



Reducing Mineral and Vitamin Deficiencies Through Biofortification: Progress Under HarvestPlus

Howarth Bouis

Founding Director, HarvestPlus

1. The Problem and Mineral and Vitamin Deficiencies

Mineral and vitamin deficiencies are a serious public health problem in developing countries. Vitamin A, iron, and zinc deficiencies affect the largest number of people throughout Africa, Asia, and Latin America. For example, in Sub-Saharan Africa the prevalence of vitamin A deficiency among preschool children ranges from 40% in west and central Africa to about 25% in southern Africa (WHO, 2009). Anemia affects about 40% of pregnant women and 62% of children in Africa, about half of which is estimated to be attributed to iron deficiency (WHO, 2015). Anemia levels have not improved over the last 20 years. Data on zinc deficiency is limited, but recent estimates suggest that 24% of Africans have inadequate zinc intakes, with pregnant women and young children at the highest risk of deficiency (Bailey *et al.*, 2015). Furthermore, half of children with vitamin and mineral deficiencies are suffering from multiple deficiencies (Micronutrient Initiative, 2009). Micronutrient deficiencies result in higher morbidity and mortality, reduced cognitive abilities and so lower educational attainment, and decreased work capacity and earning potential, with far-reaching consequences for future generations.

2. Interventions Implemented By the Nutrition Community To Combat Mineral and Vitamin Deficiencies

Several options exist to combat micronutrient deficiencies, including supplementation, fortification, and food-based approaches like dietary diversification. For children under two, breastfeeding, micronutrient powders, and nutrient-dense complementary foods can reduce the prevalence of micronutrient deficiencies.

Vitamin A supplementation is a targeted intervention that is considered as one of the most cost-effective interventions for improving child survival (Tan-Torres Edejer *et al.* 2005). Because it is associated with a reduced risk of all-cause mortality and a reduced incidence of diarrhea (Imdad *et al.* 2010), programs to supplement vitamin A are often integrated into national health policies.

Commercial food fortification, where trace amounts of micronutrients are added to staple foods or condiments during processing, allows consumers to consume recommended levels of micronutrients. Fortification has been particularly successful for iodized salt: 71% of the world's population has access to iodized salt and the number of iodine-deficient countries has decreased from 54 to 32 since 2003 (Andersson, Karumbunathan, and Zimmermann 2012). Common examples of fortification include adding B vitamins, iron, folic acid and/or zinc to wheat flour and adding vitamin A to cooking oil and sugar. Fortification is particularly effective for urban consumers, who purchase foods that have been commercially processed and fortified. Fortification is less suitable for reaching rural consumers who often do not have access to commercially produced foods. To reach those most in need, fortification must also be subsidized or mandatory, so the poor do not buy cheaper non-fortified alternatives.

An alternative to commercial fortification is home-based fortification systems, in which micronutrient powders or lipid-based nutrient supplements are added to food prepared in the home. Evidence of the acceptability and efficacy of home fortification is growing (Adu-Afarwah *et al.* 2008; Dewey, Yang, and Boy 2009; De-Regil *et al.* 2013), but concerns remain that it is difficult to implement on a large scale and costly to monitor.

Special considerations are needed for young children. The transition period from breast milk or formula to solid foods is often accompanied by micronutrient deficiency in developing countries. Food-based approaches can include additions or changes to complementary feeding practices during this period, including a focus on nutrient-dense foods and the use of specially formulated micronutrient powders.

The drawbacks are that supplementation and fortification may not reach all intended beneficiaries (particularly in rural areas) due to required behaviour change and implementation constraints and costs. Both interventions

involve yearly recurrent costs in every country; the cumulative annual costs of supplements and fortification can reach billions of dollars globally, especially if coverage rates improve over time (Bouis 2017). The need for supplements and fortification will decline as food systems provide the necessary intakes of vitamins and minerals through diverse diets at more affordable prices.

3. The Role of Agriculture To Reduce Mineral and Vitamin Deficiencies

Dietary diversity is strongly and positively associated with child nutrition status and growth, even when controlling for socioeconomic factors (Arimond and Ruel 2004). In the long term, dietary diversification is likely to ensure a balanced diet that includes the necessary micronutrients.

