Predicting the effects of genetically modified organisms – more questions than answers

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Frankenstein foods or a more sophisticated and scientific approach to feeding the world? Genetically modified (GM) crops and foods have become one of the main issues of the late 1990s, but are the critics scaremongering or the industry being complacent? The possible effects of releasing genetically modified organisms (GMOs) into the environment include those directly associated with the GMO itself, secondary effects on agricultural or other practices and socio-economic impacts, but how serious are they?

The potential for direct effects is related to the behaviour of the GMO in the environment and the particular genes which have been transferred. In the case of GM crops, if related wild plants are growing nearby, there could be cross pollination and transfer of the foreign genes into native flora. The likelihood of this depends on a host of factors, including the fertility of any hybrids formed, the relative position of the weeds and crop, and how agricultural practices affect the outcome. Since one species of weed will not be homogeneous across the UK, the likelihood of hybrid formation may even vary within a species. Thus predicting the likelihood of foreign gene flow (dubbed 'genetic pollution') is extremely complex and present knowledge remains uncertain. For crops such as sugar beet and oilseed rape, which evolved in Europe, related weeds do co-exist, have similar flowering periods and are compatible with the crop to varying degrees, so gene flow seems inevitable.

This raises the inevitable question about whether gene flow matters. Some argue that gene flow from traditionally bred crops to native flora must have been taking place for a long time with no obvious ill-effects in the UK, so why worry. However, GM crops are being altered in ways which are not possible by conventional breeding or by using techniques such as mutagenesis or irradiation, so GM-specific assessments are justified. For example, using single gene transfers (usually together with promoter and suppressor genes) crops can be made resistant to a herbicide which previously killed them, can produce a toxin which kills insect pests or resist a viral disease. If these genes are transferred into wild, weedy species under the right conditions they could give a considerable competitive advantage. One mechanism of GM disease resistance against virus diseases uses the coat protein gene of the virus itself to promote resistance by a mechanism which is not entirely understood. This is very different from conventional methods of breeding disease-resistant cultivars and, as well as wild plants acquiring a new form of resistance, there could be recombination between the transferred genes and infecting viruses leading to the emergence of new viral strains.

So gene flow may matter a lot in practical terms. However, our present understanding is so limited that accurate prediction is probably a long way off. Of course gene flow effects may not be seen for decades and become a problem inherited by our children and grandchildren.

It is not only the genes of commercial interest that may cause adverse effects. For example, the industry has been cavalier in its use of antibiotic resistance marker genes. Because the actual genetic modification technique is random and only successful in a limited number of cases, a test is needed to identify when the transformation has been successful. Therefore, an antibiotic resistance gene is generally included in the genetic material to be transferred and following treatment the cells are grown in medium containing the relevant antibiotic so only those cells where gene transfer has taken place will survive. Resistance to neomycin/kanamycin is one of the most commonly used markers, but the first commercially grown GM crop in Europe is a maize variety containing an ampicillin resistance gene as well as insect and herbicide resistance. This has raised considerable controversy because of the clinical importance of ampicillin and the risk of the antibiotic resistance gene being transferred to the bacterial flora in the intestines of animals eating the maize (which is intended for animal feed production) or in the soil. This resistance could eventually be transferred to human or animal pathogens, increasing clinical problems with antibiotic resistance. The antibiotic resistance gene plays no role in the final crop. Techniques exist to remove such unwanted genes although they increase the time and costs involved.

A recent survey by the journal *Antibiotics and Chemotherapy* revealed that 57 % of the readership who responded believed that the risk was unacceptable and the transgenic maize should be banned until the resistance gene is removed. A further 34 % considered that the risk was low but finite and that more work should be done before the maize is cleared for approval.

Despite concerns such as this, in 1998 the maize was grown on around 16,000 ha in Spain, probably about 3.5 % of the total crop, and 1,200 ha in France. It has been mixed with conventionally grown maize and is now untraceable. Undoubtedly commerce will be hoping areas will increase in future in the same way that GM crops have taken off in the USA and elsewhere. Globally (excluding China) there has been a 15-fold increase in the area of transgenic crops from 1.7 m ha in 1996, 11.0 m ha in 1997 and 27.8 m ha in 1998. It is against this background of exponential growth in the industry that the dangers have to be seen – the speed of introduction of this technology is staggering.

