

THE LEGAL FRAMEWORK FOR DECISION-MAKING ON THE RELEASE AND MARKETING OF GMOs IN THE EU

Background Paper by the UK Joint Regulatory Authority and the Secretariat to ACRE

Introduction

1. The purpose of this paper is to outline the legal framework against which decisions are made about the release and marketing of genetically modified organisms (GMOs) in the UK and EU. Releases and marketing of GMOs can only take place in the EU with the explicit consent of the regulatory authorities. Under the legislation, decisions on the granting of consents are based solely on the safety of the proposed GMO release.
2. The legislation governing GMOs covers many issues, including notifications, consents, provision of information to the public and enforcement. This paper concentrates specifically on the legal framework for decision making. The decision making process is underpinned by risk assessment. The risk assessment process is discussed in more detail in a companion paper.

European Framework

3. **The release and marketing of GMOs is controlled in the EU under Council Directive 90/220/EEC¹. The Directive defines a GMO as “*an organism in which the genetic material has been altered in a way that does not occur naturally by mating and / or natural recombination*”. The Directive requires Member States to ensure that all appropriate measures are taken to avoid adverse effects on human health and the environment that might arise from the release or marketing of GMOs.**
4. **Directive 90/220/EEC sets out some important basic principles for the regulation of GMO releases in the EU. These are:**
 - **A case-by-case environmental risk assessment should always be carried out prior to a release of a GMO;**
 - **The deliberate release of GMOs at the research stage is in most cases a necessary step in the development of new products derived from, or containing GMOs;**
 - **The introduction of GMOs into the environment should be carried out according to the ‘step by step’ principle, whereby initial releases are small and the scale of the releases increased gradually step by step, but only if the evaluation of the next steps indicate that the next step can be taken; and**

¹ Council Directive of 23 April 1990 on the deliberate release into the environment of genetically modified organisms (90/220/EEC); OJ N0 L117/15.

- **No product containing or consisting of GMOs and intended for deliberate release shall be considered for placing on the market without it first having been subjected to satisfactory field testing at the research and development stage in ecosystems which could be affected by its use.**
5. The Directive sets out two regulatory regimes; Part B for controlling releases for research and development, and Part C for placing GMOs on the market in the EU. Essentially, the Directive requires any person, before undertaking a release of a GMO or placing a GMO on the EU market, to submit a notification to the competent authority of the Member State within whose territory the release is to take place, or where the GMO is to be placed on the market for the first time. The key difference between Part B and Part C is that for research and development releases, decisions are made by individual Member States, whereas for placing GMO products on the market, decisions are made by all Member States. Part C decision making often necessitates a voting procedure to address differences in opinion on risk, and hence delays in decision making if the Commission, lead Member State and the notifier fail to find an acceptable way forward.

Part B: Research and Development Releases

6. Any person intending to carry out a research and development release of a GMO must first submit a Part B notification to the competent authority of the Member State in which the release is to take place. The notification must include a technical dossier supplying information necessary for evaluating foreseeable risks, whether immediate or delayed, that the GMO(s) may pose to human health and the environment. The detailed information required in notifications is set out in an Annex II of the Directive, which is included as an appendix to this paper. In summary, the Directive requires the following information on the:
- GMO (e.g. recipient organism, details of modification and novel trait);
 - proposed release and the receiving environment;
 - interactions between the GMO and the environment;
 - monitoring regime and procedures for controlling the release; and
 - a statement evaluating the impacts and risks posed by the GMO(s) to human health and the environment from the uses envisaged.
7. The competent authority of the Member State that receives the notification examines it for compliance with the Directive, evaluates the risks posed by the release. The information provided must be sufficient to enable a decision to be made, but further information and clarification can be sought at any time. A decision must be made within 90 days of receiving the notification, during which period comments may be received from other Member States who are informed of the notification soon after its receipt. The decision on whether or not to grant consent is made on the basis of safety to human health and the environment. No other criteria are considered in the decision making process. The notifier may proceed with the release only after receipt

of written consent of the competent authority, and in conformity with any conditions required in the consent.

8. In 1994, the First Simplified Procedure was agreed by Member States and implemented in the UK in 1995. This procedure allows releases of more than one GMO at more than one site. In the original directive a notification could only cover releases of one GMO at one or more sites or releases of one or more GMOs at one site, which raised practical problems for granting consents for official seed listing trials.
9. Under the First Simplified Procedure, one site has to be notified in the main application, but others do not have to be notified until 15 days before each proposed release takes place. However, the regulatory authorities can stop the proposed releases within this timescale, if they consider that the risk assessment in the notification is not applicable for a particular site. Certain criteria apply for this procedure to apply. The GMO has to be well characterised, and there must be information to demonstrate safety to human health and the environment. The releases must also be within a well defined programme of work. Such a procedure would not, therefore, apply to first time releases of GMOs that have not been previously considered by regulatory authorities.