In general, however, dietary quality in developing countries is poor. Low incomes and high prices for non-staple foods such as vegetables, fruits, pulses, and animal products are the major constraints to improved dietary quality. While there is great national and regional variation in diets in developing countries, most are characterized by high staple food consumption, mainly cereal or root staple crops. Access to dietary sources of micronutrients, including animal-source protein, fruits, and vegetables, is a major challenge for many. These foods are often inaccessible because of high cost, limited local availability, and distribution challenges (Fanzo, 2012).

Non-staple foods are dense in vitamin and minerals, and bioavailability is particularly high for animal products; animal products are the most expensive source of dietary energy. The poor eat large amounts of food staples to acquire dietary energy – to keep from going hungry. They spend what little money is left for some, but far too little, dietary quality.

Traditionally, public research and development strategies have focused on increasing agricultural productivity in staple crops to reduce malnutrition. The Green Revolution prioritized the development of high-yielding varieties of major staple crops and intensifying production, increasing the total output of food staples and reducing staple food prices. From the 1970s to the mid-1990s, the price of staple foods (like rice and wheat) decreased relative to the price of micronutrient-rich non-staple foods (like vegetables and pulses). As a result, micronutrient rich foods became less affordable, particularly to the poor (Bouis 2000, Kennedy and Bouis 2003).

4. The Justification for Biofortification

Biofortification, the process of breeding nutrients into food crops, provides a comparatively cost-effective, sustainable, and long-term means of delivering more micronutrients. Biofortified staple foods cannot deliver as high a level of minerals and vitamins per day as supplements or industrially fortified foods, but they can help by increasing the daily adequacy of micronutrient intakes among individuals throughout the lifecycle (Bouis *et al.* 2011). Note that biofortification is not expected to treat micronutrient deficiencies or eliminate them in all population groups. No single intervention will solve the problem of micronutrient malnutrition, but biofortification complements existing interventions to sustainably provide micronutrients to the most vulnerable people in a comparatively inexpensive and cost-effective way (Bouis 1999; Nestel *et al.* 2006; Pfeiffer and McClafferty 2007; Qaim *et al.* 2007; Meenakshi *et al.* 2010).

Biofortification provides a feasible means of reaching malnourished populations who may have limited access to diverse diets, supplements, and commercially fortified foods. The biofortification strategy seeks to put the micronutrient-dense trait in those varieties that already have preferred agronomic and consumption traits, such as high yield. Marketed surpluses of these crops may make their way into retail outlets, reaching consumers in first rural and then urban areas, in contrast to complementary interventions, such as fortification and supplementation, that begin in urban centers.

Unlike the continual financial outlays required for supplementation and commercial fortification programs, a one-time investment in plant breeding can yield micronutrient-rich planting materials for farmers to grow for years to come. Varieties bred for one country can be evaluated for performance in, and adapted to, other geographies, multiplying the benefits of the initial investment. While recurrent expenditures are required for monitoring and maintaining these traits in crops, these are low compared to the cost of the initial development of the nutritionally improved crops and the establishment, institutionally speaking, of nutrient content as a legitimate breeding objective for the crop development pipelines of national and international research centers.

There are three common approaches to biofortification: agronomic, conventional, and transgenic. Agronomic biofortification provides temporary micronutrient increases through fertilizers. This approach is useful to increase micronutrients that can be directly absorbed by the plant, such as zinc, but less so for micronutrients that are synthesized in the plant and cannot be absorbed directly (Lyons and Cakmak 2012). Conventional plant breeding involves identifying and developing parent lines with high vitamin or mineral levels and crossing them over several generations to produce plants with the desired nutrient and agronomic traits. Transgenic plant breeding seeks to do the same in crops where the target nutrient does not naturally exist at the required levels.

With the above as background, for biofortification to be successful, three broad questions must be addressed:

- Can breeding increase the micronutrient density in food staples to target levels that will make a measurable and significant impact on nutritional status?
- When consumed under controlled conditions, will the extra nutrients bred into the food staples be absorbed and utilized at sufficient levels to improve micronutrient status?
- Will farmers grow the biofortified varieties and will consumers buy/eat them in sufficient quantities?

