SESSION 1

GENETICALLY MODIFIED CROPS – THE CURRENT SITUATION

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Transgenic plants: field testing and commercialisation including a consideration of novel herbicide resistant oilseed rape (*Brassica napus* L.)

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ABSTRACT

From the first experimental field release of a transgenic plant (TP) in 1986, over 60 different species have been transformed using recombinant DNA techniques and released in confined experimental field trials. Following the first commercial TP release in 1992 the cultivated area of TP's has increased dramatically. In 1998 at least 69 million acres of TP's with novel herbicide tolerance and insect resistance were grown, predominantly in North and South America. In Europe, few TP's have received regulatory approval and cultivation of these crop varieties is very limited. Of the TP's already grown on a large acreage, *Zea mays* (maize/corn), *Brassica napus* (oilseed rape/canola) and *Gossypium hirsutum* (cotton) naturally outcross within the species, and of these *B. napus* is known to be able to outcross with certain related species that occur in some production areas. Because of this, the incorporation of novel herbicide resistance into *B. napus* using rDNA technology is viewed by many people as a major concern.

EXPERIMENTAL RELEASES OF TRANSGENIC PLANTS

Summary statistics from the OECD Field Trial Database (see Internet URL's) show that 98.3% of experimental releases of genetically modified organisms in Member countries are transgenic plants. These are made up of 38% *Zea mays*, 13% *Brassica* sp., 12% *Solanum tuberosum*, 10% *Lycopersicon esculentum*, 9% *Glycine max*, 7% *Gossypium hirsutum*, 5% *Nicotiana tabaccum*, 2% *Beta vulgaris*, with the remaining 4% made up from the other species listed in Table 1. The first experimental release[1] took place in 1986 and the number rose steadily to a maximum of just over 1400 in 1995. Releases declined to 1300 and 900 respectively in 1996 and 1997 as transgenic plant material in regulated "confined" trials in previous years were approved (deregulated) for commercial use. By far the greatest number of experimental releases amongst the OECD Member countries (70.5%) have been in the United States followed by Canada (11.9%), France (4.7%), Belgium (2%), UK (1.8%), Italy (1.7%), Holland (1.5%), Spain (1.2%) and Japan (1.2%) with 3.5% of releases in the remaining OECD Member countries. China has an active programme for testing and commercialising TP's (James, 1997), however, this data is not included in this paper.

Numerous novel traits have been introduced into TP's. Many early confined field releases were of plants that expressed marker proteins, in particular those expressed by the GUS gene, NPTII antibiotic resistance gene and herbicide resistance genes. These field tests were primarily to determine whether the growth, development and reproductive biology of the genetically modified host plant had been altered by the actual process or rDNA insertion. Apart from the delayed ripening tomato that provided benefits directly to the

[1] A release is an approval/permit to test a specific modification in a specific plant in one or more locations.

consumer, modifications were intended to be of benefit to the crop production and processing industries. TP's with novel herbicide resistance, insect resistance, virus resistance and a male sterility system for hybrid seed production, together with tomato lines with altered ripening qualities, made up the bulk of experimental field tests. More recent experimental releases have included TP's with tolerance to abiotic stress, resistance to fungal pathogens, modified quality (such as oil, starch and livestock feed components in the harvested part of the plant) and those producing specialty chemicals such as vaccines, pharmaceutical compounds and "feed" compounds for industrial processes such as plastics production.

Table 1. Plant species subject to rDNA modification and experimentally tested in confined field trials. (OECD Field Trial Database)

Actinidia deliciosa	Kiwi fruit	*Ipomea batatas*	Sweet potato
Agrostis stolonifera	Creeping bentgrass	*Juglans* sp.	Walnut
Allum cepa	Onion	*Lactuca sativa*	Lettuce
Arabidopsis thaliana	Thale Cress	*Linum usitatissimum*	Flax
Arachis hypogea	Peanut	*Liquidambar* sp.	Sweetgum
Asparagus officinalis	Asparagus	*Lupinus angustifolius*	Lupin
Atropa belladona	Belladonna	*Lycopersicon esculentum*	Tomato
Beta vulgaris	Sugar beet	*Malus domestica*	Apple
Betula pendula	Silver Birch	*Medicago sativa*	Alfalfa
Brassica carinata	Ethiopian mustard	*Nicotiana benthamiana*	Tobacco
Brassica juncea	Mustard	*Nicotiana tabaccum*	Tobacco
Brassica napus	Canola/Oilseed rape	*Oryza sativa*	Rice
Brassica oleraceae	Cabbage/Broccoli etc.	*Pelargonium* sp.	Pelargonium
Brassica rapa	Canola/Oilseed rape	*Picea abies*	Norway spruce
Capsicum annuum	Pepper	*Picea* sp.	Spruce
Carica papaya	Papaya	*Pinus sylvestris*	Scots Pine
Castanea sp.	Chestnut	*Pisum sativum*	Pea
Cichorium intybus	Chicory	*Populus* sp.	Poplar
Citrullus lanatus	Watermellon	*Prunus domestica*	Plum
Cucumis melo	Melon	*Rosa* sp.	Rose
Cucumis sativus	Cucumber	*Saccharum officinarum*	Sugar cane
Cucurbita pepo	Squash	*Sinapis alba*	White mustard
Daucus carota	Carrot	*Solanum melongena*	Eggplant
Dianthus caryophyllatus	Carnation	*Solanum tuberosum*	Potato
Eucalyptus sp.	Eucalyptus	*Tagetes* sp.	Marigold
Fragaria sp.	Strawberry	*Trifolium subterraneum*	Clover
Gladiolus sp.	Gladiolus	*Triticum aestivum*	Wheat
Glycine max	Soybean	*Vaccinium oxycoccus*	Cranberry
Gossypium hirsutum	Cotton	*Vitis vinifera*	Grape
Helianthus annuus	Sunflower	*Zea mays*	Corn/Maize
Hordeum vulgare	Barley		

