

Advice on a notification for marketing of insect resistant and herbicide tolerant GM maize 1507

Advice of the Advisory Committee on Releases to the Environment (ACRE) under S.124 of the Environmental Protection Act 1990 (Part VI) to UK ministers and ministers in the Devolved Administrations

Details of the notification

Notifier:	Pioneer Hi-Bred International Inc. and Mycogen Seeds
Notification reference:	ES/01/01
Product:	Maize genetically modified for insect resistance and herbicide tolerance, transformation event 1507
Scope:	For the cultivation, import and use of grain varieties derived from maize transformation event 1507, and conventional hybrids, as for any other maize.

Final advice

ACRE has issued advice at the three steps in the regulatory process for notifications to market GMOs in accordance with Directive 2001/18/EC, which controls the deliberate release of GMOs in the EU. These steps relate to the EU-wide assessment of the notification, the responses from the applicant to questions/ concerns raised during this assessment and finally EFSA's opinion on the issues that remain unresolved. As notification ES/01/01 has been in the regulatory system since 2001, the EU Commission has requested a number of additional updates from EFSA. These take new information in the peer-reviewed literature into account and provide further clarification on key issues. ACRE has reviewed its advice on this notification accordingly. Consequently our latest advice builds on our previous views and inevitably focuses on the key issues.

Previous iterations of our advice have established that:

- 1507 maize is very unlikely to be cultivated in the UK because the pest it targets is not a problem here;
- in addition to the pest-resistance trait, 1507 maize was modified for tolerance to glufosinate ammonium herbicides. This latter trait was used in the development of 1507 maize but any authorisation to cultivate this GMO will not include the use of glufosinate ammonium as a novel system for weed control in the commercial crop.

Since ACRE issued its advice in 2005, the EU Commission has requested that EFSA update its scientific opinion on six occasions. These updates took place in 2006¹, 2008², 2011³ and 2012a⁴ b⁵ and included a consideration of the most recent peer-reviewed literature. The updates tend to focus on two areas of the environmental risk assessment where EFSA had previously identified significant uncertainty (and recommended management options for addressing this). The uncertainty is associated with the potential for 1507 maize to (i) have an adverse effect on non-target butterflies and moths (Lepidoptera) and (ii) for target pests to develop resistance to 1507 maize.

In each update, EFSA concluded that there was no new evidence that invalidated its existing assessment of the environmental risks. This assessment concluded that 1507 maize 'is unlikely to raise a safety concern for the environment as long as appropriate management measures are implemented during cultivation'. To this end, EFSA recommended 'measures to address possible resistance in target pests to the insecticidal protein found in maize 1507 and to reduce the risk of exposure to the plant's pollen for certain highly sensitive species of non-target butterflies and moths'.

ACRE's previous advice concluded that this 'GMO is unlikely to have adverse effects on human health or the environment in the context of its proposed uses as compared with its non-GM counterparts'. This was on the basis that the likely comparator would be conventional maize sprayed with foliar insecticides and that, even if insect resistance evolved, it would be unlikely to result in environmental harm. However, there is uncertainty about whether a situation exists whereby (as yet, unidentified) highly sensitive non-target butterflies and moths are exposed to 1507 maize pollen such that the ecological impact of this interaction is greater than the consequences of applying foliar insecticides. In order to address this uncertainty, ACRE supported the applicant's proposal to carry out post-market monitoring involving experts from Spain.

In this advice, ACRE reconsiders its previous conclusions in the light of EFSA's 2012 opinion on the cultivation of 1507 maize. The result is that we discuss an alternative approach to addressing the uncertainty about the hazard posed to non-target butterflies and moths by 1507 maize pollen.

In its 2012 opinion, EFSA has endeavoured to further characterise this hazard by recalibrating a mathematical model developed for MON810 maize (Perry et al., 2010).

The model identifies hypothetical, worst case scenarios in which it is conceivable that a non-pest lepidopteran species could be adversely affected by pollen from 1507 maize (which expresses the Cry1F protein). However, this would require: (i) moderate to high

¹ <http://www.efsa.europa.eu/en/efsajournal/pub/1561.htm>.

² <http://www.efsa.europa.eu/en/efsajournal/pub/874.htm>.

³ <http://www.efsa.europa.eu/en/efsajournal/pub/2429.htm>.

⁴ <http://www.efsa.europa.eu/en/efsajournal/pub/2934.htm>.

⁵ <http://www.efsa.europa.eu/it/efsajournal/doc/2933.pdf>

adoption of 1507 maize in a maize growing region of the EU⁶ (ii) a susceptible larval stage of a species that is highly sensitive⁷ to the Cry 1F protein to be exposed to 1507 maize pollen (iii) for sufficient numbers of such individuals to be exposed over successive generations to affect an ecologically relevant change in the population of the species and (iv) for this impact to be greater than the impact associated with non-GM maize, where spraying with foliar insecticides is the most likely alternative to adopting Bt maize.

