Scientific Conference 2012

Advancing the Understanding of Biosafety

GMO Risk Assessment, Independent Biosafety Research and Holistic Analysis

28-29 September 2012
Hyderabad, India

European Network of Scientists for Social and Environmental Responsibility
TWN Third World Network
TARA FOUNDATION

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Published in 2013 by
European Network of Scientists for Social and Environmental Responsibility
Postfach 1102
D-15832 Rangsdorf, Germany
and
Third World Network
131 Jalan Macalister
10400 Penang, Malaysia
and
Tara Foundation
Rajju sah Lane, Ramna
Muzaffarpur – 482002, Bihar, India

Cover design: Lim Jee Yuan

Printed by Jutaprint
2 Solok Sungai Pinang 3, Sg. Pinang
11600 Penang, Malaysia

ISBN: 978-967-5412-84-4

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Foreword

THE European Network of Scientists for Social and Environmental Responsibility (ENSSER), Tara Foundation and Third World Network (TWN) organised our second International Biosafety Conference in conjunction with the 6th Meeting of the Parties to the Cartagena Protocol on Biosafety (COP-MOP6) in 2012 in Hyderabad, India. The conference was held on 28-29 September, right before COP-MOP6, which met on 1-5 October 2012.

The main aim of our conference was to advance the current understanding of biosafety in terms of the ecological, human health and socio-economic implications of genetically modified organisms (GMOs). The cooperation between ENSSER, Tara Foundation and TWN provided a unique opportunity to bring together independent scientists from industrialised and developing countries. This activity was 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 of our conference was to inform the delegates at COP-MOP6 about the current scientific challenges in biosafety research and assessment. To that end the conference worked towards:

- Information and experience exchange between Indian NGO-representatives/ experts and international biosafety scientists
- Capacity development of Indian NGO-representatives/experts for the national and international biosafety debates
- Discussions on strategies for sustainable GMO-free approaches to food security
- Presentation of the conference outcomes to delegates of COP-MOP6

The topics addressed by our conference included:

- Developments in GMO risk assessment, including discussion of the international standards on risk assessment in the context of the Cartagena Protocol's 'Roadmap for Risk Assessment and Management';

- Socio-economic considerations in GMO decision-making;
- Latest scientific findings generated from independent biosafety research.

As it is especially important to create linkages and synergy between the work of the different groups acting at national and international levels, the conference also brought together Indian and international expertise to discuss GM crops in India. Since the moratorium on approval of Bt eggplant for food purposes in February 2009 in India and the intense discussions on socio-economic implications of Bt cotton agriculture, the Indian debates have served as examples for success or failure – depending on the perspective of the different experts - of GM crop agriculture worldwide.

We are pleased to compile in this document the papers from the conference and hope that they will be useful for the wider biosafety audience.

For further information, please visit http://www.ensser.org/increasing-public-information/biosafety-conference-hyderabad/

Conference Papers

Key Issues for COP-MOP6

Lim Li Ching
Third World Network

THE sixth meeting of the Conference of Parties serving as the Meeting of Parties (COP-MOP6) to the Cartagena Protocol on Biosafety will be held from 1-5 October 2012 in Hyderabad, India. This paper provides an overview of some of the key issues on the agenda for COP-MOP6 and what steps need to be taken to ensure effective implementation of the Protocol.

1. Handling, transport, packaging and identification (Article 18)

COP-MOP6 will be discussing two main issues under Article 18:

(i) handling, transport, packaging and identification requirements for living modified organisms (LMOs) destined for contained use, and intended for intentional introduction into the environment and any other LMOs within the scope of the Protocol (paragraphs 2(b) and (c) of Article 18, respectively); and
(ii) standards relevant to the identification, handling, packaging and transport practices of LMOs (paragraph 3 of Article 18).

While the available information indicates that many Parties still need to develop measures to implement the documentation requirements of paragraphs 2(b) and (c) of Article 18, the following are important considerations for a decision at COP-MOP6:

- The documentation accompanying shipments of LMOs destined for contained use, or intended for intentional introduction into the environment and any other LMOs within the scope of the Protocol, must contain specific information as spelt out in paragraphs 2(b) and (c) of Article 18, and must reach the biosafety competent authorities. The information includes clear identification as LMOs, requirements for safe handling, storage, transport and use, contact point for further information, etc. It could also include the LMO's unique identifier.

- The use of a commercial invoice as the documentation accompanying shipments of LMOs is not sufficient to fulfil biosafety requirements, as the commercial invoice may inadvertently bypass the biosafety authorities. A commercial invoice is also likely to contain additional information (such as prices) and the question of what needs to be shared with the biosafety authorities might lead to confusion and delays. What is needed instead is a separate, 'stand-alone' document which would allow the competent authorities to easily and clearly identify and regulate the LMO shipments that are coming into a country.
- The stand-alone document should contain a reference to the Biosafety Clearing House (BCH) as the BCH is now the global database containing the most updated information on LMOs, and is used also by countries that are not (yet) Parties to the Protocol. This could be done by incorporating the 'LMO Quick-links' in the stand-alone document. The LMO Quick-links developed under the BCH (http://bch.cbd.int/resources/quicklinks.shtml) are bar codes for each BCH entry. They are small image files, which can be easily copied and pasted, that identify an LMO through its unique identifier, trade name and a link to the BCH where information on the LMO is available (e.g. LMO characteristics, countries' decisions, risk assessments, etc.). Through the LMO Quick-links, the relevant BCH page - in at least all UN languages – can be easily accessed by either scanning the bar code or by typing the URL in a web browser. This means that full information about a particular LMO would be available to any customs or biosafety officer with a bar code scanner or a mobile phone. Because the Quick-links are easily recognisable, they would even work if the documents are in different languages. Their use would also greatly reduce duplication of work for both exporting and importing companies as well as for the biosafety authorities.

Paragraph 3 of Article 18 requires the consideration of the need for and modalities of developing standards with regard to identification, handling, packaging and transport practices. At issue is the need to ensure that the current fragmentation of the relevant international regulations and gaps therein with respect to biosafety needs are adequately addressed. Calls to design, under the umbrella of the Cartagena Protocol, a new international standard unifying the best and most complete international norms to achieve biosafety objectives have regrettably not been acted upon.

The study commissioned by the Executive Secretary therefore provides detailed recommendations for action, a combination of which would help ensure the avoidance of adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health.

Of particular note is that Parties should support the recognition of the Cartagena Protocol standards in the list of international standards, guidelines or

recommendations applied by Members of the WTO under the Agreement on the application of Sanitary and Phytosanitary Measures (SPS Agreement). This is important, as SPS measures that conform to international standards, guidelines or recommendations are presumed to be consistent with the relevant provisions of the SPS Agreement and of GATT 1994.

2. Unintentional transboundary movements and emergency measures (Article 17)

Article 17 requires a Party to take appropriate measures to notify affected and potentially affected States, the BCH and other relevant bodies when it knows of an occurrence under its jurisdiction that leads, or may lead, to an unintentional transboundary movement of an LMO. Notifications must be provided as soon as the Party knows of such situations, and relevant information must be communicated to the affected or potentially affected States. Consultations with affected States are also necessary to enable them to determine appropriate responses and initiate necessary action, including emergency measures.

In other words, Article 17 spells out what Parties must do when LMO contamination happens. LMO contamination incidents worldwide have occurred with alarming frequency. According to the GM Contamination Register, a total of 366 known contamination cases and illegal releases have occurred since 2005, when the database was first set up (www.gmcontaminationregister.org). The GM Contamination Register is compiled from public reports and is managed by Greenpeace and GeneWatch UK. In 2012 alone, 24 individual cases have been recorded in countries in Asia, Africa and Europe, many involving unapproved LMOs.

However, from the analysis carried out by the Secretariat, very few Parties (only nine) have reported receiving information of unintentional transboundary movements arising from their jurisdiction, while the majority (133 Parties) reported that they have never received any such information, during the reporting period of the second national report. Moreover, four Parties reported unintentional introduction of LMOs into their jurisdiction in the form of imports of food or seeds, while two other Parties reported potential or unverified transboundary transfer of LMOs into their territories.

It is clear that there is a disjuncture between the known cases of unintentional transboundary movement and what is notified to Parties. This could be because the source of some contamination incidents may be from non-Parties to the Protocol. When contamination originates from Parties to the Protocol, regrettably not all have fulfilled their notification and consultation obligations.

It would be therefore important for COP-MOP6 to take a decision that includes the development of tools and guidance that facilitate implementation and assist Parties to detect and take measures to respond to unintentional releases of LMOs.

This must happen even if notification is not given directly to the affected States, but information is available from other sources, e.g. media reports, non-government organisations, etc. Furthermore, the decision should call on Parties that have not yet done so, to quickly establish and maintain measures to prevent unintentional transboundary moments, as well as mechanisms for addressing and implementing response actions and emergency measures.

Apart from the obligations of Parties that are spelt out in Article 17, the following have been identified as constituting important information and considerations that could help Parties deal with contamination incidents. These should be elements of a decision on the development of guidance to facilitate detection and response actions:

- Decisions and discussions under Article 18 (handling, transport, packaging and identification), in particular in the context of paragraph 2(a) relating to bulk shipments of LMOs intended for direct use as food, feed, or for processing (FFP). Furthermore, the decisions and discussions in relation to sampling and detection, including the establishment, through the BCH, of electronic networks of laboratories to facilitate identification, are especially pertinent.
- Risk assessment and risk management, in particular in relation to the Guidance on Risk Assessment of LMOs developed by the Ad Hoc Technical Expert Group (AHTEG) on Risk Assessment and Risk Management, which already incorporates some elements relating to unintentional transboundary movements in relation to LM trees and mosquitoes.
- Liability and redress, in particular the taking of response measures under the Nagoya-Kuala Lumpur Supplementary Protocol on Liability and Redress, in response to damage or sufficient likelihood of damage including what arises from unintentional transboundary movements.
- Capacity building, in particular in relation to determination of appropriate responses and initiation of necessary actions, including emergency measures, as well as for sampling and detection techniques.

The AHTEG on Risk Assessment and Risk Management could also be tasked with developing the guidance on measures in response to unintentional transboundary movement of LMOs.

3. Risk assessment and risk management (Articles 15 and 16)

In relation to risk assessment and risk management, several issues are to be discussed at COP-MOP6, including:

(i) The main outcomes of the process of developing guidance on specific aspects of risk assessment and risk management, as carried out by the open-ended

online forum and AHTEG on Risk Assessment and Risk Management, in particular the revised Guidance on Risk Assessment of Living Modified Organisms.

(ii) LMOs that may have or that are not likely to have adverse effects on the conservation and sustainable use of biological diversity.

The Guidance on Risk Assessment of Living Modified Organisms developed since 2009 includes the extensively 'road tested' and revised 'Roadmap' on the necessary steps to conduct a risk assessment in accordance with Annex III of the Protocol, along with the tested and revised guidance on LM abiotic stress-tolerant plants, stacked plants and LM mosquitoes. These documents were welcomed by Parties to the Protocol at COP-MOP5 and have benefited from numerous rounds of feedback and peer review. Incorporating the feedback from the first generation of documents, the AHTEG then developed new guidance on LM trees and monitoring, themselves subject to several rounds of review. Together, this package constitutes guidance in three parts that is very useful for the Parties to the Cartagena Protocol in implementing their risk assessment and risk management obligations under the Protocol and national legislation.

The package of guidance documents is both credible and consensus-building. Developed by a group of experts from industry, academia, government and civil society, it has achieved an effective compromise that adequately promotes safety without unduly burdening industry or inhibiting research, while bringing clarity and transparency to regulation.

The AHTEG has thus more than adeptly fulfilled the Parties' request for it to develop further guidance on risk assessment and risk management. It has also proved its utility in being able to respond to Parties' needs in addressing specific topics of risk assessment and risk management.

Therefore, at COP-MOP6, Parties should decide to:

- Endorse the Guidance and ensure its wide accessibility, dissemination and usage.
- Integrate the Guidance into capacity-building activities on risk assessment, including into the training manual on risk assessment that has been developed by the Secretariat and used in training courses on risk assessment.
- Integrate the Guidance within the draft Results-Oriented Capacity-Building Action Plan (2012-2020), in its Focal Area 2 on Risk Assessment and Risk Management.
- Extend the mandate of the AHTEG, with the objective of developing guidance on new topics of risk assessment and risk management, including in relation to unintentional transboundary movement of LMOs.

On the issue of identification of LMOs that are not likely to have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health, it is important to note that discussion on this issue is within the context of Article 7, paragraph 4 and is thus only relevant to the application of the advance informed agreement procedure. It cannot be used to make any extrapolations on the 'safety' of a particular LMO.

It is actually not scientifically possible to identify any LMOs that can be classified as not likely to have adverse effects. The risk assessment process set out in the provisions and Annex III of the Cartagena Protocol on Biosafety should be carried out on a case-by-case basis; the specific LMO concerned, its intended use and the likely potential receiving environment are all important considerations. The latter criteria mean that the potential adverse effects of an LMO are dependent on its specific characteristics, how it is used and where it is released. These will vary in different ways and would be influenced also by environmental, health and socio-economic factors.

Therefore, case-by-case risk assessments cannot be transferable to all potential receiving environments. It follows that any generic identification of LMOs that are not likely to have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health, is not possible. In fact, such *a priori* assumptions regarding the safety of an LMO would seriously undermine the case-by-case principle of risk assessment that is enshrined in the Cartagena Protocol. Moreover, if there is damage caused by an LMO, liability and redress applies regardless of whether that LMO has been identified as being not likely to have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health.

Parties should therefore reconsider the relevance of Article 7, paragraph 4 in light of the objectives of the Cartagena Protocol and the Nagoya-Kuala Lumpur Supplementary Protocol on Liability and Redress.

4. Socio-economic considerations (Article 26)

It is clear that the socio-economic dimension needs to be an integral part of sound and comprehensive assessments of LMOs. Many Parties have incorporated socio-economic, and even cultural and ethical considerations into their national biosafety frameworks and national laws that regulate LMOs. Nonetheless, Parties have expressed the need for further guidance to implement their policy choice to include socio-economic considerations in their decision-making on LMOs.

At COP-MOP5, the Parties considered the recommendation of the sixth Coordination Meeting for Governments and Organisations Implementing or Funding Bisoafety Capacity-Building Activities to establish an ad hoc expert group on socio-economic considerations. Some Parties at the time felt that the issue was not mature enough for consideration by an ad hoc expert group yet, thus COP-MOP5 asked

for regional online conferences and a regionally-balanced workshop to be convened first.

Together with a series of online discussion groups on socio-economic considerations, these activities were carried out successfully in 2011. The time is therefore ripe for the establishment of an ad hoc technical expert group to further progress the work on socio-economic considerations under the Protocol, to meet the needs of Parties to the Protocol. Parties should decide to do so at COP-MOP6, and the following tasks were identified by the workshop in 2011 for the ad hoc technical expert group to undertake:

- Develop conceptual clarity on socio-economic considerations;
- Compile and review information on the socio-economic impacts of LMOs, including information available on specific cases; and
- Develop guidelines on socio-economic considerations that would, among other things, identify key questions to be answered and provide minimum common elements that could be used in considering the socio-economic impacts of LMOs.

Systemic Risks of Genetically Modified Crops: The Need for New Approaches to Risk Assessment

Hartmut Meyer
European Network of Scientists for Social and Environmental Responsibility (ENSSER)

1. Genetic engineering in agriculture: impacts and restraints[1]

THE first genetically modified organism (GMO) deregulated and commercialised was the Flavr Savr tomato in 1994 in the USA, which did not prove to be commercially viable. US genetically modified (GM) agriculture actually started with Bt cotton planting in 1995, but it was only the introduction of Roundup Ready soybeans in 1996, being exported worldwide as a basic ingredient for the feed and food industry, that initiated the worldwide public debate on the use of GM crops. Meanwhile, James reports that 15 countries grow more than 50,000 ha of GM crops each with a sum of 133.9 million hectares [1]. According to Friends of the Earth International - pointing to the fact that the data presented by James are mostly based on personal communications by representatives of the biotechnology industry, which also funds his work - this area equates to 9.2% of the arable land worldwide [2].

Ninety-two per cent of this area is located in five countries (USA, Brazil, Argentina, India, Canada). GM crop agriculture relies on five plant species (soybean, maize, canola, sugar beet and cotton) predominantly producing animal feed, ethanol and fibres in high-input farming systems. Based on the data provided by James, it can be concluded that GM food products mainly comprise sugar, high-fructose corn syrup, soy protein, lecithin or different oils [1]. Some GM maize varieties can be used for direct consumption as, for example, in South Africa. In the USA, some GM papaya is marketed. The range of new properties used in GM crop agriculture is essentially limited to two features: resistance against the herbicides glyphosate and glufosinate and production of *Bacillus thuringiensis* (Bt) endotoxins that are used to kill specific lepidoptera and coleoptera larvae.

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[1] This paper is an abbreviated version of: Meyer, H. 2011. Systemic risks of genetically modified crops: the need for new approaches to risk assessment. Environmental Sciences Europe 23:7 http://www.enveurope.com/content/23/1/7 (free access paper)

The main bottleneck for developing a higher variety of commercially viable products seems to be the limited potential of the technology itself. Complex characteristics of plants such as drought or saline resistance are based on reactions of the plant organism at several levels, including, but not only, the genetic level. Many – still unknown – genes may play a role in the response to environmental condition. The application of genetic engineering alone might not lead to the improvement of such complex traits [3-5]. Only GM plants possessing genes that are supposed to work in isolation from the plant's metabolism, such as the herbicide resistance and Bt genes, are used commercially. Additionally, two GM plant types possessing pathogen-resistant genes which are supposed to interact with an invading organism could be developed into a commercial product: GM virus-resistant papaya and squash grown on 2,000 ha each in the USA [6].

Until the end of 2004 - which should have provided enough time for the development of commercial seed by 2009 – the US authorities approved 877 field trials with plants that were supposed to be virus resistant (988 by the end of 2009). Experiments with GM plants that were supposed to be resistant against fungi have not resulted in any commercial product yet; 622 field trials were approved in the USA by the end of 2004 (854 by the end of 2009). The main blocks to marketing fungal-resistant GM plants are the lack of deeper understanding of the molecular plant-fungi interactions and the unsatisfactory levels of resistance [7, 8].

Stein and Rodríguez-Cerezo predict that a turning point has been reached in the limited commercialisation of GM traits [9]. The authors estimate that in 2015 the number of traits in farmers' fields might quadruple to 120, amongst them 17 soy traits (12 herbicide tolerant, three altered oil composition, two pest resistant) or 15 rice traits (six insect resistant, four pest resistant, three herbicide tolerant, two b-carotene). This development would mainly increase the number of traits to 114. Only six traits aim at influencing more complex characteristics such as drought resistance in maize, while they still rely on single gene alterations.

2. Development of regulatory biosafety frameworks

2.1 Asilomar Conference

It was US scientists, working in the fields of cancer research and molecular biology and concerned about the potential health risks of their work, who started the scientific debate on the pros and cons of GMOs [10]. The participants of the 1973 Gordon Conference on Nucleic Acids drafted a resolution, which warned about the potential health risks of hybrid DNA molecules and called successfully upon the National Institutes for Health (NIH) to develop safety guidelines [11]. An international conference to support the development of safety standards was announced and moratoria on certain types of experiments even suggested [12]. In spring 1975, participants of the Asilomar Conference held in California recognised that more than health problems might arise from the industrial, medical and

agricultural application of genetic engineering, but they restricted their debates on this risk issue. While the conference concluded that mechanisms of self-control and voluntary guidelines should be the basis for the development of the technology, calls for a stricter and legally binding governmental oversight were launched during the emerging public debate in cities such as Cambridge, Massachusetts, harbouring major research institutions [12,13]. Envisaging a growing unease of the public, prominent molecular biologists soon questioned the value of the early risk debate [14-16].

2.2 Emerging biosafety systems in the USA

When Cohen reported that his research would enable scientists to cross species barriers, suggesting the invention or creation of new species, US politicians started, soon after, to draft regulations for the application of GMOs [17]. This in turn alerted those scientists that envisaged large economic potential based on their work and patents, and in 1977, a draft law for GMO regulation was stalled when Cohen convinced politicians that the results of the new technology could also have appeared in nature. Expecting a revolution in biology and an immense impact on business, genetic engineering was declared as equivalent to conventional breeding methods, meaning a GMO is not a new organism with unforeseeable risks and does not require specific regulation [18]. In 1976, the NIH adopted guidelines, which set up a system based on biological and physical containments.

Later, the US National Research Council formalised the risk assessment approach [19]. When in 1983 the first GM bacteria and plants were released in field trials in California, the existing health protection guideline concept was applied to assess possible environmental risks [20]. The US has opted to use existing frameworks to set up a consultation system.[2] Nowadays, genes and proteins that render herbicide tolerance to GM plants are assessed and deregulated according to the rules for food additives; plants possessing Bt genes and proteins fall under the pesticide approval rules and growth hormone-producing fish has to be checked under the procedures for approval of animal drugs. Two recent US law cases stated that the procedure agreed upon by the authorities and the applicant for deregulating herbicide-resistant golf lawn grass and alfalfa was faulty. A more rigid assessment under the norms of US environmental laws had to be conducted. With these court decisions it seems that GM plants that can interact substantially with wild or domesticated genetic resources via pollen flow must undergo a more detailed risk assessment in the US as, for example, GM soy or maize. It remains an open question pending a final Supreme Court decision, if and how these court cases will influence future GM crop regulation in the USA.

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[2] Starting points for an overview of US biosafety regulations are: http://www.aphis.usda.gov/biotechnology/index.shtml, http://www.fda.gov/Food/Biotechnology/default.htm, http://www.epa.gov/pesticides/biopesticides/pips/index.htm, http://usbiotechreg.nbii.gov/

2.3 Biosafety frameworks at the European and UN levels

In contrast to the situation in the US, the debate in European Union (EU) countries went beyond expert circles and involved more non-governmental organisations (NGOs) and citizen groups. It also lacked the strong focus on emerging commercial prospects of genetic engineering. While the model of the NIH guidelines was adopted by many European governments, the emerging public debate quickly reached the decision that an overarching, specific legal framework was necessary due to the novelty of GMOs [18, 21]. The first biosafety laws were adopted in Denmark in 1986 and Germany in 1990, and EU biosafety regulations followed in 1990.[3] Since that time, the concept of the European biosafety legislation is that the properties and behaviour of organisms whose 'genetic material has been altered in a way that does not occur naturally by mating and/or natural recombination' cannot be predicted from the current experience with and knowledge about the parent organism. Although this so-called process-based system was developed under the umbrella of the community environmental law, it did not adapt existing instruments for assessing environmental risks of technical and industrial activities, e.g. environmental impact assessment, but kept the GMO risk assessment approaches that had been developed in the context of the technology development.

In 1995, the negotiations for international binding biosafety rules under the framework of the Convention on Biological Diversity (CBD) started, which resulted in the Cartagena Protocol on Biosafety (CPB)[4] adopted in 2000 [22]. Comparable to the EU, the CPB adopted a process-based type of GMO regulation. As the Biosafety Clearing House of the CPB and other data banks show, legally binding specific biosafety legislation are currently in force or under development in 112 out of 200 countries:

- Seventy-nine states with legislation in force (amongst them 33 industrialised countries).
- Thirty-three states with legislation in development.
- Fifty states with a national biosafety framework based on the CPB.
- Eleven states having only ratified the CPB without implementing it yet.
- Countries which so far do not follow the process-based approach to biosafety legislation are the USA and Canada.
- Twenty-five states have no biosafety system at all.

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[3] A starting point for an overview of the EU biosafety legislation is: http://ec.europa.eu/food/food/biotechnology/evaluation/gmo_nutshell_en.htm

[4] The text of the CPB is available at http://www.cbd.int/biosafety/protocol.shtml

3. Conflicting concepts for assessing environmental risks of GMOs

3.1 The 'ecotoxicological approach' versus the 'environmental approach'

Ever since the first GMOs were released, it was discussed whether it is justifiable to apply methods developed for toxicology assessment of chemical substances to viable and reproducible organisms or if new methods had to be developed. The differences between the testing approaches were brought to a wider public when Hilbeck et al. and Losey et al. for the first time showed negative effects of Bt toxins and Bt maize pollen on ecologically relevant non-target organisms in laboratory experiments at a time when Bt crops where already deregulated and cultivated commercially in the US [23-25]. The US authorities did not require an ecologically oriented laboratory or even field test for the deregulation of Bt cotton in 1995 [26]. The respective risk research and assessments were largely and still are based on ecotoxicological laboratory approaches. Standard protocols and organisms are used due to the good reproducibility of experiments, easy breeding of those organisms and low costs of the work. The two different concepts for GMO risk assessment were named 'ecological approach' and '(eco)toxicological approach' [27, 28]. According to the European Food Safety Authority (EFSA), the current arguments and representatives are presented by Andow et al. and Romeis et al., respectively [29-31].

Hilbeck et al. questioned whether the design of these ecotoxicological tests would contribute to assessing the ecological risks of Bt crops [32]. For example, the water flea *Daphnia magna* was exposed to Bt maize pollen and the measurement of 'no effects' was judged as 'no risk' although the Bt toxin contained in the pollen will not dissolve in the water and Daphnia cannot eat pollen.

Similarly 'no effect' results with the earthworm *Eisenia fetida* were accepted although there was no proof that the worms actually had taken up the toxin in the feeding trials. Apart from questionable test designs, it is known that, for example, the widely used earthworm *Eisenia fetida* does not live in agricultural ecosystems [33]. The criticism on using environmentally irrelevant organisms and ill-designed tests added to the existing uncertainty on how to measure 'indirect effects'. For example the effects of herbicides used together with herbicide-tolerant crops, as demanded by the legal framework, how to deal with the foreseeable EU-wide use of antibiotic marker genes in foodstuffs made out of GM crops containing these transgenes and how to evaluate the research work pointing to considerable gene flow in GM canola [34]. It was against this background that the EU Environmental Council[5] declared the stop of all pending GMO application procedures in 1999 until the EU biosafety regulations were revised.

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[5] http://register.consilium.europa.eu/pdf/en/99/st09/st09433-re01.en99.pdf, http://register.consilium.europa.eu/pdf/en/99/st09/st09433-ad01.en99.pdf, http://register.consilium.europa.eu/pdf/en/99/st09/st09433.en99.pdf

4. Different reactions on the new EU biosafety framework

This scientific dispute in combination with societal and economic impacts influenced the revision of the EU GMO regulations [35]. The new EU biosafety Directive 2001/18/EC supports the ecological approach and prescribes a more detailed environmental risk assessment (ERA), establishes the precautionary principle as the baseline for decision making and also serves as ERA reference for the regulation (EC) 1829/2003 on GM food and feed market approval.[6] The five steps of current risk analysis procedures (hazard identification, exposure assessment, consequences assessment, risk characterisation, mitigation options) were accepted as valid for GMOs, but methodologies and interpretations should be adapted to meet the specific features of living organisms and their interactions with the receiving environment [36-39].

Although Directive 2001/18/EC establishes a new framework for ERA prescribing the testing of the GMO as such (not only of the new genes and proteins) and the consideration of the receiving environment (not only some field trial locations as basis for an EU-wide approval), a review of the soil ecotoxicological tests presented in GMO dossiers concluded that they do not reflect the new legal requirements [40]. These authors, in line with Andow and Hilbeck and Snow et al., emphasise that it is crucial not to rely on standard test species only but to choose test species representative of the agro-ecological environments in which the GM plants will be grown [41, 42]. A recent EFSA Scientific Opinion elaborates extensively on the issue of species selection that should take into account the 'ecological relevance of the species, susceptibility to known or potential stressors, anthropocentric value, testability, exposure pathways' of non-target organisms [29]. Furthermore, experiments with the actual GM crops at different levels of complexity have to be performed as a basis for a sound risk assessment [43].

The stated deficits in the GMO dossiers and a series of publications that argue against a wider application of the ecological approach in ERA show that the implications of the new legal framework are seen as critical by developers of GM crops and scientists advocating their use. A Syngenta scientist states that, 'environmental risk assessment research has often attempted to describe the multitude of potential interactions between transgenic plants and the environment, rather than to test hypotheses that the cultivation of transgenic plants will cause no harm' [28]. In this view, the ecological approach is accused of supporting decision-makers against approving GM crops, and ecologists advocate for even more research into complex ecological interactions which would increase confusion rather than create clarity. Raybould addresses not only the methodology of ERA but also the central normative problem in the relationship between risk research and risk

[6] http://ec.europa.eu/food/food/biotechnology/gmo_intro_en.htm

assessment: who determines what kind of hypothesis has to be tested, which level of scientific knowledge and certainty is needed before making decisions, and where is the border between 'need to know and nice to know'.

Developers of GM crops suggest different approaches on how to accelerate GM crop approvals under the new EU system. One basic suggestion of Raybould is that 'ecologists must avoid the temptation to test null hypotheses [of no difference between a transgenic plant and a non-transgenic comparator]' but test risk hypotheses on adverse effects of GM crops on environmental goods and processes that need to be protected [28].

With regard to the EU political and legal background, it seems questionable if this approach will lead to the desired outcome. First, the necessary decisions on protection aims have not yet been taken in the EU. Furthermore, the suggestion does not reflect the concept of the EU biosafety legislation saying that the application of gene technologies might lead to new risks and that, therefore, the first requirement of risk assessment is to test the above-noted null hypothesis on unforeseen differences between the GMO and its parents.

The second suggestion of private sector representatives in relation to the ecotoxicological approach is that field tests should not be a prerequisite for GMO approvals, but should only be demanded when literature studies or ecotoxicological experiments show significant negative effects [44]. A scientist of Monsanto suggests that this model should also be applied to his company's drought-resistant GM maize, a trait that until now was seen as a model case for more complex, ecologically oriented risk research and assessment [45]. This approach enabling a more expedient approval of GM crops was supported by US and EU governmental risk assessors and public scientists in a joint publication on risk assessment of non-target effects of Bt crops and accordingly shaped the draft guidance on GM crop risk assessment presented by EFSA [31, 46].

5. Normative dimensions of risk assessment

In those discussions, it became apparent that ERA steps 1 and 5 as described by Hill are not restricted to the application of scientific methodology but must also be based on substantial normative and thus value-loaded decisions [37]. Many authors state that step 1 indeed needs to be broadened and developed into a 'Problem Formulation'. Scientists advocating the ecological approach developed the problem formulation and options assessment (PFOA) tool, based on stock-taking exercises, stakeholder consultation and broader public participation procedures [47]. The PFOA was tested in developing countries not only to improve the ERA but as a technology assessment tool following the suggestion of the Organisation for Economic Co-operation and Development (OECD) [48-51]: 'Analyses leading to risk management decisions must pay explicit attention to the range of standpoints, in particular in situations with a high potential for controversy. This is often best

done by involving the spectrum of participants in every step of the decision-making process, starting with the very formulation of the problem to be analysed. Introducing more public participation into both risk assessment and risk decision-making would make the process more democratic, improve the relevance and quality of technical analysis, and increase the legitimacy and public acceptance of the resulting decisions.' When Raybould reflected on the UK farm scale evaluations of GM herbicide tolerant (GMHT) crops, he illustrated clearly that the problem formulation (step 1) strongly depends on the respective stakeholder interests [52].[7] From a herbicide-producing company's perspective, the preservation of arable weeds presents no value and the aim of any GMHT crop system is to reduce their abundance; from a nature conservation perspective, however, arable weeds are a valuable part of biodiversity that should not be eradicated in agro-ecosystems.

While this attitude of a scientist from the private sector is not very surprising, it can be observed that public scientists in application-oriented fields such as plant biotechnology tend to adopt comparable attitudes [53]. Kvakkestad et al. interviewed 62 Scandinavian scientists on their perspectives with regard to the deliberate release of GM crops against their professional and funding backgrounds [54]. Two perspectives prevail: the first perspective is held by many publicly funded scientists who emphasised that the environmental effects from GM crop are unpredictable, and the second perspective is held mainly by scientists from the biotechnology industry who emphasise that GM crops present no unique risks. No ecologist associated himself/herself with perspective two. Publicly funded scientists that do not hold the first perspective but promote biosafety systems that establish enabling environments for the adoption of GM crops are meanwhile organised in lobby groups such as the Public Research and Regulation Initiative (PRRI), funded by a former Syngenta manager [55].

Also, step five of the ERA and the activities leading to the final decision involve much more than pure science. Millstone et al. stated that the attitude of authorities to deal 'asymmetrically' with research that showed negative effects compared to research that could not show negative effects is interpreted by the public as support of the authorities for the developers of GMOs [56]. The Cartagena Protocol on Biosafety explicitly refers in its Risk Assessment Annex to this common attitude when it obliges its member states to consider that 'lack of scientific knowledge or scientific consensus should not necessarily be interpreted as indicating a particular level of risk, an absence of risk, or an acceptable risk'. This formulation was agreed upon by the negotiators as a way of implementing the precautionary

[7] 'In the UK Farm Scale Evaluations of GM herbicide tolerant (GMHT) crops, an assessment endpoint was the sustainability of populations of arable weeds in fields. The observed reductions in arable weed populations in some GMHT crops were considered detrimental effects, because weeds were considered to be valuable biodiversity.'

principle in GMO risk assessment and decision-making [57]. To address these normative issues in a democratic and socially acceptable way, new processes are needed, which must ensure that the point of view of every stakeholder can influence problem formulation in risk assessment and the final decision-making [58,59,51,60].

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Advancing Risk Assessment under the Cartagena Protocol on Biosafety

Beatrix Tappeser
Federal Agency for Nature Conservation (BfN), Germany
and *David Quist*
GenØk – Centre for Biosafety, Norway

1. Background

THE Cartagena Protocol on Biosafety, the first Protocol developed under the Convention on Biological Diversity (there are now three), entered into force in September 2003. It aims to ensure 'the safe handling, transport and use of living modified organisms (LMOs) resulting from modern biotechnology that may have adverse effects on biological diversity, taking also into account risks to human health'. The Protocol has currently 163 parties (as of August 2012).

