

Food and Agriculture Organization of the United Nations



Review of derivation methods for dietary intake reference values for older infants and young children

FAO request for scientific advice to develop general principles for the establishment of Codex nutrient reference values for older infants and young children

Final Draft



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CONTENTS

AC	KNOWLEDGEMENTS	V
AC	RONYMS	VI
GL	OSSARY	VII
EX		VIII
1	INTRODUCTION	1
	1.1 Recognized authoritative scientific bodies (RASBs) and FAO/ WHO Publications	/ 1
	1.2 Nomenclature	1
	1.3 Nutrients	2
2	METHODS USED TO DERIVE DIRVS	3
	2.1 Derivation Methods	3
	Category 1 Using physiological evidence from the target group	3
	Category 2 Extrapolation from DIRVs of another age group	4
	Allometric extrapolation (scaling)	5
	Isometric and linear extrapolation (scaling)	6
	Category 3 Estimated nutrient intake of the target group, or interpolation	7
	Summary of categories and subcategories	8
	2.2 Change in DIRV Classification upon Extrapolation	9
	2.3 Choice of Derivation Method	10

3 APPLICATION TO THE GENERAL PRINCIPLES 11



4 DIETARY INTAKE REFERENCE VALUES FOR VITAMINS,	
MINERALS AND PROTEIN	13
4.1 Details of Dietary Intake Reference Values in Table Series	13
RASB source publications for general population NRVs-R	13
Age ranges and sex	13
Nutrient units	14
Key to derivation methods	14
4.2 Observations on Data in Table Series	14

5 TABLE SERIES: DIETARY INTAKE REFERENCE VALUES¹⁻⁸ FOR OLDER INFANTS AND YOUNG CHILDREN WITH DERIVATION KEY 16

5.1 Protein	16
5.2 Minerals	18
5.3 Vitamins	29

6	REF	FERENCES	42
AP	PEN	DIX: REFERENCE PARAMETERS USED TO DERIVE DIRVS	44
	A1	Younger and Older Infants	44
	A2	Young Children and Adults	45

TABLES

2
2
9
10
12
15
44
45
46

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ACRONYMS

AI	Adequate Intake	
CCNFSDU	Codex Committee on Foods for Special Dietary uses	
CV	Coefficient of variation	
DIRVs Dietary Intake Reference Values		
EFSA European Food Safety Authority		
EU	European Union	
FAO	Food and Agriculture Organization of the United Nations	
INL	Individual Nutrient Level	
IOM United States Institute of Medicine		
NASEM	National Academy of Science, Engineering and Medicine	
NASEM NCM	National Academy of Science, Engineering and Medicine Nordic Council of Ministers	
NCM	Nordic Council of Ministers National Health and Medical Research Council and New Zealand	
NCM NHMRC/MOH	Nordic Council of Ministers National Health and Medical Research Council and New Zealand Ministry of Health	
NCM NHMRC/MOH NIHN	Nordic Council of Ministers National Health and Medical Research Council and New Zealand Ministry of Health National Institute of Health and Nutrition	
NCM NHMRC/MOH NIHN NRV-R	Nordic Council of MinistersNational Health and Medical Research Council and New Zealand Ministry of HealthNational Institute of Health and NutritionCodex Nutrient Reference Values-Requirement	

GLOSSARY

Nutrient Reference Values-Requirement: refers to NRVs that are based on levels of nutrients associated with nutrient requirements for the general population.

Dietary Intake Reference Values: defined as reference nutrient intake values provided by FAO/WHO or recognized authoritative scientific bodies that may be considered in establishing an NRV. These values may be expressed in different ways (e.g. as a single value or a range), and are applicable to the general population or to a segment of the population (e.g. recommendations for a specified age range).

Factorial method: defined as a modeling approach to derive requirements from equations that sums the various nutrient-related components involved in physiological maintenance and growth and accounts for nutrients lost from the body.

Extrapolation: defined as a method that derives DIRVs for older infants and young children by scaling the DIRVs of other younger or older age groups; as such it may be upward or downward in direction

Interpolation: defined as a method used to derive DIRVs for the intervening group/s when the DIRVs of the two other groups are known. For example if DIRVs for young infants and another non-consecutive older age group such as older children are established but data on which to set DIRVs for the intervening age group/s are scant or perhaps extrapolation results are not meaningful, the DIRVs for the intervening group/s are estimated and smoothed between the DIRVs of the two other groups using interpolation.



EXECUTIVE SUMMARY

This report was prepared to provide scientific advice to the Codex Committee on Foods for Special Dietary uses (CCNFSDU) on the details of Dietary Intake Reference Values (DIRVs) for protein and 24 micronutrients for older infants (6-12 months) and young children (12-36 months) in the publications of six Recognized Authoritative Scientific Bodies (RASB) and the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO). These publications were previously used to select DIRVs as the basis of Codex Nutrient Reference Values-Requirement (NRV-R) for the general population.

The scientific advice includes an assessment of the salient similarities and differences of methods used to derive the DIRVs. Ten methods were identified and grouped into three ranked categories according to discrete approach and associated level of scientific rigour. The three categories given, in order, in the following table are proposed as suitable for inclusion in the general principles for establishment of NRVs-R for older infants and young children.

	Category	Brief description
1	Use of physiological evidence from the target group	The factorial summation of the various components involved in physiological growth, maintenance and loss in the target or similar groups. Also, the estimation of nutrient intake based on maintenance of a healthy plasma or urinary biomarker, or absence of deficiency disease in the target group.
2	Extrapolation up or down from DIRVs of other age groups	Allometric, isometric and linear scaling methods using reference DIRVs from adults or young infants.
3	Estimates of nutrient intake of the target group; or inter- polation	Estimates of nutrient intake from diets of healthy older infants and young children; or interpolation between DIRVs of younger and older age groups.

The ten methods reflect the level of descriptive detail in the RASB and FAO/WHO publications and are termed subcategories in this report; however, no ranking is applied at the subcategory level.

The published DIRVs are given as a series of tables, one for each nutrient. The nutrient tables provide the following information for older infants and for young children: source publication, DIRV value and classification, as Individual Nutrient Level50 (INL50) and Individual Nutrient Level98 (INL98), or Adequate Intake (AI), applicable age range and a key denoting the derivation method subcategory. Also indicated are the RASB and FAO/ WHO publications of DIRVs previously selected for general population NRV-Rs. Three appendices provide details of the various reference parameters used to derive DIRVs for older infants and young children.

Publications describe their methods in varying levels of detail and some provide reasons for their choice of method; the European Food Safety Authority (EFSA) and the United States Institute of Medicine (IOM) publications are the most comprehensive in this regard. Review of the derivation methods indicates strong coherence across publica-



tions for some nutrient DIRVs, and limited or wide variability for others. Several factors influence the ultimate value of a nutrient DIRV – primarily the selected method subcategory, plus the specific data and parameters relevant to that method subcategory. Overall, the most common derivation category is extrapolation followed by the other two categories in approximately equal measure. This pattern also applies to older infants, but for young children, more DIRVs in the other two categories are based on physiological evidence than nutrient intake/interpolation. Each category and population group combination classifies DIRVs as INL and AI but physiological evidence is not always classified as INL, and intake estimate/interpolation is not always classified as AI. This outcome generally supports the definitions of AI and INL, noting that scientific judgement about the quality of the physiological evidence also may determine the DIRV classification.

1 INTRODUCTION

This report was developed to advise on the details of Dietary Intake Reference Values (DIRVs) for older infants (6-12 months) and young children (12-36 months) and to assess, categorise and rank the methods used to derive these DIRVs; additionally, to advise which categories are suitable for inclusion in the general principles to establish Codex Nutrient Reference Values-Requirements (NRVs-R) for older infants and young children.

1.1 Recognized authoritative scientific bodies (RASBs) and FAO/ WHO Publications

Publications from six Recognized Authoritative Scientific Bodies (RASBs)¹⁻⁶ and the Food and Agriculture Organization of the United Nations and the World Health Organization (FAO/WHO)^{7,8} that present DIRVs for older infants and young children were reviewed for this report. These publications were the source of DIRVs for the NRVs-R for the general population and cover a period of 18 years with their own style, format and level of detail.

Countries, regions and international bodies publish their DIRVs in several ways:

- 1. As a compendium of all DIRVs (Australia and New Zealand; Japan; Nordic Countries);
- In groups of related nutrients (United States of America and Canada; FAO/ WHO);
- 3. By single nutrient (European Union (EU); Food and Agriculture Organiza-

tion/World Health organization/United Nations University; International Zinc Nutrition Consultative Council).

Since the work was done to review DIRVs for NRVs-R for the general population, EU completed its publication of DIRVs, Japan released a new edition of its DIRV publication including updates to some DIRVs, and USA and Canada published revised DIRVs for sodium and potassium by a new agency. The more recent references and values are used in this report.

1.2 Nomenclature

Codex Alimentarius9 adopted the internationally recommended nomenclature for DIRVs including the relevant terms: individual nutrient level (INL) and adequate intake (AI). Where data are sufficient, an INL_{50} is determined from the 50th percentile of the distribution of requirement, and converted to the INL_{98} by a coefficient of variation (CV). Where insufficient data exist to set an INL, an AI is established by experimentally determined approximations or median nutrient intakes (usually from survey data for a healthy population). Also, for older infants, an AI can be established by extrapolation from an adult INL_{50} . No RASB publication has adopted the INL nomenclature; instead, each RASB uses its own naming convention to refer to the individual and collective sets of DIRVs FAO/WHO and Nordic Council of Ministers (NCM) do not use the AI classification or routinely include the equivalent of INL₅₀ but instead refer to all DIRVs by a single term equivalent to INL₉₈.

The RASBs and FAO/WHO, their source country or region, and adopted nomencla-ture are given in Table 1.



