

**GUIDELINES AND SPECIFICATIONS FOR DEFINING THE MICRONUTRIENT
COMPOSITION OF SINGLE SERVE SACHETS FOR SPECIFIED TARGET
POPULATIONS IN LOW- AND MIDDLE-INCOME COUNTRIES WITH HIGH
PREVALENCE OF ANAEMIA AND MICRONUTRIENT DEFICIENCIES**

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Preface

Purpose and focus of the manual

The purpose of this manual is to provide information on (single-serve) MNPs formulations that have been developed for research or program purposes; and to make recommendations for the composition of MNPs for treating or preventing anaemia and vitamin and mineral deficiencies among older infants and young children (6-23 months of age) and pregnant and lactating women in low- and middle-income countries where micronutrient deficiency disorders are moderate to severe public health problems.

The first chapter provides an overview of micronutrient powders and the concept of home fortification, as well as an introduction to the Home Fortification Technical Advisory Group (HF-TAG). Chapter Two summarizes the results of published and grey literature reviews, including agency reports and private sector contributors. Formulation-specific information, such as target population and micronutrient quantities, is presented in tabular form. The third and final chapter presents recommendations for the composition of MNPs for addressing anaemia and other vitamin/mineral deficiencies among defined target populations, including older infants and young children, as well as pregnant and lactating women.

Although this manual does not include recommendations for school-aged children, or institutional settings, and although it does not provide guidelines for implementing MNPs programs at the regional or national level, it may serve as a beneficial resource for those who are involved in coordinating such activities (e.g. policymakers, program planners, NGOs, international organizations, manufacturers, suppliers, scientists, etc.). For example, the composition recommendations provided herein can promote streamlining of standard formulation options and thus improved procurement times, and supply chain reliability. This, in turn, can help to inform the planning and development phases of nutrition-related policies, programs, and intervention or operations research.

Development process

Micronutrient powder (MNPs) composition data were collected from the following sources:

- Technical documentation from MNPs producers or developers;
- Published articles and reports from the peer-reviewed and grey literature that describe MNPs use among older infants and young children (6-23 months) or pregnant and lactating women in low- and middle-income countries (LMICs); and
- Key informants from the private sector with experience in MNPs production and distribution.

Relevant peer-reviewed publications were identified by hand-searching the reference lists of key review papers in this field [1, 2]. This initial collection of publications was then supplemented through more specific searches of peer-reviewed journal databases and agency reports (e.g. published by WHO, UNICEF, WFP, WV, and MI). Although the search strategies employed were not exhaustive, the scope was considered to be adequate in order to address the purpose and aims of this manual. Grey literature sources of MNPs composition data consisted mainly of technical specification documents from public sector organizations (e.g. UN agencies and other NGOs), and private sector companies that currently produce or distribute micronutrient powders. Composition data were not extracted if the MNPs formulations contained less than 3 micronutrients per serving/dose or a source of energy from protein, lipids, or carbohydrates (e.g. wheat or soy).

The data extracted from the literature and requested from manufacturers pertained to the composition and application of MNPs formulations either previously or currently used in research or programs, or available on the market. These data included the number and form of micronutrients, the intended target population and health issue (e.g. anemia specifically or micronutrient deficiencies generally), recommended dosing regimens, and net weight per dose. These data were then translated into a clear set of recommendations for MNPs composition by cross referencing research- and practice-based evidence from the peer-reviewed and grey literature with WHO/FAO recommended nutrient intakes for young children (6-23 months) and pregnant and lactating women.

The data collection, extraction, and synthesis results, as well as all draft versions of this manual were reviewed and approved by members of the MNPs Composition Working Group, the HF-TAG Executive Committee, and other experts or key informants as required.

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Abbreviations

DRI	Dietary reference intakes
FAO	Food and Agriculture Organization of the United Nations
GAIN	Global Alliance for Improved Nutrition
HF	Home fortification
HF-TAG	Home Fortification Technical Advisory Group
INACG	International Nutritional Anemia Consultative Group
LMIC	Low- and middle-income country
MI	Micronutrient Initiative
MNP	Micronutrient Powder
NAS	National Academy of Sciences
NGO	Non-governmental Organization
RNI	Recommended Nutrient Intake
SGHI	Sprinkles Global Health Initiative
WHO	World Health Organization
UN	United Nations
UNU	United Nations University
UNICEF	United Nations Children's Fund
WFP	World Food Program
WV	World Vision

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1

Introduction

In this chapter :

- Overview of micronutrient powders and the concept of home fortification
- About the Home Fortification Technical Advisory Group (HF-TAG)