Part C: Marketing GMOs in the EU

10. A Part C notification for placing a GMO on the EU market must be submitted to the competent authority of the Member State where the product is to be placed on the market first. For example, the UK has handled notifications for GM herbicide tolerant oilseed rape, whereas France has handled notifications for GM insect resistant maize. Notifications for placing GMOs on the EU market must, in addition to the information required under Annex II for a Part B release, provide the following extra information:
 - Extended information taking into account the diversity of sites of use of the product, including information gained from research and development releases carried out under Part B consents;
 - Information concerning the ecosystems that could be affected by the use of the product and an assessment of the risks posed to human health and the environment; and
 - Conditions for placing the GMO product on the market, including conditions for use and handling and a proposal for labelling and packaging.
11. The competent authority then reviews the notification and forms an opinion, which must be within 90 days of receipt. If that opinion is favourable, the lead competent authority will forward the dossier to the European Commission. The Commission circulates the dossier to the other 14 Member States who are given 60 days to evaluate the application in detail, taking into account the particular health and environmental safety issues unique to their territories. If no objections are made, the lead competent authority issues the marketing consent, which applies throughout the European Community.
12. If, however, another Member State objects to the GMO being placed on the market, then the Directive provides for committee procedures ('Article 21 Committee Procedure') to come to a resolution. The European Commission drafts a decision that reflects the concerns raised by Member States, on which a vote is taken using the qualified majority voting procedure. If a resolution is not possible, it falls to the Council of Environment Ministers to decide. If the Council fails to decide within

three months, the Commission can adopt its proposal. While there are procedures in place under the Directive, the decision making process has been subject to significant delays. Recent negotiations to amend 90/220/EEC sought to address these serious delays and set timescales for the European Commission to work under.

- 13. Twelve GM plants already have Part C marketing approval in Europe. These include soya beans, oilseed rape, chicory, carnations and 4 types of GM maize. The maize and soya are already imported in bulk into Europe for processing and use in animal feed.**

United Kingdom Legislation

- 14. In the UK, Directive 90/220/EEC is implemented by Part VI of the Environmental Protection Act 1990 and the Genetically Modified Organisms (Deliberate Release) Regulations 1992², as amended in 1995³ and 1997⁴. Essentially, and in line with the Directive, releases and marketing of GMOs cannot take place unless consent has been granted. Consents for releases in England are signed on behalf of DETR and MAFF Ministers, acting jointly, with the agreement of the Health and Safety Executive. Consents for releases in Wales or Scotland are signed on behalf of the appropriate Ministers of the devolved administrations, again with the agreement of the HSE. There is separate but equivalent legislation in Northern Ireland**
- 15. In making decisions on releases and marketing of GMOs, the Government is advised by the statutory Advisory Committee on Releases to the Environment (ACRE), established under Part VI of the Environmental Protection Act 1990. ACRE consists of a number of independent experts (currently thirteen), each specialising in a particular discipline, such as plant ecology, toxicology, farming, entomology, and microbiology. The joint Secretariat of ACRE is provided by DETR, and all interested Government Departments attend meetings, together with a representative of the Statutory Nature Conservation bodies.**
- 16. ACRE's main statutory role is to advise the Government on the safety of proposed releases and marketing of GMOs and non-native species. Notifications, known in the UK as consent applications, are evaluated critically by experts on ACRE, and only if the risks of the proposed release or marketing of a GMO are considered to be low will the Committee advise that consent may**

² The Regulation & Control of the Deliberate Release of Genetically Modified Organisms; DoE/ACRE Guidance Note 1.

³ Guidance to the Genetically Modified Organisms (Deliberate Release) Regulations 1995; DoE/ACRE Guidance Note 7.

⁴ Guidance to the Genetically Modified Organisms (Deliberate Release and Risk Assessment - Amendment) Regulations 1997; DoE/ACRE Guidance Note 10.

be issued. . When making decisions In issuing a consent, the Ministers will also take account of safety issues raised by experts in other Government departments, the Statutory Nature Conservation Agencies and the general public.

17. ACRE's remit also includes giving advice on the supporting GMO safety research programme (excluding the farm-scale evaluations that are overseen by an independent specialist steering group). ACRE also advise on GMO policy issues where they touch on scientific and safety related issues, particularly commenting on the development of legislation such as the amendments to Directive 90/220/EEC and the biosafety protocol. ACRE also advised on the development of the UNEP International Technical Guidelines for Safety in Biotechnology.
18. **However, ACRE's remit does not extend to giving advice on strategic (e.g. need for GMO products), ethical or public acceptance issues; the membership does not include specific expertise in these areas. The committee concentrates on scientific appraisal and advice on risks. Where ACRE identify wider issues covered under other legislation, ACRE will write to other advisory committees via the Secretariats to alert them of their concerns. For example, ACRE contacted the Advisory Committee on Pesticides (ACP) regarding their concerns about impact of herbicide use on GM herbicide tolerant crops and discussed their respective remits in detail to identify any gaps in the legislation⁵.**
19. The UK legislation has additional requirements than Directive 90/220/EEC in that there are statutory obligations to set up a Public Register on which information on consent applications and ACRE's advice are placed. Also, there are statutory requirements for Part B applicants to place advertisements in newspapers circulating in the areas where proposed releases are to take place. This enables comments to be made on proposed releases that ACRE can take into account if they pose questions about the safety of the GMO.

Recent Changes to Directive 90/220/EEC

20. In 1998, negotiations started on the amendment of Directive 90/220/EEC. Many procedural changes have been made to the Directive. Among these are two new annexes, one on Risk Assessment (Annex 2) and another on Post-Market Monitoring (Annex 7). Until December 1998, the EU competent authorities had not agreed a harmonised approach to risk assessment. Therefore, it was important that some clear principles that reflect current best practice in EU Member States for risk assessment were formalised. These are covered in more detail in the companion paper on risk assessment.
21. During the period of the negotiations to amend the technical annexes to the Directive, the UK was also preparing a paper considering the commercial introduction of GM

⁵ Genetically modified herbicide tolerant crops; Chapter 3 of the Advisory Committee on Releases to the Environment Annual Report No 4:1996/97.

crops in the light of significant farmland wildlife declines⁶. It is important that the Government's commitments under the UK Biodiversity Action Plan to reduce, and where possible reverse, such declines are not compromised by allowing GM crops to be commercially used if their use exacerbates existing wildlife declines. In order to ensure that this is addressed in subsequent risk assessments, the UK successfully introduced one key addition to the scope of the risk assessment process: the consideration of the possible adverse effects of the management of the GMO, where it was unique, in addition to the effects of the GMO itself. ACRE's remit was consequently expanded to enable to accommodate this and the ACRE Sub-Group on wider biodiversity issues has since been considering how best consent applicants consider this in future applications.

