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EURRECA—Framework for Aligning Micronutrient Recommendations

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EURRECA—Framework for Aligning Micronutrient Recommendations

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There is currently no standard approach for deriving micronutrient recommendations, and large variations exist across Europe, causing confusion among consumers, food producers, and policy makers. More aligned information could influence dietary behaviors and potentially lead to a healthier population. Funded by the European Commission, EURRECA (EUropean micronutrient RECommendations Aligned) has developed methods and applications to guide Nutrient Recommendation Setting Bodies through the process of setting micronutrient reference values. The EURRECA approach is crystallized into its framework that outlines a standard process for deriving and using dietary reference values for micronutrients in a transparent, systematic, and scientific way. The 9 activities of the framework can be clustered into four stages (i) defining the problem, (ii) monitoring and evaluating, (iii) deriving dietary reference values, and (iv) using dietary reference values in policy making. The EURRECA framework should not be interpreted as a prescriptive description of a linear process, but as a structured guide for checking that all issues essential for deriving requirements have at least been considered.

Keywords Micronutrient, recommendations, framework, Europe, dietary reference values, transparency

INTRODUCTION

Micronutrient recommendations represent the intakes of micronutrient judged sufficient to meet the requirements of the majority of healthy individuals within a population group (Pavlovic et al., 2007). Recommendations serve as a basis for national and/or regional nutrition policies, by addressing the evaluation and planning of intake as well as regulatory affairs. There is currently no standard approach for deriving micronutrient recommendations, and large variations exist across Europe, causing confusion among consumers, food producers, and policy makers. More aligned information could influence dietary behaviors and potentially lead to a healthier population.

The need for the alignment of the procedures used to derive micronutrient recommendations across Europe was recognized by the European Commission's Directorate General for Research which funded the EURRECA Network of Excellence (NoE), with a starting date of 1 January 2007, within its sixth

framework programme. EURRECA stands for "EUropean micronutrient RECommendations Aligned." Coordinated by ILSI Europe, the Network includes 38 partners comprising more than 200 individual scientists from 17 European countries, with a budget of €13.2 million spread over 5.5 years (2007–2012) (Figure 1).

EURRECA identified and developed methodologies (methods and potential applications) toward a uniform, transparent, and evidence-based process of derivation of micronutrient recommendations for all population groups (Ashwell et al., 2008; Pijls et al., 2009; Matthys et al., 2010; Matthys et al., 2011). EURRECA also explored the area of individual variability, for example, effects of polymorphisms on micronutrient metabolism, metabolomics, and elucidation of biological networks, to better understand the interplay between micronutrients and health at an individual level (van Ommen et al., 2010; Bouwman et al., 2012). EURRECA has identified ways of applying the scientific evidence into policy (Timotijevic et al., 2011; Timotijevic et al., 2013).

This introductory article provides the background and purpose of the EURRECA NoE and mentions its outcomes as described in the current issue of Critical Reviews in Food Science

