Biofortification: A new tool to reduce micronutrient malnutrition

Howarth E. Bouis, Christine Hotz, Bonnie McClafferty, J. V. Meenakshi, and Wolfgang H. Pfeiffer

Abstract

Background. *The density of minerals and vitamins in food staples eaten widely by the poor may be increased either through conventional plant breeding or through the use of transgenic techniques, a process known as biofortification.*

Objective*. HarvestPlus seeks to develop and distribute varieties of food staples (rice, wheat, maize, cassava, pearl millet, beans, and sweet potato) that are high in iron, zinc, and provitamin A through an interdisciplinary, global alliance of scientific institutions and implementing agencies in developing and developed countries.*

Methods. *In broad terms, three things must happen for biofortification to be successful. First, the breeding must be successful—high nutrient density must be combined with high yields and high profitability. Second, efficacy must be demonstrated—the micronutrient status of human subjects must be shown to improve when they are consuming the biofortified varieties as normally eaten. Thus, sufficient nutrients must be retained in processing and cooking and these nutrients must be sufficiently bioavailable. Third, the biofortified crops must be adopted by farmers and consumed by those suffering from micronutrient malnutrition in significant numbers.*

Results. *Biofortified crops offer a rural-based intervention that, by design, initially reaches these more remote populations, which comprise a majority of the undernourished in many countries, and then penetrates to urban populations as production surpluses are marketed. In this way, biofortification complements fortification and supplementation programs, which work best in centralized urban areas and then reach into rural areas with good infrastructure.*

Conclusions. *Initial investments in agricultural research at a central location can generate high recurrent benefits at low cost as adapted, biofortified varieties become available in country after country across time at low recurrent costs.*

Key words: Benefit-cost ratio, bioavailability, biofortification, consumer acceptance, efficacy, farm extension, iron, low-income countries, micronutrient deficiency, nutrition, plant breeding, provitamin A, zinc

Rationale for biofortification

Modern agriculture has been largely successful in meeting the energy needs of poor populations in developing countries. In the past 40 years, agricultural research in developing countries has met Malthus's challenge by placing increased cereal production at its center. However, agriculture must now focus on a new paradigm that will not only produce more food, but deliver better-quality food as well.*

Through plant breeding, biofortification can improve the nutritional content of the staple foods poor people already eat, providing a comparatively inexpensive, cost-effective, sustainable, long-term means of delivering more micronutrients to the poor. This approach not only will lower the number of severely malnourished people who require treatment by complementary interventions, but also will help them maintain improved nutritional status. Moreover, biofortification provides a feasible means of reaching malnourished rural populations who may have limited access to commercially marketed fortified foods and supplements.

* An important part of the overall solution is to improve the productivity of a long list of nonstaple food crops. Because of the large number of foods involved, achieving this goal requires a very large investment, the dimensions of which are not addressed here.

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Unlike the continual financial outlays required for traditional supplementation and fortification programs, a one-time investment in plant breeding can yield micronutrient-rich plants for farmers to grow around the world for years to come. It is this multiplier aspect of biofortification across time and distance that makes it so cost-effective.

Comparative advantages of biofortification

Reaching the malnourished in rural areas

Poor farmers grow modern varieties of crops developed by agricultural research centers supported by the Consultative Group on International Agricultural Research (CGIAR) and by national agricultural research and extension systems (NARES), and disseminated by nongovernmental organizations (NGOs) and government extension agencies. The biofortification strategy seeks to put the micronutrient-dense trait in the most profitable, highest-yielding varieties targeted to farmers and to place these traits in as many released varieties as is feasible. Moreover, marketed surpluses of these crops make their way into retail outlets, reaching consumers in both rural and urban areas. The direction of the flow, as it were, is from rural to urban in contrast to complementary interventions that begin in urban centers.

Cost-effectiveness and low cost

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 to bring millions over the threshold from malnourishment to micronutrient sufficiency. **Figure 1** shows this potential schematically when a high percentage of the iron-deficient population is relatively mildly deficient. For those who are severely deficient, supplements (the highest-cost intervention) are required.

In an analysis of commercial fortification, Horton and Ross in 2003 [1] estimated that the present value of each annual case of iron deficiency averted in South Asia was approximately US$20.*

Consider the value of 1 billion cases of iron deficiency averted in years 16 to 25 after the biofortification research and development project was initiated (100 million cases averted per year in South Asia). The nominal value of US$20 billion (1 billion cases times a value of US$20 per case) must be discounted because of the lags involved between the time that investments are made in biofortification and when benefits are realized. At a 3% discount rate, the present value would be approximately US$10 billion, and at a 12% discount rate, the present value would be approximately US$2 billion. This benefit is far higher than cost of breeding, testing, and disseminating high-iron and high-zinc varieties of rice and wheat for South Asia (< US$100 million in nominal costs).

