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Use of multiple micronutrient powders for home fortification of foods consumed by infants and children 6–23 months of age

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Contents

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WHO Guideline[1]

Use of multiple micronutrient powders for home fortification of foods consumed by infants and children 6–23 months of age

Summary

It is estimated that 190 million preschool infants and children are affected by vitamin A deficiency and 293 million children in the same age group have anaemia. Member States have requested guidance from the World Health Organization (WHO) on the effects and safety of the use multiple micronutrient powders for home fortification of foods consumed by infants and children 6–23 months of age in support of their efforts to achieve the Millennium Development Goals.

WHO has developed the present evidence-informed recommendations using the procedures outlined in the *WHO handbook for guideline development*. The steps in this process included: (i) identification of priority questions and outcomes; (ii) retrieval of the evidence; (iii) assessment and synthesis of the evidence; (iv) formulation of recommendations, including research priorities; and (v) planning for dissemination, implementation, impact evaluation and updating of the guideline. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology was used to prepare evidence profiles related to preselected topics, based on up-to-date systematic reviews.

The guideline development group for nutrition interventions, the Nutrition Guidance Expert Advisory Group (NUGAG), comprises content experts, methodologists, representatives of potential stakeholders, and consumers. These experts participated in several WHO technical consultations concerning this guideline, held in Geneva, Switzerland, and Amman, Jordan, in 2010 and 2011. Members of the External Experts and Stakeholders Panel were identified through a public call for comments, and the panel was involved throughout the guideline development process. NUGAG members voted on the strength of the recommendation, taking into consideration: (i) desirable and undesirable effects of the intervention; (ii) the quality of the available evidence; (iii) values and preferences related to the intervention in different settings; and (iv) the cost of options available to health-care workers in different settings. All NUGAG members completed a Declaration of Interests Form before each meeting.

Home fortification of foods with micronutrient powders containing at least iron, vitamin A and zinc is recommended to improve iron status and reduce anaemia among infants and children 6–23 months of age (strong recommendation). The overall quality of the evidence for iron deficiency was found to be high, whereas for anaemia, haemoglobin concentration, iron status and growth it was moderate. Ideally, interventions with multiple micronutrient powders should be implemented as part of a national infant and young child feeding programme.

[1] A WHO guideline is any document, whatever its title, containing WHO recommendations about health interventions, whether they be clinical, public health or policy interventions. A recommendation provides information about what policy-makers, health-care providers or patients should do. It implies a choice between different interventions that have an impact on health and that have ramifications for the use of resources. All publications containing WHO recommendations are approved by the WHO Guidelines Review Committee.

Scope and purpose

This guideline provides global, evidence-informed recommendations on the use of multiple micronutrient powders for home fortification of foods consumed by infants and young children 6–23 months of age.

The guideline will help Member States and their partners in their efforts to make informed decisions on the appropriate nutrition actions to achieve the Millennium Development Goals, in particular the eradication of extreme poverty and hunger (MDG 1) and reduction of child mortality (MDG 4). The guideline is intended for a wide audience including policy-makers, their expert advisers, and technical and programme staff at organizations involved in the design, implementation and scaling-up of nutrition actions for public health.

This document presents the key recommendation and a summary of the supporting evidence. Further details of the evidence base are provided in Annex 1 and other documents listed in the references.

Background

Iron and vitamin A deficiencies have the largest documented disease burden among micronutrients (*1, 2*), particularly in developing countries. Infants and children are the most vulnerable groups with regard to micronutrient malnutrition, given the high vitamin and mineral intake they need to support their rapid growth and adequate development (*3*). Diets that are predominantly plant-based generally provide insufficient amounts of key micronutrients to meet the recommended nutrient intakes in the age range of 6–23 months. The inclusion of animal-source foods to cover the nutrient gap has cost implications and may be not practical for the lowest income groups (*4, 5*). Although there are no global estimates of vitamin and mineral deficiencies specifically in children under the age of 2 years, 190 million preschool children worldwide are affected by vitamin A deficiency and 293 million children in the same age group have anaemia (*6*). To date, no direct estimates of zinc deficiency have been published for any age group but it is thought that it may be as widespread as iron deficiency (*2*).

Vitamin and mineral deficiencies frequently occur simultaneously, and their combined effects during the critical period from preconception to 23 months of age may be associated with increased neonatal mortality and morbidity, as well as irreversible adverse physical and cognitive (*7–9*) outcomes that lead to unfavourable lifelong consequences for health, productivity and economic growth. Nutritional risk factors, including underweight, suboptimal breastfeeding, and vitamin and mineral deficiencies, particularly vitamin A, iron or zinc deficiency, are responsible for 3.9 million deaths (35% of total deaths) and 144 million disability-adjusted life years (DALYs)[1] (33% of total DALYs) in children less than 5 years of age (*2*).