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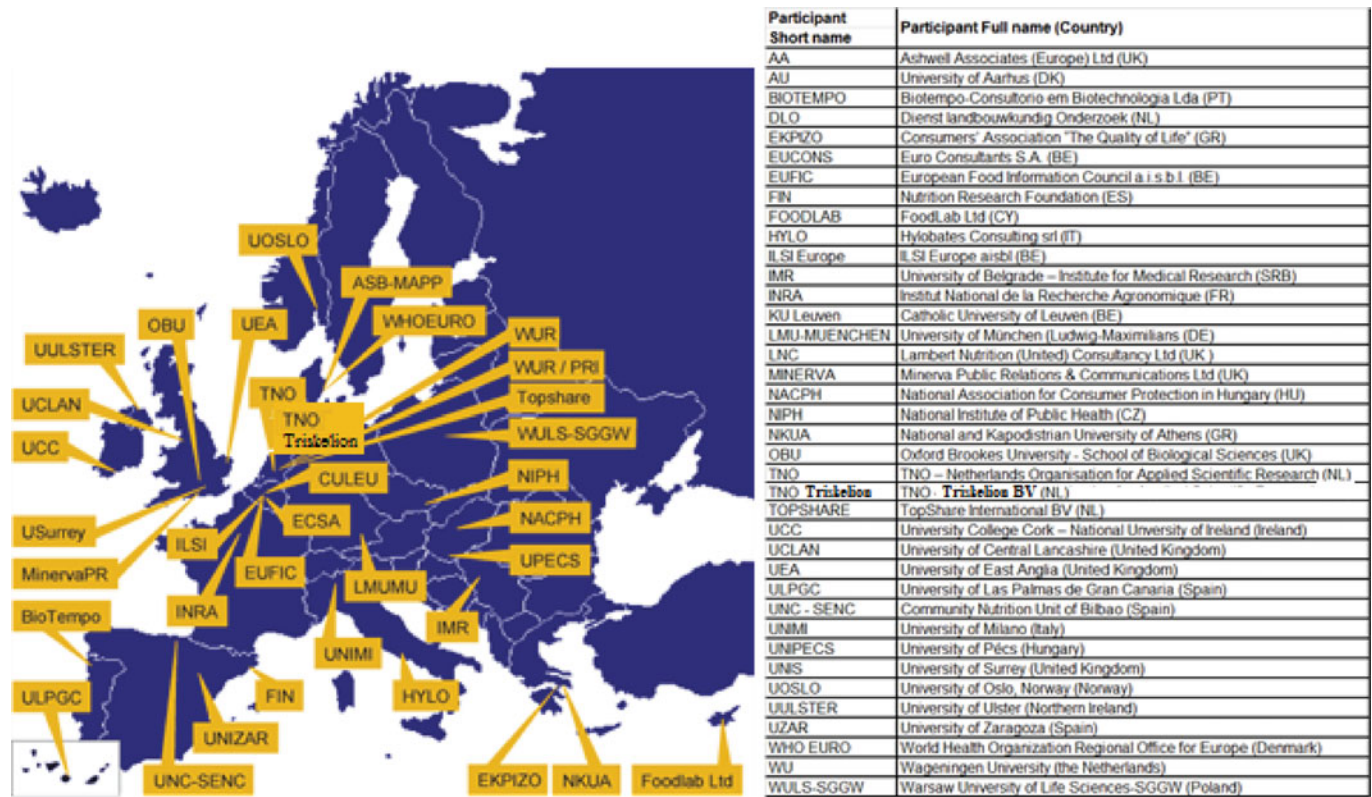


Figure 1 Geographical distribution of the EURRECA partners. (Color figure available online.)

and Nutrition. This issue, composed of a total of 10 articles, concentrates on the evidence and methodology for deriving requirements and recommendations for micronutrients (see Glossary in the Annexes of this issue for definition of terms). The resulting EURRECA approach is crystallized into its framework for deriving and using dietary reference values (DRVs) for micronutrients (see Figure 2 for graphical representation and (Dhonukshe-Rutten et al., 2013) for detailed methodological description). The 9 activities of the framework can be clustered into 4 stages (i) defining the problem, (ii) monitoring and evaluating, (iii) deriving DRVs, and (iv) using DRVs in policy making. These stages are detailed in the section “the EURRECA framework for deriving and using DRVs for micronutrients” in this article. The framework should not be interpreted as a prescriptive description of a linear process, but as a structured guide for checking that all issues essential for deriving requirements have at least been considered. As part of this report, the EURRECA framework has been applied in 6 case studies: folate (Hoey et al., 2013), iodine (Ristic-Medic et al., 2013), iron (Harvey et al., 2013), selenium (Hurst et al., 2013), vitamin D (Cashman and Kiely, 2013), and zinc (Lowe et al., 2013). The approaches and methodologies developed and the protocols available are likely to be largely applicable to all micronutrients. Claessens et al. (2013), in the conclusion article of this issue concentrate on the research needs and gaps, the potential application of the framework by the Nutrient Recommendation Setting Bodies (NRSBs) and a description of the sustainability plan following the end of the NoE life.