With decision IV/11 taken during COP-MOP4 in Bonn, 2008, the Parties mandated an Ad Hoc Technical Expert Group (AHTEG) on Risk Assessment and Risk Management to:

(i) Develop a 'roadmap', such as a flowchart, on the necessary steps to conduct a risk assessment in accordance with Annex III to the Protocol and, for each of these steps, provide examples of relevant guidance documents;

(ii) Take the identified need for further guidance on specific aspects of risk assessment into consideration, including particular types of (i) living modified organisms (for example, fish, invertebrates, trees, pharmaplants and algae); (ii) introduced traits; and (iii) receiving environments. Monitor long-term effects of living modified organisms released in the environment, prioritise the need for further guidance on specific aspects of risk assessment and define which aspects should be addressed first, taking also the need for and relevance of such guidance, and availability of scientific information into account; ...

The AHTEG was formed to reflect regional balance and a diversity of Parties and expertise. Following the rules of procedure Non-Parties and observers from industry, academia and NGOs participated as additional stakeholders in this multi stakeholder but Party-driven process. Altogether 27 experts worked together in the AHTEG.

Two years later in Nagoya, the mandate of the existing AHTEG was prolonged and the Parties recommended in their decision V/12 (among other things) that the expert group should:

- coordinate with Parties and other Governments, through their technical and scientific experts, and relevant organisations, **a review process of the first version** of the Guidance;
- **update the common format** for submission of records to the Biosafety Information Resources Centre in order to link its records on risk assessment to specific sections of the Guidance; and
- develop **new guidance** on specific topics or aspects of risk assessment.

As a result of these mandates the AHTEG will present a singular Guidance document comprised of three different parts at the upcoming COP-MOP6:

Part I: A Roadmap for risk assessment, together with a flowchart
Part II: Additional guidance on specific types of LMO and encompassing traits
- LM plants with stacked genes,
- abiotic stress-resistant LM plants,
- LM trees
- LM mosquitoes

Part III: Guidance on monitoring of LMOs released into the environment.

A first version of the roadmap and the additional guidance on stacked genes, abiotic stress resistance and LM mosquitoes were presented to COP-MOP5 in Nagoya. Some Parties had the feeling that this package needed further scientific assessment and review. This recommendation - reflecting also the diverging views on the way to translate the principles of conducting an environmental risk assessment of Annex III into real life - became part of the new terms of reference in decision V/12 of Nagoya together with the task to develop an additional new guidance according to the priorities and needs of the Parties. With their decision to extend the mandate of the AHTEG the COP-MOP also strengthened the role of the open-ended expert online discussion forum. Registered national experts from Parties and observers were asked at multiple rounds to comment on the draft version of the roadmap and the additional guidance of the first period as well as on the newly developed documents on LM trees and monitoring.

2. Outcome to date

Worldwide, different concepts exist on how to conduct an environmental risk assessment (ERA). What are the protection goals, how to define baselines, which agricultural practice shall be considered and how may the precautionary approach

be looked at and integrated? The Cartagena Protocol and especially its Annex III define the agreed steps and main points to be considered. However the conversion of the agreed steps into a real-life practical tool for the assessment of applications is not an easy task; moreover it also allows for different options.

With the development of the Roadmap and the additional guidance documents, Parties have a framework that they can use and adapt to their conditions, needs and obligations. The Guidance reflects different concepts and interpretations of risk assessment. At the same time it is a compromise between different scientific understandings of what is necessary and should be recommended during an ERA.

An important aspect of the whole Guidance package is the understanding of it as a living document. It can be and should be amended when experience about its usefulness and practicality has been gathered.

3. Innovation and strengths of the Guidance

The outcome of the AHTEG Guidance produces a number of innovations and improvements on appraising risks. Firstly, the Guidance recognises that an environmental assessment of risks does not happen in a vacuum, but criteria and needs from the risk assessment may be formed by other actors or aspects related to those of the environment. Secondly, the Guidance provides clear requirements that information should be of high scientific quality (transparency, reproducibility, and if necessary, access to research material and raw data for verification). Thirdly, the Guidance recognises the need for describing the nature and sources of uncertainty in the assessment, and communicating them to decision-makers when assessing the acceptability of risk. Fourthly, the Guidance recognises that the risk assessment is a process that may involve a stepwise and iterative advancement where risks at smaller spatial or time scales of release may be assessed before larger releases are permitted to take place. Lastly, analysing risks within the context of alternative options is also considered as important in the process of step five concerning the acceptability of risk.

4. Weaknesses of the Guidance

Despite some critical advances in thinking on risk, the Guidance contains a few general weaknesses in its approach. Most critical is the over-emphasis of the provision for comparative risk assessment. Comparing the composition, performance, and behaviour of an LMO in comparison to its conventional counterpart has historically been a cornerstone in LMO risk assessment, however this approach contains a number of flaws and disadvantages that compromise its efficacy as a measure of safety. In the current Guidance document, this limitation is apparent in the discussion of the 'choice of comparators' which effectively allows the use of very broad comparators – an approach that tends to underestimate

differences and overestimate similarity (e.g. 'equivalence') between comparators. This ultimately undermines a scientifically robust approach to the comparative feature of the risk assessment.

The other area in which the Guidance fails to deliver is in providing a link to other aspects of risk that may be taken into consideration in the entire decision-making process – socio-economic issues, legal issues, and ethical issues – at the fore. The interface between determining 'acceptability' of risks within the context of broader issues is currently subsumed by the technical provisions of risk and safety for decision-making.

5. Contentious issues

Generally speaking, the Guidance has thus far received good support. However, a few issues may undermine its support at the COP-MOP meeting, including the rejection by some to consider 'related issues' as part of the Guidance and the breadth of monitoring that should be described and possibly required (general vs. specific monitoring) after the release of an LMO into the environment. Whereas in Europe, case-specific and general monitoring are legal requirements, these provisions do not exist in other national legislations.

There were a number of smaller aspects with diverging views like the use of 'omics' technologies as a tool of evaluating differences between an LMO and its conventional counterparts, or the scope of the additional guidance of LM trees (e.g. whether scope covers fruit trees or not). These issues are likely to be discussed in Hyderabad, and the outcomes will largely determine the strength of support for the document package as a whole.

6. The way forward

The AHTEG agreed upon a set of recommendations which will be made to the COP-MOP meeting in Hyderabad:

Regarding the 'Guidance on Risk Assessment of Living Modified Organisms'

1. Endorse the 'Guidance on Risk Assessment of Living Modified Organisms'.
2. Request the Executive Secretary to make the Guidance available to Parties in all six United Nations languages through the Biosafety Clearing House (BCH).
3. Encourage Parties, as appropriate, to translate the Guidance into national languages, and make them available in the BCH for wider dissemination.
4. Encourage Parties, other Governments and relevant organisations through their risk assessors and others who are actively involved in risk assessment, to use and test the Guidance in actual cases of risk assessment and share their experiences on its practicality, usefulness and utility through the BCH, their

third national reports and any other surveys, interviews and/or questionnaires as may be organised by the Secretariat.

5. Request the Executive Secretary, subject to the availability of funds, to gather and analyse feedback provided by Parties on the practicality, usefulness and utility of the Guidance and make recommendations to the next COP-MOP on possible points for improvement.

6. Establish a mechanism to ensure the regular update of the background documents to the Guidance, as follows:

……

Regarding the development of additional guidance on specific topics

7. Extend the mandate of the Open-ended Forum and AHTEG beyond the sixth meeting of the Parties to the Protocol, with revised terms of reference, to develop guidance on new topics, taking into account any results of use and testing of the revised Guidance, as well as the needs of Parties and the list of topics in Annex IV to this report;

……

Regarding capacity-building in risk assessment and risk management

10. Request the Secretariat, subject to the availability of funds, to:

(i) Ensure coherence between the Training Manual on Risk Assessment and Part I of the Guidance (i.e., Roadmap);

(ii) Develop an advanced educational package that integrates the Guidance into the Training Manual (e.g., e-learning material);

(iii) Conduct training using the advanced educational package for risk assessors, taking into consideration actual cases of risk assessment;

(iv) Follow up on the training exercise by gathering additional feedback from Parties on the practicality, usefulness and utility of the Guidance through online discussions or other means, as appropriate;

(v) Conduct international and/or (sub-) regional workshops on Risk Assessment and Risk Management with special emphasis on applying the Guidance in the process of actual decision-making under the procedures of the Protocol.

…..

Regarding risk assessment in general

12. Urge Parties to provide the BCH with prompt and detailed information on their risk assessments of LMOs for introduction into the environment, including field trials, as well as LMOs for direct use as food, feed, or for processing (LMO-FFPs) with the view to sharing their experiences.

7. Conclusion

It can be expected that there will be some discussions on the quality of the currently developed Guidance reflecting different views on the right way to implement the principles of Annex III. Another contentious issue is whether the mandate of the current AHTEG should be extended and if there is the need for further guidance.

For some experts of the AHTEG, it was difficult to accept that the Cartagena Protocol is a Protocol to the Convention on Biological Diversity and therefore should also respect and adhere to the principles and recommendations of the Convention. They would prefer to handle the Protocol as a stand-alone document.

Besides the further development and improvement of the Guidance package, it seems to be of utmost importance to underline and strengthen this coherence to support the overall aim of conservation of biological diversity as the prerequisite for sustainable use. In our opinion, overall outcomes of the AHTEG activities, on the balance, provide good guidance for advanced understanding of risk appraisal that will be useful for the implementation of risk assessment frameworks to strengthen national biosafety legislation. Despite the challenges ahead, putting the Guidance to use will be the best measure of its ability to uphold the core objectives of the Cartagena Protocol.

Socio-Economic Considerations in GMO Decision-Making

Georgina Catacora-Vargas
Society, Ecology and Ethics Department (SEED), GenØk-Centre for Biosafety, Tromsø, Norway and
Institute of Research on Risk and Sustainability (IRIS), Department of Sociology and Political Sciences, Federal University of Santa Catarina, Florianópolis, Brazil

1. Introduction

THE inclusion of socio-economic considerations in biosafety decision-making is a widely debated issue at international, regional and national levels. Despite significant experience and acceptance of the inclusion of social and economic aspects in environmental decision-making (Freudenburg 1986; Bereano 2012), the recognition of the eco-social interrelationship and its practical implementation in regulation related to genetically modified organisms (GMOs) have been more difficult and contentious (Secretariat of the CBD 2003; MacKenzie *et al*. 2003).

The arguments both in favour and against the inclusion of socio-economic considerations in biosafety decision-making are diverse. Points of view in favour acknowledge the relevance of socio-economic considerations in risk assessment and management of GMOs due to their potential impacts on biological diversity that may in turn jeopardise rural livelihoods, indigenous knowledge, market opportunities and even national economies, etc. These concerns have been more forcefully raised by governments and institutions in countries that are centres of origin and genetic diversity (MacKenzie et al. 2003; Khwaja 2002; Secretariat of the CBD 2011; Pavone 2011). In contrast, opinions against consider socio-economic considerations of limited relevance in GMO regulation. Moreover, it is argued that their inclusion could delay the process of adoption of new technologies and increase the cost of compliance with biosafety policy (Falk-Zepeda and Zambrano 2011; Falk-Zepeda 2009, Secretariat of the CBD 2011; Secretariat of the CBD 2003).

Nevertheless, several countries have been – and are in the process of - including socio-economic provisions in their national biosafety frameworks, including countries that are not Parties to the Cartagena Protocol on Biosafety (Spök 2010; Bereano 2012). The Cartagena Protocol on Biosafety is the multilateral environmental agreement that sets international rules and procedures for the safe transfer, handling and use of GMOs in order to prevent *'adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health'* (Article 1) (Secretariat of the CBD 2000: 3).

Based on the current experience related to impacts of GMOs at the socio-economic level, and the need for greater conceptual clarity on its utility, the following sections provide some elements on the basic questions of *what*, *why*, *when* and *how* to include socio-economic considerations in GMO decision-making.

2. *What* are socio-economic considerations related to GMOs?

There is not yet a clear and agreed definition on what socio-economic considerations entail in the context of biosafety regulation, despite more mature use of the concept in other fields of environmental decision-making (e.g. Sadler and McCabe 2002). In order to advance some conceptual clarity and for the purpose of this paper, the definition of social impacts given by Sadler and McCabe (2002) in United Nations Environmental Programme training manuals could be adapted to preliminarily describe socio-economic considerations related to GMOs as *the set of the intertwined social and economic consequences resulting from the changes arising from the introduction of GMOs into the environment, which need to be taken into account in the biosafety decision-making processes*.

Three aspects need to be pointed out from this proposed description:

1. The core of the analysis is the consequences or impacts of changes rather than only the changes. This is because some changes may not result in impacts (Vanclay 2002), or more importantly, may overshadow the real relevant effects (see Box 1 for further discussion on this point).
2. The socio-economic considerations embrace two general types of impacts: i) tangible and mostly quantitatively-measured impacts, such as changes and resulting outcomes in income generation, trading opportunities, forms of livelihoods, work generation, local organisation, access to food, food quality, health status, gender equity, etc., and ii) intangible and mostly qualitatively-measured impacts such as cultural and psychological changes and related impacts, e.g. changes in values, attitudes, perceptions, communities, visions for the future, etc. (Sadler and McCabe 2002).
3. Since social and environmental contexts vary from place to place, socio-economic impacts and therefore socio-economic considerations will vary from community to community and even from group to group (Vanclay 2002). This brings methodological challenges as discussed below.

3. *Why* socio-economic considerations in decision-making related to GMOs?

A 'Nature-Society co-evolution', in development, i.e. the process of development from the mutual influence between the environmental and social systems (Norgaard and Sikor 1999) recognises that all interventions (e.g. projects and technology) have implications for both the environment and society (Pavone

Box 1. Consideration of the impacts of changes, rather than only the changes themselves

Glyphosate-tolerant soybean is promoted under the claim that its adoption will contribute to reducing the use of toxic herbicides. Since the provisional approval (in 2003) of genetically modified (GM) soybean tolerant to the herbicide glyphosate in Brazil, the use of ghyphosate has increased considerably, from 62.5 thousand kilograms of active ingredient applied in 2003 to approximately 300 thousand in 2009 (Meyer and Cederberg 2010). This change in volume equals an increase of 380% in the use of glyphosate as active ingredient. This increase results mainly from two processes: The increase in the area planted with soybean tolerant to glyphosate (Catacora *et al.* 2012), and the loss of efficacy of glyphosate in controlling weeds (Waltz 2010) due to the appearance of glyphosate-resistant weeds (Cerdeira *et al.* 2011). In order to control such weeds, herbicides more toxic than glyphosate are used, such as paraquat. Although paraquat was banned in Europe in 2007 due to its implications for neurological and reproductive disorders (Wright 2007; Frazier 2007), the import and use of paraquat is increasing in the largest (GM) soybean-producing states of Brazil (Meyer and Cerderberg 2011). In 2009 alone, 3.32 million litres of this herbicide was applied in the country (Catacora *et al.* 2012).

This case shows two changes in the production systems of soybean in Brazil: The first related to the introduction of GM soybean and the second, to increased glyphosate use. Since there is a wide controversy on the safety of GM crops and glyphosate, probably these changes may not say much. However, the consequences are the core of the socio-economic impact analysis, such as the development of glyphosate-resistant weeds that results in increased use of highly toxic herbicides, which at the same time are linked to other impacts: increased production costs as a result of the purchase of additional herbicides other than glyphosate and increased health risks. If the socio-economic assessment focuses only on the changes (e.g. introduction of glyphosate-tolerant soybean as a means of reducing the use of other more toxic herbicides) and not on the effects of those changes, there is the risk of overlooking the related consequences and, as a result, failure to consider these aspects in the GMO decision-making process.

et al. 2011). This gives the rationale for *why* socio-economic considerations are relevant in environmental decision-making processes, such as the introduction of GMOs into the ecosystems. In addition to the evident mutual relationship between the environment and society, Borrow (2002) adds two other reasons for the consideration of socio-economic aspects in decision-making: One is the growing demand for social responsibility by markets and regulations (exemplified by the growing demand for fair trade and socially-responsible products); and two, the global necessity of advancing sustainable development objectives.

4. *When* should socio-economic considerations be considered?

The debate on *when* to consider the socio-economic impacts of GMOs in the decision-making process is another unresolved issue in the biosafety discussions.

Socio-economic assessment can be performed either before (*ex-ante*) or after (*ex-post*) the GMO introduction. Both are different in purpose and information provided.

Ex-ante assessments are anticipatory, in other words, they aim to determine the potential impacts and undesired risks of GMO, information that is relevant during the decision-making process over applications of introduction of GMOs. These kinds of assessments are precautionary and have the potential to better contribute to sustainable development efforts (Borrow 2002). The Cartagena Protocol on Biosafety highlights the *ex-ante* consideration of socio-economic impacts. Article 26.1 of the Protocol mentions that for Parties who choose to include socio-economic considerations in their biosafety procedures, these are applicable in the process of reaching a decision on import of GMOs (Secretariat of the CBD 2000).

Conversely, *ex-post* assessments focus on the monitoring of the risks identified in the *ex-ante* evaluation, and detecting any potential or real unforeseen adverse effects either from approved or illegally introduced GMOs. *Ex-post* assessments are relevant for identifying and taking preventive or corrective measures in the case of risk or damage, respectively, from GMOs.

Based on the differentiated aims and types of information provided, these two types of assessments are not inter-changeable. This means that one cannot replace the other since they fulfil different purposes and provide information for different decision-making processes.

5. *How* to include socio-economic considerations?

Generally speaking, socio-economic aspects and impacts related to GMOs are complex for diverse reasons: i) they vary along time and across space, and may occur over short time periods or within locations geographically close to each other; ii) multiple factors may influence social systems simultaneously, highlighting the importance of their inclusion in the socio-economic analysis (e.g. social, economic, cultural, political, ethical, etc. factors); and iii) societies are embedded in the natural environment (a more complex system in itself) giving place to another set of socio-economic considerations arising from the Nature-Society relationship (Borrow 2002; Norgaard and Sikor 1999).

These various features described above provide the rationale for the inclusion of the following methodological assessments and decision-making approaches related to socio-economic considerations:

- ***Integrated and complementary assessment to environmental risk assessment.*** As mentioned above, ecological and socio-economic factors are intertwined and influenced mutually. This is clear in the example given in Box 1 where a socio-economic change i.e. the introduction of a GM herbicide-tolerant variety and the inherent intense use of the specific herbicide that this variety is tolerant to, resulted in ecological changes (such as appearance of herbicide-tolerant weeds) that at the same time gives place to a new set of eco-social implications: the need for other herbicides to combat weed resistance that further pollute the agro-ecosystem, increase the production costs and increase the risk to public health.
- ***Holistic by including direct and indirect as well as cumulative and combinatorial effects***. Changes and their consequences rarely occur in a linear or isolated manner in nature or societies. Since both systems are complex, changes result in direct and indirect, combinatorial and cumulative, and hence are often unforeseen impacts (Stabinsky 2001; Cardinale *et al.* 2012), out of which some may be undesirable. This justifies the need for monitoring the performance of GMOs if introduced into the environment. Following the example given above and from Box 1, the increased use of glyphosate is a direct impact from cultivating glyphosate-tolerant varieties. A reported indirect impact is the use of more toxic herbicides (e.g. paraquat) to control glyphosate-resistant weeds that appear over time. This, combined with the need for larger investments to purchase such herbicides and the higher risks to the health of ecosystems and human populations, the example of Box 1 points to a potentially unsustainable production system in the long term at ecological, social and economic levels.
- ***Multi- and transdisciplinary approaches***. The complexity of socio-economic issues, particularly the ones related to the environment, requires an assessment and decision-making process that includes different disciplines that exchange knowledge and information. In the case summarised in Box 1, ecological, health and social sciences are needed to adequately understand and estimate the corresponding risks taking place: alterations in weed populations, exposure to different herbicides, and changes to local livelihoods that may result from introductions of GMOs. Also highly relevant yet often ignored areas, such as ethics, play an important role. For instance, the ethical considerations of increasing export and use of pesticides banned in some regions (such as paraquat) and its impacts on the welfare of local ecological and social systems.
- ***Methodologically pluralistic***. Based on the above, an expected conclusion is the application of different research and decision-making approaches utilising diverse fields of knowledge; also necessitating the broader inclusion of questions to be answered and concerns from actors to be involved or impacted. The application of not only quantitative but qualitative (including participatory) methods is essential in socio-economic assessments. The

participation of an informed public is crucial for achieving societal-relevant outcomes in both GMO research and decision-making.

– ***Context specific***. As stated earlier, the eco-social interrelationship varies at temporal and geographical scales. This requires a case-by-case and regularly updated assessment of the socio-economic impacts of GMOs according to the social and ecological context where they are introduced.
– ***Long-term oriented***. Only long-term assessments will provide proper information on the socio-economic impacts of GMOs and their consequences on sustainability. The indirect, combinatorial and cumulative effects of GMO introductions in complex systems such as nature and society will not be appropriately captured or assessed in short-term scenarios.

6. Final comments

Socio-economic impacts (positive or negative, predicted or unforeseen) are an inherent part of technology introduction and adoption. This points to the need for including socio-economic considerations in biosafety decision-making related to GMOs.

The Nature-Society interface defines the complexity of the socio-economic dimension of any intervention (e.g. projects or technologies) and calls for a thoughtful and comprehensive methodological approach characterised by: a holistic view, integrative with environmental risk assessments, multi- and transdisciplinarity, methodological pluralism, context specificity and long-term orientation. In other words, proper socio-economic assessments will require going beyond the common practice of mostly economic assessments, but aiming towards sustainable-development-relevant appraisals. In order to carry out these socio-economic assessments relevant to sustainability, precautionary or anticipatory (also called *ex-ante*) assessments are needed, complemented with regular monitoring (or *ex-post*).

The challenges ahead for the appropriate assessment of socio-economic implications related to GMOs and their inclusion in environmental decision-making processes are significant. However, equally significant is their relevance, particularly in light of sustainable development. Hence, failing in the adequate consideration of the socio-economic dimension in biosafety processes may jeopardise nature's and society's welfare.

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Flaws of 'Comparative Safety Assessment' as Developed by EFSA

Hartmut Meyer and *Angelika Hilbeck*
European Network of Scientists for Social and Environmental Responsibility (ENSSER)

1. Introduction

ON 22 January 2008, the Directorate-General (DG) Environment of the European Commission asked the European Food Safety Authority (EFSA) to work on four guidelines to clearly define and describe different aspects of environmental risk assessment (ERA) of genetically modified plants (GMP).[8] In its response, EFSA suggested integrating the work in its ongoing work on reviewing the guidelines for ERA and proposed a revised version of the terms of reference.[9] On 19 March 2008, DG Environment agreed to the revised terms of reference and tasked EFSA to 'further develop and update its guidelines as regards the environmental risk assessment', covering the following points:

'1. Environmental risk assessment of potential effects of genetically modified plants on non-target organisms through
   i. Development of criteria for the selection of non-target organisms and representative species thereof, focusing on arthropods and other invertebrates, and also considering other relevant non-target organisms in different trophic levels;
   ii. Selection and recommendation of appropriate methods to study the potential effects of GM plants on these non-target organisms;
2. Development of criteria for field trials to assess the potential ecological effects of the GM plants in receiving environments (including experimental design and analysis to ensure sufficient statistical power);
3. Identification of the EU geographic regions where GM plants (combinations crop + trait) may be released and the selection of representative receiving environment(s) which reflect the appropriate meteorological, ecological and agricultural conditions;

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8 Letter ENV B3/AA/D(2008)23828
9 Letter Ref.SR/SM/shv(2008)2770072

4. Selection of appropriate techniques to assess potential long-term effects of GM plants including experimental and theoretical methodologies, and recommendations for establishing relevant baseline information.'

DG Environment further stated that 'as for the guidance presently developed for food and feed, it is our objective that this guidance document on environmental risk assessment will have regulatory status and will be adopted by the Member States with the support of risk assessors at national level.'[10] Finally, EFSA published two draft scientific opinions on 5 March 2010 and called for public comments by 30 April 2010.[11] The final document was published on 12 November 2010.[12] The European Network of Scientists for Social and Environmental Responsibility (ENSSER) sent comments on the draft scientific opinions[13] and participated at the EFSA-NGO meeting on 28 September 2010 to discuss the draft ERA guidance.[14] In this document, ENSSER would like to continue this work and to comment on the current version of the ERA guidance.

2. Implementation of the 'one door one key' procedure

The EFSA Panel on Genetically Modified Organisms (GMO) in its Guidance on the environmental risk assessment of genetically modified plants of October 2010 (Guidance) (EFSA GMO Panel 2010) aims at providing a framework for ERA as part of applications for market approval of GMOs for food and feed. The Regulation (EC) No 1829/2003 on genetically modified food and feed[15] (Regulation 1829/2003) enables a '"one door one key" procedure for the scientific assessment and authorisation of GMOs and GM food and feed resulting in a centralised, clear and transparent EU procedure where an operator is able to file a single application'.

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10 Letter ENV/B3/CB/zg(2008)D/4802

11 Public consultation on the draft scientific opinion on the assessment of potential impacts of genetically modified (GM) plants on non-target organisms (NTOs) http://www.efsa.europa.eu/en/consultations/call/gmo100305.htm
Public consultation on the draft guidance document for the environmental risk assessment of genetically modified plants http://www.efsa.europa.eu/en/consultations/call/gmo100305a.htm

12 Guidance on the environmental risk assessment of genetically modified plants http://www.efsa.europa.eu/en/scdocs/scdoc/1879.htm

13 http://www.ensser.org/activities/projects/reforming-the-gmo-approval-system/

14 EFSA Meeting with Non-Governmental Organisations on genetically modified organisms (GMOs) http://www.efsa.europa.eu/en/events/event/gmo100929.htm

15 http://eur-lex.europa.eu/smartapi/cgi sga_doc?smartapi!celexapi!prod!CELEXnumdoc&lg=en&numdoc=32003R1829&model=guichett

This means that the market approval application for a specific GM food and feed can include an application for approving the planting of the respective GM plant as well.[16] Regulation 1829/2003 foresees that the necessary ERA follows the principles and procedures described in Directive 2001/18/EC on the deliberate release into the environment of genetically modified organisms[17] (Directive 2001/18).

The applicable principles and procedures for GM food and feed risk assessment are not described by Regulation 1829/2003. GM food and feed risk assessment has to be conducted under the framework of Regulation (EC) No 178/2002, laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety[18] (Regulation 178/2002). The specific principles that should be applied for the risk assessment of GM food worldwide have been adopted by the FAO/WHO Codex Alimentarius in 2003, followed by three specific guidelines for GM plants, microorganisms and animals.[19]

In its Guidance, EFSA uses the concept of the 'one door one key procedure' to combine the established principles and procedures for, on the one hand, GM food and feed risk assessment and, on the other hand, GM plant environmental risk assessment. The Guidance does not only elaborate on one common application procedure but suggests unifying risk assessment principles and procedures that have, in our opinion, distinct, different and even incompatible features. Unfortunately, this fusion will not strengthen but will instead weaken ERA. The Guidance applies the concepts of substantial equivalence/familiarity – developed in the context of food and feed risk analysis under the US regulatory biosafety system – as methodological filters to decide whether statistically significant differences in unintended ecological effects need to be assessed through ERA or if they can be declared as biologically irrelevant, meaning ecologically irrelevant in

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16 Press Release of the EC, 22.07.2003: European legislative framework for GMOs is now in place http://europa.eu/rapid/pressReleasesAction.do?reference=IP/03/1056&format=HTML&aged=0&language=EN&guiLanguage=en

17 http://eur-lex.europa.eu/smartapi/cgi/sga_doc?smartapi!celexapi!prod!CELEXnumdoc&lg=EN&numdoc=32001L0018&
model=guichett

18 http://eur-lex.europa.eu/smartapi/cgi/sga_doc?smartapi!celexapi!prod!CELEXnumdoc&lg=EN&numdoc=32002R0178&model=guichett

19 CAC/GL44: Principles for the Risk Analysis of Foods Derived from Modern Biotechnology http://www.codexalimentarius.net/download/standards/10007/CXG_044e.pdf CAC/GL45: Guideline for the Conduct of Food Safety Assessment of Foods Derived from Recombinant-DNA Plants http://www.codexalimentarius.net/download/standards/10021/CXG_045e.pdf CAC/GL46: Guideline for the Conduct of Food Safety Assessment of Foods Produced Using Recombiant-DNA Microorganisms http://www.codexalimentarius.net/download/standards/10025/CXG_046e.pdf CAC/GL68: Guideline for the Conduct of Food Safety Assessment of Foods Derived from Recombinant-DNA Animals http://www.codexalimentarius.net/download/standards/11023/CXG_068e.pdf

the context of large-scale plantations of GMPs. The comparators on which such decisions are based are usually not the unmodified parental organisms – as required by EU legislation –but a range of currently used, foreign or obsolete plant varieties to broaden the variance range. The Guidance does not indicate which varieties and tests have to be used to assess 'familiarity'.

As laid down in the Guidance,[20] EFSA has introduced a 'comparative safety assessment' as a new and upstream decision-making step in the ERA, that will be used by the EFSA GMO Panel to decide on how to deal with documented, statistically significant differences in unintended effects prior to the conduct of the established six steps of ERA. The EFSA GMO Panel will be empowered to take decisions on the interpretation of scientific data at three points:

– Determination of the consistency of the observed differences;
– Determination of the non-transient nature of the observed differences; and
– Determination of the biological relevance of the observed differences;

based on the data mainly generated by the applicants.

With this approach, EFSA deviates from its previous guidance documents (e.g. EFSA GMO Panel 2006 & 2008) that – in accordance with EU legislation – speak of applying a 'comparative approach' as a methodological element of the ERA. It is generally accepted and indeed necessary that during an ERA a 'comparative approach' is needed to check whether through the process of genetic engineering unintended changes in the GMP have occurred. The potential of such unintended changes to cause environmental risks needs to be assessed through an environmental risk assessment. The principles and steps of such an ERA are established by the EU legislation, and it was EFSA's mandate to update certain elements in these steps of the ERA,[21] but not to add a new chapter that might render the ERA under EU biosafety legislation ineffective.

[20] see Figure 1, p.11 and Chapter 2.1, p.12-13 of the Guidance
[21] http://registerofquestions.efsa.europa.eu/roqFrontend/questionLoader?question=EFSA-Q-2008-262# to see the correspondance between the EC and EFSA, click on 'Mandate Number'.

3. Comments on Guidance Chapter 2.1

3.1 Comparative safety assessment as new principle in ERA

Firstly, ENSSER doubts that EFSA is mandated to introduce new principles in the ERA. Directive 2001/18/EC clearly defines five general principles working in accordance with the precautionary principle as basis for the ERA[22]. Based on the first EFSA presentation of the Guidance at a seminar in the European Parliament on 12 January 2011[23], it can be concluded that EFSA abandoned three of the ERA principles established by Directive 2001/18 and replaced them with two food and feed risk assessment concepts and one completely new concept (see Table 1). While EFSA does not list the reiterative nature of ERA and the analysis of long-term effects as principles any longer, these issues are still dealt with in the Guidance.

Secondly, ENSSER doubts that the comparative safety assessment – a recent rewording of the concept of substantial equivalence – is an appropriate principle guiding the implementation of the EU laws on biosafety and GMO environmental risk assessment.

The comparative safety assessment has been developed by Harry A. Kuiper – the former chair of the EFSA GMO Panel – and co-workers as an updated version of the concept of substantial equivalence in the context of the GM food approval process (Kuiper at al. 2001; Kuiper & Kleter 2003; Kok & Kuiper 2003). The comparative safety assessment has been set up in close cooperation and partly under the direct responsibility of the agro-biotechnology industry. ENSSER would like to remind of the fact that the agro-biotechnology industry and/or supporting organisations such as the Public Research & Regulation Initiative (PRRI, with

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[22] Directive 2001/18, Annex II, p.19-20: 'A **general principle** for environmental risk assessment is also that an analysis of the "cumulative long-term effects" relevant to the release and the placing on the market is to be carried out. [...]
General Principles
In accordance with the **precautionary principle**, the following **four general principles** should be followed when performing the e.r.a.:
- identified characteristics of the GMO and its use which have the potential to cause adverse effects should be compared to those presented by the non-modified organism from which it is derived and its use under corresponding situations;
- the e.r.a. should be carried out in a scientifically sound and transparent manner based on available scientific and technical data; the e.r.a. should be carried out on a case by case basis, meaning that the required information may vary depending on the type of the GMOs concerned, their intended use and the potential receiving environment, taking into account, i.e., GMOs already in the environment; if new information on the GMO and its effects on human health or the environment becomes available, the e.r.a. may need to be readdressed in order to:
- determine whether the risk has changed;
- determine whether there is a need for amending the risk management accordingly.'

[23] SEMINAR: GMO RISK EVALUATION. A contradictory debate. Brussels, 12.01.2011 http://www.alde.eu/event-seminar/events-details/article/seminar-gmo-risk-evaluation-a-contradictory-debate-35941/

Table 1: Principles for ERA

Directive 2001/18[24]	EFSA 2011[25]
1. Scientifically sound and transparent manner	1. Scientifically sound and transparent manner
2. Case-by-case basis	2. Case-by-case basis
3. Comparison of GMO with parental organisms	3. Comparative approach
4. Readdress ERA when new information becomes available	4. Concept of familiarity
5. Analysis of the 'cumulative long-term effects	5. Tiered approach

EFSA experts as members) on many occasions and in many statements[26] have rejected the approach of process-triggered biosafety regulations. This approach is the basis of the EU biosafety regulation and the Cartagena Protocol on Biosafety with its 160 Parties; it is the duty of EFSA experts to implement exactly these process-triggered regulations. The continuing collaboration between EFSA risk assessors and applicants from the agro-biotechnology industry leads to strong public concerns about the lack of distance between the respective EFSA experts and the applicants and the objectiveness and independence of the decisions they take (Then & Bauer-Panskus 2010).

