Development and Impact of Golden Rice

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Vitamin A Deficiency in the World

Degree of public health importance of vitamin A deficiency:
- clinical
- severe subclinical
- moderate subclinical
- mild subclinical
- no data, problem likely
- problem under control

SIGHT AND LIFE has supported many hundreds of projects in more than 70 countries. Millions of vitamin A capsules have been donated.

High Risk Areas:
- Iron deficient
- Vitamin A & Iron deficient
- Iodine, Vitamin A & Iron deficient
400 million poor in rice-based societies are Vitamin A deficient. 500,000 children per year go blind. 1.15 million VAD-precipitated deaths among children worldwide.

GMO-based ‘Biofortification‘ could reduce malnutrition in a cost-effective and sustainable manner if we adopted a rational deregulation process based on benefit / risk analysis.

Rice is the main staple crop for most of these children, but rice lacks provitamin A and other micronutrients.
Share of energy intake for rural Bangladesh

Source: H. Bouis, HarvestPlus
Intervention strategies and drawbacks

Intervention

- Supplementation
- Industrial fortification
- Education

Limited by

- Distribution, educated medical staff
- Centrally processed food items
- Only partially applicable
- Economically unsustainable

Alternatives required!
Cost-effectiveness of biofortification

- Centralised one-off investment.
- Recurrent costs are minimised after the initial research investment.
- Biofortified seeds can be distributed worldwide, although adaptive breeding is required.
- Biofortification complements current interventions, *all* of which are needed to help alleviate the problem.
Biofortification

No germplasm available with high provitamin A

Solution

✓ Biochemical pathway engineering using recombinant DNA technology
GR contains the genes needed to produce provitamin A.

Its content is sufficient to cover vitamin A requirements of VAD children in rice-based societies.
Carotene Desaturase (CrtI)

Phytoene Synthase (PSY)

Filling in the gaps
History of Golden Rice Development

1992 - Science - 1999 ✓
1999 - Product development – 200X

- Intellectual Property Rights 2000 ✓
- Material Transfer Agreements 2001 ✓
- HTT-competent partner 2001-2002 ✓
- Transfer to indica rice varieties 2002 ✓
  - Regulatory clean events 2002 ✓
  - Regulatory clean line at 1.6 µg/g 2003 ✓
  - Regulatory clean line at 6.0 µg/g 2004 ✓
- Experimental lines at much higher levels 2004 ✓
- Agronomic normality in field test 2004 ✓
- Regulatory clean lines at 37 µg/g 2005 ✓

Deregulation
Agronomic performance of SGR1 was not affected and pro-vitamin A content was as high as 6 µg/g.

While more than 1 million children die every year from VAD, regulatory redtape has been delaying field trials in India, Vietnam, the Philippines and Bangladesh for years, although no ecologist has come up with any substantial environmental risk stemming from Golden Rice.
SGR2
Paine et al., Nature Biotechnology 2005

- 23-fold increase of carotenoid content over Golden Rice ver 1
- Maize PSY
- 80% β-carotene
Carotenoid bioavailability

From www.sightandlife.org
Estimated vit A contribution from nutrient intake for rural Bangladesh (IFPRI)

50% RDA is sufficient to prevent malnutrition! Thus populations with 40% caloric intake from rice would be protected.
Golden Rice – going through the stances

- Bioavailability studies: USA and China.
- Field testing in India, the Philippines, Vietnam.
- Introgression into local varieties.
- Toxicology, allergenicity, substantial equivalence, etc.
- Dossiers for deregulation in India, Bangladesh, the Philippines, Vietnam, Africa, etc.
- Information, seed multiplication, distribution.
- Addition of iron, zinc, high quality protein, vit E.
- Product development and deregulation of nutritionally optimized rice.


No support from the EU Commission or EU national public granting agencies.
Introgression of the GR trait into local Vietnamese cultivars

Transfer high β-carotene from Taipei 309 into:
High Fe/yield var Khang Dan and high yield/ good grain quality/ aromatic varieties
IR1490, CS 2000, ASS 996, Jasmine 85, OM 2031, DS 2001, MTL 250 and OM 3536
Golden Rice follow-up projects

Biofortification and genetics-based improvement of the nutritional value of crops to reduce micronutrient malnutrition.