VARIATIONS IN RECOMMENDATIONS WITHIN EUROPE: WHY IS ALIGNMENT NEEDED?

The minimum amount required to maintain physiological function is traditionally referred to as the micronutrient requirement, and is defined by the body’s physiological needs. A more recent concept, which is finding favor for some micronutrients, is to define the requirement as the intake at which health and functioning is optimal (Institute of Medicine (IOM), 1994). Besides the prevention of deficiencies, the IOM introduced in 1997 requirements focusing on helping individuals optimize their health, preventing disease, and avoiding excessive consumption of a nutrient (Institute of Medicine (IOM), 1997). Furthermore, the IOM paradigm placed greater emphasis on the distribution of nutrient requirements within a population, rather than on a single value and they quantified the relationship between a nutrient and the risk of disease based on scientific evidence (Otten et al., 2006; Doets et al., 2008).

DRVs often vary widely between countries, sometimes more than two fold, even though the physiological requirements of the different populations are very similar (Doets et al., 2008). The rather small systematic physiological differences between people across Europe do not justify the currently considerable differences in DRVs. Differing national DRVs may thus not reach their goal of ensuring adequate intake. The reasons for this variation in requirements throughout Europe is not always clear and could be attributed to differences in terminology, available scientific data, expert judgment, or methodology. As populations



Note: EURRECA performed research with regard to the stage “Using dietary reference values in policy making” but did not implement any policy as this was outside its remit.

Figure 2 The final EURRECA framework describing the process for deriving and using dietary reference values for micronutrients includes activities numbered from 1 to 9 that have been clustered in four different stages.

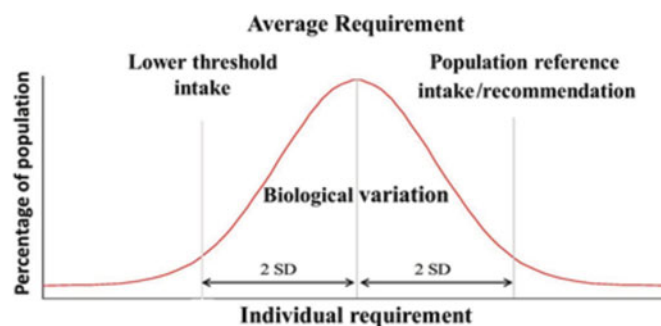
become more multicultural and more traditional foods become available internationally, harmonized DRVs based on the most up to date science are needed to compare populations on the basis of their intake. Different DRVs can also pose difficulties for food producers who market products in more than 1 country.

EURRECA initially collated data on many micronutrient recommendations (Doets et al., 2008) and developed Nutri-RecQuest, a user-friendly software tool that allows easy access of the collated data on current recommendations for 28 different micronutrients from 37 European countries, 8 key non-European countries/regions (i.e., United States/Canada, Australia/New Zealand, Japan, China, South Korea, South East Asia region, Brazil, and Mexico) as well as recommendations set by the European Commission and World Health Organization/Food and Agriculture Organization (Cavelaars et al., 2010b).

A wide range of terminologies have been used by different (inter)national agencies (see Glossary). Table 1 shows examples of different concepts and ways of defining recommendations used in Europe and North America. The most commonly given values are (i) average requirements and (ii) the average + 2 standard deviations (see Figure 3). The latter covers most of the population (97.5%, assuming the distribution of individual requirements is statistically normal) and are the most generally used recommendations. The scientific approach underlying the process followed in the EURRECA NoE is based on these generic scientific concepts, irrespective of the terminology used by authoritative bodies. For the needs of the current issue, it was decided that the European Food Safety Authority terminology shall be used to ensure coherence between the different papers.

EURRECA METHODOLOGICAL APPROACH

It was the objective of the EURRECA NoE to harmonize the process related to setting micronutrient recommendations from assessing nutritional requirements to policy applications (Pijls et al., 2009). Prior to the development of instruments for addressing differences across Europe, EURRECA initially reviewed methods currently employed in European countries to (i) estimate dietary intake (Serra-Majem, 2009; Serra-Majem et al., 2009) and (ii) evaluate biomarkers (Fairweather-Tait et al., 2009). These three journal issues describe how EURRECA has developed and adopted common concepts, definitions and terminologies and best practice methodologies for measuring micronutrient intakes and for using biomarkers of status.