The concept of substantial equivalence originates in traditional food safety assessments and has been adapted to the US approach of deregulating foodstuff derived from GMOs (FDA 1992). This approach has been set up under the lead of scientific and legal experts working in public and private entities developing or promoting GM crops and other products of modern biotechnology. The first assumption of the US deregulation system is that the process of genetic engineering will not cause greater unpredicted and unintended effects than the application of conventional methods and thus does not lead to new risks. A second assumption is that the risk assessment is based on an additive model. If a new gene with a determined level of risk is added to an organism, the risk level of that organism will only be increased by the predetermined risk level of the new gene. The rule is to assume that the GMO – apart from the intended change – is substantially equivalent to its conventional counterpart. Risk assessment under this concept does not require the testing of the GMO as such – for example in feeding studies – but can rely on chemical and physical analysis of the components of the GMO/GM food and its counterparts. The idea is that any unforeseen risk factors could be

[24] Lecture Dr. Angelika Hilbeck, page 11 (shorter wording of the original Directive 2001/18 principles) http://www.alde.eu/uploads/media/Hilbeck_ALDE_GMO_debate_12-1-2011.pdf

[25] Lecture Dr. Karine Lheureux, page 8 http://www.alde.eu/uploads/media/Lheureux_ALDE_GMO_debate_12-1-2011_01.pdf

[26] e.g. UNEP 2010a

detected through that analysis. If no substantial differences are detected this is taken as proof of the safety of the respective GM foodstuff.

In contrast to the US, the EU regulation is firstly based on the assumption that the process of genetic engineering can lead to more unpredicted and unintended effects in the GMO than conventional breeding may cause. Secondly, it is assumed that through the introduction of a gene with a predetermined level of risk, the overall risk of the GMO may be greater than the sum of the individual risks. Such potentially synergistic hazards of GMOs cannot be deduced from a compositional comparison of its components alone but requires additional testing of the whole organism. The rule is to assume that the GMO – beyond the intended change – is not equivalent to its conventional counterpart. This alternative assumption is further backed by scores of empirical evidence demonstrating such potentialities.

The notion that the concept of substantial equivalence is a safety assessment in itself has been explicitly rejected by the EU legislator and by the Codex Alimentarius.[27] ENSSER would like to remind that there is a worldwide consensus that the comparative analysis is merely a methodological element applied in the several steps in risk assessment. ENSSER also stresses that the comparative safety assessment has been developed in the context of GM food safety analysis but not in the context of conducting an ERA. The text of Directive 2001/18/EC does not give any indication that EFSA is mandated to apply such an assessment in the context of ERA. It should also be noted that the Ad Hoc Technical Expert Group on Risk Assessment of the Cartagena Protocol (UNEP 2010b) and the relevant decision of COP-MOP5 on the future 'Roadmap' for risk assessment[28] do not give any indications that a comparative safety assessment should be a new step or even principle in ERA.

3.2 Comparative safety assessment as new decision-making step in ERA

In chapter 2.1, EFSA has introduced a two-tiered approach to deal with significant differences of unintended effects. While this two-tiered approach has not been explicitly mentioned and described in previous EFSA guidance documents, it features prominently in the current Guidance. As a member of the EFSA GMO

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27 Preambular Recital 6 of Regulation 1829/2003: 'Regulation (EC) No 258/97 also provides for a notification procedure for novel foods which are substantially equivalent to existing foods. Whilst substantial equivalence is a key step in the procedure for assessment of the safety of genetically modified foods, it is not a safety assessment in itself. In order to ensure clarity, transparency and a harmonised framework for authorisation of genetically modified food, this notification procedure should be abandoned in respect of genetically modified foods.'
Para 13, Codex Guidelines for the conduct of food safety assessment of foods derived from recombinant-DNA plants, CAC/GL 45-2003: 'The concept of substantial equivalence is a key step in the safety assessment process. However, it is not a safety assessment in itself; rather it represents the starting point which is used to structure the safety assessment of a new food relative to its conventional counterpart.'

28 COP-MOP5 Decision BS-V/12 Risk assessment and risk management (Articles 15 and 16) http://www.cbd.int/decision/mop/?id=12325

Panel explains, the purpose of the comparative safety assessment is not only to compare data but also to take decisions with far-reaching consequences for the application of the ERA procedure:

> 'The comparative safety assessment is based on "four data pillars", which represent data from different sources that are frequently available in advance of the ERA to characterize the GM plant, namely: molecular characterization data; compositional data; information on agronomic and phenotypic characteristics; and information on interactions of the GM plant with its receiving environment(s). The outcome of this comparative safety assessment allows the identification of those differences and hence characteristics that need to be assessed for their biological/ecological relevance in terms of adverse effects to the environment, regardless of whether they were intended or unintended, and will thus further structure the ERA.' (Bartsch 2011)

Firstly, the Guidance states on page 12 that 'unintended effects [...] are considered to be consistent (non-transient) differences'. It is accepted and necessary to determine whether observed differences are consistent or non-transient, if they may result from methodological flaws or are based on variable behaviour of the biological material. ENSSER wants to point to the fact that the Guidance neither gives a scientific definition of the two different concepts, 'consistent' and 'non-transient', nor does it present a methodology, thresholds or any other tool to determine such consistency with respect to the non-transient status of the differences. Any decision on the non-transient nature of observed effects especially requires guidance on time frames for baseline and risk research (effects for example may only occur under particular climatic conditions or biotic conditions that may not occur every year). Although it was the mandate of EFSA to select 'appropriate techniques to assess potential long-term effects of GM plants including experimental and theoretical methodologies, and recommendations for establishing relevant baseline information', EFSA does not provide substantial guidance in this regard and leaves it almost completely to the applicant to decide what to do and how to do it. The European Commission obviously did not insist on a complete and comprehensive work based on the given mandate.

Secondly, EFSA empowers itself to determine the biological significance of such statistically significant differences without developing guidance on the crucial questions of what kinds of data are needed to judge on biological significance and what would be acceptable and not-acceptable differences in this regard. EFSA states on page 13 that 'statistically significant differences [...] should be assessed specifically with respect to their biological relevance [...]. The outcome of the comparative assessment allows the determination of those "identified" characteristics that need to be assessed for their potential adverse effects in the environment [...] and will thus further structure the ERA.' ENSSER interprets this

Example 1: Applying the concept of familiarity to avoid ERA

Swiss researchers recently applied the concept of familiarity to declare significant differences between GM wheat and its parental lines as ecologically irrelevant and thus not to be analysed through ERA before market introduction: 'We found significant effects of the different wheat lines on insect community structure up to the fourth trophic level. However, the observed effects were inconsistent between study years and the variation between wheat varieties was as big as between GM plants and their controls. This suggests that the impact of our powdery mildew-resistant GM wheat plants on food web structure may be negligible and potential ecological effects on non-target insects limited.' (von Burg et al. 2011).

Twenty-seven summer wheat varieties are currently registered in Switzerland, a handful of them are recommended and actually planted (Hiltbrunner et al. 2010, SwissSem 2010). Furthermore, the annual dynamic of the predominant varieties is very high in Switzerland (Brabandt et al. 2006). A scientifically meaningful and regulatory useful comparison should have used the main varieties grown in Switzerland in the last years – and not only one current, one obsolete and one foreign variety as von Burg et al. 2011 did. For an approval in the EU context, the application of the concept of familiarity would in addition require different comparative studies for all representative receiving environments (which are not identified in the EFSA Guidance). Van Burg et al. also declare the observed differences as 'inconsistent' based on a period of two vegetation periods. They do not attempt to relate the differences to any ecological factors, which might explain the variability and make the effects consistent.

as the introduction of a decision-making step that would serve as a bottleneck in the process of the ERA. Based on this, the EFSA GMO Panel will decide through the qualification of such differences, as either biologically irrelevant or relevant, whether the assessment of specific characteristics of GMPs will stop after the comparative safety assessment or whether their assessment will be subject to the six steps of ERA as prescribed by Directive 2001/18. EFSA seems to have an ambiguous approach towards giving guidance on the scientific criteria that can justify such decisions.

As an underlying concept, EFSA resorts to the concept of familiarity – also called the 'concept of history of safe use' – that should be applied when making decisions on biological and ecological relevance. In its second presentation of the Guidance at the workshop in January 2011, EFSA claimed that food and feed risk assessment and ERA follow the same logic,[29] a claim that cannot be supported by legal or scientific arguments. EFSA specifically states that the concept of familiarity is applicable in ERA. This logic would have severe consequences on the work of the EFSA GMO Panel when making a decision of whether documented, statistically

[29] Lecture Dr. Claudia Paoletti, page 5 http://www.alde.eu/uploads/media/Paoletti_ALDE_GMO_debate_12-1-2011_01.pdf

significant differences in unintended effects are biologically and environmentally insignificant or not. Under the concept of familiarity such differences would not only be judged with regard to the properties of the parental plants – as required by a principle of the Directive 2001/18 – but also put into relation with the natural variation of the specific property exhibited by other, non-parental plant varieties grown under the same conditions. Apart from posing technical problems, which are not solved in the Guidance (e.g. which and how many non-parental varieties need to be analysed), this approach has been judged as inappropriate for ERA by scientists and experts recently:

> 'Therefore, the concept of a history of safe use from food safety relates less easily to ERA, in which environmental harm is measured. Here, it is more fruitful to base arguments on the likely effect of a GMO, and then to contextualize whether that effect is sufficient to cause significant environmental harm. To retain the undoubted benefits of the equivalence approach, outlined above, the test must therefore be adapted. Second, for ERA, it makes little practical sense for the equivalence limits to be based on the natural variation of extraneous varieties.' (Perry et al 2009)

Based on the scientific understanding of the complex situations that need to be addressed through ERA, there is no international or EU legislation that has adopted the concept of familiarity in ERA. In its attempt to justify its proposal, EFSA had to go back as far as 1993 and quote an Organisation for Economic Co-operation and Development (OECD) (1993) report of a working group that suggested applying the concept of familiarity in ERA. When the Cartagena Protocol on Biosafety negotiations started two years after this OECD report was adopted, some of the delegations brought its recommendations into the biosafety negotiations. The inclusion of the concept of familiarity in international environmental legislation had been discussed at the second and third meetings of the Working Group on Biosafety in 1997 and was finally rejected during the fourth meeting in 1998.[30] The final text does not refer to or reflect the familiarity principle as set up by OECD.

In a second more technical approach, EFSA suggests that 'limits of concern' need to be established to support decisions on biological and ecological relevance. EFSA gives examples of such limits of concern for experiments at different scales of environmental complexity but it does not give guidance on the specific

[30] Reports available at:
Second Ordinary Meeting of the Open-Ended Ad Hoc working Group on Biosafety (BS WG 2)
http://bch.cbd.int/protocol/meetings/documents.shtml?eventid=1054
Third Ordinary Meeting of the Open-Ended Ad Hoc working Group on Biosafety (BS WG 3)
http://bch.cbd.int/protocol/meetings/documents.shtml?eventid=1037
Fourth Ordinary Meeting of the Open-Ended Ad Hoc working Group on Biosafety (BS WG 4)
http://bch.cbd.int/protocol/meetings/documents.shtml?eventid=1055
additional in-session documents can be provided by the authors

requirements of GM plant ERA. Again, it is left almost completely to the applicant to decide what to do and how to do it. In a recent scientific publication, risk assessment experts including EFSA members state that:

> 'Little guidance is available how to perform equivalence testing for GMOs in practice. Although the EFSA Guidance Document [of 2006] discusses general principles for risk assessment and recommends the use of appropriate statistical tools, detailed protocols for the design of experiments and statistical analysis are not provided.' (van der Voet et al. 2011)

These authors developed a statistical approach that combines tests for equivalence with tests on differences in order to establish a scientific approach for the application of the concepts of equivalence and of familiarity. The publication focuses exclusively on data of compositional analyses in the context of food and feed risk assessments with little or no relevance for ERA. The crucial question of which conventional varieties need to be tested in which receiving environments to establish a sound basis for the application of the concept of familiarity in GM plant risk assessment is not dealt with in this publication. In this context, the Roadmap for risk assessment of the Cartagena Protocol advises:

> 'In all cases where information, including baseline data, is derived from other sources, it is important to establish the validity and relevance of the information for the risk assessment. For instance, it should be taken into account that the behavior of a transgene, as that of any other gene, may vary because it depends on the genetic and physiological background of the recipient as well as on the ecological characteristics of the environment that the LMO is introduced into.' [31]

Despite the still-missing scientific foundation for the concept of familiarity in ERA, EFSA propagates the use of this concept for GM plant market approvals. While this would add a substantial burden of a plethora of tests on the applicants (as described in Example 1), EFSA does not give any guidance on how to plan and conduct these tests. It can be predicted that applicants will use this lack of guidance to create their own experimental protocols with the aim of declaring GM crops as safe and avoiding ERA on observed differences between the GM plant and its parents. ENSSER is of the opinion that the underlying assumptions of EFSA[32] in

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31 COP-MOP5 Decision BS-V/12 Risk assessment and risk management (Articles 15 and 16) http://www.cbd.int/decision/mop/?id=12325

32 'The underlying assumption of the comparative assessment for GM plants is that the biology of traditionally cultivated plants from which the GM plants have been derived, and the appropriate comparators is well known. To this end the concept of familiarity was developed by the OECD (OECD, 1993). In the ERA, it is appropriate to draw on previous knowledge and experience and to use the appropriate comparator in order to highlight differences associated with the GM plant in the receiving environment(s).' EFSA GMO Panel (2010), page 11

writing the Guidance with regard to the concepts of substantial equivalence and familiarity are scientifically flawed and are in addition not supported by the current international and EU legal frameworks.

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Analysis of Risk Assessment Strategies for Genetically Engineered Plants Used for Food and Feed in the EU

Christoph Then
Testbiotech, Germany

Summary

WITHIN the first ten years of its activities, the work of the GMO panel of the European Food Safety Authority (EFSA) cannot be seen as independent nor does it fulfil the requirements of EU regulations. In addition, the EU Commission fails to fulfil its task as risk manager, as it does not define sufficient risk assessment policies and neglects its duty to implement effective post-market monitoring. The flaws of current risk assessment of the EFSA will be perpetuated by a new Implementation Regulation proposed by the EU Commission. The recommendations for future risk analysis strategies include dropping the concept of comparative risk assessment and applying a comprehensive risk assessment to each application of genetically engineered organisms.

1. Overview of market authorisations in the EU

By August 2012, 46 events of genetically engineered plants had been authorised for usage in food and feed within the European Union. Most of them are for import and processing, while two events are authorised for cultivation: Monsanto's Maize MON810 and the BASF potato 'Amflora'.

The 46 events include the following species: maize (26), cotton (8), soybean (7), rapeseed (3), potato (1) and sugar beet (1). The events can be divided into four groups of technical traits (one of which overlaps with two other groups):

- 8 events producing insecticidal toxins
- 15 events tolerant to herbicides
- 22 events which are a combination of insecticidal and herbicide-tolerant plants (stacked events)
- others: one potato producing starch for industrial use, one rapeseed producing infertile pollen

2. General requirements for risk assessment of genetically engineered plants in the EU

According to the regulations of the European Union (Regulation 178/2002, Regulation 1829/2003 and Directive 2001/18), the overarching goal of EU policy is to ensure a high level of environmental and consumer protection. In case of uncertainties the precautionary principle shall prevail.

Some quotes from the EU regulations:

>> Regulation 178/2002 'the Food Safety Regulation': 'Risk assessment shall be based on the available scientific evidence and undertaken in an independent, objective and transparent manner.' (Art. 6, 2).
>> Regulation 1829/2003, 'food and feed': Products derived from genetically engineered plants 'should only be authorised for placing on the Community market after a scientific evaluation of the highest possible standard'. (Recital 9).
>> Directive 2001/18, 'deliberate release': The directive requires the examination of the 'direct and indirect, the immediate and delayed effects' of the genetically engineered plant on human health or the environment (Annex II), 'in accordance with the precautionary principle'. (Article 1)

3. Risk assessment and the comparative approach

Since 2003, EFSA has been conducting risk assessment on the basis of its own Guidance. The EFSA Guidance is built on the assumption that risks of genetically engineered plants are comparable to those of plants derived from conventional breeding. As a consequence, a comprehensive risk assessment is not conducted and only a limited set of data is requested. The so-called comparative safety assessment is explained in the current EFSA Guidance (EFSA, 2011):

'The underlying assumption of this comparative approach is that traditionally cultivated crops have a history of safe use for consumers and/or domesticated animals. These traditionally cultivated crops can thus serve as comparators when assessing the safety of GM plants and derived food and feed.'

Consequently, current risk assessment is not comprehensive. For example, there are no requests for a detailed assessment of health risks in feeding trials and in long-term studies. EFSA assumes that risks that cannot be compared to those of conventional breeding will only occur in rare cases, and only in such rare cases will a comprehensive risk assessment need to be carried out. However, so far this has never happened (EFSA, 2011):

'Where no comparator can be identified, a comparative risk assessment cannot be made and a comprehensive safety and nutritional assessment of the GM plant and derived food and feed itself should be carried out.'

The EFSA Guidance for risk assessment of genetically engineered plants refers to international standards such as set by Codex Alimentarius and the Organisation for Economic Co-operation and Development (OECD), but, taking a closer look at those standards, it is evident that the comparative approach was mostly developed by industry. Here the International Life Sciences Institute (ILSI) played a crucial role. ILSI is funded by companies such as Monsanto, Dow AgroSciences, DuPont and Bayer and it develops standards such as the comparative safety assessment on behalf of industry, and also plays an active role in introducing those standards to the Guidance of relevant state authorities.

In the case of EFSA, Harry Kuiper, who was the chair of the so-called GMO Panel from 2003-2012, not only played a decisive role in setting EFSA standards, but he was also a member of the ILSI task force which developed the concept of comparative safety assessment on behalf of the industry (ILSI, 2004; Then & Bauer-Panskus, 2010). ILSI claims the introduction of the comparative assessment was a success:

'In 2004, the task force's work culminated in the publication of a report that included a series of recommendations for the nutritional and safety assessments of such foods and feeds. This document has gained global recognition from organizations such as the European Food Safety Agency and has been cited by Japan and Australia in 2005 in their comments to Codex Alimentarius. The substantial equivalence paradigm, called the comparative safety assessment process in the 2004 ILSI publication, is a basic principle in the document.' (ILSI, 2008)

What is the general problem with the comparative approach from a scientific point of view? Conventional breeding and genetic engineering can be seen as being fundamentally different from a technological point of view as well as from a biological perspective. Unlike conventional breeding, genetic engineering inserts technically derived DNA constructs to force specific biological functions in plants by disregarding the system of gene regulation and the barriers between species. Choosing the comparative approach implies a high likelihood that risks attributed to the method of genetic engineering (such as disturbances in gene regulation) are not identified.

In the EFSA Guidance, comparative assessment is the starting point in the overall process of risk assessment. The first step in this process is the identification of potential hazards, which needs to be assessed during the later stages of the risk assessment. This starting point impacts all following steps of the risk assessment, and thus only a limited 'check up' takes place rather than a comprehensive risk assessment. As will be shown in the following section, the comparative approach is associated with flaws during other steps of the risk assessment conducted by EFSA (see also as example, Testbiotech, 2012). These flaws are also perpetuated by the Implementation Regulation of the EU Commission (EU Commission, 2012).

4. The initiative of the EU Commission

In 2012 the EU Commission published a Commission Implementing Regulation […] on applications for authorisation of genetically modified food and feed in accordance with Regulation (EC) No. 1829/2003 […] (EU Commission, 2012). As soon as this regulation is adopted, it will become the basis for the work of EFSA. However, compared with the current EFSA Guidance, this regulation is not a real improvement. The most relevant change would be a mandatory feeding study of 90 days with rats to examine health effects. However this would apply to stacked events, inheriting several additional DNA constructs, derived from crossings of genetically engineered plants. More relevant tests such as multi-generational studies are still not required. In the following section, some points are listed to show some deficiencies of the current risk assessment as well as of the proposed new regulation:

- Comparative risk assessment is still seen as the standard procedure.
- The most relevant step in comparative risk assessment (the investigation of substantial equivalence) is still based on a concept that allows the introduction of flawed historical data.
- Interactions with the environment that may impact the composition of plants are not tested sufficiently.
- Testing for health risks is still not based on a stepwise concept that entails mandatory investigations such as toxicity tests on cell cultures, targeted investigation of relevant health risks and long-term and multi-generational studies.
- There is no request to apply more recent technologies, such as metabolic profiling.
- The necessary interplay with pesticide regulations is missing.
- Bt toxins are not assessed according to pesticide regulations.
- The requirements for investigation of synergistic, additive and accumulated effects are not sufficiently defined.
- The need to establish fully evaluated methods to measure the expression of the newly introduced DNA constructs is not mentioned.
- The proposal of the Commission is missing sufficiently clear quality standards for investigations conducted by industry.
- Post-marketing monitoring to allow identification of negative health effects of the consumption of products derived is not required.

In conclusion, the current practice of post-market monitoring does not meet the requirements of existing EU regulations.

5. Conclusions and recommendations

Within the first ten years of its activities, the work of the EFSA GMO Panel cannot be seen as independent nor does it fulfil the requirements of EU regulations. Further, the EU Commission fails to fulfil its task as risk manager. It does not define sufficient risk assessment policies and it neglects its duty to implement effective post-marketing monitoring. Ethical questions and socio-economic consequences are not included in the process of risk analysis.

Some recommendations for future risk analysis strategies:

- Drop the concept of comparative risk assessment; do not presume safety, equivalence, similarity or familiarity; use comparison as a tool and not as a concept.
- Always require a comprehensive risk assessment in the case of genetically engineered organisms.
- Establish clear cut-off criteria for rejection of applications.
- Reassess EU market authorisations.
- Promote independent risk research.
- Set higher standards for the independence of EFSA.

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Intellectual Property Rights and Research Restriction

Hartmut Meyer
European Network of Scientists for Social and Environmental Responsibility (ENSSER)

1. Introduction

AFTER 15 years of genetically modified (GM) crop commercialisation a new dimension was added to the controversy about appropriate methodological approaches and interpretations in the fields of risk research and risk management. In February 2009, the *New York Times* featured a story reporting about a complaint of 26 leading US entomologists working in GM crop risk research and evaluation. The statement at the US Environmental Protection Agency (EPA) web page reads as follows:

> *The following statement has been submitted by 26 leading corn insect scientists working at public research institutions located in 16 corn producing states. All of the scientists have been active participants of the Regional Research Projects NCCC-46 'Development, Optimization, and Delivery of Management Strategies for Corn Rootworms and Other Below-ground Insect Pests of Maize' and/or related projects with corn insect pests. The statement may be applicable to all EPA decisions on PIPs [Plant-Incorporated Protectants], not just for the current SAP [Scientific Advisory Panel]. It should not be interpreted that the actions and opinions of these 26 scientists represent those of the entire group of scientists participating in NCCC-46. The names of the scientists have been withheld from the public docket because virtually all of us require cooperation from industry at some level to conduct our research.*
>
> *'Technology/stewardship agreements required for the purchase of genetically modified seed explicitly prohibit research. These agreements inhibit 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 [insect resistance management], and its interactions with insect biology. Consequently, data flowing to an EPA Scientific Advisory Panel from the public sector is unduly limited.'*

The statement finally made public what has been known to scientists in the field for many years now: those whose products are scrutinised for negative effects can determine who is conducting this research, how the research is done and what can be published. The agro-biotechnology industry claims that the intellectual property rights (IPR) laws give them the right to do so. The letter and subsequent media reports put the US biotechnology industry under pressure and resulted in the adoption of a Position Statement that enlarged the free use of patented commercialised seeds beyond purely agricultural research issues. The September 2009 document 'Research with Commercially Available Seed Products' suggests that the patent owner also should allow free research on pest resistance and environmental biosafety issues.

While this agreement was propagated as a major commitment by the biotechnology industry, it has to be stressed that it is only a recommendation and that based on the current US IPR laws, patent owners are still entitled to forbid any biosafety research with patented GM seeds that are available on the market. Still and most important, biosafety research on patented non-commercialised GMOs is not an element of the recommendation; researchers need the consent of and need to enter into an agreement with the patent owner.

2. Background on intellectual property rights

The fundamental requirements of independent research are free access to material, free choice of concepts and methodologies, and free choice of how and where to publish the results.

Tangible property laws require that scientists have to receive access permission if the material they want to analyse is under private ownership. If the material is available a as commodity in the market, the purchase renders the ownership to the buyer, in this case, the scientist. In general, the first owner of the physical material does not have legal rights to determine the use of the material by the next owner.

This is different when the potential research material is in addition covered by IPRs. The current IPRs as patents or plant variety protection based on the World Trade Organisation (WTO) Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) or the International Convention for the Protection of New Varieties of Plants (UPOV) 1991 empower the first owners of the IPR to decide about the future use of the material by the new user. According to patent laws, the owner of a patent is not the inventor but the applicant of the patent, in general a private company or in some cases a public institution.

Due to the pressure of industrialised countries and their IPR-intensive industries and contrary to older international IPR treaties, the TRIPS Agreement of the WTO obliges its members to grant IPRs in the health, food and agriculture sectors. During the negotiations, developing countries managed to obtain the concession that WTO members can exclude animals and plants as well as essentially

biological breeding methods from patentability. In the case of plant varieties, WTO members must secure effective *sui generis* protection if they do not provide patents on plant varieties. Proponents of industrial IPRs advocate the 1991 UPOV Convention on plant breeders' rights as the only appropriate *sui generis* regime.

Article 30 of the TRIPS Agreement allows its members to give limited exemptions to the exclusive rights conferred by a patent.[33] The EU Community Patent Convention specifies the circumstances for such exemptions and grants a far-reaching 'research exemption' as far as the research relates to the subject matter of the invention.[34] The patent laws of almost all EU member states have implemented this provision. The Community Patent Convention is currently under revision; the recent draft still contains this exemption.[35] However, for laypersons it is not obvious from the legal text if this research exemption would also cover experiments with the invention related to risk issues, e.g. GMO biosafety research, which might not be covered by the subject matter of the invention. Recital 14 of the preamble of the EU bio-patent directive recommends that such exemptions in the field of biotechnology must be possible 'notably from the point of view of the requirements of public health, safety, environmental protection, animal welfare, the preservation of genetic diversity and compliance with certain ethical standards'.[36]

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33 TRIPS Art 30 *Article 30 Exceptions to Rights Conferred*
Members may provide limited exceptions to the exclusive rights conferred by a patent, provided that such exceptions do not unreasonably conflict with a normal exploitation of the patent and do not unreasonably prejudice the legitimate interests of the patent owner, taking account of the legitimate interests of third parties.

34 Convention for the European Patent for the common market, Article 27 – Limitation of the effects of the Community patent:
The rights conferred by a Community patent shall not extend to
(b) acts done for experimental purposes relating to the subject-matter of the patented invention;

35 More information: http://www.epo.org/patents/law/legislative-initiatives/community-patent.html
2009 Proposal for a Council Regulation on the Community patent
Article 9 Limitation of the effects of the EU patent
The rights conferred by the EU patent shall not extend to:
(b) acts done for experimental purposes relating to the subject-matter of the patented invention;

36 Directive 98/44 on the legal protection of biotechnological inventions
Preamble Recital (14) Whereas a patent for invention does not authorise the holder to implement that invention, but merely entitles him to prohibit third parties from exploiting it for industrial and commercial purposes; whereas, consequently, substantive patent law cannot serve to replace or render superfluous national, European or international law which may impose restrictions or prohibitions or which concerns the monitoring of research and of the use or commercialisation of its results, notably from the point of view of the requirements of public health, safety, environmental protection, animal welfare, the preservation of genetic diversity and compliance with certain ethical standards;

3. Research exemption and biosafety research

One prominent issue right in the centre of the European Network of Scientists for Social and Environmental Responsibility (ENSSER)'s work and concerns is the (mis)use of IPRs, specifically patents, to restrict access to biological material and organisms necessary to conduct research for risk assessment, independent from the interests and influence of the IPR holder. These restrictions in many cases come together with giving preferential access to the necessary materials and organisms to research groups that follow the research concepts of the IPR holders and accept their conditions on interpretation and publication of data. In the field of pharmaceuticals, the research exemption contained in the patent laws of many states such as the EU is used routinely by independent research groups. This possibility is not commonly known in the circles undertaking research on environmental and health risks of other patented material such as GM seeds. It is unclear to many researchers whether the use of approved GM plants which are available on the seed market for independent risk research is legal with respect to the current provisions of the patent and seed variety laws or if approval for such research needs to be sought from the IPR holders. Access to GM seeds for pre-approval risk research is seen as impossible by many groups although the research exemption would also apply for those seeds if they are covered by IP-protection. The need to run control experiments with the non-GM parental lines which might neither be under IP-protection nor available on the market constitutes the strongest impediment for independent research. In this situation, ENSSER asked for a legal opinion to clarify the legal situation in the EU and to inform research groups about their legal possibilities to gain access to the different categories of GM seeds.

4. Summary of the legal opinion

4.1 European patent law grants a 'research exemption'

The Community Patent Convention of 1975 (the so-called Luxembourg Convention) introduced an explicit provision on the research exemption, which functioned as a model provision for all subsequent national regulations of the EU member states:

> Article 31 Limitation of the effects of the Community patent
> The rights conferred by a community patent shall not extend to:
> (a) acts done privately and for non-commercial purposes;
> ***(b) acts done for experimental purposes relating to the subject-matter of the patented invention; (....)***

A similar provision for research exemptions was introduced in the 1991 text of the UPOV Convention 1991 and subsequently signatories to this convention

started to introduce similar regulations in their national statutes. The linkage ***'relating to the subject-matter of the patented invention'*** was drafted intentionally in an imprecise and non-technical way, and therefore constituted almost a catch-all category.

4.2 Research <u>on</u> the patented subject matter versus research <u>with</u> the patented subject matter

The linkage between the subject matter of a patent and research activities was argued and interpreted in a differentiating way in only two decisions of the German Federal Court. The court distinguished between research ***on the object*** (subject matter, technical teaching) of a patent and those research activities making use of the teaching of a patent ***as an instrument*** for obtaining new knowledge. The former shall be covered by the research exemption; the latter shall fall under the scope of protection of the patent and hence be prohibited. Considering the usual types of patent claims in seed patents, as well as the type of research to be exempted or privileged, the following is an illustration of **on/with-typology** for evaluating a particular case:

Type of research	**Patent claims: Substance/seed**	**Patent claims: Process of production**	**Patent claims: Use e.g. in agriculture**
Risks to human & animal health and environment	Exempted	Exemption doubtful	Exempted
Delaying development of resistance in weeds or insects	Exempted	Exemption doubtful	Exemption doubtful
Improvements of yield and agricultural practices	Exemption doubtful	Not exempted	Not exempted

4.3 Specific issues for research on GM plant risks

a) Access to IP-protected marketed seeds

It should not be difficult for independent researchers in the EU member states to obtain access to marketed GM seeds, e.g. MON810, in sufficient quantities and in a legally not objectionable way by means of purchasing contracts and hence to become lawful owners of the GM material without legal restrictions. Contractual obligations in 'stewardship agreements' *not* to transfer these GM seeds to third parties will usually constitute 'vertical agreements and concerted practices' under Commission Regulation (EU) No. 330/2010 and hence be invalid. If accused of infringing patents of the GM producer, the researcher may not only invoke the research exemption, but can also argue that patent protection with regard to the GM material in question is at this stage already *exhausted* as a result of lawful introduction to the market.

b) Access to IP-protected seeds not yet approved for marketing

On the basis of the powers granted in administrative, e.g. environmental law, the state as represented by its organs is entitled to procure samples of GM material/organisms and to enforce access to such GM organisms even without the consent or against the explicit will of the owner, and to use the force of the law to do so. Since this power of the state administration is intended to facilitate prevention of abuse and control of risk, the right to access and procurement should include the right to examine and investigate the GM material with a view to minimising risk. As an example, the German Biotechnology Act of 1990/2008 explicitly provides for the right of the state administration to seize samples for investigations.

It seems, however, extremely doubtful whether, invoking this instrument of compulsory licensing, external researchers in the field of GM seeds will ever be granted access to GM seeds without the consent or against the explicit will of the producer of GM seeds and holder of the IPR. It is extremely unlikely that in the field of GM seed patents, the statutory requirements for such a compulsory licensing will ever be met.

In order to gain access to such material, e.g. SmartStax maize, independent researchers can refer to the research exemption but in any case need to enter an agreement with the patent holder specifying the details and aims of the intended research.

c) Access to seeds not protected by IPR and not marketed

To conduct scientifically sound risk research, the appropriate non-GM comparators, e.g. the parental varieties or breeding lines, need to be assessed in parallel to the GM plant. While in some cases the parents are commercial varieties, in others they could be breeding lines not covered by any IPR (e.g. the non-GM parent of SmartStax maize is the breeding line XE6001, itself a hybrid between the lines HCL301 of Monsanto and 5XH751 of Dow AgroSciences). The research exemption does not apply to such material, and access to this category will, as a general rule, not be granted to independent researchers by the owner(s).

5. Conclusions

Access to marketed IP-protected GM seeds should be free for independent researchers, and any restrictions seem to contradict EU law. If the IP-protected GM seeds are not marketed yet, independent researchers can refer to the research exemption but need to conclude a contractual agreement with the IP-holder to gain access. The conditions in this contract should not interfere with scientific issues such as selecting methodologies, interpreting and publishing results. The owners of those experimental, parental lines that are necessary for independent research as non-GM controls but are not IP-protected are under no obligations to grant access to these seeds. To enable independent and sound risk research, access to the appropriate non-GM comparators needs to be made possible by specific legal provisions, e.g. in the EU GMO law.

Human Cell Toxicity of Pesticides Associated with Wide-Scale Agricultural GMOs

Mesnage R., Gress S., Defarge N. and *Séralini G.-E.*
University of Caen, Institute of Biology, CRIIGEN and Risk Pole, MRSH-CNRS, France

AGRICULTURAL genetically modified (GM) plants are essentially plants that contain pesticides, because they were designed to tolerate or produce pesticides. In 2011, GM crops reached 160 million hectares, with 59% having herbicide tolerance (mainly to Roundup) mostly in soybean, maize, canola and cotton, 15% insecticide-producing varieties and 26% combining both traits (James, 2011). We characterised cellular side effects of these pesticide residues on non-target human cells and summarise here our findings.