International, multidisciplinary

Grand Challenges in Global Health

- Rice
- Sorghum
- Cassava
- Potato
- Banana

HarvestPlus CGIAR

- Rice
- Maize
- Wheat
- Cassava
- Sweet Potato
- Beans

Provitamin A: ✓
carotenoids, lutein, zeaxanthin

Iron bio-availability: ✓
Ferritin, Phytase, Cystein, conventional

Zinc bioavailability:
Ferritin, Phytase

High-quality protein : ✓
Vitamin E ✓

Background: Golden Rice field trial, Louisiana Sep 2004
A Public-Private Partnership at the core

- The Rockefeller Foundation
- ETH Zürich, Switzerland
- University of Freiburg, Germany
- Syngenta
The Fathers of Golden Rice
Golden Deal

- Inventors have assigned their rights exclusively to Syngenta.
- Syngenta, in turn, has licensed inventors for humanitarian uses, with the right to sublicense public research institutes and low-income farmers (<US$10,000 pa) in developing countries.
- Farmers can replant their seed and trade them locally.
- Syngenta continues to support inventors and the Humanitarian Board in this task.
- Syngenta retains commercial rights, although it is not pursuing any commercial plans at the moment.
Golden Rice Humanitarian Board
I Potrykus, Chair (ETH Zurich)
P Beyer, J Mayer – Univ of Freiburg
A Dubock – Syngenta
G Toenniessen – Rockefeller Foundation
G Khush – UC Davis (IRRI)
R Bertram – USAID
H Bouis – HarvestPlus, CGIAR
W Padolina, R Wang, G Barry – IRRI
R Russell – Tufts, USDA
K Jenny – SDC

HumBo preparing to visit field trial
11 Sep 2004, Crowley, Louisiana
The Golden Rice Network

• **The Philippines**
  - International Rice Research Institute (IRRI) (Management),
  - National Rice Research Institute (PhilRice).

• **Vietnam**:
  - Cuu Long Delta Rice Research Institute.

• **India**:
  - Dept of Biotechnology India,
  - Directorate of Rice Research,
  - Indian Agricultural Research Institute,
  - Univ of Delhi South Campus,
  - Tamil Nadu Agricultural Univ,
  - Agricultural Univ Patnagar,
  - Univ of Agricultural Sciences Bangalore,
  - Chinsurah Rice Research Station.

• **Bangladesh**:
  - Bangladesh Rice Research Institute.
  - Huazhong Agricultural Univ.

• **China**:
  - Chinese Acad of Sciences, Yunnan Acad. Agricultural Sciences.

• **Indonesia**:
  - Agency for Agricultural R&D, Jakarta.

• **Germany**:
  - University of Freiburg.
DO YOU KNOW WHAT THIS STUFF CAN DO TO YOU?

YES, HELP KEEP ME ALIVE.
• With a streamlined GM regulatory framework in target countries breeding would be very advanced.

• Unnecessary bureaucratic hurdles will further delay reaching a fair number of farmers until 2009, ie at least 6 years of additional waiting.

• Every day 6,000 children die from VAD, probably more than 50% in rice-based societies; thus many preventable.

Is GMO over-regulation saving or costing lives?

And who will assume political responsibility for unnecessary suffering?
The paper uses a ‘global economy-wide computable general equilibrium model’ to analyse the potential economic effects of adopting first and second generation GMO crops in Asia.

The results suggest that farm productivity gains could be dwarfed by the welfare gains resulting from the potential health-enhancing attributes of Golden Rice.

