GENETIC MODIFICATION: The need for special regulation

GeneWatch UK

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In 2003, the government will decide whether to allow the commercial growing of the first genetically modified (GM) crops – maize, sugar beet and oilseed rape – which have been made tolerant to herbicides. Some people argue that GM is an extension of conventional breeding practices and the outcomes (whether benefits or risks) could also arise from non-GM techniques of crop or animal production. Consequently, they believe that GM should not be 'discriminated' against or 'singled out' for special demands in terms of liability or other regulations such as labelling.

However, GeneWatch and many others believe that for a whole host of reasons – technical, social, cultural and economic – GM is different and demands particular attention. There are technical differences which have to be seen in the context of the forces driving the application and use of the technology. These wider issues shape the nature, scale and likelihood of different impacts. Therefore, certain regulatory responses are required and people should have the right to choose whether to buy GM products. It must also be made clear who will be responsible for any harm that arises. At such an important time for the future of GM agriculture in the UK, this briefing reviews why GeneWatch believes GM is different and requires a comprehensive approach to its regulation.

GM is promoted and supported by government and industry

GM crops are presented in official, scientific and industrial circles as having far-reaching potential. This potential, it is said, includes making industry more competitive, transforming agricultural production, and even addressing world hunger. The special ability that GM brings to transform plants in new ways - with promised advantages for industry, farmers, consumers and the environment - has driven policy in both the UK and Europe since the middle of the 1980s[1]. Under successive European Framework research programmes, genetic modification has been given special status and encouragement. Putting into place a supportive régime (including regulation to address the risks) has been a key objective of the EU in relation to biotechnology. The large majority of public funding for research on GM crops and foods has been spent on science to facilitate their development rather than research into their impacts[2]. Clearly, in science policy and elsewhere, GM has been singled out for special treatment and promotion in ways that other techniques have not. This difference for GM and other genetic technologies - that it can be a very profitable enterprise that will underpin industry - has not been argued for other methods of plant or animal breeding.

In fact, GM is treated differently at all levels in science and in science and technology policy. Efforts to downplay difference only emerge when citizens request choice, raise questions and ask for a voice in decision making. However, while bureaucrats, industry and politicians emphasise the potential benefits as a reason for special support, these benefits are contested by the public. Recent research[3] has reinforced past studies which show that the public does not accept benefits to the biotechnology industry and farmers that may arise from currently available GM crops as social benefits.

GM can change organisms in ways not possible with non-GM techniques

There are also specific differences about GM and genetically modified organisms (GMOs) from a technical and scientific perspective which demand special attention, especially when our knowledge is limited. Examples of how GM raises new questions include:

- **Entirely new compounds can be produced in plants and other organisms** – Among the next generation of GM plants - following on from those which have been developed for herbicide tolerance and insect resistance - are plants which produce drugs (vaccines, antibodies and therapeutic/diagnostic proteins). In the USA, four proteins for use in research and diagnostics are being produced commercially in GM maize by the company, Prodigene - avidin[4], β-glucuronidase[5], aprotinin[6] and trypsin[7]. These are biologically active compounds where the environmental consequences of their presence in plants are largely unresearched, although avidin, for example, is known to have insecticidal qualities. No gene containment measures are used and movement into food is possible over time if the area of use extends and controls fail. The National Academy of Sciences in the USA has criticised their relative lack of regulation[8]. Very recently (November 12th 2002), the US Food and Drug Administration fined Prodigene £2 million and ordered the destruction of soybeans grown on fields previously used by the company because they were contaminated with residues of GM maize used for the experimental production of a pig anti-diarrhoea vaccine[9,10].

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This novelty is not restricted to plants. Viruses have small genomes and genetic modification presents some limited opportunities to increase the capacity of viruses to produce new products, something which could not be achieved by other means. For example, plant viruses have been modified to produce proteins that may be useful as vaccines[11,12,13,14]. The GM viruses are then used to infect plants where the virus replicates and its vaccine protein is produced. The vaccine is then harvested from the plant. Using viruses in this way by adding to their genomes is a new technique, so we have no previous experience to inform any evaluation of its safety.

