But the fact is that at the end of the million pounds spent, there were more people disbelieving Monsanto's story.

Now everyone agrees - even the biotech companies agree - that they were shooting themselves in the foot. If they had gone about it quietly, they might have been fine, but instead they made a big deal about it. And people are not stupid. The issue is made out of all this, and people began to ask the question: what is Monsanto getting out of this?

GW: So in advertising they just drew attention to themselves.

AP: Yes. And I have great respect for the British general public. They can ask these very uncomfortable questions of the biotech industry: who is going to benefit from it? They know perfectly well that *I* didn't benefit from it! But they made a huge hullaballoo about this, and the companies know now that the right way for them would have been to put a lid on it, to keep quiet about it. But the public knows that something is happening, no matter how much they try to explain it. I know that people may not be nutrition-wise or science-wise very clever, but they have a common sense. They do understand that ... look, we are doing something that is fundamentally different from what we've done before. Therefore, just like the FDA's scientists whose sentiment was that we are doing something different, therefore the risks will be different - it is our responsibility to determine what these risks are. And if we can't come up with an acceptable answer, the next question is "who is to benefit?"

So here we are. Most importantly, what distinguishes the skeptics from the GM partisan? The skeptics try to speak to the facts. And it is therefore extremely important that the facts ought to be really facts, so that there are no mistakes. If I can help in any sense with this, then I shall do my best. ■■■

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Antibiotics in Your Corn

BY TIMO ASSMUTH AND SHELDON KRIMSKY

The risky business of pharmacrops

Biotechnology, including technologies based on genetic engineering or genetic modification, is becoming increasingly important in the global economy, ecology and politics. Agricultural biotechnology for food production has been the subject of much interest and debate in international politics, but in terms of market value, health care represents the largest sector of biotechnology, with pharmaceutical substances playing the major role. Most biotechnological pharmaceuticals are produced in microbes, but the use of genetically modified plants (often called "pharmacrops") to this end has gained increasing attention.[1] The first field trial permit for GM plants based on an application using the term "pharmaceutical" was issued in January 1991 in the U.S. By the year 2006 there had been 237 applications for field trials in the US alone; however, no commercial products have resulted to date.[2] Among the drugs being produced in plants are vaccines, antibodies, antigens, hormones, growth factors and structural proteins.

The possible advantages of plants over other systems in producing drugs include the production of larger volumes of drugs, more flexibility and cost-effectiveness in manufacture, better suitability of plant cells for production, and the potential of using plants and seeds for drug storage and delivery.[3] Plants have also some safety advantages over other pharmaceutical production systems, such as safety from contamination with human pathogens, endotoxins and tumorigenic DNA sequences.[4]

On the other hand, pharmacrops present important new risks and safety issues. By definition, they are used to produce substances that have potent biological effects on humans and

other higher animals. Pharmacrops contain higher concentrations of active substances than these animals are ordinarily exposed to in GM plants. Several genetic modifications are often carried out simultaneously, increasing risks.[5] Risks arise not only from biological but also socio-economic factors.

Pharmacrops consequently introduce special challenges to regulation. This is inherent in their position between agricultural, medical and general industrial biotechnology, and the special ecological-physical and socio-technological characteristics of these technologies. Some of these regulatory challenges include:

- The extension of new-generation GM crops to novel processes wherein the plants are not intended to be utilized as food crops but rather as plant-based 'drug factories.'
- Emergence of new forms of biopollution in possible gene transfers of GM pharmacrops to conventional crops.
- New methods required to evaluate drugs derived from plants that are grown in open fields.
- The need to align environmental, food and agricultural, as well as pharmaceutical and medicinal policies and regulatory procedures.
- The subsequent introduction of new actors, new interests and new contested issues regarding the development and application of the technology.

Risk issues are particularly urgent when pharmaceuticals are produced in plants that are potential food crops.[6] The need to control these risks has been stressed, by both consumers and food processors.[7] Currently pharmacrop risks are still addressed mainly within the conceptual frameworks of other GM food plants, and it is unclear how to accomplish the protection and management of food supplies as the distinction between food and pharmaceuticals becomes blurred.

