Provision of micronutrients in coexisting public health programs and risk of excessive intake: regulatory considerations

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Countries around the world have been implementing public health interventions to provide vitamins and minerals. There is a concern that the cumulative micronutrient contribution of coexisting programs, when targeting the same population, may exceed their safe levels of intake, thus potentially challenging the *primum non nocere* principle. We assessed the regulatory framework of such interventions and determined qualitatively whether there were provisions in the regulations that called for coordination among programs to ensure their innocuousness. Country cases from various WHO regions were selected for the study: (1) the Americas: Chile, Costa Rica, and Guatemala; (2) Africa: Malawi, Uganda, and Zambia; (3) South Asia: Bangladesh; and (4) the Western Pacific Region: China and the Philippines. We did not identify any provisions in the existing regulations requiring coordination mechanisms among interventions. However, in some countries, governments have established national micronutrient fortification commissions or alliances aimed to foster interprogram coordination. Their focus, however, has been mostly on the efficacy of the programs and less on their safety. A regulatory framework for coexisting micronutrient interventions should be comprehensive, accounting for all micronutrient sources and including regulatory provisions for coordination among programs.

Keywords: multiple micronutrient interventions; regulatory framework; excessive intake; vitamins; minerals

Introduction

Combating malnutrition in all its forms is one of the greatest global challenges. Efforts to eliminate micronutrient deficiencies are in line with the 2015 United Nations Sustainable Development Goal 2, aimed to end hunger, achieve food security, and improve nutrition ([https://www.un.org/sustainabledevelopment/hunger/](https://www.un.org/sustainabledevelopment/hunger/)). In an attempt to overcome dietary insufficiencies of vitamins and minerals, countries around the world may implement, via different actors (e.g., governments, NGOs, and international agencies), simultaneous micronutrient interventions. These may include different strategies as food fortification, micronutrients supplementation and, in some countries, biofortification initiatives, potentially creating a safety risk by exceeding the tolerable upper intake levels (UL) of nutrients.1 Such a possibility is amplified by the cumulative micronutrient intake generated by the number of overlapping public health interventions and the commercial availability of fortified processed foods and over-the-counter dietary supplements. The chronic and acute adverse effects of excessive preformed vitamin A intakes during prolonged or short periods of time are well documented and include bone fragility, liver damage, skin disorders, increased intracranial pressure, and teratogenicity.2,3 Excessive folic acid...
consumption has been associated with vitamin B12 deficiency, anemia, and cognitive impairment in the certain population groups. Adverse effects caused by a longtime exposure to iodine excess in pregnant women and particularly in children include hyperthyrotropinemia, increased risk of developing goiter, and impaired motor and verbal communication development. Some of these negative effects can be permanent but others could be corrected or prevented when returning to appropriately lower micronutrient levels.

Currently, several staple foods are used as vehicles for mandatory or voluntary fortification with one or more micronutrients, including food-grade salt, wheat, and maize flours, cooking vegetable oil, some condiments such as soy and fish sauces and bouillon cubes, milk, refined sugar, and others. In addition, supplementation programs with preformed vitamin A, iron, folic acid, or calcium are often implemented in parallel targeting specific age groups, such as children and women of reproductive age, in the same population. Furthermore, voluntary fortification of commercially available processed foods is a common practice in the food industry. More recently, biofortification of staple crops has been adopted in some countries of Latin America, Africa, and Asia, as a new strategy to address deficiencies of vitamin A, iron, zinc, and folate. Of particular concern are micronutrients, with a little margin between the Estimated Average Requirement (EAR) and the UL, such as preformed vitamin A and zinc, especially when targeting children and pregnant women. According to the European Food Safety Authority (EFSA), other micronutrients of interest from the safety point of view include iron, folic acid, iodine, copper, and calcium.

At issue is that the above interventions are often implemented independently and uncoordinatedly, most probably because there is not a regulatory framework that requires such coordination. Monitoring indicators of existing programs may also be limited, unavailable, or overseen when introducing new interventions. In some cases, it is not clear which entity at the country level is responsible for managing and governing the programs. This issue was discussed at the Global Summit on Food Fortification held in Arusha, Tanzania, in 2015, in which efforts were made to understand maximizing the benefits and minimizing the risk of interventions addressing micronutrient malnutrition.

The deliberations from this event concluded that the relationship between high intake of micronutrients and adverse health consequences is not well understood, and there are no biomarkers that can detect early adverse effects. In addition, although food standards exist in local regulations for most fortification programs, a regulatory framework linking them to other types of simultaneous interventions appears to be lacking. In summary, a comprehensive assessment of all potentially contributing factors to prevent or minimize the risk of micronutrient—short- or long-term toxicity—does not exist. Main government efforts seem to be primarily directed toward combating micronutrient deficiencies.

Our review examines whether there are regulatory provisions in the food and nutrition legislation regarding the implementation of simultaneous interventions with one or multiple vitamins and minerals in countries where such practices occur, including coordination among programs to minimize potential toxicity risks due to excessive intakes. Furthermore, a regulatory process to address their safety is suggested.

**Literature review**

We conducted a preliminary review of the global literature dealing with micronutrient interventions, using scientific databases, including PubMed and Web of Science up to September 2017. Keywords included “regulatory framework,” “micronutrient interventions,” and “excessive micronutrient intakes.” Internet searches were also performed using various search engines, such as Google and Mozilla Firefox, to identify regulatory information that could have existed in country reports and websites regarding micronutrient programs. International regulatory information was searched in the World Health Organization (WHO) Global Database on the Implementation of Nutrition Action. Whenever possible, e-mail and phone communication were unofficially initiated with government authorities, scientists, and opinion leaders at the country level. A particular effort was made to find information suggestive of some type of coordination among programs in a given country. Country cases from the WHO global regions (www.who.int/about/regions/en/) were selected for the study using the following criteria: (1) existence of multiple interventions with vitamins
and/or minerals; (2) availability and relatively easy access of regulatory information, either via the literature, existing websites of government regulatory bodies, international agencies databases, or provided by country authorities who were eager to help; and (3) existing formal evaluations of the programs at the national level. Based on the above considerations, the following nations were chosen for the investigation: (1) the Americas: Chile, Costa Rica, and Guatemala; (2) Africa: Malawi, Uganda, and Zambia; (3) South Asia: Bangladesh; and (4) the Western Pacific Region: China and the Philippines. We did not assess any country in the WHO, Europe, or Eastern Mediterranean Region.