The following three sections summarize the evidence that all three of these broad issues can be addressed in the affirmative.

5. Crop Development

Plant breeding can increase nutrient levels in staple crops to target levels required for improving human nutrition, without compromising yield or farmer-preferred agronomic traits. The crop development process entails screening germplasm for available genetic diversity, prebreeding parental genotypes, developing and testing micronutrient-dense germplasm, conducting genetic studies, and developing molecular markers to lower the costs and quicken the pace of breeding. After promising lines have been developed, they are tested in several locations across target environments to determine the genotype x environment interaction (GxE) – the influence of the growing environment on micronutrient expression. Robust regional testing enables reduced time-to-market for biofortified varieties.

Early in the conceptual development of biofortification, a working group of nutritionists, food technologists, and plant breeders established nutritional breeding targets by crop, based on food consumption patterns of target populations, estimated nutrient losses during storage and processing, and nutrient bioavailability (Hotz and McClafferty 2007). Breeding targets (Table 1) for biofortified crops were designed to meet the specific dietary needs and consumption patterns of women and children. Taking into account baseline micronutrient content in each crop, targets were set such that, for preschool children 4-6 years old and for non-pregnant, non-lactating women of reproductive age: the total amount of iron in iron beans and iron pearl millet will provide approximately 60% of the Estimated Average Requirement (EAR) (30% of the EAR for iron at baseline before breeding for high iron); zinc in zinc wheat and zinc rice will provide 60 to 80% of the EAR (40% of the EAR for zinc at baseline); and, provitamin A, the precursor of vitamin A, will provide 50% of the vitamin A EAR in the case of yellow cassava and orange maize, and up to 100% in the case of orange sweet potato (zero provitamin A at baseline). The breeding target is the sum of the baseline micronutrient content and additional micronutrient content required for each crop and micronutrient combination.[1]

Crop improvement activities for biofortification focus, first, on exploring the available genetic diversity for iron, zinc, and provitamin A carotenoids (yellow boxes in Figure 1). At the same time or during subsequent screening, agronomic and end-use features are characterized. The objectives when exploring the available genetic diversity are to identify: (1) parental genotypes that can be used in crosses, genetic studies, molecular-marker development, and parent-building, and (2) existing varieties, pre-varieties in the release pipeline, or finished germplasm products for “fast-tracking.” Fast-tracking refers to releasing, commercializing, or introducing genotypes that combine the target micronutrient density with the required agronomic and end-use traits so they can be delivered without delay.

If variation is present in the strategic gene pool (only in unadapted sources), pre-breeding is necessary prior to using the trait in final product development; if variation is present in the adapted gene pool, the materials can be used directly to develop competitive varieties (purple boxes in Figure 1). Most breeding programs simultaneously conduct pre-breeding and product enhancement activities to develop germplasm combining high levels of one or more micronutrients.

The next breeding steps involve developing and testing micronutrient-dense germplasm, conducting genetic studies, and developing molecular markers to facilitate breeding. Genotype x environment interaction (GxE) – the influence of the growing environment on micronutrient expression – is then determined at experiment stations and in farmers’ fields in the target countries (orange boxes). The most promising varieties are selected for multi-locational testing over multiple seasons by national research partners, and then are submitted to national government agencies for testing for agronomic performance and release, a process which typically takes two years, sometimes more.

International Nurseries/Global Testing

Two strategies have been used to shorten time to market for biofortified crops: 1) identifying **adapted** varieties with significant micronutrient content for release and/or dissemination as “fast track” varieties, while varieties with target micronutrient content are still under development, and 2) deploying multi-location Regional Trials

across a wide range of countries and sites to accelerate release processes by increasing available performance data of elite breeding materials. Regional Trials also include already-released biofortified varieties and generate data on their regional performance, in order to take advantage of regional variety release systems such as under SADC (Southern African Development Community). Such regional agreements harmonize seed regulations of member countries and allow any variety that is tested, approved, and released in one member country to be released simultaneously in other member countries with similar agro-ecologies.