Interventions to prevent and/or treat micronutrient malnutrition typically include exclusive breastfeeding during the first six months of life; dietary diversification to include foods with highly absorbable vitamins and minerals; fortification of staple and complementary foods; control of parasitic infections; and provision of nutritional

[1] A DALY is the sum of the years of potential life lost due to premature mortality and the years of productive life lost due to disability.

supplements (*10*). Micronutrient interventions, particularly vitamin A and zinc supplements for children, and fortification of foods with iron and iodine, are among the most cost-effective global efforts (*11*) for health improvement. However, despite the well-recognized benefits of micronutrient interventions, successful implementation of population-level programmes has been constrained by poor adherence to supplement dosing regimens and by the potential dose-related side-effects and safety concerns.

Home fortification of foods with powders containing multiple micronutrients has been suggested as an alternative to increase the vitamin and mineral intake in children 6–23 months of age. This intervention consists of the addition of a mixture of micronutrients in powder form to any semi-solid food. The mixture is provided in single-serving sachets, the contents of which are simply sprinkled over the food before consumption (*12*). With this intervention, foods can be fortified either in the home or in any other place where meals are to be consumed (for example schools, refugee camps); thus it is also referred to as "point-of-use fortification" (*13*).

Summary of evidence

A Cochrane systematic review (*13*) was conducted to assess the effects and safety of home fortification with multiple micronutrient powders of foods consumed by children under 2 years with regard to improving health outcomes. The review compared the provision of multiple micronutrient powders containing at least iron, zinc and vitamin A versus no intervention or placebo, or regular supplementation practices (i.e. iron supplements, iron with folic acid supplements or iron with vitamin and mineral supplements, given in drops or syrups), for children living in a variety of settings, including malaria-endemic areas. The outcomes considered critical by the Nutrition Guidance Expert Advisory Group (NUGAG) were anaemia, haemoglobin concentration, iron status and growth. Secondary outcomes included side-effects, morbidity, mortality and neurocognitive outcomes. The potential modifying effects of baseline anaemia prevalence and iron status, iron and zinc content of the product, provision scheme, malaria setting and duration of intervention were also evaluated.

The review included eight trials (n = 3 748 children) conducted in Cambodia, Ghana, Haiti, India, Kenya, the Kyrgyz Republic and Pakistan, seven of which were considered high quality. Six trials compared daily provision of multiple micronutrient powders versus no intervention or placebo and two compared the same with the use of daily iron drops. The interventions lasted for 2–12 months and only one study evaluated the use of multiple micronutrient powders on a flexible basis (taken at will by the participants during a given period, but no more than one sachet per day). All trials used encapsulated ferrous fumarate as the source of iron and zinc gluconate as the source of zinc. Five trials were performed in malaria-endemic areas, but it was unclear from the reports whether malaria prevention and control programmes were in place in the study sites or whether concomitant malaria interventions were made available to the study participants.

In summary, home fortification of foods with multiple micronutrient powders reduced anaemia at the end of the intervention by 31% (average relative risk (RR)

0.69, 95% confidence interval (CI) 0.60–0.78, six studies) and iron deficiency by 51% (RR 0.49, 95% CI 0.35–0.67, four trials) in infants and young children when compared with no intervention or a placebo. However, it had no effect on weight-for-age, length-for-age and weight-for-length Z-scores measured at the end of the intervention. The use of multiple micronutrient powders seemed as effective as the daily use of iron supplements in reducing anaemia (RR 0.89, 95% CI 0.58–1.39, one study) and raising haemoglobin concentration (MD –2.36 g/l, 95% CI –10.30 to 5.58, two studies), but the data need to be interpreted with caution as very few studies evaluated the equivalence between the two interventions.

The intervention seemed to be equally efficacious among infants and young children 6–23 months of age living in settings with different prevalences of anaemia (range 25–100%) and malaria endemicity versus areas with sporadic malarial cases, and regardless of whether the intervention lasted 2 months or up to 6 or 12 months.

No deaths were reported in the trials. Only scarce data were available on morbidity, neurocognitive outcomes, other indicators of vitamin and mineral status, and side-effects. Diarrhoea was reported in five trials but the differences in the definitions used by the researchers (i.e. average episodes of diarrhoea per child, number of children with at least one episode of diarrhoea or longitudinal prevalence of diarrhoea) prevented assessment with certainty of the effect of home fortification of foods with multiple micronutrient powders on this outcome. No data were available on the effects of home fortification of foods with multiple micronutrient powders on the incidence and severity of malaria.

The use of multiple micronutrient powders was well accepted by the study participants, but adherence to the intervention was variable and in several studies it was comparable with the adherence achieved for interventions involving provision of standard iron drops or syrups to infants and young children.