SD: Standard Deviation

Figure 3 Frequency distribution of individual requirements. For more information regarding the terms set by different organizations corresponding to Average Requirement, Average Requirement + 2SD, and Average Requirement – 2SD, please see Table 1. (Color figure available online.)

Table 1 A selection of concepts and acronyms used for micronutrient recommendations across the world (in alphabetical order)

Source	Set of recommendations	Mean + 2SD	Mean	Lower Threshold Intake (LTI)	Adequate intake	Reference intake range	Upper intake level
Europe-EFSA (2010)	Dietary Reference Values (DRVs)	Population Reference Intakes (PRI)	Average Requirement (AR)	Lower Threshold Intake (LTI)	Adequate Intake (AI)	Reference Intake ranges for macronutrients (RI)	Tolerable Upper Intake Level (UL)
Europe-European Commission (1993; 2000)	Recommended Dietary Allowances (RDAs)	Population reference intake (PRI)	Average requirement (AR)	Lower threshold intake (LTI)	Adequate intake	Acceptable ranges (RI)	Tolerable upper levels (UL)
France-AFSSA (2001)	Nutritional recommendations [Apports nutritionnels conseillés]	Apport nutritionnel conseillé (ANC)	Average nutritional requirement (Besoin nutritionnel moyen)	–	Apport nutritionnel conseillé (ANC)	–	Safety limit (Limite de sécurité)
Germany-Austria, Switzerland-DACH (2008)	Reference values (Referenzwerte)	Recommendations (Empfehlungen) or Recommended Intake (Empfohlene Zufuhr)	–	–	Estimated values (Schätzwerte)	–	–
International-WHO/FAO (2002)	Recommended nutrient intakes	Recommended nutrient intake (RNI)	–	–	–	–	Upper tolerable nutrient intake level (UL)
International-UNU (King and Garza, 2007)	Nutrient Intake Values (NIVs)	Individual Nutrient Level 98 (INL ₉₈)	Average Nutrient Requirement (ANR)	–	–	–	Upper Level of Safe Intake (UNL)
Netherlands-Health Council (2001)	Nutritional guidelines (Voedingsnormen)	Recommended Dietary Allowances (Aanbevolen dagelijkse hoeveelheid-ADH)	Average Requirement (Gemiddelde behoefte)	–	Adequate Intake (adequate inneming)	–	Acceptable Upper Limit (Aanvaardbare bovengrens van inneming)
Nordic countries-Norden (2004)	Nordic nutrition recommendations (Nordiska näringsrekommendationer- NNR)	Recommended intake (Rekommenderat intag -RI)	Average requirement (Genomsnittsbehov)	Lower limit of intake (Nedre gräns för intag)	–	–	Upper intake level (Högsta intag)
UK- Department of Health (1991)	Dietary Reference Values (DRVs)	Reference nutrient intake (RNI)	Estimated Average Requirement (EAR)	Lowest reference nutrient intake (LRNI)	Safe intake	–	Safe upper levels
United States-Institute of Medicine (2005; 1998; 1997)	Dietary Reference Intakes (DRIs)	Recommended dietary allowance (RDA)	Estimated average requirement (EAR)	–	Adequate Intake (AI)	Acceptable macronutrient distribution ranges (AMDR)	Tolerable upper intake level

EFSA: European Food Safety Authority, FAO: Food & Agriculture Organization, UNU: United Nations University, WHO: World Health Organization.

EURRECA studied micronutrients as described in Table 2 over the full duration of the NoE and developed a methodology to prioritize micronutrients based on the availability of new scientific evidence, public health relevance, and heterogeneity of recommendations (Cavelaars et al., 2010b). Based on this prioritization, 8 micronutrients have been included for further investigation: iodine, folate, iron, riboflavin, selenium, zinc, and the vitamins B12 and D. Population groups covered include infants (0–12 months), children and adolescents (1–18 years), adults (19–64 years), elderly (65+ years), pregnant and lactating women, furthermore, low-income groups, and immigrants have been investigated as policy-relevant population subgroups that may be at risk of low micronutrient intakes.