Low-Cost, High Throughput Methods

Biofortification breeding required developing or adapting cost-effective and rapid high throughput analytical techniques for micronutrients, as thousands of samples need to be tested for mineral or vitamin content each season. These trait diagnostics include near-infrared spectroscopy (NIRS) and colorimetric methods for carotenoid analysis. For mineral analysis, X-ray fluorescence spectroscopy (XRF) emerged as the method of choice, as it requires minimal pre-analysis preparation and allows for non-destructive analysis (Paltridge *et al.* 2012a; Paltridge *et al.* 2012b).

Releases of Biofortified Crops

Cumulatively, more than 150 biofortified varieties of 10 crops have been released in 30 countries. Candidate biofortified varieties across 12 crops are being evaluated for release in an additional 25 countries. Figure 2 depicts where biofortified varieties have been tested and released to date. Biofortified crops have been released in countries indicated in dark purple, while crops are being tested in countries in light purple. This map includes countries where the International Potato Center (CIP) has worked to release the orange sweet potato. More detailed information about the varieties tested and released in each country is given in Bouis and Saltzman 2017b, Chapter 5.

6. Nutritional Bioavailability and Efficacy

To develop evidence of nutritional efficacy food scientists first measure retention of micronutrients in crops under typical processing, storage, and cooking practices to be sure that sufficient levels of vitamins and minerals will remain in foods that target populations typically eat (for summary results, see De Moura *et al.* 2015). Genotypic differences in retention and concentrations of compounds that inhibit or enhance micronutrient bioavailability are considered. Nutritionists also study the degree to which nutrients bred into crops are absorbed, first by using animal and other models, then by direct study in humans in controlled experiments. Absorption is a prerequisite to demonstrating that biofortified crops can improve micronutrient status, but the change in status with long-term intake of biofortified foods must be measured directly. Therefore, randomized controlled efficacy trials have been undertaken to demonstrate the impact of biofortified crops on micronutrient status and functional indicators of micronutrient status (i.e. visual adaptation to darkness for vitamin A crops, physical activity and cognition tests for iron crops, etc.). Highlights are discussed below. Further detail on retention is summarized in De Moura *et al.* (2014). Annex 1 provides a list of selected references on evidence for efficacy and effectiveness.

Iron Crops

Iron nutrition research has demonstrated the efficacy of biofortified iron bean and iron pearl millet in improving the nutritional status of target populations. In Rwanda, iron-depleted university women showed a significant increase in hemoglobin and total body iron after consuming biofortified beans for 4.5 months (Haas *et al.* 2016). The efficacy of iron pearl millet was evaluated in secondary school children from Maharashtra, India. A significant improvement in serum ferritin and total body iron was observed in iron-deficient adolescent boys and girls after consuming biofortified pearl millet flat bread twice daily for four months. The prevalence of iron deficiency was reduced significantly in the high-iron group. Those children who were iron deficient at baseline were significantly (64%) more likely to resolve their deficiency by six months (Finkelstein *et al.* 2015).

Vitamin A Crops

Vitamin A bioavailability studies found efficient conversions from provitamin A to retinol, the form of vitamin A used by the body. Efficacy studies demonstrated that increasing provitamin A intake through consuming vitamin A-biofortified crops results in increased circulating beta-carotene, and has a moderate effect on vitamin A status, as measured by serum retinol. Consumption of orange sweet potato (OSP) can result in a significant increase in vitamin A body stores across age groups (Haskell *et al.* 2004; Low *et al.* 2007; van Jaarsveld *et al.* 2005).

The primary evidence for the effectiveness of biofortification comes from OSP, assessed through a randomized controlled trial. The OSP intervention reached 24,000 households in Uganda and Mozambique from 2006-2009 with adoption rates of OSP greater than 60% above control communities (Hotz *et al.* 2012a, Hotz *et al.* 2012b). Introduction of OSP in rural Uganda resulted in increased vitamin A intakes among children and women, and

improved vitamin A status among children – a decrease in the prevalence of low serum retinol by 9 percentage points. Women who got more vitamin A from OSP also had a lower likelihood of having marginal vitamin A deficiency (Hotz *et al.* 2012a). Recent research on the health benefits of biofortified OSP in Mozambique showed that biofortification can improve child health; consumption of biofortified orange sweet potato reduced the prevalence and duration of diarrhea in children under five (Jones & De Brauw 2015). For additional information on the development and delivery of OSP, see Low *et al.* (2017).