Sustainability of biofortification

Once in place, the system described in the previous section is highly sustainable. The major fixed costs of developing the varieties and convincing the nutrition and plant science communities of their importance and effectiveness are being covered by programs such as HarvestPlus (www.harvestplus.org). However, the nutritionally improved varieties will continue to be grown and consumed year after year. To be sure, recurrent expenditures are required for monitoring and maintaining these traits in crops, but these recurrent costs are low compared with the cost of the initial development of the nutritionally improved crops and the establishment, institutionally speaking, of nutrient content as a legitimate breeding objective.

Limitations of biofortification

Varying impact throughout the lifecycle

Biofortified staple foods can contribute to body stores of micronutrients such as iron, zinc, and vitamin A (the three target nutrients under HarvestPlus) throughout the life cycle, including those of children, adolescents, adult women, men, and the elderly. The potential benefits of biofortification are, however, not equivalent across all of these groups and depend on the amount of staple food consumed, the prevalence of existing

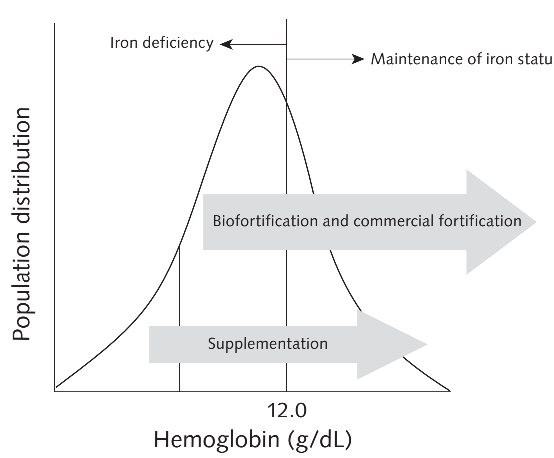

FIG. 1. Biofortification improves status of those less deficient and maintains status of all at low cost

* A World Bank study in 1994 assigned a present value benefit of US$45 to each annual case of iron deficiency averted through fortification (a mix of age-sex groups). The same study gives a present value of US$96 for each annual case of vitamin A deficiency averted for preschoolers.

micronutrient deficiencies, and the micronutrient requirement as affected by daily losses of micronutrients from the body and special needs for processes such as growth, pregnancy, and lactation [2].

Time dimension to deliver biofortified crops and to build up and maintain body stores

It will take a decade before a first wave of biofortified crops is widely adopted in several developing countries. It is only when this happens and attributable impact is confirmed, as measured by significant reductions in the prevalence of iron, zinc, and vitamin A deficiencies, that biofortification will take its place beside supplementation, fortification, and nutrition education as an effective strategy for reducing micronutrient malnutrition.

Implementing biofortification

For biofortification to be successful, three broad questions must be addressed:

» Can breeding increase the micronutrient density in food staples to reach target levels that will have a measurable and significant impact on nutritional status? [3]

» When consumed under controlled conditions, will the extra nutrients bred into the food staples be bioavailable and absorbed at sufficient levels to improve micronutrient status? [2]

» Will farmers grow the biofortified varieties and will consumers buy and eat them in sufficient quantities?

Much of the evidence available to address these questions has been generated under the HarvestPlus Challenge Program. HarvestPlus is an interdisciplinary alliance of research institutions and implementing agencies that is developing biofortified varieties of rice, wheat, maize, cassava, pearl millet, beans, and sweet potato, as shown in **table 1**. HarvestPlus activities are presented along a pathway of impact and are classified into three phases of discovery, development, and dissemination (**fig. 2**). Research developments at any one stage may necessitate revisiting the previous stages to refine and ensure high quality of the biofortified products.

Discovery and development research includes standardizing analytical methodologies, protocols, and proof of concept research in relation to crop improvement, testing, and nutritional efficacy [4]. Dissemination activities are highly dependent on the success of the discovery and development phase, as well as establishing partnerships between HarvestPlus and country agencies, which will lead to the delivery of biofortified

