

Scientific Conference

Advancing the Understanding of Biosafety

Scientific Findings

**Programme and
Extended Abstracts**

7-9 October 2010
Nagoya, Japan



TWN



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TWN
Third World Network

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**Scientific Conference: Advancing the Understanding of Biosafety – Scientific Findings
Programme and Extended Abstracts**

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PROGRAMME

Advancing the Understanding of Biosafety – Scientific Findings

Thursday, 7 October 2010

Opening

14:00	tbd Chee Yoke Ling Dr. Angelika Hilbeck	Japan Third World Network, Director ENSSER, Chairperson
Keynote Lectures		
14:45	Outlook on the Fifth Meeting of the Cartagena Protocol on Biosafety (MOP5)	Christine von Weizsäcker VDW, Germany
15:15	Native Maize Landraces, Transgenic Maize, Food Security and Cultural Conflicts in Mexico	Prof. Antonio Turrent Fernández Instituto Nacional de Investigaciones Forestales, Agrícolas y Pecuarias (INIFAP) & Unión de Científicos Comprometidos con la Sociedad (UCCS), Mexico
16:00	<i>Break</i>	
16:30	India's Bt Brinjal: From the Supreme Court to Science in Public Debate – How Civil Society Prevailed Against Monsanto and the Regulator	Aruna Rodrigues Petitioner at the Supreme Court, India
17:15	Assessing Systemic Risks – A Holistic Concept	Dr. Broder Breckling University of Vechta, Germany
18:00	<i>Summary of the Day</i>	

Friday, 8 October 2010

Risk Assessment – An Appraisal of Current Approaches

09:00	Sound Science – Assessment of Applications Sent to the European Food Safety Authority	Dr. Andreas Heissenberger Umweltbundesamt – Environment Agency Austria, Austria
09:30	Bt Crops – Controversies Around the Science Necessary for Risk Assessment	Dr. Angelika Hilbeck Swiss Federal Institute of Technology, Institute of Integrative Biology, Switzerland and GenØk – Centre for Biosafety, Norway
10:00	GM Maize and Glyphosate-Based Herbicides – Health Studies	Prof. Gilles-Eric Séralini University of Caen, France
10:30	<i>Break</i>	
11:00	Transgenic Fish – How to Assess Contained Use Applications	Prof. Antonietta Guitiérrez Rosati Universidad Nacional Agraria La Molina, Peru
11:30	<i>Discussion</i>	
12:30	<i>Lunch</i>	

Ecological Risk Research – From Organisms to Landscapes

14:00	GE Viruses – Environmental Challenges	Prof. Terje Traavik GenØk – Centre for Biosafety, Norway
14:30	Feral Growth of Genetically Modified Oilseed Rape Around Harbours in Japan and Its Impact on the Environment	Prof. Masaharu Kawata Yokkaichi University, Japan
15:00	Transgene Flow in Small-Scale Systems – Ghana as Model	Dr. Denis Worlanyo Aheto University of Cape Coast, Ghana
15:30	<i>Break</i>	
16:00	Transgene Flow in South African Commercial Maize Cultivation	Prof. Chris Viljoen Free State University, South Africa
16:30	<i>Discussion</i>	
17:30	<i>Summary of the Day</i>	

Saturday, 9 October 2010

Reality Checks

09:00	Patenting Genes and Plants: Intellectual Property Rights Transform Research and Agricultural Innovation	Lim Li Ching, M. Phil. Third World Network, Malaysia
09:30	Evaluating the Contribution of GE Traits to Crop Yield: Adoption or Alternatives for Agricultural Policy?	Dr. David Quist GenØk – Centre for Biosafety, Norway in cooperation with Dr. Doug Gurian-Sherman, Union of Concerned Scientists, USA
10:00	Bt-Resistant Target Pests – Quick Occurrence in South Africa	Prof. Johnnie van den Berg North-West University, South Africa
10:30	<i>Break</i>	
11:00	Environmental and Agronomic Issues of GE Soy in South America	Prof. Walter A. Pengue University of General Sarmiento, Argentina
11:30	Hope Not Hype: The Future of Agriculture	Prof. Jack A. Heinemann University of Canterbury, New Zealand
12:00	<i>Discussion</i>	
13:00	<i>Summary of the Day & Closing</i>	

Organizers

European Network of Scientists for Social and Environmental Responsibility (ENSSER)	http://www.ensser.org
Third World Network (TWN), Malaysia	http://www.twinside.org.sg/
Federation of German Scientists (Vereinigung Deutscher Wissenschaftler, VDW), Germany	http://www.vdw-ev.de/

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International Network of Engineers and Scientists for Global Responsibility (INES)	http://www.inesglobal.com/
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Dates & Venue

07 October 2010 (14:00 - 18:15)
08 October 2010 (09:00 - 18:00)
09 October 2010 (09:00 - 13:15)
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¹ The content of the presentations and discussions at the symposium do not reflect the views of the EEA, its Management Board, or any other institution of the European Communities.

EXTENDED ABSTRACTS

Native Maize Landraces, Transgenic Maize, Food Security and Cultural Conflicts in Mexico

Prof. Antonio Turrent Fernández

*Instituto Nacional de Investigaciones Forestales, Agrícolas y Pecuarias (INIFAP), Mexico
and Unión de Científicos Comprometidos con la Sociedad (UCCS), Mexico*

Origin of maize and of maize landraces

THE most widely accepted hypothesis on the origin of maize indicates that the valley of the Balsas river in Mexico is the cradle of domestication, more than 6,250 years ago. Teosinte (*Zea mays* L. subsp. *parviglumis*), a native grass, would have been domesticated into maize in a single event (Matsuoka et al., 2002). It took Mesoamericans some 5,000 years to develop modern maize from the early domesticate (as represented by relic ears excavated in the Guilá Naquitz caves of Oaxaca, dated 6,250 years ago). By the time of encounter of the two worlds, modern maize was already the main food crop of Mesoamerica. Developing modern maize was a product of interaction between humans and a highly diversified environment. Varied topography, climate, soil and biota interact in short geographical distances in Mexico, resulting in multiple discrete and very different ecological niches. Many of these niches were settled by some 62 ethnic groups who used the ecosystem's natural resources for subsistence, and domesticated a number of crops. Maize, their main food cereal, was introduced to most human settlements by harnessing the natural diversity of the species that included frequent gene flow from teosinte.

A consensus, collective procedure to breed maize while used as food (Hernandez X. 1987, 1993) was developed as a long-term process. This process is known as "autochthonous maize breeding" (Turrent et al., 2009) and has led to some 59 maize landraces with vast intra-racial diversity in Mexico (Sanchez et al., 2000). Some landraces were adapted to high elevations; some tolerated or escaped severe drought, and some thrived in hyper acidic soils or hyper alkaline soils. Some had a large geographic domain; some were very early or very late maturing. The 59 landraces comprise a diversity of kernel colours, endosperm texture, protein and oil content, etc., that make them suited to pluricultural food preparations on an individual basis.

The 62 ethnic groups developed some 600 food preparations from "nixtamalized" maize plus some 300 types of tamales (Perez-Sanvicente, 2003). Nixtamalization or alkaline fermentation was invented as a means to improve maize nutritional value. Maize has been the staple cereal in Mexico for centuries. After colonization, failure of the "European conquistador" to appreciate nixtamalization, which at the time was a biotechnological breakthrough, led to the pellagra epidemic of Southern Europe in the

17th and 18th centuries, as maize spread throughout and became the staple food of the poor. Unfortunately, pellagra continues to be a human threat in parts of Africa.

Autochthonous maize breeding

This is a collective procedure of the 62 ethnic groups of Mexico that involves: 1) maintaining more than one landrace in the farm for satisfying traditional uses as separate entities; 2) interchanging seed among neighbours; 3) introducing allopatric (evolutionarily distinct) maize seed, making a seed mixture with own seed and producing hybrids; 4) planting progeny and judging performance; and 5) submitting the harvested ears to the process of seed selection in the granary by the homestead woman who selects only those seeds that are “typical” of the landrace. All together, this is an open system that seeks to enrich the landrace, and does so with new alleles that directly influence stability of yield and kernel quality accordingly to cultural consensus. Currently, there are some 1.5 million farming units that apply this process akin to parallel breeding, to maize landraces. Since the important traits of yield and kernel quality are quantitative in nature and are normally linked in specific regions of the chromosome space, many crossing-over recombinations are required so as to break those linkages and accumulate the more favourable alleles through selection. This procedure has been applied to the maize agroecosystem for 5,000 years. The sources of allopatric seeds have been from within Mesoamerica and as far as South America. However, evidence from the last 50 years has shown that public hybrids distributed in the maize agroecosystem have been used as allopatric materials in autochthonous maize breeding of landraces. The seed-pollen route to gene flow has been central to such a process in the centre of origin of maize, while the sole pollen route has played a secondary role.

Food security

The Mexican farming sector includes 3.8 million farming units that have a bimodal profile: either as campesino (individual, usually subsistence) or entrepreneurial (larger scale, commercial) farming. Sixty-six percent of all farming units are managed by peasants in units smaller than five hectares. Entrepreneurial farmers manage larger, modern and market-oriented farming units. The maize agroecosystem in Mexico covers 8.5 million hectares that are currently cultivated with non-transgenic technologies. There are currently two interacting sources of technology for maize in Mexico: pre-Columbian and classical agriculture. The campesino sector includes 62 ethnic groups, plus a majority of mestizo farmers and a small fraction of the creole farmers. They use pre-Columbian technology with elements of classical agriculture. The 59 maize landraces are grown mostly as a monoculture, usually with suboptimal rates of fertilizers, pesticides and herbicides. Collectively, landraces will typically adapt to any condition ranging from marginal to optimal in the maize agroecosystem. The 59 landraces are fundamental to rural food security and are the only source for the national requirements of maize as pluricultural food.

The entrepreneurial sector, on the other hand, follows the industrial agriculture model, growing non-transgenic hybrid varieties purchased annually from the private as

well as public seed markets. This sector farms irrigated as well as rain-fed quality land. At present, only 25 percent of the maize agroecosystem is planted with annually purchased hybrid seed; 75 percent is planted with native landraces and improved open pollinated varieties. It has been shown that the maize agroecosystem of Mexico has the resources so as to increase its production to 57 million metric tons of maize annually towards the year 2025. Current apparent consumption is 33 million metric tons. However, Mexico has currently a growing dependency on the regional grain market that reaches 32 percent of apparent consumption. This deficiency explains the proclivity of the Mexican government to seek commercial planting of transgenic maize in the maize agroecosystem. Unfortunately, this strategy erroneously ignores the critical value of biodiversity that helps ensure self-sufficiency.

Transgenic maize and maize landraces

It is well known that modern recombinant DNA technology leads to a random insertion of the transgenic locus. Currently, at least 52 independent transgenic events in maize are available in the world's transgenic seed market. It is very likely that all or most of the 52 loci are dispersed throughout the chromosome space of maize. Because of this dispersion of transgenes, it should be feasible to accumulate them all in one genotype through sexual reproduction, unless there is a deleterious threshold of accumulation that is smaller than 52 loci. It is also known that commercial transgenic constructs are somatic and not designed to be regulated by endogenous DNA sequences. The transgenic promoter is permanently active and promotes transcription in the nucleus and translation of the transgenic genes in the ribosome where it competes for energy and other inputs and interacts with resident DNA. One could imagine that one or a few transgenes in one genotype would not produce a strong metabolic cost to the host organism; however, there could be a deleterious threshold of transgenes accumulated over time.

Discussion

Coexistence of native maize and transgenic maize would be nearly impossible should transgenic maize be cultivated in Mexico on a commercial scale. The conjunction of at least four factors would lead to irreversible and progressive accumulation of transgenes in native maize: 1) autochthonous maize breeding; 2) a second wave of transgenic maize adapted to Mexico that would be used as allopatric genetic material; 3) reproductive biology of maize; and 4) the previously mentioned shortcomings of current recombinant DNA technology. In the long run (possibly 20 or more years), a deleterious threshold of transgene accumulation that would decrease native maize diversity would ensue. As maize landraces and their intra-racial diversity are critical to food security and to multicultural uses of maize as food, a limited list of non-transgenic and transgenic hybrids would hardly solve food security for all and would further impact the use of diverse maize types for multicultural uses as food. The Mexican government has recently granted permission to several multinational consortia to conduct 24 field experiments with transgenic maize in the Mexican states of Sinaloa, Sonora, Chihuahua

and Tamaulipas, all located in northern Mexico. The area sampled by the experiments covers some 754,000 hectares of irrigated maize plus 284,000 hectares of rain-fed maize. This region is cohabited by five ethnic groups and is home to some 29 maize landraces. According to a law passed in the year 2005, adoption of transgenic maize should follow a three-stage process: experimental, pilot and commercial. Given the current drive for transgenic maize commercialization elsewhere, one could anticipate that the multinational seed companies wish to shorten the three-stage process to the limit and open the whole country to maize transgenic technology. Some sectors within civil society, legislature and the scientific community are very actively pursuing strategies for engaging in this process and examining the wisdom of transgenic maize introduction in the centre of domestication. Who stands to gain and who pays the costs?

Conclusions

1. Transgenic maize technology is not necessary for maize food security for all and for multicultural uses of maize as food in Mexico.
2. Native maize landraces are necessary for maize food security for all and for multicultural uses of maize as food in Mexico.
3. Autochthonous maize breeding harnesses maize genetic biodiversity and should be protected from interference or hybridization of transgenic maize.
4. For these reasons, cultivating and importing transgenic maize should be prohibited in Mexico.

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India's Bt Brinjal: From the Supreme Court to Science in Public Debate – How Civil Society Prevailed Against Monsanto and the Regulator

*Aruna Rodrigues
Petitioner at the Supreme Court, India*

THE picture is incomplete. We must still win the war of obtaining a moratorium on genetically modified (GM) crops, because they present biosafety hazards which have not been disproved by the Indian regulators and the “industry” in stringent and independent safety testing protocols. Had the approval of Bt brinjal for commercialization by the apex regulator, the GEAC (Genetic Engineering Approval Committee), not been stopped by Jairam Ramesh, India’s Minister of Environment & Forests, then that would have been “open sesame” for Monsanto and the biotech industry all the way to the last Indian food crop. That was the plan. It is still the plan.

The battle of Bt brinjal is an extraordinary one by any standard. I am told, for example, that it is a first of its kind. I would agree with that for two reasons of my own. The first is not apparent except within India. The response to the idea of a genetically engineered national vegetable, the most important vegetable in India (the potato is not a vegetable), raised a national storm in a rare demonstration of cooperation nationwide, not seen since India’s independence in 1947. Ramesh also embarked on perhaps the first democratic consultative process with civil society in India (in the spirit and letter of the CPB), in seven well-managed and fully documented public consultations conducted in carefully selected, important Indian cities (Annexures I-IV <http://www.moef.nic.in>). I can assure you that this was courageous! He was swamped (more on these aspects later). The second is also relatively unknown except to an insider like me. Bt brinjal is perhaps a unique first also because it properly belongs to the arena of international cooperation. The superstars in the galaxy of stars in this fantastic saga that is stranger than fiction are a special breed of human beings who are also eminent international scientists and acknowledged experts in their particular specialism. They rolled up their sleeves, put aside large chunks of time, burnt the midnight oil to keep timelines demanded by court schedules and plunged into the very hard work, made harder still for having to provide and explain scientific evidence to a NON-SCIENTIST! That process began six years ago. The core group of four, which later doubled and even trebled as others joined the battle over the ensuing years (and ongoing) to provide evidence that has filled numerous volumes, are: Dr Arpad Pusztai, Prof Jack Heinemann, Prof David Schubert and Dr Doug Gurian-Sherman. But my particular thanks are reserved for Providence who sees fit not to usually disclose the future. In my case, with the greatest goodwill of even these great examples of kindness, had they known what was in store for them, they would have rightly avoided me. I recall the first affidavit I

received from David Schubert. I looked at it, completely baffled and in alarm. I didn't understand a word. Finally, I put aside every shred of self-respect and said to David: "*I comprehend the verbs that join the nouns. That is all. Please would you rewrite this in plain English.*" He did. After that, it went pretty smoothly.