The main direct risks associated with pharmacrops can be categorized in terms of causative agents (for instance, the drug being produced); dispersal processes (especially gene flow) and environmental fate of the produce; exposed organisms or systems (such as animals which feed on pharmacrops in field trials); and biological (toxic, allergenic, ecological), agricultural and social effects. All of these need to be accounted for in the life-cycle of the technology (see **Figure 1**).

Indirect risks arise in complex socio-ecological processes, also from attempts to control risks which inadvertently create new risks, for instance when using unproven 'terminator' technology to render GM plants sterile, combating vandalism by non-disclosure of information on field trial sites, or causing losses of relative benefits from pharmacrops as compared with conventional drug manufacture.[8] Some risks may be irreversible, especially in regard to gene flow into the environment. Accidental outbreaks from field trials and associated food chain contamination scandals indicate that the transgenes cannot be totally contained.[9] The crucial questions become how the different kinds of risks are judged and weighed against each other, what risks are deemed acceptable and on whose criteria, and what are feasible and justified risk abatement or prevention options.

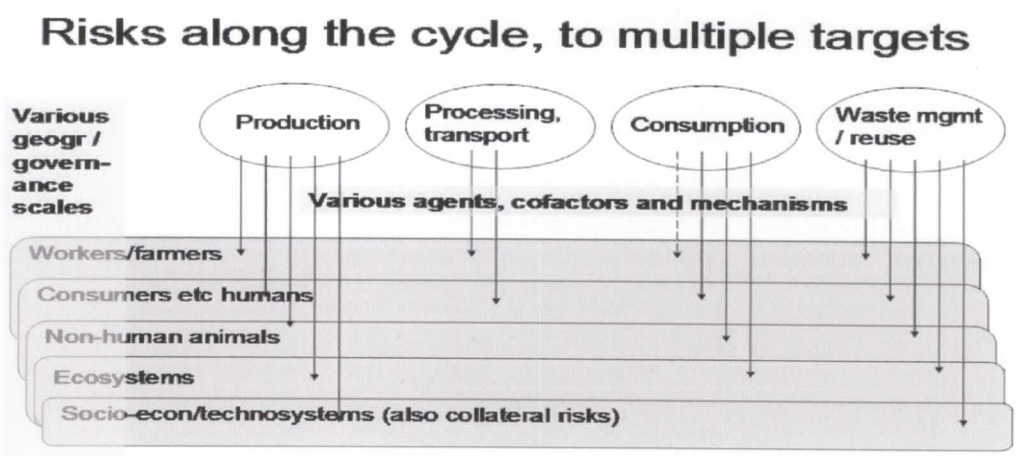

Figure 1

The risks of pharmacrops are unevenly distributed geographically. The map of field trials in the United States (**Figure 2**) shows that transgenic corn with pharmaceutical proteins has been tested mainly in the Corn Bbelt. Threats to food production systems, biodiversity, worker safety and rural development also vary according to location. If a pharmacrop is grown near fields of the same species, the risk of transferring the "drug gene" to a conventional crop is increased. The benefits are unevenly distributed as well; those who stand to directly benefit from a field test (such as a pharmaceutical companies or landowners paid to allow test plots on their land) do not necessarily share the risks, and thus the presence of potential risks does not necessarily inform decisions such as location of field plots (for a discussion of some of the political issues herein see Freese, 2002). For example, Iowa and Nebraska - two of the top corn producing states in the United States - have some of the highest numbers of corn pharmacrop test plots, despite the heightened risk of contamination or cross-pollination.