1.1 Overview of micronutrient powders and the concept of home fortification

Micronutrient powders (MNPs) are an innovation developed for home fortification (HF) to address anaemia and vitamin and mineral deficiencies in vulnerable populations. While originally designed for consumption by older infants and young children, MNPs can provide micronutrients to other vulnerable populations by enabling families to fortify many different foods in the home. This is called 'home fortification' or 'point-of-use fortification' to encompass other places where food is consumed, including schools. Home fortification is used in situations where local diets or food aid baskets (in the case of emergencies) do not provide sufficient quantities of micronutrients to meet recommended intakes. It allows caregivers to improve the quality of their family's diet by adding micronutrients to the locally available foods that are prepared at home. The approach provides the flexibility to target specific ingredients and products to population groups with increased nutrient needs, such as pregnant women or infants 6-23 months of age. In the context of complementary feeding, home fortification does not require any change in how the usual soft, mushy, semi-solid complementary foods are prepared. Adding a sachet of powdered or lipid-based nutrients to the complementary food once per day is an easy thing to do. At the same time, because home fortification is a new approach to improve the diet, and needs to be used over a relatively long period of time, there is a need for clear and unambiguous instructions on its use. Home fortification, if used correctly, does not conflict with breastfeeding or with a timely transition from exclusive breastfeeding to introduction of complementary foods at six months of age as recommended by the WHO [3]. Home fortification can even be used to reinforce messages on timely introduction of complementary food and continued breastfeeding to two years and beyond.

Home fortification products, such as micronutrient powders (MNPs), come in measured doses that are safe to consume and easy to store, transport, distribute and use. Distribution of home-fortification products can be achieved by various means including delivery by government programs, NGOs, and UN agencies free of cost to the end-user, or by market-based systems. MNPs are sachets (like small sachets of sugar) containing a blend of vitamins and minerals in powder form, usually 1 g/sachet, which instantly fortify foods after being sprinkled onto and mixed into an individual serving of food prepared at home. The micronutrient formulation should not appreciably change the taste, color or texture of the food to which it is added. MNPs can be stored for up to two years, even in hot conditions (although it is best to avoid long-term exposure above 40° C), and are low-cost, ex-factory, depending on volume produced and site of production. MNPs (Sprinkles®) were developed by the Sprinkles Global Health Initiative to prevent and treat micronutrient deficiencies among young children and other vulnerable groups [4].

1.2 About the Home Fortification Technical Advisory Group (HF-TAG)

The Home Fortification Technical Advisory Group (HF-TAG) is a community of stakeholders involved in home fortification comprised of members from the public, private, academic and non-governmental organization sectors [5]. The mission of the HF-TAG is to facilitate implementation of well-designed and effective home fortification projects at scale, based on sound technical guidance and best practices, integrated into comprehensive nutritional strategies for children. The group aims to address the most important barriers to home fortification, and to shape the market for home fortification by providing standards, guidelines and resources to policymakers, non-governmental organizations (NGOs), international organizations, corporations (manufacturers and suppliers), innovators/social entrepreneurs, academia and media.

2

Composition of current MNP formulations

In this chapter :

- Summary of findings from a review of peer-reviewed literature
- Summary of findings from a review of grey literature and private sector contributors

2.1 Summary of findings from a review of peer-reviewed literature

Table 1 presents a summary of the MNPs composition data extracted from published literature. These data were obtained primarily from reports of clinical trials investigating the efficacy (e.g. absorption, changes in micronutrient status, growth, development), safety (e.g. morbidity and mortality outcomes), acceptability (e.g. adherence, side effects), and effectiveness (e.g. coverage, program implementation and evaluation) of MNPs for young children ranging in age from 6 to 72 months living in various low- and middle-income settings. Selected papers were published between 2003 and 2012.

Overall there were 31 different formulations identified, one of which was excluded due to the inclusion of fewer than 3 micronutrients per serving/dose [6]. Of the 30 remaining formulations, 18 contained 3-5 micronutrients and 13 had more than 5 micronutrients per serving/dose (Table 1). All formulations contained iron with dose levels ranging from 2.5 mg to 45 mg. The most common form of iron used was ferrous fumarate (24/30 formulations, or 80%), while some formulations included sodium iron ethylenediaminetetraacetate (NaFeEDTA) [7] or ferric pyrophosphate [8], or the nutrient form was not specified [9-11]. In most cases (20/30 or 67%) the iron was described as being microencapsulated; although, currently, other forms of non-coated iron are used with similar shelf-life. A lack of encapsulation of iron salts, like ferrous fumarate, is likely to impart a metallic taste to the foods into which it is added and adversely affect the shelf-life of the product

Most data obtained from the peer-reviewed literature pertained to MNPs formulations designed to target either anaemia specifically or vitamin and mineral deficiencies in general among older infants and young

children older than 6 months of age. Other high-risk groups, such as pregnant women, were generally not represented as target populations. There has been only one published example of a MNPs efficacy study in pregnant women that would be eligible for inclusion in this manual [12]. Choudhury et al. conducted a cluster randomized trial to assess the relative efficacy of MNPs versus iron and folic acid (IFA) tablets among pregnant women in Bangladesh. The MNPs formulation contained iron (60 mg), folic acid (400 mcg), vitamin C (30 mg), and zinc (5 mg), and was found to be at least as efficacious as IFA tablets in controlling anaemia in the study population [12]

