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Staple crops biofortified with increased vitamins and minerals: considerations for a public health strategy

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Biofortification of staple crops has been proposed as a strategy to address micronutrient malnutrition, particularly with respect to insufficient intake of vitamin A, iron, zinc, and folate. The World Health Organization, in collaboration with the Food and Agriculture Organization of the United Nations and the Sackler Institute for Nutrition Science at the New York Academy of Sciences, convened a technical consultation entitled "Staple Crops Biofortified with Vitamins and Minerals: Considerations for a Public Health Strategy" in April 2016. Participants of the consultation reviewed the definition of biofortification of staple crops, patterns of crops production, processing, consumption, seed varieties, and micronutrient stability and bioavailability, as well as farmers' adoption and acceptability of the modified crops. Also discussed were economic, environmental, safety, and equity aspects of biofortified crops, as well as legal, policy, regulatory, and ethical issues for the implementation of biofortification strategies in agriculture and nutrition. Consultation working groups identified important and emerging technical issues, lessons learned, and research priorities to better support the evidence of improved nutrition and unintended adverse effects of biofortification. This paper provides the background and rationale of the technical consultation, synopsizes the presentations, and provides a summary of the main considerations proposed by the working groups.

Keywords: biofortification; agronomic; plant breeding; genetic modification; vitamins; minerals; objectives; technical consultation; public health

Consultation rationale

The World Health Organization (WHO) has been working toward the development of global evidence-informed guidelines on interventions to address malnutrition in all of its forms, including vitamin and mineral malnutrition. One proposed approach to improve the intake of nutrient-rich foods is to increase the nutrient content potential of staple crops through biological fortification (or biofortification), which refers to the indirect increase in the content of an essential vitamin or provitamin, mineral, or other substance in crops to support nutritional or health goals. Biofortification can be achieved through one of three main non-mutually exclusive agronomic methods: (1) application of fertilizer to the soil or leaves;[1] (2) conventional or

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traditional plant breeding;[2] or (3) genetic engineering, which includes genetic modification and transgenesis.[3]

Modified crops offer the possibility of food-based interventions that, if fully adopted and accepted, could reach remote populations with micronutrient-deficient diets. Biofortified crops, or the foods prepared with them, may not be adopted by farmers or accepted by all consumers if they are different from nonbiofortified crops in yield or organoleptic characteristics. Allergies or intolerance, particularly to crops that are bioengineered or genetically modified, have also been raised as a concern. From an environmental perspective, cross-contamination and reduced biodiversity of crops have been cited by some authors as obstacles to the acceptance of biofortification strategies.

The WHO has commissioned a systematic review of evidence to determine the effects of staple crops biofortified with increased micronutrient content on vitamin and mineral status, as well as on health, development, and cognitive function in the general population. While the review is in progress, the WHO, in collaboration with the Food and Agriculture Organization of the United Nations and the Sackler Institute for Nutrition Science at the New York Academy of Sciences, convened a technical consultation entitled "Staple Crops Biofortified with Vitamins and Minerals: Considerations for a Public Health Strategy" in New York City on April 6–8, 2016. This consultation brought together over 50 technical experts, researchers, producers, policy makers, program implementers, and other experts within the private sector and civil society to collate opinions on the agronomic technologies, feasibility, farmers' adoption and consumer acceptability, economic impact, and existing legal framework for biofortified crops and foods prepared with them. The participants also explored the applicability of country experiences where biofortification technology has been deployed. The objectives of this technical consultation were to review (1) the role of biofortified crops in improving micronutrient status as constituents of regular diets and patterns of production and consumption worldwide; (2) technical considerations with regard to variety of biofortified crops, the number and amount of nutrients that can be included in a biofortified crop, and their stability and bioavailability, as well as the acceptability of the foods prepared with these crops; (3) economic, acceptability, environmental, and safety aspects of biofortified crops and equitable marketing to ensure access by vulnerable populations; (4) legal and regulatory issues related to biofortification in agriculture and health; (5) ethics of biofortification in public health; (6) country-level experiences and lessons learned with biofortified crops; and (7) research priorities to better support evidence of improved nutrition and unintended adverse effects.