**Regulatory overview**

Globally, there are two main nutritional scenarios: (1) high-income countries experiencing the low prevalence of micronutrient deficiencies in specific population groups, and (2) low-income nations where micronutrient deficiencies are far more prevalent in the entire population and therefore considered important public health problems. In our investigation, countries focused their efforts to combat micronutrient deficiencies through mandatory mass fortification of staple foods with micronutrients affecting the general population. There was also a limited proportion of commercially driven fortified foods, which voluntarily followed established national or international food regulatory standards. In addition, countries used other strategies, aimed at specific risk groups, such as supplementation with megadoses of preformed vitamin A to children, and iron and folic acid to women of reproductive age. Other interventions included the use of multiple micronutrient-fortified powders to supplement children’s diet, and the recent introduction of biofortified crops in some countries. These combined micronutrient interventions may lead to excessive intakes of particular micronutrients beyond what might be considered safe levels. The detailed description and a number of micronutrient interventions per country are presented in Tables 1–8. Interventions targeted specific groups, such as administration of megadoses of preformed vitamin A, supplementation with iron or provision of micronutrient-fortified powders, and lacked official local government regulations but were often part of national nutrition policies and plans that followed the WHO international guidelines. One important observation regarding the implementation of these interventions was a lack of specific provisions, in any of the regulations, about coordination among programs to minimize the risk of excessive micronutrient intakes. There was no sign for use of any type of indicators to identify the risk of excessive intakes that could jeopardize the safety of the interventions. However, in some countries like Costa Rica, there was a specific regulation mandating to conform, with different stakeholders, the National Commission on Micronutrients, having as one of its functions the promotion of coordination among fortification programs (Costa Rica Government, Decree No. 27086-S). Similarly in Guatemala, by the initiative of the Ministry of Public Health and Social Assistance (MSPAS), there is the National Commission for Food Fortification, Enrichment and/or Equivalence (CONAFOR, Decree No. 4492). At the regional level, there is also an industry-government effort to coordinate fortification activities through the Regional Commission on Micronutrients and Fortified Foods in Central America (CORMAF). Nevertheless, coordination efforts from these organizations have been focused primarily on assuring the efficacy of the food fortification programs. Although most legislation allowed variability in the levels of added micronutrients to foods, only Chile had a specific regulation establishing maximum fortification limits for the addition of micronutrients to commercially fortified food products (Resol. Exenta No. 393/02).

**A regional approach to combat micronutrient deficiencies**

**The Americas**

Table 1 presents the different micronutrient interventions in Chile. The country uses two parallel strategies to combat micronutrient deficiencies. One is a mandatory fortification of staple foods targeting the general population, like salt iodization and fortification of wheat flour with vitamins and minerals. The other is the mandatory fortification of complementary feeding programs for specific risk groups like children, pregnant and lactating mothers, and the elderly. Although regulated but on a voluntary basis, there is also a limited number of commercially fortified foods that need to comply with the Chilean Sanitary Code (Decree No. 977), like fortified pasta with iron and B-complex vitamins (article 363), and vitamin A–fortified

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Table 1. Chile micronutrient programs and interventions

| Program                             | Regulation          | Enforcement | Responsibility/sponsorship | Target population | Frequency | Monitoring | Micronutrients                                                                 | Program evaluation | Interprogram coordination |
|-------------------------------------|---------------------|-------------|-----------------------------|-------------------|-----------|------------|--------------------------------------------------------------------------------|-------------------|---------------------------|
| Iodized saltab                        | Decree 977/96       | Mandatory   | Ministry of Health          | All           | Ongoing   | Ongoing    | Iodine = 0.02–0.06 g/kg of salt                                                 | 1982/2010 National Survey | No                        |
| Fortified wheat flourc                 | Decree 977/96       | Mandatory   | Ministry of Health          | All           | Ongoing   | Ongoing    | Thiamin = 6.3 mg/kg; riboflavin = 1.3 mg/kg; niacin = 13.0 mg/kg; iron = 30.0 mg/kg; folic acid = 1.0–2.6 mg/kg | 2010 National Health Survey | No                        |
| Fortified margarined                  | Decree 977/96       | Mandatory   | Ministry of Health          | All           | Ongoing   | Ongoing    | Vitamin A = 30,000 IU/kg                                                      | NA                | No                        |
| All fortified foods                  | Res. 393/02         | Mandatory   | Ministry of Health          | All           | Ongoing   | Ongoing    | Need to comply with maximum micronutrient limits established by regulation Res. 393/02 | NA                | No                        |
| Fortified purita milkd                | PNAC. Law 18.682,1987 | Mandatory | Ministry of Health          | Children and pregnant women | Ongoing   | Ongoing    | Fortified with iron, zinc, copper, and vitamin C                              | 2000 (iron status and anemia) | No                        |
| Purita mamad                          | PNAC. Law 18.682,1987 | Mandatory | Ministry of Health          | Pregnant and lactating | Ongoing   | Ongoing    | Fortified with vitamins and minerals, omega-3 fatty acids (DHA and EPA)       | NA                | No                        |
| Purita cereald                        | PNAC. Law 18.682,1987 | Mandatory | Ministry of Health          | Children aged >18 months | Ongoing   | Ongoing    | Fortified with vitamins and minerals, high in calcium and vitamins C and E     | NA                | No                        |
| Mi sopitaed                          | PNAC. Law 18.682,1987 | Mandatory | Ministry of Health          | Undernourished children | Ongoing   | Ongoing    | Fortified with vitamins and minerals                                           | NA                | No                        |
| Soup cream Atos Doradosed             | PNAC. Law 18.682,1987 | Mandatory | Ministry of Health          | Elderly       | Ongoing   | Ongoing    | Fortified with vitamins and minerals                                           | NA                | No                        |
| Dairy drink, Atos Doradosed           | PNAC. Law 18.682,1987 | Mandatory | Ministry of Health          | Elderly       | Ongoing   | Ongoing    | Fortified with vitamins and minerals                                           | NA                | No                        |

*Ministerio de Salud. República de Chile. Food Sanitary Code. Edible Salt. Article 438.
*Ministerio de Salud. República de Chile. Food Sanitary Code. Fleur Foods. Article 350.
*Ministerio de Salud. República de Chile. Food Sanitary Code. Margarine. Article 263.
*Ministerio de Salud. República de Chile. Manual de Programas Alimentarios, 2011.

Margarine (article 263). In addition, all newly introduced products containing added micronutrients need to comply with maximum limits of the addition of vitamins and minerals to foods (Resol. Exenta No. 393/02) or to dietary supplements (Resol. Exenta No. 394/02). These latter regulations in the Chilean legislation have introduced a halt in the maximum levels of all micronutrients added to foods, representing the first regulated attempt in Latin America to prevent excessive micronutrient intakes. They may also reflect the concern in the country about potential excessive levels of micronutrients in fortified foods, particularly of folic acid whose current level of addition to wheat flour has been questioned with the suggestion that it may need to be revised.

Table 2 shows the different micronutrient intervention programs in Costa Rica. The government strategy is to combat dietary micronutrient deficiencies based on mandatory fortification of six staple foods: salt with iodine; sugar with vitamin A; wheat and maize flours with iron, folic acid, and other B-complex vitamins; rice with folic acid, B-complex vitamins, vitamin E, selenium, and zinc; and milk with vitamin A, iron, and folic acid. Voluntary fortification is limited to commercially driven fortified products with little government supervision as long as they comply with product registration and labeling requirements. There are no micronutrient supplementation programs, except as needed on a clinical basis for iron and folic acid to women, but their contribution to micronutrient intake of the general population is minimal. An important feature of the Costa Rican food fortification legislation is the existence of a specific regulation conforming to the National Commission on Micronutrients (Government Decree No. 27086-S, 1998). The objectives of this regulatory body are “to promote interinstitutional coordination, among public sector, private sector, community organizations and NGOs to support the implementation of activities aimed toward the prevention and control of micronutrient deficiencies.” In this decree, there is not a specific mandate to prevent excessive...
micronutrient intakes. However, one would assume that based on this legislation, attention is also given to avoid unsafe micronutrient intake levels from combined micronutrient interventions.