EURRECA identified and developed methodologies and practical tools (e.g., databases, best practice guidelines, decision trees, and e-learning modules) that can serve as a basis for the development of DRV_s (Matthys et al., 2010; Claessens et al., 2013). This process should be easily applicable and reproducible in different settings and for different micronutrients; therefore, the methodologies developed were based on systematic reviews performed for a number of micronutrients and health endpoints. In this process, EURRECA also incorporated both the physiological and policy aspects.

Originally, a General Framework described the process leading from assessing nutritional requirements to policy applications, based on evidence from science, stakeholder interests, and the socio-political context (Dhonukshe-Rutten et al., 2010) (Figure 4). This framework envisioned the derivation of nutrient recommendations as a scientific methodology, embedded in a policy making process by distinguishing the principal components of the framework: (i) defining the nutrient requirements for health, (ii) setting the nutrient recommendations, (iii) policy options, and (iv) policy applications. However, EURRECA did not engage in applying policy options. The current practice and

the needs were identified to provide the building blocks of the process of deriving policy applications.

THE EURRECA MICRONUTRIENT FRAMEWORK FOR DERIVING AND USING DRV_s FOR MICRONUTRIENTS

Based on the scientific evidence and extensive study, the initial General Framework (Dhonukshe-Rutten et al., 2010) (Figure 4) evolved into the EURRECA flowchart (Matthys et al., 2011) (Figure 5) during a meeting with Stakeholders and NoE partners in Budapest in June 2011. One of the major revisions during this meeting was the inclusion of the evaluation of existing micronutrient intake and status of the population as an essential step between the setting of nutrient recommendations and the identification of policy options. This flowchart was further revised and evolved into the EURRECA framework for deriving and using DRV_s for micronutrients (Figure 2), following the comments of the NRSBs representatives during a workshop organized jointly by EURRECA NoE and World Health Organization in April 2012 (van 't Veer et al., 2013). The initial linear process closed-up to allow for the process to be reiterated; in the revised framework the different stages are linked in a more interactive way and do not need to be followed in a specific step-wise way. This framework should be considered as a guide for checking that all options have at least been considered, rather than all being absolutely essential for deriving DRV_s for micronutrients.

Differences in the individuals physiological processes that determine requirements may also be extremely important and lead to large variations in the requirements for some individuals; therefore, part of the work focuses on polymorphisms affecting the nutritional phenotype and defining specific requirements (van Ommen et al., 2008; van Ommen et al., 2010; Bouwman et al., 2012).

