6 September 2024

ISDI Response to CL 2024/51-NFSDU on NRVs-R For Persons Aged 6 – 36 Months

A. GENERAL PRINCIPLES FOR ESTABLISHING NUTRIENT REFERENCE VALUES (NRVs-R) FOR PER-SONS AGED 6 – 36 MONTHS (Part A) (comments at Step 6)

In response to the draft general principles for establishing nutrient reference values ISDI would like to comment the following:

ISDI generally supports the preamble and definitions as currently worded in CX/NFSDU 24/44/4, Part A, Appendix I. We also support the inclusion of the proposed definition of Adequate intake.

For section 3 GENERAL PRINCIPLES FOR ESTABLISHING NRVs-R, ISDI has the following specific comments:

- ISDI supports Section 3.1 of the general principles as worded.
- In section 3.2, ISDI agrees with the general principle that reference values or ranges recently established by RASBs may be more appropriate to consider when there is not, or there is an older, FAO/WHO DIRV for a nutrient. We also support the consideration of elements including rigour of scientific methods, the underlying data quality, the strength of the evidence, and the most recent independent review of the science when deriving NRVs-R from RASBs.

  However, ISDI does not support determining the combined NRV-R by calculating the mean value of the two age groups. ISDI asks the working group to reconsider selecting the higher value of the proposed NRVs-R for older infants and young children when determining a combined NRV-R, as long as it does not exceed the UL, where available. ISDI believes this is the best way to ensure the nutrient requirements of the combined population are met, thereby preventing deficiency while also avoiding the potential risk of toxicity by taking ULs into account.

  ISDI disagrees with the concern that choosing the higher NRV-R in the case of nutrients that have no defined UL would drive excessive intake of a nutrient to the point of toxicity or adverse events. In some cases, an UL has not been set for a nutrient because no adverse events have been identified that could be a basis for deriving an upper limit. Additionally, as the combined age range spans only 30 months, and the difference between NRVs-R for the two age ranges is not large, it is also highly unlikely that nutrients consumed at the recommended NRV-R, even at the higher NRV-R by either age group, would result in risk of adverse events or toxicity. However, chronically consuming a nutrient at levels below the NRV-R could increase the risk of deficiency. Therefore, taking the higher NRV-R would be the most conservative approach

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to balancing deficiency with toxicity. ISDI would like to ask for clarification on the concern that, for countries that label foods based on a fixed quantity versus per portion, choosing the higher NRV-R would drive higher consumption of these foods in older infants.

- ISDI supports Section 3.3 of the general principles as worded.

B. NRVs-R for persons aged 6 – 36 months (at Step 4)

In response to the stepwise process for establishing NRVs-R for persons aged 6 – 36 months and the NRVs-R for persons older infants and young children and for the combined age range of 6 – 36 months (Appendix I, CX/NFSDU 24/44/4, Part B) ISDI would like to comment the following:

- ISDI notes Member countries should have visibility to evidence included in review and process of grading the evidence by the FAO/WHO expert working group. The general principles state, "Relevant daily intake reference values provided by FAO/WHO that are based on a recent review of the science should be taken into consideration as primary sources in establishing NRVs-R." The language "taken into consideration" infers that the values should be considered or assessed in the context of new evidence. The principles also state that new relevant DIRVs from RASBs "that reflect recent independent review of the science…could also be taken into consideration." Therefore, ISDI supports an updated process:

  Step 1: Identify new or updated daily intake reference values (DIRVs) from FAO/WHO for older infants and young children and assess for establishing NRVs-R.

  Step 1a: Evaluate derivation of the new or updated FAO/WHO DIRV based on rigour of scientific methods, the underlying data quality, and the strength of evidence.

  Step 1b: Compare the new or updated FAO/WHO DIRVs to the earlier FAO/WHO DIRV and relevant DIRVs from RASBs.