It is estimated that nearly 42% of pregnant women worldwide are anaemic, and micronutrient deficiencies in pregnancy are associated with adverse health outcomes in both the mother and infant [13]. As such, Member States have requested guidance from the WHO on the use of micronutrient powders for home fortification of foods consumed by pregnant women. The WHO responded to this request by developing evidence-informed recommendations using standardized procedures outlined in the "WHO handbook for guideline development" [14]. Due to a lack of evidence, however, the benefits or harms of MNPs use among pregnant women could not be assessed [15]. While this does not necessarily imply that MNPs are not efficacious for improving micronutrient status in pregnant women or other target groups, it does highlight the need for further research and knowledge dissemination in this area [15]. Alternative strategies for effectively increasing the micronutrient intake of pregnant and lactating women may include the provision of tablets rather than MNPs. Previous programming experiences have indicated that women often prefer swallowing a tablet every day rather than adding a powder to their food, and thus may adhere more readily to this type of intervention [16].

Table 1: Summary of findings from review of peer-reviewed literature related to micronutrient powder composition

References	Publication type(s)	Target countries/ regions ¹	Target population	Target disease(s)	Micronutrient composition*	Dosing regimen	Aims of study or program	Estimated number of beneficiaries ²
Tondeur (2004) [17]	Randomized trial	Ghana	Children 6-18 months	Iron deficiency anaemia	3 Micronutrients: Iron (30-45 mg) Vit A (300 mcg RE) Vit C (50 mg)	Daily for 3 days	Efficacy	90
WHO (2011) [18]	Guideline	Settings where the prevalence of anemia in children <5y is 20% or higher	Children 6-23 months	Iron deficiency and anaemia	3 Micronutrients: Iron (12.5 mg) Vit A (300 mcg) Zinc (5 mg)	Daily for ≥2 months followed by 3-4 months off (start MNPs every 6 months)	Effectiveness	NA
Choudhury (2012) [12]	Randomized trial	Bangladesh	Pregnant women	Anaemia	4 Micronutrients: Iron (60 mg) Folic acid (400 mcg) Vit C (30 mg) Zinc (5 mg)	Daily from 2 nd trimester (14-22 weeks) until 32 weeks gestation	Efficacy	243
Christofides (2006) [19]; Hirve (2007) [8]; Lundeen (2010) [20]; Menon (2007) [21]; Ip (2009) [22]; Hyder (2007) [23]; Zlotkin (2005) [24]; Nestel (2003) [9]	Randomized trials; reviews	Ghana; India; Kyrgyz Republic; Haiti; Bangladesh; other	Children 6-36 months	Iron deficiency; Anaemia; other micronutrient deficiencies; general undernutrition	5 Micronutrients: Iron (12.5-30 mg) Vit A (300-400 mcg) Zinc (5 mg) Vit C (30-50 mg) Folic Acid (150-160 mcg)	Daily for 2 months (4 studies); 60 sachets over 2, 3, 4 months (1 study)	Efficacy; effectiveness; adherence; acceptability; feasibility	2,303
Adu-Afarwuah (2007) [25]; Christofides (2006) [19]; Giovannini (2006) [6]; Sharieff (2006a,b) [26, 27]; WVM (2005) [28]	Randomized trials; longitudinal intervention / implementation pilot study	Ghana; Cambodia; Pakistan; Mongolia; China	Children 6-72 months	Anaemia; iron deficiency; growth (stunting, wasting); diarrhea; rickets; iron overload	6 Micronutrients: Iron (12.5-40 mg) Vit A (300 mcg RE, 600 IU) Zinc (5-10 mg) Vit C (30, 50 mg) Folic acid (150-160 mcg) Vit D (D ₃ 7.5 mcg, 400 IU)	Daily for 2 months (2 studies); daily for 6, 12, or 24 months (1 study each);, daily or weekly for 13 weeks (1 study)	Efficacy; effectiveness; adherence; safety	13,823
Sharieff (2006a) [26]	Randomized trial	Pakistan	Children 6-12 months	Diarrhea	7 Micronutrients: Iron (30 mg) Vit A (300 mcg) Zinc (5 mg) Vit C (50 mg) Folic acid (150 mcg) Vit D (D ₃ 7.5 mcg) Heat inactivated L-acidophilus (1-2x10 ⁹ CFU)	Daily for 2 months	Efficacy	25
Chen (2008) [7]	Randomized trial	China	Children 2-6 years	Iron and vit A deficiency	8 Micronutrients: Iron (12 mg) Vit A (500 mcg) Zinc (12 mg) Folic acid (200 mcg) Vit B1 (0.7 mg) Vit B2 (0.7 mg) Niacin (7.0 mg) Calcium (800 mg)	Daily for 5 days/ week for 6 months	Efficacy	226