At the 3-day consultation, technical presentations followed by plenary sessions of questions and answers provided information on the critical areas related to biofortification, as summarized in the following section. Different multistakeholder working groups met to consolidate the technical considerations required for the use and impact of biofortification as a public health strategy. The participants were included in one of four domains, including (1) planning, implementing, monitoring, and evaluation of biofortification programs; (2) production, consumption, cost-effectiveness, socioeconomic, communicational, and ethical aspects of biofortification; (3) food safety, quality-control and -assurance considerations, allergies, and toxicity issues, and (4) legal framework and policy coherence.

Data on the number of crops released in different countries, processing details, and issues related to acceptance and willingness to pay were updated or presented at the consultation. Most of the information presented in this special issue, including the considerations for implementation, had not been previously published.

Summary of technical presentations

Review of biofortification crop technologies

Three agronomic technologies are available and have been used independently or in combination in selected crops to add nutritional value by increasing the content of a micronutrient or improving its bioavailability: (1) soil fertilization or foliar application, (2) conventional or traditional plant breeding, and (3) genetic engineering. It is recognized that these agronomic technologies alone or in combination can be applied to improve agricultural productivity and minimize the effects of pests and adverse environmental soil or climate conditions, but potentially produce crops with higher content of selected provitamin A carotenoid or other vitamins or minerals, such as iron or zinc, when all other conditions are optimal for crop growth. Conventional or traditional plant breeding, as well as genetic engineering, could be used alone or in conjunction with soil fertilization or foliar application.[3–5]

There is a need for a clearer definition of biofortification and related technologies, which will be addressed by the 38th Session of the Codex Committee on Nutrition and Foods for Special Dietary Uses, to be held in Germany on December 5–9, 2016. It is important to clarify that biofortification technology aims to improve the genetic potential of the seed in order to produce a crop with the desired characteristics, provided that all other factors are not limiting. While much of the focus of biofortification has been on vitamin A, iron, and zinc, some biofortification concepts apply to modifications to produce crops with altered contents of amino acids, fatty acids, or types of carbohydrates, and not only vitamins and minerals. They also apply to modifications in the plant to produce crops with changes in the contents of elements that affect the bioavailability of a nutrient, such as phytic acid, which inhibits the absorption of iron from foods by humans. Phytic acid is the principal storage form of phosphorus in plant seeds and is also an antinutrient (i.e., natural or synthetic compound that interferes with the absorption of nutrients). One of the draft definitions of biofortification proposed in preparation for the 38th Session of the Codex Committee is "the process by which the essential nutrient quality of food including essential amino acids and fatty acids, is improved through the use of agricultural methodologies, as well as reducing anti-nutritional factors with the aim of making the nutrients bio-available to the body after ingestion, in order to provide a health benefit."[6]

At the WHO consultation, the participants discussed some of the limitations of each technology. For example, for traditional plant breeding, the main limitations identified were the biological boundaries imposed by the seeds or the crop characteristics; the time-consuming nature of this manual technology; the reduced expression of desirable traits due to uncontrolled gene interactions, producing the loss of hybrid vigor that results in poor yields; and the fact that farmers had to buy new seeds every season (for hybrid seed).[7,8] Some of the proposed limitations of soil or foliar fertilization related to the need for continuous application of fertilizers, which may be detrimental to soil health; the physiological differences between plants that could affect effectiveness of absorption into grains; the geographical variations of soil micronutrient deficiencies; and the uncontrollable factors that could affect the application of fertilizers (e.g., weather conditions).[9] With regard to genetic engineering, the main limitations included the need to advance understanding of the regulation of the endogenous metabolic pathways involved, to address the food and health safety issues and ethical concerns related to the environment and conservation of genetic resources, to have labeling of products with genetically modified crops as ingredients, and to address issues related to intellectual property rights.[5]