Table 1: Countries/regions, their RASBs and DIRV nomenclature

Country/region	RASB1-8	DIRV nomenclature; <i>Term equivalent to INL</i> ₉₈
International	Food and Agriculture Organization of the United Nations /World Health Organization (FAO/WHO)	Vitamin and mineral requirements Recommended Nutrient Intake (RNI)
	World Health Organization/ Food and Agriculture Organization of the United nations/ United nations University WHO/FAO/UNU	Protein requirements Safe level of protein intake
	International Zinc Nutrition Consultative Group (iZiNCG).	Human Zinc Requirements Recommended Dietary Allowance (RDA)
Australia and New Zealand	National Health and Medical Research Council and New Zealand Ministry of Health (NHMRC/MOH)	Nutrient reference values Recommended Dietary Intake (RDI)
European Union	European Food Safety Authority (EFSA)	Dietary reference values Population Reference Intake (PRI)
Japan	National Institute of Health and Nutrition (NIHN)	Dietary reference intakes Recommended Dietary Allowance (RDA)
Nordic Countries	Nordic Council of Ministers (NCM)	Nordic Nutrition Recommendations Recommended Intake (RI)
United States of America, and Canada	Institute of Medicine (IOM)/ National Academy of Science, Engineering and Medicine (NASEM)	Dietary reference intakes Recommended Dietary Allowance (RDA)

1.3 Nutrients

this report comprise protein, 13 vitamins

The 25 designated nutrients covered in and 11 minerals as presented in Table 2.

Table 2: Nutrients

Vitamins		Minerals	
Vitamin A	Niacin	Calcium	Manganese
Vitamin D	Vitamin B6	Magnesium	Phosphorus
Vitamin C	Folate	Iron	Potassium
Vitamin E	Vitamin B12	Zinc	Sodium
Vitamin K	Pantothenic acid	Iodine	
Thiamin	Biotin	Copper	
Riboflavin		Selenium	

2 METHODS USED TO DERIVE DIETARY INTAKE REFERENCE VALUES

2.1 Derivation Methods

Methods used to derive DIRVs for 25 nutrients in the RASB and FAO/WHO publications were assessed for salient similarities and differences in order to devise a series of ranked categories of methods suitable for inclusion in the Codex general principles.

From this assessment, ten methods were identified and grouped into three categories that were ranked according to discrete approach and associated scientific rigour. The methods reflect the level of description given in the publications and are termed subcategories within each category. These method subcategories are not ranked because their scientific rigour could not be differentiated. For example, the variation in extrapolation methods is more relevant to the function and metabolism of the nutrient concerned rather than to differences in scientific rigour. RASB assessments vary from de novo reviews of the evidence base to updates or adoption of previously published DIRVs from either the same or another RASB. EFSA² and IOM⁶ publications describe their derivation methods in the most detail. The ten method subcategories arranged by category are described as follows.

Category 1 Using physiological evidence from the target group

a. Factorial method

The factorial method for older infants and young children sums the various nutrient-related components involved in physiological maintenance and growth and accounts for nutrients lost from the body. Maintenance measures the nutrient required to maintain a minimum serum level or body store that serves as a health reference, and growth accounts for the amount of nutrient incorporated into newly formed tissues. The method also measures the amounts of nutrient losses either unchanged or as metabolites via the faeces, urine and skin.

Consideration of the many physiological adaptations that occur for these population groups may also be required, such as an increased intestinal absorption, and/or greater nutrient retention. When data for some factorial components are not available from these population groups, they are extrapolated or assumed from data of other age groups. The estimated requirement is then adjusted by the fractional nutrient absorption from the intestine to derive the INL_{50} which is then converted to the INL₉₈ by applying the same CV used to convert the adult INL₅₀ to INL₉₈. Factorial methods are routinely applied to DIRVs for protein, iron and zinc; and also to some other DIRVs by some RASBs.

b. Nutrient intake needed to achieve a healthy level of biomarker; or nutrient intake associated with prevention of deficiency disease

This method determines a nutrient intake needed to maintain an adequate nutrient status as indicated by a healthy level of serum biomarker (e.g. 25(OH)D for vitamin D); or urinary level



(e.g. iodine); or more indirectly, nutrient intake known to be associated with prevention or low rates of deficiency disease such as rickets. Data may not always be available in the population group; if not, data from older children may be used.

This method relies on selection of the most appropriate physiological biomarker at a level judged to maintain health and growth, and also identification of a nutrient intake that maintains that level. For vitamin D, RASBs consistently agreed on the relevant biomarker but differed on the particular serum level associated with health; which contributed to the difference in DIRVs.

Category 2 Extrapolation from Dietary Intake Reference Values of another age group

Atkinson and Koletsko (2007)¹¹ stated in their review that "extrapolation should always be a second choice" and "there is no one 'correct' method of extrapolation and scientific judgement will probably be part of the process".

Extrapolation is the most commonly applied of all categories of methods because it is easiest to apply. Extrapolation is used in the absence of data from older infants and young children that would enable use of more reliable methods. The choice of extrapolation method depends on producing a meaningful result that can be validated by other data. For example, an extrapolated DIRV should be biologically plausible and not markedly exceed the surveyed nutrient intake of an apparently healthy population of older infants or young children in the RASB country or region.

Extrapolation derives DIRVs for older

infants and young children by scaling the DIRVs of other younger or older age groups; as such it may be upward or downward in direction. Two elements are needed in extrapolation: a reference DIRV and scaling parameters. The choice of a particular reference DIRV determines which scaling direction applies. When a young infant DIRV is used as the reference, scaling is upward; when the adult DIRV or occasionally the DIRV of another age group is the reference, scaling downward applies. The selected adult DIRV may be for young adults or a wider adult age range. The parameters used to extrapolate the reference DIRV are mostly body weights, although others such as energy or protein DIRVs (or intakes) are used when more relevant to the function of the nutrient concerned. The reference body weights are given in Appendix Table A1 for young and older infants and in Appendix Table A2 for young children and adults.

Three types of extrapolation are described in this report: allometric, isometric and linear, all of which take account of the function and metabolism of the nutrient in the body. The difference between allometric and isometric (or linear) extrapolation is that allometric applies the power exponent 0.75 to the body weight (or other parameter) quotient whereas the exponent is not used in isometric or linear extrapolation. Growth factors are used in both allometric and isometric extrapolation but only when reference adult DIRVs are scaled down to account for the additional needs for growth. The reference growth factors are given in Appendix Table A3.

Compared to isometric scaling, allometric scaling down from a higher to a lower body weight (e.g. adult to young children, body weight quotient <1) gives a higher value, whereas allometric scaling up from a lower to a higher body weight (e.g. young infant to older infant, body weight quotient >1) results in a lower value (EFSA, 2010)¹³. Because extrapolation methods are easily calculated, it would be helpful to document the reasons for the choice of direction and type of extrapolation method. Sadly, these reasons are not often recorded.

Allometric extrapolation (scaling)

Allometric extrapolation adjusts for metabolic or surface area differences between age groups. Raising the scaling parameter quotient (e.g. body weight) to power 0.75 is generally accepted as an appropriate adjustment for metabolic differences between the reference and target population groups. The history of the choice of 0.75 as the exponent is briefly discussed by Atkinson and Koletsko (2007)¹¹.

Allometric extrapolation is applied in both upward and downward directions. Scaling up is generally applied to produce DIRVs only for older infants, whereas scaling down is applied to produce DIRVs for both older infants and young children. All following equations use older infants as the example target population group.

c. Allometric scaling up — young infant DIRV to older infant DIRV

To scale up a young infant DIRV to produce an older infant DIRV, the equation is:

Alolder infant = Alyoung infant x (weightolder infant/weightyoung infant)^{0.75}

No separate factor is needed for growth in the equation because the reference AI for a growing young infant already accounts for it. The AI for young infants is nearly always set according to the mean amount of nutrient in human milk consumed daily by healthy, exclusively breastfed infants less than 6 months of age. The equation for the AI of young infants is

AI_{YOUNG INFANT} = Nutrient concentration_{mean} in human milk x daily volume_{mean} of human milk consumed/lost through lactation

RASBs prefer to use data from studies of the nutrient composition of human milk from their own population or, if not available or suitable, from comparable populations. EFSA (2013)¹⁴ made the point that the nutrient composition of human milk varies widely over the duration of lactation. between and within feeds, and also depends on maternal factors, particularly the diet, as well as sex and size of the infant and the region of the world. Nutrient composition data of human milk as the basis of a young infant DIRV should therefore be collected from a representative and sufficient sample of adequately nourished, unsupplemented lactating women that takes account of all these influencing factors and should be analysed by a certified laboratory. Reference volumes of human milk consumption by young infants differ among publications and are given in Appendix Table A1.

Not all publications formally establish AIs for young infants because the nutrient intakes of exclusively breastfed infants are assumed to be adequate for health. When an AI for young infants is not formally established but is needed to derive a DIRV, an estimate of mean nutrient intake from human milk is calculated from the above equation.

Scaling up the young infant AI to produce AIs for young children and even older age



groups is seldom used; however, some RASBs used this method to determine the biotin DIRV for older age groups.

Upward extrapolation is not used to derive the DIRVs of vitamins D and K because the concentration in human milk and therefore intake of these vitamins is insufficient to sustain health. Care is also needed to derive DIRVs for nutrients whose human milk contents reflect maternal dietary intake rather than necessarily the nutrient needs of the infant e.g. iodine and vitamin C.

d. Allometric scaling down — adult Dietary Intake Reference Values to older infant or young child Dietary Intake Reference Values

To scale down an adult Dietary Intake Reference Values to produce an older infant Dietary Intake Reference Values, the equation is:

[INL50 or AI]OLDER INFANT = [INL50 or AI]ADULT x (weightolder infant/ weightadult)0.75(1 + growth factor) Since an adult INL 50 or AI reflects maintenance needs only, adjustments for nutrient amounts incorporated into newly formed tissue for growth are needed for older infants and young children. All publications make this adjustment by multiplying by 1 + age-specific growth factor based on the proportional increase in protein requirements for growth relative to maintenance. When the resultant value for the older infant Dietary Intake Reference Values is INL₅₀, it is converted to the INL_{qg} by applying the same CV used to convert the adult INL_{50} to INL_{98} . However, this conversion is not applied to the derivation of an AI. The various growth factors used by RASBs are given in Appendix Table A3.