GM crops make for dull news. Prior to the Bt brinjal debacle, there was near-complete ignorance about these crops. There was certainly disinterest. But Monsanto, with its deep pockets, regularly beat the drum on mythical, miracle yields of GM crops, the "success" of Bt cotton (the only commercialized GM crop in India) and the easy unscientific claim that GM crops would feed the world. Yet, the battle of Bt brinjal had to be fought in the public domain if we were to succeed. The evidence in the Supreme Court had to somehow be catapulted on to the outside, broadcast and understood. Thus far, we had failed miserably. And then something happened to catalyze the required widespread agitation by civil society across India on an unexpected scale. I call it the "Rub of the Green". I'm in Japan, a golfing country, so this is a phrase that I am sure is widely understood. Like a green genie of the environment, Jairam Ramesh was the right man in the right place at the right time, driving the unique Bt brinjal orchestra of science, civil society and public debate, in an extraordinary story that has all the magic and exhilaration of deflecting a golf ball into the right lie for an eagle. The coincidence of that time and place was made possible, in my opinion, by events in the form of orders of the Supreme Court and a timely General Election! What follows is the perspective from where I stand and have stood for 5½ years on the steps of the Supreme Court of India, with Prashant Bhushan (the able advocate on this case), and onward into Court No 1, where the Chief Justice of India presides with his Brother Justices to hear, among other cases, the **Public Interest Writ Petition (PIL)** for a moratorium on GM crops. The writ petition has had its ups and downs and no doubt, this will continue, but the ups were pivotal. They represent the milestones and the watershed that made for a coalescing over time of a situation where science in the cloistered hall of the Supreme Court found its way into the public arena and an agitating civil society that took up that science, and a media that was now agog, because of that *rub of the green*. These are the highlights of that process.

The PIL and its "grounds"

The "grounds" of the Supreme Court (SC) writ petition are: (a) the scientifically unsound release of genetically modified organisms (GMOs) was in violation of the Directive Principles of the Constitution of India, specifically Article 21 whereby the right to health and a safe environment is a fundamental right; (b) the Cartagena Protocol on Biosafety, the binding international protocol to which India is a signatory; (c) the Precautionary Principle (also of the CPB), which has also been upheld in Indian law and is a precedent.

Orders of the SC: Milestones and a watershed

Acting on an "Urgent Application" filed in July 2006, the Chief Justice ordered *an interim ban on all field trials in September 2006*. The timing was crucial as it scuttled

the approval of the Bt brinjal large-scale field trials and set back the regulators' plans and Monsanto by at least one planting season or **near 12 months**.

The watershed order

In February 2007, we succeeded in obtaining an order for the biosafety raw data of Bt brinjal to be put on the Ministry's website (in the public domain). Even so it took 18 months for India's apex regulator, the GEAC, to comply, which was in August 2008. In hindsight, even this was a good thing! *Here was the watershed*. I sent out an SOS. Four scientists responded and sent in their critiques as evidence to the SC: (a) the critical evaluation of the animal feeding studies by Gilles-Eric S eralini; (b) molecular characterization and genomics by Jack Heinemann; (c) gene flow to wild brinjal relatives by Doug Gurian-Sherman; (d) sampling and statistical significance of the data of animal feeding studies by Judy Carman.

The immediate impact of these appraisals was to force the GEAC to appoint an expert committee to evaluate them, called the Bt brinjal Expert Committee II (EC II), which was convened in early 2009.

What followed

Following a General Election in May 2009 which re-elected Manmohan Singh as Prime Minister, Jairam Ramesh was appointed Minister of Environment & Forests. His appointment was to be pivotal. When on 14 October 2009, the GEAC accepted the EC II report recommendation to commercialize Bt brinjal, he stepped in the next day to bar it in a pro tem measure of review because of the nationwide criticism of the EC II Report. He had been in office just 4-1/2 months!

From October 2009 to end January 2010, Ramesh instituted a process by which he invited documented responses to the EC II Report from all stakeholders, including the international community of scientists. Ramesh's initiative was uniquely democratic. He received in excess of two dozen scientific appraisals. This was astonishing and reflects the importance of the implications of releasing the world's first major GM food crop, the brinjal, in the world's centre of diversity and origin.

The impact of the Jairam process galvanized the media. It exploded. By February 2010, India and the world had heard of Bt brinjal. The scientific data from the SC started to percolate through to our State Agricultural Ministers, NGOs and farmer organizations. When the public consultations were held between January and 6 February 2010, civil society, farmers and state governments were primed and ready. The first of their kind, fully documented and video-taped, the seven consultations proceeded with virtual pomp and ceremony uniquely Indian, the din and dust, colour and theatre and eventually order! **631 comments** from stakeholders were recorded that reflected perspicacity and a surprising level of knowledge of the science and implications of Bt brinjal. Eyeballs glued to TV screens followed the fascinating consultations and debate. Civil society did an outstanding job of management and dissemination; and science had trickled down to our NGOs and right into our farming households. Ten state governments, which include the major brinjal production centres in Eastern India, said

“no” to Bt brinjal. Agriculture in India’s federal system of government is a state subject. We have 28 states.

On 9 February 2010, Jairam Ramesh announced a moratorium on the commercial approval of Bt brinjal, citing the need for further safety testing, and declared that he had been “*responsive to society and responsible to science*”. This was an extraordinary conclusion brought about in an unlikely series of events that converged and coincided to topple Bt brinjal and stop its approval for commercial release: the Rub of the Green that brought India back from the brink.

One hour before his announcement, Nina Federoff (US science and technology adviser), who flew into India to reportedly demonstrate US support for transgenic brinjal, had special advice for the Indian government when she declared on TV that Bt brinjal is good for India.

The risk assessment of the Bt Brinjal EC II Report and gaps

Bt brinjal Event EE-1 encodes for a chimeric (Cry1 Ac and Cry1 Ab) or fusion gene to be composed of three transgenes:

- *cry1Ac*, the gene for the insecticidal protein (coupled with the heterologous promoter called 35S from the cauliflower mosaic virus);
- *npII*, a gene that confers antibiotic resistance; and
- *aad*, another gene for antibiotic resistance.

The risk assessment by the government was found deficient on the following grounds:

Health: Bt brinjal has been modified to produce an “*unknown*” chimeric insecticide toxin containing “*Cry1Ab and Cry1Ac modified sequence*. Bt brinjal has 16-17 mg insecticide toxin per kg, as compared to Bt maize (1 mg/kg) (Seralini)”. The cry gene used was in fact a chimeric arising out of the laboratory and not the soil. The case for the safety of Bt brinjal was heavily based on the GEAC supposition that Cry proteins had a history of safe use. However, as noted in submissions to the GEAC by independent scientists, this supposition lacks merit. The various Cry proteins do not have a history of safe use in the diet of mammals and there is an absence of literature to support any claim to the contrary. There were indications of a possible toxic effect to livers and kidneys from the GM plant that were revealed by a careful reading of the evidence in the dossier. (Response to EC II health impacts, **Seralini**).

A single rat feeding study of 10 rats is used to support Mahyco’s application for safety for 1.15 billion Indians (10 rats each, male and female): This small sample size is central to the “*inadequacy of the study’s statistical power to find anything adverse*”. Again, 90 days is woefully inadequate to determine long-term chronic health effects which include tumours and cancers and of 1.15 billion Indians eating GM brinjal for generations. (Monsanto’s Dossier, rat feeding studies, statistical analyses, **Judy Carman**).

Both experts conclude that the release of Bt brinjal must be forbidden because of potential serious risks to human and animal health.

Genomic analyses: A proper safety assessment includes a molecular (genomic) level profile of the modified plant. A critical first step in a comparative process of risk assessment is hazard identification. This begins with an evaluation of the GM plant and is assisted by full and accurate descriptions of both intended and unintended changes that arise from the modification or the process of making and isolating the modified plant. The GEAC cannot conclude from Mahyco's data that there is a single insert and no additional inserts of unexpected size or sequence composition. The Bt brinjal producer has not submitted, and GEAC has not claimed to have reviewed or considered such approaches and data. Hence a thorough and meaningful hazard identification has not been possible. (Response to EC II Genomic Analyses, **Jack Heinemann**).

Gene flow: Mahyco presents no data that assesses the risks of gene flow from Bt brinjal to wild relatives. The company presents data that is wholly inadequate to predict gene flow. Several wild relatives of brinjal are found in India and have been shown to be sexually compatible with brinjal. Further, methods to prevent gene flow from crops to wild relatives currently do not exist. Gene flow from Bt brinjal to wild relatives, if commercialized, would therefore be virtually certain. (Response to EC II: Gene Flow, **Doug Gurian-Sherman**).

Environmental risk assessment: Brinjal plays a unique role in Indian society. It is one of the most important vegetable crops in India, especially for the rural and urban poor. About 61% is grown in the three eastern states of West Bengal, Orissa and Bihar by **small-scale resource-poor farmers**. These states have banned the use of Bt brinjal. India is the **centre of the world's biological diversity in brinjal** with over **2,500 varieties** grown in the country. Some local varieties have significant religious and cultural value.

Event EE-1 Bt brinjal poses several unique challenges because the likelihood of resistance evolving quickly is high. Without any management of resistance evolution, Bt brinjal is projected to fail in 4-12 years. Farmers are expected to retain only 10% of the increase in profitability from Bt brinjal, but are expected to retain 63% of the increase from brinjal IPM (Integrated Pest Management).

EC II does not acknowledge this risk and the Dossier does not propose effective means to manage it. The evolution of resistance to Bt crops is a real risk and is treated as such throughout the world. ("The scope and adequacy of the GEAC environmental risk assessment"; **David Andow**)

International protocols: Despite the GEAC claim, the EC II Report does not meet India's international obligations under all relevant treaties. There are two: (a) India is bound by the provision of the Cartagena Protocol on Biosafety. The Protocol under Article 2.2 stipulates parties to ensure that the development, handling, transport, use, transfer and release of any living modified organisms (LMO) are undertaken in a manner that prevents or reduces the risks to biological diversity, taking also into account the risks to human health and socio-economic and ethical implications in the spirit of

Articles 15 and 26 of the Protocol; (b) Codex Alimentarius Commission (CAC): *Principles for the Risk Analysis of Foods Derived from Modern Biotechnology and its supporting document the Guideline for the Conduct of Food Safety Assessment of Foods Derived from Recombinant-DNA Plants (2003, CAC/GL 45-2003)* for its assessment of potential effects to human health. The lack of compliance of the EC II Report with both the Cartagena Protocol and Codex highlights a serious deficiency in the EC II assessment.

Animal feeding studies for chronic toxicity: The regulator didn't require anything more than the sub-chronic 90-day rat feeding study, yet long-term, multigenerational and lifetime animal feeding studies are required to reveal long-term effects like cancers and reproductive problems.

Allergenicity: Testing was not Codex-compliant.

Assessing Systemic Risks – A Holistic Concept

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RISK means the probability that specific decisions, actions or events could lead to a particular intended gain or undesirable damage or harm. Risks are dealt with in practically any field of human life. Risk analysis attempts to formalize procedures to identify potential pathways along which risks can develop. Usually, quantitative statements for the involved probabilities are sought.

Risk assessment of technical systems is based on well-established routines. An important part is the calculation of probabilities of failure, based on experience with similar situations. Even for complex technical systems the approach can be expanded by investigating the probability of malfunction of any of the involved components and identifying the probabilities of co-occurrences. An implicit operation basis of conventional risk assessment is the assumption of an inherent limitation of negative events: In the worst case scenario, a technical system usually could be closed down. In the case of chemical hazards, substances dilute and degrade over time. In the case of radioactive contamination, the material takes more or less time to decay.

Genetically modified organisms (GMOs) are different. With technical systems, they share the property of being engineered to serve an intended purpose. With natural living systems, they share the property that they can self-multiply, grow, disperse, recombine, and evolve beyond what was initially intended. The self-reproduction potential implies that risk assessment and safety analysis of GMOs must be stricter and more comprehensive than the assessment of physical or chemical risks and cover a wide range of risk dimensions.

If only one of the several billions of oilseed rape seeds imported to Japan for processing should get lost and give rise to an invasive population, the resulting damage could be self-amplifying and even re-growing. Therefore, the level of improbability of undesirable events which have to be evaluated or tested in advance must be accordingly low.

There are two basically different risk categories which need to be distinguished: elementary risks and systemic risks. Elementary risks are those which are based on a direct cause-effect relation and can usually be calculated in probability terms. Gain and loss in gambling or occurrence frequencies of car accidents can be considered as elementary risks. Systemic risks are different. They are not based on single interactions or direct cause-effect chains but on the overlay and the co-operation (or co-functioning) of a large number of single events, all of which, in isolation, may be harmless. Systemic

risks (sometimes also called emergent risks) arise when a larger number of elementary events come together in a particular context of boundary conditions and bring up qualitatively new effects on a higher level of organization. Systemic risks do not exist at the level of elementary interactions. A traffic jam can be considered as an example: Any single driver could go down any road when acting in isolation and no others need to be taken into account. However, if large numbers of drivers attempt to go the same direction at the same time, they may block each other. A credit crunch would be an example of systemic risks occurring in the economy.

Both types of risks need to be considered for GMOs. The GMO risk assessment must take into account all relevant types of interactions organisms are potentially involved in. GMO risk assessment must initially be based on knowledge of the biotic properties of the parent lines and the role of the hereditary material used for genetic transformation. The molecular alterations and the induced biochemical and physiological changes serve as a starting point of the analysis. It is quite obvious that some, but not all, of the potential effects can be investigated or detected at the molecular level at which the genetic transformation is done. This is because the modification itself operates at the molecular level but is intended to bring up effects at the level of the individual organism.

The consideration of potential systemic effects has an important implication. It can be used to develop a guiding framework for organization of the overall risk assessment focussing on the connectivity of effects that can potentially aggregate to unintended outcomes. A systematic assessment needs to follow the organization of science, in particular the biological sciences. This “automatically” brings up a linkage of assessing a network of elementary as well as systemic interactions. This is because the different levels of biological organization are interlinked and all have their particular properties – emergent properties, which represent the level-specific characteristics. Each level requires specialized knowledge, specific terminologies and methods to capture the particular properties of the level.

If we briefly go through the levels of biological organization for a GMO risk assessment we pass the following “stations”:

- The level of molecular interactions which take place in the cell. Cellular metabolic processes can be captured in relevant parts when employing integrative biochemical methods – among others there are metabolomic methods to quantify a large number of metabolites synchronously.
- The level of sub-organismic interactions of cells, tissues and organs up to the level of the individual. Histological methods, assessment of growth performance, and phenological rating are among the approaches used at this level.
- The level of single populations, with their characteristics of spatial distribution, age distribution, dispersal and others, are assessed using well-established methods of population ecology, including population viability analysis.
- The level of organismic interaction, bi-trophic, tri-trophic and multi-trophic interaction is highly important. For GMOs this is in particular relevant to the interaction of the GMO with target/non-target organisms. Aut-ecology of different species, taxonomic competence and physiological expertise are among the various qualifications required at this level.

- At the level of the ecosystem in particular an integrated investigation of biodiversity, the composition of the community of organisms and energy flow and matter transfer takes place. Ecosystem services are also assessed at this level: Effects of ecosystem functioning on pollination services, water budget self-regulation, nutrient retention and the ecosystem functions and services have to be assessed.
- The landscape and the regional context are the next higher level. The cultivation of GMOs can well have implications for the landscape structure and the overall landuse system, which need to be assessed. Neighbourhood relations on the larger scale require an assessment at this level. Gene flow through cross-pollination of crops and dispersal processes between different locations and ecosystems usually need to involve the expertise of landscape ecology.
- Linked to landscape processes, socio-economic implications come into the picture. Changes of landuse patterns and implications for the sustainability of the used system are of crucial interest, e.g. for regulation which does not focus on the level of single farms or ecosystem locations, but requires applicability across larger spatial extents.

It has to be emphasized that such a systematic approach in risk assessment of GMOs is not yet an established standard – neither in the biotechnology companies nor at the level of competent authorities in the course of the approval procedure. So far, GMO risk assessment operates more on a weakly structured basis of collecting case specific ideas that tend to remain incomplete, in particular regarding the characterization of the receiving environment – which for example is a requirement of the Cartagena Protocol. The method of systematization which is outlined here facilitates a targeted review of what needs to be investigated before deliberate release or placing on the market takes place. What is required is the assigning of any of the executed investigations during the risk assessment to a corresponding level of organization. This brings up a synopsis that helps to identify remaining knowledge gaps:

- Are primary and secondary metabolic changes in the GMO sufficiently understood in all relevant details?
- Is the behaviour of the organism in the target environment well tested with regard to the potentially affected parameter?
- Are effects on relevant target and non-target organisms tested to a satisfyingly representative extent?
- Are there ecosystem implications in particular on the sustainability of the cultivated systems and the ecosystem services?
- Has the receiving environment been systematically characterized and assessed?

Answering these questions yields an overview, not only of what has been done, but also of what the field of interactions is that has *not* yet been surveyed.

Is this a holistic approach?

- *No*, in the sense that no executable assessment procedure would be absolutely comprehensive. It would not provide “absolute safety” and assurance that any possible risk will be anticipated and evaluated in advance.
- *Yes*, in the sense that any potential question and issue has its well-defined location in a system where you would expect it. This increases the probability to identify existing relevant gaps and involve the required expertise. It allows a more critical and well-informed survey.