Biofortified crop production, consumption, and bioavailability

The characteristics and trends of the worldwide market for biofortified crops and consumption patterns of the different types of biofortified crops were discussed. In 2015, crops biofortified by plant breeding—including provitamin A–rich orange-flesh sweet potato, yellow cassava, and orange maize; iron-rich beans and pearl millet; and zinc-rich rice and wheat—were officially released for production in more than 30 countries and are being tested and grown in more than 50 countries.[10] In some cases, biofortification produces a crop with increased contents of a nutrient that is ready for direct preparation and consumption (e.g., orange-flesh sweet potato, iron-rich beans), while other crops require some processing, for example, wheat requires milling to become flour and eventually to be consumed as bread or porridge.

It is important to consider the factors that affect bioavailability of key micronutrients—iron, vitamin A, and zinc—in biofortified crops, particularly the chemical and physical properties of the biofortified crops, complete meals, or dietary practices. Bioavailability from biofortified foods is related to the food matrix structure and composition, especially when related to the bioavailability of provitamin A carotenoids, iron, and zinc. Processing can improve the bioavailability of carotenoids by disrupting the food matrix but could also result in carotenoid losses.[11] By degrading antinutrients, such as phytate, processing can also enhance mineral bioavailability.[12,13] In *in vivo* interventions, it has been shown that biofortified crops were efficacious overall in reducing micronutrient deficiency, with bioconversion factors varying between 2.3:1 and 10.4:1 for trans-β-carotene and with amounts of iron and zinc absorbed between 0.7 and 1.1 mg/day and 1.1 and 2.1 mg/day, respectively.[14–16]

Micronutrient bioavailability also depends on the crop type and on the presence of fat for provitamin A carotenoids and of antinutrients for minerals. There are also human factors related to micronutrient status that can be affected by inflammation and diseases and affect absorption and bioavailability. Furthermore, understanding the interactions between micronutrients is essential, for example, the synergic effect of iron and provitamin A carotenoids or the competitive effect of iron and zinc.[17]

Efficacy trials for vitamin A–rich orange-flesh sweet potato,[18] orange maize,[19] and yellow cassava[20] and for iron-rich pearl millet[21] and beans[20] all provide evidence that biofortification by plant breeding could improve micronutrient deficiency status among target populations. An effectiveness study in Uganda showed that delivery of vitamin A–rich orange-flesh sweet potato resulted in significantly increased vitamin A intakes among children and women and measurably improved vitamin A status among some children in Uganda.[22]

Economic feasibility and impact of biofortified crops: from consumers to added productivity and economic development

A review of literature on the feasibility of and financial issues related to the introduction of biofortified crops in different settings showed facilitating and hindering factors in production and consumption. Although the number of studies examining the impacts for poor farmers in rural areas was limited, these studies generally found that biofortification has a positive impact in reducing the prevalence of inadequate intakes among children and women in rural areas and that the benefits can be directed toward lower-income groups.[8,23]

Biofortification is considered to be highly cost effective (according to World Bank criteria), except in scenarios where the total substitution of biofortified crops is assumed to be less than 25% and where the average consumption of the staple crop is relatively low.[24,25]

Consumer willingness to pay is considered to be a factor in determining the adoption of biofortified crops. A meta-analysis of willingness-to-pay studies on crops biofortified either by conventional plant breeding or genetic engineering determined that consumers are generally willing to pay between 21.6% and 23.7% more for biofortified crops.[26]

