
Christine Lewis Taylor, PhD

Although adverse health effects resulting from excessive intake of nutrients have been studied for some time, nutrient risk assessment is only now gaining ground as a distinct discipline and emerging area of scientific study. Interest in such activities has been driven in part by the increased availability and marketing in all parts of the world of food/dietary supplements, fortified foods, so-called functional foods, and newer additions to the diet of nutrient-related substances. A number of diverse populations are currently “exposed to” (i.e., consuming) higher levels of nutrients and related substances than ever before. This observation raises questions concerning the impact of such intakes and the upper or safe levels of intake of these substances. For the purposes of the report described herein, upper levels of intake have been defined as: “the maximum level of habitual intake from all sources of a nutrient or related substance judged to be unlikely to lead to adverse health effects in humans.”

Key words: nutrient risk assessment, upper levels of intake, UL

© 2007 International Life Sciences Institute
doi: 10.1301/nr.2007.jan.31–38

INTRODUCTION

While nutrient risk assessment related to high levels of intake encompasses many activities beyond establishing an upper level of intake (UL), it is usually associated in the minds of many with this task. ULs serve the important purpose of providing a quantifiable demarcation for assessing risk and can provide critical assistance in the task of managing risk. It should be noted that risk associated with nutrients and related substances can in fact be of two types: risk resulting from too little intake and risk resulting from too much intake. The discussions that follow focus on the latter type of risk.

In 1996, the National Academies of Science’s Institute of Medicine (IOM) incorporated the identification of ULs and nutrient risk assessment into their process of establishing Dietary Reference Intakes (DRIs) for the United States and Canada. In addition to specifying Recommended Dietary Allowances (RDAs), Estimated Average Requirements (EARs), and at times the Adequate Intake (AI) for nutrients, the IOM has included ULs as a component of the DRIs. Moreover, nutrient risk assessment is carried out by the European Food Safety Authority as well as several national authorities as part of their food safety considerations.

The principles for nutrient risk assessment stem from those used to conduct risk assessment for non-nutrient substances such as food additives, contaminants, and pesticides. However, the physiological nature and role of nutrients and nutrient-related substances requires at times that nutrient risk assessment take into account different considerations than those used for non-nutrients. Recently, the Food and Agriculture Association of the United Nations (FAO) and the World Health Organization (WHO) undertook the task of identifying the general principles for nutrient risk assessment by convening an expert group of scientists who worked to develop an internationally applicable model. Their report is entitled “A Model for Establishing Upper Levels of Intake for Nutrients and Related Substances,” which I will refer to hereafter as the Report. While the Report contains detailed guidance on the nutrient risk assessment process, the discussion below is intended to only highlight key points.
BACKGROUND

Purpose of the Report

The Report, issued in early 2006, offers “scientific advice” regarding the conduct of nutrient risk assessment. FAO and WHO, as organizations within the United Nations, often provide scientific advice for use by member countries as well as for related programs such as the Codex Alimentarius. Codex was created in 1963 by FAO and WHO to develop food standards, guidelines, and related documents. The mission of Codex is to protect the health of consumers, to ensure fair trade practices in international food trade, and to promote coordination of all food standards work undertaken by international government and non-government organizations. Such work has included guidelines for vitamin and mineral food supplements, and Codex has requested that FAO and WHO address ULs for vitamins and minerals via a risk assessment approach.

While the ultimate goal for FAO and WHO is the establishment of internationally relevant ULs for nutrients and related substances as requested by Codex, such work could not be undertaken until an internationally applicable approach to nutrient risk assessment had been identified. A workshop of 18 scientists (see Appendix) met in May 2005 to outline such an approach. The assigned task was to specify a scientifically valid international “model” to establish ULs and conduct nutrient risk assessment. As a starting point, workshop participants considered the existing regional approaches for nutrient risk assessment and the principles established for non-nutrient risk assessment.

Conceptual Underpinnings

Differences Between Risk Assessment and Management

Those who have examined the process of risk analysis—which includes the components of risk assessment and risk management, as well as risk communication—have articulated the importance of ensuring that the activities of each do not inappropriately overlap. Risk assessment is sometimes described as “understanding,” while risk management is sometimes described as “action.” The assessment process is intended to provide scientific information for the management process, and is a set of activities that does not include policy decisions or the integration of societal concerns such as economic impact or the amount of risk that can be tolerated within the regulatory framework. For this reason, initial workshop deliberations included the distinctions between nutrient risk assessment and nutrient risk management (see Chapter 2 of the Report).