The overall quality of the evidence for iron deficiency was found to be high, whereas for anaemia, haemoglobin concentration, iron status and growth it was moderate (Annex 1).

Recommendation

Home fortification of foods with multiple micronutrient powders is recommended to improve iron status and reduce anaemia among infants and children 6–23 months of age (*strong recommendation*)[1].

A suggested scheme for home fortification with multiple micronutrient powders of foods consumed by infants and children aged 6–23 months is presented in Table 1.

[1] A strong recommendation is one for which the guideline development group is confident that the desirable effects of adherence outweigh the undesirable effects. This can be either in favour of or against an intervention. Implications of a strong recommendation for patients are that most people in their situation would desire the recommended course of action and only a small proportion would not. Implications for clinicians are that most patients should receive the recommended course of action, and adherence to this recommendation is a reasonable measure of good-quality care. With regard to policy-makers, a strong recommendation means that it can be adapted as a policy in most situations.

Table 1

Suggested scheme for home fortification with multiple micronutrient powders of foods consumed by infants and children 6–23 months

Composition per sachet[a]	• Iron: 12.5 mg of elemental iron, preferably as encapsulated ferrous fumarate[b] • Vitamin A: 300 μg of retinol • Zinc: 5 mg of elemental zinc, preferably as zinc gluconate
Frequency	One sachet per day
Duration and time interval between periods of intervention	At minimum, for a period of 2 months, followed by a period of 3–4 months off supplementation, so that use of the micronutrient powders is started every 6 months
Target group	Infants and children 6–23 months of age, starting at the same time as weaning foods are introduced into the diet
Settings	Populations where the prevalence of anaemia in children under 2 years or under 5 years of age is 20% or higher

[a] The recommendation for the composition of the powder is based on the doses and nutrients included in the systematic review (*13*). In addition to iron, vitamin A and zinc, multiple micronutrient powders may contain other vitamins and minerals at currently recommended nutrient intake (RNI) doses for the target population (*14*).
[b] 12.5 mg of elemental iron equals 37.5 mg of ferrous fumarate, 62.5 mg of ferrous sulfate heptahydrate or 105 mg of ferrous gluconate.

Remarks

- In malaria-endemic areas, the provision of iron should be implemented in conjunction with measures to prevent, diagnose and treat malaria (*15*).
- This guideline is not applicable to children with specific conditions such as human immunodeficiency virus (HIV) infection or tuberculosis as the effects and safety of the intervention in these specific groups have not been evaluated.
- Programmes involving the use of multiple micronutrient powders for home fortification of foods should be preceded by an evaluation of the nutritional status among children under 5 years of age and existing measures to control anaemia and vitamin A deficiency, such as hookworm control programmes, the provision of supplements and the use of other products for home fortification of foods and fortified complementary foods, to ensure that the daily micronutrient needs are met and not exceeded.

- Such programmes should also include a behaviour change communication strategy that promotes: awareness and correct use of the powders along with information on recommended breastfeeding practices; commencement of complementary foods at 6 months of age; preparation of complementary foods at age-appropriate frequency, amounts, consistency and variety (*16,17*); hand washing with soap and hygienic preparation of food; prompt attention to fever in malaria settings; and measures to manage diarrhoea (*18*).

- The selection of the most appropriate delivery platform should be context-specific, with the aim of reaching the least favoured populations and ensuring an adequate and continued supply of the powders.

- Given the multiple determinants of vitamin and mineral deficiencies and the range of factors affecting successful implementation of the intervention, the provision of multiple micronutrient powders on a larger scale may not produce exactly the same results as observed in the trials informing this guideline.

- In settings where iron supplementation among this population has been widely implemented and has proved to be effective, a cost-effectiveness analysis is recommended to determine whether the current intervention should be replaced by provision of multiple micronutrient powders.

Dissemination, adaptation and implementation

Dissemination

The current guideline will be disseminated through electronic media such as slide presentations, CD-ROMs and the World Wide Web, either through the World Health Organization (WHO) Micronutrients and United Nations Standing Committee on Nutrition (SCN) mailing lists or the WHO nutrition web site. Currently, the Department of Nutrition for Health and Development is developing the WHO e-Library of Evidence for Nutrition Actions (eLENA). This library aims to compile and display WHO guidelines related to nutrition, along with complementary documents such as systematic reviews and other evidence that informed the guidelines, biological and behavioural rationales, and additional resources produced by Member States and global partners. In addition, the guideline will be disseminated through a broad network of international partners, including WHO country and regional offices, ministries of health, WHO collaborating centres, universities, other United Nations agencies and nongovernmental organizations.