Isometric and linear extrapolation (scaling)

The term *isometric* is primarily used by EFSA and occasionally by the NCM. This type of extrapolation is used when data relates to less metabolically active body tissues such as minerals in bone or electrolytes so that the power exponent 0.75 is not applied although the growth factor is still included when scaling down the adult DIRV.

Isometric extrapolation is applied in upward and downward directions whereas linear extrapolation is applied only in the downward direction. Scaling up produces DIRVs only for older infants, whereas scaling down produces DIRVs for both older infants and young children. All the following equations use older infants as the example target population group.

e. Isometric/linear scaling up — young infant DIRV to older infant DIRV
To scale up a young infant AI to produce an older infant AI, the equation is:

Alolder infant = Alyoung infant x (weightolder infant/weightyoung infant)

Because neither the growth factor nor power exponent 0.75 is applied in this method, it is equivalent to linear scaling up.

f. Isometric scaling down — adult DIRV to older infant or young child DIRV To scale down an adult DIRV to produce an older infant DIRV, the equation is: [INL50 or AI]older INFANT = [INL50 or AI]ADULT X (weightolder INFANT/ weightadult)(1 + growth factor)

As for allometric extrapolation, adjustments for the amounts of nutrients incorporated into newly formed tissue are accounted for by the growth factor; conversion from the INL_{50} to the INL_{98} by applying the same CV used to convert the adult INL_{50} also applies. Occasionally alternative scaling parameters to body weights are used such as energy DIRVs, for example for sodium. The various growth factors are given in Appendix Table A3.

g. Linear scaling down — adult DIRV to older infant or young child DIRV

To scale down an adult DIRV to produce an older infant DIRV, the equation is:

[INL50 or AI]OLDER INFANT = [INL50 or AI]ADULT X (weightolder INFANT/ weightadult)

This method is similar to isometric downward scaling (2f) but without the growth factor.

EFSA's derivation of the phosphorus DIRVs as AI for older infants and young children is also included in this subcategory. In this case, the DIRVs for phosphorus are calculated by dividing the calcium DIRV for the same population group (AI or PRI) by a constant that represents the lower bound of the molar ratio of calcium to phosphorus in the whole body (1.4:1). Similarly, the NCM derived the phosphorus DIRV from their calcium DIRVs according to the equimolar ratio of calcium to phosphorus.

EFSA's and NCM's approach differs from the 2g equation above in that the reference DIRV is for another nutrient for the same age group, rather than for the same nutrient for another age group, and the body weight quotient is replaced by the ratio of atomic mass of phosphorus to calcium.

h. Linear scaling using unit measures for older infant or young child DIRVs

For a small number of nutrients, the INL_{50} /AI for older infants and/or young children is based on an amount of nutrient per unit measure such as body weight, energy DIRV or protein DIRV. This unit value may be applicable to all ages or only to infants and children.

To produce an older infant DIRV from unit measures, the equation is:

[INL50 or AI]OLDER INFANT = Nutrient amount/kg weight x weightolder INFANT

This result may be also multiplied by (1 + growth factor) to allow for growth e.g. NCM DIRV for magnesium, based on EU Scientific Committee for Food (SCF)¹⁵.

Category 3 Estimated nutrient intake of the target group, or interpolation

i. Estimated nutrient intake

An AI for older infants derived from an estimate of their nutrient intake is the sum of nutrients consumed from human milk and complementary foods. The nutrient content of human milk during exclusive breastfeeding is generally applied to all stages of infancy, although occasionally, the concentration of a nutrient in human milk from the second half of infancy is available e.g. protein DIRV. National dietary surveys or other appropriate data sources are used to estimate median nutrient intakes from consumption of complementary foods. Use of this method requires the survey data to identify foods fortified with the nutrient of interest so that nutrient intakes can be adjusted down by



tion amounts.

Also, for the three vitamin DIRVs expressed as vitamin equivalents, dietary intake estimates reflect the choice of the particular equivalence equation which may or may not account for vitamin isomers, although in reality, this is unlikely to lead to a significant difference in the DIRVs. The reference human milk volumes consumed by older infants are given in Appendix Table A1.

This method assumes that the nutrient intakes are estimated from an apparently healthy population and therefore support health, although there is no information to determine whether the amounts consumed exceed requirement. It is not clear why this method is sometimes preferred over an extrapolation method.

accounting for the additional fortifica- j. Interpolation between DIRVs for young infants and older children/adult age groups

Interpolation between the DIRVs of widely differing age groups is used when DIRVs for young infants and another non-consecutive older age group such as older children are established but data on which to set DIRVs for the intervening age group/s are scant or perhaps extrapolation results are not meaningful. In this case, the DIRVs for the intervening group/s are estimated and smoothed between the DIRVs of the two other groups. It is not clear why this method is sometimes preferred over an extrapolation method.

Summary of categories and subcategories

All categories and subcategories of methods described above are summarised in Table 3. Categories are listed in ranked order according to discrete approach and associated scientific rigour. Within a category, the subcategories are listed but not ranked.

Category number	Category description	Subcategory number and description
1	Using physiological evidence from the target group	1a The factorial summation of the various components involved in physiological growth, maintenance and loss e.g. for protein, iron and zinc.
		1b The estimation of nutrient intake based on maintenance of a healthy plasma or urinary biomarker, or absence of deficiency disease in the target group e.g. for vitamin D, iodine.
2	Extrapolation up or down from DIRVs of other popula- tion groups	2c Allometric scaling up from young infant DIRV
		2d Allometric scaling down from adult DIRV
		2e Isometric/linear scaling up from young infant DIRV
		2f Isometric scaling down from adult DIRV
		2g Linear scaling down from adult DIRV
		2h Linear scaling from unit measures
3	Estimates of nutrient intake of the target group; or interpolation	3i Estimates of nutrient intake from diets of healthy older infants or young children
		3j Interpolation between DIRVs of younger and older age groups

Table 3: Derivation methods categories and subcategories

2.2 Change in Dietary Intake Reference Values Classification upon Extrapolation

The classification of the reference DIRV in an extrapolation equation holds for the extrapolated Dietary Intake Reference Values for all age groups except in the case of older infants and INL_{50} . Downward extrapolation of INL_{50} to produce a DIRV for older infants is considered to introduce more uncertainty than for older age groups because the resultant classification is downgraded from INL_{50} to AI as shown in Table 4.

Another difference relates to the application of the CV. When an adult INL_{50} is extrapolated down for young children, the resultant INL_{50} is multiplied by the CV to obtain the INL_{98} but this step is omitted when the scaled down DIRV for older infants is classified as AI. Again, this is because of a greater level of uncertainty surrounding an extrapolated INL_{50} for older infants. Also, for both population groups, the inherent uncertainty of the reference DIRV is carried forward to the extrapolated DIRV.

Reference DIRV used in extrapolation	Extrapolation direction	Extrapolated DIRV older infant	Extrapolated DIRV young children
Adult INL ₅₀	Down	AI (or rarely INL ₅₀)	INL50
Adult AI	Down	AI	AI
Young infant AI or equiv- alent nutrient intake from human milk	Up	AI	AI Used only for biotin by two RASBs

Table 4: Change in DIRV classification upon extrapolation

2.3 Choice of Derivation Method

Although RASBs and FAO/WHO describe their derivation methods to various extents, the choice of a particular method is rarely explained in sufficient detail to enable differentiation by subcategory. Questions such as: why was upward rather than downward extrapolation applied?; or why was an estimate of nutrient intake used instead of extrapolation?; are not generally answered in the publications. The EFSA scientific opinions are a notable exception as they more consistently provide their reasons for method selection. The IOM's consideration of the thiamin DIRV for older infants is an example of an explanation of the choice of method. After rounding, the results of three methods were compared: scaling up - 0.2 mg; scaling down - 0.3 mg; intake estimate - 0.6 mg.

The intake estimate was judged to be unreasonably high compared with the two extrapolation methods because some foods in the surveyed infant diet were suspected of being fortified with thiamin. Extrapolation was the preferred approach over intake estimate but the reason for the choice of a particular extrapolation method was not discussed.

RASBs and FAO/WHO publications often do not explain the reasons for selecting one method over another when multiple methods are available and they produce different values. However, it seems that the most proportionate result relative to DIRVs of adjoining age groups is often selected. If there is no valid reason to select one DIRV over another, the values from two methods may be averaged.

3 APPLICATION TO THE GENERAL PRINCIPLES

Previously, the general principles for the establishment of NRVs-R for the general population⁹ accorded higher priority to DIRVs derived from evidence evaluated through a systematic review. A clearer ranked categorization of methods used to derive DIRVs for older infants and young children comprising three categories based on discrete approach and associated scientific rigour is available from this report. The strength of the scientific rigour associated with these method categories is further discussed in order below.

Factorial methods based on physiological evidence from the target group are regarded as more scientifically reliable than other methods even when some factorial elements are derived from adults or other age groups. These methods allow the DIRVs for older infants and young children to be classified as INL_{50} and INL_{98} because fewer assumptions underpin their derivation.

In the absence of direct evidence from the target groups, the number and validity of assumptions underpinning the other methods increase the uncertainty of the DIRV. The choice of a particular extrapolation equation should be appropriate for the known function and metabolism of the nutrient in the target and reference populations. This applies to the choice of type and value of the scaling parameters, use of modifying factors such as the 0.75 exponent and growth factor. The level of introduced uncertainty will depend on how well the chosen equation reflects the physiology.

The selection of an equation's reference DIRV will also carry forward the uncertainty associated with quality of that reference DIRV. Reference DIRVs may be derived from a higher or lower quality evidence base, or from an estimate of nutrient intake. Young infant DIRVs based on estimates of nutrient intake from human milk depend on representative sampling of milk from healthy mothers that take account of all factors that may affect data quality, together with high quality laboratory analysis. The uncertainty associated with extrapolation of DIRVs for young children is sufficiently small to allow the same classification for reference and derived DIRV but the uncertainty increases to downgrade the classification of the derived DIRV for older infants to AI when the reference DIRV is INL₅₀.