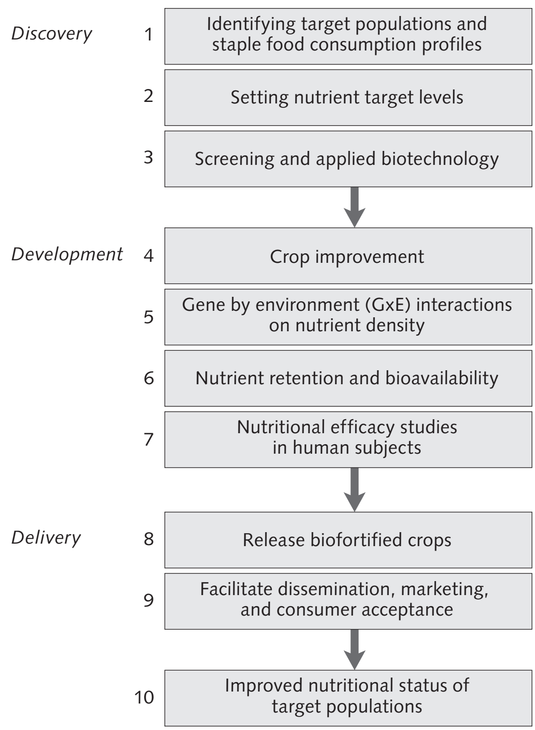

FIG. 2. HarvestPlus pathway to impact

TABLE 1. Schedule of product release of biofortified crops

Crop	Nutrient	Countries of first release	Agronomic trait	Release year[a]
Sweet potato	Provitamin A	Uganda, Mozambique	Disease resistance, drought tolerance, acid soil tolerance	2007
Bean	Iron, zinc	Rwanda, Democratic Republic of Congo	Virus resistance, heat and drought tolerance	2012
Pearl millet	Iron, zinc	India	Mildew resistance, drought tolerance	2012
Cassava	Provitamin A	Nigeria, Democratic Republic of Congo	Disease resistance	2011
Maize	Provitamin A	Zambia	Disease resistance, drought tolerance	2012
Rice	Zinc, iron	Bangladesh, India	Disease and pest resistance, cold and submergence tolerance	2013
Wheat	Zinc, iron	India, Pakistan	Disease and lodging resistance	2013

a. Approved for release by national governments after intensive multilocation testing for agronomic and micronutrient performance.

seeds to farmers and the introduction of biofortified crops to consumers.

Stage 1: Identifying target populations and staple food consumption profiles

The overlap of cropping patterns, consumption trends, and incidence of micronutrient malnutrition determines target populations. This in turn determines the selection and geographic targeting of focus crops.

For each of the seven staple food crops listed in **table 1**, the following activities have been undertaken:

» Identified countries with high per capita consumption of the food staple (based on Food and Agriculture Organization [FAO] databases);
» Established estimates of the prevalence of iron, zinc, and vitamin A deficiencies for these countries;
» Gathered information on existing and planned expansion and effectiveness of alternative micronutrient interventions in these countries;
» Information mentioned above was used to identify countries in which biofortification would have the highest potential impact;
» Preliminary evaluation of the feasibility of developing and delivering biofortified crops in the high-potential-impact countries. This included an assessment of:
» The scientific capability and institutional strength of the NARES
» Present levels of adoption of improved, modern varieties by poor farmers, the level of development of seed distribution systems, and the feasibility of realizing significant adoption of high-yielding/high-profit biofortified varieties combined with superior agronomic characteristics of newly introduced varieties;
» Political stability and strength of supporting governmental and nongovernmental enabling institutions.

Formal *ex ante* impact and benefit-cost analyses were conducted to help refine the targeting exercise. This involved developing a methodology for undertaking *ex ante* benefit-cost analysis [5]. Other publications [6–9] are based on this methodology.

Stage 2: Setting nutrient target levels

Nutritionists work with breeders to establish nutritional breeding targets based on the food intake of target populations, nutrient losses during storage and processing, and the bioavailability of nutrients related to the presence or absence of complementary compounds.

One of the first questions asked by breeders and nutritionists in the development of the HarvestPlus program strategy was “By how much do we need to increase the micronutrient content of our crops to improve the micronutrient status of their consumers?” The additional micronutrient intake resulting from biofortification, as a food-based strategy, would ideally be enough to fill the gap between current intakes and the amount that would result in the majority of the population having intakes above the theoretical mean dietary requirement level (the estimated average requirement, or EAR) for the respective micronutrient. Universal food fortification programs recommend this approach in their design [10]. However, quantitative information on micronutrient intakes for most potential target populations does not exist or exists in very limited form. There are also differences in staple food processing, storage, and cooking practices and inclusion of other foods that can result in large differences in the micronutrient content and bioavailability in the staple food across different populations.

HarvestPlus set preliminary “minimum” target levels for micronutrient content using gross assumptions about staple food intake (grams per day); bioavailability (percent nutrient absorbed) or, in the case of vitamin A, the retinol equivalency of provitamin A carotenoids; losses of the target nutrient with milling, processing, storage, and cooking; and the proportion of the daily nutrient requirement that should be achieved from the additional amount of micronutrient in the staple food. **Table 2** presents examples of the types of data used to estimate target levels for micronutrient contents of biofortified crops. As information of this type becomes available for specific populations, target levels for micronutrient contents in different staple food crops can be refined and adjusted. If preliminary target levels are determined to be inadequate for a specific population, the breeding process will continue until breeders reach or surpass the necessary micronutrient content.