Differences Between Nutrients and Non-Nutrients Relevant to Risk Assessment

Nutrient substances are not well defined as a category, and regulatory provisions around the world vary as to the specific substances that may be regarded as nutritional. Some national/regional authorities may limit nutrient substances to only those demonstrated to be biologically essential relative to preventing well-characterized deficiency states. Others may define nutrient substances more broadly, including substances with a demonstrated favorable impact on health that may be distinguished from the state of biologically essential. Many include macronutrients that are inherent constituents of foods but not uniquely essential—for example, certain carbohydrates or fatty acids—but for which recommended intakes have been specified by public health authorities either as increased or decreased levels of intake so as to have a favorable impact on health. Those associated with recommendations to lower intake may present special challenges for nutrient risk assessment. For obvious reasons, no agreed-upon listing of nutrient and related substances exists.

Due to the possibility that nutrient substances can include a range of substances, the approach developed during the workshop was intended to be relevant both to substances that are biologically essential and to substances with a demonstrated health impact. The nutrient substances considered during the workshop are those that, because they are associated with identified levels of intake known to provide a “health benefit” on the basis of essentiality or impact on health, are consistent with the unique dual-curve relationship for risk associated with nutrient substances. This well-recognized schematic, shown in Figure 1, illustrates that increasing intake of the substance first reduces the risk associated with inadequate levels of intake (left curve), then moves to what some have described as a “range of safe intake” or “an acceptable range of intake.” Next, as intake continues to increase, the potential for risk from excess intake increases (right curve). These two separate intake-response

Figure 1. Dual curves for risk relationship: percentage of population at risk of “deficiency” and then “adverse health effects” as intake levels move from low to high.
curves are almost certainly associated with different mechanisms and pathways and are not (as perhaps mistakenly understood by some) a single “U-shaped” curve. Moreover, these curves often are shown as symmetrical, but in fact may have quite different shapes and degrees of steepness depending upon the nutrient substance and the subpopulation. Substances that demonstrate these qualities of dual risk should be addressed using a risk assessment approach that incorporates special considerations related to quantitative adjustments made for the purposes of correcting for uncertainty so that the nonsensical outcome that a UL is established at a value lower than the recommended intake associated with the prevention of deficiency.

Nutrient substances are also different because they demonstrate special homeostatic mechanisms, notably those nutrients that are biologically essential. That is, specific homeostatic mechanisms exist to regulate the acquisition, retention, storage, and excretion of certain nutrient substances. No doubt both the need for and nature of these nutrient-related homeostatic mechanisms are due to the unique dual risk that is posed by inadequate intake of an essential nutrient substance in one case and by excessive intake of the substance in the other, as described above. At the extremes, as the capacity of the homeostatic mechanisms is exceeded, the incidence of adverse health effects increases. These substance-unique homeostatic mechanisms make nutrient risk assessment very much case-by-case.

Moreover, because homeostatic mechanisms vary among age and sex groups and during certain stages of the life cycle (such as pregnancy or lactation), excess intake may manifest itself not only in different intake-response relationships, but also in different adverse health effects among these groups. For this reason, ULs are most appropriately established separately for each of the relevant age/sex/life stage groups. This is in contrast to the practice of expressing ULs on the basis of lifetime exposures or body weight, as may be established for non-nutrients.

Use of the ‘Four Steps’ Approach To Risk Assessment

In specifying the model, the workshop participants initially agreed that the four widely acknowledged steps of non-nutrient risk assessment were appropriate for nutrient risk assessment. These are:

1. Hazard Identification
2. Hazard Characterization
3. Exposure (or Intake) Assessment
4. Risk Characterization

Each step is associated with a set of activities. For example, the step of hazard characterization includes the specification of the UL. Risk characterization takes into account the level of exposure in the population of interest as derived from the exposure (or intake) assessment step, compares it with the UL, and then characterizes the risk for the population providing any mitigating or relevant scientific considerations. The risk manager uses this scientific information in making policy decisions about managing the risk; however, other information must also be taken into account.