While such desk studies may be used to rule out potential hazards to non-target moths and butterflies in certain situations, it is doubtful that data exist to deal with all situations. This is not necessarily because there is a risk but because such hypothetical scenarios are very difficult to exclude. These are most likely to be found among uncommon butterfly and moth species in restricted localities; situations that will prove challenging to identify, and for which it is difficult to design effective case-specific monitoring.

An alternative approach is for Member States to implement measures that reduce exposure to 1507 maize pollen (e.g. through the use of non-Bt maize border rows or separation distances) in regions in which adoption rates of 1507 maize are likely to be moderate/ high⁶ and where significant populations of non-target butterfly and moth species are to be found in and around maize fields.

ACRE agrees with EFSA that such measures are likely to be overly precautionary for hypothetical hazards. To this end, ACRE considers it important to determine whether there is a more informed basis for predicting hazard. Further desk studies could be devised by Member States that predict whether non-target butterfly and moth species would be exposed to the pollen of 1507 maize to a significant degree by drawing together data on distribution and phenology as far as it is known. EFSA's model could provide a framework for estimating the consequences of exposure noting that any butterfly or moth species that were identified would not necessarily be highly sensitive to the Cry1F protein. If significant uncertainties remain after this exercise, then this would support the implementation of management measures.

In its 2012 opinions, EFSA has revisited its advice on insect resistance management (IRM). The evolution of resistance to pests and diseases is not a phenomenon that is specific to GM crops and ACRE is not convinced that this necessarily results in environmental harm. However in general, ACRE considers it important to implement measures that prevent or slow down the evolution of field resistance in pest species. To achieve this, ACRE agrees with EFSA's recommendations for IRM and with its advice that IRM needs to be updated periodically in the light of new information and technological advances.

⁶ For example, an uptake of 20% of 1507 maize in an area where maize represents 25% of the arable land.

⁷ The existence of highly sensitive non-pest Lepidoptera is theoretical, at present.

More detailed comment

Environmental risk assessment

There has not been any new evidence in the peer-reviewed literature or from commercial production or in EFSA's latest opinions that alters our conclusions on the environmental risks posed by the cultivation of 1507 maize.

ACRE's existing conclusions on the environmental risks posed by the cultivation of 1507 maize:

ACRE considers that 1507 maize is unlikely to pose a greater risk to human health or the environment in the context of its proposed uses as compared with its non-GM counterparts.

We consider that EFSA's successive opinions have been effective in identifying and discussing the relevance of the new evidence published in the scientific literature. Most of this evidence concerns the potential for 1507 maize to have a greater impact on non-target organisms (NTOs) compared with non-GM maize.

Potential impact on non-target organisms

This additional evidence on NTOs supports the existing conclusion that Cry1F protein is specific to lepidopteran species.

In our previous advice we highlighted the paucity of long term field data from studies involving GM maize expressing Cry1F protein (compared with studies involving GM maize events that produce Cry 1Ab protein such as MON810 and Bt11 maize). Since then Higgins et al. (2009)⁸ have published the results of a 3 year study on non-target (NT) arthropods in 1507 maize fields in the USA. No significant differences in arthropod assemblages were detected between treatments. EFSA considers that this study is relevant to the EU assessment because the range of sampled taxa were sufficiently representative of EU maize ecosystems. ACRE endorses this conclusion.

EFSA's opinion addresses the concern that NTOs that prey on, or parasitize the target pest (so-called natural enemies) may be adversely affected through a reduced or poorer quality food resource. The dependence of the natural enemy on the pest species will determine the impact. ACRE agrees with EFSA that it is inevitable that altered pest management practices will change the abundance of species in a crop. As we noted in our 2005 advice, the conventional treatment used when lepidopteran pest-pressure is high is likely to include foliar insecticides (Vasileiadis et al., 2011⁹). These would be expected to adversely affect populations of natural enemies directly.

⁸ Higgins LS, Babcock J, Neese P, Layton RJ, Mollenbeck DJ and Storer N (2009). Three-year field monitoring of Cry1F, event DAS-Ø15Ø7, maize hybrids for non-target arthropod effects. *Environmental Entomology* **38**: 281 – 292.