As with universal fortification of staple foods, biofortification will lead to some degree of increased micronutrient intakes among individuals in all life stages. A possible exception is exclusively breastfed children, but even in this case, increased intakes of provitamin A by lactating women may result in increased content in the breastmilk and hence transfer to the breastfed infant. Young children and women of reproductive age typically suffer the greatest consequences of micronutrient deficiencies because of their increased requirements for growth and for pregnancy and lactation, and hence they may be considered the primary targets for this strategy. Biofortification as the sole micronutrient strategy may not be sufficient to cover the deficit in micronutrient intakes by very young children (i.e., under 2 years of age), who have particularly high micronutrient needs and relatively low staple food intakes. Therefore, HarvestPlus estimated appropriate target levels for the micronutrient contents of biofortified foods, taking into account the potential impact in children approximately 4 to 6 years of age and in nonpregnant, nonlactating, premenopausal women (**table 2**). It is estimated that with the lower staple food intakes

TABLE 2. Information and assumptions used to set target levels for micronutrient contents of biofortified staple food crops

		Rice (polished)	Wheat (whole)	Pearl millet (whole)	Beans (whole)	Maize (whole)	Cassava (fresh-weight)	Sweet potato (fresh-weight)
Per capita consumption	Adult women (g/day)	400	400	300	200	400	400	200
	Children 4–6 yr (g/day)	200	200	150	100	200	200	100
Iron	% of EAR to achieve	~30						
	EAR, nonpregnant, nonlactating women (µg/day)	1,460						
	EAR, children 4–6 yr (µg/day)	500						
	Micronutrient retention after processing (%)	90	90	90	85	90	90	90
	Bioavailability (%)	10	5	5	5	5	10	10
	Baseline micronutrient content (µg/g)	2	30	47	50	30	4	6
	Additional content required (µg/g)	11	22	30	44	22	11	22
	Final target content (µg/g)	13	52	77	94	52	15	28
	Final target content as dry weight (µg/g)	15	59	88	107	60	45	85
Zinc	% of EAR to achieve	~40						
	EAR, nonpregnant, nonlactating women (µg/day)	1,860						
	EAR, children 4–6 yr (µg/day)	830						
	Micronutrient retention after processing (%)	90	90	90	90	90	90	90
	Bioavailability (%)	25	25	25	25	25	25	25
	Baseline micronutrient content (µg/g)	16	25	47	32	25	4	6
	Additional content required (µg/g)	8	8	11	17	8	8	17
	Final target content (µg/g)	24	33	58	49	33	12	23
	Final target content as dry weight (µg/g)	28	38	66	56	38	34	70
Provitamin A	% of EAR to achieve	~50						
	EAR, nonpregnant, nonlactating women (µg/day)	500						
	EAR, children 4–6 yr (µg/day)	275						
	Micronutrient retention after processing (%)	50	50	50	50	50	50	50
	Bioavailability ratio (µg to RAE)	12:1	12:1	12:1	12:1	12:1	12:1	12:1
	Baseline micronutrient content (µg/g)	0	0	0	0	0	1	2
	Additional content required (µg/g)	15	15	20	30	15	15	30
	Final target content (µg/g)	15	15	20	30	15	16	32
	Final target content as dry weight (µg/g)	17	17	23	34	17	48	91

EAR, estimated average requirement; RAE, retinol activity equivalent

by younger children (i.e., 1 to 3 years of age) who may still be breastfed, the same target levels for biofortified foods may still cover approximately one-quarter to one-third of their micronutrient requirements. The potential biological intake of a lower increment in micronutrient impact would need to be determined.

Researchers will compile empirical data on staple food intakes for different age groups in a variety of populations in order to refine these estimates. How these levels of increased micronutrient intake translate into changes in nutrition and health status remains to be determined. As breeding for biofortification progresses, the achievable micronutrient content may exceed the current minimum target level and thus make a greater contribution to the micronutrient needs among those groups with elevated requirements.

Stage 3: Screening and applied biotechnology

The global germplasm banks of the CGIAR institutes and the germplasm banks held in trust by national partners provide a reservoir of germplasm of staple crops for screening by HarvestPlus. Genetic transformation provides an alternative strategy to incorporate specific genes that express nutritional density.

The first step in conventional breeding is to determine whether sufficient genetic variation exists to breed for a particular trait of interest—in the specific case of HarvestPlus, whether breeding parents can be found with target levels (or higher) of iron, zinc, and provitamin A. Researchers have analyzed approximately 300,000 samples for trace minerals or for provitamin A carotenoids during screening [11]. The second step is to determine from the screening results whether sufficient genetic variation exists to breed for high-zinc rice and wheat, high-iron beans and pearl millet, and high-provitamin A cassava, maize, and sweet potato.

Stage 4: Crop improvement

Crop improvement and nutritional bioavailability and efficacy (stage 7 below) make up the two largest stages of all research activities. Crop improvement includes all breeding activities falling within a product concept that produces varieties containing those traits that (in target populations, in target areas) improve nutrient content while giving high agronomic performance and preferred consumer quality [12, 13].

Biofortification crop improvement is divided into three phases:

» Early-stage product development and parent building (phase 1)
» Intermediate product development (phase 2)
» Final product development (phase 3)

Phases 1 and 2 are undertaken at CGIAR centers. Final product development (phase 3) for a particular growing "mega-environment" may take place at the CGIAR center or at the NARES. Once promising high-yielding, high-nutrient lines emerge from final product development, they are tested by the NARES in multilocation trials throughout the target country (sometimes referred to as "genotype by environment [G × E] testing").