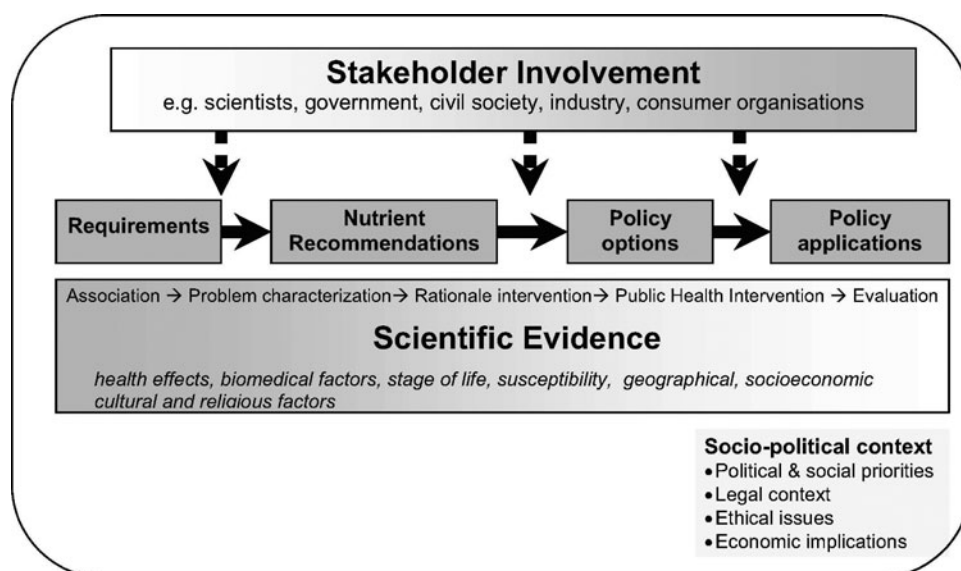


Figure 4 The EURRECA General Framework for aligning European micronutrient recommendations.

Table 2 Overview of micronutrients covered by the work of the EURRECA network

Micronutrient	Integration Activity			Research Activity												Guidance for deriving European nutrient recommendations																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																															
	Consumer understanding, stakeholder interaction	Integrating opportunities for SMEs	Influences of individuality, variability and vulnerability	Integration, Liaison & Sustainability	Define best practices			Intake-Status-Health in different population groups				Tools to derive average micronutrient requirements																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																			
					Status Assessment Methods	Concepts	Current Recommendations	Infants	Children and Adolescents	Adults	Pregnant and lactating women	Elderly	Low income and immigrants	Dose Response relationship	Factorial approach		Bioavailability	Integration and Quantification	Inadequate Intake	Aligning evidence	Planning and alignment	Individual and health space approach	Science/policy interface																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																								
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Table 2 Overview of micronutrients covered by the work of the EURRECA network (*Continued*)

Micronutrient	Integration Activity			Research Activity														Guidance for deriving European nutrient recommendations					
	Consumer understanding, stakeholder interaction	Integrating opportunities for SMEs	Influences of individuality, variability and vulnerability	Research Activity																			
				Define best practices			Intake-Status-Health in different population groups					Tools to derive average micronutrient requirements					Guidance for deriving European nutrient recommendations						
				Dietary Intake assessment Methods	Status Assessment Methods	Concepts	Current Recommendations	Infants	Children and Adolescents	Adults	Pregnant and lactating women	Elderly	Low income and immigrants	Dose Response relationship	Factorial approach	Bioavailability		Integration and Quantification	Inadequate Intake	Aligning evidence	Planning and alignment	Individual and health space approach	Science/policy interface
Iodine	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Magnesium	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Manganese			X																				
Molybdenum			X																				
Pantothenic acid			X		^a		X																
Phosphorus	X	X	X	X	^a	X	X										X		X	X			
Potassium	X	X	X	X	^a	X	X			X				X					X	X			
Selenium	X	X	X	X	X	X	X			X				X					X	X			
Sodium	X	X	X	X	X	X	X			X				X					X	X			
Zinc	X	X	X	X	X	X	X			X				X					X	X			
Phytochemicals			X		X		X																
n-3 Fatty acids	X	X	X	X	X	X	X																

^aThese nutrients were also included in the EURRECA Best Practice Guidelines: Biomarkers of status/exposure (Harvey et al.,2011).^bNo systematic review was undertaken for iodine bioavailability as there was insufficient data.