1. Toxicity of glyphosate-based herbicides

Roundup (R) was highly toxic on human cells, from 10-20 ppm, far below agricultural dilutions. This occurred on hepatic (HepG2, Hep3B) and embryonic (HEK293) as well on placental (JEG3) cell lines, but also on human placental extracts, primary umbilical cord cells (HUVEC) and freshly isolated testicular cells (Benachour and Seralini, 2009; Benachour et al., 2007; Clair et al., 2012; Gasnier et al., 2010; Richard et al., 2005). All formulations caused total cell death within 24 hours, through an inhibition of the mitochondrial succinate dehydrogenase activity, and necrosis, through the release of cytosolic adenylate kinase measuring membrane damage. They also induced apoptosis through the activation of enzymatic caspases 3/7 activities. Most importantly, the R commercialised formulation is always more toxic than the active principle alone, glyphosate (G). These effects were more dependent on the formulation and thus adjuvant content than on the G concentration. We recently measured compositions and effects of nine G-based formulations and identified ethoxylated adjuvants (commonly called POEA) as the active principle of cytotoxicity. However, these are considered as inert diluents in international regulations and are not taken into account for chronic effects, which are insufficiently tested, and only with G in pre-commercial testing. We previously underlined this loophole (Mesnage, 2010). Long-term feeding and reproductive trials with pesticides are the only tests long enough to reveal a potential endocrine disruption which was consequently never studied for R, however it was for G by itself.

We investigated it by measuring androgen-to-estrogen conversion by aromatase activity and mRNA on placental human cells and showed that G interacts with the active site of the purified enzyme (Richard et al., 2005). Both parameters were disrupted at sub-agricultural doses within 24 hours. We also observed a human cell endocrine disruption from 0.5 ppm on the androgen receptor in transfected cells, and then from 2 ppm the transcriptional activities on both estrogen receptors which were also inhibited (Gasnier et al., 2009). Aromatase transcription and activity were disrupted from 10 ppm on HepG2. On freshly isolated rat testicular cells, low non-toxic concentrations of R and G (1 ppm) induced a testosterone decrease by 35% (Clair et al., 2012). This is expected to occur in human cells which are fitted with the same steroidogenic equipment.

G-based formulations are claimed to have been extensively studied by industry and regulatory agencies and are considered as one of the safest pesticides (Williams et al., 2000). This allowed the establishment of high maximum residue limits (MRL) for GM food/feed (up to 400 ppm). For instance, 20 ppm of G is authorised in GM soy and this MRL is in the range of concentrations typically found in a GM soy harvest. In the light of our results, the safety of these thresholds is clearly challenged.

2. Toxicity of insecticidal toxins (*Bt*)

Modified toxins from *Bacillus thuringiensis* are Cry proteins forming pores in insect cell membranes (Then, 2010). They are claimed and believed to be inert on non-target species. We have tested for the very first time Cry1Ab and Cry1Ac modified *Bt* toxins (10 ppb to 100 ppm) on the HEK293 cell line, as well as their combined actions with R, within 24 hours, on three biomarkers of cell death: measurements of mitochondrial succinate dehydrogenase, adenylate kinase release by membrane alterations and caspases 3/7 inductions (Mesnage et al., 2012). Modified Cry1Ab caused cell death from 100 ppm. For Cry1Ac, under such conditions, no effects were detected. *In vivo* implications should be now assessed, as Cry1Ab does not appear to be proved as an insect-specific toxin.

3. Combined toxicity

In the new growing generation with stacked traits, G-based herbicides (like R) residues are present in the R-tolerant edible plants and mixed with modified *Bt* insecticidal toxins that are produced by the GM plants themselves. However, the toxicology of mixtures cannot be fully understood without knowing the combined toxicity of the various compounds of the formulations. In some *in vitro* conditions, G and its adjuvant synergistically damaged cell membranes in a similar manner to R (Benachour and Seralini, 2009). R adjuvants changed human cell permeability and amplify toxicity induced already by G, through apoptosis and necrosis. The real threshold of G toxicity must take into account the presence of adjuvants but

also G metabolism and time-amplified effects or bioaccumulation. For the mixtures of *Bt* toxins and R, the only measured significant combined effect was that modified Cry1Ab and Cry1Ac reduced caspases 3/7 activations induced by R; this could delay the activation of apoptosis and impact on necrosis. There was the same tendency for adenylate kinase activity and succinate dehydrogenase activity measures. Pesticides have to be tested together, as 26% of agricultural GMOs are indeed stacked events.

We also reviewed 19 studies of mammals fed with commercialised GMOs (Seralini et al., 2011). Meta-analysis of all biochemical disruptions indicated liver and kidney problems as end points of GMO diet effects. These are the major reactive organs in case of food chronic intoxication, and several contingent factors suggested that pesticide residues may be involved in the pathological features. All together, our results raise new questions in the risk assessment of food and feed derived from genetically engineered plants.

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Sources and Mechanisms of Health Risks from Genetically Modified Crops and Foods

Michael Antoniou
King's College; London School of Medicine-Guy's Hospital, UK

GENETIC modification (GM) is a purely laboratory-based method that exploits the use of recombinant DNA or genetic engineering technology to produce novel varieties of crops. It represents a radically different approach to new crop production when compared to traditional plant breeding methods, and even those using approaches such as irradiation and chemical-induced mutation. The artificial nature of GM does not automatically make it dangerous and undesirable. It is the outcome of the GM process that gives cause for concern. GM allows the transfer of any gene from any source into a crop, thereby bringing about combinations of genes that would not occur naturally. In addition, the GM transformation process as a whole is highly mutagenic. These generic properties of GM combine to generate a high risk of disturbing plant host gene function and biochemistry that could result in novel toxin and allergen production as well as a compromised nutritional value (for review see Antoniou et al., 2012).

There are three sources of health risks that can potentially arise from GM foods:

1. The introduced foreign GM gene ('transgene'):
   (a) GM gene product directly (e.g. Bt toxin);
   (b) Altered plant biochemistry caused by GM gene product (e.g. enzymes conferring herbicide tolerance);
2. Higher exposures to herbicides used in conjunction with the cultivation of GM crops (e.g. glyphosate);
3. Altered plant biochemistry caused by mutagenic effect of the GM transformation process.

This paper will focus primarily on illustrating potential sources of harm arising from points 1(a) and 3 above.

1. Feeding studies for evaluating toxicity of GM crops

There are just four major GM crops grown commercially in the world today, three of which are feed and food crops. These are soybeans, maize or corn, canola

and cotton, which collectively constitute approximately 10% of global agriculture with cultivation concentrated in North and South America. All the GM soy is engineered to be tolerant to glyphosate-based herbicide (mostly Roundup formulations) applications. Of these four GM crops, two are predominantly engineered to express versions of the insecticidal Bt toxin protein. These are corn and cotton. It should be noted that some varieties of GM corn and cotton are engineered to express both a Bt toxin and be tolerant to glyphosate. Feeding trials in established laboratory animal model systems (rats, mice) which have been routinely used to evaluate potential human toxicity have been conducted with various varieties of commercialised and non-commercialised GM crops. Although not all published animal feeding studies of this type have shown disturbances to physiological and biochemical function with potential negative health outcomes (e.g. Liu et al., 2012), many have shown very worrying results. The findings of the studies from both industry and academia that give rise to cause for concern are summarised below.

2. Studies conducted by industry

Although not mandatory, some regulators (especially within the European Union) request feeding studies with rats to evaluate potential toxicity of a GM crop as part of the industry's application for marketing approval. These studies are based on Organisation for Economic Co-operation and Development (OECD) guidelines and thus are of only 90 days duration. Nevertheless, independent academic re-evaluation of the results from these short-term feeding trials has shown:

- Rats fed insecticide-producing MON863 Bt corn grew more slowly and showed higher levels of certain fats (triglycerides) in their blood than rats fed the control diet. They also suffered problems with liver and kidney function. The authors stated that it could not be concluded that MON863 corn is safe and that long-term studies were needed to investigate the consequences of these effects (Séralini et al., 2007).
- Rats fed commercialised GM Bt corn varieties MON863 and MON810 as well as Roundup-tolerant NK603, had toxic effects on liver and kidneys. The authors of the re-analysis stated that while the findings may have been due to the pesticides specific to each variety, genetic engineering could not be excluded as the cause (de Vendomois et al., 2009).
- Various animals were fed Bt toxin-containing brinjal ('Bt brinjal') for a maximum of 90 days (rats, rabbits, goats) or 42-45 days (cows, chickens, fish). Despite the short duration of these feeding tests the results showed significant signs of toxicity to multiple organ systems in the Bt brinjal groups compared to the non-GM brinjal controls; e.g., less feed consumption in goats and rabbits; diarrhoea, higher water consumption, liver and body weight

decrease in rats; clear signs of disruption in liver function in rabbits and goats; disturbances in pancreatic, kidney and haematological function in rabbits.

Taken together, the data from these industry studies show statistically significant differences in the function of multiple organ systems between the GM and equivalent non-GM control feeding groups. There are evidently clear signs of toxicity especially with respect to liver and kidney function. Although not providing clear evidence of harm, they also do not provide clear evidence of safety.

Although these statistically significant findings with GM corn were subsequently acknowledged by both industry and EU regulators, they were dismissed as 'biologically insignificant', a scientifically meaningless term without definition. Therefore, rather than commissioning longer, life-long feeding trials to ascertain whether the statistically significant signs of toxicity observed in these short-term trials escalated to serious ill-health or not, EU regulators passed these products as substantially equivalent to non-GM corn and safe. If one is true to the science, these data suggest that approval of these GM corn varieties should be withdrawn until further long-term toxicity feeding studies are conducted because they are not substantially equivalent to non-GM corn and are potentially toxic.

Similarly, the Genetic Engineering Approval Committee, which is responsible for evaluating the safety of GM foods in India, ignored the worrying findings from the short-term feeding studies of Bt brinjal. Fortunately, the former Indian Minister for the Environment (Jairam Ramesh), responsible for overseeing the Bt brinjal application, did take note of the limitations of the safety tests available at the time as highlighted by scientists from around the world and sensibly did not approve this product for commercial use (see Jayaraman, 2009).

3. Studies conducted by academic researchers

Independent academic (university, institute)-based researchers have over the years found it very difficult to obtain GM crop material with which to conduct their own toxicity investigations. Nevertheless, following is a summary of studies with GM crops that have been completed:

- Rats fed GM Bt corn over three generations suffered damage (areas of necrosis) to liver and kidneys and alterations in blood biochemistry (Kilic & Akay, 2008).
- Old and young mice fed GM Bt corn MON810 showed a marked disturbance in immune system cells and in biochemical (cytokine) activity (Finamore et al., 2008).
- Rats fed GM Bt rice developed significant differences as compared with rats fed the non-GM isogenic line of rice. These included differences in the populations of gut bacteria – the GM-fed group had 23% higher levels of

coliform bacteria. There were differences in organ weights between the two groups, namely in the adrenals, testis and uterus. The authors concluded that the findings were most likely due to 'unintended changes introduced in the GM rice and not from toxicity of Bt toxin' in its natural, non-GM form (Schrøder et al., 2007).

- Ewes and their lambs fed GM Bt corn variety Bt176 over three generations showed hyperplasia of ruminal epithelial basal cells in ewes and a disturbed gene functioning of liver and pancreas as revealed by smaller cell nuclei containing increased amounts of heterochromatin and perichromatin granules in lambs (Trabalza-Marinucci et al., 2008).
- A short-term (31-day) feeding trial in pigs with GM Bt corn variety MON810 showed significant differences in numerous immune cell type numbers (e.g. CD4+ T cells, B cells, macrophages) and biochemistry (cytokine levels; e.g. IL-12, IFNy, IL-6, IL-4, IL-8) in the GM-fed group compared to the non-GM controls (Walsh et al., 2011). Despite the statistical significance of these differences the authors questioned the biological relevance of these observations, which is scientifically difficult to understand especially given the short duration of the investigation.
- Mice fed GM soy showed disturbed liver, pancreas and testes function. The researchers found abnormally formed cell nuclei and nucleoli in liver cells, which indicate increased metabolism and potentially altered patterns of gene expression (Malatesta et al., 2002; Malatesta et al., 2003; Vecchio et al., 2004).
- Mice fed GM soy over their lifetime (24 months) showed more acute signs of ageing in the liver than the control group fed non-GM soy (Malatesta et al., 2008).
- Rabbits fed GM soy showed enzyme function disturbances in kidney and heart (Tudisco et al., 2006).

Although narrower in scope than the industry-led studies in terms of parameters measured, these investigations showed consistent and significant signs of toxicity to multiple organ systems in response to the consumption of the GM feed.

Collectively, these industry- and academic-led feeding studies of commercialised GM soy and corn, which are already in the food and feed chain, found consistent signs of toxic effects in liver and kidney structure and function as well as some immune system disturbances. Such effects may be markers of the onset of chronic disease, requiring long-term rather than these reported short- and medium-term studies, to assess this more thoroughly. Unfortunately, such long-term feeding trials on GM foods are not required by regulators anywhere in the world (Séralini et al., 2011).

4. Mechanistic causes of negative health outcomes

What could be causing these worrying signs of toxicity in these animal feeding trials? At present we do not know. However, there are at least three logical mechanisms by which these GM crops can give rise to the disturbances in physiological and biochemical function and even signs of toxicity observed in these feeding studies:

- Bt toxin
- Herbicide residues
- Mutagenic effects of the GM transformation process

5. Effects arising from mutagenicity of GM transformation process

The GM transformation process (tissue culture plus GM transgene insertion) is highly mutagenic on two levels. Firstly, GM transgene insertion is random but with the transformation procedure ultimately selecting for insertion events within or near active plant host genes resulting in a high risk of host gene functional disruption by 'insertional mutagenesis'. The plant tissue culture component of the GM transformation process causes hundreds if not thousands of genome-wide mutations (Latham et al., 2006; Wilson et al., 2006). Although any insertional mutagenesis effects are fixed, many of the genome-wide, tissue-culture-induced mutagenic events will be bred out of the plant during production of the commercialised GM crop. Many of the remaining mutagenic events will be benign but many run the risk of causing marked disturbances to host gene structure and function resulting in altered biochemistry and composition.

Many studies using the latest 'molecular profiling' technology have now been published which clearly demonstrate the impact on food crop composition resulting from the mutagenic effect of GM transformation. Listed below are some representative examples:

1. Studies of commercialised Bt corn variety MON810 have shown that this crop displays:
   (a) A marked disturbance in protein composition profile specifically related to the GM transgene insertion event;
   (b) A newly expressed protein: zein, a well-known allergenic protein;
   (c) Differential response to environmental inputs as a result of the genome rearrangement derived from GM gene insertion;
   (d) Truncation of seed storage proteins (Zolla et al., 2008);
   (e) Disturbance in amino acid profiles (Manetti et al., 2006; Herrero et al., 2007);

2. Studies of non-commercialised GM rice have shown:
   (f) GM rice engineered to be resistant to fungal diseases showed that not only were the structure of the seeds markedly altered in some cases but more importantly varied significantly in their composition compared to their non-GM counterparts (20 to 74% for amino acids; 19 to 38% for fatty acids; 25 to 57% for vitamins; 20 to 50% for elements; 25% for protein) (Jiao et al., 2010).
   (g) GM rice engineered with CryIAc Bt toxin and sck insecticide genes showed marked biochemical and nutritional disturbances; e.g., concentrations of glycerol-3-phosphate, citric acid, oleic acid and sucrose increased considerably (Zhou et al., 2009).

These studies show that at the very least, when analysed properly in detail, no GM crop can be classified as substantially equivalent to its non-GM counterpart and on this basis passed as safe. Disturbances in plant biochemistry can result in novel toxin production, and may account at least in part for the signs of toxicity observed in animal feeding studies.

6. Bt toxin

Bt toxin is a crystalline protein complex that occurs naturally in the common soil bacterium *Bacillus thuringiensis*. Some types of Bt toxins are effective insecticides and have been used in agricultural spray form for many years by both conventional and organic farmers alike. However, Bt toxin in its native crystalline form is inactive as an insecticide. In the digestive tract of certain insects it is broken down to release the subcomponent ('Cry protein') that is active as an insecticide. This activation procedure makes Bt toxin a highly selective insecticide as only certain insects possess the appropriate acidic conditions in their digestive tracts to bring about this conversion. Once activated, the Bt toxin inserts into and causes lesions in the insect's gut epithelium bringing about death either through a disrupted digestion or systemic bacterial infection (Vachon et al., 2012).

How does native Bt toxin used as an agricultural spray compare with Bt toxin engineered into GM crops? It is important to note that Bt toxins engineered into all GM crops consist only of the active component. As a result, the GM crop contains throughout its structure high levels of constitutively active Bt toxin that is as a result approximately only 45% identical to the native form. This makes the Bt toxin in GM crops significantly different from that used as an agricultural spray; its insect target specificity is compromised (e.g. see Schmidt et al., 2009) and it may pose new health risks.

7. Why is Bt toxin a health concern?

Bt toxin has been proven to be an allergen and potent adjuvant in mammals even at low levels of exposure (Vázquez et al., 1999; Vázquez-Padrón et al., 1999 & 2000; Kroghsbo et al., 2008; Adel-Patient et al., 2011). That is, the organism can readily mount a cellular and humoral immune response against Bt toxin and that Bt toxin can markedly augment immune responses against other ingested foodstuffs. The adjuvant properties of Bt toxin have been observed in sheep as well as rodent model systems where immune response to *Salmonella abortus ovis* vaccination was more efficient in GM-corn-fed sheep than non-GM-fed controls (Trabalza-Marinucci et al., 2008). Therefore, Bt toxin possesses properties which, with sufficient exposure, could lead to allergic reactions caused directly by itself or against other ingested foodstuffs. These properties may account for the disturbing effects on immune system function observed in animal feeding studies detailed above (Finamore et al., 2008; Walsh et al., 2011). In addition, they may account for the well-documented but poorly officially investigated incidences of allergic reactions in the human population linked to exposure to GM Bt toxin-containing crops and foods. Accidental entry into human foods of GM Cry9C Bt toxin 'Starlink' corn intended only for animal feed, led to many instances of allergic-type reactions following consumption of contaminated food (CDC, National Center for Environmental Health, 2001). Workers harvesting cotton in Bt cotton fields in India suffered severe skin rashes and in some cases needed hospitalisation (Gupta et al., 2005) with farm animals feeding on the Bt cotton stubble suffering severe illness and death (Warangal District, Andhra Pradesh, 2006).

A recent finding is that Bt toxin type Cry1Ab, which is present in commercialised GM crops such as MON810 corn, binds to human cells in tissue culture, causes disturbances in energy production and exterior (plasma) membrane systems leading to cell death, albeit at relatively high levels (Mesnage et al., 2012).

Furthermore, a study conducted on pregnant and non-pregnant women in Canada found Bt toxin protein circulating in the blood of pregnant women and the blood supply to their foetuses, as well as in the blood of non-pregnant women (Aris and Leblanc, 2011). Although the source of the Bt toxin detected in these people is unknown, this study shows that Bt toxin can survive digestion and enter the circulation. This raises the possibility that people who consume Bt GM crops in moderate to large quantities as a staple food run the risk of chronic systemic exposure to this insecticide, which, based on the outcomes from animal feeding studies, may contribute to adverse health effects especially with respect to liver, kidney and immune system function. Therefore, further investigation is needed before Bt crops can be claimed to be safe for humans.

8. Conclusions

An increasing body of evidence shows the disruptive effect of the GM transformation process and clear signs of toxicity in well-controlled animal feeding studies even of a short-term nature. These observations demand that toxicity be confirmed or refuted in life-long animal feeding studies. In studies with Bt toxin GM crops that have shown signs of toxicity it is not possible at present to distinguish whether the cause is either the Bt toxin or the mutagenic effect of the GM transformation process or a combination of both. Future studies need to address this point by including a control of non-GM feed with added Bt toxin preferably from a GM plant source compared to GM and non-GM feed alone. Allergenicity needs to be evaluated with human volunteers since there are no animal model systems available for this type of clinical investigation.

Based on available evidence and inadequacy of the tests required by regulators, at present no GM crop and food can be categorically stated as safe to consume, especially on a long-term, life-long basis.

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Genetic Engineering and the Big Challenges for Agriculture – Lessons from the United States

Doug Gurian-Sherman
Union of Concerned Scientists, USA

1. Introduction

GENETIC engineering has been proposed to be a transformative technology, necessary for ensuring that agriculture is sustainable and productive in coming decades. It began in the mid-1980s, almost 30 years ago, and the first commercialised GE crops were grown in the mid-1990s, about 16 years ago. This history provides a record that is now long enough to begin to evaluate the benefits, and to understand the potential of this technology.

Genetic engineering (GE) is often evaluated based on direct risks, such as possible harm from consumption or direct harm to beneficial organisms in the environment. But another important criterion for evaluating genetic engineering, or any other practice or technology in agriculture, is how successful it has been in addressing the biggest challenges confronting food and fibre production in a sustainble manner.

The challenges to agriculture that need to be addressed are widely agreed upon, including producing enough food for a growing population, expected to reach about nine billion by mid-century. It is important to remember that poverty is the biggest reason why there is hunger in the world. We still produce enough food to feed everyone if equitably distributed. Nonetheless, producing enough food for more people while pressed by climate change is a growing concern.

In addition, the greatly increased amount of synthetic nitrogen fertiliser since the 1960s has increased crop productivity, but is causing serious pollution on a global scale, including several hundred hypoxic 'dead zones' in coastal waters that harm fisheries (Diaz and Rosenberg 2008).

Another challenge is climate change, which may exacerbate drought in some regions, as well as more extreme weather events including flooding and high temperatures that make it harder to grow our food. Agriculture already uses about 70% of extracted fresh water, with some important sources such as aquifers being depleted more rapidly than they are being recharged. Therefore, reduction of water use and more resilience in the face of drought and temperature extremes are additional important challenges for agriculture in coming decades.

To assess the progress and value of GE, we have evaluated the impact of genetic engineering in the US on three important challenges to agriculture: increasing food productivity, increasing nitrogen use efficiency, and increasing drought tolerance. These serve as indicators of how successful genetic engineering has been at addressing major challenges that must be solved if our food production system is to be sustainable and productive enough to serve humanity.

2. Genetic engineering and crop productivity in the US

To evaluate the contribution of GE to crop yield, we evaluated peer-reviewed science research and data from the US Department of Agriculture (USDA) on the yield of genetically engineered corn (maize), containing *Bt* genes or herbicide-tolerant soybeans (resistant to glyphosate herbicide) (Gurian-Sherman 2009). These are the two crops of greatest acreage in the US, with cotton between 5 and 10% of the acreage of these two crops.

When considering yield and genetic engineering, it is critically important to separate out the effects of the engineered gene(s) from other factors that influence yield. These other factors include the yield of the crop variety that the genes are inserted into, and crop management practices.

The yield effects of the crop variety are especially difficult to separate from the effects of the transgene, because both are encompassed in the growth of the plant and not readily distinguishable from each other. Farmers, for example, may buy a new engineered crop variety and obtain higher yields than for a previous non-engineered variety. It would be natural to attribute these yield gains to the engineered gene, when typically the crop variety that the gene has been placed into is already improved for yield compared to the older variety.

The most direct, and often most accurate, way to distinguish the contribution of the transgene from that of the crop variety is in controlled side-by-side field or farm trials that use typical farming practices, and where some fields contain the crop variety with the transgene, and others the same variety without the gene.

We emphasised these types of studies, but also relied on other field data, such as regional data on the periodicity of European corn borer (ECB) infestations and yield impacts in the US corn belt, to inform our analysis.

We found that the two primary types of *Bt* in corn, to control ECB and rootworms, contributed about 3-4% to the total productivity of corn in the US compared to typical non-GE corn using typical control practices, such as insecticides. Individual farmers may receive greater benefit if they encounter heavy insect infestations, but these occur sporadically: for corn borer, only about once every four to eight years, and for rootworm in most areas, only when corn is planted year after year. When the productivity contribution for all acres is estimated, this results in a 3-4% aggregate productivity increase.

This value is important because it is aggregate productivity that is relevant to society from the perspective of whether we produce enough grain to feed ourselves. Higher yield for some individual farmers, which can be as high as 10-20% in some years, is clearly important to those farmers.

We also found that available data did not support an increase in yield due to the glyphosate herbicide tolerance gene in corn. Therefore, the total impact on corn productivity is estimated to be about 3-4% over the first 12 years of commercialisation, from 1996 through 2008.

By comparison, data from the USDA show that corn productivity increased by about 28% over the same period of time. Therefore, of the 28% increase in corn productivity between 1996 and 2008, about 24 or 25% was due to factors other than GE. This is about 86% of the total increase in yield in corn in those years. Factors that typically increase crop productivity fall into two general categories: crop breeding and improved agronomy. Historically, about half of the yield increases in corn have been attributed to breeding. GE contributed about 14 percent of the yield increase between 1996 and 2008.

Recent published research has calculated that GE traits in corn have contributed about 7% or slightly higher yield increase (5% from Bt and 2% from herbicide tolerance) (Nolan and Santos 2012). Using these values, GE would have provided about 25% of the yield increase in corn, while other methods such as breeding collectively provided about 75%.

For soybeans, we found that the herbicide tolerance gene provided no clear yield advantage, while based on USDA data, yields went up about 16% from 1996 to 2008, due to breeding and agronomy.

It is also important to understand that yield is often understood as consisting of two general components: intrinsic yield, also called yield potential, and operational yield. The former is generally understood as the yield that can be obtained under favourable conditions in the absence of factors that reduce yield, such as pest infestation or stresses such as drought. The actual, or operational yield, is that obtained under normal growing conditions that include pest infestations and so on, and varies from year to year.

The yield improvements from GE discussed above are from increased operational yield, i.e., reduction of losses from insects and weeds. These are important globally, and especially in many developing countries.

On the other hand, while breeding has increased the intrinsic yield of corn and soybeans over the decades, GE has not done so. There are so far no GE crops that increase intrinsic yield.

The lesson so far is that conventional breeding and agronomy continue to contribute much more than GE to increasing crop productivity in the US, where GE can be compared to other advanced agricultural technologies and methods.

3. Reducing nitrogen fertiliser use and pollution

Synthetic nitrogen fertiliser has greatly increased crop productivity, but at the expense of great harm to the environment. It is also expensive, and is made from natural gas, a non-renewable fossil fuel that contributes to climate change. The use of nitrogen fertilisers also results in tremendous amounts of water pollution, including several hundred hypoxic 'dead zones' in coastal waters that are important for seafood production (Diaz and Rosenberg 2008). Nitrous oxide that is produced in the soil by microbes, from nitrogen fertiliser, is an important greenhouse gas about 300 times more potent than carbon dioxide (carbon dioxide is much more important overall because there is so much more of it produced by human activity than nitrous oxide).

For all of these reasons, it is important to reduce the use of nitrogen fertilisers. One way to do so is through the development of crops that use nitrogen more efficiently. Genetic engineering has been touted as one important way to develop nitrogen use efficient (NUE) crops. Our analysis of the scientific literature found that despite field trials for about a decade, no crop engineered for NUE has been successfully commercialised (Gurian-Sherman and Gurwick 2009). There had been, as of 2009, about 125 field trials for NUE crops, as compared to thousands for insect or herbicide resistance, indicating many fewer prospects for NUE.

On the other hand, the scientific literature has shown that over the past several decades, NUE has increased for several major crops through breeding and other means by about 30-40% (Gurian-Sherman and Gurwick 2009).

Our analysis of the scientific literature of the genes being considered for improved NUE through GE shows that most are plant genes that are found in crops. In addition, studies over the past two decades have demonstrated that there is considerable genetic variation in crop plants and their wild relatives, including for NUE, that may be tapped into to further improve NUE through conventional breeding. This means that GE sources for improving NUE are less varied than for the first GE crops, which relied on bacterial genes. In turn, this may mean that arguments that there are many more sources of genes to improve crops using GE compared to breeding (which uses crop plant genes) may not hold for NUE.

More importantly, non-genetic means of reducing the need for synthetic nitrogen, and the pollution it causes, are available. These include the use of cover crops, used in ecological farming systems such as organic, that can reduce pollution from nitrogen leaching into groundwater by about 40-70% (Tonitto et al. 2006). Legume cover crops, and crop rotations that include legumes such as beans, peas and lentils, supply organic nitrogen to crops which also cause less pollution than synthetic nitrogen sources (Gardner and Drinkwater 2009).

4. Drought tolerance and water use efficiency (WUE)

Drought, along with high temperature, is the single biggest cause of losses of food productivity globally. Predictions of more frequent or severe droughts and more frequent high temperature extremes with increasing climate change in coming decades mean that these losses could increase at a time when more food is needed.

In addition, agriculture is already the greatest user of water, accounting for about 70% of extracted fresh water use. This is stressing many water sources and causing competition for other human and wildlife needs.

As with other agricultural challenges, genetic engineering has been proposed as an important and necessary means of confronting the challenges of drought and for improving WUE.

We recently analysed the data on the contributions of genetic engineering to drought tolerance from the science literature and the USDA, as well as from the submission of data by Monsanto Co. to the USDA to support regulatory approval for drought-tolerant GE corn, called DroughtGard (Gurian-Sherman 2012).

Drought is complex, and can vary in severity and timing depending on its duration, when in the growth cycle of the crop the drought strikes, soil conditions, and other factors. Plants can also respond to drought in many ways, such as by increasing root capacity or length, limiting water loss through reduced transpiration (loss from the plant), reducing the timing of particularly susceptible stages of growth, such as flowering and seed filling in grain plants, and so on. The large number of different crop responses to drought reduces the possibility that a single, or even several, drought tolerance genes will be useful for all droughts or provide dramatic tolerance.

This is borne out from limited data supplied by Monsanto to the USDA, which show that its drought-tolerant corn may provide approximately a 6% reduction in yield loss on land experiencing moderate drought. For example, instead of experiencing a 15% yield loss, such corn may experience a 10% loss. In other words, in a typical year, where this type of corn may be grown on about 15% of US corn acres, it would provide about a 1% productivity benefit nationwide.

It is also likely that this corn would be of very limited or no value in severe or extreme drought, respectively.

By contrast data cited in our report from research from Iowa State University show that conventional methods have increased drought tolerance in corn over the past 30 years by about 1% per year.

Other cited data show that many crops, including several varieties of corn, are benefiting from increased drought tolerance through conventional breeding. These include sorghum, cassava, rice, pearl millet, and wheat, among others. Other studies show that, as with NUE and yield, substantial untapped genetic variation exists in crops and their wild relatives for improving drought tolerance.

Together, these data show that conventional breeding has great potential to improve NUE, drought tolerance, and many other traits in crops. Currently and for the foreseeable future, the potential of breeding to improve crops appears to be considerably higher than for GE.

Drought tolerance may also be improved through sustainable farming practices like organic and low-external-input systems that emphasise cover crops, crop rotation, including trees and other perennials in the cropping system, and use of livestock manures. All of these practices increase soil fertility, which increases the water-holding capacity of soil, making this moisture available during droughts.

Water use efficiency is also important, and has often been incorrectly considered to be synonymous with drought tolerance. Rather, scientists who study WUE have pointed out that most drought-tolerant crops have ways to prevent the plant from having reduced yields during drought, but this typically requires as much water per unit of food produced as is required by non-drought-tolerant crops. WUE and drought tolerance are therefore not typically the same thing, and most drought tolerance traits do not improve WUE.

Based on data provided to the USDA by Monsanto, this is the case for DroughtGard.

Under normal water availability, DroughtGard does not reduce corn water requirements. If water supply is reduced, DroughtGard may use somewhat less water to produce a kilogramme of corn than for normal corn, but at the expense of reduced yield, which is undesirable.

As a whole, the GE industry has invested very little in producing WUE crops. There have been only nine field tests for GE WUE since 1990, compared with about 8,000 for insect resistance and herbicide tolerance.

5. What about the future: The prospects for GE in coming years

Several lessons can be learned from our analyses of GE crops. First, the technology has made only very minor progress toward addressing the big challenges for agriculture now and in coming years. Some have argued that this is because the technology is relatively new, and that we should have confidence that it will improve in the future. But the technology is now about 30 years old—not such a newcomer—and there are biological reasons, which are discussed below, for harbouring some scepticism about the prospects of GE in the future.

Second, crop breeding and better, agrocologically-based, farming practices are much more effective than GE at confronting agriculture's challenges. In addition, those technologies are far cheaper than GE. For example, the industry's own analysis found that a typical GE trait costs about 140 million dollars to develop (Phillips McDougall 2011), while a similar trait costs about one million dollars to develop through breeding (Goodman 2002). Studies over the past two decades have demonstrated, contrary to previous belief, that crops have a large amount of genetic

diversity that can be tapped to help address agriculture's challenges (see, for example, Reif et al. 2005).

The first few commercially successful engineered traits, *Bt* insect resistance and herbicide tolerance, are genetically and physiologically relatively simple. *Bt* codes directly for a protein toxin that directly kills some insects when eaten. A single gene that is not inhibited by glyphosate herbicide is responsible for glyphosate herbicide resistance.

By contrast, many of the traits that are important for making agricultural more sustainable, better for the environment, and more resilient and productive, are complex genetically and physiologically. For example, many genes contribute to yield or drought tolerance. This generally has at least two important implications for genetic engineering.

First, this means that any given engineered gene is likely to have only a modest effect on traits like drought tolerance or intrinsic yield improvement, because it can affect only some of the responses that plants can use to improve the trait. There are some types of single genes, such as transcription factors, that can affect the function of numerous other genes. But even these are not likely to affect most of the routes that can improve these complex traits.

Second, many of the effects of genes like transcription factors may reduce the function of other, agronomically useful traits at the same time that they improve a target trait such as drought tolerance. This is because some of the genes that are affected by the engineered gene are not those that are the intended target of the engineering. This is called pleiotropy by geneticists, and its ramifications are not readily predictable. Although data are scarce, there are instances where negative pleiotropy or negative impact on gene function, some of which is documented in our reports, has been observed for some of these engineered genes. In many cases, we will not know whether such negative pleiotropy exists until after extensive field trials, or more likely, commercial planting for several years (provided that monitoring of these crops is performed).

There are no easy solutions for these two challenges going forward. Probably GE will, as is the case for DroughtGard, continue to make modest progress on these traits for the foreseeable future. But as we have seen, breeding, which can manipulate several genes at a time, is likely to do better. And neither type of genetic improvement can replace improved, sustainable farming practices.