A subset of these promising lines that do well on average across these several in-country sites is then submitted formally to Varietal Release Committees (VRCs) for testing for official release. VRCs perform independent, multilocation trials before officially approving varieties for release. During these multilocation trials, in anticipation of a favorable decision by the VRCs and to save time, often NARES begin to multiply seed prior to prelaunch.

This entire process may take up to 6 to 8 years to complete. **Table 3** characterizes current progress throughout the five-phase breeding pipeline for seven crops. Progress is measured by the nutrient levels expressed as percentages of the absolute target levels given in breeding lines in a specific phase of development. High-yielding, high-nutrient biofortified varieties currently emerging from the end of this breeding "pipeline" may have lower levels of nutrients and/or lower yields than prototype lines currently entering the front of the pipeline—owing to new discoveries, such as identification of higher-nutrient germplasm (breeding parents), while lines about to be released have been making their way through the breeding pipeline.

For example, all orange sweet potato varieties—whether currently being tested for official release (stage 5) or currently just under initial development (phase 1)—have at least 100% of the target levels of 30 μg of provitamin A carotenoids per gram.

TABLE 3. Breeding progress as of 2007/08 (iron, zinc, provitamin A expressed as percentage of breeding target in lines at indicated stage of breeding)

	Screening	Crop improvement			G×E Testing	Launch
	Screening gene/ trait identification validation	Early development parent building	Intermediate product development	Final product development	Performance G×E testing in target countries	Release prelaunch seed multiplication
Sweet potato			*NARS Uganda Program*		*Introductions*	*NARS Uganda*
Breeding	Provitamins A	100% target	100%	100%	100%	100%
Fast track	*Uganda, Mozambique*				100%	100%
Maize						
Breeding	Provitamins A	100% target	60%	50%	n.a.	
Cassava						
Breeding	Provitamins A	100% target	>75%	>75%	50%	≥30%
Fast track	*DR Congo*					n.a.
Beans						
Breeding	Iron	100% target	60%	40–50%	40–50%	
Fast track	*Rwanda*					40–50%
Rice, polished						
Breeding	Zinc	100% target	100%	75–100%	75–100%	≥30%
Wheat						
Breeding	Zinc	100% target	100%	≥30%	≥30%	
Pearl millet						
Breeding	Iron	100% target	100%	75–100%	50–75%	

By contrast, for cassava, much recent and rapid progress has been made in developing lines that meet the target of 15 μg of provitamin A carotenoids per gram. Thus, only varieties currently in phase 1 of the breeding process have 100% of the target level of provitamin A carotenoids. High-yielding yellow cassava varieties with 30% to 50% of the target level are currently being tested for release (stage 5), reflecting a relative lack of progress in attaining high provitamin A levels just 2 to 3 years ago. Even though varieties currently in stage 5 have provitamin A levels well below target levels, they are high-yielding and thus can be approved for release.

Finally, fast-track options in **table 3** refer to lines that, due to their high yields and favorable agronomic characteristics, are in the regular breeding program but have been discovered (serendipitously during germplasm screening) to be relatively high in iron, zinc, or provitamin A. Breeding for high nutrient levels is not necessary. They are coursed directly through multilocation testing and then (assuming favorable results) to the varietal release committees.

Stage 5: G × E interactions on nutrient density

Germplasm is tested in target countries for their suitability for release. G × E interactions can greatly influence genotypic performance across different crop-growing scenarios. HarvestPlus researchers are looking for high and stable expression of high micronutrient content across environments as well as alternative farming practices that enhance the uptake of nutrients in the edible portion of the crop.

By 2008, all crops were entering or were about to enter G × E trials. **Table 3** presents the progress of the first and successive generations of biofortified crops as of 2007/08. G × E analysis of sweet potato, for example, shows that varieties were demonstrating 100% of the target. G × E analyses of cassava currently finishing all stages of breeding had accomplished 50% of the target, but those improved varieties that were just entering the cassava breeding process, and had built on the successes of previous generations, were demonstrating their ability to reach 100% of target.

Stage 6: Nutrient retention and bioavailability

HarvestPlus nutrition teams are measuring the effects of usual processing, storage, and cooking methods on micronutrient retention for biofortified crops and evaluating practices that could be used by target populations to improve retention.