⁹ Vasileiadis VP, Sattin M, Otto S, Veres A, Palinkas Z, Ban R, Pons X, Kudsk P,

Another issue that EFSA discusses in its latest opinions is the potential for secondary pests to fill the niche left by the target pest. This is not a phenomenon that is unique to GM crops. A report from China linked regional Bt cotton cultivation with a mirid bug infestation (Lu et al., 2010¹⁰) and there are reports from the USA that the western bean cutworm (a pest that is not present in the EU) has increased in the corn belt as a result of decreased competition from pests targeted by Bt maize (Michel et al., 2010¹¹). However, predicting the incidence of secondary pests is difficult because it is highly dependent on the characteristics of the receiving environment, including the farming practices (Meissle et al., 2011¹²); as such, the examples of increases in secondary pests discussed above cannot be used to make predictions associated with the cultivation of 1507 maize in the EU. ACRE agrees with EFSA that for non-GM and GM agriculture, the application of integrated pest management measures is the most effective approach in managing secondary pests and minimising environmental impact.

Potential impact on non-target Lepidoptera

The hazard that EFSA has focused on in its updated opinions is the threat that 1507 maize pollen poses to highly sensitive larval stages of non-target Lepidoptera. EFSA has not addressed this through the identification of new data but through the adaptation of a mathematical simulation model that was developed initially for the environmental risk assessment (ERA) of MON810 maize (Perry et al., 2010¹³, 2011¹⁴).

In its 2012 opinion, EFSA has recalibrated the model and developed it to predict the efficacy of management strategies that could be adopted if further evidence demonstrated that the hazard characterised in the model translates into a biologically relevant risk.

ACRE considers that the model provides a useful framework for a more informed and quantitative discussion defining the circumstances when 1507 maize may present a hazard for non-target Lepidoptera, and in outlining scenarios where risk is negligible. This does not constitute new evidence that 1507 maize poses a risk to non-target Lepidoptera.

van der Weide R, Czembor E, Moonen AC and Kiss J. (2011). Crop protection in European maize-based cropping systems: Current practices and recommendations for innovative Integrated Pest Management. *Agricultural Systems*. **104** (7): 572-579.

¹⁰ Lu Y, Wu K, Jiang Y, Xia B, Li P, Feng H, Wyckhuys KAG and Guo Y (2010) Mirid bug outbreaks in multiple crops correlated with wide-scale adoption of Bt cotton in China. *Science* **38**: 1151-1154.

¹¹ Michel AP, Krupke CH, Baute TS and Difonzo (2010). Ecology and management of the western bean cutworm (*Lepidoptera noctuidiae*) in corn and dry beans. *Journal of Integrated Pest Management* **1**; 1 – 10.

¹² Meissle M, Romeis J, Bigler F (2001) Bt maize and integrated pest management – A European perspective. *Pest Management Science* **67**: 1049-1058.

¹³ Perry JN, Devos Y, Arpaia S, Bartsch D, Gathmann A, Hails RS, Kiss J, Lheureux K, Manachini B, Mestdagh S, Neeman G, Ortego F, Schiemann, Sweet J. (2010) A mathematical model of exposure of non-target Lepidoptera to Bt maize pollen expressing Cry1Ab within Europe. *Proceedings of the Royal Society B: Biological Sciences* **277**: 1417 -1425.

¹⁴ Perry JN. (2011) The effect of Bt maize on butterflies – reckoning the risk. *Outlooks on Pest Management* **22**: 199-205.

EFSA has estimated the proportion of lepidopteran species that would be highly sensitive to Cry1F protein from data available on a range of Lepidopteran species¹⁵. In establishing sensitivity categories for 'hypothetical unspecified Lepidoptera' EFSA has adopted a worst-case effect level (only a small proportion of species are expected to be highly susceptible to the Cry1F protein, and these same species will not necessarily be exposed to the protein: the worst-case scenario assumes a co-occurrence of these two elements). In dealing with uncertainty, EFSA has adopted an unrealistic scenario that over-estimates this likelihood. It suggests that risk managers use regional data to calculate exposure constants that better reflect their receiving environments. EFSA also acknowledges that more data are required to understand the ecological relevance of changes to a species that are predicted at one particular time point (1507 pollen shed) in a season at particular locations within a landscape (1507 maize fields and, where appropriate, their immediate margins).

EFSA recommends that in situations where highly susceptible Lepidoptera could be at risk, management options are adopted to either reduce exposure or to mitigate any effects.

In its 2005 opinion, EFSA concluded that the use of non-Bt maize border rows designed to prevent or delay the evolution of resistance in the target pests would also reduce significantly the exposure of non-target Lepidoptera present in the field margins to 1507 maize. It has not altered this view in its 2012 opinion. However, in further characterising the hazard, EFSA has highlighted that this is a precautionary measure that is based on hypothetical, worst case scenarios rather than empirical data. EFSA's 2012 opinion discusses other risk management options that could be adopted as a precautionary measure or if a risk were identified.