22. A further addition was that marketing notifications must now include a monitoring plan which has two objectives:
 - to confirm that any assumption about the occurrence of adverse effects of the GMO made in the risk assessment are correct; and
 - to identify the occurrence of adverse effects of the GMO or its use on human health and the environment which were not anticipated.

23. The Environment Council agreed in December 1998 that the principles in for risk assessment and monitoring be taken into account as an interim measure until the amended Directive was adopted. The UK published guidance requiring, with immediate effect, applicants for consent to apply the revised approach to risk assessment, and that for marketing applications, a monitoring plan must be submitted, and subject to any changes by ACRE, implemented if consent was granted⁷.

UK Joint Regulatory Authority and ACRE Secretariat: August 2000

⁶ The Commercial Use of Genetically Modified Crops in the United Kingdom: the Potential Wider Impact on Farmland Wildlife. A Discussion paper prepared by the Secretariat to the Advisory Committee on Releases to the Environment; published in ACRE Annual Report No 5: 1998

⁷ Guidance on Principles of Risk Assessment and Monitoring for the Release of Genetically Modified Organisms: DETR/ACRE Guidance Note 12

RISK ASSESSMENT FOR RELEASES AND MARKETING OF GMOs IN THE EUROPEAN UNION

Background Paper by the UK Joint Regulatory Authority and the Secretariat to ACRE

Introduction

1. The purpose of this paper is to explain the current approach to assessing the risks to human health and the environment of releases of genetically modified organisms (GMOs). This paper will focus primarily on GM crops, since they account for the majority of GMOs being considered at the present time.
2. Risk assessment underpins the decision making process for granting consents for the release and marketing of GMOs, since the sole basis for making decisions on the granting of consents is safety. This paper should be considered in association with the companion paper describing the legal framework for regulating the deliberate release of GMOs.

Approach to Risk Assessment: Terminology

3. The approach to risk assessment in the UK has been to:
 - identify the intrinsic properties of an activity, substance or organism that may cause harmful effects to humans or the environment;
 - to estimate the likelihood of those effects occurring under the conditions of the proposed release or use;
 - to estimate the magnitude of the harm that may arise, assuming that the effects occur; and
 - on the basis of the above steps, evaluate the overall risk.
4. This general approach has been described in other recent documents⁸.
5. The intrinsic properties of an activity, substance or organism that may cause harm are termed 'hazards' and the likelihood of hazards being realised and the magnitude of the consequences are together termed 'risks'. The process of risk assessment for GMOs is described in more detail in other specific DETR/ACRE/ guidance notes⁹.
6. The over-arching principle adopted in the risk assessment of releases of GMOs is the 'case-by-case' approach, where each GMO release is assessed according to the particular circumstances of the proposed release or use. This does not mean that every proposed GMO release is looked at in isolation of existing releases of GMOs; these are taken into account where appropriate.

Hazard Identification for GM Crops

7. Hazard identification is carried out using the information provided in applications for consent (see companion paper on the legal framework). The information requirements include information on the characteristics of the plant that has been modified ('recipient' plant), information on the genetic modification (including details of the sequences of nucleic acid inserted), and information on the genetically modified plant. This enables an understanding to be gained of the potential behaviour of the GM plant and its possible interactions in the environment and other organisms.

⁸ Guidance for Environmental Risk Assessment and Management; DETR 2000.

⁹ The Regulation & Control of the Deliberate Release of Genetically Modified Organisms; DoE/ACRE Guidance Note 1, Chapter 4.

8. The potential hazards associated with a GM crop may be:
- ***Expression of toxic or allergenic compounds;*** the genetic modification may result in the production of substances that are toxic to humans or other species, or allergenic.
 - ***Effects on biogeochemistry;*** the potential to cause changes in nitrogen and carbon recycling that depends on decomposition processes.
 - ***Increased persistence in the environment and invasiveness;*** a genetic modification may confer an ecological fitness advantage to the recipient plant, which potentially allows it to become persistent or invasive. Concerns about ‘superweeds’ have been raised regarding herbicide tolerance traits; however, traits such as disease, drought or insect resistance are more likely to confer an advantage to a recipient plant, since these pressures control natural plant populations.
 - ***Transfer of genetic material;*** cross-pollination with other crops of the same species or near-relatives can give rise to hybrids which express the traits introduced by the genetic modification. Such gene-transfer may not be a hazard in itself; this would depend on the trait being transferred.
 - ***Instability of the genetic modification;*** plants have the ability to inactivate inserted genetic material, particularly if there is a large number of copies inserted and if the constructs are large. In many cases, this may not pose a risk in itself, as the recipient plant is likely to revert to the wild-type. However, this would become an issue where a genetic modification was made to down-regulate a naturally occurring hazardous trait.
 - ***Unintended effects;*** while it is expected that inserted sequences of nucleic acid are well characterised, the exact positions of the insertion(s) cannot be predicted until more detailed analysis is completed. It is possible that the insertion can influence the expression of adjacent genes and their promoters, leading to unintended genetic modifications. These may not be hazardous, but the transformation event and its progeny would require careful monitoring.
9. If a hazard is realised in the course of a release, it may result in harm to human health if the GMO is toxic or allergenic, or to the environment, if population dynamics are affected, resulting in reductions of native species. The process of risk assessment examines whether or not it is likely that identified hazards are likely to be realised under the conditions of a proposed release.