Adaptation and implementation

As this is a global guideline, it should be adapted to the context of each Member State. Prior to implementation, interventions involving home fortification of foods with multiple micronutrient powders should have well-defined objectives that take

into account available resources, existing policies, suitable delivery platforms, and suppliers, communication channels and potential stakeholders. Home fortification programmes should start with a pilot and scaled up as experience and evidence grow and resources allow. Ideally, this intervention should be implemented as part of a national infant and young child feeding programme.

To ensure that WHO global guidelines and other evidence-informed recommendations for micronutrient interventions are better implemented in low- and middle-income countries, the Department of Nutrition for Health and Development works with the WHO Evidence-Informed Policy Network (EVIPNet) programme. EVIPNet promotes partnerships at country level between policy-makers, researchers, and civil society to facilitate policy development and implementation through use of the best available evidence.

Monitoring and evaluation of guideline implementation

A plan for monitoring and evaluation with appropriate indicators is encouraged at all stages. The impact of this guideline can be evaluated within countries (i.e. monitoring and evaluation of programmes implemented at national or regional scale) and across countries (i.e. the adoption and adaptation of the guideline globally). The WHO Department of Nutrition for Health and Development, Micronutrients Unit, jointly with the Centers for Disease Control and Prevention (CDC) International Micronutrient Malnutrition Prevention and Control (IMMPaCt) programme, and with input from international partners, has developed a generic logic model for micronutrient interventions in public health (*19*) to depict the plausible relationships between inputs and expected MDGs by applying the micronutrient programme evaluation theory. Member States can adjust the model and use it in combination with appropriate indicators, for designing, implementing, monitoring and evaluating the successful scaling-up of nutrition actions.

For evaluation at the global level, the WHO Department of Nutrition for Health and Development is developing a centralized platform for sharing information on nutrition actions in public health practice implemented around the world. By sharing programmatic details, specific country adaptations and lessons learnt, this platform will provide examples of how guidelines are being translated into nutrition actions.

The recommendation in the present guideline should be adapted into a locally appropriate document to meet the specific needs of each country and health service.

Implications for future research

Discussion with NUGAG members and stakeholders highlighted the limited evidence in some areas, meriting further research on the use of multiple micronutrient powders for home fortification of foods consumed by infants and children 6–23 years of age, in particular, in the following areas:

- side-effects associated with home fortification with multiple micronutrient powders in various settings where infection and malnutrition are common, with

emphasis on the harmonization of outcome definitions to help to assess the harms and benefits of this intervention in various contexts, particularly in areas with high transmission of malaria;

- safety and efficacy of the iron compounds (or combinations of compounds) used in multiple micronutrient powder formulations for children 6–23 months of age. If ferric sodium EDTA (FeNaEDTA) is included in clinical trials as a source of iron, the EDTA intake (including other dietary sources) should not exceed 1.9 g EDTA/day (*20*, *21*);
- determination of the safe amounts of folic acid in areas with high malaria endemicity;
- determination of the most appropriate dose of zinc and other vitamins and minerals to be included in multiple micronutrient powders and the effects of these micronutrients on indicators of nutritional status other than iron deficiency and anaemia (e.g. improvement of iodine status, prevention of vitamin A deficiency, prevention of zinc deficiency) and on important functional outcomes including growth and motor and cognitive skills;
- the most effective regimen for distribution and consumption of multiple micronutrient powders, for example intermittent or flexible schemes as alternatives to daily provision of multiple micronutrient powders;
- determination of the most appropriate foods to serve as a vehicle for multiple micronutrient powders to improve their bioavailability;
- impact of the form of delivery (single-serving sachets) of multiple micronutrient powders in areas with limited waste management strategies, to balance the benefits of this intervention against environmental concerns and overall health, that is, not only in terms of nutritional status.

Guideline development process

This guideline was developed in accordance with the WHO evidence-informed guideline development procedures, as outlined in the *WHO handbook for guideline development* (*22*).

Advisory groups

A WHO Steering Committee for Nutrition Guidelines Development, led by the Department of Nutrition for Health and Development and the Department of Research Policy and Cooperation, was established in 2009 with representatives from all WHO departments with an interest in the provision of scientific nutrition advice, including Child and Adolescent Health and Development, Reproductive Health and Research, and the Global Malaria Programme. The Steering Committee guided the development of this guideline and provided overall supervision of the guideline development process (Annex 2). Two additional groups were formed: an advisory guideline group and an External Experts and Stakeholders Panel.