The outlined approach is targeted and science-based. It would be irrational to argue that any of the organization levels listed here would not be relevant for risk assessment. Expertise at all these levels is constitutively required for a risk assessment according to the state-of-the-art. This has significant institutional implications. Risk assessment of GMOs cannot be managed as a task of “GMO-specialists” with a homogeneous qualification profile. It is practically not possible to cover expertise ranging from the molecular level to the landscape level encompassing agriculture and the full range of ecological relations without involving the full spectrum of specialized expertise. It must be demanded that for a competent assessment the coverage of expertise on both sides, the applicant as well as the risk assessors of the authorities, prove the coverage of the required expertise. In practical cases this will usually require the involvement of a network of institutions – not only a single GMO-branch or -department. The crop protection service of a country, the conservation agency, agronomic expertise, for specific purposes in land use analysis also the weather service, and remote sensing data may be required – all being required to contribute to an overall picture.

A look at the current institutional practice suggests that there is a lot of opportunity and room for improvement. A systematic coverage of relevant risk dimensions requires a structural broadening of the involvement of different levels of expertise in the assessment.

As an outlook, the presentation will point to issues so far neglected in safety assessment, in particular with regard to landscape analysis. Unintended dispersal plays an important role. If GM organisms disperse outside of their intended cultivation location, what do we need to know? In principle, precisely all of what could bring up unintended and undesirable effects – including combinatory effects that may result from interactions in a changed environment.

Sound Science – Assessment of Applications Sent to the European Food Safety Authority

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Background

IN the European Union (EU), a centralized evaluation system for the authorization of genetically modified organisms (GMOs) has been established and entered into force in November 2003. This system, according to Regulation (EC) No 1829/2003, gives a central role to the European Food Safety Authority (EFSA), located in Parma, Italy. The administrative units of EFSA are supported by Scientific Panels consisting of about 20 independent experts experienced in different fields relevant for risk assessment. The GMO Panel is responsible for evaluating the data provided by applicants in the authorization process. Based on this data the GMO Panel drafts an opinion, which is the final evaluation report and on which the authorization decision is based. The 27 Member States may provide comments but are not directly involved in drafting the opinion.

In the EFSA guidance document for the risk assessment of GM plants (EFSA 2006), EFSA describes its mission as follows: “... *EFSA’s risk assessments provide risk managers (EU institutions with political accountability, i.e. the European Commission, European Parliament and Council) with a sound scientific basis for defining policy-driven legislative or regulatory measures required to ensure a high level of consumer protection with regards to food and feed safety.*”

This so-called “sound science” is also reflected in the Directive 2001/18/EC on deliberate release of GMOs into the environment, where it reads in Annex II: “... the following general principles should be followed when performing the e.r.a. [environmental risk assessment]: ... *the e.r.a. should be carried out in a scientifically sound and transparent manner based on available scientific and technical data*”.

For GMOs this means that the opinion drafted by the GMO Panel should be based on “sound science”, and one step further down, that the applicants have to provide data which are based on experiments and trials which are designed according to high quality standards. Some Member States doubt that this is always the case and therefore the German Federal Agency for Nature Conservation commissioned the Environment Agency Austria to carry out a study on the scientific quality of data provided in the application dossiers.

Evaluation of information provided

The study (Dolezel et al. 2010) focused on data for environmental risk assessment. Food safety, toxicology and related issues were out of the scope. The evaluation therefore only contained applications for cultivation, for which the data provided have to fulfil the requirements laid down in Directive 2001/18/EC. Applications for seven different GM maize events, one GM potato, and one oilseed rape were analyzed and the main weaknesses and faults for different assessment categories identified.

Besides many cross-cutting issues, like the extrapolation of data from other GMOs or countries/continents, the insufficient documentation of experiments, lack of distinction between published and unpublished data, and cross-referencing between different applications for different GMOs, a number of specific problems have been identified. A few examples are described below:

Comparators are essential for a comprehensive risk assessment as they form the baseline for many different parameters. The comparators used are in many cases not described in detail. Only for two out of the nine GMOs discussed in this study was a breeding history of the comparator included in the dossier. For all other dossiers, the description was rather vague, e.g. “near isogenic line” or the hybrid name was given, without any details on how this hybrid relates to the GMO under study. In three notifications not even an agronomic assessment of these comparators was included. With regard to comparative treatment in the case of herbicide-tolerant GMOs, a high variability of different approaches was observed. The use of different herbicides and different ratios of treated vs. untreated plots could be observed. In many cases the description of the different field trials and the respective treatment as well as the pooling of data was not sufficient.

Data derived from **field trials** form the basis for the assessment of many different parameters, ranging from agronomic performance to compositional analysis and environmental effects. Therefore, the setup and the detailed description of the trials and selection of environments are crucial. However, the methodology (i.e. size, number of plots, comparators used, etc.) varied considerably between the different field trials even within one application dossier, sometimes being presented in an incomprehensible way. No justification is given as to why certain environments are chosen for the field trials and how the data derived from these trials reflect the “receiving environments”, in this case, Europe.

In some cases, the **statistical analysis** of the data was not based on common scientific understanding, meaning that data sets have been pooled, e.g. across locations or years, while other data sets have not been included in the analysis, e.g. one out of three growing seasons. In no case was a justification given as to why a certain approach had been followed, and neither a description if the preconditions for the used statistical tests (e.g. normal distribution of data) were met nor the statistical power of the experimental setup was given.

With regard to testing of effects on **non-target organisms**, a great variability of approaches and methodologies concerning the containment level and the used test material (isolated protein or different plant parts) could be observed. Though most of the studies used more than one setup, for some GMOs, tests were only carried out in the

laboratory, i.e. using quite artificial conditions, while others only investigated possible effects in the field, hence lacking basic and quantifiable laboratory data. The selected test organisms were usually quite similar, including honey bees, earthworms, green lacewing larvae, lepidopterans (usually the Monarch butterfly not living in the EU) and some others. An exposure assessment was only carried out in three of the nine studies. No special attention was paid to endangered species, and in no case was a species endangered in Europe tested. In general, it was observed that the species selected for testing were selected according to taxonomic rather than functional groups. No systematic approach was used for the selection.

Different **regional environments** were also not considered in the studies carried out. Most field trials have been carried out in the USA or South America. This means that little or no data from the receiving environments, i.e. Europe, were included in the dossiers. The limited European data were usually pooled with non-European data in the statistical analysis, making them inaccessible for detailed evaluation.

There is no commonly accepted definition of “sound science”, and scientific results are always subject to scrutiny. There are always discussions between scientists on conflicting results and different scientific approaches and methodologies. However, the examples discussed above show that in the risk assessment of GMOs often not even basic scientific principles are followed. This includes experimental setup, data analysis, presentation and interpretation of results, and shows a clear need for further standardization, which should lead to improved quality standards.

Recent developments

Since the finalization of the study in 2009 there have been some developments, especially with more detailed guidance and stricter requirements for the applicants. In March 2010, EFSA published a draft guidance document on environmental risk assessment, which could be considered as a major step in the right direction (EFSA 2010). It takes up at least some of the identified problems and contains, among others, more detailed requirements for testing of effects on non-target organisms, e.g. obligatory whole plant studies, selection of test organisms according to functional groups; guidance on the statistical basis for field trials by requiring a certain number of test sites and replicates and also some, though at this point quite rudimentary, guidance on how to take regional characteristics into account. It also lays down which comparators need to be included in the studies. One major drawback of this document is the continued lack of guidance on post market monitoring. However, according to the European Commission and EFSA, this will be dealt with in a next step. Currently, the document is under final revision and will be submitted to the European Commission in November 2010.

Conclusions

Though the EU has established very strict rules on how to conduct a risk assessment and has a number of guidance documents at hand, which should be followed by the applicants, the main problem is still insufficient implementation. For the environmental

risk assessment of GMOs this means that the necessary data are either not provided or incomplete and conclusions drawn are not based on science but on extrapolation or opinions. Unfortunately, this has been accepted in many cases by EFSA and the GMO Panel. This means that not even the responsible authority has implemented the legislation and its own guidance correctly. At least some progress towards better guidance and also stricter implementation has been made recently. The definition of “sound science” as a basis for GMO risk assessment and therefore as the basis for decision-making should not be subject to interpretation by applicants or any group of scientists who are members of a biosafety panel or committee. Data requirements, as well as minimum quality standards, like problem formulation, power analysis or the definition of comparators, need to be defined on a scientific basis. However, once defined, quality and scientific standards need to be followed and implemented by the competent bodies, in order to ensure a high degree of safety for consumers and the environment.

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Bt Crops – Controversies Around the Science Necessary for Risk Assessment

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DESPITE 15 years of industrial-scale production of genetically modified (GM) crops at least in five countries, no consensus on the applied environmental risk assessment (ERA) methodologies, let alone agreed standardized testing procedures exist. But all regulations of GM organisms call for some risk assessment to be carried out. Hence, I will provide a review of the current implementation of risk assessment in relation to GM crops and identify the most severe shortcomings that we propose to alleviate with an alternative concept for ERA for GM plants.

The ERA currently focuses only on the novel trait expressed by the introduced transgenes and novel substances (e.g. Bt toxins) produced in the GM plant. This current interpretation of the regulations of GM plants, including those laid down in the Cartagena Protocol, was made precedent by the US regulations (Mendelsohn et al. 2003) and is grounded in the concept of “substantial equivalence” of GM plants and their non-transformed counterparts (FAO/WHO 1996; OECD 2000). Despite the fact that OECD consensus documents on compositional considerations have been published for various crops, no obligatory guidelines exist regarding what to test and how similar the values should be in order to still comply with being “equivalent”. For example, the degree of acceptable difference between a non-transformed parent cultivar or any other cultivar of the same plant species and the GM event is not defined (Millstone et al. 1999). Often, substantial equivalence data do yield significant differences even outside of reported ranges for other (at times “historic”) cultivars but are then dismissed as “biologically irrelevant”. The substantial equivalence (or familiarity) concept is therefore highly contested in particular with regard to its relevance for biosafety evaluations as it serves as the prime screen for unintended effects (Royal Society of Canada 2001; Freese and Schubert 2004). According to the developers of GM plants and some government regulators, the declaration of substantial equivalence legitimizes the omission of testing for anything but initial acute short-term effects of the isolated microbial toxin (Garcia-Alonso et al. 2006; Romeis et al. 2008).

An improved ERA concept for the assessment of potential adverse effects of GM plants has been proposed that is tailored to the GM case and the receiving environment and system-oriented with the GM plant at the centre. The proposed testing strategy builds on the outcome of the “GMO ERA Project” produced by an international group of scientists from the global working group “Transgenic Organisms in IPM and Biocontrol” run under the auspices of the IOBC (International Organization for Biological

Control) (Hilbeck and Andow 2004, Hilbeck et al. 2006, Andow et al. 2008). It has been further developed and embedded into the EU provisions for ERA of GM plants (EC 2001 and 2002) in a project commissioned by the German Federal Agency for Nature Conservation (Hilbeck et al. 2008). The concept focuses on sequential testing from laboratory to the field and is prescriptive with regard to a procedure developed for selection of testing organisms that do occur in the receiving environment and the proper protocols for testing them. It further includes potential adverse effects arising from direct and indirect exposure to the whole GM plant and from secondary stressors that are required to realize the benefit and intended effect(s) of the GM plant, such as the application of broad spectrum herbicides.

Hazard identification

Information on the GM plant's biology, ecology and current spatio-temporal agronomic use and limitations of use is compiled. This includes comprehensive information on the molecular characterization of the GM plant, its introduced genetic material and tissue-specific expression of the novel proteins. Information on the intended effect(s) includes data on the problem to be solved with the proposed GM plant, efficacy data of it demonstrating the ability to solve that problem, the severity of the problem, how widespread the problem is and who is mostly affected by it. To do that in an inclusive and transparent manner, scientists have developed a stakeholder process and tested it for the use in ERA of GM organisms (Hilbeck and Andow 2004; Nelson and Banker 2007). Such a systematic process allows one to identify the main users of the GM plant, and to estimate the likely adoption rate and spread of the GMO after release. This in turn allows one to delineate the potential receiving environments and focus the analysis on those where the adoption is expected to be greatest with the assumption that potential adverse environmental effects will likely manifest where the GM crop is grown most frequently and is most widespread.

Selection of testing species

In current risk assessments, ecotoxicological testing that is carried out for Bt plants follows closely the methodologies developed for environmental chemicals like pesticides. Testing organisms are chosen from a list of universal standard species that are representative of trophic levels in general, rather than present in a given receiving environment (Hilbeck and Andow 2004). Our proposed methodology for testing of non-target organisms is prescriptive with regard to the use of a procedure for selection of testing species and the development of proper testing protocols and risk hypotheses tailored to each case and receiving environment.

Exposure assessment – from pathways to scenarios and protocols

For the species ranked highest in the previous component, an exposure analysis is conducted to determine whether or not and to what degree the species come into contact with the primary stressor, i.e. the GM plant including the transgene product or the

altered composition of primary metabolic compounds, or any secondary stressor required for realizing the transgenic function of the GM plant, e.g. the broad spectrum herbicide for herbicide-tolerant GM plants. Because GM plants can multiply and spread via pollen and seed flow, this exercise will differ significantly from an exposure analysis of chemicals and will include also an analysis of the spread of GM plants into other ecosystems, including aquatic systems. Currently, there exists very little if any data on biogeochemical cycling, spread and fate of transgene products in the above- and below-ground ecosystems of the receiving environments and their potentially changing bioactivity and metabolites in the varying environmental media. Some studies published to date have confirmed the suspected spread of Bt toxins through food chains (Harwood et al. 2005; Zwahlen and Andow 2005; Obrist et al. 2006; Harwood et al. 2007). However, the bioactivity of such metabolites remains unknown to date. Several experiments studied the impact of Bt crop plant material on soil organisms with variable results ranging from some effects to transient effects to no effects (e.g. Zwahlen et al. 2003; Blackwood and Buyer 2004).

Effect determination – doing the testing and generating the data

The main step here is the implementation of the testing plan developed before. However, again, controversy exists over whether the evidence for “reason for concern” should be experimental or could be extrapolated from theory and experience in related fields of science (Zwahlen and Andow 2005; Andow et al. 2006; Garcia-Alonso et al. 2006; Lang et al. 2007; Romeis et al. 2008). Secondly, whether or not an absence of a “reason for concern” (i.e. evidence) constitutes evidence for safety to the effect that no more testing at higher levels is required is subject to debate. As GM plants and their biochemical products can take on different properties in different environments and at different ecological organizational levels, data documenting/confirming the lack of evidence of adverse effects must be produced at every testing level.

Risk characterization – synthesizing all information

In this component of the ERA framework, the risk is characterized by combining and comparing the obtained data and information. While the emphasis is placed on quantitative data, all gathered qualitative information is also integrated here. The outcome of activities in this component is a list of potential risks with an estimation of their strength (high, moderate or low) that were experimentally confirmed. Rejected potential adverse effect hypotheses that could experimentally be proven as unlikely or minor or non-existent are excluded. Equally important, the delimitation of the ERA and transparent documentation of remaining uncertainties is identified here. From this, guidance for possible risk management strategies and monitoring plans can be derived. With this proposal, we distinctly disagree with the proposal that ERA of GMOs could be entirely a desk exercise based on “data collected for other purposes” and may not require the “acquisition of new data” as put forward by developers (Raybould 2006; Raybould 2007). This leads to the current situation that new GM maize cultivars combining and stacking different Bt toxins by conventional crossing of various GM

maize varieties enter the market largely untested. A Bt maize event called “Smartstax” (AGBIOS GM Database 2009) that combines 6 insecticidal Bt toxins and resistance genes for 2 broad spectrum herbicides could enter the market with close to no testing for toxic or environmental impacts relying entirely on “the environmental risk assessment of the individual events” – except for one additional study with an unspecified non-target organism, the results of which are not even summarized (EPA OPPTS 7501P). This in our view is not science-based, lacks the required precaution and entirely puts the discovery of any potential interaction, cumulative, indirect and long-term effect of the combined potpourri of 6 toxins and 2 herbicide residues on human and animal health and the environment in the marketing phase, i.e. the farmer and consumer.