In calculating the potential exposure of non-target Lepidoptera to 1507 maize pollen, EFSA has estimated the number of plants that host them in maize fields and in the field margins (where these are present); noting that maize itself is not an important food source for these species. The in-field densities of host plants (i.e. weeds) in maize are very low and are represented in the model as either 0 or 0.01 plants m⁻². This demonstrates the significance of the type of crop under cultivation in addition to the plant protection practices adopted in determining the type and abundance of non-pest Lepidoptera in-field. Consequently most host plants will be outside of maize fields and their exposure to 1507 maize pollen will be related to distance from the crop. The use of non-Bt maize buffer rows and other measures (such as maintaining separation distances¹⁶ with areas containing non-target Lepidoptera that are of conservation concern and/ or which maintain important food host-plants for local populations) will reduce exposure.

As advised previously, ACRE considers it extremely unlikely that 1507 maize will be cultivated in the UK if the EU authorises this GMO for a 10 year period. This is because pests targeted by the Cry1F protein are not a problem in the UK. In terms of whether this

¹⁵ these tend to be pest species, not species that Member States would consider require protection.

¹⁶ EFSA considers that a distance of 30 m is sufficient to reduce the local mortality of lepidopteran species to a negligible level even for extremely sensitive species.

GM maize is likely to pose a greater risk than its non-GM counterparts in potential EU receiving environments (i.e. regions of the EU where there is significant pressure from the target pests), ACRE does not consider that any new evidence has been presented in recent opinions that warrants EFSA altering its existing conclusion. However, there is uncertainty as to whether a hazard to non-target Lepidoptera exists. The key question for risk managers is how to address this uncertainty.

ACRE's view is that it may be challenging to design case-specific monitoring with the power to detect statistically significant changes against the natural fluctuations and trends in lepidopteran populations. Whilst it is achievable for species that are relatively abundant and widespread in the target regions (i.e. where 1507 maize uptake is moderate/ high), for species that are rare, including protected species, this will be difficult.

An alternative approach to such monitoring is for Member States with regions in which adoption rates of 1507 maize are likely to be moderate/ high⁶ and which may support populations of non-target lepidopteran species, to require the implementation of measures that reduce the likelihood of exposure to 1507 maize pollen. In its opinion, EFSA has also suggested that the provision of additional food resources may be an option for maintaining lepidopteran populations in regions where it is conceivable that a hazard exists. Whereas ACRE agrees with EFSA that, where appropriate, risk managers should consider a range of measures, we note that the latter approach assumes that the lepidopteran species of interest will find the additional food resources. Such an approach may not be effective where the lepidopteran species of interest is not widely / evenly distributed in the landscape.

ACRE agrees with EFSA that these measures are likely to be overly precautionary. Therefore, ACRE considers it important to determine whether there is a more informed basis for predicting a hazard. Desk studies could be used to predict where priority species of non-target Lepidoptera are likely to be exposed to the pollen of 1507 maize to any significant degree (i.e. where local mortality may impact on population levels). The exposure parameters as defined by EFSA's model provide a framework to quantify the degree of spatial and temporal overlap of 1507 pollen and the susceptible feeding stages of lepidopteran species. If significant uncertainties remain after this exercise, then this would support the implementation of management measures.

Potential impact on target organisms: insect resistance

EFSA considers 'the possible evolution of resistance to the CRY1F protein in lepidopteran target pests as a relevant environmental and agronomic concern..' ACRE is not necessarily convinced that this will result in greater environmental harm than measures used to control pests in non-Bt maize. ACRE also notes that pests are under selective pressure to evolve resistance to all pest control measures¹⁷, including pest-resistant traits in non-GM as well as GM crops. In general, ACRE considers it important to implement measures that prevent or slow down the evolution of plant resistance to pests and disease.

¹⁷ More than four hundred species of insects have evolved resistance to insecticides

There has been a report of field resistance to Cry1F protein occurring in a pest species (fall armyworm) that is not present in the EU¹⁸. This was in Puerto Rico under conditions that are unlikely to occur in the EU and where IRM measures had not been implemented. Field resistance has not been reported in other countries where 1507 maize varieties have been cultivated. This GMO has been grown in the USA since 2001 and Canada since 2002.