The Nutrition Guidance Expert Advisory Group, NUGAG, was also established in 2009 (Annex 3). NUGAG consists of four subgroups: (i) Micronutrients, (ii) Diet and Health, (iii) Nutrition in Life course and Undernutrition, and (iv) Monitoring and Evaluation. Its role is to advise WHO on the choice of important outcomes for decision-making and in the interpretation of the evidence. NUGAG includes experts from various WHO expert advisory panels and those identified through open calls for specialists, taking into consideration a balanced gender mix, multiple disciplinary areas of expertise and representation from all WHO regions. Efforts were made to include content experts, methodologists, representatives of potential stakeholders (such as managers and other health professionals involved in the health-care process) and consumers. Representatives of commercial organizations may not be members of a WHO guideline group.

The External Experts and Stakeholders Panel was consulted on the scope of the guideline, the questions addressed, and the choice of important outcomes for decision-making, as well as with regard to review of the completed draft guideline (Annex 4). This was done through the WHO Micronutrients and SCN mailing lists that together include over 5500 subscribers, and through the WHO nutrition web site.

Scope of the guideline, evidence appraisal and decision-making

An initial set of questions (and the components of the questions) to be addressed in the guideline was the critical starting point for formulating the recommendation. The questions were drafted by technical staff at the Micronutrients Unit, Department of Nutrition for Health and Development, based on policy and programme guidance needs of Member States and their partners. The population, intervention, control, outcomes (PICO) format was used (Annex 5). The questions were discussed and reviewed by the WHO Steering Committee for Nutrition Guidelines Development, and feedback was received from 48 stakeholders.

The first NUGAG meeting was held on 22–26 February 2010, in Geneva, Switzerland, to finalize the scope of the questions and rank the critical outcomes and populations of interest. The NUGAG – Micronutrients Subgroup discussed the relevance of the questions and modified them as needed. The guideline group scored the relative importance of each outcome from 1 to 9 (where 7–9 indicated that the outcome was critical for a decision, 4–6 indicated that it was important and 1–3 indicated that it was not important). The final key questions on this intervention, along with the outcomes that were identified as critical and important for decision-making, are listed in PICO format in Annex 5.

WHO staff, in collaboration with researchers from other institutions, summarized and appraised the evidence, using the Cochrane methodology for randomized controlled trials.[1] For identifying unpublished studies or studies still in progress, a standard procedure was followed to contact more than 10 international

[1] As part of the Cochrane pre-publication editorial process, reviews are commented on by external peers (an editor and two referees external to the editorial team) and the group's statistical adviser (http://www.cochrane.org/cochrane-reviews). The *Cochrane handbook for systematic reviews of interventions* describes in detail the process of preparing and maintaining Cochrane systematic reviews on the effects of health-care interventions.

organizations working on micronutrient interventions. In addition, the International Clinical Trials Registry Platform (ICTRP), hosted at WHO, was systematically searched for any trials still in progress. No language restrictions were applied to the search. Evidence summaries were prepared according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach to assess the overall quality of the evidence (*23*). GRADE considers: the study design; the limitations of the studies in terms of their conduct and analysis; the consistency of the results across the available studies; the directness (or applicability and external validity) of the evidence with respect to the populations, interventions and settings where the proposed intervention may be used; and the precision of the summary estimate of the effect.

Both the systematic reviews and the GRADE evidence profiles for each of the critical outcomes were used for drafting this guideline. The draft recommendation was discussed by the WHO Nutrition Guidance Steering Committee and NUGAG at a second NUGAG consultation, held on 15–18 November 2010 in Amman, Jordan, and at the third consultation, held on 14–16 March 2011 in Geneva, Switzerland, where the NUGAG members also voted on the strength of the recommendation, taking into account: (i) the desirable and undesirable effects of the intervention; (ii) the quality of the available evidence; (iii) values and preferences related to the intervention in different settings; and (iv) the cost of options available to health-care workers in different settings (Annex 6). Consensus was defined as agreement by simple majority of the guideline group members. WHO staff present at the meeting as well as other external technical experts involved in the collection and grading of the evidence were not allowed to vote. There were no strong disagreements among the guideline group members.

A public call for comments on the final draft guideline was then released. All interested stakeholders became members of the External Experts and Stakeholders Panel but were only allowed to comment on the draft guideline after submitting a signed Declaration of Interests Form. Feedback was received from 15 stakeholders. WHO staff then finalized the guideline and submitted it for clearance by WHO before publication.

Management of conflicts of interest

According to the rules in the WHO *Basic documents* (*24*), all experts participating in WHO meetings must declare any interest relevant to the meeting prior to their participation. The conflicts of interest statements for all guideline group members were reviewed by the responsible technical officer and the relevant departments before finalization of the group composition and invitation to attend a guideline group meeting. All guideline group members and participants of the guideline development meetings submitted a Declaration of Interests Form along with their curriculum vitae before each meeting. In addition, they verbally declared potential conflicts of interest at the beginning of each meeting. The procedures for management of conflicts of interests strictly followed WHO *Guidelines for declaration of interests (WHO experts)* (*25*). The potential conflicts of interest declared by members of the guideline group are summarized on the following page.