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GM Maize and Glyphosate-Based Herbicides – Health Studies

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Introduction and context

THE debate on the safety of genetically modified organisms (GMOs) used for food and feed is still very lively throughout the world, more than 15 years after their commercial release. Unfortunately although some stakeholders pretend there is a history of safe use of GMOs, there are no human or animal epidemiological studies to support such a claim, in particular because of the lack of labelling or traceability in GMO-producing countries. As a matter of fact, 97% of edible GMOs among cultivated ones (soy, corn and oilseed rape or canola, excluding cotton) are grown in South and North America. All these plants have been modified to tolerate and/or produce one or more pesticides, and thus contain their residues at various levels. These are mostly from Roundup, a major herbicide used worldwide and tolerated by around 80% of GMOs, or from modified Bt insecticide toxins directly synthesized by the GM plants from the transgenes. In fact, to analyze subchronic or chronic toxicological signs, it is more informative to concentrate on studies that include numerous blood and organ parameters. Most of these are 90-day-long feeding regulatory trials on rats eating GM corn or soy. It is the raw data of the companies which attracted our interest to this case; the raw data which we obtained by court order with the help of lawyers (since the data were kept confidential). We re-analyzed these data and detected significant statistical differences (~9%) which concentrated mainly on kidneys and livers. These significant effects were all interpreted as non-relevant for the safety of GMOs by the companies as well as by the official competent authorities granting approval (e.g. EFSA). While the requirement for longer and more detailed regulatory tests would change the profitability of GMOs, they would protect mammalian and human health, which seems essential to us.

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Debate on insufficiencies in the experimental design

All 90-day regulatory rat feeding studies with GMOs have been constructed according to the same scheme. The insufficiencies of the experimental design can be underlined as follows:

- a) Too small a number of animals studied: Ten individuals measured for biochemical parameters out of 20 per group. This might be enough for long-term experiments, but not for such a short period of time. A small number of effects or of low amplitude are induced, similar to when a chronic pathology is slowly developing. These kinds of protocols could result in low power of statistical tests and therefore lead to many false negative results (for example to wrongly reject a possible effect of the consumption of GMOs). In such conditions, the observed effects would hardly constitute a sufficiently coherent and consistent clinical picture for the authorities to worry about.
- b) Too many control rats: Additionally, the number of controls was four times higher in these regulatory tests, which have been used all over the world to authorize the main GMOs. Such an imbalance between control and treated rats conceals observable effects. This principle was accepted by official committees: out of 400 rats there were only 80 eating GMOs (and only 40 biochemically analyzed), thus four groups of ten animals, with two dosages (11 and 33 percent GMO in equilibrated diet), and two types of blood analyses per group (after five and 14 weeks).
- c) Too many control treatments: The 320 non-GM-fed animals were treated in fact with seven different diets which were supposed to represent a variability of the possible regimen. Six constituted the so-called “reference” groups with feed not demonstrated as substantially equivalent. Moreover, two dosages in the control groups were chemically equivalent to the GM diets; they were made with the isogenic maize or maize close to the GM variety.
- d) The rat was the only mammal fed with GMOs for three months.
- e) The regulatory test was only performed once for each GMO, which was then supposed to be eaten all over the world.
- f) The duration of 90 days is the longest test in the file and only on young adult mammals; it was not long enough to observe chronic effects.
- g) The lack of developmental, reproductive as well as chronic or multi-generational tests is the subject of a heated debate for GMOs already commercially available.

This experimental protocol from Monsanto has been uncritically accepted by many competent authorities in the world, mostly confidentially. We deeply disagree with this design. Moreover, we underline the preoccupying side effects on liver and kidney physiology in particular, because they are the major detoxifying organs reacting in case of food intoxication.

Divergent biological interpretations

The biological interpretations become crucial after global statistical agreement, to some extent. Two possible issues arise here: either a demonstration of innocuousness (Monsanto et al.'s opinion), or preoccupying disruptions that should be followed by longer-term tests prior to market approvals (our opinion). The main differences between Monsanto's biological conclusions and ours, following statistical differences in biochemical and organ parameters, are these:

- a) For the record, we would like to state that any early sign of difference should be collected in a table to get a global picture of the animal physiology after GMO consumption. It is really impossible within 90 days, with one single experiment in the world and such a small number of rats, to get a consistent toxicological picture. This is a major point because we are concerned about possible chronic pathologies. Some effects may not be of major amplitude yet; however, some are. For instance, the increase of the hearts' weight of 11 percent in males for NK603, or 40 percent increase in plasmatic triglycerides in females eating MON 863 (together with a pre-diabetic profile), could be considered as enough to trigger a moratorium. As a matter of fact, Monsanto did not repeat their studies.
- b) The statistical differences are often compared to the GM-treated groups and the so-called "historical standards of the species" which are undefined, like the also undefined "normal range". This allows one to simply consider larger variations as normal for subjective reasons. The differences have to be considered first with the closest control group, the isogenic control line. It is only afterwards that it could become possible to compare them with experimental reference groups (Monsanto et al. did that first) receiving a non-equivalent regimen (for instance at the level of salts or sugars). We recall that the reference groups are still too numerous in comparison to treated rats.
- c) The significant effects are taken into account by Monsanto et al. only if they are similar in both sexes. This is denial of common scientific knowledge. The chronic pathologies, as well as the endocrine disturbances or some cancers, are usually sex-related and not proportional to the carcinogen dose taken over a short duration.
- d) For Monsanto et al., the absence of dose-dependent effects is a reason to neglect the significant differences. This is absolutely unacceptable, just because, for instance, we need to take into account endocrine disrupting antagonist possible actions. It has to be underlined moreover that this dose-dependency cannot be approached with a two-dose study as presented to the authorities by Monsanto (11 and 33 percent of GMO in the diet).
- e) Since anatomo-pathological lesions could arise long after the beginning of a treatment or plasmatic biochemical disruptions, the necessity of correlations between these statistical differences and histopathological findings (overall within three months) cannot be requested to conclude on a preoccupying sign, by contrast to what is defended by Monsanto et al. In addition, histological slides and embedded organs are the property of the company, and were not double-checked by official

committees or independent authors. We ask for an official counter-analysis, particularly of the male kidneys in these studies, which were found to concentrate more than 43 percent of all disrupted parameters, in a meta-analysis of all published data on commercialized GMOs. We already know that during the MON 863 study, Monsanto highlighted anatomic signs of “chronic progressive nephropathy” on GM-fed male rats’ kidneys. However, Monsanto did not see these signs as being noteworthy due to the fact that, according to them, they were well known to occur in old Sprague-Dawley rats. But these rats were only five months old, and still quite young at the end of the experiment. These anatomo-pathological signs on kidneys were not noticed during the studies on MON 810 and NK603 maize. Yet the rats were the same age and from the same strain.

- f) The chemical composition of the food/feed is an important indication. However all insecticide toxins/herbicide residues/unintended or unknown metabolites (due for instance to insertional mutagenesis or new metabolites) are not assessed; thus the substantial equivalence with non-GM products is not proof of innocuousness.
- g) A bias for biological interpretations could also be seen in the fact that the regulatory toxicological tests are presented to authorities and commented on only by the companies developing industrial products. A proposal for independent studies from companies to encompass this problem has been made to the Council of European Ministers.

Conclusions and perspectives

As a conclusion, we call for the promotion of transparent, independent and reproducible health studies for new commercial products, the dissemination of which implies consequences on a large scale. Lifetime studies for laboratory animals consuming GMOs must be performed, which would be in contrast to what is done today, like the two-year-long tests on rats for some pesticides or drugs. These tests could be associated with transgenerational, reproductive or endocrine research studies. Shortcomings in experimental designs may raise major questions on other chemical authorizations.

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Transgenic Fish – How to Assess Contained Use Applications

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Introduction

SEVERAL public and private research groups are following the aim of developing and finally marketing genetically engineered (GE) fish. The commonly used methodology is the microinjection of the recombinant DNA fragment into fertilized fish eggs or early embryos. Inducing transgenesis in fish is a relatively inefficient process. Only about 1% of the treated eggs will stably incorporate the recombinant DNA into its genome and subsequently transmit the transgene to its progeny. The use of growth hormone (GH) genes has been most popular. At least 14 species of fish have been genetically modified with GH genes, and although they mostly grow faster than controls, they do not necessarily grow to a larger mature size. The economic aim of this research is a reduction of costs of feedstuff and raising time. Up to now no GE fish has been approved for commercial production. There are many concerns about the use of modern biotechnology in aquaculture in developing countries, in relation to the environment and human health but also in relation to socioeconomic considerations and intellectual property rights (IPR) and also whether or not good biosafety regulations are in place.

Impacts of transgenes

A fish which expresses the target gene at an acceptable level may not be able to transmit the gene to progeny because many GE fish are genetically mosaic individuals and unless the gonads possess the transgenes, the trait may not be heritable. Pleiotropic effects also need to be considered when assessing the properties and impacts of GE fish. When GE coho salmon was compared to a control group, it was found that the genetic engineering process had affected the activity of a number of naturally existing genes. These changes included an increased amount of the protein parvalbumin-b, a protein that has been identified as a major food allergen in fish.

Because transgenes are patentable and developing countries are forced to allow for their patenting when joining the World Trade Organization (WTO), IPR issues are of special concern. Developing countries are frequently disadvantaged in the use of, and access to, IPR because of increasingly protective attitudes taken by owners of IPR (CIPR 2002). A further area of debate concerns issues of animal welfare with regard to accelerating industrial meat production through GE applications.

Contained use

When considering adverse effects on biodiversity, it is very important to consider that the escapes of GE farmed fish are unpredictable in terms of damages, primarily due to the poor knowledge we have about aquatic biodiversity. The major focus of the relevant literature is on the effects of escaped GE fish on populations of their natural counterparts, but it is important also to bear in mind possible impacts on aquatic ecosystems as a whole. Risks might arise from the transmission of transgenes to wild fish or the establishment of the GMO itself as permanent inhabitant of an aquatic ecosystem.

To address these concerns, a number of research efforts to develop systems for sterile fish production are being made. The techniques include triploidization, antisense transgenics, ribozymes and gene targeting (Maclean & Laight 2000). According to the authors, adopting a precautionary approach should be a general rule, but still each individual case needs studies, appraisals and the establishment of best possible containment measures before approval for commercial production should be given. Scientists at the Swedish Gothenburg University recognized that GE fish has great potential to revolutionize commercial aquaculture, but advised the EU to take precautions and to avoid their culture in open systems.

GE fish risk assessment depends on a number of factors (Aleströ & de la Fuente 1999): (i) the species released and the biotope it is released into, (ii) the character of the transgene and the new phenotype, (iii) the general fitness of the GMOs versus wild populations, and finally, (iv) the number of released GE fish, which is an important factor. Many authors consider GE fish as an “exotic” species which behaviour is hard to predict. “Case by case and step by step” risk research and risk assessment, starting with physically contained testing and moving to confined field tests via small scale and intermediate scale to large scale, are necessary to decide about moving forward from research to development and finally commercialization.

Triploidization

The creation of triploid genomes is a measure to suppress the appearance of ecological risks arising from mating between GE and non-GE fish, considering that triploids are sterile. Triploids would also be economically beneficial for the developers because it hinders unauthorized breeding of the transgenes. In practice, it is possible to develop tests on triploidy, but not on sterility. In some species a certain percentage of triploid individuals could be in fact fecund. Additionally, it would be very useful to induce the reversion of sex in GE fish, so that only females grow up (Maclean & Laight 2000). However, neither of these approaches is 100% effective, nor can the genetic changes induced by triploidy be accurately assessed, monitored or controlled.

Atlantic GE salmon

The most advanced project is conducted by AquaBounty Technologies Inc, headquartered in Massachusetts (USA), which has produced and patented Atlantic GE

salmon (*Salmo salar*) with the gene construct pOnMTGH1. In patent application PCT/CA92/00109 (Hew & Fletcher 1992) gene sequences derived from ocean pout anti-freeze gene promoter and other fish gene sequences including chinook salmon GH gene are described. Some evidence is presented for increased growth rate and earlier smelting. Transgenic individuals were on average more than 11 times heavier than controls. In contrast to mammals, salmonids continue to grow throughout their entire life cycle, and even small differences in specific growth rate quickly translate into very large increases in size. Since 1996, AquaBounty has worked on receiving the approval of the US authorities to become the first producer of a GE animal for human consumption. The US Food and Drug Administration (FDA) recently announced that the risk assessment has been concluded and that neither health nor environmental risks are to be expected based on the data provided by the company.¹ Anticipating large public interest in this issue, the FDA will hold public expert meetings in September 2010 to discuss the biosafety data and conclusions, but also issues on labelling food from GE fish. The expert meeting was not able to come to recommendations, because many experts regarded AquaBounty's data as too weak and premature (Heavey 2010, Voosen 2010).

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¹ US FDA: Public Meetings on Genetically Engineered Atlantic Salmon, <http://www.fda.gov/NewsEvents/PublicHealthFocus/ucm224089.htm>

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Genetically Engineered Viruses – Environmental Challenges

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Introduction

GENETICALLY engineered or modified viruses (GMVs), from a number of taxons, are being increasingly used as live vaccine vectors. There are four broad genetically engineered virus application areas that may have environmental implications: i) Immunization against infectious disease in livestock species; ii) Immunization of wildlife species which are reservoirs of infectious agents causing disease in humans and livestock species; iii) Control of pest animal population densities by either direct lethal control operations or immuno-contraception; and iv) Human vaccination programmes with GMVs that are able to jump species barriers directly, or following recombination with naturally occurring viruses.

All these applications may, to varying extents, represent release of GMVs. The different application areas call for different considerations and options with regard to choice of virus vectors and genetic engineering strategies. Generally speaking, there are two strategies: The first is represented by gene-deleted viruses to be used for homologous vaccination, i.e. to achieve protective immunity against the GMV itself. The induced deletions most commonly concern genes that are necessary for the virus to carry out a full multiplication cycle, or are implied in viral virulence. Furthermore, non-essential genes may be deleted in order to obtain markers for monitoring unintended vaccine virus spread.

Recombinant virus vectors obtained by transgenesis represent the second strategy. Such viruses are created in cell cultures by simultaneous transfection with a plasmid carrying a gene from the virus/microbe that is to be targeted, and infection with the virus vector of choice. The plasmid construct is such that the transgene contains DNA sequences homologous to a viral gene at each end. Hence the transgene is transferred and integrated to a predetermined site in the virus vector genome by homologous recombination. The most commonly used vector viruses are members of the DNA virus families Poxviridae and Adenoviridae.

Cross-species transfer of viruses

The opportunities for cross-species transfer of mammalian viruses have increased in recent years due to increased contact between humans and animal reservoirs. It is,

however, difficult to predict when such events will take place since the viral adaptations that are needed are multifactorial and stochastic. Recent examples of viruses that have crossed species barriers are HIV, hantaviruses, haemorrhagic fever viruses, arboviruses, avian influenza virus, SARS-associated coronavirus, Nipah and Hendra viruses, and monkeypox virus. The emergence of HIV exemplifies how multiple independent cross-species transmissions of simian viruses that are not associated with disease in their natural hosts eventually resulted in the establishment of two types of HIV in the human population. While adapting to its new host the virus underwent a myriad of molecular changes. Changes in social behaviour of humans may well have offered opportunities for newly evolved HIV strains to become pandemic. Crossing the species barrier from one animal species to another is most readily noticed when it is associated with overt pathology. In the past, such events may have been overlooked as the underlying cause of the emergence of a new disease. When a virus transmitted from non-human host reservoirs to humans causes such a disease, it is called a zoonosis.

The emergence of new viral infections often follows environmental, ecological and technological changes caused by human activities (Louz et al., 2005). Such activities may lead to an increased contact between humans and livestock on one hand, and animal hosts acting as reservoirs of zoonotic viruses on the other hand. Agricultural development, an increased exploitation of environmental resources, growth and increase in the mobility of the human population and trade and transportation of food and livestock, have been identified as important factors contributing to the introduction and spread of a number of new viruses in the human population. Against this background, the intensified use of viruses and their genetically modified variants as viral gene transfer vectors for biomedical research, experimental gene therapy and as live-vector vaccines is a cause for concern (reviewed by Louz et al., 2005).

Relevant risk assessment questions for GMVs

The different virus families have their specific life cycles and host preferences. Hence it is impossible to make risk assessment schemes that are valid for all potential virus vectors. Risk assessment must be performed on a case-by-case, step-by-step basis, taking into account the characteristics of the ecosystem into which the virus will be released, and the ability of the virus to engage in transboundary movements (Traavik, 1999; McFadden, 2005). The most evident risk issues related to the release of GMVs or unmodified viruses are the known and unknown unknowns related to (i) infection of non-target species, (ii) recombinations with naturally occurring relatives and (iii) integration of GMV DNA into host cell chromosomes. Ideally, before any GMV, or unmodified virus intended for release, becomes implanted into a new location/ecosystem, a number of crucial questions should be answered, for example:

- Can the released virus engage in genetic recombination, or by other means achieve new genetic material? If so, will the hybrid offspring have changed their host preferences and virulence characteristics?
- Can the released virus or any hybrid or mutated offspring infect unintended species?