Castle (2008) singled out informed consent, risks to agricultural policy and intellectual property rights as the key global challenges for ethical production of vaccines in plants. The awareness, willingness (political) and capacity to respond to these issues varies between and within societies, and as a result there can be a mismatch between risks and responses. The geographical heterogeneity of risks and regulation increases from small nations to the US, the EU and the global systems.[10]

In the US, the policy toward pharmacrops has been relatively lax, but the regulatory procedures for assessing and

managing their risks have been upgraded in response to contamination accidents. In the EU, even after passage of a moratorium on GM plants, a more precautionary stance contributes to the lag of pharmacrop applications. The specific regulatory risk management options for pharmacrops are focused on technical measures at production sites, particularly containment, while options in other stages of the product life-cycle and risks of other dimensions have been given less attention (**Table 1**).[11] Additionally, critics point out that the seemingly self-evident options of restricting pharmacrops to closed systems and to inherently safer self-pollinating or non-food species have been a secondary consideration.[12]

In Europe, pharmacrop field trials have been carried out since 1995, but the number of trials declined after 1996; the cultivation acreage was nearly zero in 2002-2004. The onset of a more cautious approach to GM plants in general influenced these fluctuations. The regulatory approach in EU countries was pro-GM until 1990's, only later to be replaced by a *de facto* moratorium on commercial cultivation of GM crops for human consumption, due largely to growing concerns among consumers and Member States.[13]

However, even if the European stance toward GMOs has been precautionary overall for over a decade, pharmacrop risks have not been officially singled out. Increased R&D activities suggest that the EU may seek to switch back to a more pro-pharmacrop policy despite official caution, due in part to reasons of global trade policy and competition. Biopollution and other risk issues have been debated in connection with the proximity of GM crops to organic or conventional farms and with the buffer distance required to ensure safe coexistence of GM and non-GM plants.[14] These issues are potentially even more pronounced with pharmacrops, because crops can be contaminated with the pollen and residues of pharmacrops and because pharmacologically modified plants (PMPs) carry particular potency; yet such distances have not been specified in the EU for pharmacrops (**Table 1**).

The politics and practices of pharmacrop development and application involve the interplay and also tensions and clashes between different concepts of and approaches to risks, technology and regulation, and between interests and actors in various sectors and geographical regimes. Some of the polarization and conflicts in GMO politics influences pharmacrop policies, even if differently and as yet more subtly, due in part to the promises of producing wonder cures. Framing and evaluations of the risks from new-generation pharmacrops and other GMO 'industrials' are only emerging, and the confidence in their safety very greatly between and even within regulatory cultures.[15] Because of the complexity of the processes and influential factors, the trajectories of the technology and of regulation remain uncertain.

Although pharmacrops have been pursued actively, especially in the United States, some caution seems to hold commercialization back. It remains to be seen whether a fertile hybrid of pharmaceutical, agricultural and industrial technology will arise, and how the particular risks of pharmacrops will be dealt with. The development is likely to be uneven and turbulent. It will introduce the need to integrate activities on pharmacrops in partly new forms of communication, cooperation, negotiation and conflict resolution. These take time and effort to develop, due to differing concepts and traditions among actors and different views of the value-laden issues. Whatever action is taken needs to allow the legitimate involvement of a broader range of stakeholders. Even so, regulatory practices are as yet poorly equipped to deal with pharmacrops and their multi-dimensional largely unknown risks on a commercial scale. Meanwhile, certain concrete steps - such as restricting pharmacrops to closed systems and self-pollinating or non-food species - could provide a more immediate buffer against the risks, but even such solutions require the active engagement and interaction of concerned citizens including scientists and experts as well as regulators, consumer representatives and others. □□□

