



Australian Government
Department of Health and Ageing
Office of the Gene Technology Regulator

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EXECUTIVE SUMMARY
of
THE RISK ASSESSMENT AND RISK MANAGEMENT PLAN
for
APPLICATION NO. DIR 055/2004
from
MONSANTO

THE DECISION

The Gene Technology Regulator (the Regulator) has made a decision to issue a licence for dealings involving intentional release of GMOs into the environment, in respect of application DIR 055/2004 from Monsanto Australia Limited (Monsanto).

The licence allows Monsanto to conduct a large scale field trial of up to 1815 hectares over two seasons from 2005 to 2006. Summer plantings will be conducted in the cotton growing regions of New South Wales and southern Queensland from September 2005 to May 2006 on up to 1770 hectares and a maximum of 86 sites. A small part of the plantings will take place in the winter in northern Australia (potentially including northern Western Australia (WA), northern Queensland and the Northern Territory (NT)) from March to November 2006 on up to 45 hectares and a maximum of 5 sites.

The *Gene Technology Act 2000* (the Act) and the *Gene Technology Regulations 2001* (the Regulations) set out requirements which the Gene Technology Regulator (the Regulator) must follow when considering an application for a licence to intentionally release a genetically modified organism (GMO) into the environment.

For a licence to be issued, the Regulator must be satisfied that the release will not pose any risks to human health and safety or the environment that can not be managed. As part of the evaluation process, Section 51 of the Act requires the Regulator to prepare a risk assessment and risk management plan (RARMP) for each licence application, in consultation with a wide range of expert groups and stakeholders.

Under Section 52 of the Act, the Regulator is required to seek comment on the RARMP from those consulted in its preparation and to invite submissions from the public. Matters raised relating to the protection of human health and safety or the environment are taken into account in finalising the RARMP, which then forms the basis of the Regulator's decision on whether or not to issue a licence, and if so, what conditions to impose.

The Act is designed to operate in a cooperative legislative framework with other regulatory authorities that have complementary responsibilities and specialist expertise. As well as enhancing coordinated decision making, this arrangement avoids duplication. The OGTR liaises closely with other regulators to ensure the identification, evaluation and management of risks that may be associated with the development and use of gene technology.

THE APPLICATION

Monsanto Australia Ltd (Monsanto) applied for a licence (application number DIR 055/2004) for the intentional release of genetically modified (GM) herbicide tolerant (Roundup Ready[®] Flex MON 88913) and herbicide tolerant/insect resistant (Roundup Ready[®] Flex MON 88913/Bollgard II[®]) cottons into the environment, on a limited scale and under controlled conditions. Monsanto sought to conduct a large scale field trial over two seasons on up to 91 sites covering a total area of up to 1811 hectares from 2005 to 2006 in the southern summer growing season and the northern winter growing season.

Roundup Ready[®] Flex cotton MON 88913 (abbreviated to Roundup Ready[®] Flex cotton) contains two copies of a gene (*cp4 epsps*) derived from a common soil bacterium. The protein encoded by the *cp4 epsps* gene is an enzyme¹ (CP4 EPSPS) that is able to function in the presence of glyphosate, the active ingredient in Roundup[®] herbicides, whereas the enzyme expressed by the equivalent gene in other, non-herbicide tolerant cottons is inhibited by glyphosate. As this enzyme is involved in an important biochemical pathway for the synthesis of essential building blocks of cellular proteins, cottons that do not have the *cp4 epsps* gene are killed by the application of glyphosate. In contrast, the presence of the CP4 EPSPS enzyme in Roundup Ready[®] Flex GM cotton allows the application of Roundup Ready[®] herbicide for the control of weeds that emerge in the crop, without damaging the crop itself.

Roundup Ready[®] Flex cotton MON 88913/Bollgard II[®] cotton (abbreviated to Roundup Ready[®] Flex/Bollgard II[®] cotton) was produced by crossing of Roundup Ready[®] Flex cotton with GM Bollgard II[®] cotton via conventional breeding. This introduced two genes that produce insecticidal proteins which provide resistance to the major caterpillar pests of cotton. Bollgard II[®] cotton is approved for commercial release south of latitude 22° South in Australia (DIR 012/2002).