Biofortified provitamin A maize is an efficacious source of vitamin A when consumed as a staple crop. An efficacy study conducted in Zambia with 5 to 7-year-old children showed that, after three months of consumption, the total body stores of vitamin A in the children who were in the orange maize group increased significantly compared with those in the control group (Gannon *et al.* 2014). Consumption of orange maize has been demonstrated to improve total body vitamin A stores as effectively as supplementation (Gannon *et al.* 2014), and significantly improve visual function in marginally vitamin A deficient children (Palmer *et al.* 2016).

To date, only a small provitamin A cassava efficacy study has been completed in Eastern Kenya with 5 to 13-year-old children. This trial demonstrated small but significant improvements in vitamin A status, measured both by serum retinol and *beta*-carotene, in the yellow cassava versus the control group (Talsma *et al.* 2016). A larger-scale efficacy trial is underway in Nigeria.

Zinc Crops

Zinc studies have demonstrated that zinc in biofortified wheat is bioavailable (Rosado *et al.* 2009). Because plasma zinc concentration, the biomarker widely used to estimate zinc status, has limitations in measuring changes in dietary zinc, foundational research to identify and test more sensitive biomarkers is underway. These biomarkers will be tested in the zinc rice and wheat efficacy trial scheduled for 2017. A recent study showed that DNA strand breaks are a sensitive indicator of modest increases in zinc intake, such as the amount of additional zinc that might be delivered by a biofortified crop (King *et al.* 2016).

Future Areas of Investigation

Areas for further research include robust new trials that test the efficacy of biofortified crops for a wider range of age and gender groups, including infants, and over a longer time period (for example, prior to conception through infancy). Other research will test the efficacy of consuming several different biofortified crops, each providing different vitamins and/or minerals to the food basket. Nutritionists agree that biofortified crops can improve nutritional status in micronutrient-deficient populations, but additional research is needed, using other, more sensitive biochemical indicators, as well as functional indicators, to more fully understand the health impact of consuming biofortified foods.

7. Delivery Experiences in Target Counties

After biofortified varieties have been developed and released, they enter national farming and food systems. Research continues to develop evidence that farmers are willing to grow biofortified crops and that consumers are willing to eat them. An evidence base has been developed in eight target countries (Bangladesh, DR Congo, India, Nigeria, Pakistan, Rwanda, Uganda, and Zambia) by HarvestPlus and national partners. As of the end of 2016, it is estimated that more than 20 million people in developing countries are now growing and consuming biofortified crops (Bouis and Saltzman, 2017a).

Vegetatively Propagated Crops

Vegetatively propagated crops – those for which farmers plant stems, tubers or vines rather than seeds – typically have seed systems characterized by small, informal (rather than commercial) actors. Planting materials are perishable, expensive and bulky to transport over long distances, and must be replanted within several days of harvesting. The lack of commercial private sector participation creates both a challenge and an opportunity for producing planting materials of biofortified crops like orange sweet potato (distributed as vines) and provitamin A yellow cassava (distributed as stem cuttings). See Low *et al.* (2017) for additional evidence from OSP delivery.

Cassava in Nigeria and DR Congo

In parallel with strengthening the seed system through both community-based and commercial stem production, awareness of and demand for biofortified crops must be created simultaneously. In the case of provitamin A yellow cassava, extension to farmers was at the forefront of this effort. Initially, free bundles of stems were distributed to farmers, and accompanied by agronomic training and nutrition information. In the following season, farmers who received free stems were required to distribute an equal amount of free stems to two additional farmers, dramatically lowering delivery costs. This promotional strategy was effective in reaching vulnerable populations who typically do not have market access to improved varieties for planting. It also piqued

interest and allowed farmers in a low-risk way to test a new product. Many of the farmers who received and planted free stems liked the yellow cassava and are now buying additional stems from commercial traders.

