing methodologies to the safety assessment of novel foods. In particular, he highlighted the potential for “omics” technologies in the toxicological and nutritional assessment of whole foods, proteins and metabolites, and the development of appropriate methodologies for the assessment of allergenic potential of novel foods and their components.

On day 2 of the workshop, participants met in parallel working groups to consider in detail the texts on primary evaluation and pre-test considerations, toxicological and nutritional considerations in animal studies, human studies and assessment of safety in use. The ensuing lively

discussions were reported back to a plenary session on day 3 of the workshop for a concluding discussion. Generally, the draft guidance document was well received but many useful suggestions were made for additions and amendments. The

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guidance paper will be revised to reflect the best integration of the workshop’s discussions. Some issues to be resolved will be highlighted in the “future discussions” section of the document.

The revised guidance paper will be published in the *International Journal of Food Science and Nutrition* and in the *ILSI Europe Report Series*. ■

## Publication

### Article on Statistical Models for Food Allergenicity Testing Published in *Allergy*

The ILSI Europe Food Allergy Task Force initiated, in 2001, a paper to investigate whether a statistical model could be developed to estimate a "threshold" dose for foods eliciting allergic reactions in susceptible patients. The threshold dose is defined as one that elicits allergic reactions in a given (small) proportion of susceptible patients.

Based on data available from the literature, a preliminary statistical model was developed using the actual allergen

content in four foods, where data for allergen content are available (peanut, soy, egg, milk). The model demonstrated that the threshold doses giving a reaction of one in a million in susceptible patients were within the same order of magnitude for egg, milk and soy, but were an order of magnitude lower for peanut flour.

Although several assumptions were made in creating this statistical model (which needs further validation), it was demonstrated that the previously published differences in threshold doses for various foods can be largely eliminated by comparing actual allergen content; this may therefore serve as a model for further studies.



This article, written by Prof. C. Bindslev-Jensen *et al.*, was published in *Allergy* (2002;57:741-746). ■

*Free copies of the publications mentioned in this Newsletter are available from ILSI Europe upon written request (Fax: +32 2 762 00 44) or via e-mail (publications@ilsieurope.be).*

## ILSI Europe Task Forces in 2003

<i>Task Forces under the Scientific Committee on Nutrition</i>	<i>Responsible Staff Scientist</i>	<i>Task Forces under the Scientific Committee on Food Safety</i>	<i>Responsible Staff Scientist</i>
Addition of Nutrients to Food	Sonia Samartín Sandra Tuijtelaars	Acrylamide	Sandra Tuijtelaars
Alcohol	Daphne Pannemans*	Emerging Pathogens	Sandra Tuijtelaars
Antioxidants	Bernard Bottex	Environment and Health	Bernard Bottex
Dietary Carbohydrates	Daphne Pannemans*	Food Allergy	Juliane Kleiner*
Factors Affecting Hypertension	Daphne Pannemans*	Food Chemical Intake	Bernard Bottex
Functional Foods	Laura Contor Daphne Pannemans Sandra Tuijtelaars	Natural Toxins	Juliane Kleiner*
Health Science in European Countries in Transition	Onno Korver	Novel Foods	Bernard Bottex
Nutrition and Genetics	Daphne Pannemans*	Packaging Materials	Bernard Bottex
Nutrition and Mental Performance	Sonia Samartín Daphne Pannemans	Risk Analysis in Microbiology	Sandra Tuijtelaars
Nutritional Needs of Children	Sonia Samartín Daphne Pannemans	Risk Assessment of Chemicals in Food	Juliane Kleiner Sandra Tuijtelaars
Nutritional Value of Food	Sonia Samartín Daphne Pannemans	Risk Assessment for Genotoxic Carcinogens in Food	Juliane Kleiner
Nutrition and Immunity in Man	Sonia Samartín Daphne Pannemans	Threshold of Toxicological Concern	Juliane Kleiner
Nutrition and Public Health	Sonia Samartín Daphne Pannemans		
Oral Health	Daphne Pannemans*	Consumer Science	Onno Korver
Type 2 Diabetes	Daphne Pannemans*		

*\* with the assistance of Ir. Femke van Schothorst*

## Publications in brief

For many years, ILSI Japan has continuously disseminated translations of various ILSI Europe Concise Monographs. A new example is the excellent translation proposed by our Japanese colleagues of the recent ILSI Europe Concise Monograph "The Acceptable Daily Intake – A Tool for Ensuring Food Safety", into Japanese, making this concise monograph available to a wider audience. ■

## Special Announcement

Important information: The ILSI Europe workshop on Trichothecenes with a Special Focus on DON announced in our previous newsletter (*issue 48*) has been rescheduled to 10-12 September 2003 (previously 25-27 June 2003). Venue remains unchanged. ■

## Activities

### February 2003

- 06 Board of Directors
- 12 Type 2 Diabetes Task Force
- 19 ILSI Europe General Assembly Mini-workshop on "Combating Obesity Effectively", Limelette (B)
- 20 ILSI Europe General Assembly, Limelette (B)
- 28 Food Allergy Task Force

### March 2003

- 06 Acrylamide Task Force
- 11 Consumer Science Task Force
- 13 Nutritional Needs of Children Task Force
- 18 Oral Health Task Force
- 19 Dietary Carbohydrate Task Force
- 20-21 Workshop on "Structure-based Thresholds of Toxicological Concern: Guidance for Application to Substances Present at Low Levels in the Diet", Vienna (A)
- 21 Emerging Pathogen Task Force

### April 2003

- 01 Scientific Committee on Nutrition
- 04 Scientific Committee on Food Safety
- 09-11 Workshop on "Impact of Food Safety Objectives on Microbiological Food Safety Management", Marseille, (F)
- 16 Addition of Nutrient to Food Task Force
- 24 Alcohol Task Force
- 30 Risk Assessment of Chemicals in Food Task Force

### May 2003

- 08 Publications Committee
- 14-16 Nutritional Needs of Children Workshop on "Nutrition in Children and Adolescents in Europe: what is the scientific basis?", Rome (I)
- 21 Joint Scientific Advisory Committee/Board of Director Development Committee

### June 2003

- 03 Functional Food Task Force
- 12 Board of Directors
- 26 Health Science in European Countries in Transition Task Force

### July 2003

- 03 Natural Toxin Task Force

### September 2003

- 10-12 Workshop on "Trichothecenes with a Special Focus on DON", Dublin (IRL)
- 16-17 Mini-workshop on "Hypertension: Optimising Dietary and Lifestyle Factors", Brussels (B)
- 28 Sept.-1 Oct. Satellite Session at EUROTOX Conference, Florence (I)

### October 2003

- 01-04 Session on the Scientific Basis of Claims on Functional Foods, in the 9th European Nutrition Conference on Food Safety in Europe, Rome (I)



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