Table 3 depicts a wide variety of existing micronutrient interventions in Guatemala. There is a mandatory fortification of staple foods like salt with iodine, table sugar with vitamin A, and wheat and maize flours with iron and B-complex vitamins. In addition, there are other targeted interventions sponsored by the MSPAS like megadoses of vitamin A to children, iron and folic acid supplementation to women of reproductive age, and multiple micronutrient powders for the point-of-use fortification of foods consumed by children. These activities generally follow WHO guidelines. In addition, the Guatemalan government has shown great interest on biofortification, through nutritional initiatives to introduce in the country beans biofortified with iron and corn with zinc. It is relevant to mention that the latest Guatemala national micronutrient survey revealed that vitamin A deficiency was practically eradicated, but there was a 3% of children between 6 and 59 months of age with serum retinol concentrations higher than 60 μg/dL. Whether this observation has any meaning in terms of excessive intakes of vitamin A cannot be determined but raises concern about the potential effect of the multiple vitamin A intervention strategies currently used in the country. These include the program of sugar fortification with vitamin A, whose fortification level has not been adjusted since the implementation of the program in 1975. As in the case of Costa Rica, there is also the CONAFOR in Guatemala under the sponsorship of the MISPAS (Decree No. 44-92). As per its name, this collegiate organization deals exclusively with fortified foods and not with micronutrients coming from other types of interventions like supplementation.

### Africa

Table 4 shows the different micronutrient interventions in Malawi. Mandatory micronutrient interventions include fortification of salt with iodine, iron, vitamin A, and folic acid. In addition, there are other targeted interventions like megadoses of vitamin A, zinc, and vitamin B12 to women and children. These activities generally follow WHO guidelines.

| Program | Regulation | Enforcement | Responsibility/ sponsorship | Target population | Frequency | Monitoring | Micronutrients | Program evaluation | Interprogram coordination |
|---------|------------|-------------|-----------------------------|-------------------|-----------|------------|---------------|-------------------|-------------------------|
| Sugar vitamin A fortification | 27021-S | Mandatory | Ministry of Health/ sugar industry | All | Ongoing | Ongoing | Packaging: 8 ± 2 mg/kg; Processing: 15 ± 5 mg/kg | National Survey 2008–2009 | Yes, Decree No. 27086-S |
| Iodized salt | 30032 | Mandatory | Ministry of Health | All | Ongoing | Ongoing | Iodine = 30–60 mg/kg of salt | National Survey 2008–2009 | Yes, Decree No. 27086-S |
| Wheat flour fortification | 30030-S | Mandatory | Ministry of Health | All | Ongoing | Ongoing | Minimum (mg/kg): iron = 50.0 mg; vitamin B1 = 6.2 mg; vitamin B2 = 4.2 mg; niacin = 55.0 mg; folic acid = 1.8 mg | National Survey 2008–2009 | Yes, Decree No. 27086-S |
| Maize fortification | 28086-S | Mandatory | Ministry of Health | All | Ongoing | Ongoing | Thiamin = 4.0 mg/kg; riboflavin = 2.5 mg/kg; niacin = 45.0 mg/kg; folic acid = 1.3 mg/kg; iron = 22.0 mg/kg | National Survey 2008–2009 | Yes, Decree No. 27086-S |
| Rice fortification | 34394-S | Mandatory | Ministry of Health | All | Ongoing | Ongoing | Folic acid = 1.8 mg/kg; thiamine = 5.3 mg/kg; vitamin B12 = 10.0 μg/kg; niacin = 35.0 mg/kg; vitamin E = 15 IU; selenium = 105 μg, zinc = 7.5 mg | National Survey 2008–2009 | Yes, Decree No. 27086-S |
| Milk fortification | 29629-S | Mandatory | Ministry of Health | All | Ongoing | Ongoing | Per 250 mL: iron = 1.4 mg; vitamin A = 600 IU; folic acid = 40 μg | National Survey 2008–2009 | Yes, Decree No. 27086-S |

Gobierno de Costa Rica (1998). Decreto Ejecutivo No. 27021-S: Reglamento técnico para la fortificación con vitamina A del azúcar blanco de plantación para el consumo directo. La Gaceta No. 108.

Gobierno de Costa Rica (2001). Reforma Norma Oficial para la Sal de Calidad Alimentaria No. 30032.

Gobierno de Costa Rica (2002). Decreto Ejecutivo No. 30030-S: Modificación del Reglamento para el enriquecimiento de la harina de trigo de calidad alimentaria promulgado mediante Decreto No. 26381-S. La Gaceta No. 1.

Gobierno de Costa Rica (1999). Decreto Ejecutivo No. 28086-S: Reglamento para el enriquecimiento de la harina de maíz. La Gaceta No. 184.

Gobierno de Costa Rica (2008). Decreto Ejecutivo No. 34394-S: Reforma al Reglamento para el enriquecimiento del arroz. La Gaceta No. 58.

Gobierno de Costa Rica (2001). Decreto Ejecutivo No. 2969-S: Reglamento para el enriquecimiento de la leche de ganado vacuno. La Gaceta No. 131.
as well as wheat flour and maize meal fortification with iron, zinc, vitamin A, folic acid, and other B-complex vitamins. Table sugar and edible vegetable oil are also fortified with vitamin A. Targeted interventions, following international WHO guidelines, include the administration of megadoses of vitamin A to children, and iron and folic acid supplementation to pregnant women. There is also standardized fortification of skimmed milk powder with vitamins A and D. In addition, provitamin A–biofortified sweet potato, containing a high concentration of β-carotene, has been widely introduced in the country as part of the government food security and nutrition agenda. B–Carotene is not considered unsafe and there is little concern about its safety.

Table 5 illustrates the various intervention programs with micronutrients in Uganda. Emphasis
is on combating vitamin A and iron deficiencies. In addition to mandatory salt fortification with iodine, sugar and cooking oil are fortified with vitamin A and there is a program of megadoses of vitamin A targeting children, and provision to children of fortified multiple micronutrient powders containing vitamin A and iron. In addition, wheat flour and maize meal are fortified with iron, zinc, vitamin A, folic acid, and other B-complex vitamins. There is also a program of iron and folic acid supplementation during pregnancy. Biofortification also plays a role by the introduction of high iron beans and, as in Malawi, a sweet potato rich in provitamin A.8 The supervision of all fortification activities in the country is coordinated by the National Working Group for Food Fortification (NWGFF) whose secretariat is at the Ministry of Health.32 However, there are no specific provisions to coordinate micronutrient fortification levels among interventions.