Nutrient intake estimates and interpolation are regarded as having greater uncertainty than extrapolation. Intake estimates are based on food consumption surveys conducted in the same or comparable region, food composition analysis, and the assumption that the surveyed population is healthy. The quality of dietary surveys and laboratory analysis of foods consumed may vary. There is no information to determine whether the surveyed nutrient intake exceeds requirement. Interpolation relies on scientific judgement to estimate and smooth the DIRVs between those for younger and older population groups. Although these two methods have little in common, their levels of scientific rigour are not sufficiently different to place them in separate categories. DIRVs derived by these two methods are also classified as AI for older infants and young children.

The three discrete method categories, summarised in order in Table 5, are considered suitable for inclusion in the general principles for establishment of NRVs-R for older infants and young children as they are readily differentiated by approach and associated scientific rigour as well as being a practical number to facilitate decision making.

Table 5: Method categories

	Method category	Brief description
1	Use of physiological evidence from the target group	The factorial summation of the various components involved in physiological growth, maintenance and loss in the target group. Also, the estimation of nutrient intake based on maintenance of a healthy plasma or urinary biomarker, or absence of deficiency disease in the target group.
2	Extrapolation up or down from DIRVs of other age groups	Allometric, isometric and linear scaling methods using refer- ence DIRVs from adults or young infants.
3	Estimates of nutrient intake of the target group; or interpo-lation	Estimates of nutrient intake from diets of healthy older infants and young children; or interpolation between DIRVs of younger and older age groups.

Table 5 also includes a brief description of the method subcategories that may prove useful in providing an additional level of detail to assist, where necessary, the selection of DIRVs as the basis for NRVs-R for older infants and young

children. Subcategories may be particularly helpful when a nutrient's DIRV is derived by the same method but its value varies across publications, or it has the same value across publications but is derived by several methods.

4 DIETARY INTAKE REFERENCE VALUES FOR VITAMINS, MINERALS AND PROTEIN

The details of the DIRVs for older infants and young children and their derivation methods for 25 nutrients from the most recent published reports of six RASBs and FAO/WHO are compiled into a series of tables, one for each nutrient. Each nutrient table presents the following details of the DIRVs by population group and publication:

- DIRV classification (as INL₅₀ and INL₉₈, or AI)
- numerical value
- applicable age range
- subcategory key for the derivation method.

In reading the table series, it is important to note that FAO/WHO and NCM present their DIRVs only as RNI or RI respectively (see Table 1), without separation into INL_{qg} and AI on the basis of method quality. Because DIRVs from these two publications are described respectively as "meant to meet the basic nutritional needs of over 97% of the population" and "set to cover the requirements of 97% of the group", they are classified as INL₉₈ for the purposes of the table series. Occasionally, the individual nutrient chapters in these two publications also report a mean requirement or INL_{50} and where given, these are also included in the nutrient tables.

4.1 Details of Dietary Intake Reference Values in Table Series

RASB source publications for general population NRVs-R

Nearly all RASB source publications of DIRVs used to establish NRVs-R for the general population also present DIRVs for younger age groups. Exceptions are NIHN's 2015 edition which replaced the 2010 edition, and some EFSA scientific opinions that were unavailable when particular general population NRVs-R were established. Also, RASB publications were not consulted in relation to the adequacy of sodium and potassium since Codex had not established NRVs-**Requirement** for these two nutrients for the general population.

Noting the exceptions above, the RASB and FAO/WHO source publications that previously provided the DIRVs for general population NRVs-R are indicated in the table series by superscripts **A** or **B** in column 1. Superscript **A** means only one publication was the source of the selected DIRV; whereas superscript **B** means the RASB publication was one of several contributing to a mean DIRV that became the NRV-R. Details of the derivation of the general population NRVs-R are available on the Codex Alimentarius website^{16, 17}.

Age ranges and sex

The Codex age ranges are 6-12 months for



older infants, and 12-36 months for young children, with the upper bound of each range as the 1st and 3rd birthday respectively as interpreted by CCNFSDU for this work.

The age ranges for the two population groups in the RASB and FAO/WHO publications are similar to the Codex age divisions. Older infants' ages range from 6 or 7 months to 11 or 12 months. The RASB and FAO/WHO age ranges also vary with respect to their overlap or not at the 12 month/1 year boundary between older infants and young children.

The age ranges of young children all have 1 year as their lower bound but their upper bound and age range are more variable than for older infants. Several publications set their upper bounds at 3 years which is interpreted to be just before the 4th birthday because the next age group in the publication starts at 4 years. In contrast, NIHN sets 1-2 years, 3-5 years; and NCM sets 12-23 months, 2-5 yrs. Two publications also set specific ages at 6 monthly intervals for particular nutrient DIRVs such as protein.

All age ranges in the table series should be read as inclusive unless otherwise indicated by the < sign. The NIHN DIRVs for young children aged 3-5 years are not reported because only the first day of that period is relevant to this report. NIHN is the only RASB to provide

DIRVs by sex for very young children although this occurs infrequently because very few DIRVs differ between boys and girls in the first years of life. The table series present separate NIHN DIRVs for boys and for girls only when they differ.

Nutrient units

The unit of measurement of the DIRV such as gram, milligram or microgram is given according to the original publications. For a small number of nutrients, DIRVs are expressed in different units of measurement which means the tables for these nutrients have DIRVs of differing magnitudes. Also, units for folate, vitamin A, and vitamin E may be expressed as vitamin equivalents although for vitamin A, the names and associated calculation of equivalents differ across publications. The various alternatives for equivalents for all three vitamins are shown in the relevant table footnotes.

Key to derivation methods

The notation for the derivation keys in section 2.1 is also applied in the table series. For example derivation key 2c represents category 2 – extrapolation; method c – allometric scaled up metabolically. To ensure clarity, no letter is assigned to the same category number more than once i.e. there is no 1a, 2a and 3a.

Some entries in the table series show two keys joined by AND to indicate when results from two methods are averaged to produce the DIRV. Occasionally, the results of the two methods are the same but still are shown by AND as averaged. Also, the derivation key is shown as *unknown* for the occasional NCM DIRV where the DIRV is reproduced from the 2004 edition¹⁸ and no details either in the NCM publication or reproduced in the EFSA scientific opinion are given. The legend of derivation keys relevant to each table is shown in the table footnotes.

4.2 Observations on Data in Table Series

Some nutrient DIRVs are derived by the same subcategory method by all or most RASBs and FAO/WHO whereas a variety of methods is used for other nutrient DIRVs even when the DIRVs have similar value. Table 6 presents the number of subcategory methods in each category by population group and DIRV classification.

Category	Older infant	S	Young Child	TOTAL	
	AI	INL	AI	INL	
1 Physiological evidence	5	20	3	32	60
2 Extrapolation	35	24	17	63	139
3 Nutrient intake/interpolation	22	7	17	8	54
TOTAL	62	51	37	103	253

 Table 6: Number of subcategory methods* by category, and population group and DIRV classification

*Excluding methods shown as unknown or where methods are averaged

Overall as shown in the right hand column, extrapolation is the most common category followed by the other categories in approximately equal measure. This distribution of method categories also applies to older infants but differs for young children such that after extrapolation, physiological evidence is more common than nutrient intake estimate/interpolation.

Of the DIRVs in each population group, more than half are classified as AIs for older infants and about one quarter are classified as AIs for young children. Extrapolation is more likely classified as AI for older infants and as INL for young children. Across the two population groups, physiological evidence is not always classified as INL, and intake estimate/interpolation is not always classified as AI. This outcome generally supports the definitions of AI and INL, noting that scientific judgement about the quality of the physiological evidence may also determine the DIRV classification.

Apart from the selection of the methods themselves, the reasons for the differences in DIRVs include the type and basis of the original data; or the particular reference data used in extrapolation such as adult or young infant DIRVs, reference body

weights and human milk composition and volumes.

Several publications in the table series have some DIRVs for older infants that are remarkably higher than or the same as those for young children. Examples are vitamin A, vitamin C, iodine and iron. Conversely, some publications have a very large interval between DIRVs for older infants and those for young children such as for vitamin K and potassium. The reason for what appears to be biologically implausible outcomes often relates to the choice of different derivation methods for the two population groups. In such cases, not all RASBs comment on the reasons for the disparity.

5 TABLE SERIES: DIETARY INTAKE REFERENCE VALUES ¹⁻⁸ FOR OLDER INFANTS AND YOUNG CHILDREN WITH DERIVATION KEY

5.1 Protein

PROTEIN INL ₅₀ given only as /kg body wt		Olde	er Infants			Υοι	ıng Childrer	1		
Country/ region RASB	Age range [body wt]	AI	INL50	INL98	Кеу	Age range [body wt]	AI	INL50	INL98	Key
Australia & New Zealand NHMRC/ MOH(2006)	7-12mo	1.6 g/kg =14 g			3i	1-3yr		0.92 g/kg	14 g	1a
United States & Canada IOM (2002/2005)	7-12mo		1 g/kg	11 g	1a	1-3yr		0.87 g/kg	13 g	1a
Europe EFSA (2012)* DIRVs given	6mo [Boy 7.7 kg Girl 7.1 kg]		1.12 g/kg	Boy 10 g Girl 9 g	1a	1yr [Boy 10.2 kg Girl 9.5 kg]		0.95 g/kg	Boy 12 g; Girl 11 g	1a
half yearly						1.5yr [Boy 11.6 kg Girl 10.9 kg]	0.85 g/kg		Boy 12 g; Girl 11 g	
					2yr [Boy 12.7 kg Girl 12.1 kg]		0.79 g/kg	Boy 12 g; Girl 12 g		

*[Body weights for specific ages] in age range columns EFSA:

Derivation key

1a Factorial method; 3i Nutrient intake estimate INL₅₀ given only as /kg body wt INL50 INL98 INL50 Country/region AI Key Age range AI INL98 Key Age range RASB [body wt] [body wt] WHO/FAO/UNU 6mo 1.12 g/kg Boy 10.2g 1a 1yr 0.95 g/kg Boy 11.6 g; 1a (2007)* [Boy 7.8 kg Girl 9.4 g [Boy 10.2 kg Girl 10.8 g Girl 7.2 kg] Girl 9.5 kg] DIRVs given 1.5yr 0.85 g/kg Boy 11.8 g; half yearly [Boy 11.5 kg Girl 11.1 g Girl 10.8 kg] 2yr 0.79 g/kg Boy 11.9 g; [Boy 12.3 kg Girl 11.4 g Girl 11.8 kg] 3i Japan NIHN 6-8mo 1-2yr 15 g 20 g 1a g (2015)* [Boy 8.4 kg | 12.5 g** Girl 7.8 kg] 15.2 g*** DIRVs given 6-8 mo; 25 g 9-11 mo 9-11mo 22.0 g** [Boy 9.1 kg 23.8 g*** Girl 8.4 kg] Nordic 6-11mo 1.1 g/kg 1a 1-<2yr 1.0 g/kg 1a **Countries NCM** (2014)* 2-17yr [2yrs: 0.9 g/kg⁺ Boy 13.2 kg Girl 10.5 kg] DIRVs not given

Older Infants

*[Body weights for specific ages] in age range columns WHO/FAO/UNU, Japan NIHN, also Nordic Countries NCM young children **breast fed Japan NIHN;***formula fed Japan NIHN

ASingle DIRV for general population NRVs-R **Derivation key** 1a Factorial method;

3i Nutrient intake estimate

as g/day)

PROTEIN

Young Children

5.2 Minerals

CALCIUM		Ol	der Infa	nts		Young Children							
Country/region RASB	Age range	AI	INL50	INL98	Кеу	Age range	AI	INL50	INL98	Key			
Australia & New Zealand NHMRC/MOH (2006)	7-12mo	270 mg			3i	1-3yr		360 mg	500 mg	1a			
United States & Canada IOM (2011)	6-12mo	260 mg			3i	1-3yr \		500 mg	700 mg	1a			
Europe EFSA (2015)	7-11mo	280 mg			2e	1-3yr		390 mg	450 mg	1a			
WHO/FAO (2004) ^a	7-12mo			400 mg	1a	1-3yr			500 mg	Зј			
Japan NIHN (2015)	6-11mo	250 mg			Зі	1-2yr		350 mg	B) 450 mg G) 400 mg	1a			
Nordic Countries NCM (2014)	6-11mo			540 mg	unknown	1-<2yr; 2-5yr		500 mg (1-5 yr)	600 mg; 600 mg	1a			

<u>A</u>Single DIRV for general population NRVs-R Derivation key

1a Factorial method; 2e Isometric/linear scaling up from DIRV_{young infant}

3i Nutrient intake estimate

3j Interpolation

MAGNESIUM **Older Infants Young Children Country/region** Age AI INL50 INL98 Key AI INL50 INL98 Key Age RASB range range Australia & 7-12mo 75 mg 3i 1-3yr 2h 65 mg 80 mg New Zealand NHMRC/MOH (2006) United States 3i 2h 7-12mo 75 mg 1-3yr 65 mg 80 mg & Canada IOM (1997)^B Europe EFSA 7-11mo 80 mg 2e 1-<3yr 170 mg 3i (2015) and 3i WHO/FAO 7-12mo 54 mg 1-3yr 3j 3j 60 mg (2004)^{<u>B</u>} provisional Japan NIHN 3i 2h 6-11mo 60 mg 1-2yr 60 mg 70 mg (2015)[₿] Nordic 6-11mo 80 mg 2h 1-<2yr; 85 mg; 2h **Countries NCM** 2-5yr 120 mg (2014)^B

^BMultiple DIRVs for general population NRVs-R

Derivation key

1a Factorial method; 2e Isometric/linear scaling up from DIRV_{young infant} 2h Linear scaling from unit measure 3i Nutrient intake estimate 3j Interpolation

IRON		Older Infants							Young Cł	nildren	
Country/ region RASB	Age range	AI	INL50	INL98	Key		Age range	AI	INL50	INL98	Key
Australia & New Zealand NHMRC/MOH (2006)	7-12mo		7 mg	11 mg	1a		1-3yr		4 mg	9 mg	1a
United States & Canada IOM (2001)	7-12mo		6.9 mg	11 mg	1a		1-3yr		3 mg	7 mg	1a
Europe EFSA (2015)	7-11mo		8 mg	11 mg	1a		1-3yr		5 mg	7 mg	1a
WHO/FAO (2004) ^A (% bioavail- ability range 15–5%)	7-12mo (0.5-1yr)			6.2 mg (15%) 7.7 mg (12%) 9.3 mg (10%) 18.6 mg (5%)	1a		1-3yr			3.9 mg (15%) 4.8 mg (12%) 5.8 mg (10%) 11.6 mg (5%)	1a
Japan NIHN (2015)	6-11mo		3.5 mg	B) 5 mg G) 4.5 mg	1a		1-2yr		3 mg	4.5 mg	1a
Nordic Countries NCM (2014)	6-11mo			8 mg	1a		1-<2yr; 2-5yr			8 mg; 8 mg	1a

 $\underline{\textbf{A}}Single \ DIRV$ for general population NRVs-R

Derivation key 1a Factorial method

ZINC **Older Infants Young Children** Country/ AI INL50 INL98 AI INL50 INL98 Age Key Age Key region range range RASB Australia & 7-12mo 2.5 mg 3 mg 1a 1-3yr 2.5 mg 3 mg 1a New Zealand NHMRC/MOH (2006) 1-3yr United States 7-12mo 2.5 mg 3 mg 1a 2.5 mg 1a 3 mg & Canada IOM (2001) Europe EFSA 7-11mo 2.4 mg 1a 1-3yr 1a 2.9 mg 3.6 mg 4.3 mg (2015) WHO/FAO 7-12mo 2.5 mg 1a 2.4 mg 1a 1-3yr (2004) (50%) (50%) (% bioavail-4.1 mg 4.1 mg ability range (30%) (30%) 50-15%) 8.4 mg 8.3 mg (15%) (15%) Japan NIHN 6-11mo 3i 2d 3 mg 1-2yr 3 mg 3 mg (2015) and 2c Nordic 6-11mo 5 mg 1a 1-<2yr; 5 mg 1a Countries 2-5yr 6 mg NCM (2014) IZiNC^A 6-11mo 3-4 mg 1a 1-3yr 2 mg 1a 4-5 mg 3 mg

ASingle DIRV for general population NRVs-R

Derivation key

1a Factorial method; 2c Allometric scaling up from $\mathsf{DIRV}_{\mathsf{young infant}}$ 2d Allometric scaling down from $\tilde{\text{DIRV}}_{\text{adult}}$ 3i Nutrient intake estimate and: average of two specified methods

IODINE	Older Infants						Your	ıg Childr	en	
Country/region RASB	Age range	AI	INL50	INL98	Кеу	Age range	AI	INL50	INL98	Key
Australia & New Zealand NHMRC/MOH (2006)	7-12mo	110 µg			2c	1-3yr		65 µg	90 µg	1b
United States & Canada IOM (2001)	7-12mo	130 µg			2c	1-3yr		65 µg	90 µg	1b
Europe EFSA (2015)	7-11mo	70 µg			1b	1-<3yr	90 µg			1b
WHO /FAO (2004 [≜] Recommendation for 0<5 yrs from (UNU/FAO/WHO/UNICEF (2007)	7-12mo			90 µg	Зј	1-3yr			90 µg	Зј
Japan NIHN (2015)	6-11mo	130 µg			2c	1-2yr		35 µg	50 µg	2d
Nordic Countries NCM (2014)	6-11mo			50 µg	2f	1-<2yr 2-5yr			70 µg 90 µg	2f

ASingle DIRV for general population NRVs-R

Derivation key

1b Maintenance biomarker/absence deficiency; 2c Allometric scaling up from DIRV_{young infant} 2d Allometric scaling down from DIRV_{adult} 2f Isometric scaling down from DIRV_{adult} 3j Interpolation

COPPER		Olde	r Infants	5		Young Children							
Country/region RASB	Age range	AI	INL50	INL98	Key	Age range	AI	INL50	INL98	Key			
Australia & New Zealand NHMRC/MOH (2006)	7-12mo	0.22 mg			3i	1-3yr	0.7 mg			3i			
United States & Canada IOM (2001) [≜]	7-12mo	220 µg			3i	1-3yr		260 µg	340 µg	2d			
Europe EFSA (2015)	7-11mo	0.4 mg			2c and 3i	1-<3yr	0.7 mg			3i			
WHO/FAO (2004)	7-12mo	Not set	Not set	Not set		1-3yr	Not set	Not set	Not set				
Japan NIHN (2015)	6-11mo	0.4 mg			Зі	1-2yr		0.2 mg	0.3 mg	2d			
Nordic Countries NCM (2014)	6-11mo			0.3 mg	2d	1-<2yr; 2-5yr			0.3 mg; 0.4 mg	2d			

^ASingle DIRV for general population NRVs-R

Derivation key

2c Allometric scaling up from DIRV_{young infant} 2d Allometric scaling down from DIRV_{adult} 3i Nutrient intake estimate and: average of two specified methods

SELENIUM		Old	er Infant	S		You	ng Childre	en		
Country/region RASB	Age range	AI	INL50	INL98	Key	Age range	AI	INL50	INL98	Key
Australia & New Zealand NHMRC/MOH (2006) ^b	7-12mo	15 µg			2c	1-3yr		20 µg	25 µg	2d
United States & Canada IOM (2000) ^B	7-12mo	20 µg			2c and 3i	1-3yr		17 µg	20 µg	2d
Europe EFSA (2014) ^{<u>B</u>}	7-11mo	15 µg			2e	1-3yr	15 µg			2f
WHO/FAO (2004) Recommendation from FAO/IAEA/ WHO	7-12mo		8.2 µg	10 µg	Зј	1-3yr		13.6 µg	17 µg	Зј
Japan NIHN (2015)	6-11mo	15 µg			2c	1-2yr		10 µg	10 µg	2d
Nordic Countries NCM (2014) [≞]	6-11mo			15 µg	2*	1-<2yr; 2-5yr			20 μg; 25 μg	2*

