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

24 August 2005

EXECUTIVE SUMMARY OF THE RISK ASSESSMENT AND RISK MANAGEMENT PLAN FOR APPLICATION DIR 056/2004

THE DECISION

The Gene Technology Regulator (the Regulator) has made a decision to issue a licence for dealings involving the intentional release of genetically modified (GM) herbicide tolerant and herbicide tolerant/insect resistant cottons into the environment, in respect of application DIR 056/2004 from Bayer CropScience Pty Ltd (Bayer).

The DIR 056/2004 licence permits Bayer to conduct a limited and controlled field trial of GM herbicide tolerant (LLCotton25) and herbicide tolerant/insect resistant (LLCotton25/ Bollgard II®) cottons. The large scale trial may take place in up to 19 shires in the cotton growing regions of New South Wales and southern and central Queensland during the 2005-06 and 2006-07 summer growing seasons. In each season the GM cottons may be grown on up to 12 sites covering a maximum area of 500 hectares.

The *Gene Technology Act 2000* (the Act) and the *Gene Technology Regulations 2001* (the Regulations) set out requirements which 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 and the environment that can not be managed. As part of the evaluation, 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

Bayer CropScience (Bayer) applied for a licence (application number DIR 056/2004) for the limited and controlled release of herbicide tolerant (LLCotton25) and herbicide tolerant/insect resistant (LLCotton25/Bollgard II®) cottons into the environment[1]. Bayer proposes to conduct a large scale field trial on up to 24 sites covering a total area of up to 1000 hectares over two planting seasons. A maximum total area of 500 hectares would be planted in each of the 2005/06 and 2006/07 summer growing seasons in the cotton growing regions of New South Wales (NSW) and southern and central Queensland (QLD).

LLCotton25 cotton contains a single copy of a gene (*bar*), derived from a common soil bacterium. The protein encoded by the *bar* gene is an enzyme[2] (PAT) that confers tolerance to glufosinate ammonium (the active constituent in herbicides such as Basta® and Liberty®). The PAT enzyme converts glufosinate ammonium into an inactive form and thus allows the application of glufosinate ammonium-containing herbicide for the control of weeds that emerge in the crop, without damaging the crop itself.

LLCotton25/Bollgard II® cotton was produced by crossing of LLCotton25 with GM Bollgard II® cotton via conventional breeding. This introduced two genes derived from another soil bacterium that produce insecticidal proteins which are highly specific and toxic to the major caterpillar pests of cotton.

The aims of the field trial are to transfer the introduced traits into elite Australian cotton varieties, to test the agronomic performance of the GM cottons, to conduct demonstration trials for farmers, to produce seed for future releases (which would require separate applications and approval processes), and to conduct tests with material from the GM cottons in the laboratory.

Bayer proposed a number of containment and inspection measures to minimise the spread and persistence of the GMOs and the introduced genes from the trial sites. The proposed measures were considered during the risk assessment of the application and in the preparation of the risk management plan.

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. Processed 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.

Limited and controlled releases of LLCotton25 were previously approved under licences DIR 015/20002 and DIR 038/2003 (both issued to CSIRO). These field trials were/are being conducted from 2002 to 2005 in NSW and QLD. The other parent GMO, Bollgard® II cotton, was approved for commercial release south of latitude 22° South in Australia in 2002 (DIR 012/2002).

THE EVALUATION PROCESS

A risk assessment and risk management plan (RARMP) in relation to licence application DIR 056/2004 has been prepared in accordance with the Act, the

[1] Application DIR 056/2004 originally proposed an unrestricted commercial release. The application has been revised to request approval for a limited and controlled, large scale field trial. A commercial release licence may be sought in a future application.

[2] Enzymes are proteins which catalyse specific biochemical reactions.

Regulations and the Regulator's *Risk Analysis Framework*. The framework was originally developed in consultation with the public, State, Territory and Australian Government agencies, key stakeholders and the Gene Technology Technical Advisory Committee. It has recently been revised[3] in consultation with the same stakeholders in order to more fully explain the OGTR's risk analysis process and is available at *http://www.ogtr.gov.au/pdf/public/raffinal2.2.pdf*.

The revised framework introduces a *Risk Estimate Matrix* (see below) that is used to assess the combination of likelihood and consequences that leads to an estimate of risks to human health and safety and/or the environment that may be posed by dealings with the GMO.

		RISK ESTIMATE			
LIKELIHOOD	**Highly Likely**	Low	Moderate	High	High
	Likely	Negligible	Low	High	High
	Unlikely	Negligible	Low	Moderate	High
	Highly Unlikely	Negligible	Negligible	Low	Moderate
		Marginal	**Minor**	**Intermediate**	**Major**
		CONSEQUENCES			

Legend – Risk Estimate Matrix: A *negligible* risk is considered to be insubstantial with no present need to invoke actions for mitigation. A *low* risk is considered to be minimal but may invoke actions for mitigation beyond normal practices. A *moderate* risk is considered to be of marked concern that will necessitate actions for mitigation that need to be demonstrated as effective. A *high* risk is considered to be unacceptable unless actions for mitigation are highly feasible and effective.

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 detail 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 contacting the Office on 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; on the parent organism; the proposed dealings, including proposed containment conditions; and on potential impacts on human health and safety and the environment), current scientific knowledge, and submissions received during consultation with expert groups and 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 release of the GM cottons were identified. These have been evaluated to determine whether risks might arise, based on the likelihood of each

[3] Please note that this RARMP is part of a transitional process to progressively incorporate the new features of the revised *Risk Analysis Framework.*

hazard occurring and the impact of each hazard, were they to be realised. A risk assessment and risk management plan for the parental GM cotton Bollgard® II has been prepared previously as part of the application for DIR 012/2002 (available at *www.ogtr.gov.au*).