The IRM plan for 1507 maize is based on a high dose /refuge strategy. The theory is that most rare resistant pests on 1507 maize will mate with more abundant susceptible pests from nearby refuges (containing non-Bt plants) resulting in progeny that are susceptible to the Cry 1F protein. This prevents/ retards the accumulation of (recessive) resistance genes in the pest population¹⁹. The effectiveness of the strategy depends on the pests being exposed to sufficient levels of Cry1F protein as well as characteristics of the resistance genes and pest behaviour. Whereas EFSA has concluded that the high dose/ refuge strategy is appropriate to manage pest resistance in the two main target species - the European and Mediterranean corn borers, it recommends that the applicant confirms that the strategy applies to other regionally important lepidopteran pests (as appropriate). EFSA agrees with the applicant's proposal to gather more EU field data to inform scientific understanding on the effectiveness of this approach in 1507 maize. In addition to carrying out case-specific monitoring on baseline susceptibility and changes in pest susceptibility, EFSA has recommended that the applicant monitor for 'unexpected field damage'. A farm questionnaire (see below) provides a suitable tool for this monitoring.

In conclusion, ACRE agrees with EFSA's recommendations for insect resistance management (IRM) measures detailed in its 2012 opinion⁴, in particular that IRM needs to be updated where necessary in the light of new information (including case-specific monitoring). ACRE considers that the different approaches that EFSA has outlined provide flexibility that risk managers should find helpful in ensuring that IRM and measures to reduce exposure to 1507 maize pollen (or to mitigate for any adverse effects) are compatible and are not unnecessarily burdensome.

General surveillance

The legislation requires applicants to provide a post-market environmental monitoring plan in applications to market GMOs and this should incorporate general surveillance to identify unanticipated adverse effects. ACRE supports a multi-tool approach that includes literature searches, farm questionnaires and 'already established routine surveillance practices' (as appropriate).

¹⁸ Matten SR, Head GP and Quemada HD. (2008) in Integration of Insect-Resistant Genetically Modified Crops within IPM Programs, How governmental regulation can help or hinder the integration of Bt crops into IPM programs, eds Romeis J, Shelton AM, Kennedy GG (Springer, New York), pp 27–39

¹⁹ Onstad DW (2008) Insect Resistance Management: Biology, Economics and Prediction (Academic, London)

ACRE has welcomed the development of harmonised farm questionnaires by an industry (Europabio) working group as a tool for identifying unanticipated changes at the farm-scale by those working most closely with the crop. In addition, ACRE considers that farm questionnaires may contribute to case-specific monitoring in particular situations. In the case of 1507 maize, the farm questionnaire may be used to collect information relating to IRM, both in terms of determining the measures that farmers are adopting and on the efficacy of IRM (as discussed above). Member States may also use farm questionnaires to confirm that management measures are adopted where they are required to address uncertainty about impacts on populations of non-target Lepidoptera in regions where there is moderate/ high uptake of 1507 maize. As these are precautionary, ACRE has recommended that desk studies are carried out to confirm that there is a hazard.

It is likely that details of farm questionnaires will continue to develop overtime as consent-holders and risk managers become more familiar with their implementation. However, it is important that questionnaires remain practical and proportionate. ACRE has identified questions relating to soil quality that could be included in addition to existing questions concerning yield, health and vigour of the crop, which provide an indication of soil health. These questions concern ease of working the land; surface ponding, soil pan formation and erosion. ACRE also supports recent moves to ensure that information is collected in the year following cultivation.

Recently, ACRE has been considering in more detail what existing surveillance networks (ESNs) in the UK may contribute to the general surveillance of GM crops (noting that previously, ESNs have not been used routinely to investigate relationships between cause and effect). Our report²⁰ analyses the capabilities and limitations of ESNs and their power to detect change. This information should inform UK risk managers on if and how ESNs might be used in the general surveillance of GM crops in the UK, including 1507 maize.

20 January 2013

²⁰ <https://www.gov.uk/government/publications/genetically-modified-crops-post-market-monitoring>

Final advice (11 May 2005) following EFSA GMO Panel opinion

In our previous advice issued on 29 April 2004 we considered that the notifier had not adequately addressed the possible impact of the insect resistance trait on non-target insects in the environmental risk assessment or in the case-specific post-market monitoring (PMM) plan of notification C/ES/01/01. Since issuing this advice, the notifier has submitted a revised PMM plan and the EFSA GMO Panel has issued its opinion on this notification. Having considered the revised PMM plan, ACRE is now content for the notifier to extend its consideration of the potential impacts of 1507 maize cultivation on non-target insects through PMM, rather than providing more evidence in the environmental risk assessment.

In summary, ACRE is now content that notification C/ES/01/01 meets the requirements of Directive 2001/18/EC and agrees with the Spanish competent authority to issue consent.

More detailed comment

Impact of the insect-resistant trait on non-target insects

Previously we advised that the notifier had not adequately addressed the possible impact of the insect resistance trait on non-target insects (i.e. those not intended to be controlled by the GMO) in the environmental risk assessment or in its case-specific PMM plan. However, the notifier has since revised the PMM plan for C/ES/01/01 and now proposes to monitor for adverse effects on non-target organisms resulting from the cultivation of 1507 maize. In this particular case, ACRE is content for the notifier to extend its consideration of non-target insects via the PMM plan, rather than by providing more evidence in the environmental risk assessment (as previously advised).