Table 1: Summary of findings from review of peer-reviewed literature related to micronutrient powder composition

References	Publication type(s)	Target countries/ regions ¹	Target population	Target disease(s)	Micronutrient composition*	Dosing regimen	Aims of study or program	Estimated number of beneficiaries ²
Xu (2011) [29]	Randomized trial	Inner Mongolia	Children 6-24 months	Anaemia	12 Micronutrients: Iron (10 mg) Vit A (1250 IU) Zinc (4.1 mg) Vit C (30 mg) Folic acid (150 mcg) Vit D (5.0 mcg) Vit E (9.0 mg) Vit B1 (0.5 mg) Vit B2 (0.5 mg) Vit B6 (0.5 mg) Vit B12 (0.9 mcg) Niacin (6.0 mg)	Daily 5 days/ week for 4 months	Efficacy	502
Suchdev (2011) [30]; Zlotkin (2005) [24]	Randomized trial; Review	Kenya; other	Children 6-24 months	Anaemia; iron deficiency; vit A deficiency	14 Micronutrients: Iron (12.5 mg) Vit A (300-400 mcg) Zinc (5.0 mg) Vit C (30-35 mg) Folic acid (150-160 mcg) Vit D (5.0 mcg) Vit E (6.0 mg) Vit B1 (0.5 mg) Vit B2 (0.5 mg) Vit B6 (0.5 mg) Vit B12 (0.9 mcg) Niacin (6.0 mg) Copper (0.3-0.6 mg) Iodine (50-90 mcg)	Daily for 2 months (trial); daily for 12 months (review)	Efficacy; acceptability; evaluation	703
WFP/ DSM (2009) [10]	Program monitoring and evaluation	Bangladesh	Children 6-60 months	Micronutrient deficiencies	15 Micronutrients: Iron (10 mg) Vit A (100 mcg RE) Zinc (4.1 mg) Vit C (30 mg) Folic acid (150 mcg) Vit D (5.0 mcg) Vit E (5.0 mg) Vit B1 (0.5 mg) Vit B2 (0.5 mg) Vit B6 (0.5 mg) Vit B12 (0.9 mcg) Niacin (6.0 mg) Copper (0.34 mg) Iodine (30 mcg) Selenium (17 mcg)	Children: 100 sachets (every other day for 7 months); PLW: 200 sachets (2 every other day for 7 months)	Effectiveness; acceptability; coverage	Approx 100,714 children and 59,439 PLW

Table 1: Summary of findings from review of peer-reviewed literature related to micronutrient powder composition

References	Publication type(s)	Target countries/regions ¹	Target population	Target disease(s)	Micronutrient composition*	Dosing regimen	Aims of study or program	Estimated number of beneficiaries ²
WFP/ DSM/ UNHCR (2009) [11]	Program monitoring and evaluation	Kenya	Children <5 years	Iron deficiency and anaemia	16 Micronutrients: Iron (2.5 mg) Vit A (100 mcg RE) Zinc (2.5 mg) Vit C (60 mg) Folic acid (90 mcg) Vit D (5.0 mcg) Vit E (5.0 mg) Vit B1 (0.5 mg) Vit B2 (0.5 mg) Vit B6 (0.5 mg) Vit B12 (0.9 mcg) Niacin (6.0 mg) Copper (0.34 mg) Iodine (30 mcg) Selenium (17 mcg) Vit K (30 mcg)	Daily for 12 months	Effectiveness; acceptability; adherence	Approx 50,000 (women and children)
WFP/ DSM (2009) [10]	Program monitoring and evaluation	Bangladesh	Pregnant and lactating women	Micronutrient deficiencies	15 Micronutrients: Iron (10 mg) Vit A (100 mcg RE) Zinc (4.1 mg) Vit C (30 mg) Folic acid (150 mcg) Vit D (5.0 mcg) Vit E (5.0 mg) Vit B1 (0.5 mg) Vit B2 (0.5 mg) Vit B6 (0.5 mg) Vit B12 (0.9 mcg) Niacin (6.0 mg) Copper (0.34 mg) Iodine (30 mcg) Selenium (17 mcg)	200 sachets (2 every other day for 7 months)	Effectiveness; acceptability; coverage	Approx 59,439
WFP/ DSM/ UNHCR (2009) [11]	Program monitoring and evaluation	Kenya	Non-pregnant women	Iron deficiency and anaemia	16 Micronutrients: Iron (2.5 mg) Vit A (100 mcg RE) Zinc (2.5 mg) Vit C (60 mg) Folic acid (90 mcg) Vit D (5.0 mcg) Vit E (5.0 mg) Vit B1 (0.5 mg) Vit B2 (0.5 mg) Vit B6 (0.5 mg) Vit B12 (0.9 mcg) Niacin (6.0 mg) Copper (0.34 mg) Iodine (30 mcg) Selenium (17 mcg) Vit K (30 mcg)	Daily for 12 months	Effectiveness; acceptability; adherence	Approx 50,000 (women and children)