Micronutrient intervention programs in Zambia are presented in Table 6. According to the government, the main aim of the 2011–2015 National Food and Nutrition Plan was to prevent and combat micronutrient deficiencies, particularly those of vitamin A and iron.33 The programs are basically the same as in Uganda that include, in addition to mandatory salt fortification with iodine, mandatory fortification of table sugar and margarine with vitamins A and D and fortification of wheat flour with iron and B-complex vitamins. Fortification of maize meal with iron, zinc, vitamin A, folic acid, and other B–complex vitamins is currently under revision. In addition, there is periodic administration of megadoses of vitamin A to children, and iron and folic acid supplementation to women. As part of the National Food and Nutrition Strategy 2011–2015, provitamin A–biofortified sweet potato and corn, also rich in carotenoids (mainly β-carotene), have been introduced in the country.8

South Asia

Table 7 shows the different micronutrient interventions in Bangladesh. The government launched mandatory iodization of salt in 1989.34 Subsequently, a national micronutrient survey conducted in 2011–2012 revealed deficiencies in

| Program                                   | Regulation                                      | Enforcement          | Responsibility/sponsorship | Target population | Frequency | Monitoring          | Micronutrients | Program evaluation/coordination |
|--------------------------------------------|-------------------------------------------------|----------------------|-----------------------------|-------------------|-----------|---------------------|----------------|----------------------------------|
| Salt iodization                            | Iodization of salt act (52:02)                  | Mandatory            | Ministry of Health          | All               | Ongoing   | Ongoing             | Potassium iodate = 80–100 mg/kg | NA                 |
| Sugar vitamin A fortification              | MS 202, 2013                                   | Mandatory            | Ministry of Health          | All               | Ongoing   | Ongoing             | 15 mg/kg retinol | 2016 No |
| Wheat flour fortification                  | MS 30, 2011                                    | Mandatory            | Ministry of Health          | All               | Ongoing   | Ongoing             | Folic acid = 2.3 mg/kg, iron = 39 mg/kg, vitamin B12 = 0.02 mg/kg, vitamin B1 = 9.8 mg/kg, vitamin B2 = 6.6 mg/kg, niacin = 60 mg/kg, zinc = 88 mg/kg, vitamin A = 1 mg/kg | 2016 |
| Maize meal fortification                   | MS 34, 2011                                    | Mandatory, voluntary | Ministry of Health          | All               | Ongoing   | Ongoing             | Folic acid = 1.2 mg/kg, iron = 31 mg/kg, vitamin B12 = 0.015 mg/kg, vitamin B1 = 6.5 mg/kg, vitamin B2 = 4.0 mg/kg, niacin = 30 mg/kg, zinc = 49 mg/kg, vitamin A = 1 mg/kg | 2016 No |
| Cooking oil fortification                  | MS 51, 2011                                    | Mandatory            | Ministry of Health/WFP      | All               | Ongoing   | Ongoing             | Retinyl palmitate = 35 mg/kg | 2016 No |
| Mega doses vitamin A                       | National program                               | Mandatory            | Ministry of Health          | Young children    | Every 6 months | NA                  | Follows WHO guidelines | 2016 No |
| Vitamins A and D skimmed milk powder       | National program                               | Mandatory            | Ministry of Health/WFP      | All               | Ongoing   | NA                  | NA             | NA No |
| Biofortification                           | Food and Nutrition Agenda                      | Voluntary            | Department of Agricultural Research Services | All               | Ongoing   | NA                  | Sweet potato provitamin A, level NA | No No |

Malawi Ministry of Health. Iodization of Salt Act (52:02). 02-08-2015 (http://www.malawitradeportal.gov.mw/index.php?r=site/display&id=51).

WHO Global Database on the Implementation of Nutrition Action.

Malawi Standard (MS) 34:2011 (http://ffinetwork.org/about/calendar/2016/documents/Maize_Standard_Malawi_2016.pdf).

Food Fortification. United Nations World Food Programme (WFP). Malawi, August 2008.
| Program                                      | Regulation                          | Enforcement       | Responsibility/ sponsorship | Target population | Frequency | Monitoring | Micronutrients                                                                 | Program evaluation | Interprogram coordination |
|----------------------------------------------|-------------------------------------|-------------------|-----------------------------|-------------------|-----------|-----------|--------------------------------------------------------------------------------|-------------------|---------------------------|
| **Iodized salt**<sup>a,b</sup>               | Ministry of Health 1994; F&D Regulations, 2005 | Mandatory          | Ministry of Health          | All               | Ongoing   | Ongoing   | Iodine = 30–60 mg/kg                                                           | 2007–2008 food testing | NWGFF 2008                  |
| **Vitamin A fortified of sugar**<sup>a,b</sup> | Standards 2004; F&D Regulations, 2005 | Mandatory (2013)  | Ministry of Health          | All               | Ongoing   | Ongoing   | Minimum 1 mg/100 g; Maximum 3 mg/100 g                                         | NA                | NWGFF 2008                  |
| **Vitamin A fortified oil**<sup>a,b</sup>    | Standards 2004; F&D Regulations, 2005 | Mandatory (2013)  | Ministry of Health          | All               | Ongoing   | Ongoing   | Vitamin A = 2.0–4.5 mg/kg                                                      | NA                | NWGFF 2008                  |
| **Fortified wheat flour**<sup>a,b</sup>      | Standards 2004; F&D Regulations, 2005 | Mandatory (2013)  | Ministry of Health          | All               | Ongoing   | Ongoing   | Minimum (mg/100 g): vitamin A = 0.1; vitamin B1 = 0.4; vitamin B2 = 0.2; niacin = 4; vitamin B6 = 0.3; folate = 0.1; vitamin B12 = 0.0007; Minimum iron (mg/100 g): total = 2; from ferrous fumarate = 2.5; zinc = 3 | NA                | NWGFF 2008                  |
| **Fortified maize flour**<sup>a,b</sup>      | Standards, 2004; F&D Regulations, 2005 | Mandatory (2013)  | Ministry of Health          | All               | Ongoing   | Ongoing   | Minimum (mg/100 g): vitamin A = 0.05; vitamin B1 = 0.2; vitamin B2 = 0.2; niacin = 2; vitamin B6 = 0.3; folate 0.05; vitamin B12 = 0.0003; Minimum iron (mg/100 g): total = 2; from NaFeEDTA = 1; zinc = 2 | NA                | NWGFF 2008                  |
| **Micronutrient powders**<sup>a</sup>        | Ministry of Health Initiative, 2015  | National program   | Ministry of Health/ USAID/ UNICEF/ WFP | Children aged 6–23 months | Ongoing   | NA        | NA                                                                            | NA                | NA                        |
| **Vitamin A supplement** (megadoses)         | Ministry of Health Nutrition Plan   | National program   | Ministry of Health          | Children aged 1–5 years | Every 6 months | WHO guidelines | NA                                                                            | NA                | NA                        |
| **Iron and folic acid supplement**           | Ministry of Health Nutrition Plan   | National program   | Ministry of Health          | Pregnant women    | During pregnancy | WHO guidelines | NA                                                                            | NA                | NA                        |
| **Biofortification**<sup>a</sup>             | Part of government nutrition plan   | Voluntary          | Ministry of Health          | All               | Ongoing   | NA        | Beans (iron), sweet potato (provitamin A)                                      | NA               | No                        |

<sup>a</sup>Ministry of Health, the Republic of Uganda/Nutrition (Official Website).
<sup>b</sup>The Uganda Legal Information Institute. Food and Drugs (Food Fortification) Regulations 2005.

NWGFF, National Working Group for Food Fortification; USAID, the United States Agency for International Development; UNICEF, the United Nations International Children’s Emergency Fund; WFP, World Food Programme.