COMMERCIAL RELEASES OF TRANSGENIC PLANTS

The regulatory procedures for approving TP's for commercial release and marketing fall into three safety assessment and approval areas: release into the environment; human food use; and, animal feed use. They follow a step wise approach that has evolved over 20 years of collaborative work among experts from governments, international government organisations, non-governmental organisations, academia and industry associations, and although different regulatory agencies in different countries use different legal instruments for the purpose of regulation, the procedures and information required for safety assessments are remarkably similar (OECD 1995a, 1995b).

The OECD Product Database, part of the OECD "BioTrack Online" internet site (see Internet URL's) provides information on commercial TP approvals for growing, food and feed use in Member countries (Table 2). These now include some TP's with stacked genes resulting in two or more novel traits in the same plant cultivar.

Table 2. Transgenic plant species with novel traits approved for commercial release by at least one regulatory agency (OECD Product Database)

Beta vulgaris	novel herbicide[1,2,3] resistance
Brassica napus	novel herbicide[1,2,3] resistance, male sterility and novel herbicide[2] tolerance stacked, modified fatty acid profile
Brassica rapa	novel herbicide[1] resistance
Carica papaya	virus resistance
Cichorium intybus	male sterility and novel herbicide[2] resistance stacked
Cucurbita pepo	virus resistance
Dianthus caryophyllus	novel flower colour, extended vase life
Glycine max	novel herbicide[1,2] resistance
Gossypium hirsutum	lepidopteran insect resistance, novel herbicide[1,3,4] resistance lepidopteran insect resistance and novel herbicide[3] resistance stacked
Linum usitatissimum	novel herbicide[4] soil residue resistance
Lycopersicon esculentum	modified ripening, lepidopteran insect resistance
Nicotiana tabaccum	novel herbicide[2,3] resistance
*Oryza sativa**	novel herbicide[2] resistance
Solanum tuberosum	coleopteran insect resistance, virus resistance, coleopteran insect resistance and virus resistance stacked
Zea mays	novel herbicide[1,2,3,4] resistance, lepdipopteran insect resistance, lepidopteran insect resistance and novel herbicide[1,2] resistance stacked, male sterility and novel herbicide[2] tolerance stacked

* Under review by USDA (see Internet URL's)

1 Glyphosate herbicide resistance

2 Phosphinothricin (glufosinate ammonium) herbicide resistance

3 Oxynil herbicide resistance

4 Sulfonyl urea herbicide resistance

CULTIVATION OF TRANSGENIC CROPS WORLD-WIDE

James (1997, 1998) at the International Service for the Acquisition of Agri-Biotech Applications has collated data on the acreage of commercial TP production. In 1996 approximately 7 million acres of 7 transgenic crops were grown in the USA, China, Canada, Argentina, Australia and Mexico. In that year the principal crop was *Nicotiana tabaccum* (tobacco in China) followed by *Gossypium hirsutum* (cotton), *Glycine max* (soybean), *Zea mays* (corn), *Brassica napus* (oilseed rape/canola), *Lycopersicon esculentum* (tomato) and *solanum tubersoum* (potato). Of the transgenic crop area, 57% was in industrial countries and 43% in developing countries (principally China with 2.7 million acres). By trait, virus resistance (40%, again almost entirely in China) was followed by insect resistance (37%), herbicide [novel] resistance (23%) and quality traits (<1%). Data for 1996, 1997 and 1998, are presented in Tables 3 and 4, and country production for 1997 and 1988 is shown in Table 5. The adoption of TP culture, particularly in North and South America, has been rapid. (NOTE that data for China are not presented in the tables.)

Table 3. Acreages of TP's by species (James, 1997 and 1998), excluding China

By crop plant species	1996		1997		1998	
	10^6 Acres	%	10^6 Acres	%	10^6 Acres	%
G. max (soybean)	1.3	31	12.8	46	36.3	52
Z. mays (maize/corn)	0.7	17	8.0	30	20.8	30
G. hirsutum (cotton)	1.9	45	3.5	13	6.3	9
B. napus (oilseed rape/canola)	0.3	7	3.0	11	6.0	9
S. tuberosum (potato)	<0.1	<1	<0.3	<1	<0.3	<1
Total	4.2	100	27.5	100	69.50	100

Table 4. Acreages of TP's by novel trait (James, 1997 and 1998), excluding China

By novel trait	1996		1997		1998	
	10^6 Acres	%	10^6 Acres	%	10^6 Acres	%
Novel herbicide resistance	1.6	38	17.3	63	49.5	71
Insect resistance	2.6	62	10.0	36	19.3	28
Novel herbicide resistance and insect resistance stacked	-	-	<0.3	<1	0.8	1
Quality traits	<0.1	<1	<0.3	<1	<0.3	<1
Total	4.2	100	27.5	100	69.50	100

Table 5. Acreages of TP's by country (James, 1997 and 1998) excluding China, and, 1996 FAO data showing total arable land

Country	1997 acres x 10^6	%	1998 acres x 10^6	%	1996 Total arable acreage x 10^6
USA	20.3	74	51.3	74	432.098
Argentina	3.5	13	10.8	15	61.728
Canada	3.3	12	7.0	10	112.000
Australia	0.3	1	0.3	1	123.484
Mexico	<0.3	<1	0.3	1	62.444
Spain	0	0	<0.3	<1	37.615
France	0	0	<0.3	<1	45.156
South Africa	0	0	<0.3	<1	37.000
United Kingdom	-	-	-	-	15.037
Total	27.5	100	69.5	100	926.562

TRANSGENIC HERBICIDE TOLERANT PLANTS

Data for 1998 (Table 4) show that of the novel traits grown world-wide, novel herbicide resistance had the largest acreage (71%), followed by *Bacillus thuringiensis* (Bt) ∂endotoxin derived insect resistance (28%), combined Bt insect resistance and herbicide resistance (1%) and quality traits (<1%).