Also presented were aspects related to the acceptability of biofortified crops and foods and the need for changes in cultural or dietary habits. In a summary of the evidence for farmers' and consumers' acceptance and farmers' adoption, it was shown that orange-flesh sweet potato and maize were the crops most studied, whereas rice and pearl millet were the least investigated or reported. Most studies used hedonic scales, structured interviews, discrimination testing, or preference testing. The results showed that, even for yellow or orange crops, sensory acceptance for biofortified crops or innovative food preparations was generally positive, and availability and information on health benefits were the most important determinants of acceptance and adoption.[27–30]

Legal, regulatory, and intellectual property aspects of biofortification: seed markets

Regulatory considerations are rare or nonexistent for biofortification by conventional plant breeding, genetic engineering, or nutrient-enhanced soil or foliar fertilization. To date, biofortified products introduced in Latin American, African, and Asian food supply chains have been produced only by conventional breeding. Other cultivars, using different techniques, are under development. The production and marketing of these products have been conducted under a nonexistent regulatory framework and limited government control or regulatory guidance. Some countries have integrated biofortified crops in their nutrition and agriculture agendas. Although some crop modifications by conventional breeding have not been subject to regulations, an appropriate regulatory framework will be necessary when biofortification expands to include other techniques.[31]

Private companies that develop biofortified seeds rely on enforcement of intellectual property rights to ensure the recovery of invested funds and to make profits. However, there is uncertainty surrounding the implications of intellectual property rights for genetically modified and nongenetically modified biofortified varieties in the seeds business and how these rights will affect sharing of biofortified varieties with communities. In the case of access to varieties, seed markets, and intellectual property rights of small farmers growing biofortified sweet potatoes, the use of material transfer agreements has allowed the private sector to share varieties with public entities that support farmers' access to biofortified varieties of seeds. In cases of crops with low commercialization, farmer-to-farmer seed exchanges could promote access to seeds. Adoption of open-source approaches could help to increase the involvement of farmers in technology generation and acceptance of biofortified varieties.[32]

Some of the reluctance in accepting genetically modified, biofortified crops has been related to intellectual property aspects, including a concern that seeds will be owned by companies, making them unaffordable for farmers, even though the main goal and added value of biofortification are in its capacity to reach the most vulnerable populations. For example, in the case of provitamin A–enriched Golden Rice™, patent issues have delayed the approval process.[33]

Safety issues, ethical considerations, and determinants of equity in the access to biofortified seeds and foods

Biofortification research and development currently focuses on a food-based approach that increases nutrient availability in crops, simplifies production systems, and enhances crop yield. However, adverse effects on the soil or plants may critically compromise the sustainability of biofortified crop strategies, including enduring consequences on agricultural capacity. Therefore, bearing in mind that biodiversity is a key element of good agronomic practices, the interaction between biofortified crops and the environment should be an essential part of program planning and evaluation.

With respect to safety considerations, available evidence suggests that there is no high risk of direct negative impact to health. However, two important concerns have been raised related to allergies, especially to genetically modified foods, and the risk of toxicity, mainly related to soil or foliar fertilization. Concerning transgenic technologies, the processes themselves will not increase allergies, unless the genetic modification involves allergens, and the risks of increased allergen expression are minimal regardless of the crop variety.[34,35] This is important information to convey to consumers when using a biofortified crop or a product made with it. For intake of selenium and zinc, the concerns about toxicity or excess micronutrient intake have been addressed—when monitoring and control of the amounts and periodicity of applications are in place, there is no evidence of toxicity for the plant or the consumers.[4,36]

Another concern is the high variability in the desired nutrient levels between biofortified crops,[17] as factors other than biofortification can also play a role in how much of the micronutrient is contained in the edible crop. Similarly, the nutrient content can range within the same harvest, depending on factors outside of the control of the biofortification program.

The implementation of biofortification strategies needs to be considered as part of other agriculture and nutrition interventions, such as (1) concurrent fortification of staple foods with a mix of nutrients or other foods and beverages voluntarily fortified by the food industry and targeted for universal supplementation programs to avoid risks of excess micronutrient intake and (2) diet diversity and nutrition education to avoid monotonous diets that could affect field productivity, crop quality, and human health.