Vitamins A and D, iron, iodine, zinc, and calcium. Based on these findings, in 2015, the Bangladesh government established a national strategy for prevention and control of micronutrient deficiencies, 2015–2024. Various mandatory programs were then implemented by the Institute of Public Health and Nutrition under the Ministry of Health and Family Welfare. They include, besides salt fortification with iodine, mandatory vitamin A fortification of all cooking oils, distribution of fortified rice with multiple micronutrients to vulnerable groups, and multiple micronutrient-fortified powders containing iron, vitamin A, and zinc to be added to the diet of young children. In addition, a nationwide vitamin A supplementation program was launched consisting of the distribution of 100,000–200,000 IU vitamin A capsules to children, in association with immunization campaigns, and to the post-partum women in a single dose of 200,000 IU after the delivery. Most of these programs have been technically supported by the United Nations International Children’s Emergency Fund and funded
by the Global Alliance for Improved Nutrition. However, we did not find evidence of coordination among programs to prevent or minimize excessive micronutrient intakes. On the other hand, voluntary biofortification also plays an important role in this strategy. With the technical support of the Bangladesh Rice Research Institute and the Agricultural Research Institute, various biofortified crops have been introduced in the country, including biofortified rice with zinc, lentils with zinc and iron, and a sweet potato with provitamin A.\textsuperscript{8}

**The Western Pacific Region**

Micronutrient interventions in China are presented in Table 8. Salt fortification with iodine has been a highly successful mandatory program since 1994.\textsuperscript{37} It became fully regulated in 2011 under the State Council Order No. 163 to prevent iodine deficiency disorders (IDDs), previously documented in the country. Because of the initial high level of iodine fortification, there was a concern in 1995 about excess iodine intake, appropriate for pregnant women but in excess for children. Therefore, the addition level of iodine changed in 1996 from 40–60 to 20–50 ppm, and later to 14–39 ppm. In addition to salt fortification, capsules containing iodized oil are provided to high-risk populations (pregnant and lactating mothers in rural areas), and in emergencies. Currently, these successful programs provide 94% of the recommended dietary allowance for iodine, and IDD has been eliminated in the country. There is also a national standard for complementary foods aimed to improve the nutritional status of rural children by the use of multiple micronutrient-fortified powders containing vitamins and minerals, which are added at home to their meals. On the other hand, voluntary fortification of wheat flour with multiple micronutrients and of soy sauce also contributes to enhancing the micronutrient dietary availability.
Table 7. Bangladesh micronutrient programs and interventions*

| Program | Regulation | Enforcement | Responsibility/sponsor | Target population | Frequency | Monitoring | Micronutrients | Program evaluation | Program coordination |
|---------|------------|-------------|------------------------|-------------------|-----------|------------|---------------|-------------------|---------------------|
| Salt iodization | Iodine Deficiency Diseases Prevention Act 1989 | Mandatory | MOHF/UNICEF | All | Ongoing | BRAC | Iodine >15 ppm | UNICEF Survey | NA |
| Oil fortification with vitamin A | Fortification of Edible Oil with Vitamin A, law 2013 | Mandatory | MOI/UNICEF | All | Ongoing | BSTI | Vitamin A = 15–30 ppm | GAIN survey 2017 | NA |
| Fortified rice with multiple micronutrients | A rice fortification initiative 2014 | Mandatory | MWCA | Vulnerable groups | Initiated in 2014, expanded in 2015 | WFP | Vitamins A, B1, and B12, folic acid, iron, and zinc | WFP 2013 | NA |
| Multiple micronutrient powder | National strategy 2015–2024 | National program | MOHF | Subdistricts, informal urban settlements | Periodic | BRAC | Iron, vitamin A, and minerals | IL-GAIN, ICDDR,B, CEPA | NA |
| Megadoses vitamin A | Nutritional Blindness Programme 1973 | National program | MOHF | Children and postpartum women | Routinely and domiciliary visits | NA | Children 100–200K IU, Women 200K IU | PGSPH/HKI 2012; DGHS | NA |
| Iron and folic acid supplementation | National program 2001 | National program | NNS | Pregnant and nonpregnant, nonlactating women | Ongoing | MOHF | Daily 60 mg elemental iron and 400 μg folic acid | MOHF | NA |
| Biofortification | Country strategy 2014 | Voluntary | BRRI and BARI | All | Ongoing | NA | Rice (iron), lentils (iron and zinc), and sweet potato (provitamin A) | NA | NA |

*National strategy on prevention and control of micronutrient deficiencies (2015–2024), Government of the people’s Republic of Bangladesh, 2015.

The Republic of the Philippines addresses micronutrient dietary deficiencies using both food fortification and dietary supplementation with vitamin A, iron, and iodine to women and children.38 Mandatory fortification of staple foods includes an iodine-fortified salt and rice, iron and vitamin A–fortified wheat flour, and vitamin A–fortified table sugar and cooking oil. There is also voluntary use of multiple micronutrient powders targeted at young children and pregnant and lactating women, as well as voluntary fortification of processed foods with iron, vitamin A, or iodine. Commercially available fortified foods include cereal and cereal products with added iron and B-complex vitamins, milk and margarine with vitamin A, and juices, flavored drinks, and food gels enriched with vitamin C.

**Discussion**

Countries in our investigation tackled their micronutrient deficiencies by implementing both the mandatory mass fortification of staple foods aimed at the general population and the voluntary, complementary feeding and supplementation programs aimed at vulnerable groups like children, women of reproductive age, and the elderly. Biofortification has been considered and subsequently adopted by some governments. However, at present, its dietary contribution to micronutrient intake in most countries is minimal, with the exception of the African region where the dietary availability of provitamin A has been significantly enhanced by an intense introduction of various biofortified crops containing higher contents of carotenoids than their traditional counterparts.39 Mandatory mass interventions using fortified staple foods, like salt fortified with iodine, table sugar with vitamin A, and wheat and maize meal with iron, zinc, vitamin A, folic acid, and other B-complex vitamins, are clearly government regulated and the corresponding regulations are part of the country’s food laws. Targeted interventions, on the other hand, like micronutrient supplementation to specific risk groups, follow existing international regulatory guidelines adopted by the country but are not in their legislation. This
is the case of megadoses of vitamin A to children, iron and folic acid supplementation to women, and the use of multiple micronutrient powders added to children’s meals. Biofortification, by using traditional breeding techniques, is currently unregulated but has become part of the country’s nutrition policies or action plans to combat micronutrient dietary deficiencies.