- Can the released virus or any hybrid or mutated offspring integrate into the genomes of host cells?
- Can other viruses that are present within the ecosystem influence the infection with the released virus or its offspring?
- Can insects or migrating birds or animals function as vectors for the released virus or its offspring, to disseminate viruses out of their intended release areas?
- For how long can the virus and its offspring survive outside host organisms under realistic environmental and climatic conditions?
- Are the virus and its offspring genetically stable over time?
- Can the virus or its offspring establish long-lasting, clinically mute, persistent or latent infections in naturally accessible host organisms?
- Can the virus or its offspring activate or aggravate naturally occurring latent or persistent virus infections?

Some of these questions deal with the biological and phenotypical characteristics of a supposed genetically stable GMV. But the situation becomes even more complex and unpredictable if the GMV parental strain under certain conditions or circumstances is genetically unstable, giving rise to viral strains with altered characteristics (Traavik, 1999).

Gaps in information necessary to perform environmental risk assessments (ERAs) for released or escaped GMVs

So far no GMVs have been thoroughly risk assessed from an environmental point of view. Risk assessments have focused on unintended effects of the vaccine arising in the vaccinated individuals, or in individuals of the same species that are infected by viruses shed from vaccinated individuals. The main areas of information gaps related to GMVs are:

- Lack of knowledge about naturally occurring relatives in the actual ecosystem. Such information is necessary to assess the possibilities of new viruses through recombination.
- Lack of knowledge concerning recombination events and their consequences.
- Lack of knowledge concerning non-target effects and transboundary spread of the GMV or its offspring.
- Lack of knowledge concerning integration of GMV DNA, or fragments of it, into host cell chromosomes.
- Lack of knowledge concerning the genetic stability of the GMV and its offspring. If the transgene is deleted over time, monitoring of GMV spread and changed phenotypic traits may become difficult/impossible.

Current research on risk assessment of GMVs

There is little information available that relates to ERA of virus releases. To our knowledge research related to environmental effects is only being performed for

alphaherpesviruses (Thiry et al., 2006) and poxviruses (orthopox and avipoxviruses). Such environmental biosafety-related research has been performed for a number of years in Norway, but we have no present knowledge of other research groups with a similar focus. We have focused on biosafety issues of the orthopoxvirus strain MVA (Modified Vaccinia Ankara), considered to be a very safe vaccine vector because of high gene expression capacity and lack of viral replication in mammalian cells (Drexler et al., 2004).

The most relevant conclusions from our studies may be summed up as follows:

Orthopoxviruses, and hence potential recombination partners for orthopoxvirus-vectored vaccines, are common in different small rodent species populations all over the country, and small rodent predator species have antibodies to such viruses (Sandvik et al., 1998; Tryland et al., 1998).

Recombination between an influenza-transgenic MVA and a naturally occurring orthopoxvirus is readily demonstrated in cell cultures. The recombinants may have phenotypic characteristics different from the parental viruses. Recombinants may be genetically unstable and “throw out” the influenza transgene. This will eliminate the most logical tag for vaccine monitoring (Hansen et al., 2004).

The absolute and relative permissivities for MVA multiplication and viral shedding have not been thoroughly studied. GM and unmodified MVA may, contrary to the general dogma, perform fully productive infections in highly relevant mammalian cell types, and other mammalian cell cultures are semi-permissive to infection (Okeke et al., 2006).

DNA sequencing revealed that orthopoxviruses can be clearly separated into geographically distinct strains, and it was inferred that these strains have distinct evolutionary histories in different rodent lineages (Hansen et al., 2009). Upon sequencing of an orthopoxvirus isolated from a human clinical case, it was established that this strain was a naturally occurring hybrid between two distinct orthopoxvirus species. This is the first proof of concept for orthopoxvirus recombinations taking place under authentic ecological circumstances (Hansen et al., 2010).

Homologous recombination between orthopoxvirus-vectored vaccines and naturally circulating orthopoxviruses, genetic instability of the transgene, accumulation of non-transgene expressing vectors or hybrid virus progeny, as well as cell line/type specific selection against the transgene are potential complications that may result if poxvirus-vectored vaccines are extensively used in animals and humans (Okeke et al., 2009a). Phenotypic characteristics of recombinants between genetically modified and naturally occurring orthopoxviruses may be unpredictably different from any of the parental viruses (Okeke et al., 2009b). Contrary to common assumptions, some avipoxviruses may carry out productive infections in mammalian cells, and avipoxviruses within a restricted geographical area may be more genetically diverse than realized so far (Weli et al., 2004 and 2005).

The implications of these studies for ERA of transgenic viruses, and the lack of GMV biosafety relevant research will be further discussed.

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Feral Growth of Genetically Modified Oilseed Rape Around Harbours in Japan and Its Impact on the Environment

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Introduction

JAPAN imports more than two million tons of oilseed rape (OSR) a year for food oil, of which 90 percent are from Canada. In 2009, about 90 percent of OSR in Canada was genetically modified, most of which was herbicide-tolerant. As a result, many volunteers of GM-OSR are found around harbours in Japan. We have surveyed the feral GM-OSR around harbours to consider how we can conserve the domestic Brassicaceae from introgression of modified genes since 2004, because commercial cultivation of GM-OSR is not carried out in Japan. The main survey areas are the ports of Yokkaichi and Nagoya. The concern over gene transfer from GM-OSR to other Brassicaceae is realistic because many experiments and natural surveys show genetic crosses between *B.napus* and other Brassica species and Brassicaceae genera (Chevre et al. 1997; Brown et al. 2005; Beckie et al. 2006). Our research shows that gene introgression has occurred in domestic crops and natural weeds in Japan over these years.

Materials and methods

The samples were collected around the roads from ports to seed processing factories. Thirty surveys were carried out around Yokkaichi port since 2004. Many feral *B.napus* are growing and sometimes flowering year round at the roadsides, although most domestic Brassicaceae plants grow annually from winter to spring. *B.napus* and domestic species of *B.rapa*, *B.juncea* and *B.oleracea* were analyzed. Plants from a different genus, *Sisymbrium sp.*, were also collected in 2009 and 2010 in Yokkaichi region. The samples were analyzed by simple lateral flow test. The method used immunochromatography to detect the proteins produced by herbicide-tolerant genes. Two types of herbicide tolerance, glyphosate and glufosinate, were checked for. Glyphosate tolerance was detected by the CP4EPSPS protein from *Agrobacterium tumefaciens* and glufosinate tolerance was detected by the PAT protein from *Streptomyces hygroscopicus*. Transgenes were also detected by PCR methods if necessary.

Results

A lot of feral *B.napus* were discovered around Yokkaichi harbour in July 2004. They were found also outside of the Yokkaichi port area, along roads to an oil factory 40 km away from the harbour. The cause of feral OSR was spilling of the seeds during truck transportation. Roadside OSR sometimes bloomed and were germinating or producing seeds year round. This means that the feral OSR became perennial, although most domestic Brassicaceae are usually annuals. The season independent growth of *B.napus* may increase the chance of hybridization with related domestic cultivar species and wild *B.juncea* and other Brassicaceae. As a result of perennial growth of *B.napus*, sometimes large feral plants were observed. Some of the OSR developed to large populations and others grew as single plants in this area. Generational alterations of feral OSR were also observed. Feral OSR scatter seeds, giving rise to offspring around themselves. So, even if efforts were successful in stopping trucks carrying GM-OSR from spilling seeds, this would not effectively influence the situation.

The contamination rate of GM-OSR has increased considerably over these seven years. More than 70 percent of feral OSR were herbicide-tolerant in 2009. There were two kinds of OSR: glyphosate- and glufosinate-tolerant. In the surveys of 2008 and 2009, we found stacked GM-OSR that show tolerance to the two herbicides, glyphosate and glufosinate. The samples were analyzed by PCR method and confirmed the existence of the two kinds of herbicide-tolerant DNA sequences. This means genetic crosses have occurred naturally between the two kinds of GM-OSR by co-existent growth. By sympatric co-existence of herbicide-tolerant OSRs and other domestic Brassicaceae, possibilities of out-crossing increase between them. We found some hybrid plants between glyphosate-tolerant *B.napus* and wild *B. juncea*, and hybrid plants between glyphosate-tolerant *B. napus* and *B.rapa* in Toyokawa city in Aichi prefecture in 2008 and 2009, near an OSR processing factory. The factory produces machine oil from imported OSR which was contaminated with fungi or soil during the shipping procedures and could not be used for food oil. There are big populations of *B.juncea* and *B.rapa* on riverbanks near the factory. In addition, we found glyphosate-tolerant broccoli (*B.oleracea*) on the roadside in Yokkaichi region in 2009.

In 2009 and 2010, we found another example of cross-hybridization between GM-OSR and a plant from a different genus, *Sisymbrium sp.*, a Brassicaceae weed, which grows all around Japan. The hybrid plant shows different morphology from Brassica species, but exhibited herbicide tolerance. Usually *Sisymbrium altissimum* grows near the hybrid, which may be one of the parents of the hybrid. Both glyphosate- and glufosinate-tolerant weeds were observed. A stacked hybrid weed tolerant to both glyphosate and glufosinate was also found in Yokkaichi region. These were confirmed by the existence of nucleotide sequences via PCR. Most of these *Sisymbrium* weeds do not produce seeds and show sterility. However, sometimes, small amounts of seeds are found which are different from *Sisymbrium*'s. One weed was found in 2009, but 13 were found in 2010. 92.5 percent of the weeds are herbicide-tolerant, which shows an abnormally high rate of the modified genes.

Discussion

Japan imports over two million tons of OSR seeds a year, mostly from Canada. In 2009, more than 90 percent of OSR from Canada was genetically modified. Reflecting the situation in Canada, the feral OSR around Japanese harbours contains a considerable rate of herbicide tolerance, as described in the results. The Japanese situation was reported by Saji et al. (2005) and Kawata et al. (2009). The possibility of hybridization between OSR and its wild relatives has been discussed by many authors since the development of genetically modified crops, because of the concern about potential introgression of genetically modified genes into cultivated or wild relatives (Mikkelsen et al. 1996; Timmons et al. 1996). Brown et al. (1996) carried out extensive experiments on pollination by herbicide-tolerant *Brassica napus* with its wild relatives in field conditions, before commercial cultivation of GM-OSR. They suggested that transportation would give rise to volunteer weeds by seed spillage, pollen movement would be affected by wind direction, hybridization would occur between GM canola and its wild relatives in field conditions, and bridge crosses between the hybrid and its relatives could play a major role in the movement of herbicide-resistant genes into the natural weed population. FitzJohn et al. (2007) reviewed many articles on hybridization within Brassica species and allied genera and estimated potential transgene escape. They reported at least 23 Brassicaceae that can hybridize successfully with *B.napus*, including *B.rapa*, *B.juncea* and *B.oleracea*. Sixteen different genera containing *Sisymbrium* can also hybridize with *B.napus*. Hansen et al. (2001, 2003) demonstrated extensive introgression between *B.napus* and *B.rapa* in the natural population and persistence of the introgressed gene in the following generations. Transfer of modified genes from *B.napus* to *B.rapa* was genetically analyzed in detail under Japanese conditions by Lu et al. (2002).

Perennial growth of GM-OSR increases the chance of hybridization and gene transfer to related cultivars and weed plants. We have many agricultural cultivars for food of *B.rapa* and *B.oleracea* in Japan. Wild *B.juncea* grows around many riverbanks. Our findings of hybrids between GM-OSR and *B.rapa*, *B.juncea* and *B.oleracea* show that the possibilities have become reality. The occurrence of the herbicide-tolerant weed, *Sisymbrium sp.*, is the first case reported in the Japanese natural environment. Although most hybrids are sterile, some of the plants have seeds. If the hybrid seed grows and back-crosses with the parent weed, gene introgression may occur into the environment, which influences the conservation of biological diversity.

Conclusion

Unintended dispersal of GM-OSR around Japanese harbours was surveyed, especially around Yokkaichi port since 2004. Many glyphosate and glufosinate herbicide-tolerant feral OSRs were discovered. Perennial growth and generational alteration of the OSR were confirmed. The cause of volunteer growth of OSR was transportation and spillage of the seeds from trucks moving from the import harbour to an oil factory and to another seed processing factory. Stacked gene herbicide-tolerant OSRs were also discovered. This means that natural pollination and hybridization between two kinds of GM-OSRs have occurred. We have discovered several hybrids between

herbicide-tolerant *B.napus* and cultivars (*B.rapa* and *B.oleracea*). In addition, hybrids were also discovered with weeds, *B.juncea* and with a different genus, *Sisymbrium sp.*, in 2008 and 2010. The modified gene transfer to weedy plants may influence the natural conservation of biological diversity.

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Transgene Flow in Small-Scale Systems – Ghana as Model

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TO allow for a fuller consideration of the implications of GMOs in developing countries relative to the developed-country context, this paper will present an account of a project that assessed the implications of GMOs in small-scale agricultural systems in Africa by focusing on a specific sector of agricultural food production in Ghana. Maize cultivation has been used in this instance to distinguish the differences that exist between agriculture in the US or Europe and elsewhere in other developed countries and those under African conditions. In particular, the following elements are considered: the agricultural structure, the landscape, crop field locations, isolation distances and spatial patterns of agricultural fields which are completely heterogeneous. On the basis of a modelling approach, representative scenarios are calculated to address the possible impacts of gene flow between GM and conventional fields due to cross-pollination. An extension into the topic will be made to gain an understanding from the perspectives of the farmers themselves, as to which seed sources and factors they consider most relevant or useful in terms of accessibility to seeds, agricultural productivity and economic considerations. These data are highly relevant to the biosafety discussion because of the urgent need for scientifically acceptable and applicable guidance on small-scale monitoring of GMOs, particularly the need to identify suitable test parameters to assess gene flow for the receiving environments.

This study aimed to bridge the gaps by developing appropriate sampling methods for estimating potential impacts of gene flow due to the introduction of GMOs in small-scale systems. So far, large-scale data on the ecological impacts of GMOs in small-scale agricultural systems are still very limited. This paper will address the topic in two distinct parts. First, it will provide data on the location and general field geometries, as well as the isolation distances of the prevailing cropping conditions. Based on these data, estimates are calculated for gene flow within sown conventional maize due to the introduction of GM crops. Thirdly, the paper will discuss possible socioeconomic impacts on farmer livelihoods and assess implications for seed diversity as well as the biosafety implications. These are of utmost relevance for Ghana since the Seed Bill, which addresses seed use, exchange and distribution, is presently before parliament for consideration alongside the Biosafety Bill, yet to come into force. The Seed Bill was reviewed to include biotechnology and the consideration of genetically modified crops. Amendments are being made to ensure not only the protection of the environment and genetic diversity of landraces but also health issues including food safety relative to

seed distribution due to the introduction and use of GMOs in the country. Also of great concern is that in Ghana, nearly 70 percent of agriculture is carried out under the smallholder context, and over 90 percent of Ghanaian farmers rely on saved seeds from previous harvests or exchanged for their annually sown crops, rather than through purchase of certified seeds. Furthermore, maize serves as the basic food necessity for the greater part of the country's population. On the one hand, GM maize is advertised by the developers as providing an added value by improving upon weed management and a reduction in costs and amount of herbicides applied to field crops. Resistance to insect pest attack is additionally an alternative trait promoted by the developers.

Therefore, to strengthen the understanding of biosafety, it is important for all stakeholders, decision-makers and policy-makers to consider from a scientific perspective whether seed segregation or trait traceability is feasible following the introduction of GMOs into small-scale agriculture, taking into account the Ghanaian agricultural, social and environmental conditions. Gene flow is discussed in this context. Gene flow is a relevant ecological process, but the effects which it may have must be fully assessed. For a complete risk assessment, this is required in accordance with the Cartagena Protocol on Biosafety (2000). Gene flow incorporates genes into the gene pool of one population from one or several populations, eventually determining the genetic structure of natural populations. Dispersal of seeds and pollen are important mechanisms leading to gene flow in plant populations. In the context of GMOs, concerns have been raised over possible agronomic and environmental impacts. Agronomic impacts could result from the incorporation of transgenes from GM crops into native crop species, with potential adverse effects for the conservation of landraces and plant breeding. Some environmental effects relate to impacts on non-target insect species or herbicide resistance leading to persistence or invasiveness of species. The economic value to GM growers or of hybrids due to transgenes in conventional harvests is highly uncertain. Again, the potential loss of farmer livelihood and seed security is an additional concern.