For some years the popular press has given much attention to the issue of transgenic herbicide resistant crop plants, though generally not identifying this as "novel" herbicide resistance, and has emphasised the potential for development of superweeds (not clearly defined), generating much public concern and scientific and political debate. This is particularly true in the case of transgenic herbicide resistant oilseed rape/canola (*B. napus*). because of its natural ability to exchange genes, as either father or mother, with certain of its related species (OECD, 1997).

HERBICIDES - *BRASSICA NAPUS*: THE EXISTING PARADIGM

The development of new crop plant varieties results from a collaborative effort among several interested parties, and the growth of the Canadian oilseed rape/canola industry over the past 40 years is a good example of this. Food retailers in many countries provide information of their, and their consumers', preferences to the food processors and commodity shippers who in turn advise the plant breeders and the farming community of the quality requirements of the oilseed. Farmers also provide the plant breeders with the agronomic quality characteristics they require. This close collaboration among plant breeders, growers, processors and oilseed marketers has resulted in the regular setting of ever higher standards which have to be met by new canola cultivars (*B. napus* and *B. rapa*) if they are to become registered varieties. Processors have required higher seed oil and

protein with low to zero levels of erucic acid in the oil and glucosinolates in the meal. Growers have required higher seed yield, improved disease and insect resistance, reduced shattering and lodging, and uniform plant growth and time to maturity (Downey and Röbbelen, 1989).

During this same time selective herbicides have been used by growers to control weeds with little or no damage to the crop plant, increasing yields for farmers and reducing weed seed "dockage" for processors. Selective herbicides have been a key part of the Canadian canola industry success story. Quality for the oilseed processors was further improved with the introduction of selective herbicides controlling species closely related to canola e.g., *Sinapis arvensis* (wild mustard) that when harvested with the crop could elevate levels of both erucic acid and glucosinlates in the final product. This was the existing canola variety breeding paradigm when rDNA technologies first became available to plant breeders.

HERBICIDE RESISTANT WEEDS: THE EXISTING PARADIGM

It is doubtful that all of the almost 1 billion acres of arable land shown in the countries listed in Table 5 have herbicide applied to crops grown on them, yet it is questionable that any of those acres are sown to crops that don't have tolerance[2] to one or more selective herbicides, i.e., their billion acres already have had herbicide tolerant crops growing on them. A major goal of herbicide producers over 50 years has been to develop "selective" herbicides that control as many weed species as possible without damaging crop plant species, and in this there has been good success. However, as predicted by Harper (1957) ill conceived management practices that relied on the same herbicidal mode of action in the same fields for several years resulted in the selection of those rare, naturally occurring, individuals within weed species populations that are resistant. The Weed Science Society of America (WSSA) provides data on weed species that have developed populations resistant (novel resistance) to specific herbicidal modes of action (Heap: see Internet URL's). WSSA reports 216 instances worldwide; 120 dicots and 216 monocots. Triazine herbicides have the most resistant weed species (60) the acetolactate synthase (ALS) disrupting herbicides (53), bipyridliums (26) and ACCase inhibitors (19). Some species, especially grasses, now have multiple herbicide resistances. These naturally occurring, but rare herbicide resistances can also be found in somaclonal variants, and in weed species closely related to crop plants. Some of these resistances have been incorporated into commercially available *B. napus* and *B. rapa* varieties. In Canada, plants with novel herbicide resistance (plants with novel traits) are subject to safety assessment no matter how they are developed, however, in other countries they are not subject to the same regulation and safety assessment as their rDNA derived counterparts, even should they have resistance to the same herbicide family.

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[2] The Weed Science Society of America uses the term "resistance" to describe the inherent ability of a plant to survive and reproduce following exposure to a dose of herbicide normally lethal to the wild type. In a plant, resistance may be naturally occurring or induced by such techniques as genetic engineering or selection of variants produced by tissue culture or mutagenesis.
Herbicide "tolerance" is the inherent ability of a species to survive and reproduce after herbicide treatment. This implies that there was no selection or genetic manipulation to make the plant tolerant; it is naturally tolerant.

HERBICIDE RESISTANT *BRASSICA NAPUS*: THE NEWER PARADIGM

Maltais and Bouchard (1978) discovered triazine tolerant birds rape (*B. campestris* [=*B. rapa*]) in corn (*Z. mays*) fields in Québec where triazine herbicides had been applied over many years. This maternally inherited triazine resistance was incorporated into cultivated lines of *B. napus* and *B. rapa* oilseed rape (Beversdorf *et al.* 1980) and it was suggested the acquired triazine resistance could facilitate new and additional methods of weed control in oilseed rape. Triazine tolerant oilseed rape/canola varieties (*B. napus* and *B. rapa*) were developed, registered and have been grown in Canada especially where there are severe problems with related weed species, in particular *Thlaspi arvense*. Acreages have never been great since the reduced photosynthetic ability of the triazine resistant varieties resulted in a penalty, associated with a mutant photosystem II protein that prevented triazine herbicide binding, which lowered seed yielding ability.