In 2015 it was estimated that about 75% of all biofortified harvested roots were consumed on farm, as many households were not yet producing excess from the stem packs they received for trial. Increased commercialization is expected going forward. As farmers began to produce yellow cassava in excess of their household food security needs, several activities were undertaken to increase awareness and demand from the food market for biofortified cassava. These efforts include consumer marketing via print, radio, and television media (even feature-length movies), and market development efforts by linking commercial food processing investors to supplies of yellow cassava roots.

Self-Pollinated Crops

Self-pollinated crops – those which produce seed true to their parent characteristics – can be replanted year after year. While farmers do need to periodically replace their seed to maintain its desirable agronomic traits, the possibility of self-production for seed typically limits private sector investment in producing seed for self-pollinated crops.[1] In many countries, the public sector instead multiplies and distributes self-pollinated seed, and further farmer-to-farmer dissemination is common. Self-pollinated biofortified crops include iron beans, delivered in Rwanda and Democratic Republic of Congo, zinc rice in Bangladesh, and zinc wheat in India and Pakistan.

Delivery has progressed most quickly in Rwanda, where initial public sector investments have now spurred private sector interest in meeting growing demand for iron bean seed. Significant delivery has also taken place in Bangladesh, where demand is driven by the zinc rice varieties that have attractive agronomic traits, including a short duration variety that allows for production of a third crop between the wet and dry season rice crops. Delivery of zinc wheat in India and Pakistan is just beginning. In India, zinc wheat is predominantly marketed by the private sector as truthfully labeled seed (TLS), and six private seed companies had incorporated zinc wheat into their product lines. In Pakistan, the first zinc wheat variety was released in 2016, and delivery through public and private sector partners is now underway.

Beans in Rwanda and DR Congo

In Rwanda, HarvestPlus worked closely with the Rwanda Agriculture Board (RAB) to facilitate production of bean seed through contracted farmers, cooperatives, and small seed companies. From 2011-2015, 80% of certified seed was procured through registered seed farmers under the supervision and certification of RAB, with the remainder being produced through contracts with local seed companies. To increase available seed for the 2015 planting season and beyond, established local and regional seed companies were engaged for seed multiplication, with RAB certifying the biofortified seed. A new seed class was proposed, #Declared Quality Seed# (DQS) or Certified II seed, first in Rwanda and then in DRC. DQS is produced from certified seed and is priced between certified seed and grain, bridging a price gap for farmers who are inclined to plant recycled grain rather than purchase certified seed.

Farmers initially accessed iron bean seed either in small quantities through direct marketing (via established agrodealers or in local markets) or in larger quantities through a payback system that also included cooperatives. By the end of 2014, marketing data showed that an increasing number of farmers were purchasing seed, a trend that is expected to continue. Farmer-to-farmer dissemination is also an important delivery channel; an impact assessment conducted in 2015 found that nearly half of farmers growing iron bean had received their planting material from a person in their social network (Asare-Marfo *et al.* 2016).

Because the iron trait is invisible and iron beans are not easily distinguished from conventional varieties, the primary approach has been to gain market share for biofortified beans due to their superior agronomic and consumption qualities. Over time, a high percentage of the total national supply of beans is expected to contain the biofortified trait, allowing access to additional iron for much of the population. A variety of delivery methods have been tested, including “swapping” biofortified seed for conventional seed, to ensure a high rate of farmer trial and adoption. Only five years after the first iron bean release, iron beans make up more than 10% of national bean production in Rwanda (Asare-Marfo *et al.* 2016).

Rice in Bangladesh

At the core of the Bangladesh strategy are rice varieties with attractive agronomic properties and a robust farmer demonstration program. One released zinc rice for the wet season (BRRI dhan 64) is a short duration variety (100 days as compared with 140 days), which allows production of a third crop of lentils or other food between wet and dry season rice crops. Other biofortified zinc rice varieties carry different farmer-preferred agronomic traits, like high height at maturity, which is beneficial for flooded areas in Southern Bangladesh. A

robust demonstration program provides farmers a chance to observe these new varieties, as well as training on growing the biofortified rice and the health benefits of zinc.