¹ Country or region where study conducted or program implemented; NA = not applicable

² Sample size (enrolled and/or randomized) of the MNPs arm or estimated program coverage

*Reported nutrient types, forms, and elemental amounts per serving (ranges represent variation in amounts reported across publications). Nutrient forms/salts (if specified): Iron (ferrous fumarate; microencapsulated ferrous fumarate; Micronized ferric pyrophosphate; sodium iron EDTA; ferrous lactate); Vitamin A (Retinyl acetate; Beta carotene); Zinc (Zinc gluconate; Zinc oxide); Vitamin C (Ascorbic acid); Vitamin B (B1 = Thiamin mononitrate; B2 = Riboflavin; B6 = Pyridoxine; B12 = Cobalamin); Calcium (Calcium carbonate); Vitamin E (Alpha tocopherol)

IU = International units; CFU = Colony forming units; RE = Retinol equivalents

2.2 Summary of findings from a review of grey literature and private sector contributors

The findings summarized in Table 2 represent MNPs formulations that are available or currently in use across various low- and middle-income countries worldwide. Micronutrient composition data were obtained for a total of 32 different MNPs formulations. Of these 4 were excluded due to the inclusion of macronutrients (1 formulation), or because they were designed to target populations in high-income countries (3 formulations). Of the 28 remaining formulations, the majority (71%) consisted of 12 or more micronutrients to a maximum of 16 micronutrients per serving/dose. Similar to the above findings from peer-reviewed literature, most data obtained from technical specifications and manufacturer reports pertained to MNPs formulations designed to target either anaemia specifically (14 out of 32 formulations) or vitamin and mineral deficiencies in general (in addition to anaemia) among infants and young children older than 6 months of age. Further, the majority of the anaemia-specific formulations tended to

consist of 5 or fewer micronutrients per serving/dose. Formulations for target populations other than children were generally not well represented. One formulation for pregnant and lactating women contained 4 micronutrients: iron, zinc, vitamin C, and folic acid. The 5-micronutrient formulations (7 formulations in total) differed from those containing 4 micronutrients primarily through the inclusion of vitamin A, and were all designed for use in older infants and young children ranging from 6 to 60 months of age. All of the multiple micronutrient formulations (i.e. those containing 12 or more micronutrients per serving/dose) targeted children at risk of vitamin and mineral deficiencies, with the exception of one 15-micronutrient formulation for pregnant and lactating women. Similar to the micronutrient compositions described in section 2.1 (and Table 1), the forms of iron (e.g. ferrous fumarate; ferrous lactate; sodium iron EDTA) and corresponding amounts (ranging from 2.5 to 27 mg) also varied across the formulations described here (and Table 2). Half of all formulation descriptions specified encapsulation of the iron, including those for pregnant and lactating women.

Table 2: Summary of findings from review of grey literature and private sector contributors

Formulation names	Target population	Target disease(s)	Target countries/ regions	Micronutrient composition*	Dosing regimen	Net weight per sachet
Chispaz; Sprinkles; MNPs	Children 6-24 or 6-59 months	Anemia	Ecuador; Uganda; Bangladesh; not specific	5 Micronutrients: Iron (12.5 mg) Vit A (300 mcg RE) Zinc (5.0 mg) Vit C (30 mg) Folic acid (150-160 mcg)	Daily; 60 sachets over 60-120 days; 2 sachets /week	1.0 g ($\pm 0.05-0.1$ g)
NurtureMate	Children 6-36 months	Micronutrient deficiency	China	12 Micronutrients: Iron (6.0 mg) Vit A (200 mcg RE) Zinc (4.8 mg) Folic acid (66 mcg) Vit D (5.0 mcg) Vit E (1.55 mg) Vit B1 (0.3 mg) Vit B2 (0.5 mg) Vit B6 (0.3 mg) Vit B12 (0.3 mcg) Niacin (3.0 mg)	Daily	1.0 g
Sprinkles; Sprinkles Plus; MNPs; Vitalita	Children 6-24 or 6-59 months or school-aged	Anemia; micronutrient deficiency	North Korea; Algeria; Indonesia; not specific	14 Micronutrients: Iron (10-12.5 mg) Vit A (100-500 mcg RE) Zinc (4.1-5.6 mg) Vit C (30-35 mg) Folic acid (150-300 mcg) Vit D (5.0 mcg) Vit E (5.0-7.0 mg) Vit B1 (0.5-0.9 mg) Vit B2 (0.5-0.9 mg) Vit B6 (0.5-1.0 mg) Vit B12 (0.9-1.8 mcg) Niacin (6.0-12 mg) Copper (0.34-0.6 mg) \pm Iodine (50-90 mcg) \pm Selenium (17 mcg) \pm Vit K1 (1.2 mg)	Daily; 60 sachets over 60-120 days; 0.5 g/ serving (20 servings/ sachet)	1.0-8.0 g ($\pm 0.05-0.1$ g)

