HarvestPlus Statement on the Potential Benefits of Biofortification on the Nutritional Status of Populations

Biofortification is an intervention strategy currently being researched and developed for increasing the bio-absorbable content of micronutrients in the edible portion of staple food crops. The micronutrients currently being targeted by the HarvestPlus biofortification program are iron, zinc, and provitamin A. When consumed regularly, biofortified staple foods should lead via increased intakes of these micronutrients to improved health outcomes. HarvestPlus' methodology involves mainly conventional plant breeding, but other paths to biofortification (biotechnology, fertilizer enhancement) are being explored too.

BIOFORTIFICATION AS A MICRONUTRIENT INTERVENTION STRATEGY

The Goal of Biofortification

The goal of biofortification is to contribute to reducing the high prevalence of specific nutritional deficiencies, especially of iron, zinc and vitamin A, that commonly occur in low income populations. This is to be achieved by improving the micronutrient density of staple food crops that are produced and consumed by these populations and hence, if bioavailability is demonstrated, increasing the adequacy of micronutrient intakes. Biofortification is intended to contribute to the prevention of micronutrient deficiencies by reaching all household members.

The Niche for Biofortification

The four ways to tackle micronutrient deficiency are diet diversification, food supplementation, traditional food fortification, and biofortification. Diversification is the long-term solution but is often unaffordable by the very poor and by remote dwellers, usually those at greatest risk of deficiencies. Supplementation (e.g. vitamin A mega doses) requires permanent, medically skilful backup. Traditional fortification (e.g. iodized salt) requires central processing. After a one-time investment in developing seeds that naturally fortify themselves, biofortification has lower recurrent costs, especially as germplasm may be shared internationally. It is this multiplier aspect of plant breeding across time and distance that makes it so cost effective. Therefore, this strategy has the potential to fill the gap in coverage left by other interventions as it can be more accessible to those who consume staple foods from local or self production. The latter populations are typically rural-based and more vulnerable to micronutrient malnutrition. Biofortification is also suitable for reaching food buyers who cannot yet afford or access more diverse diets with widely released varieties from national or international crop research units.

Updated 08-17-2010

Intended Contribution of Biofortification to Reducing Micronutrient Deficiencies
The biofortification strategy intends to contribute toward the *prevention* of micronutrient deficiencies by increasing the daily adequacy of micronutrient intakes among nearly all individuals throughout the lifecycle. It should be viewed as a strategy that will contribute to the overall reduction of micronutrient deficiencies in a population. Some of this contribution (e.g. to lower visual impairment among vitamin A deficient children) may be quick, but some is long term. Also, gains can later be lost if nutrition worsens. Therefore, nutrition improvement strategies once initiated should be sustained. For biofortification, this is cheap and administratively sustainable. Note that biofortification is not expected to *treat* micronutrient deficiencies or eliminate them in all population groups.

THE EXPECTED BENEFITS AND LIMITATIONS OF BIOFORTIFICATION AS A MICRONUTRIENT INTERVENTION STRATEGY

What is the Expected Contribution of Biofortified Foods to the Adequacy of Iron, Zinc, and Vitamin A Intake of Different Population Groups?
The target increment in the iron, zinc, and provitamin A content of staple foods was estimated on the basis of providing a minimum percentage of the daily intake requirements for those nutrients based on estimated staple food intakes and micronutrient requirements for nonpregnant women and for children roughly 4–6 years of age. Using assumptions about daily staple food intake, micronutrient retention after storage, processing, and cooking, and micronutrient bioavailability, target increments for iron, zinc, and provitamin A content were set to provide 30 percent, 40 percent, and 50 percent, respectively, of the Estimated Average Requirement[1] for those nutrients. These minimum target levels were set as the first goals to be achieved through breeding because the process typically takes several years. For some crops, it will be possible to exceed these minimum levels, in which case continued increases in the micronutrient content should be pursued.

Who is Likely to Benefit—and How Much—from Biofortification
Biofortified staple foods can contribute to body stores of iron, zinc, and vitamin A throughout the lifecycle, including those of children, adolescents, adult women, men, and the elderly. The potential benefits from biofortification are, however, not equivalent across all of these groups and depend on the amount of staple food consumed, the prevalence of existing micronutrient deficiencies, the micronutrient requirement as affected by daily losses of micronutrient from the body, and special needs for processes such as growth, pregnancy, and lactation. Some special considerations are noted in the following points.