- **Completely novel mechanisms for agronomic properties can be achieved** – Conventional breeding and non-GM methods using chemicals or radiation to mutate a plant's genes (mutagenesis) can achieve herbicide tolerance and disease resistance. However, GM has introduced completely new mechanisms to achieve these and other traits, often through the introduction of genes from different species. In relation to viral disease resistance, this has been accomplished through the introduction of genes from viruses which confer resistance through unknown mechanisms. Professors Alan Gray and Ian Cooper have observed that[15]:

> *"When the transgenes derive from viruses, they are substantially different from current 'natural' resistance/tolerance traits in terms of context and ubiquity. Their presence introduces a substantially new dimension into the dynamics of plant/virus coevolution, even though virus-derived nucleic acids are normal constituents of natural plant populations where they undoubtedly contributed to the evolution of viruses. Hitherto, virus evolution has been affected by multiple infections constrained, at least in part, by the serendipitous behaviour of vectors. There is a risk that the spread of virus-derived transgenes will eliminate this element of chance as the presence of viral nucleic acid becomes uncoupled from vector behaviour".*

Other mechanisms to produce viral resistance in plants include the use of a human viral defence mechanism where a gene coding for a protein triggered by interferon in mammals is introduced into the plant[16].

GM techniques are also being used to 'improve' plant breeding using mutagenesis by chemicals and radiation because these techniques have a random and unpredictable effect. A faulty human gene implicated in hereditary colon cancer in humans has been used in GM animals, plants, human cells and microorganisms[17]. The faulty gene leads to the failure of normal gene repair mechanisms and makes cells become 'hypermutable' – that is, they are likely to mutate very easily, especially when exposed to chemicals or radiation, but even when they are not. To have more control over the mutations produced, the faulty gene is linked to a 'gene of interest' so only this gene mutates and not others. However, the plant kingdom does not appear to have this gene repair mechanism at all (it is restricted to animals and microorganisms), let alone a defective version.

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Transferring mechanisms from one kingdom to another (e.g. animal, human or viral to plant) is not possible through non-GM methods and raises complex questions about potential impact, particularly if these techniques become widely used and the organisms are multiplied on a large, commercial scale. There is no evolutionary precedence for such organisms and there are no data upon which to base an assumption that GM plants will behave in a similar way to changes induced by other methods – they may or may not. There are very few data which compare the behaviour of plants produced using different methods. The advent of genetic modification heralds the introduction of completely new mechanisms of disease control, insect resistance and herbicide tolerance, not only into crop species but most likely, over time, into related wild species.

- **GM allows the same genes and constructs to be used across all species globally** – The development of GM has led to the same genetic constructs being used across a variety of different crop species and across several continents. GM insect resistant cotton based on the *Bt* Cry1A gene is being used in North and South America, Africa, Australia and Asia. Monsanto's GM herbicide tolerant *Roundup Ready* soybean, cotton, maize and oilseed rape are also in commercial use. *Roundup Ready* potatoes and wheat are expected shortly and many other *Roundup Ready* crops are likely to follow. This raises whole new questions for genetic vulnerability – for example, could resistance emerge on a global scale? This risk is intensified by the prevailing economic incentives and intellectual property arrangements which encourage the use of the same genes and techniques in as many varieties of the same crop and in as many different crops as possible[18]. It is not possible through conventional breeding or mutagenesis to impose this form of genetic uniformity across species and continents. There are real issues for food security should there be rapid emergence of insect and weed resistance, for example.

Genetic modification may result in lack of operation of genes, instability or interference with other gene functions

- **Novel unpredicted effects may arise** – GM, like chemical and radiation induced mutagenesis, can cause unintended changes to the genome. Genes may be disrupted and normal function affected. However, in contrast to mutagenesis, where changes are made to the existing genome, genetic modification may - and usually does - involve the addition of genes. A particular additional issue for genetic modification is that many copies may be integrated, additional fragments inserted, gene sequences rearranged and deleted[19,20,21], which may result in lack of operation of the genes, instability or interference with other gene functions. In farm animals, it is quite clear that GM brings a raft of completely novel potential impacts, completely outside any experiences with conventional breeding[22].