In terms of coordination among interventions, we did not find specific provisions in the actual regulations requiring coordination among programs to avoid excesses of micronutrient intakes. There were neither requirements in the regulations for use of biomarkers or program indicators to identify potential toxicity. Moreover, with the exception of data on fortification, centralized information that accounted for all sources of micronutrients was not available. Therefore, a true estimate of how far from the UL is the actual level of micronutrient intake and the risk of overconsumption cannot be made in the studied countries. Only Chile had a specific regulation establishing maximum limits of micronutrient fortification of foods and dietary supplements. Although this is an important step in the safety of the programs, there was no clear connection among interventions. However, it is interesting to find in Central American countries like Costa Rica and Guatemala, the national commissions for micronutrient fortification established by a government mandate. Formed by different stakeholders, these collegiate organizations include government, industry, community organizations, and NGOs. A somewhat similar government-sponsored organization in Africa is the NWGFF (2008). One of the functions of these collegiate bodies is to coordinate micronutrient initiatives and advise governments on micronutrient policies. This could be a mechanism of controlling excessive micronutrient intakes from multiple interventions; however, the scope of these commissions is primarily food fortification, not including other types of interventions. Moreover, their coordination efforts seem to be directed primarily to ensure the effectiveness of the fortification programs. In summary, it can be concluded that the regulatory framework for the existing multiple interventions to combat vitamins and mineral

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**Table 8. China micronutrient program and interventions**

| Program                                      | Regulation             | Enforcement       | Responsibility/ sponsor | Target population | Frequency | Monitoring | Micronutrients | Program evaluation | Interprogram coordination |
|----------------------------------------------|------------------------|-------------------|-------------------------|-------------------|-----------|------------|---------------|--------------------|--------------------------|
| Salt iodization. Elimination of iodine deficiency disorders (IDD)³⁴ | GB 14880, 2011          | Mandatory         | NHFPC, MIIT, Salt industry | All               | Ongoing   | IDD Survey System, National Salt Monitoring | 14–39 ppm | GAIN 2014, National IDD survey 1995–2014 | NA                       |
| Iodized oil capsules³⁴                       | State Council Order 163³⁴ | Mandatory routine and emergency capsule distribution to specific groups | NHFPC               | High-risk populations (pregnant and lactating women) | Ongoing   | High-risk areas monitoring | 300–960 mg/12 months (1 capsule, 0.4 mL; 200 mg iodine) | IDD Surveys 1995–2014 | NA                       |
| Iron fortified soy sauce GB 1480, 2012       | Voluntary              | The Food Fortification Office at China CDC | All population in nine provinces | Ongoing           | China CDC | 180–260 mg/kg | Calcium, iron, zinc, folic acid, niacin, and vitamins A, B1, and B2 | GAIN 2003–2013 | NA                       |
| Fortified wheat flour GB/T 21122, 2007, GB 14880, 2012 | Voluntary              | China CDC         | All                      | Ongoing           | China CDC | 72 mg/kg | Calcium, iron, zinc, folic acid, niacin, and vitamins A, B1, and B2 | NA                      | NA                       |
| Multiple micronutrient powder (Ying Yang Bao program) National Standard complementary food supplements, 2009 | Voluntary point-of-use home fortification (sprinkles) | China CDC | Infants and young children in rural areas | Ongoing | China CDC | Per 12-g sachet: iron = 7.5 mg, zinc = 5 mg, calcium = 200 mg, vitamin A = 250 µg, vitamin D = 5 µg, vitamin B1 = 0.5 mg, vitamin B2 = 0.5 mg, vitamin B12 = 0.5 µg, and folic acid = 75 µg | China CDC | NA                       |
deficiencies in the selected countries lacks mandatory requirements to coordinate their implementation in such a way that the risk of excessive micronutrient intakes is minimized. In general, countries have regulations that set levels of addition of micronutrient to foods, and in some cases maximum limits, but only within the individual program without considering the contribution of micronutrients from other sources.

Concerns about excessive intakes of micronutrients due to food fortification exist since the 1980s. The issue was first addressed in 1987 by the Codex Alimentarius publication titled “General Principles for the Addition of Essential Nutrients to Foods” (CAC/GL 9-1987. Amended in 1989 and 1991. Revised in 2015). This clear set of principles intends to provide guidelines and legal texts to country authorities for implementation of rational and safe fortification programs. One of these principles clearly states, “The amount (of micronutrient) added should not result in either an excessive intake or an insignificant intake of the added essential nutrients, considering total daily intakes from all relevant sources, including supplements.” Furthermore, those maximum amounts of added micronutrients should be set taking into account ULs of micronutrients established by scientific risk assessment and generally accepted scientific data. Within this context, the Codex General Guidelines also indicate the importance of monitoring and evaluation of the programs. In 2006, the WHO/Food and Agriculture Organization of the United Nations published the Guidelines on Food Fortification with Micronutrients. Again, the main objective of this latter publication was to assist countries in the design and implementation of appropriate food fortification programs. In this report, it is recommended that setting of fortification levels of micronutrients should be based around the EAR and considering ULs. In addition, those levels of added micronutrients above the Recommended Nutrition Intakes (RNIs) should be avoided. A refinement in optimizing the setting of adequate and safe levels of micronutrients in foods has been described by Bruins et al. In all these guidelines, monitoring and the use of program indicators to identify potential toxicity, risk assessments, and periodic program evaluations are considered part of the safety equation. In this respect, centralization and compilation of data on dietary intake from all sources, program coverage, and biomarkers to identify excessive intakes and morbidity among vulnerable population groups are essential. Thus, after a risk–benefit analysis, decisions can be made regarding adjustments or termination of an existing program or even not starting a new intervention.

Food fortification in high-income countries is tightly regulated by government food safety agencies. In member countries of the European Union, the addition of vitamins and minerals to foods is regulated by the EFSA under Regulation (EC) No. 1925/2006. Such legislation is aligned with a regulatory committee procedure with scrutiny by regulation (EC) No. 108/2008 by which new vitamin and mineral substances, not in a positive list, need to go through evaluation by the agency based on a scientific dossier regarding the safety and bioavailability of the individual micronutrients, including intake data and proposed maximum levels.

The United States allows the addition of vitamins and minerals to foods according to the U.S. Food and Drug Administration Fortification Policy (21-CFR 104.20, 1980). It is based on a positive list of nutritional substances that can be used in food fortification and on a negative list of food vehicles that cannot be fortified like meat products and foods with a standard of identity. According to this policy, to add nutrients to foods, there should be sufficient information available to identify the nutritional problem and the affected population groups and that the food is suitable to act as a vehicle for the added nutrients. In addition, that the added nutrient is present at a level at which there is a reasonable assurance that consumption of the food containing the added micronutrient will not result in an excessive intake considering cumulative amounts from other sources in the diet.

In Canada, fortification is a process by which vitamins, minerals, and amino acids are added to foods to provide consumers with sufficient but not excessive amounts of certain nutrients in the diet. The Canadian Food and Drug Regulations (FDR) set the framework for the fortification of foods, including which ones are required or permitted to be fortified, and the applicable conditions. For some foods, fortification is mandatory; for example, the standard for skim milk requires the addition of vitamins A and D, including the range of acceptable amounts.
Voluntary fortification is also permitted in the regulations for certain foods. The requirements and voluntary permissions for fortification are set out in food standards under parts B and D, Division 3 of the FDR as well as they meet the compositional, packaging, labeling, and advertising requirements under the Food and Drug Act.

It appears then that there is already a body of regulatory information, including country experiences, regarding principles and regulatory procedures to ensure safe implementation of micronutrient interventions. However, most information comes from food fortification and connection among programs is missing. Therefore, there is a need to design comprehensive guidelines and a regulatory framework considering all intake sources of micronutrients, the use of program indicators to identify the risk of overconsumption, and a centralization of the data of all existing programs. Regarding food fortification, key elements needed for implementing safe interventions include setting safe levels of micronutrients (including maximum levels), food intake data of the food vehicle and from other sources that may contain the same micronutrient, monitoring of food compliance, and periodic evaluation of the programs using biological indicators so that adjustments to the interventions can be periodically made. Monitoring and evaluation are of foremost importance as illustrated in Costa Rica in which table sugar fortification with vitamin A was suspended by the government in 1981 based on the program evaluation indicating that vitamin A deficiency did not longer exist. The program was reinitiated in 2003 when the new survey data showed that hypovitaminosis A reappeared and became again a public health concern.