Other genetic material may also have unwanted effects. Although most risk assessment focuses on the gene causing the desired effect (such as disease or herbicide resistance), promoter and suppressor genes may behave unexpectedly. One common source of such genes is the cauliflower mosaic

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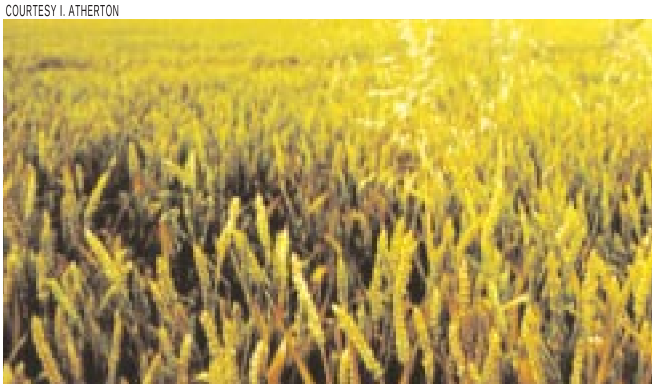

virus (CaMV). Studies looking at plant viral disease pathogenesis have shown that when transgenic brassicas containing CaMV sequences as suppressors or promoters are infected with CaMV, the functional transgene (such as herbicide resistance) may be switched off, presumably as a result of co-suppression following recognition of the homologous gene sequence. This is not just of research interest – commercial varieties of herbicide-resistant oilseed rape (a brassica) containing CaMV sequences are in the final stages of approval without the potential for crop failure (as a result of gene suppression) should a CaMV virus infection arise having been considered.

Concerns have also been raised about the potential for harmful effects arising as a result of the vectors that are used to transfer genetic material. In broad-leaved dicot crops the ability of *Agrobacterium tumefaciens* to transfer genetic material into the genome of the affected cell has been adapted for use in genetic engineering. Other vectors have been developed from bacteria and viruses to transform other bacteria, viruses and animal cells in many laboratories worldwide. How might the distribution of genetic material which facilitates gene transfer affect organisms? The likelihood that an organism may acquire characteristics which increase pathogenicity or alter host range could be increased. There has been little serious investigation of such risks, even though the outcome could be extremely serious.

The GMO may also behave unexpectedly in the environment. A GM disease or herbicide-resistant crop could become a troublesome weed in the right conditions. Crops are often weeds anyway, for example when seed is shed at harvest and it germinates and emerges in the following season or seasons. If these so-called 'volunteer weeds' were herbicide-resistant, farmers' weed control options may be made more difficult. This may be especially true for farmers who have fields of non-GM crops bordering those where a GM crop is grown. Pollen from oilseed rape can travel well over 1 km and thus cross-fertilization could result in a non-GM crop being partially pollinated by a GM crop. Completely unexpected herbicide resistant volunteer weeds could be the result. Organic farmers wanting to produce a GM-free crop will face similar problems if GM crops are grown close by.

The problem with all the direct risks is that the safety regulations rely completely on a case-by-case, step-by-step evaluation. The step-by-step approach takes testing from the laboratory to the greenhouse to small and then larger field trials. The assumption is that at each stage any adverse effects will be identified and only if it is safe will the containment be reduced. The difficulties are that each trial is contained, so that adverse effects will not be seen; most of the trials are looking at agronomic, not environmental, impacts and are small-scale and short-term. As well as having limited predictive capacity, each crop is assessed individually, neglecting the potential for cumulative effects. Thus considerable uncertainty remains even after supposedly rigorous safety testing.

For secondary effects on agricultural practice the situation is even worse. Little or no notice has been taken as to whether the introduction of GM crops will potentiate the effects of intensive agriculture. English Nature and the Royal Society for the Protection of Birds (RSPB) have called for a moratorium on the commercial use of GM crops until their potential impacts on biodiversity have been considered in more detail. The use of crops resistant to broad-spectrum herbicides could alter weed flora and remove important food sources for birds already under pressure from conventional agricultural systems. Insect-resistant crops, where the toxin is expressed throughout the life of the crop, could harm non-targeted beneficial insects ingesting pests which have fed on the crop. If many different crops are modified in this way, the effects on the food web could be very serious. There are few data on these aspects.

Socio-economic impacts have received even less official attention. The presumption behind policy is that GMOs are good for competitiveness, jobs and agriculture. If the US are doing it, so must we. However, whether jobs will be created is questionable – more 'efficient' intensive agriculture has been paralleled by job losses, not gains. The biotechnology industry will also be replacing traditional crop breeders. Public opinion shows there is a healthy market for non-GM foods which will have to go outside Europe to be met if GM crops are grown here. Again there remain more questions than answers.

Considerable uncertainty remains around all the possible impacts of GMOs. People are right to be asking questions and demanding a say in whether risks are justified or not. But to evaluate the potential impacts takes time. With a technology having such a broad spectrum of possible effects, an integrated approach needs to be developed. Our present approach cannot deal with such complexities and before embarking on wholesale adoption of the technology with its irreversible consequences we need to take a break, have a moratorium, look more deeply at the issues and develop the systems to cope with them. Now is the time to do that before it's too late.

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Further reading

Pechere, J.-C. (1998). Concerns about the presence of a β-lactamase gene in a transgenic maize. *Newsl Int Soc Chemother* Dec, 16.