*extrapolation method unknown

Multiple DIRVs for general population NRVs-R

Derivation key

2c Allometric scaling up from DIRV_{young infant} 2d Allometric scaling down from DIRV_{adult} 2e Isometric scaling up from DIRV_{young infant} 2f Isometric scaling down from DIRV_{adult} 3i Nutrient intake estimate 3j Interpolation and average of two specified methods

B

MANGANESE **Older Infants Young Children** Country/ Age AI INL50 INL98 Key Age AI INL50 INL98 Key region range range RASB Australia & 7-12mo 0.6 mg 3i and 1-3yr 2 mg 3i 2d New Zealand NHMRC/ MOH(2006) 3i and 3i United 7-12mo 0.6 mg 1-3yr 1.2 mg States & 2d Canada IOM (2001)₿ Europe EFSA 7-11mo 0.02-0.5 mg 2e -1-3yr 0.5 mg 2g (2013)[₿] (2g and 3i) WHO/FAO 7-12mo Not set Not 1-3yr Not Not Not Not ----(2004) set set set set set Japan NIHN 6-11mo 3i 1-2yr 2d 0.5 mg 1.5 mg (2015) Nordic 6-11mo Not set Not Not 1-<2yr; Not Not _ _ Not --Countries set set 2-5yr set set set NCM (2014)

BMultiple DIRVs for general population NRVs-R

Derivation key

2d Allometric scaling down from DIRV_{adult} 2e Isometric scaling up from DIRV_{young infant} 2g Linear scaling down from DIRV_{adult} 3i Nutrient intake estimate and average of two specified methods

PHOSPHORUS		Olde	er Infants	5			Υοι	ing Childro	en	
Country/ region RASB	Age range	AI	INL50	INL98	Key	Age range	AI	INL50	INL98	Кеу
Australia & New Zealand NHMRC/ MOH(2006)	7-12mo	275 mg			3i	1-3yr		380 mg	460 mg	1a
United States & Canada IOM (1997) [≜]	7-12mo	275 mg			3i	1-3yr		380 mg	460 mg	1a
Europe EFSA (2015)	7-11mo	160 mg			2g	1-3yr	250 mg			2g
WHO/FAO (2004)	7-12mo	Not set	Not set	Not set		1-3yr	Not set	Not set	Not set	
Japan NIHN (2015)	6-11mo	260 mg			3i	1-2yr	500 mg			3i
Nordic Countries NCM (2014)	6-11mo			420 mg	2g	1-<2yr; 2-5yr			470 mg; 470 mg	2g

<u>A</u>Single DIRV for general population NRVs-R

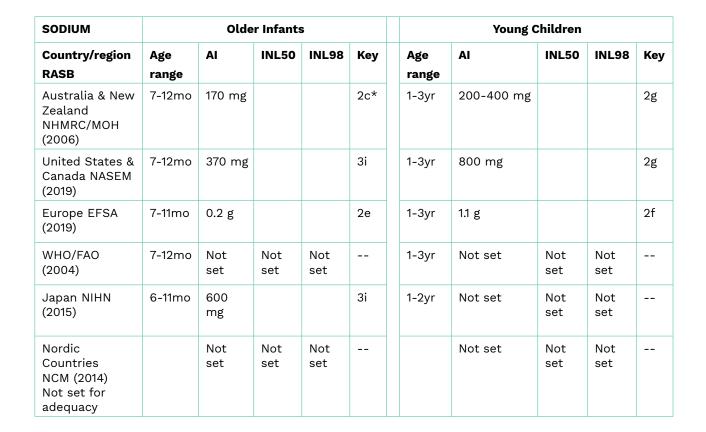
Derivation key

1a Factorial method 2g Linear scaling down from DIRV_{adult} 3i Nutrient intake estimate



POTASSIUM		Olde	r Infants	i			Young C	hildren		
Country/region RASB	Age range	AI	INL50	INL98	Key	Age range	AI	INL50	INL98	Key
Australia & New Zealand NHMRC/MOH (2006)	7-12mo	700 mg			3i	1-3yr	2000 mg			3i
United States & Canada NASEM (2019)	7-12mo	860 mg			3i	1-3yr	2000 mg			3i
Europe EFSA (2016)	7-11mo	750 mg			2f	1-3yr	800 mg			2f
WHO/FAO (2004)	7-12mo	Not set	Not set	Not set		1-3yr	Not set	Not set	Not set	
Japan NIHN (2015)	6-11mo	700 mg			3i	1-2yr	Boy 900 mg Girl 800 mg			2d
Nordic Countries NCM (2014)	6-11mo			1.1 g	2f?	1-<2yr; 2-5yr			1.4 g; 1.8 g	2f

Derivation key 2d Allometric scaling down from DIRV_{adult} 2f Isometric scaling down from DIRV_{adult} 3i Nutrient intake estimate



Derivation key

2c Allometric scaling up from DIRV_{young infant} *Extrapolation parameter is product of body weight and DIRV_{energy} (not body weight alone)

2e Isometric scaling up from DIRV_{young infant}

2f Isometric scaling down from $\mathsf{DIRV}_{\mathsf{adult}}$

2g Linear scaling down from DIRV_{adult}

3i Nutrient intake estimate

5.3 Vitamins

VITAMIN A		Old	er Infants	5				Young Chi	ldren	
Country/region RASB	Age range	AI	INL50	INL98	Key	Age range	AI	INL50	INL98	Key
Australia & New Zealand NHMRC/MOH (2006)	7-12mo	430 µg RE			3i	1-3yr		210 µg RE	300 µg RE	2d
United States & Canada IOM (2001) [≜]	7-12mo	500 µg RAE			2c and 3i	1-3yr		210 µg RAE	300 µg RAE	2d
Europe EFSA (2015)	7-11mo		190 µg RE	250 µg RE	1a	1-3yr		205 µg RE	250 µg RE	1a
WHO/FAO (2004)	7-12mo		190 µg RE	400 µg RE	Зј	1-3yr		200 µg RE	400 µg RE	Зј
Japan NIHN (2015)	6-11mo	400 µg RAE			2c	1-2yr		B) 300 μg RAE G) 250 μg RAE)	B) 400 μg RAE G) 350 μg RAE	1a
Nordic Countries NCM (2014)	6-11mo			300 µg RE	2d	1-<2yr; 2-5yr			300 µg RE 350 µg RE	2d

RE = retinol equivalents; 1 RE =1 μ g retinol +6 μ g β -carotene +12 μ g other pro-vitamin A carotenoids RAE = retinol activity equivalents; 1 RAE = 1 μ g retinol +12 μ g β -carotene +24 μ g other pro-vitamin A carotenoids

<u>A</u>Single DIRV for general population NRVs-R

Derivation key

1a Factorial method 2c Allometric scaling up from DIRV_{young infant} 2d Allometric scaling down from DIRV_{adult} 3i Nutrient intake estimate 3j Interpolation and: average of two specified methods



VITAMIN D		Olde	er Infants	5		Young C	hildren			
Country/region RASB	Age range	AI	INL50	INL98	Key	Age range	AI	INL50	INL98	Key
Australia & New Zealand NHMRC/MOH (2006)	7-12mo	5 µg*			1b	1-3yr	5 µg**			1b
United States & Canada IOM (2011) [≞]	6-12mo	10 µg*			1b	1-3yr		10 µg*	15 µg*	1b
Europe EFSA (2016) ^{<u>B</u>}	7-11mo	10 µg*			1b	1-3yr	15 µg*			1b
WHO/FAO (2004) [₿]	7-12mo			5 µg*	1b	1-3yr			5 µg*	1b
Japan NIHN (2015)	6-11mo	5 µg**			1b	1-2yr	2 µg***			2d
Nordic Countries NCM (2014)	6-11mo			10 µg*	1b	1-<2yr; 2-5yr		7.5 μg; 7.5 μg	10 µg; 10 µg	1b

* limited/no sunlight including in winter with previous sun exposure in summer **adequate & limited/no sunlight

***free living subjects, unknown exposure to sunlight

<u>B</u>Multiple DIRVs for general population NRVs-R

Derivation key

1b Maintenance biomarker/absence deficiency; 2d Allometric scaling down from DIRV_{adult}

VITAMIN C		Olde	er Infant	S			Y	oung Chil	dren	
Country/region RASB	Age range	AI	INL50	INL98	Key	Age range	AI	INL50	INL98	Key
Australia & New Zealand NHMRC/MOH (2006)	7-12mo	30 mg			2c	1-3yr		25 mg	35 mg	Зј
United States & Canada IOM (2000)	7-12mo	50 mg			2c and 3i	1-3yr		13 mg	15 mg	2d
Europe EFSA (2013)	7-11mo		Not set	20 mg*	1b	1-3yr		15 mg	20 mg	2g
WHO/FAO (2004)	7-12mo			30 mg	Зј	1-3yr			30 mg	Зј
Japan NIHN (2015)	6-11mo	40 mg			2c and 2d	1-2yr		30 mg	35 mg	2d
Nordic Countries NCM (2014)	6-11mo			20 mg	2f	1-<2yr; 2-5yr			25 mg; 30 mg	2f

*EFSA - Arbitrary, 3 times amount to prevent scurvy, (SCF, 1993)¹⁶

<u>B</u>Multiple DIRVs for general population NRVs-R

Derivation key

1b Maintenance biomarker/absence deficiency; 2c Allometric scaling up from DIRV_{young infant} 2d Allometric scaling down from DIRV_{adult} 2f Isometric scaling down from DIRV_{adult} 3i Nutrient intake estimate 3j Interpolation and: average of two specified methods