Recent research results are suggestive that retention of micronutrients may also be genetically determined, which then adds retention heritability to the plant breeding portfolio. Nutritionists use various methods to study the degree to which the nutrients bred into crops are absorbed by using *in vitro* and animal models and, with the most promising varieties, by direct study in humans in controlled experiments. These studies guide plant breeders in refining their breeding objectives [14–31].*,**

Stage 7: Nutritional efficacy studies in human subjects

Although nutrient absorption by the body is a prerequisite to preventing micronutrient deficiencies, ultimately the change in prevalence of micronutrient deficiencies with long-term intake of biofortified staple foods needs to be measured directly. Thus, randomized, controlled efficacy trials demonstrating the impact of biofortified crops on micronutrient status will be required to provide evidence to support the release of biofortified crops at the level of nutrient density thus far achieved (i.e., the minimum target level).

As outlined under stage 2 above, nutrient targets have been set for breeders based on assumptions about retention of micronutrients in the staple food crop following usual processing and cooking methods and how bioavailable these nutrients will be when consumed by micronutrient-deficient populations. These assumptions need to be studied and tested empirically. Eventually, efficacy needs to be evaluated as well [32, 33].

In general, the findings show that retention and bioavailability are higher than assumed. If these promising results are validated with further research to be undertaken under HarvestPlus II, this could eventually allow for a lowering of minimum target levels for breeders. If, however, breeders can attain the targets already set, the thus-far-promising results suggest that impacts could be higher than expected.

Stage 8: Release biofortified crops

Varietal release regulations differ by country and often by states within countries. Proof that the variety is new and distinguishable and adds value must be established in order to register new varieties of crops. HarvestPlus works with NARES to gather the relevant information for registration and formal release of biofortified crops in target regions.

* Chavez AL, Sanchez T, Tohme J, Ishitani M, Ceballos H. Effect of processing on beta-carotene content of cassava roots. Poster. Sixth International Scientific Meeting of the Cassava Biotechnology Network, 8-14 March 2004. Centro Internacional de Agricultura Tropical, Cali, Colombia.

** Bechoff A, Westby A, Dufour D, Dhuique-Mayer C, Marouze C, Oworі C, Menya G, Tomlins KI. Effect of drying and storage on the content of provitamin A of orange fleshed sweet potato (*Ipomoea batatas*): Direct sun radiations do not have significant impact. Poster. Proceedings of the 13th International Society for Tropical Root Crops Symposium, Arusha,Tanzania, 2003.

Stage 9: Facilitate dissemination, marketing, and consumer acceptance

Market chain analysis, seed development and production capacity, consumer acceptance studies, and the cultivation of an enabling policy environment for the uptake and production of biofortified crops in country are essential cornerstones for the development of a sustainable, independent, demand-driven, national biofortification research and implementation program.

The dissemination strategy for nutrients that are invisible (iron and zinc) is to “piggy-back” on superior agronomic characteristics that will drive adoption of the newly introduced varieties and capture a large share of total supply and thus consumption in a given country. For example, high-iron beans that are drought and heat tolerant are undergoing national release trials in Africa. High-zinc wheat varieties to be released in India and Pakistan will be resistant to newly evolved yellow rust viruses, to which current popular varieties are not resistant.

For nutrients that are visible—high-provitamin A sweet potato, maize, and cassava are orange or yellow—nutritional messages must be delivered simultaneously with the release of high-yielding, high-profit biofortified varieties to effect a switch from production and consumption of white varieties (which is currently the norm) to production and consumption of orange or yellow varieties.

HarvestPlus’s experience in the dissemination of biofortified crops is limited to orange sweet potato, which is very high in provitamin A. A published pilot study in Mozambique showed that behavior can be changed among farmers who switched from production of white to orange varieties, and whose families then consumed orange varieties. As a result, vitamin A deficiency among preschoolchildren in treatment villages declined from 60% to 38%, while vitamin A deficiency remained constant in control villages [34]. HarvestPlus is now concentrating on identifying activities and messages that will effect this same behavior change at the lowest cost possible.

In 2006, HarvestPlus embarked upon its first dissemination activity of high-provitamin A carotenoid (pVAC) sweet potato in Uganda and Mozambique. Researchers and implementation specialists are gathering lessons learned in strengthening seed systems, developing markets, and generating consumer demand through behavior change for this nutrient-dense orange variety of sweet potato. Best practices will be applied to expansion of sweet potato to other regions of the world and to instruct dissemination strategies of other pVAC-dense (orange) biofortified staple crops.

Stage 10: Improved nutritional status of target populations

Ultimately, biofortified crops are expected to improve the nutritional status of populations. Baselines and post-dissemination impact and effectiveness surveys are conducted in target regions with and without the intervention to determine whether biofortified crops can improve human health in the absence of experimental conditions.

Some work is ongoing related to the dissemination of orange sweet potato in Uganda and Mozambique (see above). Final results will be reported in 2011.

Conclusions

The biofortification strategy seeks to take advantage of the consistent daily consumption of large amounts of food staples by all family members, including women and children, who are most at risk for micronutrient malnutrition. As a consequence of the predominance of food staples in the diets of the poor, this strategy implicitly targets low-income households.

After a one-time investment in developing seeds that fortify themselves, recurrent costs are low and germplasm can be shared internationally. It is this multiplier aspect of plant breeding across time and distance that makes it so cost-effective.