Biofortification has clear nutritional goals but cannot be, in any way, considered as a stand-alone solution; rather, it should be considered as part of a comprehensive approach that addresses food insecurity, extreme poverty, and social injustice.[37] More research is necessary on ethical aspects of biofortification in order to understand the impacts of biofortification on issues of self-determination, liberties, and food justice with regard to production and dietary choices. Early involvement of farmers and the community, including women, in understanding the biofortification process and its importance and in finding local solutions could facilitate acceptance, adoption, and implementation.[38] In addition, fair access of farmers and consumers to seeds and foods should be considered.

Biofortification of staple crops may face implementation bottlenecks that hinder its effectiveness in improving the nutritional status of populations and their economic potential. Implementing strategies that carefully address socially determined factors (e.g., access to information and training by producers and consumers, empowerment of women in rural settings, skills development in frontline health workers, addressing opposing groups and stances, promoting inclusive approaches for less powerful stakeholders, and developing partnerships for sustainability and scale-up) could improve acceptability, adoption, and sustainability of the intervention. There is a need for more practical guidance on intersectoral approaches to deal with equity in health.

Country experiences and case studies

Nigeria. Biofortified crops were formally released in Nigeria as national pilot initiatives involving yellow-flesh cassava, yellow maize, and orange-flesh sweet potato, all bred to have increased contents of provitamin A, as well as quality protein maize fortified with protein and amino acids (lysine and tryptophan).

Although no biofortification effectiveness studies have been conducted in Nigeria, one randomized controlled efficacy trial showed high consumption of biofortified cassava by women and children in Akwa Iborn.[39] Currently, 672 communities and 450,000 Nigerian households have received vitamin A–rich cassava stem cuttings. Furthermore, 1,300,000 cassava stems have been disseminated and 245 processing centers have been established. To date, over 20,000 farming households have received bundles of orange-flesh sweet potato vines to plant, which may possibly be replanted after harvest. However, since the potatoes are usually harvested at the beginning of the dry season, the vines usually dry up before or after harvest due to the dry season, making replanting difficult for some farmers. Since 2012, awareness of orange-flesh sweet potato has been growing to the point that cooperative farming groups have been formed.[40]

Uganda and Zambia. Results from the experiences related to orange-fleshed sweet potato in Uganda and to orange maize in Zambia were presented at the WHO consultation, including the challenges, essential elements for success in introducing these biofortified crops, achievements, initial impacts, and plans for sustainability of the programs. Behavioral change was a major obstacle to overcome in the adoption of the biofortified orange crops by farmers and in increasing acceptability by consumers. To overcome obstacles in the adoption of the crops, the release of the biofortified crops was supported in Uganda and Zambia by many activities, such as radio shows, distribution of samples of meals prepared with biofortified crops, and market development. The involvement of ministries of health, stakeholders, and local researchers and the dissemination of research findings have also been effective in facilitating adoption.[19,22,41]

Breakout sessions

Participants were assigned to one of four working groups, with key aspects and critical questions to address for discussion. Table 1 summarizes the topics covered by each group. All groups were advised to (1) address unresolved issues that emerged during the discussions and build on the conclusions from the discussions to propose group recommendations; (2) focus on technical needs related to biofortification interventions that have a significant public health impact; (3) produce feasible, executable considerations for implementation; and (4) focus on implementation, recognizing the need for research only when critical. The considerations and conclusions are summarized below by topic.

Planning, implementing, monitoring, and evaluating programs involving biofortification of crops with micronutrients

Planning a program that involves biofortification of crops with one or more micronutrients requires a robust rationale to be developed on the basis of market analysis, government endorsement, evaluation of food consumption patterns, analysis of food production systems, and nutritional assessment of micronutrient status for important groups of the target population. Once the rationale has been established and accepted, the planning activities can begin with the identification of existing coordinating bodies (public, private, and voluntary sectors), a feasibility assessment of capacity for implementing and monitoring and evaluation, and the development of a roadmap and timeline.