WSSA data show that *Brassicaceae* weed species related to the oilseed rapes that have developed (been selected for) populations with novel herbicide resistance are *Brassica campestris* [=*rapa*] (oilseed rape/canola, bird rape, turnip), *B. tournefortii* (wild turnip), *Capsella bursa-pastoris* (shepherd's purse), *Raphanus raphanistrum* (wild radish), *Sinapis arvensis* (wild mustard), *Sisymbrium orientale* (Indian hedge mustard) and *S. thellungii* (African turnip weed). Of these, *B. rapa* and *R. raphanistrum* may naturally exchange genes with *B. napus*, although the potential for an exchange resulting in fertile offspring with *B. rapa* is very much greater that for *R. raphanistrum,* the latter being remote. As *B. napus* is an interspecific amphidiploid (n=19) sharing chromosomes from its two parents, *B. oleraceae* (n=9) and *B. campestris* [=*rapa*](n=10) this is expected (OECD, 1997). The probability of selecting mutant herbicide resistant *R. raphanistrum* compared with the probability of introgressing a transgene from *B. napus* conferring the same herbicide resistance is not known. These issues are discussed in detail in later papers.

Table 6 shows estimated acreages of Canadian registered varieties of *B. napus* resistant to glyphosate, phosphinothricin and imidazolinone herbicides. All have received regulatory approval (see Canadian Food Inspection Agency: Internet URL's).

Table 6. Estimated acreages of novel herbicide resistant oilseed rape/canola (*B. napus* and *B. rapa*) grown in Canada, 1996 – 1998. (Zeph: Pioneer HiBred International, pers. comm.)

Plant type	1996		1997		1998	
	10^6 Acres	%	10^6 Acres	%	10^6 Acres	%
B. napus varieties	6.21	69.0	10.41	86.0	12.24	92.0
B. rapa varieties	2.60	62.0	1.69	14.0	1.06	8.0
TOTAL	9.00	100.0	12.10	100.0	13.30	100.0
Glyphosate resistant	0.05	0.5	0.73	6.0	3.19	24.0
Phosphinothricin resistant	0.40	4.5	2.06	17.0	2.00	15.0
Imidazolinone resistant*	0.54	6.0	1.57	13.0	2.13	16.0
TOTAL novel herbicide resistant	0.99	11.0	4.36	36.0	7.32	55.0

*Imidazolinone resistance is NOT transgenic, but has been developed through somaclonal variation.

ENVIRONMENTAL SAFETY ASSESSMENT PARADIGMS FOR TRANSGENIC HERBICIDE RESISTANT *BRASSICA NAPUS*

In North America, the environmental safety assessment paradigm for TP's is based on a comparison of the novel varieties with their traditionally developed counterparts. This follows the environmental safety assessment model developed by the OECD Member countries (OECD 1993). The considerable "familiarity" gained from variety development and agronomic management practices have been used as a baseline in evaluating the potential risk of hazard of crops with novel herbicide resistance. Of course, the potential for different environmental interactions resulting from the presence of the novel proteins/enzymes conferring the novel trait are also considered. In the case of oilseed rape/canola it is accepted that gene flow between *B. napus* and certain related species, depending on the location of the release, might occur and that even though there is a remote possibility of introgression of herbicide resistance genes into these species, other existing cultural and chemical means can be used to control them. A more probable outcome is that gene exchange among oilseed rape/canola crops and its volunteers will lead to stacked transgenes in certain individual volunteer plants (see Canadian Food Inspection Agency Decision Documents: Internet URL's). Nonetheless it is considered that sound management practices will prevent serious problems from arising, whilst at the same time providing growers and oilseed rape/canola processors with improved "quality" oilseed rape/canola varieties.

In Europe there does not yet appear to be a consistent safety assessment and approval paradigm for oilseed rape/canola varieties with novel herbicide resistance. Recombinant DNA derived herbicide resistant varieties are subject to EC 90/220 regulation and safety

assessment, whereas wide cross and somaclonal variant derived varieties with novel herbicide resistances are not. This suggests that the existing paradigm for breeding and growing oilseed rape varieties using registered selective herbicides may not be considered adequate as a baseline for evaluating the new transgenic herbicide resistant varieties.

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Deliberate release of genetically modified organisms: the UK regulatory framework

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ABSTRACT

This paper reviews the development and operation of the regulations covering the release of genetically modified organisms (GMOs) in the UK. The regulatory framework aims to prevent or minimise damage to the environment by establishing a statutory system of risk assessment and prior consent, before any GMO can be released or marketed. Directive 90/220/EEC *on the deliberate release into the environment of genetically modified organisms* does much to harmonise the release of GMOs across the European Community. The Directive recognises two classes of release depending of the purpose; Part B releases for research and Part C releases for marketing. Individual Member States differ in how the Directive has been implemented and in the UK. No GMO may be released without the express consent of the Secretary of State. All UK applications for Part B (research) releases are submitted to the Department of the Environment Transport and the Regions, and the Advisory Committee on the Releases to the Environment (ACRE) advise whether the release should be allowed. In issuing consent the Secretary of State will also take account of views expressed by other Government Departments, the Statutory Nature Conservation Bodies and the general public. Applications for Part C (marketing) consent follow a different procedure and are submitted initially to any one of the 15 Member States, which then review the application and form an opinion. The other 14 States then evaluate the application. If there are no objections the lead Member State issues the marketing consent which applies throughout the European Community. If one or more State objects to the application then it falls to the Commission and Council to resolve. The current system, based on Directive 90/220/EEC, has been criticised mainly because of lengthy delays in obtaining marketing consent. Discussions are in progress to revise it in a number of key areas. An overview of the main proposed changes is given in the paper.