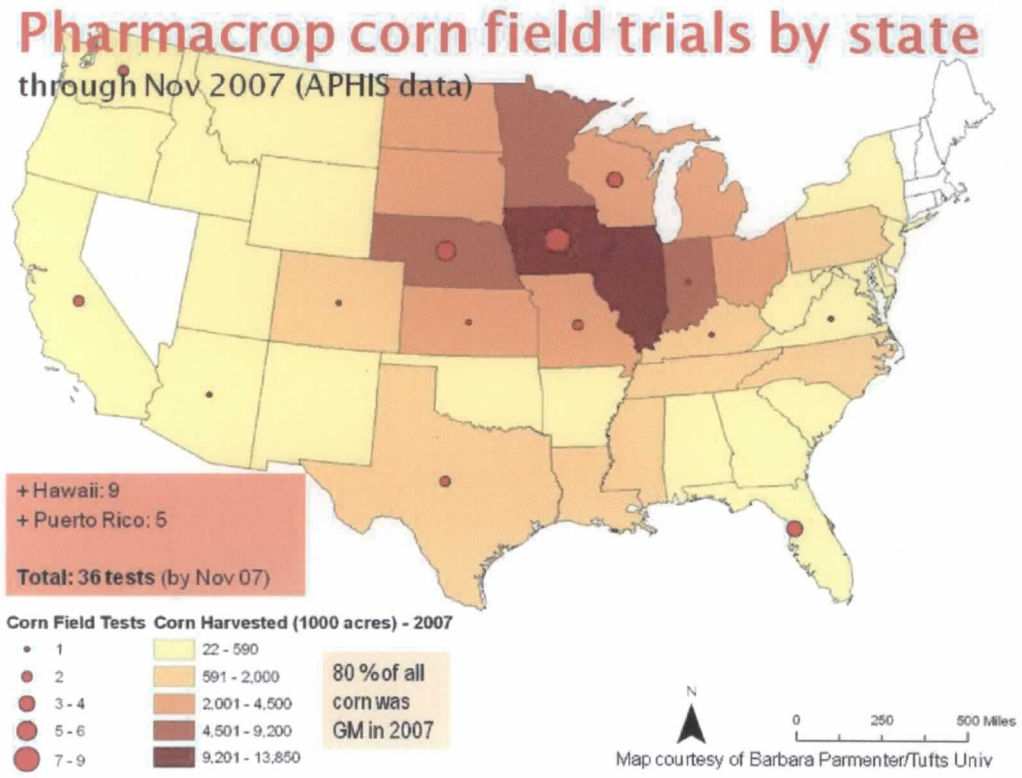

Figure 2

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mental sciences at the Universities of Turku and Helsinki, Finland, where he is affiliated as adjunct professor, and on a Fulbright grant at Tufts University Department of Urban and Environmental Policy and Planning in 2007. He has worked for 25 years in the Finnish Environment Institute, a government R&D organization, on wastes, soil protection, chemicals, GMOs, and environmental and health risks, with increasing interest in the human aspects of risk assessment and management.

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Type of measure	*Inclusion in US procedures*	*Inclusion in EU procedures*
Selection of plant species	Low (little requirements for inherently safer species)	Moderate (high dispersal potential species not favored)
Selection of GM type	Low (many types of GM)	Low-moderate
Preparation of cultivation material, incl. sterilization and non-dispersing constructs	Moderate (developing, inherently risky)	Moderate
Selection of place of application (coexistence rules)	Low (non-GM crops often nearby)	Moderate (greenhouse not required)
Selection of timing and duration (coexistence)	Low (up to 1 year fallow period)	Low
Containment or buffer zones	Low to moderate	Emerging/unspecified for PMPs
Eradication of offspring	Moderate	As above
Prevention of seed transport	Moderate (failures occurred)	As above
Protection and control of wildlife	Low-moderate (few provisions)	As above
Cleaning of agricultural/processing machines	Moderate (failures occurred)	As above
Purification of products	Moderate (private interest)	As above
Testing of cultivar and product safety	Low-moderate?	As above
Occupational safety measures	Low-moderate?	Moderate (high overall)
Liability, insurance etc risk management provisions	Low-moderate (improved post-2002)	Emerging/unspecified for PMPs
Monitoring and oversight	Low-moderate; self-monitoring allowed	As above
Confidentiality of information	Moderate; low transparency	Moderate
Transparency and public availability of information	Low-moderate (improved post-2002)	Moderate (still cryptic for PMPs)
Inherently contained culture (greenhouse)	Low (not a focus)	Low (not a focus)
Labeling / consumer information	Low (resisted)	Moderate (partial)

Table 1. Inclusion of specific risk management measures in regulatory planning and implementation processes for pharma-crop applications mainly in field trials (based on U.S. and Canadian regulations and proposals).[16]