1. Children between 6 and 23 months of age are particularly vulnerable to micronutrient deficiencies and are the most gravely affected by their consequences. However, breastfed children in this age range consume relatively smaller amounts of staple foods and have

[1] The EAR is the equivalent to the median of the nutrient requirement distribution and is specific for age, sex, and physiological status; it is the intake level at which approximately half of the population will meet its requirements, and half will not.

Updated 08-17-2010

relatively higher micronutrient requirements compared to other age groups. Biofortified nutrients do reach such children via breast milk and complementary foods; the scale of such contributions to the needs of under-twos and ways to increase them are important research topics for HarvestPlus. However, the contribution of biofortification to the micronutrient adequacy in this vulnerable group may well be low in comparison with requirements, and hence, biofortification alone will not always be sufficient to meet a significant proportion of their micronutrient requirements, particularly for iron.

However, due to the particularly high provitamin A content of several orange-fleshed sweet potato varieties, regular consumption of these varieties can contribute substantially to vitamin A requirements of breastfed children 6–23 months. In addition, zinc and iron content of some staples used for complementary foods is already substantially increased by biofortification (e.g. rice variety IR68144 with 24 µg Zn/g milled; pearl millet varieties MLBH504 and MRB204 with ~80 µg Fe/g and ~60 µg Zn/g; and Peruvian bean G23834E with 102 µg Fe/g and 35 µg Zn/g). Research must be completed to confirm that consumption will improve zinc and/or iron status of children under two.

2. Breast milk vitamin A concentration decreases as a result of maternal vitamin A deficiency. Maternal consumption of provitamin A biofortified staple foods may help to maintain normal breast milk vitamin A concentrations. Therefore, all breastfed children, particularly those for whom breast milk provides a major source of total energy (such as those up to 6 months of age) *may* benefit indirectly from biofortification with provitamin A due to increased intake of vitamin A from breast milk. However, research is needed to quantify the potential benefits to the suckling from different amounts, times, and durations of biofortified staples consumed by the mother. Breast milk iron or zinc content is not significantly affected by maternal dietary iron or zinc intake or status, so maternal consumption of iron and zinc biofortified foods is not expected to provide direct nutritional benefits to the breastfed child. However, indirect and long-term, but potentially large, benefits to breastfed infants may accrue as biofortification increases iron and zinc uptakes from girlhood, and thus to iron and zinc stores in mothers.

3. Biofortified staple foods may also contribute to maternal micronutrient adequacy during pregnancy when requirements are substantially increased. A potentially more significant contribution of biofortification to women's iron status is through improving their iron intake and status before entering into pregnancy. However, due to the particularly high requirements for iron *during* pregnancy, the additional amount of iron contributed from biofortification or even a typical meat-containing diet will be low in relation to requirements. Additional means of meeting iron requirements during pregnancy are required.

For iron and zinc, improved adequacy of maternal status during pregnancy may also lead to increased transfer of iron and zinc to the fetus in late gestation and during birthing through cord blood. Infants are believed to rely on these stores for the balance of their iron and zinc requirements during the first 4–6 months of life.

Are There Any Risks from Biofortification?

In the particular case of populations living in areas where malaria transmission is very high, children under two years without iron deficiency may experience substantially more adverse health events when provided with daily, low-dose iron supplements (~12 mg/day) for prolonged periods, as recommended by current international regimes for preventive iron supplementation. However, it may not be the case that iron in home-prepared or industrially processed weaning foods will reproduce the untoward effects of iron-and-folic-acid supplements, even in similar climate and malaria conditions, as food dampens the absorption of iron, an already highly guarded process in human nutrition. Additionally, consumption of biofortified foods high in iron will typically contribute less than half the amount of iron provided by supplements, and the total food iron is divided into several meals throughout the day.

In light of recent technical consultations, the World Health Organization has recommended that in areas with high malaria prevalence, iron supplements be given to children under two years of age only after diagnosis of iron deficiency has been made. Fortified complementary foods are considered safe in any circumstance.

Biofortified crops with high iron intended for complementary feeding of children 6 to 24 months of age should be of greatest benefit to populations where the intervention is mainstreamed in concert with complementary feeding education and malaria prevention, so that the benefits of the interventions are maximized, and the hopefully remote risk of damaging side effects minimized. Despite all the theoretical differences between pharmaceutical iron and food iron, interventions (e.g. biofortification) should be implemented after careful planning and integrated with other relevant public health interventions (i.e. malaria control and prevention).