6. Conclusions and further thoughts

Genetic engineering has made some minor contributions toward addressing major challenges in agriculture. These are often discussed uncritically by the media and many scientists in ways that magnify and distort the contributions of GE. This occurs because the small magnitude of the contributions is often glossed over, and especially because it is almost never discussed by proponents of GE in the context

of other approaches to agriculture that are proven, like breeding, or show much more promise, and much better results, at lower cost.

At other times, numbers are presented in a way that also magnifies their importance. For example, it has been said that about 13 million small farmers use GE. Without context, this sounds impressive. But when framed by an understanding that there are up to two billion people engaged in farming or related activities worldwide, the percentage of farmers using GE is shown to be very small.

This problem is exemplified by comparisons of GE to conventional industrial monoculture agriculture, which while productive is not sustainable, and already causes huge environmental and public health problems. Studies that show minor improvements compared to these types of agriculture myopically magnify the value of GE. By contrast, as our work has shown, when breeding and agroecology are contrasted with GE, the latter shrinks greatly in importance.

In addition, GE has reinforced the industrial model of agriculture. Higher input costs from more expensive seeds may result in a relatively larger percentage of profits going to large seed companies. This is a pattern repeated by other farming-input industries and technologies (as well as by large food processors and aggregators). This forces farms that grow commodity grain crops in the US to continue to grow in size to make more money on higher volume. And current GE crops, by reducing labour inputs, facilitate this trend.

But the increasing simplification of agriculture systems that results from this ongoing process is the opposite of farms based on sound biology and ecology, which is facilitated by biological complexity, such as longer crop rotations, the use of cover crops and trees, which reduces pest problems and recycles crop nutrients. These latter functions improve sustainability and resilience and reduce cost to farmers, but are generally not favoured by big companies because they rely more on knowledge than products that those companies sell.

The problems that result from this decreased biological complexity, in addition to the environmental impacts of nitrogen that have already been discussed, are the rise of herbicide-resistant weeds in the US due to the excessive use of herbicides on GE crops, and now the advent of resistant insects. The answer from GE seed companies is more herbicide-resistant crops, using older herbicides, which will greatly increase herbicide use. These older herbicides, such as 2,4-D, developed in the 1940s, may also be more harmful to the environment and people. This ‘pesticide treadmill’ is ultimately not sustainable (Mortensen et al. 2012). Resistance to herbicides and insecticides has always occurred in industrial agriculture. But the fact that GE also has this serious problem is a compelling argument against it.

And in addition, the scale of resistance of weeds due to use of glyphosate on GE crops greatly exceeds what has come before, and this is directly connected to how these herbicides are used on GE crops.

The best answer to these problems is a large shift in the dedication of public resources to those types of agriculture that we know can improve sustainability, resilience, and productivity, and support farmers in their livelihood.

These include research, policy incentives, and information on agroecology and breeding, especially participatory breeding.

Genetic engineering could make small contributions, but at great cost. As such it is largely a distraction from better approaches to agriculture. But since it is one favoured by the economically and politically powerful companies that sell GE seed, only an informed process supported by popular demand is likely to reverse the overemphasis on GE technology at the expense of vitally important alternatives.

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Erring on the Side of Caution: A Case for Increased Regulatory Oversight of Genetically Modified Organisms in the United States

Cynthia L. Sagers[1] and *Robert Finlay*[1,2]
[1]Department of Biological Sciences
[2]Department of History
University of Arkansas Fayetteville, Arkansas USA 72701

Abstract

REGULATORY oversight of genetically modified organisms in the United States has been weakened in the decades since recombinant DNA technologies first emerged. Erosion of regulatory control should be questioned inasmuch as that contamination by genetically engineered (GE) products has imposed a burden for US food producers in lost market share while generating only marginal gains in productivity (Foley et al. 2011). Moreover, the adventitious presence of transgenes in the human food supply has created an environment of mistrust for regulatory oversight. Yet advocates of biotechnology continue to lament the cost of approving new GE events (Borlaug 2000, Federoff et al. 2010, Giddings et al. 2012). In this brief, we identify shortcomings in the rationale for limiting regulation and instead make the case that now is the time for increased regulatory oversight.

1. Introduction

Soon after the first demonstrations of recombinant DNA technology, the potential risks to the environment and human health became evident. In 1975, a global moratorium halted research on recombinant forms until risks could be defined and confinement protocols established. Concerns were so great and an understanding of risks so limited that the decision was made to err on the side of caution (Andow & Zwahlen 2005). Leading researchers convened a meeting at Asilomar, California, to identify potential biohazards and to recommend standardised lab practices for handling GE organisms (Berg et al. 1975). The conference resulted in the US National Institutes of Health (NIH) guidelines for laboratory research on recombinant DNA (Andow & Zwahlen 2005). The recommended *modus operandi* was deemed the 'precautionary principle' and adopted as the 'precautionary approach' in the Cartagena Protocol on Biosafety. It maintains that when risks to human well-being are in doubt, the wise course of action is to take precautionary steps until the significance of those risks is clear (Rio Declaration on Environment

and Development 1992). Thus in 1975, independent scientists, alarmed at the hazards arising from the new technology, signed onto the moratorium; but in the decades since, there has been a radical shift in perspective, with industry-scientists now maintaining that the technology is safe and that a moratorium on its use represents a relic of unconstructive thinking.

The NIH guidelines were put into place early in the evolution of the biotech industry when few could have envisioned the scale on which GE organisms would be produced. There has been a striking record of growth since the first intentional releases of GE organisms in the mid-1990s (Nap et al. 2003). Genetically engineered crops now grow in all ecosystems that support plant life, approximately 160Mha worldwide (FAOSTAT 2012). Despite the widespread use of GE products and their cultivation in diverse ecosystems, there has been no clear-cut environmental calamity, no loss of human life, no evident spread of plant blight. The biotech industry and its advocates have championed the safety of GE organisms, arguing that threats to human health have been exaggerated and that delays stemming from regulatory approval have harmed the industry (Fedoroff 2011). They maintain that because there has been no acute, irreversible harm, the regulatory control of biotech developments should be minimised (Borlaug 2000, Federoff et al. 2010, Giddings et al. 2012). In this brief we discuss some fallacies in this reckoning and argue that regulatory oversight of GE products should be strengthened.

In the years since Asilomar, US scientific organisations have weighed in with concerns regarding the widespread adoption of genetically engineered plants and animals. Members of the Ecological Society of America (ESA) summarised the potential environmental risks of transgenic organisms in 1984, 1989 and 2005 (Brown et al. 1984, Tiedje et al. 1989, Snow et al. 2005). The most recent report summarised likely hazards to the environment and formalised recommendations for development of GE organisms. A tacit assumption of these cautionary reports was that should any of these concerns be realised, the offending GE organism would be withdrawn from commercial production. Of the six environmental concerns listed by Snow et al. (2005), four have been realised in North America: the persistence of GE organisms outside of cultivation (‘escapes’) (Watrud et al. 2004, Warwick et al. 2008, Zapiola et al. 2008, Schafer et al. 2011), their potential to interbreed with related taxa (Reichman et al. 2006, Zapiola et al. 2008, Wegier et al. 2011), direct and indirect effects on non-target species (Rosi-Marshall et al. 2007), and the potential for the evolution of resistance to herbicides and pests (Warwick et al. 2008, Heap 2012). Unfortunately, there has been no regulatory backlash and no government action to eradicate the escapees; nor has there been litigation concerning intellectual property rights and responsibility for clean-up. A case in point is the report of GE canola escaped from cultivation throughout North Dakota, USA. Schafer et al. (2011) reported large populations, occasionally thousands of individuals, of GE canola resistant to glyphosate or glufosinate herbicides growing outside cultivation. Among the plants sampled in the study,

several expressed resistance to both herbicides (glyphosate and glufosinate resistance), a phenotype that has not been commercially released (Schafer et al. 2011). Discovery of plants with 'stacked traits' indicates that new genetic forms of GE canola are evolving outside of both cultivation and regulatory oversight. The discovery brought global attention to the issue of commercial production of GE crops. Nevertheless, there has been no subsequent monitoring or clean-up by regulatory agencies or private industry. In 2012, GE canola was still cultivated on more than 90% of canola acres in North Dakota (FAOSTAT 2012).

Despite evidence that genetically engineered crops contribute to significant environmental disruption, the industry and its advocates persist in arguing that regulatory protocols should be streamlined for approval of new biotech products (Bourlaug 2000, Fedoroff et al. 2010, Federoff 2011, Giddings et al. 2012): 'Despite the excellent safety and efficacy record of GM crops, regulatory policies remain almost as restrictive as they were when GM crops were first introduced' (Federoff et al. 2010). Such appeals for limiting regulatory oversight are premature, however: evidence for the biosafety of most GE crops is scarce and regulatory oversight remains insufficient. Lack of transparency in the risk assessment process coexists with inadequate regulatory supervision. Given this, it is not surprising that emerging problems in the regulation of GE organisms have not been fully articulated. In this brief, we present three fallacies in the argument for streamlining regulatory approval of new biotech products. These fallacies are:

- Absence of evidence is not evidence of absence
- One problem can be solved by another
- Substantial equivalence is actual equivalence

2. Absence of evidence is not evidence of absence

Environmental effects of GE crop cultivation, unlike acute economic results, have failed to materialise on a large scale (Federoff et al. 2010). Only a limited number of studies have linked the cultivation of GE crops to possible changes in native communities or ecosystem function. For example, several studies have documented the persistence of transgenic protein products outside the GE organism (Saxena et al. 2002, Zwahlen et al. 2003, Chambers et al. 2010), while others report effects on plant and soil (Watrud et al. 2011). Nonetheless, even under close scrutiny, large-scale effects of GE crops have not been reported (Squire et al. 2003). This absence of evidence, industry and its advocates argue, is confirmation that environmental effects are not taking place. Such an argument entails some dubious assumptions, however. Consider an alternative explanation: that the environmental effects of GE crops are undetected by current approaches or under-reported because monitoring efforts are deficient.

Community and landscape level effects will likely be cumulative and detectable only when they can be distinguished from other complex phenomena in agricultural landscapes, such as effects of herbicide overspray, declines in pollinator abundance and diversity, and climate change. Further, the effects may be taking place below detection levels because effects on soil processes, growth rates of native populations, or the structure of native communities will seldom be acute. Effects on biodiversity may be measurable only after generations of exposure and only when there is a pre-cultivation baseline available for comparison. Moreover, they are most likely to affect remote, sparsely populated areas, and only a small number of scientists are currently monitoring crop-wild boundaries. Evidence that current oversight and monitoring efforts are inadequate is underscored by the previously cited report of GE canola escape in the US. In the first year of a USDA-funded study, Schafer et al. (2011) documented the escape from cultivation of GE canola years after gene flow and crop migration had been reported in the United Kingdom, Denmark, Canada, Australia, Japan and France (Crawley & Brown 1995, Mikkelsen et al. 1996, Pessel et al. 2001, Rieger et al. 2002, Simard et al. 2002, Beckie et al. 2003, Aono et al. 2006, Warwick et al. 2008). In Switzerland, where federal law mandates the eradication of GE products when discovered in the environment, a federal task force seeks out and eliminates escaped plants.

Regulatory agencies in the US, however, eschew such aggressive action. The long lag time in discovering escapes supports the contention that regulatory and monitoring practices are inadequate for the scale at which GE crops currently are grown. To argue that the absence of evidence is evidence of absence is valid only if adequate monitoring and assessment efforts are in place to identify and track long-term effects of GE crops and their management on natural communities. In short, the lack of reports of environmental effects in the US almost certainly is due to lack of investigating and reporting of such effects.

3. Substantial equivalence is not actual equivalence

According to current US regulation, if a new food or food component is found to be 'substantially equivalent' to an existing food or food component, it can be treated in the same manner with respect to safety (Isham 2006). When deemed 'substantially equivalent' to its conventional counterpart, a new GE product requires fewer regulatory steps and reduced scrutiny for approval for commercial production than a novel transgene in a different crop species. Moreover, the concept of 'substantial equivalence' carries with it the assumption that existing food sources can be used as a basis for comparison when assessing the safety of GE products (Mayers et al. 2002). The questions of what constitutes 'substantial' – that is, what characters are to be evaluated and what represents an adequate basis for comparison – have not yet been satisfactorily challenged in the US. Indeed, without clearly

established criteria for evaluating 'substantial' or what characters must be considered 'equivalent', any degree of equivalence may capriciously be labelled 'substantial'.

Selection of a conventional crop variety as a standard of comparison for GE products unduly limits the scope of risk assessment to the effects of the transgene itself. This procedure has already created an unfortunate reputation for US regulatory agencies. A case in point is LL601, an experimental rice cultivar that carries a transgene for glyphosate herbicide resistance. LL601 was grown in field trials in several US states from 1998 to 2001 until the owner of the product, Bayer CropScience, decided against further commercial development (Vogel 2006). In 2006, however, evidence of LL601 contamination was discovered in rice stores in Missouri and Arkansas. Soon after this was made public, LL601 contamination was reported in Sweden, France and Germany. In response, the European Union, Japan and South Korea banned imports of US rice. On the very day that the contamination came to public notice, Bayer CropScience applied to the US Department of Agriculture for retroactive approval of LL601 for commercial distribution. The USDA responded with a risk assessment from which it concluded that the appropriate decision was to approve the variety based on 'substantial equivalence' to a non-GM rice cultivar and a transgene already approved for use in the human food supply (APHIS/USDA 2006). Thus a new transgenic product was approved by the USDA after it had contaminated rice stores intended for humans because it was deemed 'substantially equivalent' to approved products. The criterion of 'substantial equivalence', especially when a judgement is made after release, cuts short regulatory review and provokes mistrust and suspicion of the regulatory process. The case of LL601 suggests that the USDA acted less as a regulatory agency than as an institution poised to approve whatever a corporation placed before it.

In addition to its conceptual inadequacy, the notion of 'substantial equivalence' fails to acknowledge that management of new GE varieties may differ fundamentally from conventional crops. The clearest example is the management of GE herbicide-resistant varieties for which the costs of transformation for herbicide resistance are recouped only when crop fields are sprayed with herbicide. From 1996 to 2011, the cultivation of herbicide-resistant crops increased from 12 million to 160 million hectares worldwide (FAOSTAT 2012). Increased herbicide use is now linked to the rapid evolution of herbicide-resistant weeds (Powles 2008, Heap 2012). In addition, the mounting use of herbicide poses threats to native vegetation, neighbouring crops, and open water sources, especially when recalcitrant herbicides such as 2,4-D (2,4-Dichlorophenoxyacetic acid) are part of the package. The vertical integration of seed source with herbicide use carries additional risks linked to herbicide application for conventional crops. Application of herbicide should therefore be incorporated into the risk assessment of herbicide-resistant GE products. Operating under the rubric of 'substantial equivalence', then, fails to acknowledge the full risks of the GE product and creates vulnerability in risk assessment protocol.

4. One problem cannot be solved by another

GE organisms increasingly involve individual plants expressing multiple transgenic traits. For example, in response to the evolution of herbicide-resistant weeds, multiple herbicide-resistances are now 'stacked' in single plants. Stacking allows farmers to treat crop fields with a cocktail of herbicides that can effectively eliminate those weedy plants that have evolved resistance. Similarly, stacking pest resistances with a family of Bt cry transgenes makes a single variety resistant to a suite of harmful insects. Multiple pesticides will only delay the evolution of Bt resistance; resistance to herbicides and pesticides evolves quickly in organisms with short generation times. Stacking multiple resistances therefore will merely delay the evolution of more resistant plants and insects. Under strong selection and with gene flow, novel combinations of resistances evolve rapidly. The spontaneous evolution of multiple resistances has already been demonstrated in feral canola populations (Knispel et al. 2008, Schafer et al. 2011). Release of commercial varieties with multiple beneficial transgenes will create even greater problems for weed and pest control. Products like SmartStax corn, which carries eight transgenes for resistance to herbicides and insects, have been released in the US. The risk of releasing multiple, effective resistance to all families of pesticides poses a serious threat to agricultural productivity when nearly every major crop can hybridise with a native species in its geographic distribution (Ellstrand et al. 1999). Plants bearing stacked traits demand more careful scrutiny that any single transgene inasmuch as risks of escape pose problematic issues whose resolution will be costly to the individual farmer as well as to society as a whole.

The three fallacies detailed above reveal their pernicious consequences when placed in the nexus between commercial enterprise and public policy. It is a truism of both economics and cognitive science that perceived advantage, such as commercial profit or self-aggrandisement, almost always trumps objectivity. Profit is one of the most potent incentives known to man; but the profit motive does not inevitably align incentives in a socially desirable way. Ever since the Progressive Era (1890s to 1920s), the federal government has created regulatory agencies to oversee finance, medicine, schooling, and industry as a consequence of the recognition that the public must be protected by private or corporate interests seeking profit. The case of GE commodities should be treated in the same, well-tried fashion.

Corporations argue that making public the details of the GE organism, that is, the transgene sequence, its promoter, and its protein product, would expose them to exploitation. They argue that the GE organism represents confidential information, a source of deserved revenue. To protect commercial interests, regulatory agencies allow the corporation to complete a suite of toxicology studies and report their findings in confidence to the regulating agency. In the previously mentioned case of widespread contamination by LL601 rice, 40% of the industry-generated risk

assessment data were judged 'confidential business information' and not available to the public - even after it had contaminated the food-supply chain (Clapp 2008). In the US, independent risk assessment by academic researchers or even federal regulatory agencies such as the US Environmental Protection Agency (US EPA) is prohibited without a Memorandum of Understanding (MOU) that must be negotiated with the corporation. The MOU is developed after corporate review of the research plan of the submitting agency and is signed by both parties. As a result, the corporation regulates who has freedom to operate with the GM organism in question. In short, pre-release risk assessment is done by profit-seeking corporations; review by outside scientists or by federal regulatory agencies is fatally restricted.

Clearly, there is a conflict of interest when a corporation assesses the risks of a GE organism from which it will profit. Bringing GE products to the approval stage typically costs tens of millions of dollars (Isham 2006). With so much at stake, it is surely not advisable to expect a corporation responsibly to evaluate potential risks. Independent investigation by the public sector is the only guarantee that the effects of a transgene product will be effectively assessed within the context of public policy (NAS 2002).

5. Conclusion

The concerns spelled out in reports by the Ecological Society of America (2005) and the National Academy of Science (2005) are clear: prudence is warranted and existing regulatory policies are inadequate to prevent harmful release of genetically engineered organisms. Crops already recognised as problematic have been approved for engineering and release. Alfalfa (*Medicago sativa*) is known to grow outside of cultivation (Bagavathiannan et al. 2010), yet a cultivar engineered for herbicide resistance recently was cleared for release in the US. SmartStax corn, which is widely distributed, contains eight unique transgenes that confer resistance to multiple herbicides and herbivores. Similarly, corn with multiple resistances to herbicides, glyphosate and 2,4-D has been approved for production despite the long half-life of 2,4-D and its toxicity to pollinators (Zepp et al. 1975).

In a larger perspective, agronomists, ecologists and conservationists recognise that herbicide-resistant weeds are evolving rapidly following the release of glyphosate- and glufosinate-resistant GE crop cultivation. Yet GE cultivars with resistance to multiple environmental challenges have been approved for release in the US. In contrast, countries from Sweden to South Korea have taken action based on the precautionary principle; but the latter is rarely cited in US courts (Foster et al. 2000) and regulatory oversight accordingly has slackened across the board.

The issues at stake can hardly be exaggerated. Sustainable agriculture, land management, crop production, indigenous cultures, food security, dietary regimes, and public health are all potentially at risk as GE crops gradually expand around the world. GE organisms now flourish in all arable ecosystems. In the near future,

without appropriate restriction, they will surely prosper in the cultivated fields of all nations. They have gained a secure global foothold in 160 million hectares – an area the size of the subcontinent of India – and can look forward to overrunning the remaining 13.4 billion hectares of the planet in the future. Furthermore, when the balance tips in that remote prospect, and GE crops come to dominate, a return to the *status quo ante* will be impossible. We will all live under a radically altered botanical regime.

To be sure, some of these GE products may confer immense benefits on humanity; but others, as research already confirms, decidedly will not. This is an argument to err on the side of caution. 'First do no harm' – the equivalent in medicine to the precautionary principle in scientific research, is a standard that researchers, corporations, regulatory agencies, and governments would do well to adopt in considering the future of GE products. The Cartagena Protocol should guide future action: 'Where there is uncertainty as to the existence or extent of risks to human health, the institutions may take protective measures without having to wait until the reality and seriousness of those risks become fully apparent.' (Rio Declaration on Environment and Development 1992)

Acknowledgements

Thanks to ENSSER – European Network of Scientists for Social and Environmental Responsibility – for organising this symposium and encouraging us to develop this document; thanks to Drs Johnnie van den Berg (North West University, South Africa) and Doug Gurian-Sherman for interesting and provocative discussions.

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Transgene Flow into Native Seed and Ecosystems in Mexico

Ana Wegier
National Institute for Research in Agriculture, Forests and Lifestock (INIFAP), Mexico

1. Introduction

TO understand the context in which many of the centres of origin of important crops exist, we have to imagine how they emerged and the processes that have sustained them until today. Only by understanding their evolution will we know how to conserve them. Among the biological and cultural mega-diversity of Mesoamerica, one of the cradles of agriculture emerged. Mesoamerica is the centre of origin of about 150 crops like corn, beans, squash, chilli and several others that constitute the nutritional basis of the region. The environmental heterogeneity together with the diversity of customs and traditions maintain this centre of origin.

How can we identify areas that are centres of origin and diversity, to document and propose conservation strategies that include biosafety measures?

Nothing makes sense except in the light of evolution. The conservation of genetic diversity is not a fad, since it represents the possibility of adapting to new environmental scenarios. The higher the genetic diversity, the higher are the chances of surviving in new conditions by natural selection processes. In addition, *in situ* conservation is critical to the continuation of the process of domestication (another evolutionary process that is not static), because it offers not only the opportunity to make improvements with modern and traditional techniques, but the option to start the development again, in the event that something happens to all domesticated varieties (as has happened with the potato and banana), and as often as desired. However, if transgenes are present in wild plants and traditional or native cultivars, this possibility is ruled out, since these genes have been patented and nobody can make commercial use of the material without a licence while the protection period is effective.

Here we will discuss the case of cotton in Mexico from the beginning and then update on the history of maize and its current consequences.

2. Cotton

At first, we investigated the actual and potential distribution of wild cotton populations, as well as the contribution of historical and recent gene flow in shaping cotton genetic diversity and structure. We evaluated historical gene flow using chloroplast microsatellites and recent gene flow through the assessment of transgene presence in wild cotton populations, exploiting the fact that genetically modified cotton has been planted in the North of Mexico since 1996. Assessment of geographic structure through Bayesian spatial analysis, BAPS and Genetic Algorithm for Rule-set Production (GARP), suggests that *G. hirsutum* seems to conform to a metapopulation scheme, with eight distinct metapopulations. Despite evidence for long-distance gene flow, genetic variation among the metapopulations of *G. hirsutum* is high (He = 0.894 ± 0.01). We identified 46 different haplotypes, 78% of which are unique to a particular metapopulation, in contrast to a single haplotype detected in cotton cultivars. Recent gene flow was also detected (m = 66D† 270 = 0.24), with four out of eight metapopulations having transgenes. The percentage of positive individuals with 'wild haplotypes' and the percentage of individuals with transgenes that are not commercially available, in combination or alone, show that evidently introgression has occurred and more research is needed (Wegier et al 2011 Molecular Ecology 20(19): 4182-94).

Many challenges arise from these findings: How can we know the impact of the insertion of a new gene on the ecosystem? How can we measure the environmental impact caused by GM crops in ecosystems?

3. Maize

Scientific papers document the presence of transgenes in Mexican native maize varieties: 1) In Sierra Juárez, state of Oaxaca in 2000: Quist and Chapela. (2001) Nature, 414, 541-543; 2) In the conservation area of the Federal District (Mexico City), in 2003: Serratos-Hernández et al. (2007) Frontiers in Ecology and the Environment, 5(5): 247–252; 3) In Sierra Juárez, state of Oaxaca in 2001 and 2004: Piñeyro-Nelson et al. (2009) Molecular Ecology, 18:50-761; 4) In localities of the states of Guanajuato, Veracruz, Oaxaca and Yucatán in 2002: Dyer, G. et al. (2009) PlosOne. Vol. 4(5): e5734 doi: 10.1371/journal.pone.0005734; 5) Peer-reviewed papers addressing other transgene biomonitoring efforts made by governmental agencies and NGOs in Mexico: Mercer and Wainwright (2008) Agriculture, Ecosystems and Environment, 123, 109-115. To date, at least 12 papers can be found online on gene flow in Mexico. Recent projects, involving great sampling, have also found evidence of gene flow but indicate that they are still not ready for publication.

Since 2009, after demolishing several legal obstacles, the planting of GM maize in Mexico began. The Union of Scientists Committed to Society (UCCS,

México) presented a document with a synthesis of the main issues that translate into important uncertainties and potential risks, which have not been adequately addressed with scientific research:

1) There is still insufficient scientific evidence on the technological potential and risks of the present-day GM maize lines, and the ones being proposed for release are already obsolete. Alternative technologies should be explored before adopting this transgenic maize technology, which has been tailored for different environmental and socio-economic conditions. Some examples that support this statement: Pests for which maize transgenic lines have been engineered are not important or present in Mexico. Local maize varieties are well adapted to resist important pests in each locality and the introduction of transgenic lines may also affect the ecological balance of different pests and create new pest problems for Mexican agriculture. The use of maize genetic variation combining bioinformatics, contemporary molecular biology approaches and the use of novel transgenic approaches that overcome some of the limitations and risks of the first generations of GMO are promising.
2) Uncertainties related to the interpretation of the law and its violation.
3) Recent scientific evidence has shown that transgenes have made their way into native maize varieties within several different agricultural zones in Mexico. This data suggest that coexistence of GM maize lines with conventional maize varieties without gene flow is virtually impossible once the former are planted in the field.
4) Mexican Government agencies in charge of biosafety (Agriculture, Environment and Health, among others) have been unable to detect, investigate and prevent the introduction or impact of transgenes in Mexican native maize varieties.
5) Mexico comprises the centres of origin, domestication and diversification of maize and thus, harbours the majority of the genetic diversity of maize worldwide, while being home of all its known wild relatives. This genetic diversity is dynamically recreated in the fields of many small-scale farmers that produce maize for their subsistence, for local or regional markets. Farmers in the diverse agronomical systems present in different parts of Mexico rely on saving seed from one agricultural season to the next as well as on frequent seed exchange among farmers within and outside of the communities. These activities are at the heart of the dynamic system that ensures the generation and maintenance of genetic diversity in maize. This system also implies that dispersal of GM maize and introgression of transgenes into native maize varieties cannot be avoided in Mexico if GM maize lines are planted in open fields.
6) Maize is a basic staple of the country, consumed daily with little processing and in large quantities, and thus possesses a critical agricultural, nutritional,

economic and cultural significance for Mexican people. Furthermore, it's the third staple of the world, with increased consumption in countries within Africa and an important source of feed in many other nations. The health consequences of GMO consumption under these regimes have not been investigated thoroughly, but the few available appropriate experiments point to possible negative effects.

7) Multiple maize lines expressing pharmaceuticals and other industrial substances (so-called pharma and industrial crops) should not be consumed by animals or humans. Companies have not been able to keep transgenic and non-transgenic lines segregated and several escapes from experimental plots of pharma-crops unauthorised for consumption have been reported. Therefore, even if such events occur at very low probabilities and have limited impact on maize stocks in the USA, once in the Mexican territory, the frequency and dispersal of such sequences could be amplified. For that reason, the probabilities of occurrence of such escapes in Mexico should be estimated rigorously in order to establish efficient monitoring and biosecurity methods.
8) Once GM maize lines are released, transgenes will insert and accumulate in landraces and wild maize relative species (teosintes). It is well documented that the phenotypic effect of a transgene largely depends on the genome context and background where it is inserted.
9) There is ample evidence demonstrating that stable alternatives exist that meet and even exceed the needs which transgenic maize is purported to meet, without the risk its release would involve.

In 2011, the global project about maize coordinated by CONABIO concluded. Two hundred and thirty-five researchers from 70 institutions participated (http://www.biodiversidad.gob.mx/genes/proyectoMaices.html). This effort culminated with a greater knowledge about the distribution of the native maize races of Mexico and the generation of multiple maps that are available at (http://www.biodiversidad.gob.mx/usos/maices/razas2012.html). However, the current initiative to determine the centre of origin and diversity of maize in Mexico, does not respect the results obtained in this project nor the rest of the scientific information generated on the subject.

4. Conclusions

The interplay of historical long-distance gene flow and geographic barriers in Mexico has shaped the genetic structure of extant populations of *G. hirsutum.*

The hypothesis is rejected: geographic distance is not a measure that can prevent gene flow between cotton populations.

We need to incorporate ecological and evolutionary research to GMO risk assessments.

With this research, Mexico has demonstrated that it is not ready to release, monitor, or experiment with species of which it is the centre of origin or diversity, or that endanger human health or ecosystems.

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Bt Eggplant Field Trials and Biosafety Regulations in the Philippines

Ruth U. Gamboa
University of the Philippines Mindanao, Philippines

1. Introduction

EGGPLANT is a household vegetable and the most consumed in the country. It accounts for about 28% of the vegetable production and is grown in more than 20,000 hectares across the archipelago. Its most significant insect pest is the Fruit and Shoot Borer (FSB) that can lead to yield losses of 20-92% (Francisco, 2010).

2. From India to the Philippines

In June 2006, seeds of the FSB-Resistant eggplants, or simply *Bt* eggplants, were turned over from India to the Agricultural Biotechnology Support Project II (ABSPII) at the Institute of Plant Breeding, University of the Philippines Los Banos (UPLB). This came six months after a royalty-free licence was granted to the university by the Indian Maharashtra Hybrid Seeds Company Limited (Mahyco) to use its eggplant lines as source of the mentioned trait for the development of selected Philippine varieties. ABSPII and Mahyco are partnering with USAID, Cornell University, the International Service for the Acquisition of Agri-biotech Applications and the Department of Agriculture (Phil) for this particular project. Local adoption of an existing technology is viewed as a practical approach in the Philippines, which has limited budget allotment for biotech research and development (Cabanilla, 2007).

The stages in the development of *Bt* crops as prescribed in the country's Guidelines for Biosafety start from Contained Trials moving to Confined Field Trials then to Multi-location Field Trials and finally to Propagation/ Commercialisation. The first two stages for *Bt* eggplant were completed in 2009. The following year, multi-location trials were conducted and continue to date. Seven locations were identified across the country; the choice was primarily based on the volume of locally produced eggplants. The first trials in three provinces in the northern island of Luzon proceeded smoothly until they reached Davao City in the southern island of Mindanao.

3. From Luzon to Mindanao

On 13 December 2010, the mayor of Davao City issued a Cease and Desist Order (CDO) for the field trial being conducted inside the campus of the UPMindanao (UPMin). This was implemented on 17 December, by the uprooting of all the plants. The Order cited the project's failure to comply with several conditions highlighting the failure to 'conduct a public consultation through the posting of a Public Information Sheet (PIS)' – a requirement under Administrative Order No.8 (2002) of the Department of Agriculture. The issuance of the CDO was preceded by a resolution emanating from the city's Legislative Body declaring, 'There is no compelling reason for the city…to welcome *Bt* eggplant as it is provided under the Organic Agriculture Ordinance that *Bt* eggplant is a complete departure from the city's stance on sustainable agriculture and fisheries.'

By 29 December, the Bureau of Plant and Industry (BPI), the national agency responsible for the regulation of GM crops, suspended the biosafety permits for the field testing at UPMin. BPI's review of pertinent documents also led them to the suspension of the same permit granted earlier to the Visayas State University in central Philippines for likewise failing to post the PIS and conducting the consultation with the municipal officials.

The *Bt* eggplant project team in Davao claimed Public Information Sheets were posted in designated areas prior to the start of the trial. The city, however, argued that for such a controversial project no one came purposely to invite them to a public consultation more so that there is local ordinance on organic agriculture. The project team did arrange public engagements but according to opposing groups those took place only after the experimental plot had been made ready and the seeds were about to be transported from UPLB. The guidelines specifically state that consultations should be done prior to the application of a permit. A farmer-scientist group, MASIPAG, expressed that concerns about GM crops stem from the fact that the government has not done any monitoring on the impacts of *Bt* corn ten years after its commercialisation.

The experience in Davao prompted a neighbouring location to 'start right'. The provincial government of North Cotabato and the municipal government of Kabacan initiated public consultations themselves. The host academic institution, the University of Southern Mindanao, likewise conducted its own in-house consultations. Both local governments as well as the university gave their support for the project.

The following year, in June 2011, BPI granted the request of ABSPII to resume the field trials at UPMindanao. The proponents went through the requirements again including the posting of the PIS. By this time, however, the city mayor and the council were more straightforward in their objection. The stand of the city is basically based on its Organic Agriculture Ordinance which organic farmers and anti-GMO groups strongly pointed out to the local officials.

Early this year, groups from various sectors including the local government of Davao City signed a petition to the Supreme Court (SC) asking for a total ban of *Bt* eggplant trials. On 2 May, the highest court issued a Writ of *Kalikasan* (nature) where all respondents will be summoned to present 'all possible defences' in favour of the field trials. The Writ also temporarily stops new applications for field testing. On 15 June, more activist groups joined the petitioners in urging the SC to likewise issue a Temporary Environmental Protection Order and a Writ of Continuing Mandamus that will put a stop on all on-going field tests. To date, the SC has yet to act on these petitions. Meanwhile, trials on the *Bt* eggplant are now for the hybrid variety. According to ABSPII Newsletters, results of the open pollinated variety tests showed that *Bt* eggplant lines had 'high resistance against the FSB'.

4. From written provisions to real practice

The legal framework for biosafety in the Philippines is very comprehensive and involves about four sets of documents: from a policy statement to specific guidelines. Its strategy serves as a model among Asian countries (Cabanilla, 2007) and its guidelines are among the most stringent (Cruz, 1999). As an example: each stage of *Bt* crops, from contained laboratory trials to commercialisation, has to be assessed and approved by two departments: Science and Technology and Agriculture. In the US, the notification is only with the Department of Agriculture.