The EFSA GMO Panel has concluded that there is no reason to believe that 1507 maize will cause changes to non-target species that differ significantly from those caused by conventional farming and that it does not consider that potential impacts on non-target Lepidoptera should be addressed in the PMM plan²¹. Whilst ACRE recognises that there have now been several long term field studies looking for adverse impacts of Bt crops on non-target insects and none have been found (e.g. Pons et al. 2005), ACRE also notes that many of these studies have involved GM maize containing the Cry1Ab gene (present in Bt11 and Bt176) rather than the Cry1F gene, which is present in 1507 maize. Consequently, ACRE considers it appropriate to generate more field data for the Cry1F trait through monitoring. Hence we are pleased to note that the applicant proposes to carry out such monitoring of non-target organisms and intends to call upon the expertise of Spanish researchers (who have carried out detailed long term studies with Bt maize) to develop the monitoring protocols. Our advice on the consideration of non-target insects in this notification has therefore evolved to reflect both the greater availability of ecological

²¹ Section 5.2.4 of EFSA's Opinion: http://www.efsa.eu.int/science/gmo/gmo_opinions/827_en.html

data and the revisions the applicant has made to the notification and monitoring plans over time.

ACRE recognises that in some, but not all cases, the relevant comparator will be non-GM maize crops treated with insecticide to control Lepidopteran pests. We anticipate that it is extremely unlikely that GM maize containing the 1507 transformation event would be cultivated in the UK as pests targeted by the Bt protein are not a problem in the UK.

Impact of altered weed management

The scope of notification C/ES/01/01 is limited to the cultivation of 1507 maize without the application of glufosinate ammonium until the herbicide is licensed for this use. ACRE accepts this position but advises that if consent for cultivation of 1507 maize is issued, this should anticipate the licensing of glufosinate ammonium herbicides for use with GM maize. The results of the UK's Farm-Scale Evaluations (FSE²²) showed that under the particular conditions used in these trials, the cultivation of GM herbicide tolerant (HT) maize did not adversely affect wildlife as compared with typical management regimes used in the cultivation of non-GM maize crops. However, as farmers may not use the herbicide regime used in the FSE and as herbicide management regimes are likely to change over time (for example, with the phasing out of certain herbicides such as atrazine and as farmers become more familiar with managing herbicide tolerant crops) ACRE advises that the relative impact on farmland biodiversity of cultivating GMHT maize (in association with its respective broad spectrum herbicide) should be monitored. Therefore, ACRE agrees with the EFSA GMO Panel's recommendation that observation of general weed abundance and diversity should be included in the general surveillance plan of 1507 maize.

Post-market monitoring

The EFSA GMO Panel has agreed in principle with the general methods and approach to the general surveillance plan but has made recommendations for improving the farmer questionnaire. We also welcome the inclusion of the proposed farmer questionnaire in the notifier's revised PMM plan but concur with the EFSA GMO Panel that it requires further development along the lines of the recommendations made in the GMO Panel's Opinion.

11 May 2005

Reference

Pons X, Lumbierres, B, Lopez, C, Albajes, R. 2005. European Journal of Entomology 102: 73-79. Abundance of non-target pests in transgenic Bt-maize: a farm-scale study

²² Link to ACRE advice on Farm-scale Evaluation results:

http://webarchive.nationalarchives.gov.uk/20080306073937/http://www.defra.gov.uk/environment/acre/advice/pdf/acre_advice44.pdf

Advice (29 April 2004) after the 45 day assessment period

ACRE has considered this notification for the import, use and cultivation of insect resistant and herbicide tolerant maize based on transformation event 1507. ACRE has assessed the notifier's responses to the further information the Committee requested (see ACRE advice dated September 2003) and also the information provided in response to comments from other Member States. ACRE considers that the notifier has not adequately addressed the possible impact of the insect resistance trait on non-target insects in the environmental risk assessment or in its case-specific post-market monitoring plan. Consequently ACRE advises that consent for the cultivation of 1507 maize is not issued at this stage.

Comment

ACRE first considered this notification in September 2003 and advised that further information was required for it to be able to assess whether the cultivation, import and use of 1507 maize poses a risk to human health and the environment. The notifier's response has been assessed by the Committee:

Event-specific detection

ACRE is content with the notifier's response to the request for clarification on the event-specific detection protocol for 1507 maize, but notes that whilst the DNA sequence targeted for detection is event-specific (because it includes a rearranged fragment of insert DNA) it does not include any flanking host DNA.