- Dr Héctor Bourges Rodriguez declared being chair of the executive board of the Danone Institute in Mexico (DIM), a non-profit organization promoting research and dissemination of scientific knowledge in nutrition, and receiving funds as chair honorarium from DIM. Some of the activities of the DIM may generally relate to nutrition and are funded by Danone Mexico, a food producer.

- Dr Norm Campbell at the first meeting declared owning stock in Viterra, a wheat pool for farmers that neither manufactures products nor has activities related to this guideline. In 2011 Dr Campbell declared no longer owning stocks in this company. He serves as a Pan American Health Organization (PAHO) consultant and has been an adviser to Health Canada and Blood Pressure Canada, both of which are government agencies.

- Dr Emorn Wasantwisut declared serving as a technical/scientific adviser to the International Life Sciences Institute (ILSI)/South East Asia's Food and Nutrients in Health and Disease Cluster and as a reviewer of technical documents and speaker for Mead Johnson Nutritionals. Her research unit received funds for research support from Sight and Life and the International Atomic Energy Agency (IAEA) for the use of stable isotopes to define interactions of vitamin A and iron.

- Dr Beverly Biggs declared that the University of Melbourne received funding from the National Health and Medical Research Council (NHMRC) and Australian Research Council (ARC) for research on weekly iron and folic acid supplementation in pregnancy, conducted in collaboration with the Research and Training Center for Community Development (RTCCD), the Key Centre for Women's Health and the Murdoch Childrens Research Institute.

- Dr Gunn Vist co-authored the systematic review on the use of multiple micronutrient powders in children under 2 years of age. Dr Vist did not vote on the final draft recommendation but remained in the room during the discussions in order to answer questions regarding the systematic review.

Plans for updating the guideline

This guideline will be reviewed in 2013; there are at least six ongoing trials which may be able to provide the evidence that is currently lacking, particularly in malaria-endemic settings. The Department of Nutrition for Health and Development at the WHO headquarters in Geneva, along with its internal partners, will be responsible for coordinating the guideline update following formal *WHO handbook for guideline development* procedures (*22*). WHO welcomes suggestions regarding additional questions for evaluation in the guideline when it is due for review.

References

1. Black RE et al. Maternal and Child Undernutrition Study Group. Maternal and child undernutrition: global and regional exposures and health consequences. *Lancet*, 2008, 371:243–260.

2. *Global health risk. Mortality and burden of disease attributable to selected major risks.* Geneva, World Health Organization, 2009 (http://www.who.int/healthinfo/global_burden_disease/GlobalHealthRisks_report_full.pdf, accessed 21 June 2011).

3. Dewey KG, Brown KH. Update on technical issues concerning complementary feeding of young children in developing countries and implications for intervention programs. *Food and Nutrition Bulletin*, 2003, 24:5–28.

4. PAHO/WHO. *Guiding principles for complementary feeding of the breastfed child.* Washington, DC, Pan American Health Organization, 2001 (http://www.who.int/nutrition/publications/guiding_principles_compfeeding_breastfed.pdf, accessed 21 June 2011).

5. *Guiding principles for feeding non-breastfed children 6–24 months of age*. Geneva, World Health Organization, 2005 (http://whqlibdoc.who.int/publications/2005/9241593431.pdf, accessed 21 June 2011).

6. WHO/CDC. *Worldwide prevalence of anaemia 1993–2005. WHO Global Database on Anaemia*. Geneva, World Health Organization, 2008 (http://whqlibdoc.who.int/publications/2008/9789241596657_eng.pdf, accessed 21 June 2011).

7. Lozoff B. Iron deficiency and child development. *Food and Nutrition Bulletin*, 2007, 28:S560–S571.

8. Sanghvi T, Ross J, Heymann H. Why is reducing vitamin and mineral deficiencies critical for development? The links between VMD and survival, health, education and productivity. *Food and Nutrition Bulletin*, 28 (Suppl. 1):S167–S173.

9. WHO/UNICEF/UNU. *Iron deficiency anaemia assessment, prevention and control: a guide for programme managers*. Geneva, World Health Organization, 2001 (http://www.who.int/nutrition/publications/en/ida_assessment_prevention_control.pdf, accessed 21 June 2011).

10. De Maeyer EM et al. *Preventing and controlling iron deficiency anaemia through primary health care*. Geneva, World Health Organization, 1989 (http://www.who.int/nutrition/publications/micronutrients/anaemia_iron_deficiency/9241542497.pdf, accessed 21 June 2011).

11. Horton S et al. *Scaling up nutrition: what will it cost?* Washington, DC, International Bank for Reconstruction and Development/The World Bank, 2010 (http://siteresources.worldbank.org/HEALTHNUTRITIONANDPOPULATION/Resources/Peer-Reviewed-Publications/ScalingUpNutrition.pdf, accessed 21 June 2011).