For implementation, securing adequate financial resources from governments is important in establishing and strengthening program monitoring and to add the new components needed for modification of the crop supply chain. A multistakeholder–coordinating secretariat or body with the mandate to ensure that elements addressed during the planning phases are actually in place (e.g., stakeholder dialogue/advocacy/quality control/assurance) is of high value. In addition, the education and advocacy efforts of different members of civil society can prove essential by encouraging countries to integrate nutrition education activities in primary school

Table 1. Topics covered by each working group at breakout sessions

Topic	Key considerations
1. Planning, implementing, monitoring, and evaluating biofortification programs	• Available biofortification technologies and assessment of needs • Rationale for a biofortification program • Stakeholder engagement, program funding • What to monitor? (the process, the final outcome) • Identify appropriate indicators of biofortification, especially to identify the technology used to produce the biofortified product (e.g., genetic engineering, traditional plant breeding) • Who will monitor? • How to monitor? (Production at the local level; sales of biofortified products or seeds; consumption at national level and disaggregated in subgroups (through indicators or purchase or intake); reduction in deficiencies at population level) • Internal and external quality control implemented by industry and regulatory programs. What is realistic and appropriate to guide programing? Who uses and analyzes the data? • Setting indicators and key performance indicators • Evaluation
2. Production, consumption, cost-effectiveness, socioeconomic communication, and ethical aspects of biofortification	• Production and consumption of biofortified staples • Communication and social marketing strategies • Ethical considerations • Strategies to be used by countries to consolidate a strategy and overcome implementation barriers, particularly among low-income groups • Acceptability • Willingness to pay
3. Food safety, quality-control and -assurance considerations, allergies, and toxicity issues	• How to evaluate the risk for excessive intake? • What are the greatest concerns in terms of quality controls? • Existing surveillance systems for food safety • Allergies and toxicity issues • Environmental considerations
4. Legal framework and policy coherence	• International standards and national laws on content information, health claims, trade, and seeds markets • Is there a need for a guided process to help countries select their fortification strategy? • What needs to be in place for biofortification to be successful from a regulatory standpoint? • Policy coherence: biofortification in the context of other public health strategies and other micronutrient interventions • Key elements that are needed to ensure a balanced approach to biofortification • Harmonization with other public health strategies. What is the best way to pilot such a strategy?

curricula in order to generate acceptance and create demand for agronomic technologies in farming and in consumer preferences.

Process monitoring to improve acceptance of biofortification programming, both from health and agronomic perspectives, is required. This monitoring includes a wide range of process and outcome indicators, both pre– and post–farm gate, including nutrient content of germplasm over time, activities from national agricultural research and extension systems, volume of seeds being distributed, compliance by farmers, postharvest uptake and processing activities, acceptance by consumers, actual micronutrient intake, and nutrition status outcomes. The agency responsible for monitoring will depend on where along the value chain the monitoring is taking place.

The establishment of baseline conditions during the planning and initial implementation stages and the use of simple indicators that are integrated into preexisting national surveys, with focus on reach, coverage, and the target micronutrient(s) intake, are important for decision making, as is information on negative health outcomes/side effects and economic impact. Consultation participants recognized the need to establish baselines and the challenge of data availability, and noted the potential for household consumption and expenditure surveys (e.g., living standards measurement surveys) to include biofortified crops.

Socioeconomic communications and ethical considerations for biofortification of staple crops with micronutrients

From a communications perspective, ministries of health and agriculture need to collaborate with other governmental organizations and stakeholders to communicate the initiatives, using the available nutrition-related fora and including communities at all levels. This should be accomplished with cost-effective and efficient ways of educating, informing, and creating awareness about biofortified crops. It will also be important to communicate not only with allies or those who are undecided, but also with opponents of biofortification to ensure that they are well informed before influencing their constituents. There is also a need to fill in some research gaps, especially on the effectiveness of biofortified crops.