Risk Assessment

10. The likelihood of a hazard being realised and the magnitude of the consequences will depend on the characteristics of the release or use of the GMO, including the features and position of the release site, or the scale of use. There is a significant difference between a small-scale research plot (covered under Part B of Directive 90/220) and unrestricted commercial use (covered under Part C).
11. Estimating the likelihood of an event in an ecological system is not an exact process, and extremely difficult to quantify in terms of probabilities. As with all risk assessment, there is an element of uncertainty. With respect to GMOs, this has been handled in a number of ways:

- adopt a worse case scenario approach in the evaluation process, assuming the consequences will definitely occur, and assign a magnitude to those consequences;
 - request further information from the consent applicant to address specific areas of concern, and require an amended risk assessment;
 - impose a higher degree of risk management of the release until more information is available to address the issues; or
 - require monitoring during and after the release of the GMO.
12. As pointed out above, there is a significant difference between Part B release applications for small scale field plots and Part C notifications for unrestricted commercial cultivation of a GM crop. In the case of a small scale field plot, it is possible to have close control over the site and impose risk management measures to isolate the trial from important habitats and commercial crops to prevent or minimise cross-pollination and thus gene transfer by:
- planting a border row around the GM plants to act as a pollen barrier;
 - isolation distances;
 - bagging plants during flowering; or
 - cutting the developing flower buds off; and
 - destroy all harvested material.
13. In accordance with the ‘step-by-step’ principle explained in the companion paper on the legal framework, small trials are necessary to gather more information on the crop and its safety, before a scaled up release can take place. More information reduces the uncertainty and enables ACRE to advise accordingly on subsequent releases. For Part C notifications, ACRE must consider the potentially wide use of a GM crop within the EU. ACRE is in the position of taking into account the realities of commercial agriculture, and the limited scope for onerous restrictions on use, in giving advice. If it is considered necessary to impose onerous risk management in commercial use order to address safety concerns, then it is likely that a consent would not be granted. In a Part C situation, the GM crop and its use must be intrinsically low risk.
14. In considering applications for both Part B and Part C consents, ACRE has often taken the approach of assuming that the hazard, if present, will be realised, and to focus on the consequences. For example, the release of GM oilseed rape raises the issue of gene transfer, since this crop readily cross-pollinates with nearby oilseed rape crops and there is some evidence of spontaneous hybridisation with some wild relatives. Experience in crop breeding and seed production has enabled separation distances that can be recommended to minimise cross-pollination and thus gene transfer. However, it has always been accepted that gene transfer between crops such as oilseed rape and maize can never be prevented, so ACRE has focussed attention on the consequences of the event occurring, even it occurs at a low frequency.
15. In the case of tolerance to glufosinate ammonium herbicides, ACRE concluded that any resulting feral populations or oilseed rape crops and wild relatives were unlikely to gain

any selective advantage by inheriting this specific trait¹⁰. However, this would not necessarily be the case for other traits inserted by genetic modification. ACRE has considered applications for consent to release glyphosate tolerant oilseed rape on an experimental basis, and have concluded that it should be separated from other oilseed rape by 50m to minimise gene-transfer. The issues relating to multiple herbicide tolerance have been explored by ACRE¹¹, but the committee has yet to advise on a marketing notification for GM glyphosate tolerant oilseed rape.

16. Similarly, the consequences of gene-transfer of traits such as reduced pod shatter, insect or fungal resistance could also be viewed very differently from herbicide tolerance, since it could result in decreased or increased ecological fitness of wild relatives, thus potentially affecting population dynamics. ACRE has taken the view that cross-pollination can only be minimised – not prevented – and if there are safety implications associated with the genetic modification, then the committee would advise that a consent should not be granted for the release or marketing of a GM crop¹². This illustrates the case-by case approach, and that existing GM crop consents are taken into account in the risk assessment process.
17. The estimation of overall risk takes into account the combination of the likelihood of hazards being realised and the magnitude of the consequences. The likelihood of harmful effects being realised may be high, medium, low or negligible. Similarly, the magnitude of the harmful effects may be severe, moderate, low or negligible. This approach illustrates the qualitative and descriptive nature of assessing the magnitude of harmful effects and the risk of releases of living organisms. Further guidance on what is meant by low, moderate or severe effects has been offered to applicants in DETR/ACRE Guidance. The behaviour of any organism in the environment is influenced by many interacting factors, and we are not yet in a position to take a quantitative approach with any confidence.
18. It should be stressed that a risk assessment is not a closed issue if a consent has been granted to allow a release or marketing to proceed in the EU. There is a statutory requirement that all consent holders keep themselves informed and alert the regulatory authorities of new information which has significance for the risk assessment. A risk assessment should only be carried out with the latest information available, and which is based on credible scientific studies. But the option for a re-appraisal is always available if new information becomes available.

Changes to the Risk Assessment Process

19. In the latter half of 1998, negotiations to amend Directive 90/220/EEC resulted in a new technical annex on risk assessment being agreed, which the UK played a key role in developing. This was an important step, since until then there had been no formally agreed approach to risk assessment for GMOs within the EU. The technical annex formalises some important principles, which reflect existing best practice among EU Member States¹³. These include:

- That potential adverse effects may be direct, indirect, immediate or delayed;

¹⁰ Environmental Risks of Herbicide-Tolerant Oilseed Rape. A Review of the PGS Hybrid Oilseed Rape. GMO Research Report No 15.

¹¹ Genetically Modified Herbicide Tolerant Crops; Chapter 3 of the Advisory Committee on Releases to the Environment Annual Report No 4: 1996/97

¹² ACRE response to the MAFF Consultation on Separation Distances – July 2000.