The framework is also very inclusive. The National Committee on Biosafety, the lead body coordinating and harmonising inter-agency and multi-sectoral efforts to develop biosafety policies, involves three more national agencies (Health, Environment and Natural Resources, Trade and Industry); five scientists from various disciplines; and three community representatives from the consumer, industry, and agriculture sectors. The framework upholds public participation, transparency, and consensus as principles in reaching biosafety decisions. It invokes constitutional policies such as the right to information, the right to participation, and local autonomy as among the basis for framing and implementation guidelines.

This 'spirit of the law' came to life in the Davao experience when stakeholders made local officials accountable in interpreting the biosafety provisions vis-à-vis an existing local ordinance and a national law on organic agriculture. From then on, the Bureau of Plant Industry, the *Bt* eggplant project itself and the succeeding implementers all made sure no short cuts were resorted to. Eggplant farmers supportive of the technology are pushing for more and continuing education. Such adherence by the key players and vigilance by stakeholders will ultimately benefit the country which regards biotechnology as 'one of several means' to achieve and sustain food security.

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Field-Resistance of the African Maize Stem Borer to Bt Maize: What Did We Learn?

Johnnie van den Berg
Unit of Environmental Sciences and Management,
North-West University, South Africa

1. Introduction

IN 1997 South Africa became the first country in Africa to commercially produce genetically modified (GM) crops. Farmers started adopting Bt yellow maize (mainly used as animal feed) during the 1998/99 season. Bt white maize (mainly used for human consumption) was introduced during the 2001/02 season and the 2002/03 season saw the first large-scale Bt white maize production. Up to 2006, when event Bt11 was commercially released in South Africa all Bt maize hybrids contained event MON810. These hybrids therefore all have the same gene that encodes for the Cry1Ab protein that is selectively toxic to larvae of the Lepidoptera.

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 effectively control moth larvae of other economically important pests in Africa, which include *Chilo partellus* and *Sesamia calamistis* (Van Rensburg, 1999; Van den Berg & Van Wyk, 2007). Until 2006, effective control of the main target pest of Bt maize, *Busseola fusca*, was also reported in South Africa.

Since the first deployment of GM crops with insecticidal properties, there has been concern with regard to resistance development of target pests and possible non-target effects (Tabashnik, 1994; Gould, 1998). Resistance development as well as ineffective management thereof once reported could have several significant adverse effects. Firstly, if continuing product failures occur and resistance becomes an area-wide problem, farmers will be back to where they were with management strategies 15 years ago. This will imply repeated application of broad-spectrum insecticides. Secondly, continued cultivation of specific GM events (for example Cry 1Ab-producing maize cultivars) may compromise the future use of cultivars with similar stacked events, when these are deployed to control resistant pest populations.

2. Farmers' perceptions of Bt maize in South Africa

Surveys conducted by Kruger *et al*. (2009, 2012) showed that the greatest benefit associated with Bt maize was the convenience of target pest management. An important advantage in the cultivation of Bt maize is the reduction in the number of insecticide applications. However, Bt maize is only an advantage when target pests are present and there is no advantage in areas where infestation pressure is generally low. Stem borer populations can vary in abundance from year to year and their pest status is not predictable. This is evident from research done by Van Rensburg *et al*. (1987) on *B. fusca*, which indicated large-scale variation in infestation levels over seasons. In South Africa farmers have benefited from the adoption of Bt maize since its deployment during 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.

3. Resistance development

Two years after that start of planting Bt maize in South Africa, at harvest of the 1999 growing season, crop damage to the lower stems caused by *B. fusca* was noticed on a considerable scale at a number of localities, involving various Bt maize hybrids (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 seemed to have been raised about resistance development at that time. These observations were the first that should have indicated the possibility of resistance development and should have stimulated actions to address the issue.

4. First report of resistance

The first official report of resistance of a maize pest to Cry 1Ab maize was made in South Africa during 2007 (Van Rensburg, 2007). This report of field resistance of *B. fusca* to Bt maize showed that some larvae on Bt maize at certain locations were able to survive in the presence of the Bt-toxin but not without some detrimental effect on larval growth rate.

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. Results from studies on the fitness of the stem borer population collected at the latter site showed that larvae survived on Bt maize and field-collected larvae were reared without problems for four generations

on Bt maize plants in the laboratory. This study also indicated that larvae collected from non-Bt maize refugia, adjacent to maize fields, survived until the moth stage on Bt maize. This indicates that the high dose/refuge strategy (see below) may be compromised in effectiveness in this geographical area.

Follow-up surveys conducted between 2010 and 2011 showed that resistant pest populations occurred in many areas within the maize production region of the country (Kruger *et al*., 2012). Based on the incidence of farmers that spray insecticides for borer control on Bt maize, it can be concluded that *B. fusca* resistance to Bt maize (MON810) is widespread in the country. The study by Kruger *et al*. (2012) showed irresponsible management of GM crop technology by the maize industry.

5. Insect resistance management (IRM)

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*., 2008a). 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; Tabashnik *et al*., 2008b) and *Spodoptera frugiperda* (Lepidoptera: Noctuidae) in Puerto Rico (Matten *et al*., 2008). Pink bollworm *Pectinophora gossypiella* (Lepidoptera: Gelechiidae) resistance to Bt cotton has also recently been reported from India and *Diabrotica virgifera virgifera* (Coleoptera: Chrysomelidae) resistance to Bt maize in the USA (Gassmann *et al.*, 2011). Except for the case of MON810-resistance of *Spodoptera frugiperda* (Lepidoptera: Noctuidae) in Puerto Rico, poor refuge compliance was put forward as the major reason for resistance development in two of the three lepidopteran and one coleopteran species that have developed resistance to Bt crops.

6. Refugia

The importance of refugia in the delay of resistance development has been pointed out by several studies. Refuges are defined as habitats in which the target pest is not under selection pressure due to the toxin and it therefore provides 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 to one another. The principle underlying this strategy is that any resistant insects emerging from Bt crops are more likely to mate with the 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.

7. How did resistance develop so quickly in South Africa?

An effective high dose/refuge strategy requires three main components. Firstly, the increase in fitness conferred by resistance alleles must be recessive. Secondly, resistance alleles must be rare so that few homozygotes survive on the Bt crops. Thirdly, one of the assumptions of the strategy is that resistant insects selected on Bt crops mate randomly, or preferentially, with susceptible insects preserved on non-Bt crops (Bourguet, 2004).

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, 2012). Furthermore, Van Rensburg and Van Rensburg (1987) indicated that rainfall and humidity are important environmental factors affecting the abundance of *B*. *fusca* moths. Moths possibly give preference to 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*. (2008) 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 result in strong selection pressure for evolution of resistance.

The increased levels 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, 2012). However, in retrospect it appears that the Bt-events currently available for control of *B. fusca* do not meet the high dosage requirement (Tabashnik *et al*., 2009). Pest resistance to Bt maize most likely resulted from a combination of late planting dates with consequent increased levels of infestation and variance in time of planting providing a continued supply of moths. Increased pest pressure combined with non-compliance with refuge requirements probably contributed to selection pressure that resulted in increased levels of pest tolerance to the Cry 1Ab toxin.

8. Lessons learned

Poor monitoring (and reporting?) of compliance to refugia requirement was shown to have played an important role in resistance development. Rapid adoption of Bt-technology, up to a level of nearly 100% over a short period of nine years, probably created an environment in which farmers and seed companies did not foresee or realise the absence of refugia and the problem this was creating. A lesson that could be learned from this is that in areas were Bt-technology adoption rate is very high, refuge compliance should be followed up on and enforced.

No information exists on the levels of protein expression in Bt maize hybrids in South Africa. Low-dose expression of Cry1Ab protein can contribute significantly

to resistance development and the role that it could have played in this case should not be underestimated.

Apart from increased refuge compliance monitoring, no other actions relating to insect resistance management were taken in South Africa. Continued selection pressure could therefore have contributed to the evolution of a pest population that could also rapidly evolve resistance to new Bt maize events.

The stacked event, MON89034, which expresses two different cry proteins, Cry1A.105 and Cry2Ab, was commercially released in South Africa during 2011 and large-scale planting is expected from the 2012/13 growing season onwards. Only time will tell whether the continued planting of Cry1Ab-expressing maize after the first reports of resistance six years ago, will have an effect on the sustainability of the newly released stacked event in the country.

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Influence of the Fast Spread of Bt Cotton on Organic Cotton Production: Examples from India and Burkina Faso

Matthias Klaiss[1], Monika Messmer[1]*, Dionys Forster[1], Rajeev Verma[2], Rajeev Baruah[2], Vivek Rawal[2], Lokendra Singh Mandloi[2], Yogendra Shrivas[2]*

[1] Research Institute of Organic Agriculture, Ackerstrasse, CH-5070 Frick, Switzerland, Matthias.Klaiss@fibl.org, Monika.Messmer@fibl.org

[2] bioRe India, Kasrawad, Madhya Pradesh, India

* Corresponding authors

1. Introduction

COTTON is grown in more than 120 countries by over 20 million cotton producers on 35 million ha in 2012 (Truscott, 2010, www.fas.usda.gov).

In 2011, around 27 million tons of cotton were produced, mostly by smallholder producers in 'developing' countries which cultivate cotton as a cash crop on their own land averaging under 2 ha in size, or as contracted workers for bigger land owners. Cotton is usually grown as a monoculture. In industrialised countries, the level of mechanisation is high, thus cotton production does not provide a lot of work in rural communities. In contrast, in developing countries, the cultivation and harvest is mostly done by hand labour and thus provides a lot of work for the rural population. Cotton, particularly as a monoculture, uses significant amounts of pesticides, fertilisers, fossil fuels and water (Truscott, 2010).

There are four commercially exploited cotton species: *Gossypium hirsutum* and *G. barbadense*, the 'New World Species', and *G. arboreum* and *G. herbaceum*, the Old World Species. Though Old World cottons are still grown in some areas of Africa and Asia, they have been almost totally replaced by New World cottons. Most dominant today are *G. hirsutum* cultivars, which are spread across 45 countries. About 90% of the annual global cotton harvest is derived from *G. hirsutum*. One negative outcome of the wide cultivation of *G. hirsutum* cultivars is the increased pest attacks, particularly by the American bollworm. Hence, cotton cultivation had a very bad reputation as the single largest user of pesticides in the world (Truscott, 2010).

In the mid-1990s, conventional cotton production posed a serious threat to the environment, farmers' health and the economy. At one stage cotton accounted for the use of 15% of the world's pesticides and 25% of the world's insecticides.

This resulted in two major responses. One response was the development of genetically modified (GM) insect-resistant cotton cultivars, which were rapidly adopted by many countries since its first commercial introduction in 1996. Approximately 82% of the world's cotton-growing area was grown under genetically modified cotton in 2011 (www.isaaa.org2).

The other response was the adoption of organic methods of cotton production by farmers who believed that holistic, earth-friendly responses, optimised crop rotation and organic fertiliser could reverse the trend of the soaring use of chemical pesticides.

The rapid spread of GM seeds in cotton has resulted in problems for the organic cotton sector, a few of which can be briefly examined, taking India and Burkina Faso as examples (Truscott, 2010).

2. Organic cotton

The production of organic cotton is more knowledge intensive than resource intensive, thus less dependent on fossil fuels and synthetic inputs. Organic farmers rely on understanding the ecology of their farm in building up and maintaining an agro-ecological balance of the complex farm system, increasing soil fertility, micro and macro fauna etc. This investment in the ecology of the farm system in turn contributes to the efficiency – and quality – of crop production.

Organic agriculture is proven to be highly suitable for small-scale farming in developing countries (Truscott, 2010, IAASTD, 2008).

Organic cotton has experienced years of unprecedented growth. In 2005 only 0.1% of global cotton production was organic, in 2010 it was already 1.1%, which is an increase of 1100% in five years (Truscott, 2010). By 2010, organic cotton was grown in 23 countries. The top five organic cotton-producing countries were India, Syria, Turkey, China, and USA (Texas). Countries in West Africa, Latin America and the Middle East are also well-established organic cotton producers. Some organic cotton producers are also certified according to fairtrade standards; particularly in West Africa and Central-South East Asia (Truscott, 2010). More than 94% of organic cotton was produced by India, Syria and Turkey alone in 2010 (Textile Exchange 2012). Neither recession nor unstable economies have put a damper on the growth of the organic textiles industry which grew 20% to an estimated $5.16 billion in 2010 (www.naturalnews.com). Several brands and retailers more than doubled their usage of organic cotton alone and plan to do so in 2012 as well. Others with large programmes are staying the course. As a result, Textile Exchange projects the global organic cotton market will increase another 20% to result in an estimated $7.4 billion market in 2012 (Textile Exchange, 2011a). According to a very optimistic market analysis, the world market for organic cotton is projected to exceed $19.8 billion by the year 2015, mainly driven by growing

awareness and interest for eco-friendly products among consumers (www.strategyr.com).

However, despite all this breath-taking developments, organic cotton production dropped by 37% in 2011 (Textile Exchange, 2012). This was especially true for India.

One of the main reasons for the sharp decline of organic cotton production may be the rapid expansion of GM cotton in cotton-producing countries. This dominance leads to the decline of diversity and neglect of local/native species of cotton. Organic cotton producers face new challenges as in some areas the availability of appropriate non-GM cotton seed has become increasingly limited. Moreover, the quality of such seeds is often dubious. To overcome this problem, the role of local, native or specially bred cultivars should be recognised. Local varieties, especially locally adapted species, play an important role for conservation of a broad range of biodiversity of the cotton gene pool.

Increasingly, the governments leave the seed sector to private companies and corporations. A considerable amount of resources are spent on R&D of GM seed development, hence, there is little interest and little funding and priority on improving non-GM seed. This leads to a dependency on a small number of patented brands/company monopolies.

GM cotton is found in at least ten cotton-growing countries now – and tested in others. The lobby promoting GM (supported by multinational agrichemical suppliers) is very powerful (Truscott, 2010). Organic production does not permit the use of GMO (www.ifoam.org). Contamination issues are a severe threat to organic production: if organic cotton is contaminated by GM, organic certification is lost. Due to patents on GM crops, traditional seed exchange cannot be practised anymore, even among conventional farmers. Moreover, there is evidence now of secondary pest attack problems and pests exhibiting resistance to Bt cotton (TE Cotton Briefing 2011).

3. West Africa

Most West African countries have ratified the Cartagena Protocol on Biosafety; however, only Burkina Faso, Mali, Ghana and Nigeria have functioning legislation allowing field trials of GM products. Bt cowpea is expected to be introduced shortly in West Africa, which is the most important food crop in dry regions (www.aatf-africa.org). In Mali, authorities are allowed to approve applications for trials. There are no applications for trials to test GM crops yet, but they are likely to adopt Bt cowpea (www.nepadbiosafety.net[1]).

In Mozambique, the biosafety bill is in progress, an application for trials is expected. Senegal has no functioning biosafety framework yet. Benin renewed in 2008 the five-year moratorium set up first in 2002 and will again discuss and decide on the matter in 2013 (www.arkansasonline.com).

Ghana has a functioning biosafety framework that allows trials (www.nepadbiosafety.net[2]).

4. Burkina Faso

In Burkina Faso, cotton is cultivated on a total of 424,810 hectares (ISAAA, 2012). Cotton farmers represented almost 1/6 of all rural households in Burkina Faso in 2006, being the largest employment group in the country. Thirty-five per cent of GDP comes from the cotton sector, and about 18% of the people live from cotton growing (www.cotton-made-in-africa.com).

Cotton is generally produced by smallholder farmers with household labour. The former governmental company was split into three private companies working in assigned zones: SOFITEX, SOCOMA and Faso Coton. Hence, there is a high market concentration. SOFITEX, being the former governmental company, still acts as a gatekeeper and dominates the sector. These companies also define the cotton cultivar(s) that have to be grown in their specific zone.

The average area dedicated to cotton production is 45% of the total land available for a farm. Rural incomes are largely shaped by the seasonal cotton yield and market price.

Conventional cotton growing relies heavily on costly agro-chemical inputs that leave producers indebted to the cotton companies, encourages ecologically questionable farming practices, and promotes a strong bias in favour of male cotton producers through extension services and access to credit (Coulter, 2011).

4.1 Bt cotton in Burkina Faso

In 2000, a joint collaboration between Burkina Faso's national cotton companies and Monsanto started. Burkina Faso signed the Cartagena Protocol on Biosafety and put in place the regulatory process after GM cotton had been (illegally) tested in the country. NGOs have played a major role in ensuring that national legal frameworks for GM crops admission are implemented (Kone and Lanting 2011).

Starting in 2003, official experiments with American GM cotton cultivars (DP50 and Cooker) were conducted under controlled conditions in research centres. In 2006, the Bollgard II event containing the stacked Cry2Ab and Cry1Ac genes was transferred into local varieties. Monsanto assisted the introgression of these Bt genes into the two regional cotton varieties – STAM 59 and STAM 103 – that were widely grown by conventional cotton farmers (Vitale, 2010).

In 2007, field trials were conducted to test these GM cotton varieties with 20 participating farmers on 20 ha under controlled conditions. The 2006 biosafety law was reviewed in 2008 and a contract was signed with Monsanto. In 2008, an area of 8,500 ha was planted with Bt cotton. Finally, in 2009, the first local cotton varieties containing Bollgard II were commercially released. This was the result of

several years of coordinated efforts on behalf of various Burkina Faso cotton stakeholders. A large portion of the resources required for the testing and commercialisation process was provided by Monsanto.

In 2009, 125,000 ha of these local Bt cotton varieties were grown. In the 2009/2010 season, Bt cotton was grown on 128,563 hectares (Vitale 2010). In 2011, Bt cotton area doubled to 247,000 hectares or 58% of the total cotton area (www.isaaa.org[1]), making Burkina Faso the second largest producer of GM cotton in Africa behind South Africa.

In Burkina Faso, Monsanto owns the events that have been introduced into commercial Bt cotton seeds, which entitles it to up to 28% royalties. The current model of seed sales in Burkina Faso gives about 60% profit to the seed farmers, 28% to Monsanto, and 12% to research (Kone and Lanting, 2011) .

4.2 Situation arising from spread of Bt cotton for non-GM cotton farmers

The rapid large-scale introduction of Bt cotton caused several disturbances. Due to price struggles with the companies, farmers decided to boycott cotton production. This matter led the main cotton company to use subtle influence on farmers, which caused even riots and deaths.

With the increase in Bt cotton production in Burkina Faso, isolation zones between GM cotton and non-GM cotton fields were often neglected, which is against recommended practice and leads to genetic contamination of non-GM cotton. However, leaving a 100m distance in a smallholder context is difficult. There are now problems with contamination of non-Bt fibre due to improper handling during sales and transport. There is an emerging competition for availability of land for organic or conventional cotton and Bt cotton (Ngang in DDS, 2012).

Four years after the introduction of GM cotton, there were reports that farmers were switching back to conventional, or non-GM seed. Many farmers in Burkina Faso experienced shorter fibre length which resulted in lower cotton prices than before. The GM cotton was introduced in the area with the promise of 30% higher yields, reduced pesticide use, and higher net income overall. After several years, none of these promises have been realised. Crop yields even dropped in some cases (www.organiccotton.org). The ‘rumours’, that Burkina Faso farmers would abandon GM cotton, were immediately denied and the success of GM cotton underlined by SOFITEX (www.lobservateur.bf).

4.3 Organic cotton in Burkina Faso

In 2011, Burkina Faso produced 252 metric tons of organic cotton, 0.17% of world organic cotton production and was ranked 13th in the world organic cotton producers list. Compared to the previous year, there was a decrease of 15% (Truscott, 2010). The organic programmes in Burkina Faso have been in place since 2004 and operate under the direction of Helvetas, a Swiss non-governmental organisation (NGO). Despite the high level of interest of rural producers in organic cotton

production and the support of an NGO, there is a discrepancy between the ability to start such production and the demand of growers for market entry. Organic cotton programmes operate under the auspices of the cotton company that controls the particular zone, and it is dependent on the goodwill of each cotton company. The three companies derive their profits from conventional and GM cotton. Thus, their support for the lower-yielding organic cotton is limited. Additionally, the recent introduction of GM cotton further endangers the feasibility of organic cotton production. Organic farmers are concerned about contamination of their fields with Bt cotton, whereas cotton companies strive to expand the more profitable conventional and Bt cotton. There is huge pressure on organic farmers, as GM-contaminated cotton fibre obtains no organic premium price. Thus, their investments and efforts are at risk. These developments limit the interest of smallholder producers and thus the expansion of organic cotton production (Coulter, 2011). As the recruiting of new farmers became very difficult, the priority is now to retain farmers who invested in organic. In 2010, the number of farmers dropped to almost one-third of the amount of farmers participating in the programme the year before, which was around 7,000. An explanation for this drop could be the stringent measures that farmers are required to take to minimise contamination.

Organic cotton can be contaminated in many ways. Organic cotton seed can be mixed with GM or conventional seed before planting. Cross-pollination is possible between neighbouring fields of GM or conventional and organic cotton. Contamination can occur through mixing (whether unintentional or intentional) during storage, transport or processing. Even under laboratory conditions, it is difficult to prevent contamination of pure varieties (farmhub.textileexchange.org). Measures taken by organic producers to prevent GM contamination would be to keep a 100m distance between organic and GM cotton fields, which is difficult in a smallholder context and might be not enough to prevent cross pollination (Pierre et al. 2010). The cultivation of GM cotton, which is usually grown by men, and organic cotton, which is grown by women, on the same farm was banned. This led to exclusion of women.

5. India

India is the only country to produce and market all of the four commercial cotton species (Nemes, 2010). In 2010, 80% of global organic cotton production was grown in India, which was 195,412 metric tons (Textile Exchange, 2012).

In 2011/12, total cotton production area in India was 12,178 million ha. Total production of cotton was approximately six million tons of cotton, mostly of *G. hirsutum* (calculation based on figures from cotcorp.gov.in/national-cotton.aspx).

The history of cotton cultivation in India can be traced back thousands of years. At the time of India's independence in 1947, 97% of the cotton grown were the so-called Desi-cotton varieties, *G. arboreum* and *G. herbaceum*, which were

adapted to local conditions after centuries of development and cultivation. Only 3% was *G. hirsutum*, which was introduced by the British at the end of the 18th century to cater for their spinning mills. The American cotton species *G. hirsutum* has longer and stronger fibres than the Desi cotton, but requires more fertiliser and is highly susceptible to drought, water logging, diseases and insect pests. By 1965, after Indian scientists intensified efforts to breed American cotton for Indian conditions, *G. hirsutum* was grown in 40% of the total area under cotton cultivation. The remaining area was under Desi varieties. By 2002, when Bt cotton was introduced, Desi cotton acreage was further reduced to 25%. At the moment, the area under Desi cotton is estimated at 3% in the country (www.financialexpress.com).

India's seed industry was dominated by public-sector seed companies until the end of the 1980s. After India's decision to embrace biotechnology, the seed sector was deregulated and in 1988 a New Seed Policy was implemented. This development, as a means of achieving food security, has attracted several leading biotechnology-focused multinational seed companies to India. Nowadays, 60% of the turnover in the seed sector is made by private companies (Sangar et al., 2010). In 1970 the Gujarat Agricultural University in Surat released the world's first intra-specific (*G. hirsutum x G. hirsutum*) hybrid (H-4) and in subsequent years further intra- as well as inter-specific (*G. hirsutum x G. barbadense*) hybrids were released (CICR 2010).

5.1 Bt cotton in India

In 2002, Mahyco (MAharashtra HYbrid Seed COmpany) in collaboration with Monsanto was the first to receive approval for three Bt cotton hybrids for commercial cultivation in the Central and Southern cotton-growing zones in India. Around 54,000 farmers in India grew these Bt cotton hybrids on 50,000 hectares of land in 2002 (Choudhari and Gaur, 2010, www.isaaa.org[3]).

India ratified the Cartagena Protocol on Biosafety in 2003 (www.siliconindia.com). In 2003/04 Monsanto sublicensed the Bollgard gene to other companies. India's 3rd Amendment to its Patent Act in 2005 has allowed patents for GM seeds, and created a situation where the importance and dominance of the public sector and state seed supplies has diminished. This has paved the way for the private sector to take more control of seed supply (Truscott, 2010). Until 2005, Mahyco-Monsanto Biotech (MMB) dominated the market for cotton hybrids, either directly through selling hybrid seeds or indirectly through sub-licensing the Bollgard events to private seed companies. India's regulatory system gave them a temporary monopoly on the Bt gene. Companies that licensed Bt had to pay a fee, leading to an increase in seed prices (Arora and Bansal, 2012). In 2006, the Indian government adopted a case-by-case method of approval, and shifted later to event-based approvals. Bt cotton hybrids are the principal commercial crops planted, increasing from three Bt cotton hybrids in 2002-03 to 884 Bt cotton hybrids in 2011/12 (www.isaaa.org3). By 2009 the area under GM cotton increased 168 fold to 8.4

million hectares. The Indian seed market suffered proliferation (Ramaswami et al. 2009). In 2010, already 780 Bt cotton hybrids were on the market in India. Six events were approved by government (Choudhari and Gaur, 2010). By 2011, seven million farmers had adopted Bt cotton on 26 million acres, around 90% of the total Indian cotton area (James, 2011, in Kathage and Qaim, 2012).

The march of time and commercially-prioritised technology poses a threat to agricultural traditions of centuries, and ironically in an era of the patent regime, makes seed-saving a criminal act punishable under intellectual property (IP) law. So far in India only Bt cotton has been approved, while the release of Bt eggplant and other food crops has been turned down.

5.2 Organic cotton in India

For the first time in years, the global organic cotton production declined by 37%. India, which produced 80% of world organic cotton in 2010, experienced the greatest reduction, 48% less in 2011 compared to 2010 (Textile Exchange 2012a). Four reasons were found to have the most severe impact. To prevent fraud and control contamination, India mandatorily implemented the comprehensive quality control system Tracenet by APEDA (the Agricultural Produce Export Development Authority). The additional cost caused by this system has to be borne by the organic sector. There is an environment of continued economic uncertainty, which keeps commodity prices down and endangers farmers' stability. There has also been a shift by some companies from established programmes such as organic and fair trade to newer initiatives like Better Cotton Initiative with less strict regulations (allowing the use of GM cotton as well as pesticides) offering a lower barrier to entry.

Due to the ubiquitous presence of GM cotton, it has become increasingly difficult to produce organic cotton. There is a severe shortage in the availability of non-GM cotton seed, and even this seed is often contaminated with GM cotton. The ways of contamination are numerous (see Blake, 2010) and force organic cotton producers to take measures which cause a lot of additional cost and effort (Textile Exchange 2012a). On the other hand, farmers have lost their traditional knowledge on seed production. Hybrid seeds have to be purchased each season and therefore organic cotton farmers depend today on a diminishing supply market of non-GM cotton seed (Stone, 2007).

Recent experience has been that available non-GM seed is of doubtful quality (expired, chemically pre-treated, segregating) and based on only a few hybrids selected for responsiveness to fertiliser and chemical pest control that might not be adapted to rain-fed and low-input conditions (Felkl et al. 2010). While new cultivars are tested routinely under conventional growing conditions (Surulivelu 2011 and Rathore et al., 2011), no systematic cultivar trials were conducted for organic and low-input farming. Moreover, there is a big risk of physical and genetic

contamination of organic cotton with GM cotton and the loss of locally adapted genetic resources. It has become very difficult to produce and maintain non-GM seed. A lot of cultivars are already contaminated (Patil in Forster et al., 2011).

6. The Dharwad Declaration

Stakeholders of the organic movement are highly concerned about this development in the cotton sector in India. Organic farming can only present a viable alternative to conventional production if farmers have access to suitable cultivars. A national workshop on 'Disappearing non-GM cotton – ways forward to maintain diversity, increase availability, and ensure quality of non-GM cotton seed' (Forster et al., 2011) initiated by bioRe India (Ltd.), the Research Institute of Organic Agriculture (FiBL Switzerland) and the University of Agricultural Sciences (UAS) Dharwad presented the first agreement, the 'Dharwad Declaration' (www.fibl.org) towards safeguarding the heritage of Indian Desi cotton, maintaining genetic diversity, avoiding GM contamination as well as supporting the organic farmers with suitable cultivars.

7. Outlook: The Green Cotton project

FiBL, together with bioRe and the University of Dharwad, took immediate action and started with preparations for a participatory breeding project in 2011. Participatory plant breeding is a proven method to develop locally adapted cultivars and to maintain and to increase genetic diversity (Nkongolo et al. 2008; Djaboutou et al., 2007; Lancon et al., 2004).

The short-term aim of the project is to provide organic cotton farmers with high-quality seeds. In the mid term, new cultivars need to be developed that fit the needs of organic cotton farmers and processors. Seed sovereignty and autarky of smallholder cotton farmers should be improved by capacity building and establishing decentralised participatory breeding initiatives. Farmers' experience and breeders' knowledge is combined to develop cotton cultivars adapted to the local conditions of organic cotton farmers. To achieve this goal the following objectives were defined:

(i) Networking with all stakeholders in the organic cotton value chain to achieve coordinated cooperation.
(ii) Collection and conservation of genetic resources.
(iii) Testing of existing cultivars under organic conditions.
(iv) Training farmers in seed multiplication, crossing and selection.
(v) Establishing participatory cotton breeding programmes.
(vi) Re-establishing the non-GM seed chain.

Currently, the following activities are taking place:

Fifty different non-GM cultivars provided by the UAS Dharwad are being tested in 2012 under optimum and water stress conditions with low-input organic management. Different cultivar types (*G. hirsutum* vs. *G. arboreum* (Desi cotton) species, hybrids vs. varietal lines) are being tested assessing yield, resistance traits, and fibre quality according to the market demand. In addition, the optimal planting density for the different cultivar types is being tested. Workshops are conducted with farmers to teach them on cultivar testing, crossing techniques, selection of segregating material and cultivars and seed propagation. In these workshops, the farmers' knowledge is assessed to define the most important traits and ideal cotton genotype under different growing conditions. Farmers manage on-farm cultivar tests in different soil types with and without irrigation. Currently, a socio-economic evaluation of different models for the establishment of a seed supply chain for non-GM cotton in India is being carried out. For the future, it is foreseen to build up further participatory breeding programmes in various cotton-growing regions and countries (Tanzania, Uganda, Benin, Mali, Burkina Faso) by South-South transfer relying on our international networks (Messmer et al., 2011; Roner, 2012; Roner et al., 2012).

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Interrogating the Science of Safety: Unknown Aspects of Bt Toxin that Continue to Pose a Threat to the Health of Domestic Animals in India

Sagari R Ramdas
ANTHRA

1. Introduction

SINCE 2005, shepherds and farmers from different parts of India - particularly from the states of Andhra Pradesh, Haryana, Karnataka and Maharashtra have reported that their animals (cattle, buffaloes, sheep and goat) that have grazed on genetically modified cotton or have been fed genetically modified cotton seeds or cotton seed cake have fallen sick and in some instances have died. Despite several reports and representations to concerned regulatory and research institutions at both national and state levels, alerting them to the seriousness of the issue, there has been a persistent reluctance amongst the scientific establishment to respond, investigate and research into the problem. On the contrary, the reaction of the establishment has been bureaucratic, dismissive of the field and clinical observation of shepherds whose animals suffered, and of non-government veterinary scientists who have been tracking the problem, describing these as being 'unscientific', 'exaggerated and blown out of proportion', and not based on sufficient research and hard facts.

The Indian regulatory authorities such as the Genetic Engineering Approval Committee (GEAC) and top Indian research universities have regrettably exhibited incapacity to rigorously investigate the problems experienced and observed by farmers and shepherds, and instead consistently argue that because all safety tests in the 'pre-commercialisation' stage provided beyond doubt proof of safety of the technology, the GM toxin simply could not be the cause of morbidity and mortality. To date not one public research institution has undertaken to systematically investigate the problem at the farmers' field.

In this paper, we critically highlight the numerous unanswered questions with respect to the effects of the Bt toxin on animals, which continue to be unaddressed. We discuss the absence of scientific rigour by regulatory authorities, in particular their circular arguments of safety, being cited as 'evidence' that animal deaths were not caused by Bt toxin. The evidence of safety would not stand any kind of international scientific scrutiny based as it is on incomplete testing/investigation protocols, compounded by admissions by top Indian research institutions of the

absence of facilities to test for the effects of the toxin on animals, and citing company data on toxin-safety levels. The paper concludes arguing for the critical need for comprehensive risk-assessment and biosafety protocols, which are completely absent today from the required portfolios for GMO testing.

2. The case of Bt cotton and animals in India: Warangal district, Andhra Pradesh, India

Grazing on harvested crop residues that remain on the fields is a regular and common practice of livestock owners in villages across the length and breadth of India, including in Warangal district, AP. Cotton cultivation in Warangal district was minimal in the 1960s, and gradually increased in area, peaking in the mid-1990s replacing the dryland food crops which predominated the region. Livestock owners had no option but to graze their animals on harvested cotton fields, which began to dominate the landscape. They continued to do so for nearly 12 years, prior to the entry of Bt cotton. Not once did farmers or shepherds experience morbidity or mortality in their animals due to the effects of their animals grazing on cotton fields. Bt cotton was commercially released in Andhra Pradesh in March 2002, after the Government of India granted permission to Mahyco-Monsanto, to market its Bt cotton variety in South India. In the Kharif season of 2002 the company released two Bt cotton hybrids MECH Bt 12 and MECH Bt-162. It was sown in approximately 9,500 acres in Andhra Pradesh, which stands third in cotton cultivation in the country, with an area of 887,000 ha under cotton. In Warangal district of Andhra Pradesh, approximately 1,200 farmers planted Bt cotton over 1,500 acres in Kharif 2002-03.

The first reports of morbidity/mortality in animals after grazing on Bt cotton, occurred in January 2005, which coincided with the third year (2004-05) of Bt cotton in Warangal district. Between 2005 and 2009 Anthra[37] has been closely investigating reported morbidity and mortality observed in sheep and goat flocks, in selected regions in the state, where shepherds specifically contacted the organisation and in turn the organisation was able to respond through fact-finding teams to collect retrospective information, as well as on-site clinical observations. The detailing is not a comprehensive summary of events/reports from the entire state (Table 1, Table 2).