With respect to adoption, acceptability, and willingness to pay, evidence from farmers and consumers to date suggests that acceptance may not be an issue, although access to the technology may be a limiting factor. Behavioral changes are not expected to be drastic—the premise of biofortified crops, as currently proposed, is that farmers will grow the crops and consumers will eat the crops similarly to nonbiofortified crops, with the main difference being the genetic potential of the crops to have a higher content of a selected micronutrient considered to be deficient in the diets of the population, in addition to other crop yield–related modifications.

From the perspective of a framework for public health ethics, there is a need to evaluate how the individual principles will be contextualized by country, crop, and micronutrient. It is likely that some ethical dilemmas will need further discussion.

Food safety, quality control and assurance, and allergy and toxicity issues

The risk of excessive micronutrient intake through biofortified crops or the combination of biofortified crops and other fortified foods or supplements was discussed by the consultation participants. There is limited evidence on the safety of existing biofortified crops used for human and animal consumption. There appear to be some concerns of skin coloration following excessive intake of carotenoids but no risk of toxicity or allergies.

In countries where industrial fortification and/or supplementation are taking place, it is thought that the addition of biofortified crops poses a small or no risk of excessive intake of a particular micronutrient. Nonetheless, caution should be taken to ensure that consumers are aware of the different sources of micronutrients and of what constitutes appropriate intake. The concentrations of biomarkers of micronutrient status among target groups may be periodically monitored as part of the surveillance systems in the country or area covered by the micronutrient-biofortified crops.

The need for consumer education is increasing, owing to the rapid expansion of industrial fortification of staple foods, such as wheat and maize flours, rice, salt, vegetable oil, and some condiments, and the importance of increasing awareness of the general public and policy makers regarding the potential contribution of biofortified crops relative to other approaches. It was noted by the consultation participants that much more communication is needed with the general public about biofortified crops, specifically about their benefits to increase the intake of a particular micronutrient or provitamin, fears concerning biodiversity, diet diversification, and issues related to genetic modification of food.

Criteria for minimum micronutrient levels should be set during the varietal release stage, taking into account losses expected during cooking and monitoring of the quality of the seed or stem being distributed as part of the normal inspection services of seed or stem regulators. After such standards are set, it should be ensured that the levels of the micronutrient being modified in food products using biofortified crops meet the established food standards. It was noted that technical inspection or monitoring at the consumer stage would not be cost effective. The implementation of these quality-control points may require product labeling (indicating biofortified, processed products) in formal marketing systems, research on the stability of biofortified traits in processed products over time (i.e., products for formal markets where claims are being made), and detection kits for easily determining the levels of the micronutrients in food products at reasonable costs.

There appear to be no new environmental concerns beyond the preexisting concerns about pollution, water use, sustainability of monoculture, and decreasing biodiversity currently under debate. However, biofortified crops, as proposed, are part of the agricultural system and part of the food systems. Breeding micronutrient density to obtain an adapted, acceptable variety requires crossing micronutrient-dense parents with locally adapted varieties, hence preserving the locally adapted genes in the existing system and increasing the number of varieties available. From this point of view, micronutrient biofortification of selected crops would not undermine biodiversity.

The possible negative consequences of zinc foliar sprays, if overused, were discussed as a potential research topic. It was also noted that actions concerning biofortified crops should be more systematically integrated into diet diversity–promotion efforts.

Legal framework and policy coherence

An explicit definition of biofortification by the Codex Alimentarius is a key starting point, leaving the definition of agricultural methods open to cover future innovations and identifying member states that will provide comments and help to shape and reach agreement on a definition.