Once in place, production and consumption of nutritionally improved varieties are highly sustainable, even if government attention and international funding for micronutrient issues fade.

Biofortification provides a feasible means of reaching malnourished populations in relatively remote rural areas, delivering naturally fortified foods to people with limited access to commercially marketed fortified foods, which are more readily available in urban areas. Biofortification and commercial fortification, therefore, are highly complementary.

Ultimately, good nutrition depends on adequate intakes of a range of nutrients and other compounds, in combinations and at levels that are not yet completely understood. Thus, the best and final solution to eliminating undernutrition as a public health problem in developing countries is to provide increased consumption of a range of nonstaple foods. However, to be realized, this will require several decades, informed government policies, and a relatively large investment in agricultural research and other public and on-farm infrastructure [35].

In conceptualizing solutions for a range of nutritional deficiencies, interdisciplinary communication between plant scientists and human nutrition scientists holds great potential. Human nutritionists need to be informed, for example, about the extent to which the vitamin and mineral density of specific foods, as well as compounds (e.g., pre-biotics) that promote and inhibit their bioavailability, can be modified through plant breeding. Plant breeders need to be aware of both the major influence that agricultural research may have had on nutrient utilization in the past (e.g., the bioavailability of trace minerals in modern varieties versus bioavailability in traditional varieties) and the potential of plant breeding for future improvements in nutrition and health.

References

1. Horton S, Ross J. The economiics of iron deficiency. Food Pol 2003;28:51-75.
2. Hotz CC, McClafferty B. From harvest to health: Challenges for developing biofortified staple foods and determining their impact on micronutrient status. Food Nutr Bull 2007;28:S271-9.
3. Pfeiffer WH, McClafferty B. Biofortification: breeding micronutrient-dense crops. In: Kang MS, Priyadarshan PM, eds. Breeding major food staples for the 21st century. Oxford: Blackwell Publishing, 2007:61-91.
4. Grusak MA, Cakmak I. Methods to improve the crop-delivery of minerals to humans and livestock. In: Broadley MR, White PJ, eds. Plant nutritional genomics. Oxford: Blackwell Publishing, 2005:265-86.
5. Stein AJ, Meenakshi JV, Qaim M, Nestel P, Sachdev HPS, Bhutta ZA. Analyzing the health benefits of biofortified staple crops by means of the disability-adjusted life years approach: a handbook focusing on iron, zinc and vitamin A. HarvestPlus Technical Monograph Series 4. Washington, DC: International Food Policy Research Institute, 2005.
6. Stein AJ, Nestel P, Meenakshi JV, Qaim M, Sachdev HPS, Bhutta ZA. Plant breeding to control zinc deficiency in India: how cost effective is biofortification? Public Health Nutr 2007;10:492-501.
7. Qaim M, Stein AJ, Meenakshi JV. Economics of biofortification. Agric Econ 2007;37:119-33.
8. Meenakshi JV, Nancy J, Manyong V, De Groote H, Javelosa J, Yanggen D, Naher F, Garcia J, Gonzales C, Meng E. How cost-effective is biofortification in combating micronutrient malnutrition? An *ex ante* assessment. HarvestPlus Working Paper 2. Washington, DC: International Food Policy Research Institute, 2007.
9. Stein AJ, Meenakshi JV, Qaim M, Nestel P, Sachdev HPS, Bhutta ZA. Potential impacts of iron biofortification in India. Soc Sci Med 2008;66:1797-808.
10. Allen L, de Benoist B, Dary O, Hurrell R, eds. Guidelines on food fortification with micronutrients. World Health Organization/Food and Agriculture Organization, 2006. Available at: http://www.who.int/nutrition/publications/guide_food_fortification_micronutrients.pdf. Accessed 29 October 2010.
11. Menkir A, Liu W, White WS, Maziya-Dixon B, Rocheford T. Carotenoid diversity in tropical-adapted yellow maize inbred lines. Food Chem 2008;109:521–9.
12. Harjes CE, Rocheford T, Bai L, Brutnell TP, Kandianis CB, Sowinksi SG, Stapleton AE, Vallabhaneni R, Williams M, Wurtzel ET, Yan J, Buckler ES. Natural genetic variation in lycopene epsilon cyclase tapped for maize biofortification. Science 2008;319:330-3.
13. Stangoulis JCR, Huynh BL, Welch RM, Choi EY, Graham RD. Quantitative trait loci for phytate in rice grain and their relationship with grain micronutrient content. Euphytica 2007;154:289-94.
14. Pedersen B, Eggum BO. The influence of milling on the nutritive value of flour from cereal grains. Plant Foods Hum Nutr 1983;33:267-78.
15. Iglesias C, Mayer J, Chavez AJ, Calle F. Genetic potential and stability of carotene content in cassava roots. Euphytica 1997;94:367–73.
16. Kósambo LM, Carey EE, Misra AK, Wilkes J, Hagenimana V. Influence of age, farming site, and boiling on pro-vitamin A content in sweet potato (*Ipomoea batatas* (L.) Lam.) storage roots. J Food Compos Anal 1998;11:305–21.
17. Hagenimana V, Carey EE, Gichuki ST, Oyunga MA, Imungi JK. Carotenoid contents in fresh, dried and processed sweetpotato products. Ecol Food Nutr 1999;37:455–73.
18. Villareal CP, Maranville JW, Juliano BO. Nutrient content and retention during milling of brown rices from the international rice research institute. Cereal Chem 1991;68:437-9.
19. Sungpuag P, Tangchitpianvit S, Chittchang U, Wasantwisut E. Retinol and beta carotene content of indigenous raw and home-prepared foods in Northeast Thailand. Food Chem 1999;64:163-7.
20. Grewal HK, Hira CK. Effect of processing and cooking on zinc availability from wheat (*Triticum aestivum*). Plant Foods Hum Nutr 2003;58:1-8.
21. Van Jaarsveld PJ, Marais DW, Harmse E, Nestel P, Rodriguez-Amaya DB. Retention of β-carotene in boiled, mashed orange-fleshed sweet potato. J Food Compos Anal 2006;19:321–9.
22. Sison MEGQ, Gregorio GB, Mendioro MS. The effect of different milling times on grain iron content and grain physical parameters associated with milling of eight genotypes of rice (*Oryza sativa* L.). Philipp J Sci 2006;135:9-17.
23. Howe JA, Tanumihardjo SA. Carotenoid-biofortified maize maintains adequate vitamin A status in Mongolian gerbils. J Nutr 2006;136:2562-7.
24. Li S, Tayie FAK, Young MF, Rocheford T, White WS. Retention of provitamin A carotenoids in high β-carotene maize (*Zea mays*) during traditional African household processing. J Agric Food Chem 2007;55:10744-50.
25. Kidmose U, Christensen LP, Agili SM, Thilsted SH. Effect of home preparation practices on the content of provitamin A carotenoids in coloured sweet potato varieties (*Ipomoea batatas* Lam.) from Kenya. Innov Food Sci Emerg Technol 2007;8:399-406.