During the first three years of investigation, symptoms reported by shepherds were confounded by the concurrent incidence of other common contagious diseases that affect small ruminants, such as peste-du petits ruminants (PPR) and blue tongue.

[37] Anthra is an organisation led by women veterinary scientists, works on issues related to livestock, people's livelihoods and the environment and has been researching the impact of Bt cotton on animals in different parts of India.

By 2008-09 the symptoms could be isolated, due to the in-situ presence of Anthra's veterinary scientists who continuously monitored the village flocks, which we ensured were vaccinated/protected against all other possible preventable contagious diseases, and thus we were able to narrow down and be precise about the specific morbidity and mortality patterns exhibited by animals that grazed on harvested Bt cotton. Our clinical findings were:

a) Morbidity *selectively* manifests itself symptomatically in animals by the 3rd or 4th day of consuming Bt cotton foliage/bolls and seeds as *nasal discharge, cough, respiratory distress*, *occasional bloody urine and the absence of fever.*
b) Mortality occurs in some animals, especially if untreated, but not in all.
c) Mortality and morbidity are observed to occur in those animals that have had a cumulative exposure to the Bt toxin – in the form of grazing/being fed the cottonseeds/cottonseed cake, over a number of years.

In Haryana, there was a strong correlation between feeding Bt cotton seeds and cotton seed cake to milch animals, and drop in milk yield and several reproductive disorders such as prolapse of uterus, premature birth of calves, increase in the incidence of abortions and decrease in conception rate.

3. Investigating the problem: the response by the research institutes and government departments and the absence of standardised protocols of testing

In 2006 and 2007, shepherds directly approached the local government veterinary doctors in government veterinary hospitals appealing to them to treat their animals, and also to advise them on what to do. In both years, the government veterinarians treated the sick animals with a combination of drugs that are typically used to treat cases of toxicity (Ramdas, 2009). The local veterinary doctors after noting the history of feeding reportedly asked the shepherds to stop grazing their sheep on the harvested Bt cotton fields. The sheep were treated with a combination of drugs (Atropine, Dexamethasone, Pregneselone) which are commonly used to treat cases of toxicity. The government veterinarians carried out post-mortems on the dead sheep and sent them to different government laboratories. In 2006 the samples were tested in state and national laboratories, and in 2007 samples were tested in state laboratories.

By 2008 and 2009, veterinary scientists from Anthra were located directly with communities in select villages, and carried out post-mortems of dead sheep and goats that had died after grazing on Bt cotton, and sent tissue samples to top research institutions of the country such as the Indian Veterinary Research Institute (IVRI), with a specific request that these be tested for Bt toxin. In 2008, the IVRI reported their *inability to test for Bt toxin*. The IVRI in 2008 and 2009 recorded

Table 1: 2005-2008: Shepherds' observations on morbidity/mortality in flocks grazed on harvested Bt cotton fields

	2005 **Jan**	**2006** **Jan-Mar**	**2007** **Jan-Feb**	**2008** **Jan-Mar**	**2009** **Dec-Jan**
Location	1 district 3 villages 1 Mandal	1 district 4 villages 3 Mandals	2 districts Warangal-3 Mandals Adilabad-6 Mandals	2 districts Warangal - 2 Man Medak -1 Man	Warangal 1 Mandal 1 Panchayat
History	Bt l	Grazed for 2-4 days on Bt l	Grazed for 3-4 days Bt 1	Grazed for 3-4 days in Warangal BT 1 & 2 Grazed for 3 wks in Medak (1st exposure)	Grazed for 3-4 days on Bt 1 and Bt 2
Species	cattle, goats, sheep	sheep, goats	sheep, goats - Warangal sheep, goats, cattle - Adil	Sheep - Warangal Sheep - Medak	Sheep, goat, cattle
Sympt reported by shepherds	Imprecise information	dullness, cough, nasal discharge, reddish and erosive lesions in the mouth bloat, blackish diarrhoea occasional red coloured urine	**Sheep/Goats/Cattle** difficulty in breathing, nasal discharge, mucopurulent/ blood tinged red coloured urine, bloat Eye/face swelling difficulty in standing occasional diarrhoea Vomiting, convulsion, salivation	Medak - Anorexia Nasal discharge, slight fever. 1 death PM performed Warangal: As above confounded with PPR symptoms	
Vets Clinical observations		NA	As above in S/G - no fever As above in Cattle	As above in Medak Fever, anorexia, mouth lesions, frothing	nasal discharge, cold, cough, respiratory distress (in some cases) Occ. red urine
Vaccines	No details	Not vaccinated against PPR, HS	Not vaccinated against PPR, HS	Medak - HS, PPR, ET	HS, PPR, ET

Table 2: Summary of Morbidity and Mortality in Animals as recorded by Anthra

Year	District	Population	Morbidity	Mortality
2006 (March)	Warangal retrospective	8869 sheep	No information	1825
2007 (February)	Warangal (clinical observations)	350 sheep	40	–
2007 (February)	Warangal (retrospective)	300 sheep		30
2008 (January)	Medak Vaccinated PPR	1000 sheep	3	1
2008 (January)	Warangal Not vaccinated	1000 sheep	40	
2009 (January)	Warangal Vaccinated PPR, HS, SP	7500 sheep 500 goats	31 (21 sheep, 8 goats, 2 cattle)	2 (1 sheep, 1 goat)

histo-pathological lesions in the kidney (chronic nephrosis), liver (chronic hepatitis) and intestinal tissues (chronic enteritis) of the post-mortem sheep/goat, indicative of some kind of 'chronic' factor at play.

In 2006, 2007 and 2008, plant and animal tissue samples were sent for testing, and the results do not lend themselves to drawing any conclusions, as the information of the tests differed (Table 3). Identical samples of plant sent to different laboratories actually yielded completely different and contradictory sets of information[38]. Except for 2008, where Bt toxicity testing was specifically requested and the institution specifically responded stating their inability to test as they lacked facilities. There is no information on whether animal tissues were tested for Bt toxicity in the previous two years.

The chronic nature of the tissue lesions should have alerted scientists within these research institutions, as to what could possibly be causing this chronic effect. It matched with the history of mortality in those animals that had been exposed to the Bt toxin over an extended period of time. The admission of lack of facilities to test, coupled with contradictory information emerging from different laboratories, should have alerted the scientific establishment to the urgency and need to

[38] Letter sent to the GEAC by the Director, Animal Husbandry Department (AHD), Andhra Pradesh, dated May 2007 ref: No 3531/Epid/2006.dated 9/5/2007.

systematically research into the problem observed by the shepherds. It also raises several unanswered questions regarding the testing protocols used:

- Did these laboratories test the post-mortem animal tissue samples?
- What was the entire list of test protocols followed by each of the laboratories for animal tissue and plant tissue alike to arrive at a cause of death?
- If we assume it was the identical plant samples sent to all laboratories what explains the different findings?
- The presence of a mineral (e.g. nitrate/nitrite/organophosphate etc.) in the plant sample is completely insufficient evidence to deduce/derive that this mineral was the cause of animal death.
- Were animal tissue samples tested for Bt toxin or Bt immune response? Going by IVRI's response of 2008, these facilities do not exist at these state and national-level 'disease investigation laboratories', leave aside district-level investigative labs.

One of the test results, which warranted further inquiry, was the report that the Bt toxin found in the plant samples were within 'safe and tolerable levels of Bt toxin' – **'***The Bt protein level detected in the samples of Bt cotton bolls and leaves sent for analysis was recorded as 5*μ*/gm. This level is within the tolerable range which is said to be 5-10*μ*/gm*.'[39]

In a subsequent right to information (RTI) request filed to the Department of Agriculture Biotechnology by Anthra, to obtain the source of this 'tolerable' range, the department responded that this was Mahycos data of safety, accessible on the official IGMORIS website[40]. They also mentioned that the Bt cotton had been well tested, including testing of foliage, which is a blatant piece of misinformation, as the protocols of testing were on cotton seeds/cotton seed cake and not foliage. Hence what we have is the public sector research institutions citing company data as proof of safety, once again exhibiting scientific incompetency in conducting their own research and evolving their own protocols.

From 2006 onwards, Anthra and other civil society organisations submitted their observations, fact-finding reports and concerns regarding the test results to the Genetic Engineering Approval Committee (GEAC), Veterinary Universities and Research Institutions and the Department of Animal Husbandry. In response to repeated submissions by civil society organisations, the Department of Animal Husbandry also sent their letters of concern to the GEAC.

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39 letter roc no: 14627/Epid/2006/, dated 20/9/2006.

40 ABT/ Let No 427 dated 15 Dec 2009

Table 3: Contradictory Results of Testing

Abstract of Tests done: Bt cotton plant samples and animal tissue of animals that died after grazing on Bt cotton (2006-2009) and their implications				
Year	**Institution that conducted tests**	**Plant**	**Institution that conducted tests**	**Animal Tissue**
2006 **State and National**	Andhra Pradesh Forensic Science Laboratory, Red Hills Western Regional Disease Diagnostic Laboratory, Pune Veterinary Biologicals Research Institution (VBRI, AHD, AP) Department of Agriculture Biotechnology, ANGRAU, Hyderabad	+ve organophosphates +ve Nitrates and Nitrites -ve HCN +ve Nitrites +ve HCN Traces of pesticides Bt protein in leaf and boll: 5 ppt 'tolerable range - 5-10 ppt'	Veterinary Biologicals Research Institution (VBRI, AHD, AP)	??? no information Not tested for Bt protein/Bt antibodies
2007 **State**	Veterinary Biologicals Research Institution (VBRI) Animal Husbandry Department, AP	+ve HCN (VBRI) no report of Bt protein content	Veterinary Biologicals Research Institution (VBRI)	rumen content and spleen and lung -ve HCN Not tested for Bt protein/Bt antibodies
2008 **National**	Indian Veterinary Research Institution (IVRI), Izzatnagar. (Bt cotton samples grazed by the dead sheep in Medak district, AP)	Pods: +ve: saponin, -ve: nitrates and alkoloids Plant: -ve: saponin, nitrates, Nitrites, alkaloids Leaves: +ve nitrate/ nitrite -ve: saponins and alkaloids no mention of Bt protein levels	i) Indian Veterinary Research Institution (IVRI) Izzatnagar 1 dead sheep (Medak district, Andhra Pradesh ii) Swab samples collected from 3 sheep in Warangal, AP (VBRI)	All Toxicology tests are negative: -ve: phosphine, nitrate/nitrite, alkaloid, heavy metals, organochlorine/ organophosphate are negative Chronic Hepatitis Lack facilities to test for Bt toxin ii) Tested only for 'Blue tongue' – result is negative No other tests conducted

4. Response by the regulatory authorities and circular arguments of safety provided as evidence/proof of safety

In response to the reports received from civil society organisations regarding mortality in sheep flocks after grazing on Bt cotton fields in Warangal, Andhra Pradesh, the GEAC records in the minutes of its 78th meeting held on 22 June 2007 that the committee deliberated at length and arrived at a *general opinion that the report was highly exaggerated and is based more on hearsay than scientific facts.* The committee cited various feeding studies conducted as evidence and proof of safety. They recommended that the Department of Biotechnology (DBT) sponsor a study to assess the problem at Warangal District with the help of the local Veterinary Hospital in the district. *The Committee also agreed that, in future, leaf toxicity studies need to be included as part of the bio-safety studies.* The Committee further decided to refer the matter to the State Department of Agriculture for a factual report on the allegation made by the NGOs and the findings of the post-mortem report. Exactly six months later on 11 January 2008, the GEAC committee in their 82nd meeting, reversed their decision to have additional animals feeding studies on new events, as taken in the 78th GEAC meeting, citing that they (GEAC) had received foolproof evidence that the death of sheep was due to other causes and not Bt toxin. They state in the minutes that the proof of this was analytical reports that the GEAC received from the IVRI and Department of Animal Husbandry, Andhra Pradesh wherein the latter confirmed that the sheep deaths could not have been due to Bt cotton. The minutes record that a representative of the State Department of Agriculture was present in the sub-committee meeting held on 11 January 2008.

Anthra decided to access this evidence of safety. It first filed an RTI dated 5 February 2008 to the IVRI requesting a copy of their 'Submission of Safety' to the GEAC. The IVRI responded on 25 February 2008, stating '*no studies have been done by them and that the Animal Nutrition Department of IVRI has not submitted any reports to the GEAC'*.

Anthra then filed an RTI to the GEAC dated 5.3.2008, requesting them for the dossier of safety.

Their dossier of safety sent to Anthra by the GEAC consisted of four letters:

a) A letter from the Department of Animal Husbandry, AP to the GEAC[41]
b) A letter from the IVRI to the GEAC
c) A letter from the Sri Venkateshwara Veterinary University (SVVU), AP
d) A letter from a Joint Director (AHD) of a district (Ranga Reddy) in Andhra Pradesh, which never reported any sheep deaths.

[41] Letter Roc. No. 3531/Epid/2006 Dated 9/5/2007

In the first 'proof', the then Director, Department of Animal Husbandry, Andhra Pradesh stated that Bt cotton samples were sent to four different laboratories and (abstracted in Table 3) based on these above reports, concludes that the death of sheep might be due to high content of nitrate/nitrite/HCN/organophophates. The results from each laboratory contradict the other (Table 3). The Bt cotton sample is negative for HCN in results from Western Regional Disease Diagnostic Lab, and positive for HCN in VBRI, Hyderabad. The Bt cotton sample is positive for nitrite in VBRI results, and positive for organophosphate in the AP Forensic Science Lab, Hyderabad, results. Further, the presence or absence of a mineral deposit in a plant sample does not automatically translate into that being the cause of death in the animal.

In addition, *three of the four letters clearly stated the need for further biosafety studies.*

Anthra filed another RTI to IVRI (dated 20 March 2008) requesting IVRI to send us the copy of a 'Bt Cotton feeding study on goats', which they mentioned in their letter to the GEAC, which GEAC produces as the 'evidence of safety'. This resulted in a response from IVRI dated 26 April 2008, sending copies of research protocol and methodology to test for HCN, glyphosate, alkaloids, nitrites and nitrates. They also sent a report of toxicity assessment of feeding Bt cottonseeds to rats; but no studies on goats, which was specifically asked for.

It is critical to note here that there appears to be direct factual conflict between the first and subsequent responses from IVRI. One of these is simply not truthful. Not one of these 'proofs' can even remotely be construed as 'rigorous testing to research the field problem to arrive at a conclusive result'.

The GEAC consistently referred to the 'tolerable' range of Bt protein as evidence that death in the animals was due to nitrate/nitrite/organophosphates/ other diseases. Apart from the fact that the department was citing company data, there was absolutely no logic to this value, which was borne out by another set of 'safe toxic levels', cited by the GEAC-appointed Expert Committee II's report on Bt brinjal. In this report (point 3.1.5), the expert committee describes the level of Bt protein (Cry1Ac protein) found in different parts of the crop to vary between 5 and 47 ppm in shoots and fruits. *For the sake of argument, if we are to go by the earlier submission of all institutions concerned (Agriculture university, cited by Animal Husbandry Department, cited by GEAC) that the reports of Bt toxin (Cry 1 AC protein) are safe and tolerable if they are between 5-10 ppm then it follows that the levels detected in Bt brinjal reported in the biosafety studies and Expert Committee Report are not tolerable, as they are way above the supposed tolerable levels, which are cited as being safe for sheep!*

This raises serious questions on supposed 'tolerable' and safe levels of Bt toxin in plants. Who has decided on this supposed safe level for Bt toxin? What is the scientific evidence for safety? How can there be a safe level of 'toxin' with a food product, when the very definition of a 'toxin' indicates a poison, or something that is harmful?

What is of serious concern is that in the name of evidence-based decisions of safety, we have instead, clear evidence of deception and fraud on the part of all the regulatory bodies in India, and the duplicity of passing of circular arguments of safety as 'fool proof evidence of safety':

a) The absence of protocols to test for proving/disproving the role of Bt toxin, results in the non-testing for the toxin/immune response.
b) The non-testing results in 'non-detection' and a negative result.
c) The negative result of having 'not detected Bt toxin' is passed off as proof of safety.

It is scientifically untenable that without performing any tests, its absence is cited as evidence that the toxin is safe. This circular argument of 'safety' is the basis on which the GEAC claims that reports of animal deaths are 'unsubstantiated', and reversed its decision to carry out further risk assessment tests on goats, as cited earlier.

Regrettably the above 'laboratory reports' are the scientific evidence of 'safety of the toxin for animals' which have been included in the letter of Shri Prithvi Raj Chauhan, the then Minister of State (Independent Charge) for Science & Technology and Earth Science to Dr. Ramadoss, the then Minister for Health & Family Welfare, to instil confidence in the technology and to disprove any risks involved[42].

Subsequent studies on the effects of Bt toxin on sheep were carried out in 2007 by a Veterinary University in Andhra Pradesh, and in 2008 by the Central Sheep and Wool Research Institute. Neither of the studies were designed keeping in mind the field observations of how symptoms were observed in sheep which had been repeatedly exposed to Bt toxin, and moroever were one-time studies. The researchers chose to conclude that no untoward impacts/effects were detected, even though there were some troubling results, which raised several unanswered questions:

The 2007, season-long study by the Sri Venkateshwara Veterinary University found:

i) The presence of higher toxic heavy metals in Bt plants (842.25 ppm of lead in Bt cotton as compared to 134.62 ppm of lead in non-Bt cotton after 45 days), which is 6.25 times higher after 45 days, as compared to the non-Bt cotton[43].

[42] www.indiagminfo.org
[43] Studies on the toxicity of Bt cotton plants incorporated in the feed of small ruminants. Project Report. Sri Venkateshara Veterinary University, Tirupati page 27,Table 18

ii) The liver marker AST, which is known to increase after hepato-cellular injury, as the author of the experiment indicates, increased in the protocol by 37% in Bt-treated sheep in comparison to the untreated group of sheep fed on regular cotton, by the second month[44].

The feeding trial study carried out by CSWRI in 2008 was designed for only a three-month period, with a first-time exposure of animals to Bt toxin. It detected a higher liver weight, testicular weight and fat deposits in sheep fed on Bt diet. These results only served to reinforce the urgent need for more systematic, comprehensive long-term studies on the effects of GMOs on animals.

5. Conclusion

It is evident from the above that there is much to worry about.

The inconclusive nature of Bt toxin in Bt cotton and its impact on animals remains. Is Bt toxin acting as a stress factor that is eliciting in a select fashion, a morbid possible allergenic response in sheep, goats, and other animals, manifested as cold, cough or nasal discharge in animals? Is the intense stress a trigger for *Pasteurella haemolytica*, in some of the animals with resultant death? Is the stress factor Bt toxin? Is it some unknown/new toxin? Is it a new allergenic protein? Is it macro/micro mineral imbalances in the Bt cotton plant (e.g. excess or deficiency of nitrate, nitrite, selinium, etc.) as a result of the Bt protein, which elicits a response from the animal?

There are obvious untruths and a host of contradictions within the 'safety' parameters being presented to us citizens by those who are 'regulating' the technology. There is clearly failure and inability of our existing public research institutions and national regulatory bodies (GEAC), to investigate/test/rigorously examine, prove or disprove these field observations, preferring to dismiss the reports as 'unsubstantiated', 'exaggerated, and unscientific', refusing to conduct a single field-based study and instead placing the onus of 'proof' on shepherds, farmers and civil society groups who have reported the problem. The argument that the latest guidelines do not require the suggested new risk assessments tests and hence have been dispensed with, negates and ignores the field realities where 'non-target organisms' have been affected by the Bt toxin. On the contrary, these unique field experiences and observations urgently invite new and additional specific regulatory and risk assessment protocols.

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[44] Studies on the toxicity of Bt cotton plants incorporated in the feed of small ruminants. Project Report. Sri Venkateshara Veterinary University, Tirupati page 20, Table 20

There is a clear need for new risk assessment and biosafety protocols: chronic and long-term toxicity and allergenic tests and inter-generational studies so as to deepen our understanding on long-term implications for human and animal health to understand the unattended effects which often only come to light after several years of exposure of the organism to the GM technology (in this specific case GM cotton containing Bt toxin). There is a clear need to *put into place a reliable and citizen-accountable regulatory and monitoring mechanism, that will respond to problems when they are experienced, and not ignore/dismiss them.* There is an urgent need that India sets up *independent labs for testing* which are fully functional and certified to international standards. These must be capable of conducting all the required tests, standardised and exhaustive testing protocols. It is important that India *institutes capability/capacity for independent oversight, outside of the regulatory mechanism that is free of both government and bureaucratic/ corporations' involvement*.

Until such time that these can be carried out, it is absolutely necessary that we invoke the precautionary principle and impose a moratorium on all further open-field trials of GM crops, until safety is proved without doubt.

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Technology, Liberalisation and Farmer Suicides in Vidarbha (Maharashtra State, India)

Vijay Jawandhia
Shetkari Sanghatana, India

1. Saved from reaping a deadly harvest

THERE have been several attempts to undermine the irrefutable evidence against GM crops presented by the Parliamentary Standing Committee on Agriculture by labelling it as the work of 'green activists'. This 450-page report was the outcome of a two-and-a-half-year study prepared by 31 MPs from diverse political parties – both ruling and opposition, left and right wing, who normally do not agree with each other! It is therefore a unanimous and landmark refutation of the false propaganda that has been fed to the press, public and policy-makers all these years by the GM seed manufacturers, their sponsored NGOs, PR agencies, and 'farmer leaders'. To say it was prepared by 'green activists' is an insult to their work. The Parliamentary Committee has recorded the public consultations it held, considered thousands of pages of depositions, including those of leading Indian scientists, and cited highly reputed studies such as the International Assessment of Agricultural Science, Technology and Knowledge for Development (IAASTD Report) commissioned by the World Bank, FAO, WHO, GEF and several UN agencies and conducted by 400 outstanding scientists from across the world. The IAASTD Report did not find that GM crops are the answer for global agriculture, poverty and hunger and highlighted that traditional agricultural practices can provide superior yields and incomes than high-input corporate agriculture – of which costly, patented, genetically engineered seeds are a prime example. The Parliamentary Committee not only exposed the falsehoods of the pro-GM propaganda but also rightly castigated the Genetic Engineering Appraisal Committee for regulatory failures that put Indian consumers, farmers, biodiversity and national seed sovereignty at risk. Its recommendations of a cessation of all open-air field trials should be immediately implemented until a new and publicly debated bio-safety regulatory process is in place. Let our Government play its role now to protect Indian citizens and not foreign corporations and their Indian partners.

2. Does GM increase yield?

The propaganda that GM crops are the only way to increase yield is refuted by a number of independent studies e.g. the Union of Concerned Scientists did a 13-year study of GM crop yields aptly entitled 'Failure to Yield'. In India, cotton production has increased because the area under cotton has increased, at the expense of food crops, due to government policies. Cotton yields have increased when irrigation increased as in Gujarat. Initial increases due to bollworm control have been followed by increases in bollworm resistance, and in the increase of secondary pests. The area under Bt cotton has increased because these are now the only seeds that are available in the market. These are not indicators of the success of Bt cotton but indicators of why farmer indebtedness has increased, and why desperate farmers are leaving the failed gamble of Bt cotton for soya in Vidarbha. As a farmer, and honorary worker for farmers' organisations for over 40 years, I can say that yield is a product of many factors – quality of seeds, soil, nutrition, water and climate - and there is no gene which magically increases intrinsic yield. About 99% of GM seeds transfer only two traits – a 'toxin- producing' gene (such as Bt) which leads every cell of the plant to produce an insecticide which cannot ever be washed away, or a 'herbicide-tolerant' gene which enables a crop to withstand a herbicide – usually produced by the same GM seed company! Let us not for a moment think that companies like Monsanto, Cargill, Syngenta, Dow and their Indian licencees have the interest of the Indian farmer at heart. When their seeds fail do they compensate them or point to the small print on the seed packets regarding timely watering, pest epidemics, refugia etc., which can never be ensured by small rain-fed farmers? Hybrid Bt cotton has contributed to GM seed company's profits, but farmers and the nation are dangerously losing self-reliance in seed production. There are over 70 GM crops awaiting clearance – which would be a monumental disaster for Indian consumers and farmers, making no sustainable increase in yield and undoubtedly increasing the national shame of being a global leader in farmer indebtedness and suicides.

3. Is GM the answer for our food requirements?

Are costly, patented, not-reusable GM seeds needed to meet our food requirements? The farmers of our country have proved that they are more than capable of producing enough food to feed our growing population. The overflowing godowns of wheat and rice – which are neither GM nor even hybrid seeds – demonstrate what happens when farmers are given irrigation and price support. As of 1 June 2012 we had over 800 lakh tons of surplus food grain. Yield is not our problem. Our problem is that much of this food grain is eaten by rodents or simply rots, is stolen from centralised godowns by the powerful for profit, while the poor starve. Instead of shifting to a technology that makes highly questionable claims of

providing higher yields, the focus should shift to build food storage and small food-processing facilities at the village level, to improve food distribution and minimise spoilage, loss of produce in transport and theft of centrally procured food grain. We need to ensure better prices to farmers and not to middlemen or foreign retail giants who seek to replace them.

4. Poverty and malnutrition needs a different approach

Those who produce our food cannot afford to buy it, and Dr. M.S. Swaminathan, who chaired the National Farmers Commission, rightly pointed out that the focus of agricultural policy now needs to shift to securing farmer incomes and not to production. GM has benefitted the seed companies, and perhaps a very small number of well-off irrigated farmers and not the 80% of our farmers who are small and marginal and the 65% of our farmlands, which are rain-fed. The members of the Parliamentary Committee indeed visited the famers of Vidarbha and their report correctly and poignantly states that the 'villagers implored upon the Committee to voice their request to the concerned central authorities to ban farming of Hybrid BT Cotton in the country'.

5. All Indians as consumers need safe food

We are asked to put aside our 'baseless fears of GM crops'. On what grounds are these fears 'baseless'? A number of studies are emerging on the detrimental health impacts of GM crops, which give sufficient 'base' to consumer fears. The US population is now demanding labelling based on reports from doctors who have found a number of illnesses linked to GM. Reportedly Monsanto, the leading GM manufacturer, does not supply GM food in its own canteen. Yet Indian consumers are being fed GM cotton seed oil which is mixed into our edible oil, without labelling.

6. Global position on GM crops

GM crops are being produced in only 29 nations across the world, but only six countries account for 95% of all GM crops grown: the USA, Brazil, Argentina, India, Canada and China. Significantly China has now started proceeding with extreme caution and has less area under GM crops compared to India. Many countries have rejected or are strictly regulating genetically modified crops with heavy penalties and strict labelling laws, and one must congratulate our Parliamentary Standing Committee on Agriculture for sounding a timely warning to stall the UPA Government's headlong drive towards GM food in response to corporate-sponsored 'educational visits', research funding and other incentives to our agricultural establishment. If GM is such a successful, farmer-friendly

technology it is pertinent to ask why the US cotton farmers have to be given an annual subsidy of US$4.6 billion, and why our taxpayer's money has to be spent on loan write-offs which have increased astronomically after the arrival of Bt cotton in Vidarbha.

Ecological Agriculture for Food Security and Climate Resilience

Doreen Stabinsky
College of the Atlantic, USA

1. Introduction

AGRICULTURE is the most important sector in many developing countries and is central to the survival of hundreds of millions of people. In most developing countries, agriculture, which provides the bulk of employment, is not a commercial activity per se, but a way of life. Most agricultural production in these countries involves small land holdings, mainly producing for self-consumption. Women are the key agricultural producers and providers. Hence agriculture is critical for food and livelihood security, and for the approximately 500 million smallholder households, totalling 1.5 billion people, living on smallholdings of two hectares of land or less (De Schutter, 2008). Smallholdings account for 85% of the world's farms.

The impacts of climate change will fall disproportionately on developing countries, despite the fact that they contributed least to the causes. Furthermore, the majority of the world's rural poor who live in areas that are resource-poor, highly heterogeneous and risk-prone will be hardest hit by climate change. Smallholder and subsistence farmers, pastoralists and artisanal fisherfolk will suffer complex, localised impacts of climate change and will be disproportionately affected by extreme climate events (Easterling et al., 2007). For these vulnerable groups, even minor changes in climate can have disastrous impacts on their livelihoods (Altieri and Koohafkan, 2008).

2. Ecological agriculture is essential to meet the climate challenge

Climate change will require a range of adaptation approaches across many elements of agricultural production systems, from small changes in the crop varieties grown to decisions to abandon cropping completely. For example, in some rain-fed regions in Africa, there just will not be enough predictable moisture to continue to grow crops; in these areas, agriculturalists may change to livelihood strategies based entirely on pastoralism, or they may need to move to other regions or to

cities. In other areas more animals may be integrated into the farming system to reduce dependency on crop production (Jones and Thornton, 2008).

In all areas, farmers working to adapt to climate change will need to adopt new practices that help to increase the resilience of their cropping systems – through building healthier soils, increasing the biological diversity of the system and, particularly in rain-fed regions (where most poor farmers farm), incorporating more water-harvesting and water management techniques.

3. Building healthy soils

By increasing the health of soils, farmers can increase the water-holding capacity of the soil and the infiltration capacity – augmenting the speed at which water can percolate into soils and thus the ability to take more advantage of heavier rains that are expected under climate change (Tirado and Cotter, 2010). Moreover, by building healthier soils, farmers can increase productivity. Given that climatic changes will likely significantly reduce yields over time, any increase in productivity through better soil health and fertility will serve to moderate the productivity reduction expected.

Many well-established agroecological practices increase soil health and fertility, and with these, productivity. Prominent among these practices is the addition of manure or compost. At the same time that these additions bring necessary nutrients into the system, they also improve the structure of the soil, making it better able to hold onto both nutrients and water. And with an improved soil structure, water is able to infiltrate better and more water is captured during periods of intense rainfall. Evidence from the Tigray region in Ethiopia shows that compost can increase crop yields significantly; on average, composted fields gave higher yields, sometimes double, than those treated with chemical fertilisers (Edwards et al., 2009).

Other ecological agriculture practices that can improve soil structure and increase fertility include growing green manures (crops that are tilled into the soil after they are grown to add nutrients and structure), cover cropping to add nutrients and keep soil covered during a fallow season, mulching and crop rotation (Magdoff, 1998). These are all standard practices in agroecological systems, which work to increase fertility naturally and use the diversity of the system to control pests and diseases, while increasing habitats for pollinators and other beneficial organisms.

4. Building resilience through diversity

System resilience can be built through increasing biological diversity (Altieri and Koohafkan, 2008). Practices that enhance biodiversity allow farms to mimic natural ecological processes, enabling them to better respond to change and reduce risk. Experience suggests that farmers who increase diversity suffer less damage

during adverse weather events, compared to conventional farmers planting monocultures.

In cropping systems, diversity can be increased through increasing the variety of crops grown at one time on the parcel of land, and by adding trees and/or animals into the system. Farmers can also increase the diversity of the system by increasing crop diversity itself, growing different varieties of the same crop that have different attributes, for example, shorter-season varieties that may be beneficial if the season is shortened by inadequate rainfall, or varieties that provide more nutritious forage for animals. Supporting soil health increases the diversity of organisms in the soil, which are responsible for benefits such as increased access to nutrients and reduction of overall disease burden.

It is important to note here the role of women, as they play a key role in managing biodiversity, and thus in adapting to climate change. For example, women in Rwanda produce more than 600 varieties of beans; in Peru, Aguaruna women plant more than 60 varieties of manioc (CBD, 2009).

5. Emphasising water management and harvesting techniques

Adapting to climate change will require even more emphasis than is currently given to improving water management and water harvesting in rain-fed regions. Many traditional techniques already in use to improve rainwater use efficiency can be shared using farmer-to-farmer methods.

For example, the zaï techniques of the Sahel have received much attention: water pits used by farmers in Burkina Faso and Mali to reclaim thousands of hectares of degraded lands in the last decades. Farmers have become increasingly interested in the zaï as they observe that the pits efficiently collect and concentrate runoff water and function with small quantities of manure and compost. The practice of zaï allows farmers to expand their resource base and to increase household security. Yields obtained on fields managed with zaï are consistently higher (ranging from 870 to 1,590 kg/ha) than those obtained on fields without zaï (average 500-800 kg/ha).

6. Increasing productivity in the face of climate change

Given the threats posed by climate change to crop yields, it is important that agriculture practices are able to maintain and even increase productivity. Fortunately, the practices that enhance climate resiliency that are found in ecological agriculture also work to raise productivity, primarily because they improve soil structure and increase fertility.

7. A roadmap towards ecological agriculture through climate resilience

Adaptation of agricultural systems to changing climates is an enormous challenge that will require the concerted effort of governments, researchers and farmers, working together and starting immediately. Because temperatures will continue to rise over the coming decades, we find ourselves in a race against time, to an unknown destination. The effort to create climate-resilient agricultural systems must be prioritised at all levels – from the local to the global, with an important role for national governments to coordinate efforts. Lack of a well-coordinated and well-funded adaptation strategy threatens the lives and livelihoods of millions.

An essential component of climate-resilient agriculture, as explained above, is ecological agriculture. To move on the road to a climate-resilient agriculture, agricultural practices and policies, at the national and international levels, must be systematically and urgently redirected towards ecological agriculture, in order to ensure it can reach its full potential, especially in addressing this enormous challenge.

Farmers, in particular women, who make up the majority of the world's small producers, must play a key role on the road to climate-resilient agricultural systems. To do so, they must be integrated into the research and development systems and given tools to do their own on-farm research and the capacity to share their knowledge with other farmers in farmer-to-farmer networks. The challenges facing agriculture are too great to ignore the important potential of farmers, their knowledge and their innovation skills to contribute to the creation of climate-resilient agriculture.

A roadmap towards climate resiliency contains five essential elements:

- Increasing investment in ecological agriculture;
- Managing climate risks and reducing vulnerability;
- Stopping climate-destructive agriculture by dismantling perverse incentives and subsidies that promote unsustainable and high-emissions agriculture;
- Implementing a research agenda for climate-resilient ecological agriculture;
- Building supportive international policy frameworks.