The identified potential hazards relate to:

- **toxicity and allergenicity to humans:** could LLCotton25 or LLCotton25/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 resulting from the introduced genetic material?
- **toxicity to non-target organisms:** could LLCotton25 or LLCotton25/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 LLCotton25 or LLCotton25/Bollgard® II cottons to establish as a problematic weed?
- **transfer of introduced genes to other organisms:** could there be adverse consequences from potential transfer of the introduced genetic materials to non-GM cotton crops, feral or native cottons, or to other organisms? and
- **herbicide and insecticide resistance:** could weeds develop resistance to glufosinate ammonium (if the LLCotton25 crop-herbicide combination were used inappropriately) and could target insects develop resistance to the insecticidal proteins produced by the introduced insecticidal genes in LLCotton25/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 herbicide, 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 provided below, and in Chapter 1 and Appendix 6 of the RARMP.

CONCLUSIONS OF THE RISK ASSESSMENT

The Regulator has concluded that the limited and controlled release of LLCotton25 and LLCotton25/Bollgard® II cottons on up to 24 sites covering a total area of up to 1000 hectares, over two planting seasons, does not pose any significant risk to human health and safety or the environment.

The effect of combining glufosinate ammonium tolerance and 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. It is considered unlikely that the combination of the two unrelated traits in LLCotton25/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

LLCotton25 and LLCotton25/Bollgard® II cottons are unlikely to prove more toxic or allergenic to humans via occupational exposure than conventional cotton or commercially released GM cotton. The introduced proteins are the same as those expressed by existing commercially approved GM crops (InVigor® hybrid canola and Bollgard® II cotton). GM cottons expressing PAT proteins have been field trialled in Australia since 2000. None of the introduced proteins have any known toxicity or allergenicity to humans and these, and similar, proteins are naturally widespread in the environment.

Food Standards Australia New Zealand (FSANZ) is responsible for human food safety assessment and FSANZ approval would need to be obtained before products of these GM cottons could be used in human food. Oil and linters from one of the parental GMOs, Bollgard® II cotton, have previously been approved by FSANZ for use in human food. GM corn and canola expressing the same gene introduced into LLCotton25 have also been approved for use in human food in Australia. FSANZ is currently evaluating an application from Bayer to approve food products derived from LLCotton25. Accordingly, cottonseed and derived products (e.g. oil, linters and meal) produced during the proposed trial is not permitted to be used in human food or animal feed.

The sale of lint[4] will be allowed for use in fabric, upholstery and other non-food products. Processed lint does not contain DNA or protein.

Toxicity to non-target organisms

LLCotton25 and LLCotton25/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 approved GM crops. Potential non-target effects of the insecticidal proteins expressed in LLCotton25/Bollgard® II cotton have been considered in detail in the risk assessment and risk management plan prepared for the commercial release of 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. 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 LLCotton25 or LLCotton25/Bollgard® II cottons establishing as environmental weeds in the cotton growing regions of NSW and QLD is negligible, and not likely to be greater than that of non-GM cotton or other commercially released GM cottons. This is because the major constraints on weediness of both GM

[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 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.

and non-GM cotton south of latitude 22° South in Australia are water availability, nutrient availability, plant competition, frost and fire. 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. No unintended effects on agronomic characteristics, including characteristics indicative of weediness, have been observed in field trials of LLCotton25 conducted to date in Australia and the USA.

Other GM cottons expressing a different herbicide tolerance gene and/or the same insecticidal genes have been grown commercially in Australia and have not become problematic weeds.

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 (including the commercially released GM 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 or similar risks as the risks posed by the GM cottons themselves. If gene transfer to commercially released GM cottons that are tolerant to a different herbicide (glyphosate) occurred, other herbicides or cultivation could be used to control these plants. 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

Glufosinate ammonium herbicide is not currently registered for use on cotton. However, the APVMA has issued a permit to Bayer which allows the use of glufosinate ammonium on the GM cottons as part of this release. The risk of development of herbicide-resistant weeds has been assessed in parallel with this application, and is managed by the APVMA through permit conditions. The existing registration for the use of the insecticidal proteins produced by the *cry1Ac* 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 was developed to address the risks identified in the risk assessment process. A number of containment measures proposed by the applicant to minimise exposure to the GMOs and the spread and persistence of the GMOs and introduced genetic materials in the environment were also considered.

The key licence conditions imposed by the Regulator to protect human health and safety and the environment are outlined below. Chapter 2 of the RARMP provides a tabulated summary of the risk assessment conclusions and the corresponding management measures. 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:

- prevent GM plant materials 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.

Weediness

Licence conditions have been imposed which require the applicant to:

- limit the scale and duration of the release;
- prevent GM cottonseed 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;
- surround the GM cottons with a 20 m pollen trap of non-GM cotton or Bollgard II® cotton which is approved for commercial release in southern Australia;
- 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 insecticide or herbicide resistance, 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 also 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.

It should also be noted that the use of LLCotton25, or products derived from it, in food would require approval from FSANZ.

Identification of issues to be addressed for future releases

The following information would be required if the applicant were to submit an application for commercial release:

- compositional analysis of the GM cottonseed; and
- data on the expression levels of the introduced PAT protein under Australian conditions.

It should be noted that provision of the above data during the release is not required to manage risks to human health and safety and the environment from the release. This will be achieved by the risk management measures summarised in Chapter 2 (Table 2) and given effect by the licence conditions.

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 will be 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 unforeseen problems.

FURTHER INFORMATION

Detailed information on the evaluation of the application, including the licence conditions, is available in the risk assessment and risk management plan document for this application. This 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 056/2004).