Impact of altered weed management

In the further information provided, the notifier states that the scope of notification C/ES/01/01 is limited to the cultivation of 1507 maize without the application of glufosinate ammonium until the herbicide is licensed for this use. ACRE accepts this position but advises that if consent for cultivation of 1507 maize is issued, this should anticipate the licensing of glufosinate ammonium herbicides for use with GM maize and restrict the herbicide regime to that used in the Farm-scale Evaluation (FSE). This is line with ACRE advice on the FSE results, which concludes that cultivation of GM herbicide tolerant maize will not adversely affect the environment if cultivation is managed as in the FSE²³. If alternative herbicide regimes are proposed the Committee would expect to see evidence to demonstrate that these would not adversely affect the environment as compared to conventional management regimes with non-GM maize crops.

²³ Link to ACRE advice on Farm-scale Evaluation results:
http://webarchive.nationalarchives.gov.uk/20080306073937/http://www.defra.gov.uk/environment/acre/advice/pdf/acre_advice44.pdf

Impact of the insect resistant trait on non-target insects

ACRE advises that the environmental risk assessment (ERA) for 1507 maize does not adequately consider the potential impact of the insect resistance trait on non-target Lepidoptera. Whilst the notifier has provided strong supporting evidence that there is a high degree of specificity in the biological activity of CRY1F protein against target lepidoteran pests, it has not considered what Lepidoptera are associated with maize fields (including hedgerows) or provided experimental data that supports the prediction that these insects would not be adversely affected by the cultivation of 1507 maize. The Committee is aware that numerous studies have been conducted into the potential impact of the insect resistant trait on a diversity of non-target organisms besides the Monarch butterfly, however this information has not been included in the notification.

Post-market monitoring plan: case specific

As the aim of the case-specific part of the post-market monitoring plan is to investigate risks identified in the ERA and also to test any assumptions included in the ERA, the Committee considers that case-specific monitoring for assumptions about the impact of the insect resistance trait on non-target Lepidoptera is relevant to this release. The plan should identify the insect species to be monitored and a description of the experimental design, which should include details of the experiment's duration, the selection of study sites including comparators and a consideration of its statistical power.

ACRE has taken into account the further information requested from the notifier by other member states. In particular, the Committee discussed the potential adverse effects on non-target organisms caused by tritrophic effects. Whilst the known target organisms of the CRY1F protein are not present in the UK (i.e. *Ostrinia nubilalis* and *Sesamia nonagrioides*), ACRE notes that the case-specific monitoring plan does not address assumptions about the potential indirect effects that the cultivation of 1507 maize might have on predators and parasitoids associated with these target organisms in European countries where they are found. An important consideration in designing such monitoring experiments is the baseline against which levels of non-target organisms in 1507 maize fields should be compared. In areas of Europe where the target pest occurs, the conventional alternative to cultivating insect-resistant maize is to treat non-resistant varieties with chemical sprays.

General surveillance

In its considerations, ACRE has taken into account the further information requested from the notifier by other member states. In particular, the Committee discussed the general surveillance plan for unanticipated adverse effects on non-target organisms.

Whilst ACRE agrees with the principles of the surveillance plan outlined by the notifier, it considers the detail and timeframes suggested to be inadequate. Before this maize is cultivated in the EU the notifier should provide a more detailed general surveillance plan for monitoring unanticipated effects, which should include (1) the strategy for identifying

which organisms will be monitored for in different member states (2) the strategy for identifying resources that will be used to provide information, including (where appropriate), which national surveillance programmes will be used (3) the monitoring frequency and the type of information that will be collated and (4) how the company will ensure participation to ensure a robust assessment. The Committee also recommends that monitoring reports be provided by the applicant on an annual basis.

In accordance with its advice on the FSE results²⁴, ACRE advises that as atrazine (the principal management practice for conventional maize) is to be phased out in April 2005, monitoring of the indirect effects associated with the management of 1507 maize in the UK should include a comparison of the impacts of new conventional management regimes with those of glufosinate ammonium herbicides used in association with 1507 maize. The FSE results show that weed seed biomass is a key indicator in such monitoring.