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Early Warning on Food Safety Issues: How Regulators Got It Wrong on dsRNA

Jack A. Heinemann
Centre for Integrated Research in Biosafety (INBI)
School of Biological Sciences
University of Canterbury, Christchurch, New Zealand

Abstract

CHANGING the nature, kind and quantity of particular regulatory-RNA molecules through genetic engineering can create unique risks. For some GMOs, this outcome is intended but for many others it is not. To characterise, assess and then mitigate potential adverse effects arising from changes to RNA will require a different approach to food and environment risk assessments of GMOs. I will discuss the advice offered to a government regulator during official risk evaluations of GM plants for use as human food, how the regulator dismissed those risks *a priori*, and what that experience teaches us about the risk assessment framework.

1. Introduction

All commercialised GM plants at this time are created through *in vitro* DNA modification. However, not all of them are created with the intention to produce a new protein. A growing minority are designed to change their RNA content (Table 1). The reason for this is the finding that RNA, specifically double-stranded RNA (dsRNA), is an important regulator of gene expression (Appendix 1 of Heinemann, 2009). In the near future, GM products may arise from only *in vitro* RNA modification (Heinemann, 2009).

RNA is an intermediate molecule used in the cellular reactions of translation to synthesise proteins. The most familiar form of RNA is mRNA, the single-stranded messenger. However, it is only in the last 10-15 years that small dsRNA molecules have become known for their role in regulating gene expression (Hutvágner and Simard, 2008).

dsRNAs are variously called siRNA (short-inhibitory RNA), miRNA (microRNA), shRNA (short-hairpin RNA) and so on and are foundation substrates in biochemical pathways that cause RNAi (RNA interference), PTGS (co-suppression, post-transcriptional gene silencing) and TGS (transcriptional gene

Table 1. Various GM crops with intended RNA changes in the food approval pipeline

Product	Status	Ref/Application Code
Flavr Savr Tomato	withdrawn from market	(Sanders and Hiatt, 2005)
High oleic acid soybean lines G94-1, G94-19 and G168[2]	FSANZ[1] approved (2000)	A387
New Leaf and New Leaf Plus Potatoes[3]	FSANZ approved (2001)	A383 and A384
High oleic acid soybean line DP-305423-1	FSANZ approved (2010)	A1018
Herbicide-tolerant, high oleic acid soybean line MON87705	FSANZ approved (2011)	A1049
Golden mosaic virus-resistant pinto bean	Brazil approved (2011)	(Tollefson, 2011)
papaya ringspot virus-resistant papaya	USA (1996), Canada (2003) and Japan (2011)	USDA[4] GMO Compass[5]

[1] Food Standards Australia/New Zealand (FSANZ) http://www.foodstandards.gov.au/consumerinformation/gmfoods/gmcurrentapplication1030.cfm

[2] 'Withdrawn from [FSANZ] Standard 1.5.2 in 2011 because never commercialised.'

[3] The way the virus protein gene used as a transgene causes resistance to the potato viruses (Y and PLRV) was unknown at time of approval. However, it is well known now that gene duplications (which occur when the virus infects the GM plant) cause silencing of both copies of the gene through RNAi.

[4] http://gain.fas.usda.gov/Recent%20GAIN%20Publications/Japan%20approved%20GM%20papaya_Tokyo_Japan_12-19-2011.pdf

[5] http://www.gmo-compass.org/eng/database/plants/59.papaya.html

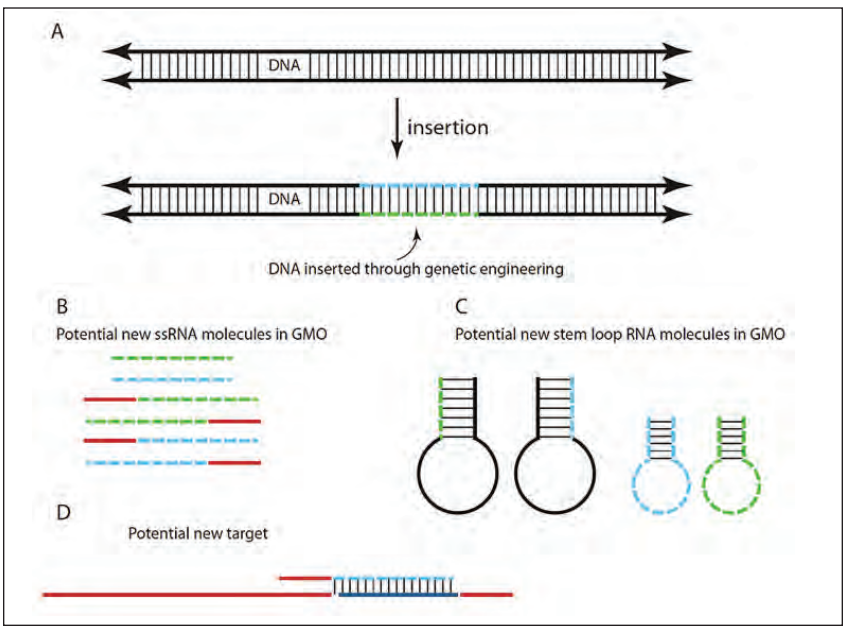
silencing). In short, RNAi, PTGS and TGS are caused by gene silencing: disrupting the connection between genes and the production of the proteins specified by genes[45].

dsRNAs form when both strands of a DNA molecule are transcribed to synthesise complementary RNA molecules (which then bind together in the same way as strands of DNA), or when stretches of intra-molecular complementarity create stem-loop structures (Figure 1). A long dsRNA molecule (e.g., pre-mature miRNA) is processed into a shorter dsRNA (e.g., miRNA) and then one strand is retained – the guide strand – to direct protein complexes to target mRNA molecules and prevent their translation (cytoplasmic pathways), or to target and chemically modify DNA sequences by addition of methyl groups and cause modification of DNA-associated histone proteins (nuclear pathway). The nuclear pathway is known to inhibit transcription and to seed heterochromatin formation (Ahlenstiel et al., 2012, Grewal and Elgin, 2007, Reyes-Turcu and Grewal, 2012, Zhang and Zhu, 2012).

[45] For an excellent animation, see http://www.nature.com/nrg/multimedia/rnai/animation/index.html.

Figure 1: source of new dsRNA molecules from genetic engineering.

(A) Regardless of the source of the DNA inserted (dashed blue and green lines in the black double stranded DNA molecule) into a genome by genetic engineering, it creates new sequences. The DNA used will create new sequences because it will be bordered (boundary between dashed and solid lines) by different sequences than in the source genome by the engineering process, or may be sourced from a genome that has no or few sequence matches. (B) Transcription will produce new RNA molecules (red and dashed blue and green lines) that might be able to form dsRNA because of complementarity or (C) because of internal base-pairing causing stem-loop structures to form (base-pairing illustrated with thin black connecting lines). (D) This may lead to intended and off-target (red line with purple target section) gene silencing in the GMO or in organisms that eat the GMO.



Once a silencing effect is initiated, the effect may be inherited. The biochemistry of this process varies depending on organism and remains an area of active research with many unknown aspects. Nevertheless, it is known for example that human cells can maintain the modifications necessary for TGS, creating actual or potential epigenetic inheritance within tissues and organisms (Hawkins et al., 2009).

Unintended gene silencing is a common outcome of the genetic engineering process. Indeed, most cells initially engineered using *in vitro* nucleic acid techniques ultimately 'silence' the gene inserted because of the engineering-associated production of dsRNA (Denli and Hannon, 2003, Weld et al., 2001). The new RNA

sequence may be created when the DNA strand not normally used as a co-factor for transcription is used as such (perhaps because the insert had a cryptic promoter activity or inserted near a promoter). The resulting single-stranded RNA may bind to the target mRNA to create regions of linear dsRNA that can be processed into siRNA (Figure 1). Another possibility is that the insert contributes to the formation of a stem-loop, from which the 'stem' may be processed into an miRNA-like molecule (Figure 1).

2. Summary

dsRNAs are remarkably stable in the environment. Insects and worms that feed on plants that make dsRNA can take in the dsRNA through their digestive system, where it remains intact (Gordon and Waterhouse, 2007, Mao et al., 2007). Worms can absorb dsRNA through their skin when dsRNA is suspended in liquid (Cogoni and Macino, 2000, Tabara et al., 1998). Once taken up, the dsRNA can circulate throughout the body and alter gene expression in the animal (Mello and Conte Jr., 2004). In some cases, the dsRNA taken up is further amplified or causes a secondary reaction that leads to more and different dsRNAs ("secondary" dsRNAs) with unpredictable targets (Baum et al., 2007, Gordon and Waterhouse, 2007).

New dsRNA molecules can be made as a side effect of genetic engineering (or existing dsRNA molecules can be made in higher or lower quantities), and some GMOs were created for the purposes of generating new dsRNA molecules. Some dsRNA molecules can have profound physiological effects on the organism that makes them. Some dsRNA molecules can be transmitted through food or other means to other organisms and can have effects on these organisms that are not yet understood. "A daunting outcome is raised, that each [dsRNA] formulation might have its own risks" (p. 514 Aronin, 2006).

There are no validated procedures for excluding either exposure pathways or potential adverse effects of particular dsRNA molecules that may be produced as a result of genetic engineering, whether intended or otherwise. Therefore, for the foreseeable future, all GMOs intended for release or food should be submitted to a battery of testing for unknown dsRNAs and unintended effects of dsRNAs. The testing should provide empirical evidence capable of providing confidence for claims of the absence of any unintended dsRNAs or of an unintended effect.

Acknowledgements

I am grateful to Dorien Coray, Brigitta Kurenbach and Judy Carman for helpful discussions, and to past and present members of INBI for their contributions during the writing of submissions to FSANZ.

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If Not GM and Factory Agriculture, What and Who Will Nourish the World?

Hans R. Herren
Millennium Institute, Washington and Biovision Foundation, Zurich

1. Introduction

GENETIC modification (GM) does not produce more food. By contrast, many studies reveal that smallholder farmers often have higher productivity than large farms on a per hectare basis without using transgenic crops. The problem of producing food for a growing and more demanding world population lies in improving soil fertility, closing of the yield gap between low-productivity and high-productivity farmers, improving water access and conservation, and protecting biodiversity. These issues can be addressed with agronomic practices that improve climate-change adaption on the one hand, while also providing much needed climate-change mitigation. Modelling of the sustainable farming methods recommended by the widely-supported IAASTD study demonstrates that agriculture can be transformed so that all major sustainability indicators are improved, as well as productivity.

This type of agriculture, which relies on fewer expensive, scarce, and often harmful purchased inputs, including genetic engineering, also results in higher income and more jobs. Key points on this are outlined below.

2. Productivity of smallholder farmers without GM seeds

For an overview from the FAO on smallholders and family farmers and their relationship to sustainability and high productivity, see FAO (2012). Drawing on Pretty et al., smallholders adopting sustainable agriculture have increased their crop yields on average by 79%.

2.1 Sub-Saharan Africa

In line with the Green Revolution approach to achieve agricultural growth in Africa, the genetic modification of crops, hand in hand with synthetic fertiliser applications, has risen to the forefront as a viable alternative – technological solution – to the current traditional agriculture methods. While some of its most vocal proponents (Paarlberg and Collier) contend that biotechnology is currently kept

out of African countries at the cost of starving and poor farmers, I argue that numerous and scientifically backed-up agro-ecological alternatives exist to increase productivity – sustainably and with a proven track record – to the benefit of these small-scale farmers, as well as the local consumers in sub-Saharan Africa and beyond.

In addition to the traditional herbicide- and pest-tolerant varieties, GM technologies developed for African farmers include newer generation varieties. One example is a drought-tolerant variety 'Water Efficient Maize for Africa (WEMA)' – managed by the African Agricultural Technology Foundation (AATF). Although it has stimulated high hopes, to date, however, AATF has yet to release to the public the yield results from its ongoing trials. Since yield increases from similar genetic modifications were limited in the US (around 10%), it is very likely that existing local and improved (CGIAR and National Research Institutes) drought-tolerant varieties might yield better results.

Single approaches to increasing yields through genetic improvement do not address the need to consider the farming system as a whole, in which any improvements need to 'take root'. While I support advancements in seed technologies, sustainable agricultural methods promoted by the Biovision Foundation in Africa and implemented by thousands of East African farmers are effective in not only substantially increasing yields, but at the same time improving soil fertility, increasing soils' abilities to retain moisture, preventing soil erosion, reducing carbon emissions, and increasing biodiversity among other benefits (see for example Niggli et al. 2009; UNEP 2011; Khan et al. 2008a, b).

In an African low-input environment, sustainable agricultural practices can not only reduce costs of synthetic inputs (i.e. pesticides replaced by push-pull methods), but also increase yields, enhance economic diversification and strengthen household self-sufficiencies and food securities (UNEP and UNCTAD 2008, FAO 2007). Furthermore, smallholder farmers can take advantage of both domestic and international markets for organic and other products derived from such productions.

These multipronged efforts aim at improving the livelihoods of farmers across the scales: moving from soil and the seed to the crop and animals, and finally to the household and the social, economic and ecological sustainability of the region as a whole. While GM seeds have the potential to save input costs (such as labour) or under optimal conditions increase yields, these solutions do not pay off for the smallholder farmer, as they often demand additional fertiliser use, access to irrigation and access to credit and the needed complementary insurances, none of these readily available nor affordable.

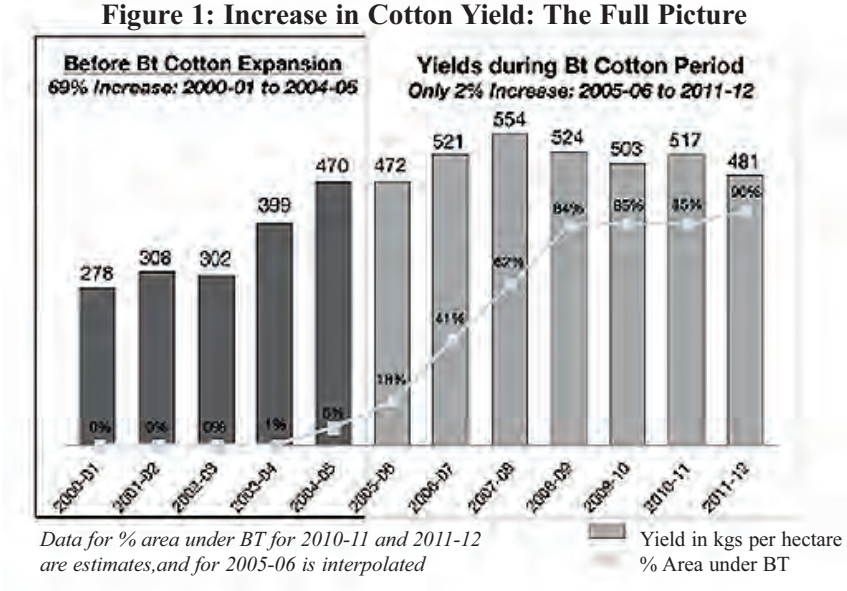
2.2 On India

In regard to genetic modification, studies have found sustained yield increases for Bt cotton compared to conventional cotton. For example, Kathage and Qaim (2011) compared data of over 500 farmers between 2002 and 2008. They estimated

that Bt cotton farmers had a net yield gain of 24%. Over the last five years, Bt yields however are described as stagnating, with improper pest management and an overall decrease in soil fertility mentioned as two main culprits (DownToEarth 2011). When focusing on smaller, more marginal farmers who were using intercropping strategies (i.e. sorghum and mungbeans; Swaminathan and Rawal 2011) and focusing on rain-fed, as opposed to irrigated cotton (i.e. Greenpeace 2010), benefits for growing Bt cotton diminish, are non-existent or as new evidence suggests, negative. In contrast, a previous study by Eyhorn et al. (2007) showed significant increases in income at the farm level for organic farmers compared to Bt cotton farmers in India. Fair comparisons between Bt cotton and best practice conventional and organic agriculture are missing. These would be long-term comparisons that have all the same agronomic practices, soil fertility levels at the start of the experiment, irrigation levels as well as equivalent varieties. Environmental and social data need also to be considered in such studies. Until such data exist it will be meaningless to draw definitive conclusions.

A recent publication reviewing a decade of Bt cotton in Madhya Pradesh (where Bt adoption has risen from 6% in 2004-5 to 90% by 2011-12 (measured in percentage of area under production) by Hamara Beej Abhiyan and Beej Swaraj Abhiyan (2012) highlights how yield increased by nearly 70% from 2000 till 2005 prior to the expansion of Bt cotton. After 2005 and with the expansion of Bt cotton, yield increases were only 2% (Figure 1).

Figure 1: Increase in Cotton Yield: The Full Picture



Source: Data used from Office of Textile Commission of India, cited by cotton Advisory Board (www.txindia.com) and Cotton Corporation of India (cotcorp.gov.in/state-operations.aspx)

Due to the very widespread adoption of Bt cotton (90%+), it has become nearly impossible for organic cotton contractors - India produces up to 80% of the world's organic cotton - to obtain non-GM seeds. Current efforts are underway to establish a long-term participatory plant-breeding programme to develop locally adapted cultivars and maintain and increase genetic diversity (Roner et al. 2012). These efforts - led by FiBL, bioRe an organic cotton producer in Central India and the University of Agricultural Sciences (UAS) Dharwad - are focusing on safeguarding the heritage of Desi cotton for the benefit of organic farmers. Given the high costs associated with these initiatives (and the lack of private seed company interest given the importance of the Bt seed market) this type of initiative clearly would offer a great opportunity for government involvement to strengthen public research for the benefit of rain-fed small-scale farmers, sustainable agriculture and maintaining biodiversity.

3. Challenge of soil fertility

Fertile land is the precondition for successful agricultural production. However, land is becoming scarce, with increasing degradation due to unsustainable practices and growing global competition for productive agricultural land. Land degradation, and poor soil fertility in particular, is widely accepted as the most critical limiting factor in constraining agricultural production in sub-Saharan Africa (IAASTD 2008; 2009). There are some five billion hectares of land presently available for the global food supply: 1.5 billion hectares of farmland and permanent crops and 3.5 billion hectares of grassland, grazing land and extensively used steppe (Harder 2008). Of this land, 1.9 billion hectares have already been degraded to a greater or lesser extent due to intensive and improper use (IAASTD 2008; i.e. UNEP 1999; Eswaran et al. 2006). Additionally, ten million hectares are lost to erosion every year. The need to stop the loss of farmland is urgent, and this includes regenerating depleted soils so they can be used in the future with sustainable production methods (Herren 2012).

Fertile soils are also crucial to mitigating climate change and building resilience for adaptation as discussed below. There is a need to consider the feedback system from agriculture to climate change and climate change to agriculture. Clearly, a continuation of present farming practices contributing some 50% of the GHG needs a major change in direction. In particular, any practice, such as the ones promoted and underscoring the Green Revolution, need to be dumped in favour of ecologically based practices that are regenerative.

4. Challenge of yield gap

'The challenge is to find ways to close this yield gap by overcoming the constraints to innovation and improving farming systems in ways that are appropriate

to the environmental, economic, social and cultural situations of resource-poor small-scale farmers. An additional requirement is for farm products to be fairly and appropriately priced so that farmers can spend money on the necessary inputs.' (IAASTD 2009, p.223)

Proposed methods from the IAASTD (2009, pp. 382-383) include:

- improve practices for root health management;
- conventional breeding/rDNA assisted;
- transgenics;
- improve the performance of livestock in pastoral and semi-pastoral subsistence communities;
- rain water harvesting, supplemental and small-scale irrigation for rainfed systems;
- integrate soil water and soil fertility management;
- multiple water use systems, domestic and productive uses, crops/livestock/ fisheries.

Closing the gender gap in agriculture would have a substantial impact on increasing yield. According to the FAO's State of Food and Agriculture 2010–11 report on the topic: 'If women had the same access to productive resources as men, they could increase yields on their farms by 20-30 percent. This could raise total agricultural output in developing countries by 2.5 to 4 percent, which could in turn reduce the number of hungry people in the world by 12-17 percent.' (FAO 2011, p.5f)

5. Challenge of improving water access and conservation

Sustainable use of natural resources is also especially relevant when we look at the use of water in agriculture. Agriculture accounts for 70% of global freshwater consumption today – yet it is possible to limit water use while still meeting global food and nutritional needs. In various regions such as India, China, North Africa and the Middle East, depletion of water resources is already a serious problem. Groundwater levels are falling rapidly. Further, groundwater resources are only renewable over the very long term, if at all. Climate change will exacerbate water shortages in drier parts of the world. Sustainable small-scale farming exhibits a great deal of potential with regard to reducing water consumption. Efficient irrigation systems – such as drip irrigation – could reduce consumption by several degrees of magnitude. Case studies in developing countries have demonstrated that water consumption can be reduced by 40-80% yet increase yields by up to 100% (i.e. for drip irrigation see Burneya et al. 2009; Sivanappan 1994, Belder et al. 2007). In 2011 the United Nations Environment Programme (UNEP) Green Economy report confirmed that production with sustainable methods, which is adequate to cover

humanity's food needs in the year 2050 with limited use of water, is now feasible (UNEP 2011) and should be implemented without delay in order to avert a catastrophic temperature rise beyond two degrees Celsius (Stern, 2010).

6. Challenge of protecting biological diversity

Biological diversity is crucial for sustainable food production, but it is currently under considerable threat. Over centuries, humanity has used over 10,000 edible plants: today we use only 150 and just 12 species make up 80% of plant-based food production (FAO 2008). The edible plants being grown are becoming increasingly similar to one another. The enormous wealth of cultivars that the world's farmers have created through cultivation under a variety of conditions has shrunk in parallel with the rapid rise to dominance of a few globally grown high-yield cultivars. An estimated 75% of all economically useful plant cultivars have vanished from the world's farms (Forum Biodiversität Schweiz, 2005, p.18). With every species that disappears, valuable genes are lost. Considering that 90% of pest species have natural antagonists – predatory or parasitic insects – and over thousands of species of pollinating insects provide their services to the agriculture sector, this matters a great deal. This is why diversity in the animal kingdom and plant species is an insurance against pest problems, and key to ensuring food and nutrition for all; allowing higher productivity, adaptation, and maintenance of ecosystem functions (see also FAO and Platform on Agrobiodiversity Research 2011).

The conservation of agricultural biodiversity is unique, in that it depends on the use and practices of farming communities, in their fields. Diverse smallholder farming systems with farmer-selected seeds not only foster genetic diversity and adaptation to climate change, but provide an environment that is very beneficial to natural enemies and pollinators. These beneficial insects may be far more diverse in farmers' fields than even in natural habitat (Gikungu 2011). The contrary is also true, however, that the uniformity of industrial farming and use of pesticides, whether sprayed or coated on seeds, is highly damaging to agrobiodiversity in all forms.

7. Agroecology fosters climate-change adapation and mitigation

Intensive industrial farming is one of the causes of climate change, and we need to switch to ecological methods to provide relief. Agriculture accounts for 47-55% of man-made greenhouse gas emissions. Livestock contributes 18% of the global warming effect, which is even more than the total from global transport. Agriculture accounts for 50-60% of emissions of nitrous oxide (N2O) and methane (CH4), which are both potent greenhouse gases: one kilogramme of methane has the same impact as 21 kilogrammes of carbon dioxide (CO2), and nitrous oxide has 310 times the impact. Animal factory farms have the highest greenhouse gas

emissions in the agriculture sector. Moreover, the potential impact of climate change on agricultural production is huge (see IAASTD 2008, 2009; Steinfeld et al. 2006).

On the other hand, some methods of sustainable and organic farming can reduce climate change impact while increasing resilience (Niggli et al. 2009). One example is the sequestration of CO2 in fertile soils where the humus content is higher.

CO2 from the atmosphere ends up in dead plant materials in the soil, where it is mineralised before being released again as CO2, but some of it is also stored in the humus for a long time. If the humus content increases, more CO2 will be stored in the soil than will escape. Studies have shown that soils on organic farms are richer in humus than soils on conventional farms. Furthermore, ploughless farming techniques can further increase CO2 capture in soils, because ploughs promote the breakdown of humus.

8. Modelling of sustainable agriculture demonstrates how productivity and sustainability can be improved

There are a number of recent studies that provide evidence from both experiments and computer simulation models to justify a change in course in agriculture and the wider food system, as both are closely connected. Maeder et al. (2002) reported on soil fertility and biodiversity. The Rodale Institute (2011) published extensively on yield and profitability under sustainable production systems and also FiBL (2011) on farming system comparisons in the tropics. Some of these and many other studies have provided the needed input into the agriculture chapter of the UNEP 'Green Economy' Report, supported by a system dynamics model of agriculture and related sectors (UNEP 2011). The UNEP study shows how an investment in a global change from brown to green agriculture would result in benefits on all key social, environmental and economic sustainability indicators (Figure 2).

9. Benefits of a revolution based on sustainable agriculture: knowledge- and labour-intensive, vs capital-intensive

Public investments in sustainable agricultural productivity will result in clear pro-poor growth. Improving productivity of small-scale agriculture in sub-Saharan Africa by 10% can lift almost seven million people above the dollar-a-day poverty line (McIntyre, B., Herren, H. R., Wakhungu, J., & Watson, R. T., 2009, p.2).

The benefit of agro-ecological agriculture is its focus on knowledge-intensive nature, which means that the technologies can be adapted and disseminated amongst farmers, including their own innovations. Depending on the agro-ecological technology, higher labour-intensiveness in agriculture - coupled with increased

Figure 2: Summary of results from the Green Economy Agriculture chapter

Green Agriculture can.... (UNEP GER Report - 2011)
Investing 0.1% or 0.16% of total GDP ($83-$141 Billion) / year

Year		2011	2050	
Scenario	*Unit*	*Baseline*	*Green*	*BAU*
Ag production	Bn US$/Yr	1,921	2,852 ↑	2,559
Crops	Bn US$/Yr	629	996 ↑	913
Employment	M People	1,075	1,703 ↑	1,656
Soil quality	Dmnl	0.92	1.03 ↑	0.73
Ag water use	KM3/Yr	3,389	3,207 ↓	4,878
Harvested land	*Bn ha*	*1.20*	*1.26* ↓	*1.31*
Deforestation	*M ha/Yr*	*16*	*7* ↓	*15*
Calories p/c/day for consumption	Kcal/C/D	2,081	2,524 ↑	2,476

productivity – can also result in improved employment opportunities and wages for rural, landless poor classes.

This stands in stark contrast to previous experiences of the Green Revolution, where the introduction of high-input agriculture resulted in increases in inequalities as the poorest farming households or regions were unable to benefit from such capital-intensive technologies.

Even proponents of the Green Revolution are beginning to moderate their assessments of its success: 'The direct benefits to the poor through their own on-farm adoption, greater agricultural employment, and empowerment have been more mixed and depend heavily on local socioeconomic conditions. In many cases inequalities between regions and communities that adopted Green Revolution technologies and those that did not also worsened. At the same time, the Green Revolution had many negative environmental impacts that have still to be adequately redressed.' (IFPRI, 2003, p. 4)

10. The way forward

In order to change the way food is produced, there will be a need to change the ways food is being processed, marketed and consumed. In particular, consumption patterns will have to change drastically, as in no way can the planet sustainably produce food at the rate it is being consumed and wasted in the Western world today. Consumers have the ultimate decision power over their preferences, and information needs to be given to them in order that they can make informed choices. This is not the case today in most instances. But there is also a trend in the

right direction on the horizon, despite the fact that agribusiness is trying hard to thwart any effort in that direction. Scare tactics such as the spectre of additional costs, or the 'impossibility' of labelling foods that contain GMOs, for example, are being widely adopted. The IAASTD report 'Agriculture at a Crossroads' could not have delivered a stronger message than 'business as usual is not an option'; the world needs a paradigm shift if it wants to reach the goal of food security for all for the long term. Simple solutions for complex problems - as they are being proposed with GMOs as the solutions to production problems of today and climate change impacts of tomorrow - are not credible. Scientists and policy-makers need to start to think in systems, and see agriculture and food as an integrated system that is interconnected across all the dimensions of development. System tools and scenario models, allowing people to play out options for the future and to inform sustainable development policies that take into account the world's boundaries, are urgently needed. We can't afford to keep our heads in the sand and hope for the crises to pass, or throw some reductionist solution(s) at them, in the hope that they will miraculously disappear. The time for realism and above all courage to make the tough decisions today has come, for the sake of our children and theirs too.

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Annex:
Conference Programme

European Network of Scientists for Social and Environmental Responsibility (ENSSER)

TWN
Third World Network

Advancing the Understanding of Biosafety

Friday, 28 Sept 2012

Opening		
09:00	**Dr. Angelika Hilbeck** **Lim Li Ching** **Christine von Weizsäcker**	**ENSSER, Chairperson** **Introduction** **Third World Network** **ECOROPA** **Key Issues of COP-MOP-6**
Developments in GMO Risk Assessment		
09:40	**Legal and Scientific Background of Risk Assessment Models**	**Dr. Hartmut Meyer** ENSSER, Germany
10:10	**The Roadmap on Environmental Risk Assessment of the Cartagena Protocol on Biosafety**	**Dr. Beatrix Tappeser** Federal Agency for Nature Conservation (BfN) Germany **Dr. David Quist** GenØk - Centre for Biosafety, Norway
10:40	**Socio-economic Considerations in GMO Decision-making**	**Georgina Catacora-Vargas** GenØk - Centre for Biosafety, Norway / Institute of Research on Risk and Sustainability (IRIS), Federal University of Santa Catarina, Brazil
11:10	*Break*	
11:40	**Appraisal of New Approach on Environment Risk Assessment of the European Food Safety Agency (EFSA)**	**Dr. Angelika Hilbeck** Swiss Federal Institute of Technology Zurich (ETH), Switzerland
12:10	**Appraisal of New Approach on Health Risk Assessment of the European Food Safety Agency (EFSA)**	**Dr. Christoph Then** Testbiotech, Germany
12:40	*Lunch*	
14:00	**Discussion Panel – Audience**	
Independent Biosafety Research - Hurdles and Results (1)		
14:45	**Introduction**	**Lim Li Ching** Third World Network (TWN), Malaysia
15:00	**Sources and Mechanisms of Health Risks from GM Foods**	**Prof. Michael Antoniou** King's College London, UK
15:30	**Health Impacts of Glyphosate-based Herbicides and Roundup-tolerant GM Plants**	**Robin Mesnage** University of Caen, France
16:00	**Access to GE Seed and Research Control Through Patents**	**Dr. Hartmut Meyer** ENSSER, Germany
16:30	*Break*	
17:00	**Glyphosate-resistant Weeds and Bt-resistant Insects in US Agriculture**	**Dr. Doug Gurian-Sherman** Union of Concerned Scientists (UCS), USA
17:30	**Discussion Panel - Audience**	
18:15	*Closure*	

European Network of Scientists for Social and Environmental Responsibility (ENSSER)

TWN
Third World Network

Advancing the Understanding of Biosafety
Saturday, 29 Sept 2012

GM Crops in India		
09:00	**Influence of the Fast Spread of Bt Cotton on the Organic Cotton Production**	**Matthias Klaiss** Research Institute of Organic Agriculture (FiBL), Switzerland
09:30	**Interrogating the Science of Safety: Unresolved Effects of Bt Toxin on the Health of Domestic Animals in India**	**Dr. Sagari R Ramdas** Anthra, India
10:00	**Technology, Liberalisation and Farmer Suicides in Vidarbha (Maharashtra State, India)**	**Vijay Jawandhia** Shetkari Sanghatana, India
10:30	**Discussion Panel - Audience**	
11:15	*Break*	
Independent Biosafety Research - Hurdles and Results (2)		
11:45	**Domestication, Feral Species and the Future of Plant Diversity**	**Prof. Cynthia L. Sagers** University of Arkansas, USA
12:15	*Lunch*	
13:45	**Transgene Flow into Native Seed and Ecosystems in Mexico**	**Dr. Ana Wegier** National Institute for Research in Agriculture, Forests and Lifestock (INIFAP), Mexico
14:15	**Field Trials of Bt Eggplant and Regulatory Policies in the Philippines**	**Associate Prof. Ruth Gamboa** University of the Philippines Mindanao, Philippines
14:45	**Insect Resistance Against Bt Maize in South Africa and Management Challenges for African Farmers**	**Prof. Johnnie van den Berg** North West University, South Africa
15:15	**Discussion Panel - Audience**	
16:00	*Break*	
Holistic Analysis - Joining the Pieces		
16:30	**Introduction**	**Dr. Angelika Hilbeck** Swiss Federal Institute of Technology Zurich (ETH), Switzerland
16:45	**Early Warning on Food Safety Issues: How Regulators Got it Wrong on dsRNA**	**Prof. Jack Heinemann** University of Canterbury, New Zealand
17:15	**Ecological Agriculture for Food Security and Climate Resilience**	**Prof. Doreen Stabinsky** College of the Atlantic, USA
17:45	**Business as Usual is No Longer an Option - Paths to a Sustainable Future**	**Dr. Hans Herren** Millennium Institute, USA
18:15	**Discussion Panel - Audience**	
19:00	*Closure*	

This conference was made possible by the funding through EMstitut, Germany; Fondation pour le Progrès de l'Homme, France; Heinrich-Böll-Stiftung, Germany; Third World Network, Malaysia; Zukunftsstiftung Landwirtschaft, Germany

This is a compilation of papers from the second Scientific Conference jointly organised by the European Network of Scientists for Social and Environmental Responsibility (ENSSER), Tara Foundation and Third World Network (TWN), in conjunction with the 6th Meeting of the Parties to the Cartagena Protocol on Biosafety (COP-MOP6) in Hyderabad, India, in 2012.

The main aim of the conference was to advance the current understanding of biosafety in terms of the ecological, human health and socio-economic implications of genetically modified organisms (GMOs).

Another aim was to inform the delegates at COP-MOP6 about the current scientific challenges in biosafety research and assessment.

Topics covered by the conference included:

- Developments in GMO risk assessment, including discussion of the international standards on risk assessment in the context of the Cartagena Protocol's 'Roadmap for Risk Assessment and Management'
- Socio-economic considerations in GMO decision-making
- Latest scientific findings generated from independent biosafety research

ISBN 978-967-5412-84-4