INTRODUCTION

No discussion of gene flow in agriculture can currently stray far from the challenges - real or imaginary - presented by the environmental release of genetically modified organisms (GMOs). The anti-GM pressure groups are quick to raise the spectre of gene flow from GM crops to wild relatives leading to 'superweeds' or, at the very least, the 'genetic pollution' of our botanical national heritage. In response it is often pointed out that herbicide tolerant weeds and hybridisation between conventional crops and their wild relatives or sexually compatible neighbouring crops are already common in the agricultural environment and not a feature unique to GM. Although they might be described as a nuisance in some agricultural situations they are not a significant threat to the environment.

Faced with the media hysteria that has surrounded GM crops and GM food in recent weeks, it comes as a surprise to many genuinely concerned observers that genetic modification is actually tightly regulated in the UK. In fact there are several layers of risk assessment and safety testing that take the GMO right from initial research and development in the laboratory through to testing in the environment and finally placing a product on the market.

This paper outlines briefly the regulatory framework in the UK[1] in as far as it controls the deliberate release of GMOs. The emphasis is placed on the *process* whereby the regulations are put into action and consent may be obtained to release GMOs either for experimental purposes or for commercialisation.

DEVELOPMENT OF THE DELIBERATE RELEASE REGULATIONS

The regulation of genetic modification has its roots in the early 1970s when scientists working at the forefront of the emerging technology recognised its potential power and called for a 'moratorium' until a number of safety concerns had been considered. In 1976 the Genetic Manipulation Advisory Group (GMAG)[2] was set up to consider proposals for work involving genetic manipulation. Soon afterwards, the *Health and Safety (Genetic Manipulation) Regulations 1978* came into force and required that any activity involving genetic manipulation [modification] should be notified to the Health and Safety Executive (HSE). These regulations only covered GM work in containment[3], and at this time the release of GMOs to the environment was controlled by a voluntary code of practice overseen by HSE.

The first specific controls over the environmental release of GMOs in the UK were provided by Part IV of the *Environmental Protection Act 1990*. At the same time the Environmental Protection Act was being drafted the European Commission was also preparing community legislation to control deliberate release, this later emerged as the now familiar *Council Directive 90/220/EEC on the deliberate release into the environment of genetically modified organisms*. Directive 90/220 was implemented in the UK by the *Genetically Modified Organisms (Deliberate Release) Regulations 1992*[4] (amended 1995 and 1997) and came into force on 1 February 1993.

AIMS AND PROVISIONS OF THE REGULATIONS.

The regulatory framework provided by these various statutory instruments aims to prevent or minimise damage to the environment by establishing a statutory system of 'prior informed consent' before any GMO may be released or marketed. In the UK this means that no GMOs may be released without the express consent of the Secretary of State. The regulations set out prescribed information (see below and Box 1) which must be supplied in an application for consent to do a deliberate release. Central to the approval process is an *environmental risk*

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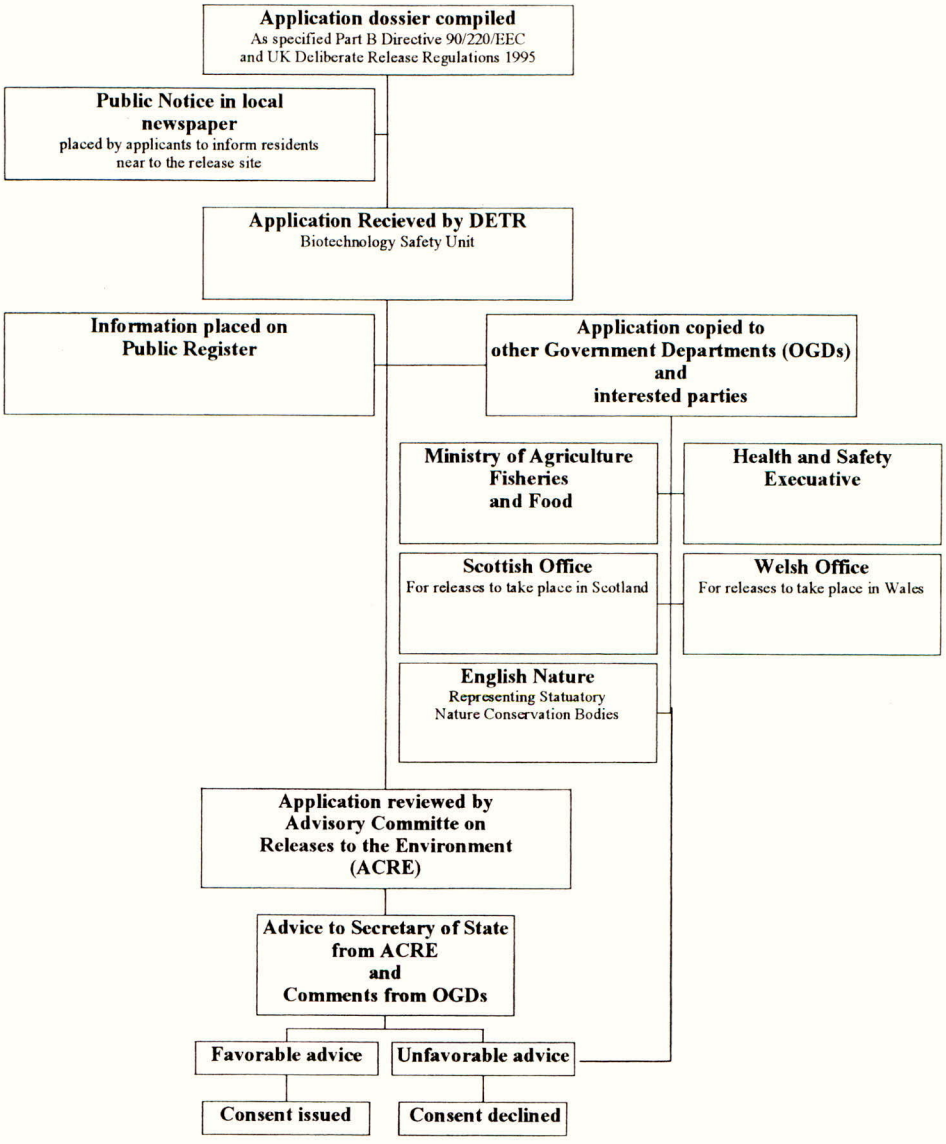
[1] The UK regulatory framework is intimately linked to the wider European Community controls over GMOs