Table 2: Summary of findings from review of grey literature and private sector contributors

Formulation names	Target population	Target disease(s)	Target countries/ regions	Micronutrient composition*	Dosing regimen	Net weight per sachet
Sprinkles; MNPs; Daminaide	Children 6-24 or 6-60 months or school- aged	Anemia; micronutrient deficiency	Mongolia; Nepal; Bangladesh; not specific	15 Micronutrients: Iron (10-12.5 mg) Vit A (400-500 mcg RE or 1332 IU) Zinc (4.1-5.6 mg) Vit C (30 mg) Folic acid (150-300 mcg) Vit D (0.5-5.0 mcg or 200 IU) Vit E (5.0-7.0 mg or 7.46 IU) Vit B1 (0.5-0.9 mg) Vit B2 (0.5-0.9 mg) Vit B6 (0.5-1.0 mg) Vit B12 (0.9-1.8 mcg) Niacin (6.0-12 mg) Copper (0.56-0.6 mg) Iodine (90-120 mcg) ± Selenium (17 mcg) ± Vit K1 (60 mcg)	Daily; 60 sachets over 60-120 days or every 6 months up to 5 years; 2 sachets/ week; Once or twice daily ± fortified food rations (during emergencies); 0.4 g/serving (20 servings/ sachet)	1.0-8.0 g (±0.05-0.1 g)
Nurture Mate MMNPs; MNPs for malaria areas; Little Bits	Children 6-59 or 24-60 or ≥6 months	Anemia; micronutrient deficiency	India; Mexico; Zambia; malaria areas	16 Micronutrients: Iron (2.5-12.5 mg) Vit A (100-400 mcg RE) Zinc (2.5-10 mg) Vit C (30-60 mg) Folic acid (50-150 mcg) Vit D (5.0 mcg) Vit E (5.0-6.0 mg) Vit B1 (0.5-0.7 mg) Vit B2 (0.5-0.8 mg) Vit B6 (0.5-1.0 mg) Vit B12 (0.7-0.9 mcg) Niacin (6.0-7.0 mg) Copper (0.34-1.0 mg) Iodine (30-90 mcg) Selenium (17-30 mcg) ± Vit K (30 mcg) ± Calcium ± FOS	Daily; daily for 2 or 6 months	1.0-1.34 g (±0.05-0.1 g)
Sprinkles	Pregnant & lactating women	Anemia	Not specific	4 Micronutrients: Iron (60 mg) Zinc (10 mg) Vit C (30 mg) Folic acid (400 mcg)	60 sachets over 60-120 days	1.0 g (±0.1 g)
Sprinkles	pregnant & lactating women	Anemia	North Korea	15 Micronutrients: Iron (27 mg) Vit A (800 mcg RE) Zinc (10 mg) Vit C (55 mg) Folic acid (600 mcg) Vit D (10 mcg) Vit E (15 mg) Vit B1 (1.4 mg) Vit B2 (1.4 mg) Vit B6 (1.9 mg) Vit B12 (2.6 mcg) Niacin (18 mg) Copper (1.15 mg) Iodine (250 mcg) Selenium (30 mcg)	NA	1.0 g (±0.1 g)

* Nutrient types, forms, and elemental amounts per serving (ranges represent variation in amounts reported across formulations). Nutrient forms/salts (if specified): Iron (descote ferrous fumarate; encapsulated ferrous fumarate; ferrous fumarate; ferrous lactate; NaFeEDTA = sodium iron EDTA); Zinc (zinc gluconate; zinc oxide); Vitamin C (ascorbic acid; L-ascorbic acid); Vitamin A (retinyl acetate; retinyl palmitate); Vitamin D (D2; D3; cholecalciferol); Vitamin E (alpha tocopherol; alpha-TE = alpha tocopherol equivalent; alpha-TE acetate); Vitamin B (B1 = thiamin mononitrate; B2 = riboflavin; niacin = B3, niacinamide; B6 = pyridoxine, pyridoxine HCl; B12 = cobalamin, cyanocobalamin); Copper (copper sulfate); Iodine (potassium iodide); Vitamin K (K1 = phylloquinone or phytonadione); Selenium (sodium selenate/ selenite); Calcium (tri-calcium phosphate)

Excipients: Maltodextrin; Silicon dioxide; Aerosil; Dextrose

PE = polyethylene; PET = polyethylene terephthalate; LDPE = low-density polyethylene; RE = retinol equivalent; MNPs = micronutrient powder; MMNPs = multiple micronutrient powder; IU = international units; FOS = fructo-oligosaccharide

3

Recommendations for MNP composition

Recommendations for MNP composition

The composition specifications for each recommended formulation are presented in Table 3. Further details on the target populations and health conditions to which these recommendations apply are included below. This is followed by a discussion on recommended micronutrient amounts and forms.