VITAMIN K		Olde	er Infants	S		Young Children Age AI INL50 INL98					
Country/region RASB	Age range	AI	INL50	INL98	Key	Age range	AI	INL50	INL98	Key	
Australia & New Zealand NHMRC/MOH (2006)	7-12mo	2.5 µg			2c	1-3yr	25 µg			3i	
United States & Canada IOM (2001)	7-12mo	2.5 µg			2c	1-3yr	30 µg			3i	
Europe EFSA (2017)	7-11mo	10 µg			2g	1-3yr	12 µg			2g	
WHO/FAO (2004) [≜]	7-12mo			10 µg	2g	1-3yr			15 µg	2g	
Japan NIHN (2015)	6-11mo	7 µg			Зі	1-2yr	60 µg			2d	
Nordic Countries NCM (2014)	6-11mo	Not set	Not set	Not set		1-<2yr; 2-5yr	Not set	Not set	Not set		

<u>A</u>Single DIRV for general population NRVs-R

Derivation key

2c Allometric scaling up from DIRV_{young infant} 2d Allometric scaling down from DIRV_{adult} 2g Linear scaling down from DIRV_{adult} 3i Nutrient intake estimate

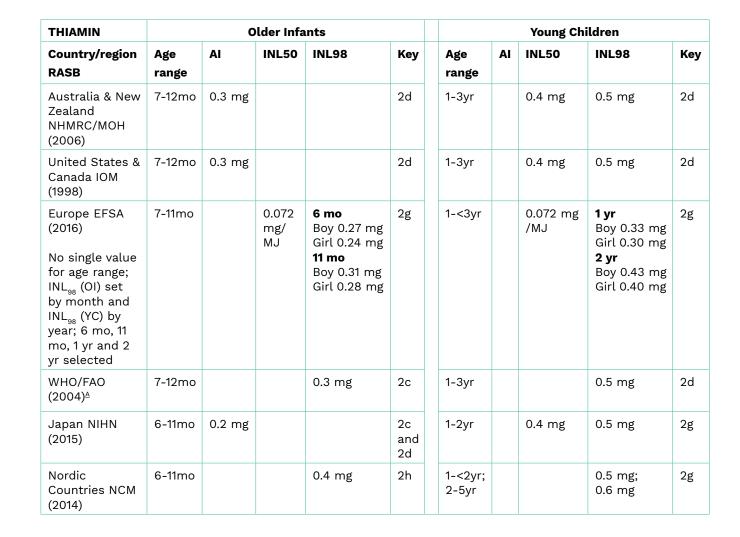
VITAMIN E		Olde	er Infant	S			You	ng Childı	ren	
Country/region RASB	Age range	AI	INL50	INL98	Key	Age range	AI	INL50	INL98	Key
Australia & New Zealand NHMRC/MOH (2006) ^B	7-12mo	5 mg α-TE			2c	1-3yr	5 mg α-TE			3i
United States & Canada IOM (2000)	7-12mo	5 mg α-toc			2c	1-3yr		5 mg as α-toc	6 mg α-toc	2d
Europe EFSA (2015) [≞]	7-11mo	5 mg α-toc			2c	1-3yr	6 mg α-toc			3i
WHO/FAO (2004) ^E * Best estimate	7-12mo			2.7 mg α-TE*	Зј	1-3yr			5 mg α-TE*	Зј
Japan NIHN (2015) [≞]	6-11mo	4.0 mg α-toc			2d	1-2yr	3.5 mg α-toc			3i
Nordic Countries NCM (2014) [®]	6-11mo			3 mg α-toc	2h	1-<2yr; 2-5yr			4 mg αtoc; 5 mg α-toc	2h

 α -toc = α -tocepherol; 1 mg α -toc = 1 mg RRR- α -tocopherol (d- α -tocopherol) α -TE = α -tocepherol equivalents; 1 mg α -TE =1 mg α -tocopherol + 0.4 β -tocopherol + 0.1 γ -tocopherol

BMultiple DIRVs for general population NRVs-R

Derivation key

2c Allometric scaling up from DIRV_{young infant} 2d Allometric scaling down from DIRV_{adult} 2h Linear scaling from unit measure 3i Nutrient intake estimate 3j Interpolation



ASingle DIRV for general population NRVs-R

Derivation key

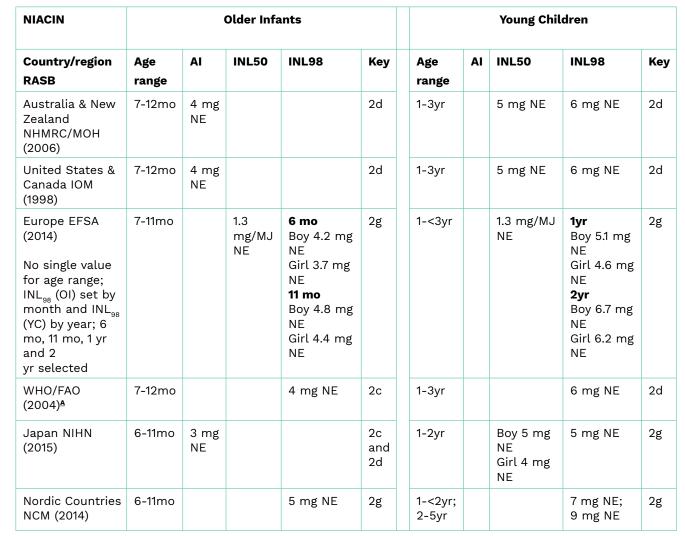
2c Allometric scaling up from DIRV_{young infant} 2d Allometric scaling down from DIRV_{adult} 2g Linear scaling down from DIRV_{adult} 2h Linear scaling from unit measure and: average of two specified methods

RIBOFLAVIN		Olde	er Infants	5			١	oung Chi	ldren	
Country/region RASB	Age range	AI	INL50	INL98	Key	Age range	AI	INL50	INL98	Key
Australia & New Zealand NHMRC/MOH (2006)	7-12mo	0.4 mg			2c and 2d	1-3yr		0.4 mg	0.5 mg	2d
United States & Canada IOM (1998)	7-12mo	0.4 mg			2c and 2d	1-3yr		0.4 mg	0.5 mg	2d
Europe EFSA (2017)	7-11mo	0.4 mg			2c	1-3yr		0.5 mg	0.6 mg	2d
WHO/FAO (2004) ^a	7-12mo			0.4 mg	2c	1-3yr			0.5 mg	2d
Japan NIHN (2015)	6-11mo	0.4 mg			2c and 2d	1-2yr		0.5 mg	B) 0.6 mg G) 0.5 mg	2g
Nordic Countries NCM (2014)	6-11mo			0.5 mg	2g	1-<2yr; 2-5yr			0.6 mg; 0.7 mg	2g

 $\underline{\textbf{A}}Single \ DIRV$ for general population NRVs-R

Derivation key

2c Allometric scaling up from DIRV_{young infant} 2d Allometric scaling down from DIRV_{adult} 2g Linear scaling down from DIRV_{adult} and: average of two specified methods



NE means niacin equivalents; 1 mg NE = 1 mg niacin +60 mg tryptophan

<u>A</u>Single DIRV for general population NRVs-R

Derivation key

2c Allometric scaling up from DIRV_{young infant} 2d Allometric scaling down from DIRV_{adult} 2g Linear scaling down from DIRV_{adult} and: average of two specified methods

VITAMIN B6		Old	er Infan	ts			Y	oung Chilo	dren	
Country/region RASB	Age range	AI	INL50	INL98	Key	Age range	AI	INL50	INL98	Key
Australia & New Zealand NHMRC/MOH (2006)	7-12mo	0.3 mg			2c	1-3yr		0.4 mg	0.5 mg	2d
United States & Canada IOM (1998)	7-12mo	0.3 mg			2c and 2d	1-3yr		0.4 mg	0.5 mg	2d
Europe EFSA (2016)	7-11mo	0.3 mg			2c and 2d	1-3yr		0.5 mg	0.6 mg	2d
WHO/FAO (2004) [≜]	7-12mo			0.3 mg	2c	1-3yr			0.5 mg	2d
Japan NIHN (2015)	6-11mo	0.3 mg			2c and 2d	1-2yr		0.4 mg	0.5 mg	2g
Nordic Countries NCM (2014)	6-11mo			0.4 mg	2g	1-<2yr; 2-5yr			0.5 mg; 0.7 mg	2g

$\underline{\textbf{A}}Single \ DIRV$ for general population NRVs-R

Derivation key

2c Allometric scaling up from DIRV_{young infant} 2d Allometric scaling down from DIRV_{adult} 2g Linear scaling down from DIRV_{adult} and: average of two specified methods

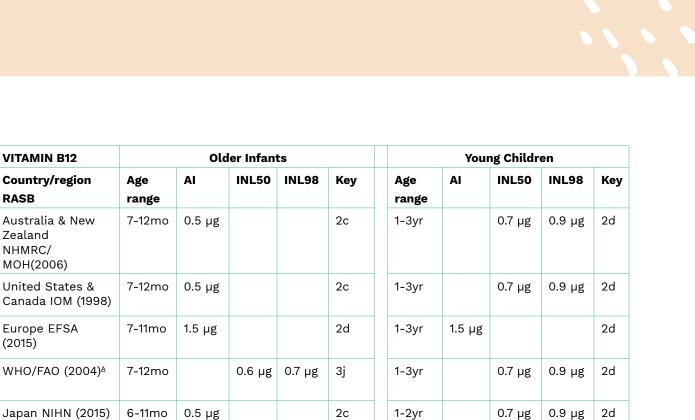
FOLATE		Old	er Infant	S			Y	oung Chil	dren	
Country/region RASB	Age range	AI	INL50	INL98	Key	Age range	AI	INL50	INL98	Key
Australia & New Zealand NHMRC/MOH (2006)	7-12mo	80 μg DFE			2c and 2d	1-3yr		120 µg DFE	150 μg DFE	2d
United States & Canada IOM (1998)	7-12mo	80 µg DFE			2c and 2d	1-3yr		120 µg DFE	150 µg DFE	2d
Europe EFSA (2014)	7-11mo	80 µg DFE			2c	1-3yr		90 µg DFE	120 µg DFE	2d
WHO/FAO (2004) [≜]	7-12mo			80 µg DFE	2c and 2d	1-3yr		120 µg DFE	150 µg DFE	2d
Japan NIHN (2015) As folic acid	6-11mo	60 µg			2c and 2d	1-2yr		70 µg	90 µg	2d
Nordic Countries NCM (2014) Not DFE	6-11mo			50 µg	2h	1-<2yr; 2-5yr			60 µg; 80 µg	2h

DFE = dietary folate equivalents; μ g dietary folate equivalents (DFE) = μ g food folate + 1.7 μ g folic acid added to food or as supplement).