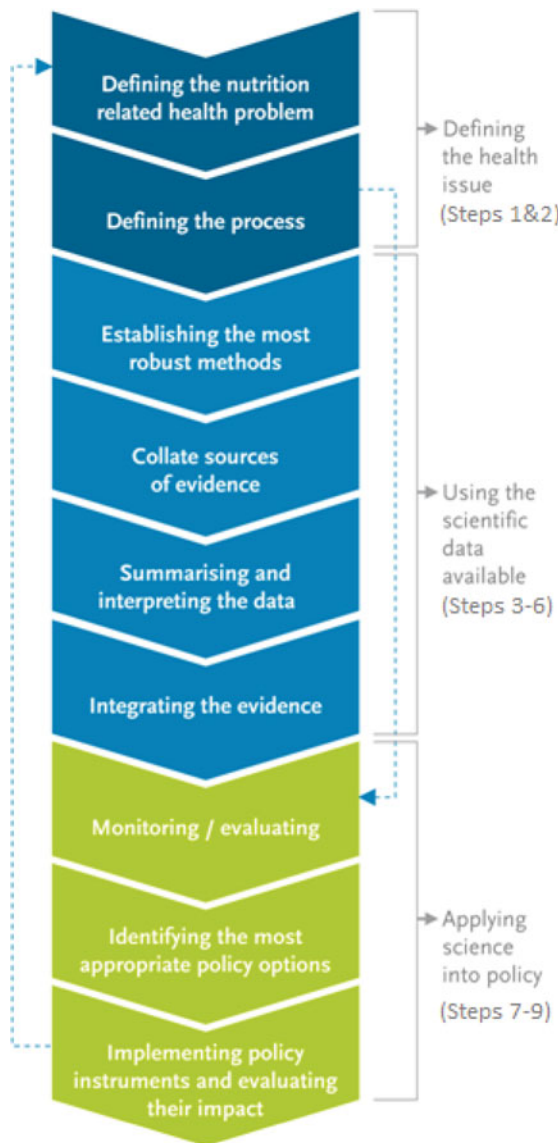


Figure 5 The EURRECA micronutrient requirement process flowchart that was discussed during the EURRECA/WHO workshop in April 2012 (van 't Veer et al., 2013). Following the comments of the workshop participants, it was changed to lose its linear format, steps were transformed into activities and re-grouped into four stages. The final refined version appears in Figure 2. (Color figure available online.)

Another crucial aspect is to determine the nutritional inadequacy of vulnerable groups, including social lower classes and immigrants, infants and children, pregnant and lactating women, and the elderly (Roman-Vinas et al., 2009; Cetin et al., 2010; Ngo et al., 2011; Roman-Vinas et al., 2011).

The nine activities of the framework can be clustered into 4 stages (i) defining the problem, (ii) monitoring and evaluating, (iii) deriving DRVs, and (iv) using DRVs in policy making (Dhonukshe-Rutten et al., 2013).

Defining the Problem

Defining the problem in terms of nutrition and health includes the identification of health endpoint(s), population group(s), and

micronutrient(s) of concern. EURRECA also identified, compared, and evaluated existing published recommendations for micronutrients in and outside Europe, which were collected in Nutri-RecQuest (Cavelaars et al., 2010b). Once the health issue is characterized, a committee should be established to address it. The remit of the committee, the choice of the committee members as well as the criteria on which to base the requirements and/or recommendations need to be carefully defined.

Monitoring and Evaluating

Valid information on the micronutrient intakes and status of a population, as well as on the effect of micronutrient intake/status on health (relationship between intake-status-health outcomes) is fundamental for deriving micronutrient DRVs and establishing recommendations. In Europe, data collected by surveillance are used to evaluate population nutritional health and give early warning information on malnutrition and nutrition health related problems. Through the adoption of clearly defined processes, EURRECA has established a series of approaches that assure the identification, and ultimately provision, of robust micronutrient dietary intake, and status data. The network specifically identified that the risk of dietary inadequacy is dependent on the dietary assessment methodology employed in combination with the micronutrient under evaluation. Therefore, a set of Best Practice Guidelines were developed to facilitate identification of the most robust data for setting DRVs (available at www.eurreca.org). The resulting Best Practice Guidelines, whilst highlighting the most robust indicators currently available, also exposed the lack of appropriate status markers for several micronutrients.

Deriving Dietary Reference Values

Once the best practice methodology was agreed, scientific data was collected to estimate the micronutrient requirements. Two different approaches were explored by EURRECA. The association approach addresses the dose–response relationship between dietary micronutrient intake and body status, and the effect of the intake/status on health outcomes. The second approach is the factorial approach which addresses micronutrient losses and maintenance, absorption/bioavailability, and additional requirements for specific life stages, to give factorial estimates of micronutrient requirements. Based on these approaches, a series of systematic literature searches were conducted. The current quantitative methodologies used to derive requirements do not generally integrate all of the intake, status, and health data. EURRECA has developed a statistical model to combine a maximum amount of all available quantitative evidence into the process. The integration of the evidence has also to accommodate systematic variations (between studies) originating from (i) differences in study quality, (ii) study population, (iii) micronutrient dose, and (iv) other population characteristics (growth, pregnancy, lactation, etc.).