- Projected gains from Golden Rice adoption by developing Asia would amount to US$ 15.2 bn per year globally.
- Enhanced productivity of Asian unskilled labor in bn US$:
  - China 7.2; India 2.5; other countries in S+SE Asia 4.1.
- Export losses due to import ban from Europe are < 0.5%!
## Food-Related Illness and Death in the US 2002

Mead et al., Centers for Disease Control and Prevention, Atlanta GA

<table>
<thead>
<tr>
<th></th>
<th>Known Pathogens Non-Gastroenteritis</th>
<th>Known Pathogens Acute Gastroenteritis</th>
<th>Unknown Etiology Acute Gastroenteritis</th>
<th>GMO-derived Health Problems</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Illness</strong></td>
<td>120,000</td>
<td>14,000,000</td>
<td>62,000,000</td>
<td>0</td>
</tr>
<tr>
<td><strong>Hospitalization</strong></td>
<td>5,000</td>
<td>55,000</td>
<td>263,000</td>
<td>0</td>
</tr>
<tr>
<td><strong>Deaths</strong></td>
<td>900</td>
<td>900</td>
<td>3,400</td>
<td>0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>Illness</strong> 76,000,000</td>
<td><strong>Hospitalizations 323,000</strong></td>
<td><strong>Deaths 5,200</strong></td>
<td><strong>GMO-derived 0</strong></td>
</tr>
</tbody>
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\textbf{Nuffield Council on Bioethics}

‘The current evidence from safety assessments of GM crops does not suggest any significant risk to people who eat them.’ (or to the environment).

‘An excessively \textit{conservative interpretation} of the precautionary approach ... is fundamentally at odds ... and essentially impractical.’

‘The European Union is ignoring a “\textit{moral imperative}“ to promote genetically modified crops for their great potential for helping the developing world.’

‘We believe EU regulators have not payed enough attention to the \textit{impact} of EU regulations on agriculture in developing countries.’
Moral dilemma

• Social needs and moral imperatives are not reflected in the present regulatory framework.

• Numerous scientific success stories with the potential to benefit the poor will be incapable of making it through present regulatory requirements, thereby wasting public and private investment.
Hundreds of accumulated genome alterations don’t attract regulatory oversight.

Add two defined genes and regulation kicks in.
GMO Product Development:

Proof-of-concept → hundreds of events → regulatory clean event → product development → biosafety assessment

4-8 years of intensive experimental work with no publications even though data produced must be of scientific quality.

Very expensive process!

GMO Deregulation:

Exposure evaluation
Protein production and equivalence
Molecular characterization and genetic stability
Expression profiling
Phenotype analysis
Compositional analysis
Environmental risk assessment, etc
New crops from the public sector have little chance to contribute to this optimistic scenario in the near future, if the present regulatory regime is maintained.

Progress with biotech crops looks impressive, however ...

... the increase is based on only two traits and four species, all developed and deregulated by the private sector in the U.S. and subsequently adopted by developing countries (cotton, maize, soybean, canola with herbicide-tolerance and insect-resistance).
Hundreds of ‘food-security‘ transformation events produced in the public domain in Egypt, Kenya, South Africa, Zimbabwe, China, India, Indonesia, Malaysia, Pakistan, Philippines, Thailand, Argentina, Brazil, Costa Rica, and Mexico,

... established in rice, maize, pearl millet, sorghum, wheat, potatoes, cassava, sweet potatoes, melons, cucumbers, squash, watermelons, tomatoes, bananas, plantain, beans, papaya, sunflower, soybean, ground nut, chickpea, oil palm, cabbage, cauliflower, cacao, mango,

... with improved agronomic performance, stress tolerance, and nutritional value, *)

which all are facing the same regulatory, ie huge financial obstacles.

*) Data from J.I. Cohen, Nature Biotechnology 23 (1) 2005
Within 2 years one seed has the potential to produce a one-year supply of food for 100,000 poor reducing VADD in a sustained and cost-effective manner.

Over-regulation and uncertainty have delayed the process in a morally unjustifiable way.
Health Effects Studies

Vitamin A is involved in many physiological functions and processes

"Improvement of vitamin A status in young child populations ... leads to a reduction in all-cause mortality rates of about 23%"
United Nations, 1993

"Improved vitamin A nutriture would be expected to prevent approximately 1.3-2.5 million deaths annually among children aged under 5 years."
Bulletin of WHO, 1992

You'll find excellent information about the health effects of vitamin A at the «Sight and Life» website in their Manual on Vitamin A Deficiency Disorders.

Vision and good health go together with a bright smile. Impaired vision, a terrible condition in itself, is but one manifestation of the disorders caused by vitamin A deficiency (VAD). More than one million children a year die as a consequence of a number of diseases precipitated by VAD.