ASingle DIRV for general population NRVs-R

Derivation key

2c Allometric scaling up from DIRV_{young infant} 2d Allometric scaling down from DIRV_{adult} 2h Linear scaling from unit measure and: average of two specified methods



Japan NIHN (2015)	6-11mo	0.5 µg		2c and 2d	1-2yr	0.7
Nordic Countries NCM (2014)	6-11mo		0.5 µg	2h	1-<2yr; 2-5yr	

ASingle DIRV for general population NRVs-R

VITAMIN B12

RASB

Zealand NHMRC/ MOH(2006) United States &

Country/region

Australia & New

Europe EFSA

(2015)

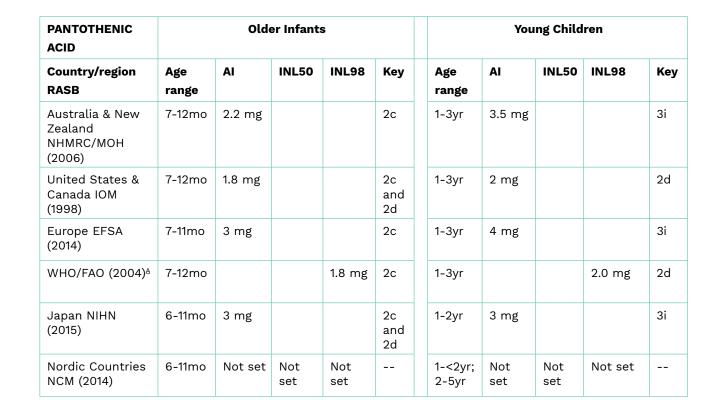
Derivation key

2c Allometric scaling up from DIRV_{young infant} 2d Allometric scaling down from DIRV_{adult} 2h Linear scaling from unit measure and: average of two specified methods

0.6 µg;

0.8 µg

2h



ASingle DIRV for general population NRVs-R

Derivation Key

2c Allometric scaling up from DIRV_{young infant} 2d Allometric scaling down from DIRV_{adult} 3i Nutrient intake estimate and: average of two specified methods

BIOTIN		Old	der Infar	its		Young Children				
Country/region RASB	Age range	AI	INL50	INL98	Key	Age range	AI	INL50	INL98	Key
Australia & New Zealand NHMRC/MOH (2006)	7-12mo	6 µg			2c	1-3yr	8 µg			2c
United States & Canada IOM (1998)	7-12mo	6 µg			2c	1-3yr	8 µg			2c
Europe EFSA (2014)	7-11mo	6 µg			2c	1-3yr	20 µg			3i
WHO/FAO (2004) ^a	7-12mo			6 µg	2c	1-3yr			8 µg	2d
Japan NIHN (2015)	6-11mo	10 µg			2c and 2d	1-2yr	20 µg			2d
Nordic Countries NCM (2014)	6-11mo	Not set	Not set	Not set		1-<2yr; 2-5yr	Not set	Not set	Not set	

$\underline{\textbf{A}}Single \ DIRV$ for general population NRVs-R

Derivation Key 2c Allometric scaling up from DIRV_{young infant} 2d Allometric scaling down from DIRV_{adult} 3i Nutrient intake estimate and: average of two specified methods

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APPENDIX: REFERENCE PARAMETERS USED TO DERIVE DIRVS

The following reference data used by the RASBs to derive the AI and INL_{50} DIRVs for older infants and young children are presented in the next three tables.

A1 Younger and Older Infants

The age ranges, body weights of infants and volumes of breast milk used to derive DIRVs for older infants are shown in Table A1. The body weight data varies slightly among RASBs depending on the data source, usually drawn from national or international growth charts or databases.

Age range **Reference body weight** Breast milk volume for **Country/region** RASBs¹⁻⁸ Older infant (mean of both sexes unless nutrient intake specified) Young **Older Infants** Young Older Infants Infants Infants Australia & New Zealand 7-12mo 7 kg 9 kg 0.78 L 0.6 L NHMRC/MOH (2006) United States & Canada IOM 7-12mo 0.78 L 0.6 L 6 kg 9 kg (1997, 2001, 2005) Boy 6.4 kg 0.8 L Europe EFSA (2010, 2013, 7-11mo Boy 8.9 kg _ _ Girl 5.8 kg Girl 8.6 kg 2014, 2017) Mean 6.1 kg Mean 8.6 kg WHO/FAO (2004) 7-12mo 6 kg 9 kg 0.75 L -0.65 L 0.85 L WHO/FAO/UNU (2007) 6 mo Boy 7.8 kg (Protein) Girl 7.2 kg Boy 10.2 kg 1 yr Girl 9.5 kg 0.78 | 0.60 | Japan NIHN (2015) 6-11mo Boy 6.3 kg Boy 8.8 kg Girl 5.9 kg Girl 8.1 kg (6-8mo) 0.45 L (9-11mo) 0.53 L (6-11mo) Nordic Countries NCM (2014) 6-11mo 0.75 L --9 kg _ _ IZiNC (2004) *0.776 L 6-11mo 9 kg *0.714 L (6-8mo); (0-2mo); 0.616 L 0.784 L (9-11mo) (3-5mo)

Table A1: Reference data for age range, infant body weights and breast milk volume

*from lactation estimates

A2 Young Children and Adults

The age ranges, and body weights used to derive DIRVs for young children vary slightly among RASBs as shown in Table A2. The body weights for young children are drawn from national or international survey data. Adult body weights are taken from national or international survey data as measured body weights or derived from median heights and a BMI of 22 or 23 kg/m² for young adults only or a broader age range as indicated in Table A2. Some RASBs updated body weights during the period of publication.

During the period of development of DIRVs in the United States and Canada, and the European Union, the reference adult body weights were adjusted downward from measured body weights to those corresponding to median height and ideal BMI.

Country/region RASBs ¹⁻⁸	Age range Young children	Reference body weight		
		Young children	Adults	
Australia & New Zealand NHMRC/MOH (2006)	1-3yr	13 kg	Young adult 19-30 yrs Male 76 kg; Female 61 kg	
United States & Canada IOM (1997, 2001, 2005); 2019)	1-3yr	13 kg to 2001 12 kg from 2002	Young adult 19-30 yrs Male 76 kg; Female 61 kg (to 2001) Male 70 kg; Female 57 kg (from 2002)	
Europe EFSA EFSA (2010, 2013, 2014, 2017)	1-3yr	Boy 13.0 kg; Girl 12.5 kg (2012) Boy 12.2 kg; Girl 11.5 kg (from 2013) Mean 11.9 kg	Adult 18-59 yrs (to 2012) Male 74.6 kg; Female 62.1 kg Adult 18–79 yrs (from 2013) Male 68.1 kg; Female 58.5 kg Mean 63.3 kg	
WHO/FAO (2004) WHO/FAO/UNU (2007) (Protein)	1–3yr 1 yr; 2 yr	12 kg (Zn, Mg) or 13 kg (Fe) Boy 10.2 kg; 12.3 kg Girl 9.5 kg ; 11.8 kg;	Adult 19–65 yrs Male 65 kg (Zn, Mg); 75 kg (Fe); Female 55 kg (Zn, Mg); 62 kg (Fe)	
Japan NIHN (2015)	1-2yr;	Boy 11.7 kg; Girl 11.0 kg	Young adult 18-29 yrs Male 63.2 kg; Female 50.0 kg	
Nordic Countries NCM (2014)	2yr 2-5yr	Boy 13.2 kg Girl 12.5 kg 16.1 kg	Adult 18-74 yrs Male 75.4 - 72.1 kg; Female 64.4 - 61.8 kg	
IZINC (2004)	1-3yr	12 kg	Adult 19+ yrs Male 65 kg; Female 55 kg	

Table A2: Reference data for age range, body weights for young children and adults



A3 Growth Factors

The growth factors shown in Table A3 used in downward extrapolation methods 2d and 2f represent the approximate proportional increase in protein requirements for growth relative to the maintenance requirement at the different ages. These factors are used because adult reference DIRVs are based only on maintenance and allowance is needed for incorporation into newly formed tissues for growth when extrapolating DIRVs for older infants and young children. Growth factors are not needed in extrapolating up from young infants as growth is already accounted for in their reference DIRVs.

Table A3: Growth factors

17,18

Country/region RASBs1-8	Growth factor		References
Australia & New Zealand NHMRC/MOH (2006)	0.3	(7mo-3yr)	United States & Canada (1998)
United States & Canada IOM (1997, 2001, 2005).	0.3	(7mo-3yr)	United States & Canada (1998)
Europe EFSA EFSA (2010, 2013, 2014, 2017)	0.57 0.25	(7-11mo) (1-3yr)	EFSA DIRV for Selenium, Appendix G
WHO/FAO (2004)	0.3	(7mo-3yr)	United States & Canada (1998)
Japan NIHN (2015)	0.3	(6mo-2yr)	United States & Canada (1998)
Nordic Countries NCM (2014)	0.3 0.15	(6mo-<2yr) (2-13yr)	Adapted from United States & Canada (2001, = same data as 1998)
IZINC (2004)	Not applica- ble		



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