26. Chavez AL, Sanchez T, Ceballos H, Rodriguez-Amaya DB, Nestel P, Tohme J, Ishitani M. Retention of carotenoids in cassava roots submitted to different processing methods. J Sci Food Agric 2007;87:388–93.
27. Wu X, Sun C, Yang L, Zeng G, Liu Z, Li Y. β-Carotene content in sweet potato varieties from China and the effect of preparation on β-carotene retention in the Yanshu No. 5. Innov Food Sci Emerg Technol 2008;9:581–6.
28. Bengtsson A, Namutebi A, Alminger ML, Svanberg U. Effects of various traditional processing methods on the all-trans-β-carotene content of orange-fleshed sweet potato. J Food Compos Anal 2008;21:134–43.
29. Bechoff A, Dufour D, Dhuique-Mayer C, Marouzé C, Reynes M, Westby A. Effect of hot air, solar and sun drying treatments on provitamin A retention in orange-fleshed sweetpotato. J Food Eng 2009;92:164–71.
30. Tako E, Laparra JM, Glahn RP, Welch RM, Lei XG, Beebe S, Miller DD. Biofortified black beans in a maize and bean diet provide more bioavailable iron to piglets than standard black beans. J Nutr 2009;139:305-9.
31. Thakkar SK, Huo T, Maziya-Dixon B, Failla ML. Impact of style of processing on retention and bioaccessibility of β-carotene in cassava (*Manihot esculenta*, Crantz). J Agric Food Chem 2009;57:1344–8.
32. Haas, JD, Beard JL, Murray-Kolb LE, del Mundo AM, Felix A, Gregorio GB. Iron-biofortified rice improves the iron stores of non-anemic Filipino women. J Nutr 2005;135:2823-30.
33. Van Jaarsveld PJ, Faber M, Tanumihardjo SA, Nestel P, Lombard CJ, Benadé Spinnler AJ. β-Carotene–rich orange-fleshed sweet potato improves the vitamin A status of primary school children assessed with the modified-relative-dose-response test. Am J Clin Nutr 2005;81:1080–7.
34. Low JW, Arimond M, Osman N, Cunguara B, Zano F, Tschirley D. A food-based approach introducing orange-fleshed sweet potatoes increased vitamin A intake and serum retinol concentrations in young children in rural Mozambique. J Nutr 2007;137:1320-7.
35. Graham RD, Welch RM, Saunders DA, Ortiz-Monasterio JI, Bouis HE, Bonierbale M, de Haan S, Burgos G, Thiele G, Dominguez MRL, Meisner CA, Beebe SE, Potts MJ, Kadian M, Hobbs, Gupta RK, Twomlow S. Nutritious subsistence food systems. Adv Agron 2007;92:1-74.