



ADVISORY COMMITTEE ON RELEASES TO THE ENVIRONMENT

Advice on a notification for marketing of herbicide tolerant GM oilseed rape

Notifier: Monsanto Europe S.A.

Notification Reference: C/NL/98/11

Product: Oilseed rape genetically modified for tolerance to glyphosate herbicides, line GT73

Scope: For import into the European community and use for processing for food and feed of GT73 oilseed rape and from any progeny derived from line GT73 by conventional breeding methods with non-genetically modified oilseed rape. This notification does not include cultivation.

Date: 24th September 2003

Advice of the Advisory Committee on Releases to the Environment (ACRE) under S.124 of the Environmental Protection Act 1990 (Part VI) to the Secretary of State for Environment, Food and Rural Affairs, Scottish Ministers, Ministers of the Welsh Assembly Government and the Department of Environment (Northern Ireland).

Secondary advice: ACRE is not fully satisfied at this stage on the basis of the evidence provided that the risk to human health and the environment arising from marketing of this product for importation and processing in the UK will be no different from that of other oilseed rape imported for processing and animal feed purposes. In coming to this conclusion ACRE have taken account of the advice of the Advisory Committee on Animal Feedingstuffs (ACAF).

ACRE considered the notifiers responses to three requests for further information (see Appendix 1). ACRE was satisfied with the response provided regarding flanking sequences. However ACRE still has concerns regarding seed spill and remains of the opinion that the post market monitoring plan should include active monitoring for spillage of GT73 seed during import, transportation and processing and include tests for the establishment of feral populations of GT73 oilseed rape. The plan should also include appropriate emergency plans should such populations be identified.

In addition, ACRE and ACAF are not satisfied that the notifiers have supported the hypothesis that increased liver weight in rats fed GT73 compared with controls is attributed to higher glucosinolate content levels in the test material. A satisfactory explanation for this potentially adverse response observed in the rat feeding study is required.

Comment

ACRE considered the risks to human health and the environment posed by the release of genetically modified herbicide tolerant oilseed rape. In its primary advice (Appendix 1) the committee requested three pieces of further information from the notifier:

1. Sequences of the DNA on either side of the insertion site of the *epsps* and *gox* gene cassette in the oilseed rape genome. The requested information was provided by the notifier in full. ACRE considered the flanking sequence data and the analysis provided by the notifier and was content that they confirmed that the inserted DNA had not disrupted any endogenous genes. As a result ACRE concluded that they were now content with this aspect of the risk assessment.
2. Details of the likely point(s) of import and processing of GT73 oilseed rape in the UK, and information concerning standard operating procedures for handling GT73 seed. The notifier reported that the main port of import in the UK is Liverpool and that most oilseed rape grain is unloaded and crushed in the port area. As a result Monsanto do not expect seed spill to be a problem. ACRE noted that the notifier had not provided any supporting evidence to demonstrate that loss of material will be minimal hence the Committee is not convinced that seed spill will not occur and that feral populations will not materialise.
3. The post market monitoring plan should include monitoring for spillage of GT73 seed during import, transportation and processing and test for the establishment of feral populations of GT73 oilseed rape. The plan should also include appropriate emergency plans should such populations be identified. The notifier provided a revised and more detailed post market monitoring plan. In particular the area of general surveillance for unanticipated effects had been expanded and focuses on the use of existing networks.
ACRE was disappointed that Monsanto still have not acknowledged that one of the purposes of post-market monitoring is to confirm any assumptions which underpin the risk assessment. One such example would be to confirm that the assumptions made regarding seed spill are valid and to confirm that herbicide tolerant feral oilseed rape populations do not result. Hence ACRE remains of the view that the post market monitoring plan should include active monitoring for spillage of GT73 seed during import, transportation and processing and include tests for the establishment of feral populations of GT73 oilseed rape between the point of import and final destination. The plan should also include appropriate emergency plans should such populations be identified.

Animal Feed Safety

The Advisory Committee on Animal Feedingstuffs (ACAF) considered additional information provided in the dossier from the perspective of animal feed safety. Further consideration of the compositional equivalence data concluded that GT73 is substantially equivalent to its parental control and that its composition falls within the range of values seen in other non-transgenic commercial varieties.