In summary, there are substantial prospects for improving nutritional status of children under two years of age through biofortification of major dietary staples. These benefits depend on a combination of direct effects through consumption and indirect effects through breast milk and maternal health. Biofortified varieties already exist or are in various stages of development for achieving these prospects in the case of vitamin A and zinc. In the particular case of iron, biofortification offers fewer short-term prospects for preventing the putatively irreversible developmental damage associated with deficiency during infancy. However, even in that case, biofortification can improve the prospects for later generations by improving female micronutrient intake from conception through girlhood to pregnancy.

THE STRATEGY FOR RELEVANT RESEARCH ON THE IMPACT OF BIOFORTIFICATION

Ideally, research on the biological impact of biofortification on micronutrient status and health should be conducted in those groups at greatest risk of micronutrient deficiencies *and* those most likely to benefit either directly or indirectly from the intervention. At present, the efficacy of biofortification is still in proof-of-concept stage, and the sample populations chosen for the first efficacy studies may be based on convenience. As proof of concept is established for each micronutrient, the research program should become more strategic, focusing on priority groups based on the relative risk and potential for impact. A summary of the relative level of risk to micronutrient deficiencies and the potential direct and indirect benefits and risks of biofortification by age and physiological status groups is given in Table 1, together with a rationale for current priority research at HarvestPlus. One way in which HarvestPlus optimizes its work is through collaboration with other areas of expertise. HarvestPlus adopts a risk-benefit-cost effectiveness approach to its work and has the regular input of an ethicist on its Advisory Board. All projects are assessed by an independent ethics committee.

Table 1. Potential Benefits of Biofortification on Different Age and Physiological Status Groups and Priorities for Research

AGE/ PHYSIOLOGICAL STATUS	RISK OF MICRONUTRIENT DEFICIENCY	POTENTIAL DIRECT AND INDIRECT* BENEFITS OF BIOFORTIFICATION	PRIORITY FOR HARVESTPLUS RESEARCH OF DIRECT AND INDIRECT NUTRITIONAL EFFECTS (next 5 years)
< 6 mos	Low-high; depending on maternal status during pregnancy/ lactation and gestational age at birth	**Direct:** none or negligible **Indirect:** via maternal intakes: -Increased content of breast milk vitamin A -Possible via increased maternal stores of Fe/Zn transferred to fetus in late gestation and during birthing for use in infancy	**Direct:** low **Indirect:** high for vitamin A contribution via breast milk; for maternal transfer during fetal development, priority is high but requires complex and expensive intergenerational studies from pregnancy to post-partum
6-23 mos	High	**Direct:** probably low at current target levels; moderate for provitamin A and zinc crops **Indirect:** via maternal intakes: -Increased content of breast milk vitamin A	**Direct:** low *at current target levels,* except for absorption of micronutrients from biofortified weaning foods **Indirect:** high for vitamin A contribution via breast milk
Preschool children	High-moderate	**Direct:** high	**Direct:** high-moderate due to risk level
School children / adolescents	Moderate	**Direct:** high	**Direct:** moderate due to risk level
Adult women	High-moderate	**Direct:** high	**Direct:** high-moderate due to risk level
Pregnancy	High	**Direct:** high for zinc and vitamin A; lower for iron. **Indirect:** via preconception intakes: moderate to high for improving stores prior to conception	**Direct and Indirect**: high but requires complex recruitment procedures and hence long studies to study women preconception or at early stages of gestation
Lactation	High	**Direct:** high	**Direct:** high; may often be included in studies of non-pregnant women due to high rates of lactating women in target populations
Adult men	Low [?]	**Direct:** high	**Direct:** low due to generally low risk

* For some age/physiological status groups, availability of biofortified foods in the population may lead to either direct benefits (i.e., through direct consumption of the biofortified food) or indirect benefits. For infants and young children, indirect benefits occur through improvements in maternal micronutrient status either passed on to the developing fetus or via breast milk. In the case of pregnancy, biofortified foods may contribute to the increased requirements for micronutrients during pregnancy, but biofortification may indirectly assist in maintaining adequate maternal micronutrient stores prior to conception.