**Harmonization**

One of the goals of an international model is to foster harmonization to the extent possible. In the case of a model for nutrient risk assessment, an important consideration is which of the outcomes of risk assessment can be harmonized. That is, is it possible for all of the components of nutrient risk assessment to be addressed globally, or are there some components that may be amenable to internationally consistent approaches and principles, but that produce different outcomes because they must take regional considerations into account? The nature of the data to be used for risk assessment makes it clear that there are globally relevant steps and population-specific steps.

Globally relevant steps in the nutrient risk assessment process are based on the available scientific/medical literature. These steps identify and interpret the biological, physiological, and chemical evidence for relationships between intake and the potential for harm to humans. By their nature, these data are relevant across wide and diverse populations. That is, they reflect science pertaining to humans regardless of their region of origin and they have global relevance and application. This global relevance does not, of course, preclude the possibility of subpopulation-specific hazard.

Other, population-specific steps use information on the population being targeted for risk assessment. This information includes data about the consumption of foods and supplements and about the composition of the food and supplements consumed—data used in the exposure/intake assessment step. The exposure/intake assessment is population relevant. That is, it is dependent on the types of foods and supplements consumed and on dietary patterns within a region or nation-state. Since risk characterization includes considerations of the globally relevant hazard characterization within the context of the exposure/intake assessment, risk characterization is also population relevant.

These differences relative to the four steps of risk assessment are depicted in Figure 2, where the outcomes of hazard identification and characterization, notably the UL, are shown as globally relevant. On the other hand, exposure/intake assessment and risk characterization produce outcomes that are population relevant. This means that risk characterizations can be inherently different depending upon the target population. This holds true even when the assessments are conducted in a consistent manner using internationally applicable guiding principles.
At the outset of the workshop, discussions took place regarding the applicability of evidence-based systematic review in nutrient risk assessment. The rating of study quality and the use of tables to summarize the data and the ratings were deemed highly useful and relevant to transparency. For these purposes, certain aspects of evidence-based systematic review were viewed as providing valuable techniques that enhance documentation and thereby transparency. Such techniques include a priori definitions for data searches, the use of summary tables, and ratings for individual studies. However, as currently practiced, other aspects of evidence-based systematic review, notably the kinds of questions it works to address, were generally viewed as not appropriately suited at this time to nutrient risk assessment in that the questions key to nutrient risk assessment are different from those for developing clinical practice guidelines or for identifying research needs. The workshop highlighted interest in adapting existing evidence-based systematic review approaches to make them applicable to nutrient risk assessment.

Data Gaps and Research Needs

An important agreement among participants was that the ability to address specific ULs for nutrients and related substances, as well as the ability to refine the model for doing so, is dependent upon targeted research to fill existing data gaps. As identified by the workshop participants, these research needs are myriad and critical (see Chapter 10 of the Report). They range from additional elucidation of biological mechanisms concerning nutrients and related substances to guidelines concerning data selection and review, and even to clarification of the types of information that would be most useful to risk managers. Considerable discussion was devoted to the need to identify and validate biomarkers of effect for adverse health effects associated with nutrients and related substances. It is impractical (and at times unethical) to rely on data related to the clinical manifestation of adverse health effects. Moreover, the use of biomarkers in setting the UL may offer a margin of safety relative to protecting public health, because biomarkers identify a situation in which metabolic dysfunction or abnormal gross features may not yet be present but, if left uncorrected, could result.

Given these conceptual underpinnings, the workshop participants worked to: 1) develop the essential components/characteristics of hazard identification and hazard characterization to provide for a uniform approach to these activities internationally, and 2) identify general principles for harmonizing the process (rather than the outcome) of exposure assessment and risk characterization, which by their nature vary from region to region because the relevant data vary from region to region. Risk characterization and application of the model were also addressed.

MAJOR COMPONENTS OF THE NUTRIENT RISK ASSESSMENT MODEL

Figure 3 illustrates the final model developed during the workshop and identifies key activities associated with each step of nutrient risk assessment. Problem formulation is conducted as a preliminary step to the four steps of risk assessment. Ideally, problem formulation is a dialogue among the key players and stakeholders, including the risk managers who will use the outcomes of the assessment and the assessors who will conduct it.

Hazard Identification and Characterization

The goals of nutrient hazard identification and characterization are to identify hazards and evaluate available data in order to establish ULs and to describe the nature of the hazard. The tasks include: 1) identifying adverse health effects associated with the intake; 2) selecting the critical adverse health effect that will serve as the basis for the UL; 3) deriving the UL after taking into account uncertainties; and 4) characterizing the nature of the hazard and specify vulnerable subpopulations.