ACAF considered the animal feed studies provided in the dossier. No significant differences in growth were observed between rats fed GT73 or Westar parental variety oilseed rape (Naylor, M. W. 1995; MSL-14164). However, the relative liver weights for the rats fed 15% processed GT73 oilseed rape were found to be significantly higher than controls. This was attributed by the notifiers to higher glucosinolate concentration in the GM diets compared with the corresponding control diets. This adverse effect was not observed in a subsequent rat experiment (Naylor, M. W. 1996; MSL-14778), ACAF is not satisfied that the subsequent feeding study satisfactorily supports this hypothesis as the two studies are not equally comparative.

Therefore ACAF remains of the view that the adverse response in rats to a diet containing 15% GT73 requires further explanation.



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Advice on a notification for marketing of herbicide tolerant GM oilseed rape

Notifier:	Monsanto Europe S.A.
Notification Reference:	C/NL/98/11
Product:	Oilseed rape genetically modified for tolerance to glyphosate herbicides, line GT73.
Scope:	For import into the European community and use for processing for food and feed of GT73 oilseed rape and from any progeny derived from line GT73 by conventional breeding methods with non-genetically modified oilseed rape. This notification does not include cultivation.
Date:	10 th March 2003

Advice of the Advisory Committee on Releases to the Environment (ACRE) under S.124 of the Environmental Protection Act 1990 (Part VI) to the Secretary of State for Environment, Food and Rural Affairs, Scottish Ministers, Ministers of the Welsh Assembly Government and the Department of Environment (Northern Ireland).

Primary advice: ACRE is satisfied at this stage on the basis of the evidence provided that the risk to human health and the environment arising from marketing this product for importation and processing in the UK will be no different from that of other oilseed rape imported for processing and animal feed purposes. This advice is pending receipt of further information as outlined below. In coming to this conclusion ACRE have taken account of the advice of the Advisory Committee on Animal Feedingstuffs (ACAF). Further information required is as follows:

1. Sequences of the DNA on either side of the insertion site of the *epsps* and *gox* gene cassette in the oilseed rape genome
2. Details of the likely point(s) of import and processing of GT73 oilseed rape in the UK, and information concerning standard operating procedures for handling GT73 seed.
3. The post market monitoring plan should include monitoring for spillage of GT73 seed during import, transportation and processing and test for the establishment of feral populations of GT73 oilseed rape. The plan should also include appropriate emergency plans should such populations be identified.

Comment

On the basis of the information provided regarding characterisation and risk assessment of GT73 ACRE were content with this notification for genetically modified oilseed rape in terms of risk to human health and the environment. However, the Committee would like to comment that they were disappointed with the presentation of this dossier which was difficult to navigate. In addition ACRE commented that as the dossier was submitted in 1998 the supporting scientific literature was now a number of years old. However, the Committee agreed that this did not significantly affect the risk assessment of GT73.

Genetic modification and molecular characterisation

ACRE noted that the data relating to molecular characterisation of GT73 was poorly presented, in particular the quality of reproduction of the Southern blots was criticised. On a specific point, on several occasions in the dossier Monsanto refer to restriction enzyme digests with *EcoR1* which they state does not cut inside plasmid PV-BNGT04 (e.g. part D, 2, d). *EcoR1* does in fact cut within this plasmid. It would be appreciated if Monsanto could clarify this.

The genetically modified oilseed rape line GT73 was created by *Agrobacterium tumefaciens* mediated transformation. The *cp4epsps* and *goxv247* genes were inserted into the plant genome resulting in tolerance of the GM oilseed rape to glyphosate herbicides. Southern blot and PCR analysis was performed to demonstrate that the plasmid DNA is inserted at a single locus in the nuclear chromosome and that vector backbone sequences are absent from line GT73. On the basis of the data supplied by the applicant, it is likely that a single copy insert is present in line GT73 and that vector backbone sequences are most likely absent.