[2] GMAG latter became the Advisory Committee on Genetic Modification (ACGM) which still advises Government today on the contained use of GMOs

[3] Contained Use of GMO refers to activities in, for example, research laboratories and industrial facilities

[4] These regulations also gave effect to the substantive provisions in Part IV of the *Environmental Protection Act 1990*

Figure 1. Flow diagram for obtaining deliberate release consent (Part B) in the UK



assessment which considers the potential risk to human health and the environment posed by releasing a particular GMO and, where necessary, identifies risk management procedures to avoid or minimise any damage. The regulations are framed in such a way that if it can be shown, to the best of current scientific understanding, that a release poses a low or negligible risk to the environment then it should be given the necessary consent to proceed.

Directive 90/220 recognises two broad categories for the deliberate release of GMOs[5] depending on the proposed purpose:

I. releases for *research and development*, which are made under *Part B* of the Directive, cover a number of activities but, in particular, are used mostly for conducting experimental field trials with GM crops.

II. releases for *placing on the market* are made under *Part C* of the Directive. Part C consent is necessary before a GMO may be used commercially or marketed within the European Community.

The principal procedural difference between these two categories of release is that Part B consents are granted at the national level on an individual Member State by Member State basis, whereas Part C marketing consents are granted at the European Community level. Once issued they apply across all Member States.

THE REGULATORY PROCESS: PUTTING THE REGULATIONS INTO ACTION

Although Directive 90/220 does much to harmonise the deliberate release of GMOs across the European Community there are nevertheless differences between the individual Member States in the ways in which the Directive has been implemented and the national procedures followed to obtain release consent. By way of illustration, the following section describes the process in the UK whereby Part B and Part C consent may be obtained. The example of seeking approval to release a GM plant will be used, but the process is essentially the same for all GMOs covered by the Directive.

Part B consent - releases for research and development

Applicants wishing to conduct an experimental field trial in the UK with GM crops must apply to the Secretary of State for consent to conduct the deliberate release (figure 1). The application is submitted to the Biotechnology Safety Unit of the Department of the Environment, Transport and the Regions (DETR). Applications consist of a dossier of information substantially composed of the responses to 41 prescribed questions (box 1) which are set out in schedule 1 to the 1995 regulations[6]. Taken together the questions and answers build up a detailed description of the GM plant, how it has been modified and the conditions of the proposed release. Importantly, each application dossier also contains a detailed environmental risk assessment which considers the potential harm that may be caused to

[5] Which are also reflected in our national deliberate release regulations

[6] *Genetically Modified Organisms (Deliberate Release) Regulations 1995*

Box 1. Information required under Schedule 1 of the 1995 Regulations for the Deliberate Release of Genetically Modified Higher Plants

General information

1. The name and address of the applicant.
2. The title of the project.

Information relating to the parental or recipient plant

3. The full name of the plant: family, genus, species, subspecies, cultivar,
4. Information on reproduction of plant: mode, generation time and the sexual compatibility with other cultivated or wild plant species.
5. Information on the survivability of plant: survival structures, dormancy etc.
6. Information concerning dissemination of plant: means, extent and factors affecting dissemination
7. The geographical distribution of the plant.
8. If the plant species is not normally grown in Member States, describe the natural habitat
9. Information on any significant interactions of the plant with organisms other than plants in the ecosystem where it is usually grown, including toxicity to humans, animals and other organisms.

Information relating to the genetic modification

10. A description of the methods used for the genetic modification.
11. The nature and source of the vector used.
12. The size, function and donor organism(s) of each DNA sequence intended for insertion.

Information relating to the genetically modified plant

13. A description of the trait(s) and characteristics of the GM plant which have been modified.
14. Information on sequences inserted or deleted: size/structure, copy number of insert, information on any vector sequences or foreign DNA remaining in the GM plant. The size/function of any deleted regions. Cellular location of insertion (e.g. chromosomal, mitochondria, chloroplast etc.).
15. Information on the expression of the insert: expression and parts of the plant where expressed.
16. How does GM plant differ from the recipient plant in: mode/rate of reproduction, dissemination, survivability
17. The genetic stability of the insert.
18. The potential for transfer of genetic material from the GM plants to other organisms.
19. Information on any toxic/harmful effects on human health and the environment arising from the genetic modification.
20. The mechanism of interaction between the genetically modified plants and target organisms.
21. Any potentially significant interactions with non-target organisms.
22. A description of detection and identification techniques for the genetically modified plants.
23. Information about previous releases of the genetically modified plants.