Roundup Ready[®] Flex cotton differs from GM Roundup Ready[®] cotton (also approved for commercial release south of latitude 22° South; DIR 023/2002) in that the former has two copies of the *cp4 epsps* gene, under the control of two different novel promoters², while the latter only has one. This means that tolerance to Roundup Ready[®] herbicide is prolonged in Roundup Ready[®] Flex cotton due to enhanced expression of the CP4 EPSPS enzyme in both level and duration. Yield loss occurs if Roundup Ready[®] herbicide is applied to Roundup Ready[®] cotton beyond the four-leaf stage of growth (approximately five weeks after planting). The applicant anticipates that Roundup Ready[®] Flex cottons will be able to tolerate application of Roundup Ready[®] herbicide at later stages of plant growth without yield loss, allowing a wider window to apply herbicide during growth of the cotton crop. This is intended to increase growers' flexibility in the timing of herbicide application for integrated weed management and is not expected to increase the overall amount of herbicide use.

The aims of this field trial are to transfer the Roundup Ready[®] Flex trait into elite Australian cotton varieties, to test the agronomic performance of the GM cottons under Australian field conditions, to produce seed for future releases (which would require separate applications and approval processes), to set up demonstration sites for industry, government, researchers and the wider community and to collect data required for future applications.

The applicant proposed a number of containment measures to minimise the spread and persistence of the GMOs and the introduced genes from the trial sites. These include:

¹ Enzymes are proteins which catalyse specific biochemical reactions.

² The term 'promoter' refers to a regulatory sequence that controls the expression of the gene that is linked to it.

- surrounding the trial sites by pollen traps or isolation zones;
- destroying all viable GM materials that remains on the trial sites following harvest;
- ensuring that trial sites are not within 50 metres of natural waterways;
- destroying any volunteer GM cotton plants that may occur at the release sites after completion of the plantings; and
- implementation of a management plan which will prevent unintended dispersal of GM cottonseed from demonstration sites by visitors .

None of the cotton plants from the release, or their by-products, will be used in animal feed or human food. However, the applicant has been given approval to sell lint from the release. Lint does not contain genetic material or protein. Transport of the GMOs and materials from the GMOs will be in accordance with the transport guidelines issued by the Regulator.

A limited and controlled release of Roundup Ready[®] Flex and Roundup Ready[®] Flex/Bollgard II[®] cottons was previously approved under licence DIR 035/2003. This field trial is being conducted from 2003 to 2005 in NSW, Queensland, NT and northern WA. The licence conditions for DIR 035/2003 contain a requirement to conduct a research program and a range of data on Roundup Ready[®] Flex cotton relevant to the assessment of this application have been collected and provided to the Regulator.

THE EVALUATION PROCESS

A risk assessment and risk management plan (RARMP) has been prepared in relation to licence application DIR 055/2004 from Monsanto in accordance with the Act, the Regulations and the Risk Analysis Framework. This framework was developed as part of the establishment of the regulatory arrangements in consultation with the public, State, Territory and Australian Government agencies, key stakeholders and the Gene Technology Technical Advisory Committee³. It is available at www.ogtr.gov.au.

Details of the process that the Regulator must follow, including the prescribed consultation process on the application, and the matters that she must consider in preparing a RARMP, are set out in Appendix 8 of the RARMP. The complete RARMP along with a review document 'The Biology and Ecology of Cotton (*Gossypium hirsutum*) in Australia' (produced to further inform the risk analysis) and a set of 'Questions and Answers' on the evaluation of the application can be obtained from the OGTR by calling 1800 181 030 or from the OGTR's website at www.ogtr.gov.au.

The risk assessment considered information contained in the application (comprising: information required by the Act and the Regulations on the GMOs; the parent organism; the proposed dealings, including proposed containment conditions; and potential impacts on human health and safety and the environment), current scientific knowledge and submissions received during consultation with expert groups, authorities and the public (issues raised in submissions are summarised in Chapter 2 and Appendix 9 of the RARMP).

Through this process, potential hazards to human health and safety or the environment that may be posed by the proposed release of the GM cottons were identified. These have been

³ This RARMP was prepared and consulted on prior to the OGTR finalising a review of the framework. Therefore, new terminology selected to distinguish between the different elements of risk characterisation have not been applied.

evaluated to determine the likelihood of each hazard occurring and the likely impact of each hazard, were it to be realised.