Beyond a concrete definition, more measurable standards on crops and food products are needed, including quality standards for different stakeholders and standards on nutrient levels in products (industrial or other) to provide criteria on what constitutes a food containing biofortified ingredients. Also necessary is harmonization with existing regulation on labeling and with nutrition and health claims. Furthermore, there is a need to build on existing regulations on agriculture, genetically modified organisms, and industrial food fortification and to consider existing Codex Alimentarius principles for the addition of essential nutrients to foods. Most of these standards are thought to be applicable to foods prepared with micronutrient-biofortified crops.

Relevant gaps in existing agricultural and food regulations need to be identified and addressed. With respect to this challenge, it was proposed that the WHO, FAO, and other international organizations expand existing policy recommendations and tools to include biofortified crops. It was also proposed that the FAO establish a portal on micronutrient biofortification similar to the platform for genetically modified organisms.

Final considerations

The topics discussed at the technical consultation and covered in this paper highlight the importance of biofortification technologies in increasing micronutrient contents in selected crops and in helping to address a micronutrient intake gap in populations with the modification of one or more staple crops. Participants of the consultation considered it necessary to clearly define the terms “biofortification” and “micronutrient biofortification.” Although the Codex Alimentarius is reviewing this particular issue related to definitions, the consultation participants raised the importance of clarifying the procedure for biofortification with micronutrients, using the different agronomic methods, and also including the term “micronutrient” to clearly identify the nature of the nutritional modification being made. Furthermore, it is important to clarify that the technology allows modifying the potential for increased content of a provitamin or micronutrient, usually in addition to other agronomic modifications related to crop yield, growth, resistance to pests, or other adverse environmental conditions. This potential will become reality if other conditions for optimal agriculture are not limiting. It should be noted that the increased content of the selected provitamin or micronutrient can vary within an expected range, with variations that could affect the expected impact of the crop in its contribution to the dietary intake of populations.

Other critical points raised include the need to build capacity for local seed systems and management of biofortification programs, as well as the importance of having more robust communication and advocacy strategies for increased uptake and application of biofortification technologies, if the approach is to be considered at scale as a public health strategy for vitamin and mineral deficiencies.

It is clear that there are a number of unanswered questions to be further explored from a scientific research perspective and in the context of ethical, policy, and legal considerations, as well as from the perspective of program implementation. The above discussions from the working groups identified many of these unanswered questions, which may require in-depth consideration before scaling up this technology for expected impact on micronutrient malnutrition of vulnerable populations.

Acknowledgments

This paper summarizes presentations and working group conclusions at the WHO/FAO technical consultation "Staple Crops Biofortified with Vitamins and Minerals: Considerations for a Public Health Strategy," held in collaboration with the Sackler Institute for Nutrition Science at the New York Academy of Sciences, on April 6–8, 2016 in New York City. This paper is being published individually but will be consolidated with other manuscripts as a special issue of *Annals of the New York Academy of Sciences*, the coordinators of which were Drs. Maria Nieves Garcia-Casal and Juan Pablo Peña-Rosas. This special issue is the responsibility of the editorial staff of *Annals of the New York Academy of Sciences*, who delegated to the coordinators 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 the WHO, the FAO, and the Sackler Institute for Nutrition Science at the New York Academy of Sciences. 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.*

Conflicts of interest

Maria Nieves Garcia-Casal and Juan Pablo Peña-Rosas are authors of a Cochrane Review on the effects of biofortification of staple crops with increased micronutrient contents. Juan Pablo Peña-Rosas is a staff member of the WHO. The authors alone are responsible for the views expressed in this article and they do not necessarily represent the views, decisions, or policies of the institutions with which they are affiliated or the decisions, policy, or views of the WHO. The WHO gratefully acknowledges financial support from the Bill & Melinda Gates Foundation, the U.S. Centers for Disease Control and Prevention, the Micronutrient Initiative, the U.S. Agency for International Development, the United Nations Children's Fund, the Global Alliance for Improved Nutrition, and HarvestPlus for its work in nutrition.

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