As a recent paper noted[23]:

> *"It is incorrect to assume that the current methods of genetic engineering used to express single transgenes in plants are completely targeted and will have no, or minimal, effects on unrelated biochemical pathways in untransformed plants".*

This paper was reporting on unintended and unforeseen changes in GM insect resistant potatoes based on introduced lectin genes (including one of the same lines of GM potatoes used in Arpad Pusztai's infamous experiments – see GeneWatch Briefing No 9[24]). Levels of glycoalkaloids (chemicals naturally present in potatoes and thought to be associated with a natural insect resistance mechanism) were reduced in the GM plants compared to controls. The effect was considered to be attributable to *"target gene insertion, marker gene insertion, chromosomal re-arrangements, altered gene expression and/or tissue culture"*. GM was found to increase changes seen in tissue culture alone.

- **Knowledge of gene function is limited and prediction difficult** – Some people have argued that because GM involves the use of genes with well known functions, this makes it less 'risky' and more predictable in outcome than when other techniques are used. However, our knowledge of genetics is limited and findings from studies such as the Human Genome Project have shown that there are far fewer genes in higher organisms than was predicted – 30-40,000 in humans rather than the 120-140,000 originally estimated[25]. This means that genes or parts of genes may be involved in different functions, depending on how they are 'read' by the cell and which other genes are involved. This undermines the assumption that adding a gene with one known function means that this is the only way it will behave in practice[26]. Indeed, the detailed functioning of DNA is not well understood. The introduction of a gene into two different cells can result in different outcomes and the overall pattern of gene expression can be altered by the introduction of a single gene making the prediction of outcomes extremely difficult if not impossible[27]. Scientific theories and understanding of the ways in which genes work are constantly developing, giving new insights into the complexity of gene function[28].

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GM has led to monopolisation of genes and genetic technologies

The advent of GM and associated technologies has driven changes in the accepted rules of intellectual property rights and what is termed 'discovery' and 'invention'. The biotechnology industry has insisted on having intellectual property protection (patents) for genes and the cells, plants and animals developed using genetic techniques. A new Directive was introduced in Europe in 1998 which facilitated the patenting of living organisms. Pressure is being exerted on developing countries to bring their intellectual property protection for plants and animals in line with that in the developed world through the TRIPs agreement (trade-related aspects of intellectual property rights).

Patents on genes, cells, plants and animals and the techniques used in their production are leading to the monopolisation of certain species by private interests. This can lead to the virtual monopoly control of future modification of crops. One example is cotton, where Monsanto has patents on the genes for tolerance to the herbicide glyphosate and for *Bt* insect resistance. On acquiring the company Agracetus in 1997, it also gained access to its patent portfolio which included US patent 5,159,135, which has exceptionally broad scope, covering all GM cotton. Monsanto has also made 90% of the patent applications for cotton genes[29]. Other companies are using Intellectual Property Rights (IPRs) to gain control over other staple crops. This situation raises important questions for the control of GM science and for food security.

Two recent UK reports have now questioned whether allowing patents on genes is in the public interest because innovation may be stifled, not encouraged[30], and have recommended that developing countries do not allow patents on genes, plants and animals in order to protect their food security[31].

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GM has intensified concentration of the seed market

The advent of genetic modification and the potential to alter organisms more rapidly and in ways not achievable through conventional breeding attracted the agro-chemical industry to invest in GM crops. Through a series of acquisitions of seed companies and mergers between agrochemical companies, there has been a consolidation of the seed market. In the US, concentration of the seed market and of transgenic crop research is at levels where action to prevent excessive monopoly control could be considered[18]. Ten seed companies now own one third of the world's commercial seed market. The Commission on Intellectual Property Rights recorded in its report[31] (p65) that:

> *"…in Brazil, following the introduction of plant variety protection in 1997 (but presumably also related to the expected permission to grow GM crops) Monsanto increased its share of the maize seed market from 0% to 60% between 1997 and 1999. It acquired three locally based firms (including Cargill as the result of an international deal), while Dow and Agrevo (now Aventis) also increased their market share by acquisition. Only one Brazilian-owned firm remained with a 5% market share. This trend appears widespread in developing countries".*

This consolidation of seed markets, facilitated by GM technology and favourable intellectual property arrangements, poses real dangers for food security if seed becomes too expensive for poorer farmers and no alternative exists. Such consequences are related to GM, not other plant breeding techniques. It is sometimes argued that these changes would have arisen anyway and are not associated with the genetic modification technique. To some extent this will be true, but the way in which GM and large corporate interests intersect and drive each other can be seen in the statement by the Chairman of Syngenta's Board in their latest (2002) Annual Report:

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> *"Industry consolidation in pursuit of economies of scale will continue. Research in biotechnology, with seeds as the key platform for delivering biotech traits, offers opportunities for higher-value, higher-quality outputs and increased returns in future…Finally, consolidation at the dealer and distributor level will continue".*

As the Food Ethics Council argued in its recent report, *"TRIPS with everything"*, the technology of GM allows patentable products to be produced which influences the market structure[32].