A suggested regulatory procedure at the country level to initiate a micronutrient intervention could be the submission of a scientific dossier containing relevant efficacy and safety data to a collegiate technical/regulatory body, like the one already established in Costa Rica, conformed by all stakeholders, including technical and regulatory personnel. The dossier should contain a comprehensive analysis and evaluation of all existing programs, including dietary intake, prevalence of deficiency, morbidity data, and a risk assessment of implementing the new intervention. This scientific/regulatory body will then review and advise the government about the appropriateness of the proposed program, as well as the needed legislation. The resulting regulatory framework should contain provisions requiring coordination among interventions to assure the safety of the multiple programs considering the intake contribution of micronutrients coming from all sources, and the use of appropriate program indicators to identify excessive micronutrient intakes. Building and operating this regulatory framework will also require management responsibility for centralization, compilation, assessment, and availability of all relevant data.

Acknowledgments

This work was commissioned and financially supported by the Evidence and Programme Guidance Unit, Department of Nutrition for Health and Development of the World Health Organization (WHO), Geneva, Switzerland.

Statement

This manuscript was presented at the World Health Organization (WHO) technical consultation “Risk of Excessive Intake of Vitamins and Minerals through Public Health Interventions—Current Practices and Case Studies,” convened on October 4–6, 2017, in Panamá City, Panamá. This paper is published individually and with related manuscripts as a special issue of Annals of the New York Academy of Sciences, the coordinators of which were Drs. Maria Nieves García-Casal and Juan Pablo Peña-Rosas. The special issue is the responsibility of the editorial staff of Annals of the New York Academy of Sciences, who delegated to the coordinators the preliminary supervision of both technical conformity to the publishing requirements of Annals of the New York Academy of Sciences and general oversight of the scientific merit of each article. The workshop was supported by WHO, the United States Agency for International Development (USAID), and the Bill & Melinda Gates Foundation. The authors alone are responsible for the views expressed in this paper; they do not necessarily represent the views, decisions, or policies of the WHO. The opinions expressed in this publication are those of the authors and are not attributable to the sponsors, publisher, or editorial staff of Annals of the New York Academy of Sciences.
Competing interests
The authors declare no competing interests.
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References
1. World Health Organization. 1998. Vitamin and mineral requirements in human nutrition. 2nd ed. Bangkok: World Health Organization.
2. Penniston, K.L. & S.A. Tanumihardjo. 2006. The acute and chronic toxic effects of vitamin A. Am. J. Clin. Nutr. 83: 191–201.
3. Bhattacharya, S. & A. Singh. 2017. Time to revisit the strategy of massive vitamin A prophylaxis dose administration to the under-five children in India—an analysis of available evidence. Clin. Nutr. ESPEN 21: 26–30.
4. Selhub, J. & I.H. Rosenberg. 2016. Excessive folic acid intake and relation to adverse health outcome. Biochimie 126: 71–78.
5. Pearce, E.N., J.H. Lazarus, R. Moreno-Reyes, et al. 2016. Consequences of iodine deficiency and excess in pregnant women: an overview of current knowns and unknowns. Am. J. Clin. Nutr. 104: 918S–923S.
6. Chen, W., Y. Zhang, Y. Hao, et al. 2018. Adverse effects on thyroid of Chinese children exposed to long-term iodine excess: optimal and safe tolerable upper intake levels of iodine for 7- to 14-y-old children. Am. J. Clin. Nutr. 107: 780–788.
7. Aakre, I., T.A. Strand, K. Moubarek, et al. 2017. Associations between thyroid dysfunction and developmental status in children with excessive iodine status. PLoS One 12: e0187241.
8. Mejia, L.A., O. Dary & H. Boukerdennia. 2017. Global regulatory framework for production and marketing of crops biofortified with vitamins and minerals. Ann. N.Y. Acad. Sci. 1390: 47–58.
9. Bruins, M.J., G. Mugambi, J. Verkaik-Kloosterman, et al. 2015. Addressing the risk of inadequate and excessive micronutrient intakes: traditional versus new approaches to setting adequate and safe micronutrient levels in foods. Food Nutr. Res. 59: 26020.
10. Scientific Committee on Food/Scientific Panel on Dietetic Products Nutrition and Allergies. 2005. Tolerable upper intake levels for vitamins and minerals. European Food Safety Authority. Accessed August 25, 2018. http://www.efsana.europa.eu/sites/default/files/efsna_rep/blobserver_assets/ndatablerueil.pdf.
11. Bruins, M.J., R. Kupka, M.B. Zimmermann, et al. 2016. Maximizing the benefits and minimizing the risks of intervention programs to address micronutrient malnutrition: symposium report. Matern. Child Nutr. 12: 940–948.
12. World Health Organization. 2012. Global database on the Implementation of Nutrition Action (GINA). World Health Organization. Accessed August 20, 2018. http://www.who.int/nutrition/gina/en/.
13. World Health Organization. 2011. Guideline: vitamin A supplementation in infants and children 6–59 months of age. World Health Organization. Accessed August 25, 2018. http://apps.who.int/iris/bitstream/handle/10665/44664/9789241501767_eng.pdf?sequence=1.
14. World Health Organization, A.L. Williams, W. van Dromgelen, et al. 2012. Guideline: daily iron and folic acid supplementation in pregnant women. World Health Organization. Accessed August 25, 2018. http://apps.who.int/iris/bitstream/handle/10665/77770/9789241501996_eng.pdf?sequence=1.
15. World Health Organization. 2016. WHO guideline: use of multiple micronutrient powders for point-of-use fortification of foods consumed by infants and young children aged 6–23 months and children aged 2–12 years. Geneva: World Health Organization.
16. Gobierno de Costa Rica. 1998. Decreto No. 27086-S. Crea la comision de micronutrientes. Gobierno de Costa Rica. Accessed August 20, 2008. https://reventazon.meic.gob.cr/informacion/gaceta/1998/junio/27086.pdf.
17. República de Guatemala. 2010. Comisión nacional para la fortificación, enriquecimiento y/o equiparación de alimentos (CONAFOR). República de Guatemala. Accessed August 20, 2018. http://www.conafor.org/main.asp?clc=326.
18. Comité de Nutrición y Tecnología de Alimentos. 2016. Fortificación de alimentos en Centroamérica y el Caribe. ILSI Mesoamérica. Accessed August 16, 2018. http://ilsismesoamerica.org/wp-content/uploads/sites/14/2016/08/Mono graf%C3%ADAs-Fortificaci%C3%B3n-de-alimentos-para-Centroam%C3%A9rica-para-el-Caribe.pdf.
19. Ministerio de Salud. 2002. Exenta 393. Fijación directrices nutricionales sobre uso de vitaminas, minerales y fibra dietética. Exenta. Chile: República de Chile. Accessed August 20, 2018. https://www.leychile.cl/Navegar?idNorma=194952.
20. Pizarro, T., L. Rodr & X. Benavides. 2004. Programas de Suplementación Alimentaria y de fortificación de alimentos con micronutrientes en Chile. Cuad. Médico Soc. 43: 53–60.
21. Ministerio de salud. 2011. Manual de programas alimentarios. Santiago, Chile: República de Chile. Accessed August 25, 2018. http://www.minsal.cl/portal/Url/item/caa1783sed97a1425e04001016401099p.pdf.
22. Ministerio de Salud. 2016. Decreto No. 977/1996 que aprueba reglamento sanitario de los alimentos (modificado por el Decreto No. 29/2016). República de Chile. Accessed August 20, 2018. http://www.wipo.int/wipolex/en/details.jsp?id=16357.
23. Ministerio de Salud. 2002. Exenta No. 394. Fijación directrices nutricionales sobre suplementos alimentarios y sus contenidos en vitaminas y minerales. República de Chile. Accessed August 20, 2018. https://www.scribd.com/document/248959423/Resolucion-Exenta-394-de-2002.
24. Araya, H.L. & M.O. Ruz. 2007. Evaluación del riesgo para vitaminas y minerales en alimentos fortificados. Departamento de Nutrición, Facultad de Medicina, Universidad de Chile. Accessed August 20, 2018. http://www.minsal.cl/portal/url/item/62ddc6f7a969153bbe0400101e1f5a76e.pdf.
25. Castillo, C.L., J.A. Tur & R. Uauy. 2010. Fortificación de la harina de trigo con ácido fólico en Chile. Consecuencias no intencionadas. Rev. Med. Chil. 138: 832–840.
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26. Castillo-Lancellotti, C., J.A. Tur & R. Uauy. 2013. Impact of folic acid fortification of flour on neural tube defects: a systematic review. Public Health Nutr. 16: 901–911.