ACRE has previously issued advice on the import and use of 1507 maize, excluding its cultivation²⁵ (notification C/NL/00/10), where it advised that consent for release be conditional on the applicant providing a more detailed plan for monitoring animal feed safety before this maize is imported into the EU. Further details should include: (1) precisely who will be requested to provide information; (2) what type of information will be requested and the frequency of requests and (3) how the company will ensure participation to ensure a robust assessment. The Committee also recommends that monitoring reports should be provided by the applicant on an annual basis

29 April 2004

²⁴ Link to ACRE advice on Farm-scale Evaluation results:
http://webarchive.nationalarchives.gov.uk/20080306073937/http://www.defra.gov.uk/environment/acre/advice/pdf/acre_advice44.pdf

²⁵ Link to ACRE advice on C/NL/00/10:
http://webarchive.nationalarchives.gov.uk/20080306073937/http://www.defra.gov.uk/environment/acre/advice/pdf/acre_advice45.pdf

Advice (September 2003) after the 60 day assessment period

ACRE has considered this notification for the import, use and cultivation of insect resistant and herbicide tolerant maize based on transformation event 1507. The Committee does not consider that sufficient information has been provided by the notifier to allow a full assessment of potential risks to human health and the environment of the cultivation of maize 1507. In coming to this conclusion ACRE have taken account of the advice of the Advisory Committee on Animal Feedingstuffs (ACAF) Before ACRE can complete its assessment the following information is required..

1. Further details concerning the PCR-based event-specific detection protocol
2. An environmental risk assessment of the impacts of altered management practices associated with the cultivation of 1507 maize, including consideration of the impact of the insect resistance trait, altered herbicide regime and any potential cumulative effects of the two traits and associated changes in management
3. An improved post-market monitoring plan that takes into account any risks identified in the environmental risk assessment, and tests any assumptions made in the environmental risk assessment

Comment

Molecular characterisation

ACRE considered carefully the thorough molecular characterisation of transformation event 1507 provided. The Committee is content that the data provided support the conclusions, and that the event (including rearrangements) has been thoroughly characterised and potential risks evaluated appropriately. The Committee requests clarification concerning the PCR-based event-specific detection protocol. On page 63 of the notification it is stated that the amplified fragment is between the 3' end of the insert and adjacent sequence showing homology to the ORF25PolyA terminator whereas in Annex 15 states that the primers span the 3' end of the insert and an inverted repeated version of the Cry1F gene.

Animal feed safety

On the basis of the evidence supplied by the notifier (including information provided as part of notification NL/00/10) ACRE and ACAF are satisfied that maize line 1507 is as safe as any other commercial maize line when used as feed for animals and that its use poses no risks for consumers of animal products. The Committees are also satisfied that the Cry1F protein does not pose a risk for animals consuming maize line 1507 or for consumers of products derived from animals fed this line.

Environmental risk assessment

ACRE considered carefully the environmental risk assessment (ERA) for 1507 maize provided by the notifier. The Committee did not consider that this assessment had been carried out in full, especially as 1507 maize is both herbicide tolerant and insect resistant. In particular, the ERA does not consider the possible indirect effects due to changes in management associated with the use of 1507 maize. There are a number of areas that need to be addressed before the ERA is complete:

- Impact of altered weed management. The notifier states that the glufosinate tolerance trait would allow alternative weed management strategies based on the use of this broad spectrum herbicide to be used. This may have an impact on the biodiversity of organisms dependent on weeds for food, which, in turn, may impact on higher trophic levels. The results of the Farm Scale Evaluations of herbicide tolerant crops in the UK, which will be published shortly, will inform this part of the risk assessment.
- Impact of insect resistance trait on target insects. While the notification considers the impact of the insect resistance trait on insects not targeted by the Bt toxin, the ERA does not consider fully the potential wider biodiversity impact of the insect resistance trait resulting from the effect on Lepidoptera. This consideration should not only include consideration of the primary targets *Ostrinia nubilalis* and *Sesamia nonagrioides* but also other potential maize or grass feeding Lepidoptera.
- Cumulative effect of changing management practices. As well as the assessment of the wider biodiversity impacts of the individual traits in 1507 maize, and their associated management practices, the ERA should also consider the potential cumulative impact of the traits. For example, is the impact of the insect resistance trait on non-target Lepidoptera likely to be exacerbated by altered floristic balance within fields caused by changes in herbicide use?

Post-market monitoring

The aim of the case-specific part of the post market monitoring plan is to investigate risks identified in the ERA, and also to test any assumptions included in the ERA. The current plan for case-specific monitoring is focussed on monitoring to test the effectiveness of the Insect Resistance Management (IRM) strategy. While the Committee consider the IRM and monitoring of resistance to be adequate, the notifier will need to modify considerably the case-specific monitoring plan to take into account the additional requirements for the ERA outlined above. For example, depending on the outcome of the revised ERA, it may be appropriate to monitor changes in populations of target and non-target insects. In drawing up a revised case-specific monitoring plan the notifier should also consider the appropriate timeframe for reporting the outcome of monitoring to the regulatory authorities – this should be as frequent as is compatible with the type of monitoring study being carried out.

September 2003