The identified potential hazards relate to:

- **toxicity and allergenicity to humans:** could Roundup Ready® Flex or Roundup Ready® Flex/Bollgard II® cottons be more toxic or allergenic than non-GM cotton to humans as a result of the novel gene products or because of unintended effects?
- **toxicity to non-target organisms:** could Roundup Ready® Flex or Roundup Ready® Flex/Bollgard II® cottons be harmful to non-target organisms as a result of the novel gene products or because of unintended effects?
- **weediness:** could the genetic modifications be harmful to the environment by increasing the potential for the Roundup Ready® Flex or Roundup Ready® Flex/Bollgard II® cottons to establish as a problematic weed compared to non-GM cotton?
- **transfer of introduced genes to other organisms:** could there be adverse consequences from potential transfer of the introduced genetic materials to other cultivated cotton crops, feral or native cottons, or to other organisms? and
- **herbicide and insecticide resistance:** could weeds develop resistance to glyphosate (if the Roundup Ready® crop-herbicide combination were used inappropriately) and could target insects develop resistance to the insecticidal proteins produced by the introduced insecticidal genes in Roundup Ready® Flex/Bollgard II® cotton?

The Australian Pesticides and Veterinary Medicines Authority (APVMA) has a complementary regulatory role in respect to this application due to its responsibility for agricultural chemical use in Australia, including insecticides and herbicides, under the *Agricultural and Veterinary Chemicals Code Act 1994*.

For commercial products, the normal form of approval is through registration, but the APVMA may also issue permits allowing restricted use of an insecticide or herbicide, for example, for a limited period of time or for a limited area. The APVMA can impose conditions on the use of insecticides and herbicides in registrations and permits. Further information about the APVMA's assessment and approval processes is contained in Chapter 1 and Appendix 6 of the RARMP.

CONCLUSIONS OF THE RISK ASSESSMENT

The Regulator has concluded that the proposed limited and controlled release of Roundup Ready® Flex and Roundup Ready® Flex/Bollgard II® cottons on up to 91 sites covering a total area of up to 1811 hectares, over two planting seasons, does not pose any significant risks to human health and safety or the environment.

The effect of combining the glyphosate tolerance and the insecticidal genes in the GM cotton plants was considered, in particular whether this could result in new or increased risks over and above those posed by the individual traits. This was also assessed in the RARMP for DIR 012/2002 (commercial release of Roundup Ready®/Bollgard II® cotton expressing the same introduced proteins). It is considered unlikely that the combination of the two unrelated traits in Roundup Ready® Flex/Bollgard II® cotton will present new or increased risks to human health and safety, or to the environment.

The risk assessment of each potential hazard identified above is summarised under a separate heading below.

Toxicity or allergenicity to humans

Roundup Ready[®] Flex and Roundup Ready[®] Flex/Bollgard II[®] cottons are unlikely to prove more toxic or allergenic to humans via occupational exposure than conventional cotton. The introduced proteins are the same as those expressed by existing commercially released GM cottons (Roundup Ready[®], Roundup Ready[®]/Bollgard II[®] and Bollgard II[®] cottons). None of the introduced proteins have any known toxicity or allergenicity to humans and the proteins are naturally widespread in the environment.

Food Standards Australia New Zealand (FSANZ) is responsible for human food safety assessment, and FSANZ approval will need to be obtained before products from these GM cottons could be used in human food in Australia. Oil and linters from Roundup Ready[®] cotton and from one of the parental GMOs, Bollgard II[®] cotton, have previously been approved by FSANZ for use in human food. FSANZ is currently evaluating an application from Monsanto to approve food products derived from Roundup Ready[®] Flex cotton. Accordingly, cottonseed produced during this trial is not permitted to be used in human food or animal feed.

The sale of lint⁴ will be allowed for use in fabric, upholstery and other non-food products. Lint does not contain DNA or protein.

Toxicity to non-target organisms

Roundup Ready[®] Flex and Roundup Ready[®] Flex/Bollgard II[®] cottons are unlikely to prove more toxic to non-target organisms than conventional cotton. The introduced proteins are the same as those expressed by existing commercially released GM cottons. Potential non-target effects of the insecticidal proteins expressed in Roundup Ready[®] Flex/Bollgard II[®] cotton have been considered in detail in the risk assessment and risk management plans for Bollgard II[®] cotton (DIR 012/2002) and INGARD[®] cotton (DIR 022/2002), available at www.ogtr.gov.au. The toxicity of the introduced insecticidal proteins is highly specific to larvae of lepidopteran insects, including the major caterpillar pests of cotton, and none of the other introduced proteins have been shown to be toxic to any organism. The introduced proteins, or similar proteins, are naturally widespread in the environment. However, exposure of non-target organisms to the introduced proteins will be low and cottonseed from the release will not be used for stockfeed.