Information relating to the site of release

24. The location and size of the release site or sites.
25. A description of the release site ecosystem, including climate, flora and fauna.
26. Details of any sexually compatible wild relatives or cultivated plants present at the release sites.
27. The proximity of the release sites to officially recognized biotopes or protected areas.

Information relating to the release

28. The purpose of the release.
29. The foreseen dates and duration of the release.
30. The method by which the genetically modified plants will be released.
31. The method for preparing and managing the release site, prior to, during and after the release.
32. The approximate number of genetically modified plants (or plants per m^2) to be released.

Information on control, monitoring, post-release plans and waste treatment plans

33. A description of any precautions to minimize or prevent pollen or seed dispersal from GM plant.
34. A description of the methods for post-release treatment of the site or sites.
35. A description of post-release treatment methods for the GM plant material including wastes.
36. A description of monitoring plans and techniques.
37. A description of any emergency plans.

Information on potential environmental impact of the release of the genetically modified plants

38. The likelihood of the GM plant becoming more persistent or invasive than recipient plants.
39. Any selective advantage or disadvantage conferred to other sexually compatible plants species, which may result from genetic transfer from the genetically modified plant.
40. Potential environmental impact of the interaction between the GM plant and target organisms.
41. Any possible environmental impact resulting from potential interactions with non-target organisms.

human health and the environment and identifies ways in which the risks may be avoided or minimised.

On receipt of the application dossier, it is initially reviewed by specialist scientists (case officers) in the DETR Biotechnology Safety Unit who copy it for comment to other Government Departments which also have an interest. These Departments are the Ministry of Agriculture Fisheries and Food, the Health and Safety Executive, the Scottish Office[7] and the Welsh Office[8]. Details of each application and the environment risk assessment are also copied to English Nature, which in GMO matters represents the statutory Nature Conservation Bodies.

The deliberate release regulations also specify certain information[9] about each application which is required to be placed on a statutory public register[10] within 12 days of receipt of the application by DETR. This information includes, among other things, a summary of the application written in non-technical language, the location at which the release will take place and the environmental risk assessment. In practice, DETR go much further than is required by law and make all of each application available to the public, excluding the names of private individuals and any information agreed to be 'commercial in confidence'.

To aid transparency in the regulatory process the applicants are required to place an announcement of the proposed release in a newspaper circulating in the area where the release is planned. The announcement must be placed within 10 days of submitting the application to DETR and it gives concerned or curious members of the public the opportunity to write the Secretary of State to object or seek further information about the release.

Most applications when they are first submitted to DETR contain inadequate or ambiguous information and the case officer has the statutory power to request more information from applicants or clarify specific points. Once the case officer is content that the application contains sufficient detail and is compliant with the regulations then the dossier is put before the statutory Advisory Committee on Releases to the Environment (ACRE). ACRE is a scientific and technical committee made up of leading experts in subjects such as ecology, plant breeding, microbiology, plant and animal molecular biology and toxicology. The Committee advises the Government on the potential risks to human health and the environment from the release of genetically modified organisms. All members of ACRE are appointed by the Secretary of State for the Environment, together with the Secretaries of State for Scotland, Wales and Northern Ireland and the Minister for Agriculture Fisheries and Food. Members are appointed on the basis of their technical and scientific expertise. They do not represent any particular stakeholder interests such as the biotechnology industry or environmental pressure groups.

ACRE reviews all of the information in applications put before it with particular emphasis on the risk assessment and any proposed risk management procedures. Gene flow is always an

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[7] If a release is to take place in Scotland

[8] If a release is to take place in Wales

[9] Information prescribed under Part V section 17 of the Genetically Modified Organisms (Deliberate Release) Regulations 1992

[10] Held at DETR in London. Copies of the register are also held at regional offices of the Environment Agency and at the Scottish Office in Edinburgh

important part of the risk assessment where both the potential for gene flow and its consequences are considered. Often the Committee will advise that the risk management is not sufficient and indicate what must be done to make it acceptable. Similarly the Committee may instruct the Secretariat (provided by DETR Biotechnology Safety Unit) to seek more information from applicants. When ACRE is content that the proposed release poses a low risk to human health and the environment, then the Committee will advise the Secretary of State that the consent may be granted. In reaching a final decision the Secretary of State will also take into account views expressed by other Government Departments, English Nature and any letters received from the general public in response to the initial Public Notice placed in a local newspaper. If ACRE have expressed a favourable opinion and there are no scientific objections from the other parties then consent will be granted.

Part C consent - for placing on the market

Marketing applications (also called 'notifications') are submitted initially to any one of the 15 Member States. The selected country then takes the regulatory lead on that particular application. The lead Member State has 90 days in which to form an opinion on the application. During this time additional information may be requested from the applicants and the clock is stopped while this is supplied. Marketing notifications that come to the UK, as the lead competent authority, go through the same strict evaluation process outlined for the Part B releases above, in that information is placed on the statutory public register and the dossiers are copied to other Government Departments, including Northern Ireland in the case of marketing, and English Nature. ACRE is asked to advise the Secretary of State whether the proposed commercialisation of a particular GMO poses a risk to human health and the environment.

After reviewing the dossier, if the lead competent authority is content for the GMO to be placed on the market in the European Community then the application dossier is forwarded to the Commission with a favourable opinion. The Commission must then circulate the dossier to the other 14 Member States who have 60 days in which to comment. During the 60 days Member States can request further information but there is no opportunity to stop the clock. If none of the Member States object to the application then the Commission instructs the lead country to issue the marketing consent which applies across all Members States.