27. Comisión Intersectorial de Guías Alimentarias para Costa Rica. 2007. Actualización de lineamientos técnicos para la elaboración de guías alimentarias de la población costarricense. San José, Costa Rica: Comisión Intersectorial de Guías Alimentarias de Costa Rica. Accessed August 16, 2018. https://www.ministeriodesalud.go.cr/index.php/biblioteca-de-archivos/tecnico-ciencia/documentos-2/2684-plan-de-accion-de-reduccion-y-control-de-las-deficiencias-de-micronutrientes-2011-2020-costa-rica/file.

28. Ministerio de Salud. 2013. Plan de acción de reducción y control de las deficiencias de micronutrientes 2011–2020. San José, Costa Rica: República de Costa Rica. Accessed August 16, 2018. https://www.ministeriodesalud.go.cr/gestores_en_salud/guiasalimentarias/actualizacion%20lineamientos.pdf.

29. Ministerio de Salud Pública y Asistencia Social. 2012. Encuesta nacional de micronutrientes 2009–2010. Guatemala: MSPAS/Instituto Nacional de Estadística (INE). Accessed August 16, 2018. https://www.scribd.com/doc/272127322/Informe-Final-ENMICRON-2009-2010.

30. Mazariégos, M., C. Martínez, D.I. Mazariegos, et al. 2016. Análisis de la situación y tendencias de los micronutrientes clave en Guatemala, con un llamado a la acción desde las políticas públicas. Food and Nutrition Technical Assistance. Washington, D.C. FHI360/FANTA. Accessed August 16, 2018. https://www.fantaproject.org/sites/default/files/resources/Guatemala-Micronutrient-Analysis-Sep2016.pdf.

31. Arroyave, G. & L.A. Mejía. 2010. Five decades of vitamin A studies in the region of Central America and Panama. Food Nutr. Bull. 31: 118–129.

32. Ministry of Health. 2008. Quality of fortified foods in Uganda 2007–2008. National Monitoring Report. Republic of Uganda. Accessed August 16, 2018. http://a2zproject.org/pdf/Uganda_FC_Report_Round3_Formated180409.pdf.

33. National Food and Nutrition Commission of Zambia. 2011. National food and nutrition strategic plan for Zambia 2011–2015. Republic of Zambia. Accessed August 16, 2018. http://scalingupnutrition.org/wp-content/uploads/2013/02/Zambia_FNFC-Strategic-Plan-2011-2015.pdf.

34. Counts, E.W., Z. Mahmud & S.A. Chowdhury. 1997. General review of iodine deficiency in Bangladesh and policy implications. In Bangladesh Rural Advancement Committee Micronutrient Series. pp. 1–18. Dhaka: BRAC, Health and Population Division.

35. Bangladesh UNICEF. 2013. National micronutrients status survey. Institute of Public Health and Nutrition. Accessed August 16, 2018. https://static1.squarespace.com/static/56424f6ce4b0b552eb7dfc4e8/t/57490d3159827c39bd4d2314/1464405328062/Bangladesh_NMS_final_report_2011-12.pdf.

36. Institute of Public Health Nutrition Directorate General of Health. 2015. National strategy on prevention and control of micronutrient deficiencies, Bangladesh (2015–2024). Ministry of Health and Family Welfare, Government of the People’s Republic of Bangladesh. Accessed August 16, 2018. http://iphn.dghs.gov.bd/wp-content/uploads/2016/01/ NMDCS-.pdf.

37. Sun, D., K. Codling, S. Chang, et al. 2017. Eliminating iodine deficiency in China: achievements, challenges and global implications. Nutrients 9: 361.

38. National Nutrition Council. 2017. Philippine plan of action for nutrition 2017–2022: an urgent call to action for Filipinos and its leadership. Department of Health, Republic of The Philippines. Accessed August 16, 2018, http://www.nnc.gov.ph/downloads/technical-papers?download=870:philippine-plan.

39. Food and Agricultural Organization (FAO) and World Health Organization (WHO). 2015. General principles for the addition of essential nutrients to foods CAC/GL 9–1987 Adopted in 1987. Amendment: 1989, 1991. Revision: 2015. Codex Alimentarius. Accessed August 16, 2018. http://www.fao.who-codexalimentarius/sh-proxy/ip/?lnk=1&url=https%253A%252F%252Fworkspace.fao.org%252Fsites%252Fcodes%252FStandards%252FCAC%252FGL%252F%252F%252F9-1987%252FCXG-009e_2015.pdf.

40. Allen, L., B. de Benoist, O. Dary, et al. 2006. Guidelines on food fortification with micronutrients. WHO, FAO, UN. Accessed August 16, 2018. http://www.unscn.org/layout/modules/resources/files/fortification_eng.pdf.

41. European Parliament. 2000. Regulation (EC) No. 1925/2006 of the European Parliament and of the Council of 20 December 2006 on the addition of vitamins and minerals and of certain other substances to foods. Official Journal of the European Communities. Accessed August 16, 2018. https://eur-lex.europa.eu/eli/reg/2006/1925/oj.

42. Food and Drug Administration. 2017. 21-CFR 104.20. Nutritional quality guidelines for foods, sub-part b- Fortification policy. Code of Federal Regulations. Accessed August 16, 2018. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=104.20.

43. Government of Canada. 2018. Food and Drug Regulations, CRC, c 870. Food and Drug Act. Government of Canada. Accessed August 16, 2018. http://laws-lois.justice.gc.ca/eng/regulations/C.R.C.,_c._870/FulText.html.