12. Zlotkin S et al. Micronutrient sprinkles to control childhood anaemia. *PLoS Medicine*, 2005, 2(1):e1.

13. De-Regil LM et al. Home fortification of foods with multiple micronutrient powders for health and nutrition in children under 2 years of age. *Cochrane Database of Systematic Reviews* 2011, (9): CD008959.

14. WHO/FAO. *Vitamin and mineral requirements in human nutrition*, 2nd ed. Geneva, World Health Organization, 2004 (http://whqlibdoc.who.int/publications/2004/9241546123.pdf, accessed 21 June 2011).

15. *Global malaria report 2010*. Global Malaria Programme. Geneva, World Health Organization, 2010 (http://whqlibdoc.who.int/publications/2010/9789241564106_eng.pdf, accessed 21 June 2011).

16. PAHO. *Guiding principles for complementary feeding of the breastfed child*. Pan American Health Organization, 2003. (http://whqlibdoc.who.int/paho/2003/a85622.pdf, accessed 21 June 2011).

17. *Guiding principles for feeding non-breastfed children 6–24 months of age*. Geneva, World Health Organization, 2004 (http://www.who.int/child_adolescent_health/documents/9241593431/en/index.html, accessed 21 June 2011).

18. WHO/UNICEF joint statement. *Clinical management of acute diarrhoea*. Geneva, World Health Organization, 2004 (http://whqlibdoc.who.int/hq/2004/WHO_FCH_CAH_04.7.pdf, accessed 21 June 2011).

19. WHO/CDC. Logic model for micronutrient interventions in public health. Vitamin and Mineral Nutrition Information System. Geneva, World Health Organization, 2011 (WHO/NMH/NHD/MNM/11.5; http://www.who.int/vmnis/toolkit/WHO-CDC_Logic_Model.pdf, accessed 21 June 2011).

20. FAO/WHO. *Evaluation of certain food additives and contaminants. Sodium iron (III) ethylenediaminetetraacetate, trihydrate*. Sixty-eighth report of the Joint FAO/WHO Expert Committee on Food Additives. Geneva, World Health Organization, 2007 (WHO Technical Report Series 947; http://whqlibdoc.who.int/publications/2007/9789241209472_eng.pdf, accessed 21 June 2011).

21. European Food Safety Authority, Panel on Food Additives and Nutrient Sources added to Food. Scientific opinion on the use of ferric sodium EDTA as a source of iron added for nutritional purposes to foods for the general population (including food supplements) and to foods for particular nutritional uses. *EFSA Journal*, 2010, 8(1):1414 (http://www.efsa.europa.eu/de/scdocs/doc/1414.pdf, accessed 21 June 2011).

22. *WHO handbook for guideline development*. Guidelines Review Committee. Draft March 2010. Geneva, World Health Organization, 2010.

23. Guyatt G et al. GRADE guidelines 1. Introduction – GRADE evidence profiles and summary of findings tables. *Journal of Clinical Epidemiology*, 2011, 64:383–394.

24. *Basic documents*, 47th ed. Geneva, World Health Organization, 2009 (http://apps.who.int/gb/bd/, accessed 19 May 2011).

25. *Guidelines for declaration of interests (WHO experts)*. Geneva, World Health Organization, 2010.

Annex 1 GRADE "Summary of findings" tables

Provision of multiple micronutrient powders versus placebo/no intervention in infants and children 6–23 months of age

Patient or population: Children 6–23 months
Settings: Community settings
Intervention: Home fortification with multiple micronutrient powders
Comparison: Placebo/no intervention

Outcomes	Relative effect (95% CI)	Number of participants (studies)	Quality of the evidence (GRADE)*	Comments
Anaemia (haemoglobin less than 110 g/l)	**RR 0.69** (0.60–0.78)	1447 (6 studies)	⊕⊕⊕⊖ **moderate**[1]	
Iron deficiency (as defined by the trialists)	**RR 0.49** (0.35–0.67)	586 (4 studies)	⊕⊕⊕⊕ **high**[1,2]	
Haemoglobin (g/l)	**MD 5.87** (3.25–8.49)	1447 (6 studies)	⊕⊕⊕⊖ **moderate**[1]	
Iron status (ferritin concentrations in g/l)	**MD 20.38** (6.27–34.49)	264 (2 studies)	⊕⊕⊕⊖ **moderate**[1]	
Weight-for-age (in Z-scores)	**MD 0** (–0.37 to 0.37)	304 (2 studies)	⊕⊕⊕⊖ **moderate**[1]	

CI, confidence interval; RR, risk ratio; MD, mean difference.
*GRADE Working Group grades of evidence:
High quality: We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate quality: We have moderate confidence in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low quality: Our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of the effect.
Very low quality: We have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of the effect.
[1]One study (Adu-Afarwuah, 2007) has serious risk of bias because the control group was not randomized. There was considerable unexplained heterogeneity, but because of the clear conclusion in the summary results, we have chosen not to downgrade.
[2] Assessors upgraded the quality of the evidence (from moderate to high) because of the large effect of the intervention: RR 0.49 (95% CI 0.35-0.67)

For details of studies included in the review, see reference (*13*).