If however one or more Member States objects then it falls to the Commission to make the decision. In practice, to do this the Commission seeks advice from the Scientific Committee on Plants (SCP) which serves a purpose much the same as ACRE. If the SCP reaches a favourable opinion on the marketing application the Commission will propose that it is given consent, and asks Member States to participate in a qualified majority vote (QMV) on whether to adopt the Commission's proposal to place the GMO on the market. If the QMV is in favour then the original lead country issues the consent. If the QMV is against placing the product on the market (i.e. the Member States reject the Commission's proposal) then the final decision is referred to the Council of Ministers. The Council have 90 days to reach a decision but at this stage according to the comitology (the voting and administrative procedures) it can only block the GMO from getting marketing consent by a unanimous decision. Otherwise the Commission's original proposal is accepted and the product is given consent.

THE DELIBERATE RELEASE REGULATIONS: FUTURE DEVELOPMENTS

With the current scepticism and mistrust of GM in Europe it is unlikely that there will be any major effort, at least in the next several years, to deregulate GMOs - even if increasing experience world wide in releasing and using GMOs begins to suggest that our worst fears are unfounded. Nevertheless something may be done to make the existing regulations work better.

The current Directive 90/220 has been in operation for several years and has attracted some criticism mainly because the procedures for getting marketing consent are slow and lack transparency. Furthermore, like all legalisation of this sort it is only when it has been operating for some time that areas in which there is room for improvement are revealed. Discussions are currently in progress to revise Directive 90/220 based on a text put forward by the Commission early in 1998. The main elements[11] of the proposed revision are set out in the paragraphs below. However, it should be emphasised that there is still great deal of negotiating to be done within the EU system and it is not at all certain what form the revisions will take in the final text. There have already been several rounds of talks at Member State level during the Austrian presidency and the European Parliament has recently commented on the proposal. It is already clear that some of the proposed changes are significantly more 'problematic' than others.

The main proposed changes to Directive 90/220 are:

I. procedural time limits - clear time limits are set out in which particular actions must be taken during consideration of marketing applications. Even if all of the proposed procedural steps are taken to the allowed time limit it should still be possible to get marketing consent within one year from submitting the dossier to the lead Member State.

II. risk assessment - clarification of the risk assessment and harmonisation cross Member States. The scope of the risk assessment is to include 'direct, indirect, immediate and delayed' effects.

III. monitoring and time limited marketing consents - specific provision is included for mandatory monitoring of commercial releases post marketing consent. Marketing consents will have a time limit after which they are again reviewed. The time limit suggested by the Commission is seven years.

IV. transparency and labelling - the Commission will make the content of the marketing applications available for public comment and there will be greater transparency at Community level. There is commitment for GMOs to be labelled 'in accordance with Community policy'. Current requirements are that the GMO product is labelled where the gene or gene product can be detected.

V. ethics - the Commission will be able to consult a committee that it appoints on the ethical issues raised by biotechnology.

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[11] for a more detailed consideration and comment on the proposed changes to Directive 90/220 see *EC Regulation of Genetic Modification in Agriculture*, House of Lords Select Committee on the European Communities 2nd report, 15 December 1998. London; the Stationary Office.

VI. comitology - this is essentially a change in the regulatory committee procedures followed by the Commission[12] in reaching a decision. The main effect is to strengthen the role of the Council of Ministers in agreeing or blocking proposals for marketing put forward to it by the Commission. For example, under the proposed new comitology the Council may agree a Commission proposal to give marketing consent by a QMV, or reject it by a simple majority.

OTHER CHANGES

When Directive 90/220/EEC was first produced it covered the environmental release of all GMOs, but over the past few years the primary regulatory responsibility for some GMOs has been removed. GM medicines and vaccines[13] and novel foods[14] consisting of or containing GMOs are now covered by separate regulations. There are future plans to remove responsibility for other GMOs such as GM seeds and animal feed containing GMOs. Eventually it is expected that Directive 90/220 will cease to exist, as all of its elements are covered by other regulations.

CONCLUDING REMARKS

The deliberate release of GMOs is tightly regulated in the UK and intimately linked to the wider European Community. It is accepted that the regulations may not be completely perfect and there is always room for improvement, but despite what is claimed in sensational stories in the press the regulations do provide a very effective safeguard for human health and the environment. The UK is generally regarded as being a 'Gold Standard' in Europe and other Member States look to us for a lead on key policy issues.

It is difficult to imagine a greater contrast in acceptance of GMOs between that which currently exists in the USA and that in Europe. It is important that those who have responsibility for regulating Biotechnology do not themselves get swept along in the highly charged debate. We have a science based regulatory system in the UK and science/safety decisions should not be made on emotional grounds. That said, science alone cannot address all of the concerns of society over Biotechnology and there is a good argument for a wider debate on ethics and, more generally, what society actually wants from agriculture.

It is often said that we do not know the long term consequences of releasing GMOs. This is true, but no field of human endeavour is absolutely free from risk, nor can long-term consequences ever be foreseen at the outset. This is as much true for new advances in engineering or medicine as it is for agriculture. Given that there will always be some uncertainty, then the long-term unpredictability of a new technology should not be used as a reason for not taking the first cautious steps. Genetic modification may bring great benefits for the environment but we must recognise that there is also potential for harm. The challenge for us all is to get the good bits without the bad.

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[12] technically this is a change from IIIa to IIIb regulatory committee procedures
[13] GM medicines regs
[14] Novel foods and food ingredients