Target populations

In keeping with the original intent and most widely used application of MNPs, the primary target population for these recommendations is older infants and young children (6-23 months of age); although they may also be applied to all preschool aged children (including those aged 24-59 months). While recommendations for school aged children have not been formally established at this time, the micronutrient formulation used by WFP for school feeding programs may be considered as the current 'standard'. Despite the current lack of evidence for the use of MNPs in pregnant and lactating women, a general recommendation for this target population is also included herein.

Target health conditions

Although the flexibility of MNPs formulations allows the number and amounts of vitamins and minerals to be adjusted in order to target specific micronutrient deficiencies or related diseases (according to the needs of the target population), the recommendations described in this chapter are focused only on the two most commonly targeted health issues: 1) anaemia; and 2) general dietary micronutrient inadequacies. Anaemia formulations for young children should contain a minimum of 3 micronutrients, including iron, vitamin A, and zinc, according to the WHO 2011 guideline [18]. Multiple micronutrient formulations, for addressing general dietary micronutrient inadequacies in addition to anaemia in children, should consist of at least the 15 micronutrients that make up the HF-TAG recommended formulation (Table 3).

Micronutrient amounts and forms

The amount of each micronutrient should at least correspond with recommended nutrient intakes (RNIs) [31], unless otherwise indicated by the specific needs of a target population. Recommended nutrient intake is defined by the WHO and Food and Agriculture Organization (FAO) as the daily dietary intake of a nutrient sufficient to meet the nutrient requirements of nearly all apparently healthy individuals in a specific population group [31]. This definition is equivalent to that of the recommended dietary allowance (RDA) used by the Food and Nutrition Board of the United States Institute of Medicine [32]. The recommended nutrient amounts in Table 3 correspond to the WHO/FAO RNIs. In some cases, the recommended dose of a micronutrient may be adjusted in order to adhere to country level standards or regulations, or to account for potential variations in nutrient requirements (for example, reduced bioavailability of iron due to consumption of plant-based complementary foods high in phytates; or high prevalence of vitamin D deficiency among susceptible populations). However, unless there is clear indication for making such alterations to individual micronutrient amounts, it is recommended that standard MNPs formulations to be used in public health interventions contain no more than 1 RNI of each nutrient, and that the specific needs of a target population be met by adjusting the dosing regimen (i.e. the number of sachets per month). For example, where there is a high prevalence of micronutrient deficiencies and high incidence of infections, the recommendation may be to take 1 sachet daily or 30 per month. In circumstances where the prevalence of micronutrient deficiencies is low, the recommendation may be reduced to 15 sachets per month or alternatively 60 sachets over six months. For more information on recommended dosing regimens, please see the HF-TAG Programmatic Guidance Brief on Use of Micronutrient Powders (MNPs) for Home Fortification [33].

In terms of micronutrient forms, it should be noted that iron is a potent oxidizing agent and most forms of iron have a strong metallic taste. Because of its oxidizing capacity (it is a potent catalyst for fat oxidation), iron will have significant nutrient-nutrient or nutrient-food interactions as evidenced by a change in colour and taste (flavour) of the food to which it is added. As a general recommendation, the form of iron used for home fortification should have the following properties:

- a) High bioavailability
- b) Minimal effect on the taste or colour of the food it is mixed with
- c) Minimal or no interaction with other micronutrients

Currently, there is evidence to suggest that sodium iron EDTA (NaFeEDTA), ferrous bisglycinate, and ferrous lactate meet the above criteria [29, 34-40]. Where such evidence is lacking, however, **it is strongly recommended that iron be micro-encapsulated in order to mask any metallic taste and prevent oxidation through nutrient-nutrient or nutrient-food interactions.**

The use of NaFeEDTA in MNPs formulations has recently been explored, since EDTA can improve iron absorption by preventing the formation of insoluble complexes with other dietary components (e.g. iron-phytate) [41]. An additional advantage of EDTA compounds is that they are relatively stable and thus suitable for use in foods that are stored for long periods of time [42]. The Joint WHO/FAO Expert Committee on Food Additives (JECFA) has evaluated the safety of using sodium iron EDTA (NaFeEDTA) in infants and children up to the age of 13 years, and determined that the acceptable level of intake for EDTA is 1.9 mg/d/kg body weight, which equates to 0.37 mg iron/kg body weight [43]. Using mathematical models, Yang et al. calculated a dose range of 1.8 mg to 2.2 mg NaFeEDTA for fortifying the

complementary foods of 6- to 8-month old children with a prevalence of underweight of 40% and 5%, respectively [44]. It should be noted that these levels of intake do not meet the RNIs for dietary iron for infants and children 0.5 to 3 years of age (using a mean body weight of 9-13 kg and assuming 15% bioavailability) [45]. Thus for MNPs manufacturers who have chosen to include NaFeEDTA in the MNPs formulation, these formulations have also usually included a second form of iron in order to increase the dose in each sachet to desired fortification levels. Another chelated form of iron, called ferrous bisglycinate, has similar features to NaFeEDTA in terms of higher absorption and resistance to inhibition of absorption by phytates [38-40]. Reviews of the literature have demonstrated that ferrous (bis) glycinate is safe for consumption by adults and young children with normal iron status (including pregnant and non pregnant women); and is well suited for use as an iron fortificant [46, 47]. As such, ferrous glycinate has been approved by FAO for use both as a direct food fortificant and as a food supplement.