These tasks are classically portrayed as two separate sequential steps of identification and characterization. However, during the workshop it was noted that nutrient hazard identification and characterization are better reflected as a closely linked, integrated activity performed for the most part as a single step—one that is iterative with refinements in data gathering and evaluation. Moreover, nutrient hazard identification and characterization, as well as nutrient risk assessment in general, are most useful when the approach to and results of an objective...
data review are clearly and adequately described and a detailed documentation is provided about the decisions made throughout the process.

**Combining and Evaluating Data**

The initial review of the available data and the development of a data set suitable for the hazard characterization pose challenges. One such challenge is the need to combine available data in order to establish the link between intake and a response. Although human data are preferable to animal data for establishing this link, in reality, human data for nutrient substances are limited. Human studies often fail to provide complete information on causal linkages, yet the risk assessment will need to rely upon a causally associated link. Combining information from human, animal, and in vitro studies can provide a more complete picture of the relationship between intake and adverse health effect. As a companion activity to combining data, the risk assessor needs to gather information that is relevant to interpreting the findings from the studies. In the likely event that this need for information could not be specified a priori, then the risk assessor would call for additional data searches as the process proceeds, underscoring the iterative nature of the data searches. The Report outlines approaches to identifying and selecting data and provides guidelines for conducting the initial review of data, such as rating data quality and the use of meta-analysis techniques (see Chapter 4 of the Report).

**Establishing the Upper Level of Intake**

After compiling and summarizing data pertaining to candidate adverse health effects, the process generally moves to the derivation of the UL. This activity is shown schematically in Figure 4.

**Selection of Critical Adverse Health Effect.** In order to establish a UL, a critical adverse health effect must be selected to serve as the basis for it. By definition, the “critical effect” is the adverse health effect(s) judged to be most appropriate for deriving the UL. Consistent with physiological and metabolic differences, different critical adverse health effects may be used for each age/sex/lifestage UL. For example, the UL for vitamin A in infants could be based on an effect associated with increased intracranial pressure, while that for pregnant women could be based on teratogenicity.

Adverse health effects can range from what may be considered “less serious,” such as osmotic diarrhea, to “more serious,” such as hypertension or liver damage. However, the severity of an effect does not always enter into the process for selecting the adverse effect used as
the basis for setting a UL. Rather, the workshop participants considered the goal to be the selection of the adverse health effect that occurs at the “intake of greatest concern.” The intent is to provide public health protection by maximizing the protection of the population. While at times the selected intake level may be one associated with the most sensitive members of the population or perhaps even with the steepest intake-response curve, in practice, it is likely to be the effect occurring at the lowest intake within the range of intakes investigated. Protecting people from the effects seen at the lowest intakes will also protect them from more serious effects seen only at higher intakes.

Although judgments concerning seriousness or even reversibility do not form the basis for selecting the critical adverse health effect, the overall hazard characterization should contain a description of the nature and health impact of different adverse health effects at different intakes and of related factors such as reversibility.

Intake-Response Analysis. An examination of the data available for the response or effect seen at a measured level of intake is carried out so as to describe the relationship between different levels of intake, the occurrence of an adverse health effect, and the changing impact of that effect (such as an increasing loss of renal tubular function as the intake increases). The intake-response relationship is a hallmark of hazard identification and characterization. It allows for the specification of a no observed adverse effect level (NOAEL), which is the highest intake of a nutrient at which the critical adverse health effect has not been observed. If data are not sufficient, then the lowest observed adverse effect level (LOAEL) is used. While it is possible to obtain data to bypass the use of NOAELs or LOAELs and instead establish a more precise benchmark intake (called by others a benchmark dose), such data are currently rare.

Correction for Uncertainty and Extrapolation to Unstudied Groups. The NOAEL or LOAEL cannot be used as the final value for the UL except in the unlikely situation that the value was derived from a large study that is truly representative of the exposed population and contains no uncertainties and negligible errors. Given that available data will contain uncertainties, risk assessment principles stipulate that the risk assessor must take these into account. Therefore, the NOAEL or LOAEL value is adjusted upward or downward in order to establish a UL. This process involves quantitative adjustments as well as the use of a composite uncertainty factor (see Chapter 4 of the Report). The Report points out that precautionary default corrections appropriate for non-nutrient substances pose a potential problem for nutrient substances in that the resulting UL could be a value that is below the intake required to ensure nutritional adequacy.