GM has driven the privatisation of biological research

The advent of genetic modification coincided with a political change in science policy and funding. The drive towards wealth generation as a fundamental aim of science funding rather than, say, knowledge acquisition, has forced the biological sciences to focus on those areas where commercial applications are more likely. This has led to genetic technologies being favoured over other areas of science.

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This privatisation of scientific knowledge in the biological sciences is not restricted to genetic technologies but because of the emphasis that has been placed on this area of research and development, it has shaped the trajectory of genetic science. It has determined what questions have been asked and those that have remained unanswered. In this way, GM is being introduced under a different approach than for plant or animal breeding in the past, where the enterprise was centred in the public sector. This affects the purposes to which GM is put and, therefore, the consequences will be different too.

GM alters accepted notions of species barriers

The movement of genes between unrelated species challenges accepted social and cultural (and scientific) meanings of species. As such, it raises questions about our sense of order in the natural (non-human) world. Moving genes between species will, as out-crossing takes place between GM and wild species, raise questions for conservation and the value that is being placed on conserving genetically distinct populations and sub-species of organisms. Not only will there be movement from domesticated species to wild populations but genes from unrelated species may enter certain populations and pose challenges for species preservation.

Like the contamination of Antarctica and its ecosystems with persistent chemicals, the movement of genes will be unseen, but human actions will have irreversibly altered the evolutionary divergence between species in fundamental and possibly dramatic ways. This basic intrusion of human activity into the genetic make-up of other species raises ethical and cultural concerns. Whether we want to take this step or not under the present or different conditions is an important question and marks GM as a watershed.

Conclusions – If GM is different, what does this mean for regulation?

A whole range of issues marks GM as ‘different’, so what does this mean for policy and regulation?

The risks may not be evaluated fairly or the research to do so will not be supported

Firstly, there are powerful interests pushing the technology, attracting financial investment and establishing intellectual property rules that support a certain industrial model which is consolidated and global. This brings with it certain hazards, including that the risks may not be evaluated fairly or the research to do so will not be supported. It also raises questions about food security, particularly for the developing world. There needs to be some balance introduced into this:

- Other agricultural strategies should be supported, not just biotechnology exclusively (or largely).
- Intellectual property laws need to take account of the developing world as well as the developed world.

- The global nature of the industry and risks has to be reflected in regulatory mechanisms.

Secondly, because current risk assessments tend to be narrowly focused, they do not capture the potential problems adequately. This is particularly true because of the far-reaching changes that GM can introduce, the possibility that impacts may not be reversible, the likelihood of surprises given our current state of knowledge, and the types of GMOs being produced because of a privately driven research agenda. Therefore, the framing of assessments should include comparative evaluations (other food production systems, for example), the question of need, and socio-economic criteria. Because of past institutional denial of scientific uncertainty and the potential for surprises, there should be greater exploration of their implications for our ability to predict harm through sensitivity analysis and other techniques. Monitoring, through labelling and traceability, is one other important dimension of a precautionary approach to GMOs.

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Thirdly, and as importantly, there is an underlying dispute about the benefits of GM for the current generation of products at least. A lack of public acceptance that the benefits will be 'social' (rather than largely for the biotechnology industry) drives three clear regulatory demands:

- that there must be labelling and choice;
- that non-GM options must be available and given social support;
- that liability (or clear responsibility) for any economic harm to non-GM farmers and for damage to the environment and human health should not fall on society or individuals but lie with the industry.

As the debate about whether to grow GM crops commercially in the UK proceeds, GeneWatch UK believes that all these dimensions must form part of the discussion about the 'terms and conditions' under which we proceed or not.

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GeneWatch UK

The Mill House, Manchester Road, Tideswell, Buxton, Derbyshire, SK17 8LN, UK
Phone: 01298 871898   Fax: 01298 872531   E-mail: mail@genewatch.org

Website and online database: http://www.genewatch.org

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