¹³ Guidance on Principles of Risk Assessment and Monitoring for the Release of Genetically Modified Organisms. DETR/ACRE Guidance Note 12.

- The risk assessment should be carried out on a case by case basis; this implies that the required information may vary depending on the type of GMOs concerned, their intended use and the potential receiving environment, taking into account, among other things, GMOs already in the environment;
 - If new information on the GMO and its effects on human health and the environment becomes available, the risk assessment should be re-examined;
 - That the information required in notifications must include possible impacts of the specific techniques used for the management of GMO where these are different from those used for non-GMOs. This particular principle is a new addition to GMO risk assessment.
20. At the Environment Council in December 1998, Ministers agreed that until the revision was complete, competent authorities could take into account the underlying principles for risk assessment resulting from the work done, particularly when considering Part C notifications. Whilst the Directive as a whole is currently under the conciliation stage, this Annex is largely agreed and will be formally adopted with these important principles intact.

Baselines on Environmental Harm

21. The assessment of the risk of a GMO needs to be placed in the context of existing agricultural activities, whether non-GM or organic, and which also have the potential to cause adverse environmental effects. The baseline against which the risk of a GMO can be compared has been the subject of discussion in ACRE. All agricultural activities result in adverse effects on the environment, and there are serious concerns about farmland wildlife declines that have occurred during the last fifty years. With GMOs, it has been common to compare the risks of a GM crop with the unmodified crop. DETR and ACRE have commented that it is inappropriate to demand non-target effects from the use of GM crops, while tolerating them from the use of non-GM crops whether they are grown conventionally, organically, or in accordance with Integrated Crop Management (ICM) methods¹⁴.
22. Given the UK Biodiversity Action Plan commitments to stop and where possible reverse wildlife declines, it is important that the risk assessment process now identifies GM crops whose use may lead to increasingly intensive agricultural management practices. This is why the recent amendments to the risk assessment process to evaluate the effects of the management of GMOs as well as the GMO itself are so important. At present, the debate is focussed on whether GM crops tolerant to broad-spectrum herbicides will lead to increased weed control and less resources for farmland wildlife to feed on. This is why the farm-scale evaluation research programme was set up, and the results, whatever the final conclusions, will provide a greater understanding of arable ecology that can be used to underpin this process.
23. Work is currently being carried out by the ACRE Sub-Group on Wider Biodiversity Issues to develop guidance on how the effects of the management of GM crops should be assessed in the context of Biodiversity Action Plans and other farmland and habitat conservation targets. A draft will be issued for consultation shortly.

Joint ACRE Secretariat: August 2000

¹⁴ The Commercial Use of Genetically Modified Crops in the United Kingdom: the Potential Wider Impact on Farmland Wildlife; Chapter 3 of the Advisory Committee on Releases to the Environment Annual Report No 4: 1996/97.

THE HISTORY OF THE FARM-SCALE EVALUATIONS

Background paper by DETR

Introduction

1. The purpose of this paper is to provide a summary of the development of the Farm-Scale Evaluations (FSE) of herbicide-tolerant genetically modified crops (GMHT).
2. In 1998 three types of GMHT crops were on the verge of entering commercial agriculture in the UK when real concerns were raised about the impact the management of these crops would have on the environment. The Government, through a voluntary agreement with industry, has halted their commercial introduction until further evaluations are completed.
3. European legislation covering the release of GMOs in Europe (90/220/EEC) is currently under revision. Part of the revision will require that an assessment of such changes in the management of the crops is included in the application for consent for the GM crop to be marketed in the EU. Environment ministers in December 1998 agreed that the updated risk assessment requirements in the proposed revision of the directive should be implemented straight away using the powers in the existing directive. In future all applications will automatically have to consider the likely impact on wildlife brought about by changes in management practice.

Chronology

4. The first releases of GM herbicide tolerant crops took place in the UK in the late 1980s. Following the step by step approach in the European legislation plant breeders developed and tested a small number of GM crops. GMHT oilseed rape was first considered for placing on the European market in 1994 closely followed by various maize varieties. In advising the UK government on the application, the Advisory Committee on Releases to the Environment (ACRE) was concerned that while the risks of the GM crop by itself appeared to be low, the potential environmental effects associated with the use of broad spectrum herbicides on the crop should also be assessed.
5. In 1996 ACRE discussed the specific issues relating to GM herbicide tolerant crops in detail, with officials from the Pesticides Safety Directorate (PSD) in attendance. ACRE's main concern was to identify whether or not impacts of the use of herbicides are adequately covered under the Pesticides legislation, and whether there are any gaps in the legislation. Their discussions and conclusions are published in Chapter 3 of the ACRE Annual Report No 4 (1996/7).
6. In subsequent marketing notifications, ACRE continued to raise issues regarding the impact of herbicide use on GMHT crops with the Pesticides Safety Directorate.