Provision of multiple micronutrient powders versus daily use of iron supplements in infants and children 6–23 months of age

Patient or population: Children 6–23 months
Settings: Community settings
Intervention: Home fortification with multiple micronutrient powders
Comparison: Iron supplements

Outcomes	Relative effect (95% CI)	Number of participants (studies)	Quality of the evidence (GRADE)*	Comments
Anaemia (haemoglobin less 110 g/l)	**RR 0.89** (0.58–1.39)	145 (1 study)	⨁⨁⨀⨀ **low**[1]	
Iron deficiency (as defined by the trialists)	Not estimable	0 (0 studies)		None of the trials reported on this outcome
Haemoglobin (g/l)	**MD –2.36** (–10.30 to 5.58)	278 (2 studies)	⨁⨁⨁⨀ **moderate**[2]	
Iron status (ferritin concentrations in g/l)	Not estimable	0 (0 studies)		None of the trials reported on this outcome
Weight-for-age (in Z-scores)	Not estimable	0 (0 studies)		None of the trials reported on this outcome

CI, confidence interval; RR, risk ratio; MD, mean difference.
*GRADE Working Group grades of evidence:
High quality: We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate quality: We have moderate confidence in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low quality: Our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of the effect.
Very low quality: We have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of the effect.
[1]Only one study provided data for this comparison.
[2] 58% were anaemic at start of the 2-month intervention in one study (Hirve, 2007).

For details of studies included in the review, see reference (*13*).

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Annex 5 Questions in Population, Intervention, Control, Outcomes (PICO) format

Effects and safety of multiple micronutrient powders for infants and young children

a. Can multiple micronutrient powders be used in infants and young children 6–23 months of age to improve health outcomes?
b. If so, at what dose, frequency and duration?

Population: **Infant and young children 6-23 months**
Subpopulation:
Critical
- By malaria transmission (four categories: no transmission or elimination achieved, susceptibility to epidemic malaria, year-round transmission with marked seasonal fluctuations, year-round transmission with consideration of *Plasmodium falciparum* and/or *Plasmodium vivax*)
- By use of concurrent antimalarial measures
- By prevalence of anaemia in children 6–23 months of age: countries with a public health problem (5–19.9%, mild; 20–39.9%, moderate, 40% or more, severe) versus no public health problem (less than 5%)
- By individual anaemia status: anaemic children versus non-anaemic children (defined as haemoglobin less than 110 g/l)
- By iron status: iron-deficient versus (non-iron-deficient) children (as defined by ferritin, transferrin receptor, and/or zinc protoporphyrin/haem ratio (ZPPH) cut-offs)

Intervention: Multiple micronutrient powder formulations containing iron, zinc and vitamin A, with or without other micronutrients
- Subgroup analysis:

Critical
- By content of product:
  - Iron: less than 12.5 mg versus 12.5 mg or more
  - Zinc: less than 5.0 mg versus 5.0 mg or more
- By number of micronutrients: 5 or fewer versus 6 or more
- By frequency: daily versus weekly versus flexible
- By duration of intervention: less than 6 months versus 6 months or more
- By level of exposure to the intervention: high versus low

Control:
- No provision of multiple micronutrient powders, or placebo
- Provision of iron supplements

Outcomes: *Critical*
- Haemoglobin values
- Anaemia
- Iron status (as defined by the trialists)

For malaria-endemic areas only
- Malaria incidence and severity (parasitaemia with or without symptoms)

Setting: All countries

Annex 6 Summary of NUGAG members' considerations for determining the strength of the recommendation

Quality of evidence:	• The quality of the evidence for anaemia and iron deficiency was considered sufficient to support recommendation in all settings, including areas of malaria transmission
Values and preferences:	• Large groups of children under 2 years are affected by iron deficiency and may benefit from this intervention. Other options (i.e. fortification) may be preferred in order to reach a larger proportion of the target population
Trade-off between benefits and harm:	• This intervention is effective for prevention of iron deficiency and anemia but there is still uncertainty regarding adverse effects, particularly diarrhoea and malaria
Costs and feasibility:	• This intervention may be more expensive than drops but is feasible • Cost-effectiveness analyses in different settings are needed

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