Seed is produced by both the private and the public sector. A private seed association called SeedNet produces truthfully labeled seed alongside the foundation and certified seed produced by government entities. HarvestPlus initially both guarantees a market for a portion of the private sector production and subsidizes the price for any seed that the private sector markets directly to consumers. Free seed is distributed by NGO and government partners in small seed packs, and all free seed recipients agree to pass on the same amount of seed to three neighboring farmers in the subsequent season. As an increasing amount of zinc rice is available on the market, efforts to increase consumer and miller awareness have increased, including outreach via SMS and programs on local television and community radio channels.

Hybrid Crops

Hybrid crops – those for which seed must be replaced each year to maintain the same yield and agronomic traits – offer the most potential for private sector commercialization. While utilizing the private sector for delivery may lead to long-term sustainability, the speed of private sector uptake is dependent on their assessment of demand. Therefore, the activities of biofortification proponents must focus on targeted demand creation for both farmers and consumers.

Maize in Zambia

Because private seed companies dominate the hybrid maize seed market in Zambia, upon release, biofortified hybrid varieties were licensed to companies for commercialization of seed production and distribution. As biofortified maize is scaled up to reach more households in more provinces, the main challenge is to ensure extensive distribution through private networks to outlying areas. Because many rural households purchasing from agro-dealers cannot afford to buy large quantities of seed, private seed companies have begun to ensure that large quantities of smaller, affordable pack sizes will be available. The Zambia National Farmers Union and government extension services disseminate information to farmers about the availability of vitamin A maize seed in their local areas. The inclusion of orange maize seed in the Zambian government's Farmer Input Support Programme (FISP) has further facilitated access to orange maize, including for vulnerable households. FISP provides at least a 50% subsidy for maize seed and fertilizer to farmers considered economically disadvantaged. The quantity of orange maize seed distributed under FISP grew by 400% between the first and second year of inclusion in the program.

A central element of the delivery strategy is to create awareness and acceptance of orange maize through the use of social marketing campaigns and advertisements placed in public media, including TV, radio, newspapers, and popular music. Educational and awareness-creation activities stimulate consumer demand for orange maize products, while engagement with the private sector helps meet growing consumer demand.

To further stimulate cultivation of orange maize, creating markets for surplus production was essential, considering that 20 to 50% of rural households sell maize after satisfying their own food needs. HarvestPlus therefore links major grain buyers to farmers and offers grain samples to millers and food processors interested in incorporating orange maize in their product lines. The multi-lateral AgResults initiative also incentivizes millers to produce and market vitamin A maize products. Strong interest from farmers and food processors encourages increased private sector seed production.

Pearl Millet in India

Crop development and delivery in India is implemented through public and private sector partnerships. In crop development, ICRISAT supplies parental materials/breeder seeds for next stage seed multiplication. Partners now testing and developing their iron pearl millet varieties for seed sales include fifteen private seed companies, two public seed companies and five public organizations. ICRISAT develops high iron hybrid parental lines and to test hybrids with farmer-preferred traits, including of course high yields. This unique crop development arrangement supports and encourages companies to develop their own biofortified varieties for their target market segments. This approach is expected to more quickly increase the number and range of biofortified varieties available in the years to come.

Lessons Learned from Delivery

While delivery experiences vary widely by country and seed system, a few common themes have emerged from the delivery experience. First, multiplication of sufficient planting material is a crucial first step – without planting material to “prime the pump”, farmers cannot be made aware of and will not be able to test biofortified crops. For example, there has been a focus on both strengthening capacity in the public and private sector to produce high quality seed and reducing risk, to ensure that quality planting material is available for farmers.

Second, demonstration trials have been key demand drivers at the farm level. Decentralized field demonstrations and the availability of small promotional seed packs have allowed interested farmers to view and try the new product without taking on a great deal of risk in cultivating a crop for which the market has not yet been tested. Third, nutrition messaging aimed at both men and women has also been key, and in general, involving women farmers has led to increasing demand for biofortified crops. While many biofortified crops are acceptable to farmers and consumers without further information about their nutrition traits, nutrition information helps ensure that the biofortified foods are integrated into child diets (Birol *et al.* 2015).