Methods

A Global Positioning System (GPS) receiver was used to determine maize cultivation locations. Data collected were systematized in a database and field acreages calculated based on their geometries that were estimated using GIS software. A quantitative model was applied to estimate gene flow through representative scenarios of actual field practices in a 20 km² area. Subsequently, cross-pollination rates between GM fields and conventional fields were calculated. Questionnaire surveys were conducted with about 200 farmers to evaluate the extent of seed acquisition sources and their preferences, examining also the socioeconomic conditions of the smallholders.

Analysis and conclusions

Traceability ensures quality control in seed supply systems. The data indicates that once GM products are introduced, traceability of GMOs would be very difficult in case adverse impacts eventually emerge. Secondly, the very small nature of fields and

their close proximity would not allow for the implementation of isolation distances between GM and conventional fields as a management strategy. This poses a high probability for transgene contamination of local seed varieties as a potential consequence. Thirdly, the large number of smaller fields suggests a larger number of potentially different seed varieties being sown by smallholders potentially leading to increased genetic exchange and genetic variability. Cultivation of GM maize will come with a high probability of impacting on the seed landraces and genetic diversity including areas where conventional farming is likely practised. Fourth, the highly informal nature of the small-scale agriculture or open space farming in backyards or in marginal spaces already makes it very difficult to regulate the cropping situation and agricultural markets, including any GM seeds that may be introduced in the future. These conditions only pose a major difficulty since options that would allow for consumer choice and trait segregation are substantially less. Therefore, the containment of GM products, including mitigation or removal from the environment, would require very heavy investments and political commitment to implement. The use of isolation distances as a management requirement to control gene flow between GM and conventional fields is challenged. An estimated 98% of all fields numbering about 1,300 documented for the study area had a maximum of 3, 4, 5, 7 and 8 field neighbours at distances of 20 m, 40 m, 60 m, 80 m and 100 m respectively. With a minimum nearest neighbour distance of 5 m and a maximum nearest distance of 459 m, the practice of co-existence of GM and conventional cropping would not be possible. In terms of field sizes, nearly 98% of all fields encountered were below 0.5 Ha in size, with the remaining 2% ranging from 0.5 to 2 Ha and above. On-farm conservation of maize genetic resources would be unlikely due to higher cross-pollination in smaller and adjacent fields as indicated by the model. The size of a recipient field, its location and the distance to a GM field proved to be very important parameters to estimate the probability of transgene introgression. The assessment allowed testing potential cross-pollination rates even for a single GM field as the most minimal scenario, which turned out to be unfavourable with a conclusion that with an introduction of a GMO, areas cropped to conventional agriculture will gradually be impacted by the GMO and this will potentially increase across the landscape.

In relation to seed use, seeds sown by farmers are obtained from a wide range of sources. The use of food grains as seed grains was most significant, and often not distinguishable as such. However, seeds from previous harvests are also a crucially relevant source. Farmers confirmed that the varieties sown are mostly landraces because they provide economic advantage due to savings on the cost of acquiring certified seeds. Seeds that were sown from previous harvests are significant and largely influenced by the availability of financial resources. Thus, the growing of GM crops could pose additional difficulties to the farmers, in particular through the payment of technology fees that could be an economic threat to the security of farmer livelihoods. The model confirmed that a single GM field for example, comprising 0.2% of conventional cropping area could potentially lead to gene flow in the considered region up to 0.12% of transgenes in harvested crops. This data indicated that very small fractions of transgene introgression in the order of magnitude of up to 2.61% in conventional fields are possible under the various tested conditions. In comparison to the EU regulatory standards for GM labelling threshold of 0.9%, any increasing condition of transgene presence in conventional

harvests from any magnitude above 0.9% is sufficient to be labelled, considered or sold as GM. For the African conditions, the consequences would be immense. In the first place, it will limit the potential to expand agricultural food exports and deepen existing trade barriers between the continent and developed nations. The study showed that local farmers would have difficulty differentiating between conventional and GM at the smallholder level, which introduces a further complexity. With the introduction of GMOs, the area cropped to GM would most likely increase over time due to transgene flow into conventional fields and further exacerbate the impacts. In conclusion, it is important to note that the agro structure and seed exchange practices would make it possible that gene flow even at low frequencies may easily be detected in conventional production, possibly with legal repercussions for the small farmers if patent infringement clauses are applied by the developers. It is also worth noting that the usefulness of isolation distances under the described conditions is challenged. Finally, with the introduction of GM, on-farm conservation of conventional seeds would be very unlikely due to increasing content of GM traits in farm-saved seeds. The implications of this outcome seem to be an issue and should therefore be a subject of further discussions.

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Transgene Flow in South African Commercial Maize Cultivation

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Background and aim

SOUTH Africa is one of the few countries in Africa that have introduced genetically modified (GM) crops. First-generation GM maize has been commercially grown in SA since 1997 (Department of Agriculture 2005). In 2008, South Africa was ranked eighth in terms of global commercial GM production that included cotton, soybean, yellow and white maize (James 2009). Gene flow from GM crop to non-GM crop may have several consequences including: the development of resistance in target insects for Bt crops; the contamination of landraces; loss of trade in processed and bulk grain commodities; the contamination of the food chain by experimental, industrial or pharmaceutical GM crops. Thus, similar to other GM producing countries, SA has to deal with considerations to minimize or prevent comingling through the use of isolation distances, where necessary, for GM field trials and coexistence (Huffman 2004; Moschini 2006). A further consideration is that specialist GM crops, e.g. for pharmaceutical production, nutritional enhancements, and bio-fuels, are expected to become a reality within the near future. Minimizing gene flow for different applications from contained use through to environmental release is an important consideration. In the past, several studies have recorded different distances of cross-pollination for maize, using a variety of field trial designs under different environmental conditions (Aylor et al. 2003; Bannert and Stamp 2007; Burris 2001; Byrne and Fromherz 2003; Della Porta et al. 2008; Garcia et al. 1998; Henry et al. 2003; Jemison and Vayda 2001; Luna et al. 2001; Ma et al. 2004; Paterniani and Stort 1974; Stevens et al. 2004). However, these trials have usually been small plots and not on the scale of commercial farming. Furthermore, very few of these studies have made specific recommendations with regard to the ideal isolation distance required in terms of different stringencies for minimizing cross-pollination. For example, different tolerances for comingling may apply to field trials under contained use compared to the production of maize engineered for bio-fuels. There is also no published data regarding the extent of cross-pollination for maize in South Africa and regulators have to base decisions on available data not necessarily applicable to South Africa. Thus the aim of this study, conducted from 2005 to 2007, was to determine

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the extent of maize cross-pollination under South African conditions in the context of commercial farming practice, which could inform the regulatory decision-making process with regard to GM field trials.

Materials and methods

Field trials were planted with a central plot of yellow GM maize (0.0576 Ha) surrounded by white non-GM maize (13.76 Ha), in two different geographic regions over two seasons with temporal and time isolation to surrounding commercial maize planting. Cross-pollination from GM to non-GM maize was determined phenotypically, across 16 directional transects, every 2 m up to 100 m and thereafter every 10 m up to 300 m. Pollen was captured during flowering in four wind directions and genotyped using PCR. Pollen counts during flowering were compared to weather data as well as percentage cross-pollination. The data was transformed logarithmically and mean percentage cross-pollination compared to high cross-pollination.

Results and discussion

Although there was general congruency between wind data, pollen load and cross-pollination, it is evident that wind data and pollen load do not solely explain the directional extent of cross-pollination. We suggest that swirling winds and other biotic factors may have contributed to this incongruence. The highest cross-pollination ranging from 54% to 82% occurred at 2 m from the pollen donor and declined sharply up to between 20 and 25 m, a trend similar to other studies (Henry et al. 2003; Jemison and Vayda 2001; Luna et al. 2001; Ma et al. 2004). Interestingly, a low percentage plateau of cross-pollination was observed up to the furthest distance sampled. There was a high correlation of logarithmically transformed mean percentage cross-pollination of distance ($R^2=0.97$). Based on the logarithmic transformation of cross-pollination over distance, 50 m is sufficient to minimize cross-pollination to between <1.0% and 0.1%, 159 m for <0.1% to 0.01% and 501 m for <0.01% to 0.001%. However, an important consideration when using mean cross-pollination values is that the potential of cross-pollination to occur may be underestimated. To test this hypothesis, we performed a logarithmic transformation of high values of cross-pollination over distance. It is interesting to note that there was a high correlation for high values of cross-pollination over distance ($R^2=0.95$). Based on these values, a theoretical isolation distance of 135 m is required to ensure a minimum level of cross-pollination between <1.0% and 0.1%, 503 m for <0.1% to 0.01% and 1.8 km for <0.01% to 0.001%. However, it is not practical to apply such stringent isolation distances, especially when different minimum levels of comingling may be required. We therefore suggest that a combination of temporal and distance isolation be combined, taking into account the GM maize pollen sources within the radius of the most stringent isolation distance required. We also investigated graphical shifts in percentage cross-pollination over distance, over the different locations at which trials were planted. We noted that a shift in percentage cross-pollination over distance was similar to the comparison of mean compared to high values for cross-pollination. Based on the incongruence between pollen load, environment and cross-pollination, as

well as taking into consideration the comparison of mean compared to high values of cross-pollination, we suggest that pollen load, environment and reproductive physiological characteristics are factors in determining cross-pollination.

Based on these data, the following is recommended to achieve minimal cross-pollination at different threshold levels:

- **Field trials:** To minimize out-crossing to a non-detectable level (0.01%-0.001%) the isolation distance should be at least 1.87 km. It may be difficult to achieve this in practical terms and it is suggested that a combination of spatial and temporal isolation be used taking the following into consideration:
 - o Apply a four-week temporal isolation up to a minimum distance of 503 m to the nearest maize planting.
 - o Apply a two-week temporal isolation up to a minimum distance of 1.87 km to the nearest maize planting.
- **GM seed production:** To prevent the development of illegal stacked events during seed production the recommendations for field trials should be applied.
- **Non-GM seed production for export purposes:** In order to comply with export requirements for non-GM seed, i.e. GM is not detectable, the recommendations for field trials should be applied.
- **Non-GM production:** Depending on the required threshold for non-GM production the following measures can be applied:
 - o 1% threshold: A minimum isolation distance of 135 m should be applied. It may be difficult to achieve this in practical terms; instead it is suggested that a combination of spatial and temporal isolation be used taking the following into consideration:
 - o Apply a four-week temporal isolation up to a minimum distance of 36 m to the nearest maize planting
 - o Apply a two-week temporal isolation up to a minimum distance of 135 m to the nearest maize planting.
 - o 0.1% threshold: A minimum isolation distance of 503 m should be applied. It may be difficult to achieve this in practical terms; instead it is suggested that a combination of spatial and temporal isolation be used taking the following into consideration:
 - o Apply a four-week temporal isolation up to a minimum distance of 135 m to the nearest maize planting
 - o Apply a two-week temporal isolation up to a minimum distance of 503 m to the nearest maize planting.

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Patenting Genes and Plants: Intellectual Property Rights Transform Research and Agricultural Innovation

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Introduction

INTELLECTUAL property rights (IPRs) are exclusive (monopoly) rights granted to an inventor for a limited period of time in exchange for a public disclosure of an invention. Patents are one type of intellectual property protected by national law and are legally enforceable in the country where it has been applied for and obtained. A patent may be granted if it meets the following criteria: new, involves an inventive step and industrially applicable (useful). Minimum global intellectual property rights standards are set by the World Trade Organization's (WTO) Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement), for WTO members to implement nationally. Patents must be available for any inventions, whether products or processes, in all fields of technology. Exceptions for certain public interests are allowed. Under TRIPS, the minimum term of patent protection is 20 years.

Patenting genes and plants

Living organisms were initially not considered patentable subject matter, but that changed with the US Supreme Court decision in *Diamond v. Chakrabarty* in 1980, which upheld the patenting of a genetically engineered (GE) oil-eating bacterium. Since then, many national laws have opened the possibility of patenting microorganisms, cells, genes and other sub-cellular components (Correa, 2010). At the same time, Article 27.3(b) of the TRIPS Agreement obliges WTO members to patent microorganisms and to protect plant varieties (by patents, an effective *sui generis* system, or a combination of both). While under the TRIPS Agreement plants and animals may be excluded from patentability, on the flip side this means that they may be patented. A significant number of free trade agreements promoted by the US and the EU have required the expansion of patent protection over biological materials, particularly plants (Correa, 2010). As a result, "patents on life" have been granted on DNA sequences, genes, cell lines, microorganisms, GE organisms, plants and animals, etc. Such patents reflect the commodification of genetic resources, and the potential monetary returns have provided incentives for "biopiracy" – the monopolization of genetic resources and associated traditional knowledge taken from peoples or farming communities that developed and nurtured these resources, without their prior informed consent or even knowledge.

What are the implications?

This discussion is focused on the implications of patents on GE genes, seeds and organisms, which have raised several worrying prospects relevant to livelihoods and food security, agricultural innovation, ownership and control of agricultural resources, and research, including biosafety research. The increasing use of these patents is aiding the consolidation of the seed, agrochemical and biotechnology companies, with food and agriculture increasingly dependent on a small number of powerful multinational corporations (Heinemann, 2009). An example of the vast reach of these corporations is embodied in the Monsanto ownership, since 1996, of the European patent covering all GE soybeans and seeds. This patent was revoked in 2007 after challenges brought by civil society. In that period Monsanto cornered 90 percent of the GE soybean market globally. Such monopolies lead to lower competitiveness, and increased costs for farmers (IAASTD, 2009). Broader still are patents that rely on genetic homologies to claim genetic components of organisms across taxonomic groups, such as Syngenta's attempt to claim monopoly control of basic gene sequences that regulate flowering and plant architecture in rice. The scope of this patent application was so wide that it extended to other major cereals and flowering plants (Oldham, 2005).

Another aspect of concern is the recent attempt by Monsanto to extend the scope of patents from genetic information to derived products even where such information performs no function (Correa, 2007). Monsanto had sued European importers of soybean meal produced with Roundup Ready seeds in Argentina, erecting barriers to trade to force the Argentine government to impose on farmers a "technology fee", even though the transgene was in the public domain in Argentina. Monsanto withdrew the suit in 2010 and the European Court of Justice later ruled against the company.

As transgenes are patented, saving GE seeds in countries like the US now constitutes a patent infringement and has resulted in lawsuits against farmers for suspected seed saving. As of 26 October 2007, Monsanto has filed 112 lawsuits, involving 372 farmers and 49 small farm businesses, and has won more than \$21 million (Center for Food Safety, 2005, 2007). However, the majority of cases brought by Monsanto have ended in confidential, out-of-court settlements, so the aggressive defence of its patents is not truly reflected. Farmers' rights to save, use, exchange and sell seeds are thus threatened by such patents, with potential food security implications. In many developing countries, farm-saved seed is a large percentage of seed used, reaching above 80 percent for self-pollinated and subsistence crops (Correa, 2010). Furthermore, farmer experimentation is also potentially restricted, curtailing the crucial contribution of farmers to agrobiodiversity and seed development (Heinemann, 2009; IAASTD, 2009).

Parallel to the trend of corporate concentration in agriculture is the increasing privatization of agricultural research, with the private sector outspending the entire CGIAR international agricultural research system by 30 times in 2000 (Kiers et al., 2008, cited in Heinemann, 2009). This shift from the public to private sector has various implications on the innovation pipeline, with biotechnology products attracting a disproportionate share of funding. Beyond this, it channels science education and training down certain pathways at the expense of others (IAASTD, 2009). Patents on genes and

plants can also become a barrier to access and rapid adoption of new products as they create new hurdles for local research and development (IAASTD, 2009). Moreover, owning the DNA sequence of a gene implies an extension of ownership to the enabling technologies behind, and applications of, this information, e.g. the diagnostic used to identify the gene as a molecular marker in applications such as marker-assisted breeding (Heinemann, 2009). An example from the medical field is Myriad Genetics' patents on the BRCA1 and BRCA2 genes, associated with greater susceptibility to hereditary breast and ovarian cancers, that secured the exclusive right to the diagnostic tests. Myriad's patents were recently ruled invalid, although the company will appeal.