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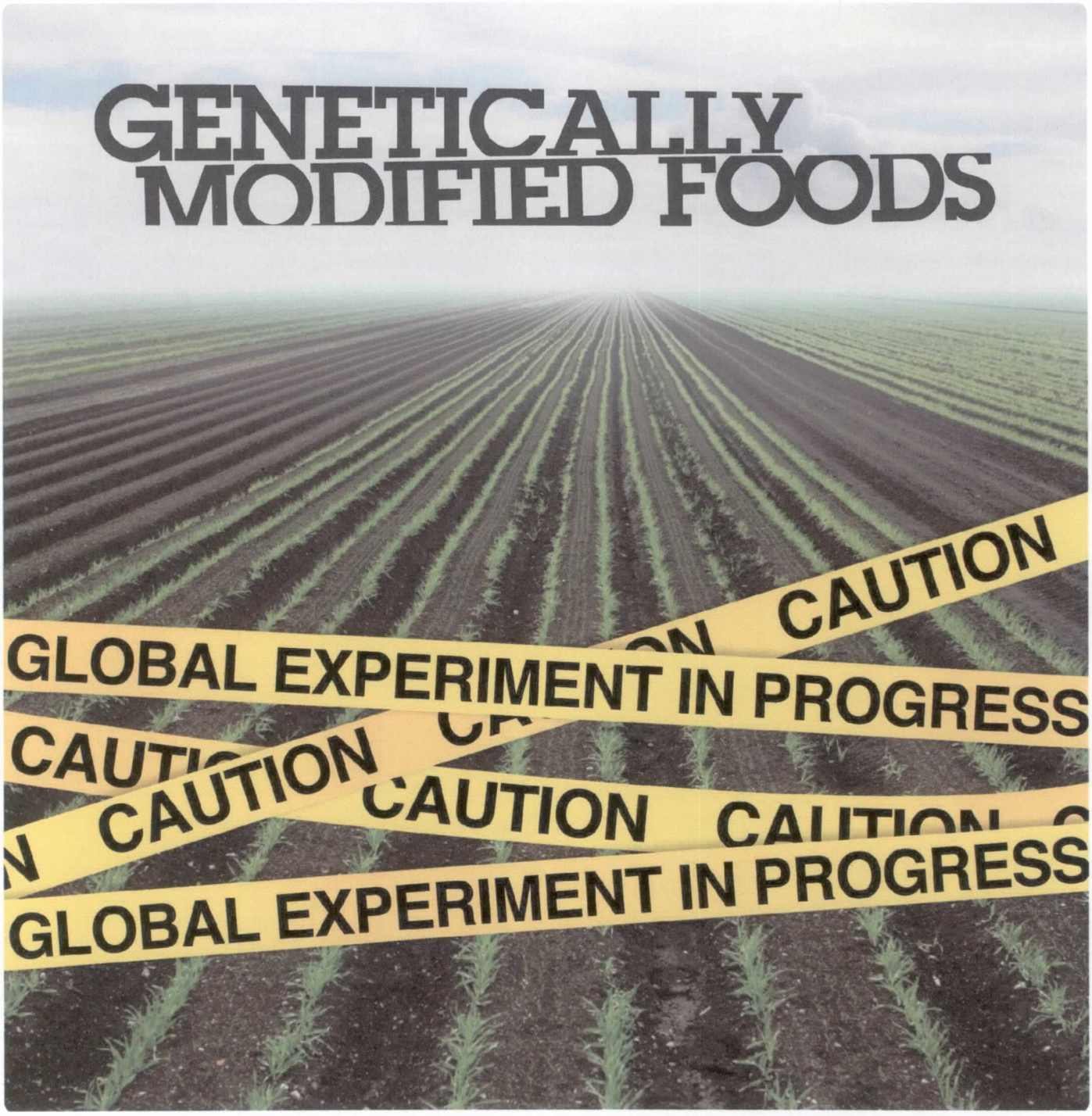

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