Data are scarce for many age/sex/life stage subpopulations other than adults. Therefore, although it is desirable to establish ULs based on data and end points relevant to the specific population group, it may be necessary to establish them by extrapolating from the adult value. Although an approach based on knowledge of differences in the metabolism, homeostatic mechanisms, and toxicokinetics between children and adults would be preferable, in the absence of such data appropriate scaling is needed. To adjust or “scale” adult ULs in order to estimate levels relevant to children, three possibilities exist: adjustment based on 1) the quantified reference body weight established for the age group; 2) body surface area, which is calculated using the reference body weight taken to the power of 0.66 (i.e., BW^{0.66}); or 3) energy requirement, which is sometimes referred to as metabolic body weight and is calculated using the reference body weight taken to the power of 0.75 (i.e., BW^{0.75}). Scaling according to basal metabolic rate, which is a function of metabolically active body mass, appears to be a more logical approach than scaling according to body weight (see Chapter 4 in the Report).

Hazard Characterization. At the final stages of nutrient hazard identification and characterization, the risk assessor characterizes the hazard by preparing a concise narrative that summarizes the conclusions reached and the basis for those conclusions, identifies vulnerable subgroups, and indicates other pertinent information about the hazards associated with the intake of the nutrient substance. The purpose of the narrative is to present scientific information in an organized way so that it can be used in the next steps of nutrient risk assessment.
Dietary Intake Assessment

By providing a quantitative estimate of the intake of a nutrient substance by the population of interest, dietary intake assessment provides the information needed to estimate the proportion of the population that is likely to exceed the UL. When combined with the UL and other information gleaned from hazard identification/characterization, the dietary intake assessment is essential to describing the risk associated with excessive intake. A major task of dietary intake assessment is to use data about the composition and the amounts of the dietary items consumed to estimate the total nutrient substance intake for the population of interest. The risk assessor compiles data, conducts analyses, makes the appropriate statistical adjustments, and then compares intakes with the UL.

Dietary consumption, which determines dietary intake of a nutrient substance, varies in different parts of the world for a wide range of environmental and cultural reasons. Thus, as discussed earlier, dietary intake assessment is population relevant rather than globally relevant, so the workshop participants worked toward identifying a harmonized process for conducting dietary intake assessment (i.e., they worked to identify methods and practices that can assist with harmonizing and improving the process for deriving the estimate).

The Report chapter focused on dietary intake assessment contains considerable in-depth discussions about the process of dietary intake assessment (see Chapter 5 of the Report). Using such a process would result in comparisons to the UL that are as accurate and relevant as possible. Specific topics covered include use and modification of composition data, techniques for maximizing the utility of available consumption data, and acceptable approaches to combining consumption data to estimate total intake. Because many regions in the world lack adequate data to readily conduct dietary intake assessment, strategies for dealing with this problem were outlined and included dealing with national food balance sheets or regional representative diets.

Risk Characterization

Nutrient risk characterization focuses on risk estimation and is the final step of nutrient risk assessment. It integrates the outcomes of the preceding steps to provide an estimation of risk for the specified population. It also provides descriptions of strengths and weaknesses of the estimates and other characterizing information about the risk. Furthermore, risk characterization outlines all key assumptions and gives a clear explanation of the uncertainties involved in the assessment. For example, when the risk assessment is based on animal data, the validity of such data needs to be specified and supported. Also, uncertainties associated with the extrapolation of data from studies in animals to predict human risk should be presented. Finally, scientific information should be specified on susceptible subpopulations, including those with greater potential exposure and/or specific physiological conditions or genetic factors.

To facilitate improved communication, the information for risk managers should be in the form most useful to them. The workshop participants saw value in developing either a standard approach to nutrient risk characterization and format for presentation of information, or at least an identified process to ensure that the risk characterization contains the needed components. Such an approach or process could help ensure that basic scientific components of nutrient risk characterization are addressed consistently, and it could help differentiate between risk assessment and risk management. In both cases, consideration should be given to the format and organization of the characterization. The Report identifies the key components of the scientific information needed to provide a nutrient risk characterization (see Chapter 6 of the Report).