Also of concern are the difficulties faced by biosafety researchers in obtaining samples to conduct independent research on the risk aspects of GE crops, which is needed to ensure that their impacts are properly measured, assessed and understood (Heinemann, 2009; Scientific American, 2009). Twenty-six leading corn insect scientists working at public research institutions in the United States submitted a statement to the Environment Protection Agency in 2009, stating: "Technology/stewardship agreements required for the purchase of genetically modified seed explicitly prohibit research... inhibit[ing] public scientists from pursuing their mandated role on behalf of the public good unless the research is approved by industry. As a result of restricted access, no truly independent research can be legally conducted on many critical questions regarding the technology, its performance, its management implications, IRM, and its interactions with insect biology." (Anonymous, 2009). The warning is "relevant to all transgenic crops and all public-sector scientists of any discipline who seek to conduct research on transgenic crops" (Sappington et al., 2010). While researchers are expected to seek permission from the seed companies, this is sometimes denied or research agreement terms may include limit or control of publication of the study, while the design and dissemination of the research may be unduly influenced by industry partners (Sappington et al., 2010). An attempt to resolve the issue resulted in a draft set of principles designed to protect the legitimate property rights of companies while affording public scientists independence to conduct research on commercialized transgenic seed (Sappington et al., 2010). It remains to be seen whether this effort will address all the issues, although both sides acknowledge progress. In addition, the increasing involvement of and funding by the private sector influences how research is conducted, raising conflict-of-interest issues and questions over biases in results (IAASTD, 2009). Finally, regulatory agencies may also face difficulty in obtaining patented GE materials, for example to detect the presence of transgenes to monitor for contamination.

Conclusion

Significant calls have been made for a reform of the global IPRs framework, and in particular the patent system, also in relation to agriculture (IAASTD, 2009). Within the WTO, there are discussions and proposals for clarification and amendment of the TRIPS Agreement to, among others, ensure that living organisms are not patentable and to ensure that any patent applications involving genetic resources and traditional knowledge are accompanied by disclosure requirements. At the national level, there is still considerable space for the design of pro-development intellectual property policies

and laws that are sensitive to agriculture interests (Correa, 2010). The recognition of farmers' rights and the contribution of indigenous and local communities to agricultural biodiversity and the elaboration of the Access and Benefit-Sharing Protocol under the Convention on Biological Diversity (CBD) are also steps in the right direction.

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Evaluating the Contribution of Genetically Engineered Traits to Crop Yield: Adoption or Alternatives for Agricultural Policy?

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INCREASING prices, inadequate food distribution, rapid population growth and poverty – and more recently, climate change – are all central issues for global food production. While agricultural research has long been focused on the goal of increasing yields, effective and sustainable means to increase crop productivity can be highly context-dependent in different growing regions and socioeconomic conditions. Genetic engineering (GE) of crop plants has been promoted as an important means for dramatically improving the yields of staple food crops, and has enjoyed widespread public perception as an important means for improving yields. Teasing apart the contribution of the different variables that affect crop productivity has rarely been considered in evaluating the way forward in agriculture. A recent investigation has attempted to understand the contribution of genetic engineering to increases in crop yield.

The report *Failure to Yield* (Gurian-Sherman 2009) shows that, despite tremendous effort and expense, genetic engineering (specifically looking at soy and maize productivity) has only succeeded in measurably increasing the yield of one major food or livestock feed crop in the US – and this contribution has been small compared with other methods available. Based on this report, it seems that data to date on GE's contribution to yield has not justified the massive investment of resources that has gone into their research and development. In this presentation, the findings in *Failure to Yield*, based on over a decade of cultivation and dozens of studies on yield from the US, will be discussed. The report draws four distinct, empirically based conclusions:

1. Genetic engineering has not increased intrinsic yield

No currently available transgenic varieties enhance the intrinsic yield of any crops. The intrinsic yields of maize and soybeans did rise during the 20th century, but not as a result of GE traits. Rather, they were due to successes in traditional breeding.

2. Genetic engineering has delivered only minimal gains in operational yield

Herbicide-Tolerant Soybeans and Maize. Although not extensive enough to develop precise yield estimates, the best data show that transgenic herbicide-tolerant soybeans

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and maize have not increased operational yields, whether on a per-acre or national basis, compared to conventional methods that rely on other available herbicides. That herbicide-tolerant soybeans have been so widely adopted suggests that factors such as lower energy costs and convenience also influence farmer choices, and may produce benefits unrelated to yield.

Bt Maize to Control Insect Pests. Combining the values for Bt European corn borer maize and Bt rootworm maize gives an estimated operational yield increase from the Bt traits of 1.3-5.5 percent. An increase of about 3.3 percent, or a range of 3-4 percent, is a reasonable intermediate. Averaged over the 13 years since Bt maize was first commercialized in 1996, this equates roughly to a 0.2-0.3 percent yield increase per year.

3. Most yield gains observed are attributable to non-genetic engineering approaches

In the past several decades, overall maize yields in the United States have increased an average of about 1 percent per year, or considerably more in total than the amount of yield increase provided by Bt maize varieties. More recently, US Department of Agriculture data indicate that the average maize production per acre nationwide over the past five years (2004-2008) was about 28 percent higher than for the five-year period 1991-1995, an interval that preceded the introduction of Bt varieties – an average of close to 2 percent per year.² But our analysis of specific yield studies concludes that only 3-4 percent of that increase is attributable to Bt, meaning an increase of about 24-25 percent must be due to other factors, such as conventional breeding and the number of maize plants per unit area. Yields have also continued to increase in other major crops, including soybeans (which have not experienced increases in either intrinsic or operational yield from GE) and wheat (for which there are no commercial transgenic varieties). Comparing yield increase over recent intervals, the increases were about 16 percent for soybeans and 13 percent for wheat. Overall, as discussed above, GE crops have contributed modestly (at best) to yield increases in US agriculture in comparison to that provided by breeding practices.

4. Experimental high-yield genetically engineered crops have not succeeded

Several thousand experimental GE-crop field trials have been conducted since 1987. Although it is not possible to determine the precise number of genes for yield enhancement in these trials (given the confidential-business-information concerns among commercial developers), it is clear that many transgenes for yield have been tested over the years. Despite these efforts, still only the Bt and herbicide-tolerance transgenes and five transgenes for pathogen resistance have been commercialized on limited acreage, and only Bt has had an appreciable impact on aggregate yields.³

² Operational and intrinsic yields cannot be distinguished in these aggregate yield numbers.

³ Virus-resistant GE papaya has prevented substantial yield loss, but it is grown only on several thousand acres in Hawaii and therefore has not contributed significantly to overall agricultural yield in the United States.

What are genetic engineering's prospects for increasing yield?

Genetic engineers continue to identify new genes that might raise intrinsic and operational yields. How likely is it that these genes will produce commercially viable new crop varieties? Given the variety of transgenes tested, it would be expected that some of them may eventually be successful in increasing yield. But in light of their biological and physiological complexity, and their unpredictable side effects, it is uncertain how many will become commercially viable, and their past track record for bringing new traits to market suggests caution in relying too heavily on their success. To summarize, the only transgenic food/feed crops that have shown significant improvement to yield in the US are varieties of Bt maize, and they have contributed gains in operational yield that were considerably less over their 13 years than other means of increasing yield. Further, the emerging evolution of resistance by the target pest (Tabashnik et al. 2009) – prompting some farmers to spray pesticides on their Bt crops – suggests that this effect may be shortlived.

Discussion: Alternative approaches to increasing yield

Given the large investment and little return by GE to significantly improve crop yield, it may be time to look more seriously at the other options in the agricultural toolkit. In order to invest wisely in the future, we must evaluate agricultural tools to see which ones hold the most promise for increasing intrinsic and operational yields and providing other resource benefits. Several recent studies have shown that low-external-input methods such as organic can improve yield by over 100 percent in these countries, along with other benefits (Badgley et al. 2007). Such methods have the advantage of being based largely on knowledge rather than on costly inputs, and as a result they are often more accessible to poor farmers than the more expensive technologies (which often have not helped in the past). Meanwhile, conventional breeding methods, especially those using modern biotechnology approaches (often called marker-assisted selection and distinct from GE), have the potential to increase both intrinsic and operational yield. Also, more extensive crop rotations, using a larger number of crops and longer rotations than current ecologically unsound maize-soybean rotations, can reduce losses from insects and other pests.

Implications and future options

Where can investment of R&D in agriculture yield the most benefits with the fewest risks and least regulatory burden? What types of agricultural development can lead to the most sustainable solutions in a given context? What access, ownership and stewardship regimes will most contribute to future food security? The evidence reaffirming the importance of breeding and genetic diversity of crop plants should put the effects of consolidation of access and ownership of the world's crop genetic diversity clearly as a priority issue for national and international agricultural policy. Therefore, putting too many of our crop-development eggs in the GE basket could lead to lost opportunities. National, state and local agricultural agencies, and public and private

universities should consider redirecting substantial funding, research, and incentives toward approaches that are proven and show more promise than genetic engineering for improving crop yields, especially intrinsic crop yields, and for providing other societal benefits. These approaches include modern methods of conventional plant breeding as well as organic and other sophisticated low-input farming practices. Improving the genetic basis of yield increase and maintenance of genetic diversity, through breeding and selection (which may or may not include biotechnology), will likely be essential for sustainable crop production.

Biotechnology will undoubtedly have a distinct role to play in increasing future crop yield, but the evidence to date suggests that genetic engineering (as only one form of biotechnology) is not likely to contribute substantially to sustainable or predictable benefits to yield. Given the uncertainties of climate change and in the sustainability of dominant models of agriculture, it seems that traditional breeding and selection still possesses the greatest capacity to ensure both a sustainable and productive global food harvest for the foreseeable future.

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Bt-Resistant Target Pests – Quick Occurrence in South Africa

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MAIZE is the staple diet of people in Africa. Lepidopterous stem borers seriously limit potentially attainable maize yields by infesting the crop throughout its growth, from seedling stage to maturity. The most important of these species are the spotted stem borer, *Chilo partellus* (Lepidoptera: Crambidae), and African stem borer, *Busseola fusca* (Lepidoptera: Noctuidae).

The advent of Bt maize

Through the use of modern biotechnology some very effective solutions for maize stem borer control have been developed. Bt maize expressing Cry1Ab protein was initially developed for the control of two stem borer species in North America, i.e., *Ostrinia nubilalis* (Lepidoptera: Crambidae) and *Diatraea grandiosella* (Lepidoptera: Crambidae). These products also provide effective control of moth larvae such as those in the genus *Chilo*, and provide partial to very good control of noctuid moths in the genera *Sesamia* and *Busseola* (Van den Berg and Van Wyk, 2007).

Since the first deployment of genetically modified (GM) crops with insecticidal properties, there has been concern with regard to resistance development in target pests and possible non-target effects (Tabashnik, 1994; Gould, 1998). When resistance to Bt maize develops farmers will be back to where they were with management strategies 15 years ago and if the Bt protein disrupts beneficial interactions in agro-ecosystems it may lead to increased pest presence and/or development of secondary pests.

Between 1994 and 1997 various Bt events were evaluated under artificial pest infestation in South Africa. The event MON810 of the Cry1Ab gene provided superior control to all other events tested and subsequently approved for release (Van Rensburg, 1999). Bt maize has been planted in South Africa since 1998 and the country is the 8th biggest producer of GM crops in the world.

Farmers' perceptions of Bt maize in South Africa

A survey conducted by Kruger et al. (2009) showed that the greatest benefit associated with Bt maize was the convenience of target pest management. However, Bt maize is only an advantage when target pests are present. In South Africa farmers have benefited from the adoption of Bt maize since its deployment in 1998 (Gouse et al.,

2005). Despite paying more for seed, adopters enjoyed increased income over conventional maize varieties through savings on pesticides and increased yield due to better pest control. Farmers also indicated that they did not need to scout their fields for pests any more since they assumed the technology was effective.

Resistance development

Two years after the planting of Bt maize in South Africa stem borer damage was noticed involving various Bt maize hybrids (Van Rensburg, 2001). Van Wyk et al. (2007) also reported the presence of *B. fusca* larvae on mature Bt maize plants. Since no leaf feeding damage occurred during the vegetative growth stages of these plants, this damage indicates survival of larvae on plants during the period from tasseling to grain filling (Van Rensburg, 2001). No yield losses could be attributed to these infestations, but the observation caused concern due to the possibility that similar infestations may in future result in significant damage to maize ears. This concern was therefore only of “importance” due to the fact that it may result in yield loss and no alarm seems to have been raised about resistance development at that time.

The first official report of resistance of a maize pest to Cry1Ab maize was made in South Africa in 2007. This report of field resistance of *B. fusca* to Bt maize (Van Rensburg, 2007) showed that in certain locations some larvae were able to survive on Bt maize.

Within one year of the first report of resistance of *B. fusca*, another reportedly resistant population was observed by farmers at the Vaalharts irrigation scheme, approximately 50 km from the initial site. Follow-up studies showed that larvae survived on Bt maize and field-collected larvae were reared for four generations on Bt maize plants in the laboratory. The latter study also indicated that larvae collected from non-Bt maize refugia could survive on Bt maize. This indicates that the effectiveness of the high dose/refuge strategy may be compromised in this geographical area.

Analysis of more than a decade of resistance monitoring data up to 2008 for six Lepidoptera species targeted by Bt maize and cotton suggested that the principles of the refuge strategy may apply in the field to limit resistance development (Tabashnik et al., 2008). To date field evolution of resistance has been detected only in *B. fusca* in South Africa (Van Rensburg, 2007), *Helicoverpa zea* (Lepidoptera: Noctuidae) in the south-eastern United States (Tabashnik, 2008) and *Spodoptera frugiperda* (Lepidoptera: Noctuidae) in Puerto Rico (Gassman et al., 2009). Pink bollworm *Pectinophora gossypiella* (Lepidoptera: Gelechiidae) resistance to Bt cotton has also recently been reported from India.

The increased appearance of these Bt-resistant pests during the last 4 years indicates that the predicted rate of evolution of resistance was seriously underestimated and casts doubts on the use of this technology in future.

Refugia

Refugia form an important part of insect resistance management strategies. Refuges are defined as habitats in which the target pest is not under selection pressure due to the

toxin and therefore provide a sustainable habitat for pest development. The high dose/refuge strategy, employed to limit resistance development, comprises a combination of Bt maize plants producing high doses of toxin and non-Bt plants in close proximity. The principle underlying this strategy is that any resistant insects emerging from Bt crops are more likely to mate with one of the much larger number of susceptible pest insects emerging from refuges than with each other, thereby decreasing the selection for Bt-resistant alleles.

How did resistance develop so quickly in South Africa?

Although the planting of refugia is compulsory, the level of compliance between 1998 and 2006 was shown to be low in the region where resistance was reported in South Africa (Kruger et al., 2009). Research has also shown that *B. fusca* moths prefer irrigated maize, which could have contributed to increased selection pressure towards the evolution of resistance to the Bt toxin (Van Rensburg, 2007). Van Wyk et al. (2007) also indicated that the strong linkage of stem borers to the maize ecosystem in irrigation areas and especially the planting of Bt maize in these systems results in strong selection pressure for evolution of resistance.

The increased level of resistance recorded for *B. fusca* was at least in part due to non-compliance by producers with the refuge principle (Kruger et al., 2009). However, in retrospect it appears that the Bt events currently available for control of *B. fusca* may not meet the high dosage requirement. Pest resistance to Bt maize most likely resulted from a combination of late planting dates with consequent increased levels of infestation combined with non-compliance with refuge requirements which contributed to selection pressure for Bt resistance. A lesson that could be learned from this is that in areas where the adoption rate of Bt technology is very high, refuge compliance should be followed up and enforced.

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Environmental and Agronomic Issues of Genetically Engineered Soy in South America

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OF all human activities, farming presents the greatest conflict between satisfying our basic needs and maintaining the sustainability of the natural environment. Some types of farming impact the environment more than others. For several thousands of years in Latin America, highly diversified ecological farming systems evolved that fostered the sustainable use of resources. Different cultural groups developed various complementary cropping methods: maize, beans and squash in Central America; tubers, roots and maize in the Andes; and camote and yucca in the Caribbean. These practices have been progressively undermined by the influence of colonization, modernization and globalization, which have replaced them with systems that encourage **extractive processes and the mining of resources. Latin America's natural and human resources could sustain its own long-term development.** Some 23 percent of its land is suitable for farming and another 23 percent is tropical rainforest (almost half the world's tropical rainforests are found in Latin America). Some 13 percent of the surface area is grassland and the region holds 31 percent of the planet's available fresh water. Furthermore, it is home to rich reserves of renewable and non-renewable energy, and the wealthiest biodiversity on the planet. Of the twelve so-called "mega-diversity" countries, five are in Central and South America: Mexico, Colombia, Ecuador, Peru and Brazil. Nevertheless, that wealth has not created the quality of life or environment for Latin America's peoples that it should. This is because governments have focused on a defective development model that has excluded the majority of people, especially over the last thirty years.