7. **By early 1998**, DETR had started in depth discussions with English Nature to lay the ground for development of policy to address wider biodiversity issues related to GM crops. English Nature (EN) with the other statutory nature conservation bodies called publicly for a moratorium on the commercial use of herbicide tolerant or insect resistant GM crops until further research is carried out. They were specifically concerned about the continuing impact of farming practices on farmland wildlife. GM crops could exacerbate wildlife declines if they encouraged higher levels of weed control than necessary, which in turn would reduce invertebrate and bird numbers.
8. In June 1998 Michael Meacher hosted a meeting to discuss the wider biodiversity issues with experts from English Nature, RSPB, Green Alliance, National Institute of Agricultural Botany, MAFF and ACRE members. The feedback from this meeting was used to prepare the more detailed draft paper. In consultation with ACRE, other Government Departments and English Nature the text was developed along the lines of:
 - Severe declines in farmland wildlife have been detected, which are the result of increasingly intensive agricultural practices;
 - Biodiversity Action Plans are in place to address this;
 - Decisions on the marketing of GM crops must not encourage further intensification, or Biodiversity Action Plan targets will be prejudiced;
 - Investigation of potential adverse effects on farmland wildlife of GM crop management is needed as well as statutory investigations already carried out on the GM crop itself;
 - A more strategic approach is needed, in terms of what is wanted from agriculture in terms of food and biodiversity, against which regulatory decisions can be made.
9. **By October 1998:** DETR was exploring the possibilities of a moratorium on the commercial planting of GM crops. Discussions were held with Friends of the Earth (FoE), English Nature (EN), RSPB and Genewatch and separately with industry. Calls for a moratorium (which would be illegal under EU law) were rejected but instead the Government introduced a programme of closely monitored commercial-scale plantings of GM crops to assess the impact on wildlife of the new herbicide regime. A voluntary agreement was made with industry to delay commercial planting of GM crops for one year whilst research was carried out. On 21 October, Michael Meacher and Jeff Rooker appeared before the House of Lords European Communities Committee on Agriculture and announced the concept of managed development and the agreement with industry.
10. Following the announcement the specifications for the letting of contracts for the ecological research were developed in consultation with English Nature and well known ecologists. The research is funded by DETR with contributions from MAFF and the Scottish Executive. Then 15 major research organisations were invited to tender for research contracts investigating effects of management of herbicide tolerant oilseed rape (both spring and autumn sown) and maize. The organisations were:

ADAS Consulting Ltd
Central Science Laboratory
Game Conservancy Trust
Horticulture Research International
Imperial College, London
Institute of Arable Crops Research, Long Ashton
Institute of Arable Crops Research, Brooms Barn
Institute of Arable Crops Research, Rothamsted
Institute of Terrestrial Ecology (now CEH)
Institute of Grassland and Environmental Research
John Innes Centre, Norwich
National Institute of Agricultural Botany
Scottish Agricultural College
Scottish Crops Research Institute
University of Birmingham

11. DETR consulted on the proposals in February 1999.
12. **In autumn 1998** negotiations started in earnest under the EU Austrian Presidency about the amendment of Council Directive 90/220/EEC on the release of GMOs into the environment. The UK was instrumental in the development of the technical annexes on risk assessment and included text to ensure that the potential impact of the management of GM crops is considered in addition to the impact of the crops themselves. The UK also played a key role in developing a technical annex on post-market monitoring.
13. At their Council **in December 1998**, EU environment ministers agreed that the technical annexes on Risk Assessment and Post-Market Monitoring should be implemented with immediate effect whilst other provisions of the Directive continued to be negotiated.
14. **In February 1999** public concern about GM crops reached fever pitch with daily headlines in the media. ACRE published the discussion paper entitled 'The commercial use of GM crops in the UK: the potential wider impact on farmland wildlife' prepared by the ACRE Secretariat. The following month the ACRE Sub-Group on Wider Biodiversity Issues was appointed and held its first meeting, adopting the 'Wider Issues' Paper as the basis for its deliberations. Its agreed priority was to develop guidance for consent applicants on how the wider biodiversity impacts of the management of GM crops should be addressed in future applications for consent to market.
15. **In April 1999** the contract for the farm scale evaluations was let to a Consortium of three research organisations: Institute of Terrestrial Ecology (ITE), now (Centre for Ecology and Hydrology, CEH), Institute of Arable Crops Research (IACR) and Scottish Crop Research Institute (SCRI). The Evaluations started with pilot plantings of 2 spring oilseed rape fields and 4 fodder maize fields, followed by three autumn sown rape fields. One field of sugar beet was also sown, with the ecological research funded by SCIMAC using the same protocols.
16. The Secretary of State appointed an independent Scientific Steering Committee (SSC), chaired by Professor Chris Pollock to oversee the evaluations. The members of the committee are Professor Mick Crawley,

Imperial College, London, Dr David Gibbons, RSPB, Dr Nick Southerton, Game Conservancy Trust, Mr Jim Orson, Morley College, Dr Alastair Burn, English Nature and Dr Nicholas Aebisher, GCT. The SSC first met in June 1999 and endorsed the FSE programme. They have subsequently met four times. The minutes of meetings and interim reports are published on the FSE page of the DETR web site.

17. After the pilot phase of the programme, in **November 1999**, the government negotiated a new agreement with the industry body SCIMAC. There will be no widespread planting leading to general market access of GM crops grown in the UK until farm-scale evaluations are complete. Subsequent freedom to pursue widespread plantings leading to general market access of GM crops grown in the UK will be dependent upon the recommendations and advice Government receives from the Scientific Steering Committee and ACRE. This advice will be based on the results of the Farm Scale Evaluations (FSE), together with all other relevant approvals required under current UK and EU legislation.
18. **In spring 2000** SSC met twice and agreed the programme for the first full year of the evaluations. They have set criteria for the type of farms to be included and the minimum number of fields. The Committee approves the number and types of farm presented by SCIMAC and selected as suitable for research by the Consortium. They also agreed the inclusion of GMHT beet, both sugar and fodder, in the programme.
19. The FSE for this year have included 12 spring rape, 12 maize and 23 beet. There was one rape site in Scotland and one maize in Wales, otherwise all the sites were in England. In August 25 winter oilseed rape FSE sites were announced.
20. Since 1996 ACRE has completed consideration of dossiers supporting applications for five GMHT crops, three rape and one maize tolerant to glufosinate ammonium and one fodder beet tolerant to glyphosate. In each case they have advised that, subject to the outcome of the FSE, there are no human health or environmental reasons why consent should not be granted.
21. Before GMHT crops can be exploited commercially they also need separate approvals under
 - seeds legislation,
 - pesticides legislation and
 - novel foods regulations.