Using Dietary Reference Values in Policy Making

The derivation of recommendations from DRVs is not undertaken by EURRECA. It is the responsibility of decision and policy makers to set the most appropriate recommendations based on the current situation in a country or region and their public health priorities. To facilitate this, EURRECA has developed the Public Health Nutrition Policy-Making Framework to guide policy makers in integrating nutrition science with other types of scientific evidence (economics, social, and consumer science, etc.) and nonscientific evidence (policy, institutional, and wider context) (Timotijevic et al., 2013). After the implementation of a policy, impact assessment enables the risk assessors and decision makers to assess changes in the nutrition situation due in part or wholly to a nutrition policy. This evaluation may lead to revisions in existing recommendations or the identification of new problems, in which case the process can be reinstituted.

CONCLUSIONS

Alignment in micronutrient DRV setting is needed in the way in which scientific evidence is gathered, managed, interpreted, and communicated to the users (European Commission, 2001; Dhonukshe-Rutten et al., 2010). Scientific alignment includes the scientific content (objectivity, transparency, and common basis), processes to collate and summarize evidence, and application of results by regional and international users who evaluate their policy options and implement the chosen applications. (Dhonukshe-Rutten et al., 2010).

The EURRECA framework (Figure 2) aspires to be used as a practical tool for defining the appropriate process for deriving DRVs. It brings together scientific research and evidence base with policy decision making to achieve a transparent and systematic approach to derive micronutrient DRVs. At present, policy advice is partially evidence based, but the process of translating the evidence into degrees of (un)certainity and the subsequent formulation of nutrition and food recommendations largely remains a matter of valuable eminence-based logical reasoning and agreement by the responsible committees. In the future, this part of the process will gain further confidence and transparency through the development and use of methods that have been subjected to scientific scrutiny. A further value added by the EURRECA approach is the identification of the type of evidence and new data that are needed for the update of DRVs for micronutrients [see also (Claessens et al., 2013)]. EURRECA focused on the micronutrients that were highlighted following the prioritization methodology it developed (Cavelaars et al., 2010a) and has further prioritized these according to relevance to the European setting. The EURRECA process of deriving micronutrient DRVs is illustrated in this issue by means of six of these prioritized micronutrients (Cashman and Kiely, 2013; Harvey et al., 2013; Hoey et al., 2013; Hurst et al., 2013; Lowe et al., 2013; Ristic-Medic et al., 2013; Timotijevic et al., 2013), thereby providing an example for similar cases in the near future.

Moreover, EURRECA considered a wider range of population groups than usual for panels setting DRVs, focusing on vulnerable groups such as low income and immigrant groups as well as the more traditional population groups based on gender and the life cycle (infants, children, adolescents, pregnant and lactating women, and the elderly). EURRECA engaged with partners outside the scientific community; the involvement of many stakeholders and end-users helped EURRECA to adapt to their needs. These include consumers, research scientists, NRSBs (nutrition societies, health ministries, and health councils), government sectors, the European Union institutions, WHO, United Nations (UN) organizations, nongovernmental organizations, and the private sector. In this context, a workshop organized jointly by EURRECA NoE and WHO, and its resulting publication addressed the needs of the NRSBs (van 't Veer et al., 2013).

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ABBREVIATIONS

DRVs	= Dietary reference values
EC	= European Commission
EFSA	= European Food Safety Authority
EURRECA	= EUROpean micronutrient RECommendations Aligned
FAO	= Food and Agriculture Organization
IOM	= Institute of Medicine
NoE	= Network of Excellence
NRSBs	= Nutrient Recommendation Setting Bodies
SD	= Standard Deviations
UNU	= United Nations University

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