The B-vitamin, folate, may be expressed on nutrition information panels as 'folate' (the natural form found in food), or 'folic acid' (the synthetic form found in supplements). Due to differences in bioavailability, the amounts of each form must also be adjusted accordingly, such that 1 mcg of dietary folate (or 1 dietary folate equivalent, DFE) is equated to 0.6 mcg of folic acid. The recommended formulation (for children 6-23 months) presented in Table 3, below, includes the RNI for folic acid (90 mcg), which is equivalent to 150 mcg of folate. MNPs producers may also consider encapsulating the B vitamins for taste and odour masking purposes, as well as to prevent colour changes in certain types of food. Lastly, all micronutrient formulations should include at least 25 mg of vitamin C, which is known to enhance the absorption of iron from food [45, 48].

Table 3: Recommended micronutrient powder formulations and specifications

Target population	Purpose	Micronutrient composition ^{†*}	Notes
Children 6-23 months (and 24-59 months)	Address anaemia and vitamin/ mineral deficiencies	<u>Multiple Micronutrient Formulation:</u> Iron (EFF 10 mg) ¹ Vitamin A (400 mcg RE) Zinc (ZnG 4.1 mg) Vitamin C (AA 30 mg) Folic acid (90 mcg) ² Vitamin D3 (5.0 mcg) Vitamin E (TE 5.0 mg) Vitamin B1 (0.5 mg) Vitamin B2 (0.5 mg) Vitamin B6 (0.5 mg) Vitamin B12 (0.9 mcg) Niacin (6.0 mg) Copper (CuS 0.56 mg) Iodine (KI 90 mcg) Selenium (NaS 17 mcg)	10mg iron recommended by HF-TAG See reference [49] for more information on dosing regimens
Pregnant and lactating women	Address anaemia and vitamin/ mineral deficiencies	<u>Multiple Micronutrient Formulation:</u> Iron (30-60 mg) ³ Vitamin A (800 mcg) Zinc (15 mg) ³ Vitamin C (70 mg) ³ Folic acid (400 mcg) Vitamin D3 (5.0 mcg) Vitamin E (10 mg) ³ Vitamin B1 (1.4 mg) Vitamin B2 (1.4 mg) Vitamin B6 (1.9 mg) Vitamin B12 (2.6 mcg) Niacin (18.0 mg) Copper (2.0 mg) ³ Iodine (150 mcg) ³ Selenium (65 mcg) ³	30 mg iron recommended by WHO/UNICEF/UNU for multiple micronutrient formulations 60 mg iron recommended by INACG/WHO/UNICEF for formulations containing iron and folic acid only

[†] Micronutrient amounts correspond with WHO/FAO recommended nutrient intakes 2004 [31]

*Nutrient forms: Iron (EFF = encapsulated ferrous fumarate, or NaFeEDTA for 2.5 mg Fe combined with other form of iron); Vitamin A (ACET = acetate; RET = retinol; RE = retinol equivalent); Zinc (ZnG = zinc gluconate); Vitamin C (AA = ascorbic acid); folic acid; Vitamin D3 (cholecalciferol); Vitamin E (TE = alpha tocopherol; acetate); Vitamin B1 (thiamin mononitrate); Vitamin B2 (riboflavin); Vitamin B6 (pyridoxine HCl); Vitamin B12 (cyanocobalamin); niacin or niacinamide (Vitamin B3); Copper (CuS = copper sulfate); Iodine (KI = potassium iodide); Selenium (NaS = sodium selenate/selenite)

¹ Intake requirements for children based on assumed bioavailability of dietary iron, which can vary with age [45], and overall diet composition. Research has shown that doses of 12.5 mg encapsulated ferrous fumarate are also effective for reducing iron deficiency. However, for practical reasons, the HF-TAG recommends a standard dose of 10mg iron for all MNPs formulations targeted towards children 6-23 months (and 24-59 months) of age.

² Equivalent to 150 mcg folate (150 dietary folate equivalents, DFE) of age.

³ WHO/WFP/UNICEF recommendations for populations affected by an emergency: 27 mg iron, 10 mg zinc, 55 mg vitamin C, 600 mcg folic acid, 15 mg vitamin E, 1.15 mg copper, 250 mcg iodine, 30 mcg selenium

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