No information is provided in the dossier regarding the location in the oilseed rape genome where the genetic material is inserted. ACRE acknowledge that, on the basis of the animal feed data provided, that GT73 oilseed rape is substantially equivalent to its non-GM counterparts hence, insertion of the additional genetic material does not affect the phenotype of GT73 (with the exception of glyphosate tolerance) and therefore has not disrupted a gene that affects growth and agronomy of GT73. However, ACRE consider it important to know and understand the nature and location of the insertion of the genetic material, hence, request that the notifier provide this information, specifically sequence information of the flanking regions of the inserted genetic material. This should include details of any genes disrupted as a result of the insertion and their possible phenotypic effects on the GM plant.

Animal feed safety

ACRE asked the Advisory Committee on Animal Feedingstuffs (ACAF) to assess GT73 from the perspective of animal feed safety. ACAF, like ACRE, noted that the dossier was poorly presented and randomly organised, making it difficult to find the relevant data. ACAF considered the dossier with respect to the safety of the expressed proteins, safety of rapeseed GT73 and animal studies.

Safety of the expressed CP4 EPSPS and GOX proteins was assessed by over expression in *E coli*, extraction and tests in simulated gut environments and in acute toxicity studies in mice. The CP4 EPSPS protein has been widely studied in previous constructs, on the basis of this and the evidence presented by Monsanto, ACAF conclude that this protein is safe for use. In comparison the GOX protein has not undergone the same level of scrutiny. The evidence provided to ACAF concluded that the GOX protein is degraded in simulated gut environments, activity is lost at temperatures greater than 60°C and when fed to mice in an acute toxicity study no adverse responses were noted. On the basis of this information ACAF were content with the safety and toxicity analysis of the GOX protein.

ACAF considered the safety of GT73 oilseed rape on the basis of comparative compositional data. The data provided generally showed no significant differences between GT73 and the parental Westar variety. Although none of the data provided would appear to show cause for concern, ACAF is reluctant to draw conclusions on the composition equivalence of GT73 to its parental Westar control on the basis of the available information. ACAF noted the variation in the concentration of alkyl glucosinolates in samples of GT73 compared with the Westar parental control. However, all values were well below the levels set for alkyl glucosinolates hence, this variation was not considered a safety issue. ACAF advised that a possible course of action could be to require regular analysis of imported GT73 alkyl glucosinolates concentrations to ensure they do not exceed the limits set by European legislation as part of the post-market monitoring plan.

ACAF considered the animal feed studies provided in the dossier. No significant differences in growth were observed between rats fed GT73 or Westar parental variety oilseed rape. However, the relative liver weights for the rats fed 15% processed GT73 oilseed rape were found to be significantly higher than controls. This was attributed to higher glucosinolate concentration in the GM diets compared with the corresponding control diets. This adverse effect was reportedly not observed in a subsequent rat experiment, although ACAF have not seen the relevant data.

Although, on the basis of the summary compositional data provided in this dossier ACAF would expect GT73 oilseed rape to behave as any other oilseed rape variety, they could not reach this conclusion without seeing further information.

Post market monitoring plan

The post market monitoring plan is a new requirement under Directive 2001/18/EC. The plan provided by the notifier is brief and limited. On the basis of the risk assessment for GT73 Monsanto do not propose to carry out any case-specific monitoring. ACRE agree with this conclusion as the risk assessment does not identify any risks in relation to human health or the environment from the use of GT73 oilseed rape as defined in the notification (i.e. for import and processing).

Directive 2001/18/EC places a requirement to provide a monitoring plan for the occurrence of adverse effects not anticipated in the environmental risk assessment. ACRE consider that the proposal in response to this requirement put forward by the notifier is unsatisfactory. In particular the plan does not take into account monitoring of the occurrence and effects of seed spill during transportation and processing of the oilseed rape seed. Based on current experience regarding movement of non-GM oilseed rape in the UK seed spill is likely to occur and will result in the survival and establishment of feral oilseed rape populations and their hybridisation with crop and other feral populations. It is accepted that the risk of harm to human health and the environment from seed spill is low, however there is an issue, in the UK, regarding the segregation of transgenic and non-transgenic material. Hence, ACRE request that Monsanto review their monitoring plan taking into account methods of monitoring and reporting seed spill, incorporating a proposal as to how seed spill may be controlled. It should also include plans for monitoring and controlling establishment of feral populations as a result of seed spill.