During this period, the agricultural sector – one of the most promising productive sectors of the region – changed dramatically. Large-scale, export-oriented production requiring the intensive use of chemical inputs started to dominate the agricultural landscape. **This Green Revolution-style approach to farming started to suffocate the diversified local and self-sufficient farming practices of small and medium-sized farmers. Traditional campesino (peasant) culture had demonstrated a high degree of sustainability within its own historical and ecological contexts, and fulfilled the vital needs of the population even under adverse environmental conditions.** Farming practices were built on sophisticated social, geographical and cultural frameworks, appropriate processing technologies, and a precise knowledge of resources, consumption and labour habits, all adjusted to the conditions of each locale. These diverse farming systems fed millions of Americans five hundred years ago. Today

they are largely relegated to the poorest 10 percent of agricultural land, yet they still generate 40 percent of the region's livestock and agricultural produce. In Central and South America, campesinos comprise up to 80 percent of the rural producers, and they supply 51 percent of the most important grain harvested in the region: maize. In at least seven countries (Brazil, Chile, Colombia, El Salvador, Guatemala, Mexico and Paraguay), campesinos are primarily responsible for their own food security. Nevertheless, their farming methods – so successful from a social and environmental point of view – have not received the support or the official backing of the governments.

Since the mid-nineties, South America, and Argentina initially, were confronted with a **new twist to the Green Revolution model**, with the introduction of genetically modified (GM) crops. Transgenic soybean is the flagship of this transformation. The GM Revolution extends the logic of the Green Revolution from controlling the inputs (seeds and chemicals) to controlling the whole chain of agro-industrial activities from seed to supermarket packaging. **New technologies, regulatory measures, patents, commercial agreements, cheaper lands and territories, new global demand for feeding animals and biofuels, were the keys to introducing GM products in South America.** Argentina has allowed the most extensive introduction of transgenic crops and has rushed through oversight mechanisms for genetically modified organisms (GMOs), via its governmental agencies and private sector. Similar agencies have been set up in Brazil, Uruguay, Bolivia and Paraguay. Most of them have been more involved in matters regarding the promotion of the new technologies than with their regulation, largely ignoring integrated social-environmental impact studies. There have been no instances of broad-based public participation, nor are the decisions of the agencies subject to review by independent researchers. Argentina was the spearhead of this agricultural transformation, with the releasing of transgenic soybean resistant to glyphosate (Roundup) in 1996. **For the farmers, Roundup Ready (RR) soybean was a solution for one of the main problems in farm management, namely weed control.** With “only one herbicide”, farmers could control a broad spectrum of weeds (including the most conspicuous weed problems such as *Sorghum halepense*, *Cynodon dactylon*, *Cyperus rotundus* or *Chenopodium album*) and at a very low cost. A reduction in the herbicide price, less fossil energy consumption and simple application made the offer of the technical package very attractive. The other aspect of this model presents **no tillage** as a unique alternative that avoids the ploughing of the soils and gives more time for the acceleration of agricultural alternatives, giving the farmers three harvests (RR soy/wheat/RR soy) every two years. The rural and natural environment is under this process and an important portion of the country is being transformed in a cluster productive of commodities, especially cake, oils and soybeans. The shift in production systems has resulted in the **agriculturization phenomenon**. That is, the displacement of cattle production to marginal areas and the concentration in the use of land for agricultural production, with a main crop at the centre of the model – transgenic soybean. It is associated with the agricultural management implementation of “technological packages” and land concentration of the Pampean and extra-Pampean regions. This has meant significant changes during the last 15 years in the agrarian structures and technologies and has resulted in the expansion of monocultures that substituted previous rotation systems of crops and pasture lands (a historical agronomic way of production

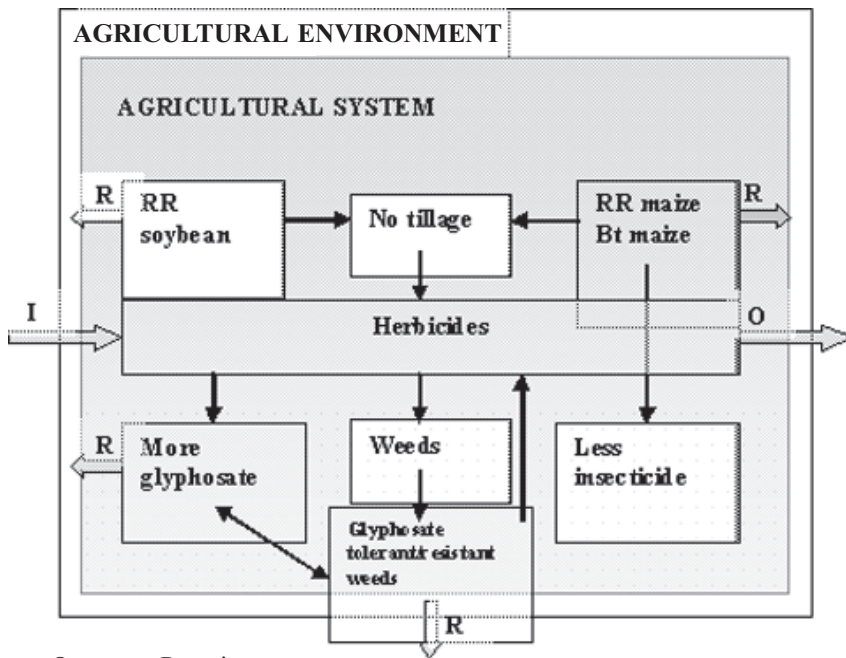
under rotation of cattle and soy production, that allows a “sustainable agriculture” during the short agricultural history of South America). This model has spread not only in the Pampas (55,000,000 hectares of the richest soils in the world), but also over other very rich areas with high biodiversity, opening a new agricultural border in important ecoregions such as the Yungas, Great Chaco and the Mesopotamian Forest.

The **dominant technology is monoculture glyphosate-resistant soybeans associated with no-tillage practices and the use of glyphosate** (see figure 1). Of the total soybean production, 99 percent are genetically modified glyphosate-resistant soybeans. The simplicity of weed management under the glyphosate scheme allows farmers to manage more hectares and increase overall productivity and profitability based on a vertical integration model. In the extra-Pampean areas, with more complex environments, the system also implies a growing application of external inputs related to weed and pest control. Demand for new lands in this area implies a complete deforestation. Argentina is leading the rates of deforestation, 0.85 percent, greater than those of Africa (0.78 percent) or the average of South America (0.50 percent). The process, called “**pampeanization**”, implies the importation of the technological, financial and agronomical model of the Pampas into other ecoregions with different types of soils, biodiversity and climate, such as the Great Chaco (Paraguay, Bolivia and Argentina), the Yungas (Bolivia and Argentina), the Pantanal (Brazil), and the savannas (Pampas) (Uruguay).

In most countries, formal agricultural research has historically been linked with a process of technological modernization and agronomical transformation that only benefited large-scale farmers. The research agenda of national agricultural research institutes – many of which have now been privatized – focusses largely on extensive cropping for export markets. In the nineties, many of these institutes received the direct benefit of a small percentage of the resulting export sales, which further skewed their research priorities. In these agencies, as in the universities and public-private joint ventures, research was done “on demand”, which is dangerous territory for determining research and development policy. Very little independent research was developed focussing on environmental, social or health issues related to transgenic releases. While Argentina, Brazil, Bolivia, Uruguay and Paraguay were advancing and allowing the release of transgenic soybean on their own territories, environmental impacts and social conflicts have started to appear and cannot be hidden. In the south centre of South America, environmental impacts have resulted: Deforestation of very high biodiversity areas, appearance of herbicide-tolerant weeds (*Parietaria debilis*, *Petunia axillaris*, *Verbena litoralis*, *Verbena bonariensis*, *Hybanthus parviflorus*, *Iresine diffusa*, *Commelina erecta* and *Ipomoea sp*) (Pengue 2004), appearance of herbicide-resistant weeds (such as the case of *Sorghum halepense*) (Binimelis et al. 2009), soil depletion and virtual soil exportation (Pengue 2010), agrochemical contamination, soil structure degradation with potential desertification processes, and a loss of food diversity and food sovereignty are some of the consequences.

Transgenic soybean is not a demand of the small farmers and peasants. The main demands of these millions of small farmers responsible for the majority of agricultural production in South America favour the implementation of agricultural policies that are consistent with and adequate for their own needs. Their message is simple: **the GM**

Figure 1: The agricultural environment and the simplification of weed management via RR soybean



I: input, O: output, R: resistance

soybean developed to date does not provide solutions for the small family farm. The evaluation of a new technology and its risks should involve providing complete information about all the possible alternatives, as well as a comparative analysis of the benefits, risks, means of distribution and the variety of alternatives. The evaluation should involve broad, complex and holistic criteria that our authorities and scientists in South America need to take into account and implement to change the environmental and health effects of the dark side of this agricultural history.

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Hope Not Hype: The Future of Agriculture

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A SYNTHESIS of the best science on agriculture was the immodest goal of a project initiated in 2003 under the title of the International Assessment of Agricultural Knowledge, Science and Technology for Development, abbreviated as IAASTD (Heinemann, 2009). It was a joint project of the world's major agriculture and development institutions initiated by the World Bank and conducted in partnership with the United Nations Food and Agriculture Organization (FAO), UN Environment Programme (UNEP), UN Development Programme (UNDP), UN Educational, Scientific and Cultural Organization (UNESCO), World Health Organization (WHO) and the Global Environment Facility (GEF) (IAASTD, 2008).

The large Assessment is comprised of a multi-chapter global and five multi-chapter sub-global reports with two overarching documents, the Global Summary for Decision Makers (SDM) and the Synthesis Report (SR). The entire project was supervised by a multi-stakeholder governing Bureau composed of representatives of the funding agencies, governments, private sector and non-governmental organizations (NGOs). It is the single largest and most diverse global appraisal of agriculture ever undertaken (Rivera-Ferre, 2008). Hopefully, it has not been completed too late. Agriculture is coming under greater scrutiny than ever before as it is increasingly clear that the benefits and impacts of agriculture are not evenly shared between the rich and the poor. The Assessment was set the ambitious task of answering the central question of how agriculture in 2050 will contribute to a well-fed and healthy humanity despite the challenges of vast environmental degradation, population growth and climate change, and do so in a way that the potential to produce food has not been lost because of how we farm. One answer was simple: Business as usual is not an option. How we farm now will fail to achieve this goal. How we should farm was not as easy a question to answer.

No one can know for sure if there will be a technology capable of feeding the world forever. At least for now, we must be as concerned with our appetites as we are with our capacity to produce food, fuel and materials. The Assessment had hard words for the societies that have long disproportionately consumed. Harder words still for their attempts to maintain their consumption using subsidies and market-distorting trade mechanisms and asymmetric intellectual property rights (IPR) frameworks. What is clear is that genetic engineering cannot feed the world, at least not the way we have been developing and using it.

What the Assessment found with regard to GMOs was:

1. There is no evidence of a general, sustained or reliable increase in yield from GM crops over the 14 years since the first commercial release.
2. There is no evidence of a sustained reduction in costs to farmers adopting GM crops, nor a sustained and reliable increase in profits to such farmers.
3. There is no evidence of a sustainable reduction in pesticide use. In fact, there is a dramatic increase in some herbicides and the special way that they are used on GM crops is undermining the conventional farmer's weed control options.
4. The overwhelming majority of GM crops were not designed to increase yield, they were designed to sell particular agrochemicals or biological insecticides.
5. There is no evidence that genetic engineering has produced crops needed by the majority of the world's farmers.
6. The wholesale grab of plant germplasm as the intellectual property of a few mega-corporations is consolidating the seed industry and threatens long-term plant agrobiodiversity and biodiversity. Should GM animals ever become viable commercial products, there is every reason to expect the same contraction in animal germplasm.

New GMOs must be subject to uniform safety and ecological assessments of higher standard, transparency and independence than has benefited existing GM crops. The adoption of GM crops is consistent with a number of "oversimplification", or monoculturalization, trends in agriculture over the last few decades. The most literal are the large monocultures that characterize cropping systems in countries such as the US, Canada and Argentina, which also boast some of the biggest GM crop production. Monocultures require high levels of external inputs to attempt to restore the soil and high pesticide use because of the large populations of specialist pests that they support. Oversimplification of the agricultural landscape through both intensive plant and animal monocultures undermines agroecosystem resilience and thus sustainability. GM crop commercialization shows no signs of working outside the monoculture model. The attempt to simplify pest management through genetic engineering has resulted in increased applications of a very small number of agrochemicals. This practice has increased the frequency of resistance to those chemicals and reduced the diversity of alternative products. Consequently, it threatens the sustainability of yields in both GM and non-GM agroecosystems. Finally, the industrial model of agriculture is also correlated with the oversimplification of diets (Chávez and Muñoz, 2002; Hawkes, 2006; Scialabba, 2007; Tee, 2002). In many countries, malnutrition is marked by larger numbers of both the underweight and the overweight, often within the same households. The sources of fats, proteins and carbohydrates are from fewer kinds of plants and animals, leaving people vulnerable to disease because of micronutrient malnutrition.

What the Assessment found with regard to other solutions was:

1. There is substantial evidence that investment in agroecological methods would contribute to feeding the world in a sustainable way.

2. We must immediately re-invest in proven technologies such as conventional breeding and marker-assisted breeding.
3. IPR frameworks must be urgently revised. If biological material is to continue to be protected by patent and patent-like instruments, then the way in which intellectual property is described and the incentives on public institutions to develop intellectual property must be changed.
4. Large agriculture exporting countries must immediately adopt trade and aid policies that promote food security and sovereignty outside their own borders.

What characterizes the present is that the world lacks the will and not the means to feed everyone. What characterizes the future is that we may also lack the means. We must prepare now for that day.

The purpose of this talk is not to pit genetic engineering against other biotechnologies, but to chart the course for development of the right biotechnology to meet our mutual goals of having plentiful nutritious and tasty foods that are fit for purpose and locally prized, and to do so without losing the ability to continue to feed future generations. It is also essential that the pathway to this future of food also strengthens local communities and builds local economies. The Assessment is confident that the pathway to feeding the world in a sustainable way will not only achieve a more resilient agriculture, in the process it will restore our diverse global ecosystem and halt the loss of our diverse human agricultures. To the degree that modern biotechnology, genetic engineering included, can contribute and be compatible with these larger social and ecological solutions, it is welcome. But it is time, as they say, for GMOs to put up or shut up.

To feed the world and build sustainable agroecosystems and societies at the same time will require more than current knowledge of agroecology (Tilman et al., 2002). Governments, philanthropists and industry must invest in research and institutions that will build knowledge and improve methodology, as well as help to customize implementation. This knowledge must be made in collaboration with farmers and be distributed through extension services, non-governmental organizations, and the private sector.

Can the world follow agroecological agriculture and make a profit? The likelihood is high but there is no question that we need new economic models. To meet the goals discussed above requires more than tinkering with technology and tariffs. We need to be able to account for the true cost of using non-renewable resources, such as fossil fuels. The value of “marginal land” and water as ecosystem services must be identified. The contribution of *in situ* conservationists, largely farmers, must be recognized. Ultimately, we have to change the question from “How much can be made on the crops from this land, or the animals grazed on this paddock?” to “How much will it cost to not have this land, these crops, these animals or these farmers?”.

The right biotechnologies are both sophisticated and effective at what they do. “A frequent misconception is that organic agriculture means turning back the clock to a primitive mode of farming. While organic agriculture does build on traditional knowledge and practices, what it offers is a modern, ecologically intensive farming system that can perform successfully without any synthetic fertilizers or pesticides” (p. 217 Scialabba, 2007).

A return to low-yield low-input agricultural systems is not the answer. But modern agroecological approaches are not low-yield. However, they are comparatively low-input in many cases. Reducing input in most agroecosystems will provide the necessary flexibility to apply external inputs in others, without losing global sustainability. The right biotechnology is available. It can be implemented right now, provided that poor and subsistence farmers receive access to institutions that build local knowledge and spread innovation, and are not prevented from developing their own markets. The recipe for success is in the Assessment.

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The foremost aim of the Scientific Conference is to advance the current understanding of biosafety in terms of the ecological, human health and socio-economic implications of genetically modified organisms (GMOs). To that end, the event works towards:

- Sharing the most recent scientific findings of biosafety research with a wide range of Japanese stakeholders and, during the 5th Conference of the Parties serving as the Meeting of the Parties to the Cartagena Protocol on Biosafety (COP-MOP 5) in Nagoya, also with negotiators and observers from other countries;
- Providing opportunities for exchange of experiences and views related to biosafety policy and regulation; and
- Promoting public participation in framing risk research, technology assessment and decision-making related to biosafety.

The cooperation between ENSSER, TWN and the VDW provides a unique opportunity to bring together independent scientists from industrialized and developing countries. This activity is seen as critical to maintain and demonstrate diversity in scientific approaches in the fields of risk research and research addressing socio-economic issues.

The second aim is to inform the delegates at the COP-MOP 5 about the current scientific challenges in biosafety research and assessment, and to contribute effectively to the political and legal discussions at the Nagoya meeting.

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