Weediness

The risk of Roundup Ready[®] Flex or Roundup Ready[®] Flex/Bollgard II[®] cotton establishing as environmental weeds in the cotton growing regions of NSW and Qld and the areas of the release in northern Australia is very low, and not likely to be greater than that of non-GM cotton. This is because the major constraints on weediness of both GM and non-GM cotton in Australia are water availability, nutrient availability, plant competition, herbivory by non-lepidopteran species, fire and (in southern Australia) frost. It is highly unlikely that the genetic modifications will affect the response of the GM cottons to these variables and thereby alter the weediness of the GM cottons.

⁴ The long cotton fibres which are separated from the cottonseed during the ginning process are called lint, whereas the short, fuzzy fibres that remain on the cottonseed after ginning are known as linters. Lint is used to produce fabric, whereas linters (after being separated from the cottonseed) are used in a variety of products including food.

Roundup Ready® Flex and Roundup Ready® Flex/Bollgard II® cottons express the same introduced proteins as the commercially released Roundup Ready® and Roundup Ready®/Bollgard II® cottons, which have not become problematic weeds. However, the site of insertion and level of expression of the introduced herbicide tolerance genes differ. Therefore, there is a very low possibility that potential unintended effects resulting from the genetic modification could alter some aspect of the GM cottons' biology that may affect weediness. No unintended effects on agronomic characteristics, including characteristics indicative of weediness, have been observed in field trials of Roundup Ready® Flex cotton conducted to date in Australia and the USA.

Licence conditions have been imposed to minimise the spread and persistence of the GM cottons in the environment, including cleaning of release sites and equipment after harvest, secure wrapping of GM materials, post harvest inspections and destruction of volunteer cotton after harvest (refer to key licence conditions, below).

Transfer of introduced genes to other organisms

Some gene transfer from the GM cottons to other cultivated cottons would be likely under uncontrolled conditions, although the overall frequency of out-crossing would be very low as cotton is primarily self-pollinating. Transfer of the introduced genes to other cultivated cotton would pose the same risks as the risks posed by the GM cottons themselves. Licence conditions have been imposed to minimise the potential transfer of the introduced genetic materials to other cotton crops (refer to key licence conditions, below).

Gene transfer to naturalised cotton populations is unlikely because of the geographic distances between these naturalised populations and the cotton growing regions of NSW and Qld. However, herbarium records of *G. hirsutum* and *G. barbadense* suggest that naturalised populations may occur, or may have occurred in the past, in northern, central and south eastern Qld, in northern NT and in northern WA. The remnants of some of these populations, which may be within pollinating distance of cotton crops, has not been confirmed.

Licence conditions have been imposed to limit cross-pollination with compatible plants outside the release sites (refer to key licence conditions, below)..

The possibility of transfer of the introduced genes to native cotton, other plant species or other organisms is negligible because of well established genetic incompatibility. Even if such transfer occurred it would be unlikely to pose any hazard to human health and safety or the environment.

Herbicide and insecticide resistance

Roundup Ready® herbicide (containing glyphosate as the active ingredient) is not currently registered for use on cotton beyond the four-leaf stage of growth. Monsanto has submitted an application to the APVMA for a permit to use Roundup Ready® herbicide on Roundup Ready® Flex and Roundup Ready® Flex/Bollgard II® cottons beyond the four-leaf stage during the trial. The risk of development of herbicide-resistant weeds is being assessed in parallel with this application, and if necessary, will be managed by the APVMA through permit conditions. The existing registration for the use of the insecticidal proteins produced by the *cryIAc* and *cry2Ab* genes in Bollgard II® cotton as insecticidal products contains conditions to address the risk of development of insecticide resistant pests.

THE RISK MANAGEMENT PLAN (KEY LICENCE CONDITIONS)

As part of the evaluation process for this licence application, a risk management plan has been developed to address the risks identified (refer to Conclusion of the Risk Assessment, above).

The applicant proposed a number of containment measures to minimise the spread and persistence of the GMOs and introduced genetic materials. In addition to these, the Regulator has imposed other licence conditions to implement the risk management measures that will minimise the potential exposure of humans and other organisms, and limit the likelihood of spread and persistence of the GMOs or the introduced genetic materials in the environment. The key licence conditions are outlined below.