APPLICABILITY OF THE MODEL

Regarding the model’s general applicability to the range of nutrient substances, the workshop participants noted that a very wide range of adverse health effects can be taken into account by the model; effects as diverse as cancer, heart disease, reduced kidney function, and liver toxicity can all be addressed. In short, the nature of the end point does not change the applicability of the model. While the ability to determine valid biomarkers for the end points of interest (e.g., cancer) may be challenging, once they are determined the model can be applied. However, the model’s apparent flexibility cannot be relied upon to readily address nutrient substances that do not demonstrate a threshold level for an adverse health effect or nutrient substances for which the levels of intake associated with risk appear to overlap with levels associated with biological essentiality or favorable impact on health. These situations require further study; the Report offers interim strategies (see Chapter 8 of the Report).

Regarding the model’s applicability to all populations, the workshop participants noted that nutrient risk assessment in general has recognized applications for populations that are both adequately nourished and “generally healthy.” These populations usually consume an array of fortified foods, formulated foods, so-called functional foods, and supplements. Existing models for nutrient risk assessment at the national/regional level have been developed consistent with the characteristics of such populations. However, not all populations that may receive such foods and supplements are adequately nourished and “generally healthy.” Certain populations in the
world and many subpopulations within adequately nourished populations may not be receiving adequate levels of nutrients, may be experiencing nutritional deficiencies, and may be in environments in which disease or other adverse conditions affect their metabolic states.

The workshop participants came to the conclusion that the appropriateness of a UL established for adequately nourished populations cannot be assumed to transfer to inadequately nourished populations. Although the basic process of nutrient risk assessment decision-making would remain the same regardless of the nutritional status of the population of interest, it is likely that inadequately nourished populations would need a different set of ULs because of important differences in metabolism and the vulnerability that can result from these differences. However, too little is known about the effects of inadequate nutrition on the absorption, distribution, metabolism, and elimination of nutrient substances to allow specification of considerations relevant to adjusting ULs to make them appropriate for inadequately nourished populations.

NEXT STEPS

FAO and WHO are currently working to create awareness for the Report and to discuss its utility with stakeholders. It would also be worthwhile to conduct targeted activities to enhance and refine the use of the model. These can be accomplished in several ways, including small case studies to explore aspects of nutrient risk assessment for certain representative nutrient substances. The studies and associated discussions could be carried out by involving a range of scientists and stakeholders, including representatives from industry, non-government organizations, and professional associations. The development of ULs, as requested of FAO/WHO by Codex, will require considerable resources, scientific expertise, and technical support. In the meantime, the harmonization of nutrient risk assessment would benefit from efforts to put in place ad hoc task forces among interested international parties. The goal would be to identify opportunities for coordination and further discussions.

REFERENCE


Appendix

List of Workshop Participants

Dr. Peter AGGETT, University of Central Lancashire, Preston, United Kingdom
Dr. Alicia CARRIQUIRY, Iowa State University, Ames, Iowa, USA
Dr. Namsoo CHANG, Ewha Woman’s University, Seoul, Republic of Korea
Dr. Margaret CHENEY, Ottawa, Ontario, Canada
Dr. Silvia COZZOLINO, Universidade de São Paulo, São Paulo, Brazil
Dr. Omar DARY, Guatemala (Arlington, Virginia, USA)
Dr. Cuthberto GARZA, Cornell University, New York, USA
Mrs Katharine GOURLIE, Ottawa, Ontario, Canada
Dr. Barry HALLIWELL, National University of Singapore, Singapore
Dr. Lena HULTHEN, Göteborg University, Göteborg, Sweden
Dr. Anna LARTEY, University of Ghana, Legon, Ghana
Dr. Barry HALLIWELL, National University of Singapore, Singapore
Dr. Lena HULTHEN, Göteborg University, Göteborg, Sweden
Dr. Anna LARTEY, University of Ghana, Legon, Ghana
Dr. Joseph LAU, Tufts - New England Medical Center, Boston, Massachusetts, USA
Dr. Jean-Charles LEBLANC, National Institute of Agronomical Research, French Food Safety Agency, Paris, France
Dr. Hildegard PRZYREMBEL, Federal Institute for Risk Assessment, Berlin, Germany
Dr. Andrew RENWICK, University of Southampton, Southampton, United Kingdom
Dr. Omid SABZEVARI, Tehran University of Medical Sciences, Tehran, Islamic Republic of Iran
Dr. Bhattiprolu SIVAKUMAR, National Institute of Nutrition, Hyderabad, India
Dr. Songsak SRIANUJATA, Mahidol University, Nakhonpathom, Thailand