  Step 1c: If derivation of the new or updated FAO/WHO DIRV are the same or higher than relevant DIRVs from RASBs on the elements of rigour of scientific methods, the underlying data quality, and the strength of the evidence, then select the new FAO/WHO DIRV as the recommended NRV-R. If not, then go to step 2.*

  **As per Step 2 note 1, the new FAO/WHO data would then replace the older FAO/WHO data*

- ISDI agrees that DIRVs from RASBs that are based on recent independent review of the science should be taken into consideration, with higher priority given to values where evidence has been evaluated by a systematic review.

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However, as outlined in our proposed Step 1, we believe DIRVs from RASBs should also be taken into consideration alongside new or updated DIRVs from FAO/WHO and values from both FAO/WHO and RASBs should be evaluated based elements outlined in the General Principle: rigour of scientific methods, the underlying data quality, and the strength of the evidence. If the new or updated DIRVs from FAO/WHO are evaluated in the context of DIRVs from RASBs and ranked the same or higher on the elements of rigour of scientific methods, the underlying data quality, and strength of the evidence, the new or updated DIRV from FAO/WHO should be selected as the NRV-R. To align with the proposed Step 1, ISDI suggests the following edit to Step 2:

> *Step 2: Aligned with General Principle 3.1, when new or updated DIRVs by FAO/WHO are not selected for establishing NRVs-R OR when updated DIRVs have not been established by FAO/WHO for the vitamins and minerals, relevant DIRVs that reflect recent independent review of the science from RASBs can be considered, with higher priority given to values where evidence has been evaluated by a systematic review.*

- ISDI agrees with Step 3 of the process as being in line with the General Principles. This approach is also consistent with the weighting of evidence by other authoritative groups. This method is also outlined as the appropriate scientific methodology for developing DIRVs as published in the FAO "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". ISDI also agrees with the use of the median vs the mean as it is less prone to the effect of outliers.

- ISDI supports selection of Option 1 to determine the combined NRV-R for 6-36 months, as this ensures that the highest nutrient requirements of the population are reasonably met, as long as the lowest UL is not exceeded. This approach manages both the potential risks of toxicity and deficiency. In cases when the combined NRV-R exceeds the lowest UL, ISDI believes using the most sensitive population's UL would be appropriate and safe.

- ISDI agrees with Step 5 of the process as being in line with the General Principles.

With regards to the summary table Summary Tables of NRVs-R for Older Infants and Young Children and for the combined age range 6-36 months Appendix II CX/NFSDU 24/44/4 Part B (for comments at Step 3), ISDI would like to comment the following:

- ISDI supports use of Approach 1 (consideration of data from FAO/WHO & 'more recent RASBs' only) as in line with the general principles, which states "relevant DIRVs that reflect recent independent review of the science from RASBs can be considered".

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- For vitamin D, supplementation studies and dose-response modelling have generally concluded that a vitamin D intake of 10 µg /day in infants 6-12 months and 10-15 µg /day in children 1-3 years is adequate to obtain a serum 25(OH)D concentration of 50 nmol/L, considering minimal exposure to sunlight. Recent recommendations by IOM, EFSA, and Nordic Council of Ministers are higher than 5 µg. This is likely due to determination that a target serum 25(OH)D concentration of 50 nmol/L is indicative of vitamin D sufficiency, as well as more recent availability of data to generate dose-response models. ISDI recommends in that context to consider RASBs values as more up to date than the 2004 FAO/WHO DIRV and recalculate the NRVs values accordingly.

- For magnesium, with Approach 1, because of the RASBs values considered for older infants versus young children, the Stepwise Process leads to a lower NRV-R for young children as compared to older infants, which does not seem to be the intent of DIRVs. This should be reviewed before final agreement.

- ISDI supports selection of Option 1 to determine the combined NRVs-R for vitamins for 6-36 months, as this ensures that the highest nutrient requirements of the population are reasonably met, as long as the lowest UL is not exceeded. This approach manages both the potential risks of toxicity and deficiency.

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