Finally, multi-stakeholder platforms are crucial to scaling up the early uptake and success of biofortified crops. In target countries, there has been rapid acceptance of biofortification by government entities, and national governments have proactively integrated it into their agriculture and nutrition policies. Integrating private and public sector actors and interests around shared goals reduces barriers to scaling.

8. Future Directions for Biofortification: Transgenic Approaches

Because conventional plant breeding does not face the same regulatory hurdles and is widely accepted, it is considered to be the fastest route to getting more nutritious crops into the hands of farmers and consumers. However, one of the very significant limitations thus far to conventional plant breeding is that the density of a *single* nutrient has been increased for each staple food crop – and that particular nutrient has been dictated by the variation of the nutrient density available in varieties stored in germplasm banks maintained by agricultural research centers.

In crops where the target nutrient does not naturally exist at the required levels in the tens of thousands of varieties in germplasm banks, transgenic plant breeding is a promising approach to produce biofortified crops with the desired nutrient and agronomic traits – for single nutrients and for multiple nutrients as well.

For example, transgenic iron and zinc rice has been developed and tested in confined field trials that can provide +30% of the EAR for iron and +50% of the EAR for zinc in the same event (Trijatmiko *et al.* 2016). As can be seen in Figure 3, the event tested in two locations (IRRI in the Philippines and CIAT in Colombia) meets the iron target of (14 ppm Fe total or +12 ppm Fe) and exceeds the target for zinc by a very large margin (45 ppm Zn or +30 ppm Zn), in a high-yielding background.

Golden Rice, which contains beta-carotene, can provide more than 50% of the EAR for vitamin A. Despite being available as a prototype since early 2000, Golden Rice has not been introduced in any country, in large part due to highly risk-averse regulatory approval processes (Wesseler and Zilberman 2014). High iron-zinc and high provitamin A rice can be crossed to give transgenic rice with high levels of all three nutrients.

While these transgenic varieties have tremendous potential for nutritional impact, release to farmers depends on approval through very strict national biosafety and regulatory processes, which ignore scientific recommendations that transgenic crops are safe (European Commission 2010; Nicolai *et al.* 2014; National Academies of Sciences, Engineering and Medicine 2016; The Royal Society 2016).

9. Conclusion

Currently in Africa, maize is the most widely consumed food staple. Most maize is white. White varieties are often highly preferred, white varieties contain no provitamin A, yet vitamin A deficiency is a serious public health problem in Africa. High-yielding, orange varieties, high in provitamin A are now available to farmers consumers – at the same price (due to high yields) as white varieties. Consumers like the taste of orange varieties and other sensory attributes (e.g., aroma and texture) of vitamin A varieties, often in the absence of information about their nutritional benefits (Stevens and Winter-Nelson 2008, Pillay *et al.* 2011, Meenakshi *et al.* 2012). The value proposition to mothers is obvious: which do they grow/buy and consume – orange or white – to protect their families from vitamin A deficiencies?

Currently, the private sector completely dominates the production and marketing of white varieties. The task ahead is to motivate consumers to demand orange varieties, and for the private sector again to dominate the production and marketing of orange varieties. Twenty years from now, a granddaughter will ask her grandmother – did there used to be such a thing as white maize? And her grandmother will reply, yes, when she was a child maize was mostly white. After all, carrots used to be white.

The vision of HarvestPlus, the global leader in biofortification science and policy, is that one billion people will be benefitting from biofortified crops by 2030. If 20 to 25% of the primary staple food supplies are biofortified in a subset of the 60 countries where biofortified crops will have been released (see Figure 2), then one billion people will have been reached. If fully committed to, biofortification will be one of largest nutrition interventions ever implemented.

End notes

[1] For crops with a low seed rate, like pearl millet, farmers are more likely to purchase seed annually. An open-pollinated variety of biofortified iron pearl millet, which combines the iron trait with 10% higher yield, has been successfully deployed through the private sector in India, where farmers generally purchase seed annually.

[2] The breeding targets shown in Table 1 take into account per capita consumption, bioavailability, and retention during processing, storage, and cooking. All these parameters vary by crop. For details see Bouis and Saltzman, 2017b, chapter 1, especially Table 1.2.

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