Biotechnology Safety Unit

Department of the Environment Transport and the Regions: August 2000

THE SCIENCE OF THE FARM SCALE EVALUATIONS

Background paper by Biotechnology Safety Group, DETR

Introduction

1. The Farm-Scale Evaluations (FSE) of genetically modified herbicide tolerant (GMHT) crops have become one of the most controversial ecological research programmes ever undertaken. The research has received great public attention partly because its outcome will influence Government policy on commercial use of these crops, and partly because of direct action by pressure groups concerned about genetically modification technology. This paper describes the rationale and science behind the FSE and should be read in association with the paper on the History of the FSE.
2. A small number of crop varieties genetically modified to be tolerant to broad spectrum herbicides have almost completed all the necessary approvals to permit them to be grown commercially in the UK. The furthest forward are oilseed rape, maize, sugar beet and fodder beet. The approval process includes a comprehensive assessment of the genetically modified (GM) plant and the possible risks it may pose to human health and the environment. However, a number of bodies, including the statutory nature conservation agencies, (such as Scottish Natural Heritage) are concerned that the commercial planting of GMHT crops may lead to changes in agricultural practice that will adversely affect farmland wildlife. The increasing intensity of agricultural production systems has already had severe effects on farmland wildlife, causing decreases in many once common species such as brown hares and skylarks. The concern is that management (especially herbicide use) associated with GMHT crops could exacerbate these effects, further reducing the quality of the agricultural ecosystem for wildlife. Increases in agricultural intensity would make it impossible for the UK to meet Biodiversity Action Plan targets, agri-environment commitments and pesticide regulations. This has been discussed in detail in a discussion document published in February 1999¹⁵.
3. In response to these concerns, the UK successfully introduced the need for the management of GMOs to be considered in risk assessments in the recent negotiations to amend Directive 90/220/EEC. This is discussed in more detail in the paper on risk assessment. However, there was an urgent need for the UK Government to address the potential effects of management of GMHT crops on farmland wildlife, because a number of products were close to being placed on the EU market.
4. Even though these GMHT crops are not considered directly harmful to humans and the environment, the FSE research will allow an evaluation of the potential indirect effects of the management associated with GMHT crops, especially herbicide use, on the farmland environment. Herbicides can indirectly affect wildlife by reducing or eliminating the food resources such as weeds and insects available to them in an ecosystem. This has knock-on effects through food chains to higher feeding (trophic) levels. Investigation is needed of the potential large-scale effects of herbicide management associated with these crops, were they to become a part of commercial agriculture. Small-scale evaluation in experimental plots or laboratory conditions cannot provide information on the complex ecology of the agricultural ecosystem and no existing research is available to help answer the question. The current pesticide legislation now includes provisions to address the issue of indirect effects of herbicides on farmland wildlife.
5. If GMHT herbicide management does exacerbate the adverse effects of conventional agriculture, the FSE results will provide the evidence needed to modify or delay EU directives covering the commercialisation of GMHT crops until risk associated with the management of these crops has been fully assessed. The FSE are probably one of, if not, the largest ecological investigation of their type in the world and will provide invaluable information about the indirect effects of non-GM conventional farming as well as those of new GM technology.

GMHT crops

¹⁵ The Commercial Use of Genetically Modified Crops in the United Kingdom: the Potential Wider Impact on Farmland Wildlife: Chapter 3 The Advisory Committee on Releases to the Environment Annual report No 5: 1998.

6. The GMHT crops have been modified to be resistant to broad-spectrum herbicides such as glyphosate and glufosinate ammonium. This means that broad-spectrum herbicides that would normally kill the crop as well as the weeds can be applied to remove all weeds without damaging the crop. In practice it is difficult to control effectively broad-leaved weeds in broad-leaved crops because the crop is often susceptible to a herbicide. This means that existing herbicide programmes are complex and there is a need to control weeds either at a very early stage of growth, or use persistent soil acting herbicides to prevent weed seed germination in anticipation of them being a problem at a later stage when the crop is susceptible to competition. It is argued by the proponents of the GM crops that these crops have the potential to allow much greater flexibility in the timing of herbicide application, help control herbicide resistant weeds and reduce the quantity of persistent and more hazardous chemicals (such as Atrazine on maize) that are currently in wide use in the UK. To date, the Government has seen no evidence that this is the case; nor is there evidence that the use of herbicides on these GM crops will exacerbate farmland wildlife declines, hence the need for specific field studies.

The Farm Scale Evaluations

7. The farm scale evaluations of GMHT crops are designed to investigate the effect on the agricultural ecosystem of the management associated with their production. The crops themselves: forage maize, oilseed rape (winter and spring varieties) and beet (fodder and sugar varieties) have already cleared most of the regulatory procedures, designed to investigate their safety to human health. However, potential effects on the agricultural ecosystem resulting from the novel herbicide management that can be used with these crops have not been investigated. Industry has entered a voluntary agreement with the Government that commercial development of GMHT crops will not continue until biodiversity effects relating to their management are understood (see 'History of the Farm Scale Evaluations' paper).
8. The farm scale evaluations are comparing the impact on farmland biodiversity of two different herbicide regimes. They are not evaluating the safety of the GM plants themselves. There has been a widespread misunderstanding the FSE have been designed to investigate the potential effects on the environment of the GMHT crops themselves. This has already been done in the laboratory and in small-scale field trials. Consent to grow these crops at the scale of the farm scale evaluations would not have been granted if these plants were not already considered safe.