Chapter 2 of the RARMP provides a tabulated summary of assessment conclusions and corresponding management conditions. Full details of the licence conditions are provided in Appendix 7.

Toxicity or allergenicity to humans

Licence conditions have been imposed which require the applicant to:

- limit the scale and duration of the release;
- prevent GM plant materials and materials from the pollen trap from being used in human food;
- destroy all GM seed not required for testing or future release;
- securely transport and store retained GM plant materials and seeds; and
- report any adverse effects on human health and safety.

Toxicity to non-target organisms

Licence conditions have been imposed which require the applicant to:

- limit the scale and duration of the release;
- prevent GM cottonseed and cottonseed from the pollen trap from being used as stockfeed;
- destroy all GM seed not required for testing or future release; and
- securely transport and store the retained GM plant materials and seeds;

Weediness

Licence conditions have been imposed which require the applicant to:

- limit the scale and duration of the release;
- prevent GM cottonseed and cottonseed from the pollen trap from being used as stockfeed;
- securely transport and store the retained GM plant materials and seeds;
- clean the release sites and equipment used at release sites after harvest; and
- inspect release sites after harvest and destroy volunteers.

Transfer of introduced genes to other organisms

Licence conditions have been imposed which require the applicant to:

- limit the scale and duration of the release;
- at sites south of latitude 22° South, surround the GM cottons with a 20 m pollen trap of non-GM cotton, or Bollgard II[®], Roundup Ready[®] or Bollgard II[®]/Roundup Ready[®] GM cottons which are approved for commercial release in southern Australia;

- at sites north of latitude 22° South, surround the GM cottons with a 50 m isolation zone (monitored for volunteers) surrounded by a 400 m zone free of any cotton populations that would be able to cross with the GM cottons;
- securely transport and store the retained GM plant materials and seeds;
- clean the release sites and equipment used at release sites after harvest; and
- inspect release sites after harvest and destroy volunteers.

Herbicide and insecticide resistance

No conditions have been imposed in relation to management of herbicide resistance in weeds or insecticide resistance in pests, as the APVMA has responsibility for these issues. The requirement to comply with any conditions imposed by the APVMA has been noted in the licence.

General conditions

Any licence issued by the Regulator contains a number of general conditions that are also relevant to risk management. These include, for example:

- identification of the persons or classes of persons covered by the licence;
- a requirement that the applicant allows access to the release sites by the Regulator, or persons authorised by the Regulator, for the purpose of monitoring or auditing; and
- a requirement to inform the Regulator if the applicant becomes aware of any additional information about risks to human health or safety or to the environment.

Research requirements

As mentioned above (see under 'The Application'), data relevant to the assessment of the application was supplied from the current trial with the same GM cottons being conducted under DIR 35/2003. For the current application (DIR 055/2004), no additional research requirements have been imposed. In addition, a gene flow research program is being coordinated by the OGTR with GM cotton licensees, including Monsanto, in a range of current and potential cotton growing areas.

Identification of issues to be addressed for future releases

In addition to the extra data on gene expression and agronomic characteristics that are expected to be provided from the trial currently being conducted under DIR 35/2003, the following information would be required if the applicant were to submit an application for the commercial release of these GM cottons:

- the complete sequence of the introduced DNA; and
- sequences of the DNA regions flanking the introduced DNA and results of database homology searches.

Monitoring and enforcement of compliance by the OGTR

As well as the legislative capacity to enforce compliance with licence conditions, the Regulator has additional options for risk management. The Regulator can direct a licence holder to take any steps the Regulator deems necessary to protect the health and safety of people or the environment. The OGTR also independently monitors releases that the Regulator has authorised. At least 20% of all field trial sites are inspected each year, in

accordance with a monitoring and compliance strategy based on risk profiling (which takes into account biological, seasonal, geographical and ecological risk factors), to determine whether licence holders are complying with the licence conditions, or whether there are any unintended effects.

FURTHER INFORMATION

Detailed information on the evaluation of the application, including the licence conditions, is available in the risk assessment and risk management plan for this application, which can be obtained from the website of the Office of the Gene Technology Regulator (www.ogtr.gov.au), or by calling 1800 181 030 (please quote application number DIR 055/2004).