The research consortium

9. The Government invited 15 organisations to submit proposals for the evaluations, including the experimental design. As a result the ecological research is being carried out by a consortium of independent scientists from the Centre for Ecology and Hydrology (CEH), the Institute of Arable Crops Research (IACR) and The Scottish Crop Research Institute (SCRI). The scientific validity of the research is being overseen by a Scientific Steering Committee (SSC) of independent experts in agriculture and ecology drawn from Universities and organisations such as The RSPB and The Game Conservancy Trust (GCT).

Farm and site selection

10. The industry body SCIMAC (Supply Chain Initiative on Modified Agricultural Crops) finds farmers willing to offer fields for the evaluations. From these, a suitable number are selected by the researchers to be representative of regional geographical differences and the range of current farming methods, biodiversity and production intensities throughout the British Isles. The SSC approves the suitability of these sites for the FSE research. The experimental fields need to be large enough to allow commercial style crop management and to prevent edge effects from compromising the results. Field sizes are in the range 3-12 hectares.

Experimental design

11. The FSE experiment has been designed by the research consortium to test the statistical 'null hypothesis' that there is no significant difference in the effects on biodiversity from herbicide management in GM crops when compared with herbicide management in equivalent non-GM

varieties of these crops. The use of a 'null hypothesis' is a standard part of designing scientific experiments and not unique to the FSE. It allows statistical analysis of data to seek for both potential positive and potential negative effects.

12. At each site, the field is split and one side sown at random with the GM crop while the other side is sown with an equivalent non-GM variety of the crop. This experimental design means that initial differences in biodiversity between the two halves are minimised and any differences in biodiversity detected during the course of the experiment will be the result of the herbicide treatment. As this is a manipulative experiment looking at differences between the crops, no baseline data on biodiversity are required, provided that the pairing is efficient. The grower is advised on herbicide use in the GM part of the field by the company providing the GM seed, but continues to manage the non-GM part in their usual way. The management in each FSE field is audited to ensure that herbicide use provides cost effective weed control, and that herbicide is not applied in a way that is unrepresentative of commercial practice.

Number of sites

13. The research consortium carried out a statistical power analysis to determine just how many fields would be needed in the experiment to allow the null hypothesis to be tested reliably and take into account natural variability. Overall, the analysis indicated that 60 sites would be necessary over the whole programme to give sufficient results. Ideally this meant 20 starts each year. However with the difficulty in obtaining sites, for the first year of research, the analysis indicated that 12-15 fields of oilseed rape, 12-15 fields of maize and 20-25 fields of beet would be a sufficient minimum to allow analysts to be confident that the hypothesis could be tested reliably. Ecological experiments are always subject to complications and the number of fields available in a given year of the FSE can fall below the optimum minimum, provided additional fields are added to the study in subsequent years.

Duration of the research programme

14. The evaluations are a four-year programme. In the first year, 1999, a small number of fields of each crop were sown to test the evaluation protocols. The main project started in spring 2000 and is due to end in autumn 2002 for the spring crops and summer 2003 for the autumn sown rape.

Species being monitored

15. It is not possible to monitor all biodiversity indicators in the FSE ecosystem, so a number of sensitive species that can be studied reliably have been selected. These are shown in the box below.

In practice, the variation in biodiversity can not be recorded for all species. The approach is to compare key indicators of biodiversity between the GM HT and non-GM HT cropping systems. In reporting these effects, they will be placed into the context of national recording schemes that can help to show the relationships between the biodiversity associated with the study sites and arable areas in general.

The indicators being measured are:

- soil seed bank;
- arable plant diversity, biomass and estimated seed return;
- field margin and boundary vegetation, noting species in flower and signs of spray drift;
- Gastropods (slugs and snails) abundance, activity and diversity measures;
- Arthropods on vegetation, concentrating on plant bugs (Heteroptera), spring tails (Collembola), and the caterpillars of butterflies, moths, (Lepidoptera) and sawflies; diversity and biomass measures;
- Carabid beetles and other ground dwellings arthropods; abundance and diversity measures;
- bees and butterflies; observational studies;
- birds and small mammals, observational studies.

16. At this stage the emphasis is on studying species at the lower end of the food chain, although monitoring of the birds and mammals using the FSE fields for foraging or breeding is also

underway. This work is being done by the British Trust for Ornithology. The assessment methods are based on existing protocols, which have been modified appropriately for this project. In addition to studying animal indicator species, protocols are being used to investigate seed and plant biodiversity in and around the study fields. The study is limiting the number of confounding factors by using a split-field design and controlling for all the variables except the herbicide treatment. The monitoring takes place throughout the growing season in relation to herbicide applications. After the first year the studies will continue in the subsequent follow-on conventional crops.

Publication of the results

17. Publication of the results will be supervised by the SSC. They have advised that the results and analysis should be published in peer-reviewed scientific journals at the end of the three years of research. All the data collected will also be made available at that time. The research contractors produce interim reports on progress with the evaluations every six-months. After review by the SSC these are published in the FSE web site, www.environment.detr.gov.uk/fse/index.htm.

Other studies

18. The opportunity is being taken to use the FSE fields for other work where this does not interfere with the evaluations themselves. The decision to allow such additional studies lies with the SSC.
19. The main additional project is monitoring gene flow from the GM half of the fields of rape and maize to the non-GM half. Both the flow of pollen and the extent of cross-pollination is being monitored. The work is being done by the Central Science laboratory and where appropriate they are also monitoring cross-pollination in nearby fields.
20. The Centre for Ecology and Hydrology is monitoring any cross-pollination with wild relatives of rape within the fields themselves and within a margin of 10metres. Maize has no wild relatives present in the UK agricultural ecosystem.

DETR Biotechnology Safety Unit: August 2000