



16 February 2006

**TECHNICAL SUMMARY OF THE RISK ASSESSMENT AND
RISK MANAGEMENT PLAN**
for
APPLICATION NO. DIR 059/2005
from
MONSANTO AUSTRALIA PTY LTD

INTRODUCTION

The Gene Technology Regulator (the Regulator) has decided to issue a licence (DIR 059/2005) to Monsanto Australia Ltd (Monsanto) for dealings involving the intentional release of herbicide tolerant and herbicide tolerant/insect resistant genetically modified (GM) cotton into the environment.

The DIR 059/2005 licence permits commercial release of the two GM cotton lines on an unrestricted basis south of latitude 22° South. The licence also permits the use of seed from the GM cotton plants as stockfeed, including in northern Australia where measures to limit the spread and persistence of the GMOs have been imposed.

The *Gene Technology Act 2000* (the Act), the Gene Technology Regulations 2001 (the Regulations) and corresponding state and territory law govern the comprehensive and highly consultative process undertaken by the Regulator before making a decision whether or not to issue a licence to deal with a GMO.

The Regulator's *Risk Analysis Framework* explains the approach used to evaluate licence applications and to develop the Risk Assessment and Risk Management Plans (RARMPs) that form the basis of her decisions¹.

The RARMP for DIR 059/2005 has been finalised in accordance with the gene technology legislation. Matters raised in the consultation process regarding risks to the health and safety of people or the environment from the dealings proposed by the applicant were taken into account by the Regulator in deciding to issue a licence and the conditions that have been imposed.

Consistent with Australia's integrated regulatory framework for gene technology, the Regulator has also liaised closely with other regulatory agencies that have been considering parallel applications relating to this release, namely Food Standards Australia New Zealand (FSANZ) and the Australian Pesticides and Veterinary Medicines Authority (APVMA), to avoid duplication and enable coordinated decision making.

¹ More information on the assessment of licence applications and copies of the *Risk Analysis Framework* are available from the Office of the Gene Technology Regulator (OGTR). Free call 1800 181 030 or at <http://www.ogtr.gov.au/ir/process.htm> and <http://www.ogtr.gov.au/pdf/public/raffinal2.2.pdf> respectively.

SECTION 1 APPLICATION

Title:	Commercial release of herbicide tolerant (Roundup Ready Flex [®] MON 88913) and herbicide tolerant/insect resistant (Roundup Ready Flex [®] MON 88913/Bollgard II [®]) cotton south of latitude 22° South in Australia*
Applicant:	Monsanto Australia Ltd
Common name of the parent organism:	Cotton
Scientific name of the parent organism:	<i>Gossypium hirsutum</i> L.
Modified trait(s):	Prolonged herbicide tolerance and/or insect resistance, antibiotic resistance, reporter gene expression
Identity of the gene(s) responsible for the modified trait(s):	<ul style="list-style-type: none">• Two copies of the <i>cp4 epsps</i> gene from the bacterium <i>Agrobacterium</i> sp. strain CP4 (herbicide tolerance)• <i>cry1Ac</i> and <i>cry2Ab</i> genes from the bacterium <i>Bacillus thuringiensis</i> (insect resistance)• <i>nptII</i> gene from the bacterium <i>Escherichia coli</i> (antibiotic resistance)• <i>uidA</i> gene from the bacterium <i>Escherichia coli</i> (reporter gene)
Proposed location(s):	South of latitude 22° South and use of seed as stockfeed, including in northern Australia
Proposed release size:	Phased introduction commencing with 20,000 hectares in current cotton growing areas of NSW and QLD in 2006 to commercial scale planting in subsequent years, potentially including other areas suitable for cotton growing south of latitude 22° South
Proposed time of release:	Ongoing from 2006

*The title of the licence application submitted by Monsanto is *Licence Application to the OGTR for agricultural use of Roundup Ready Flex[®] technology (MON 88913) in cotton*

Monsanto applied for a licence to release herbicide tolerant and herbicide tolerant/insect resistant GM cotton lines, Roundup Ready Flex[®] MON 88913 (referred to as Roundup Ready Flex[®]) and Roundup Ready Flex[®]/Bollgard II[®] respectively, into the environment. Monsanto is seeking approval for unrestricted, commercial scale planting of the two GM cotton lines south of latitude 22° South.

The company anticipates a phased introduction in the current cotton growing areas of New South Wales and southern Queensland. Future plantings may occur in other areas south of latitude 22° South that are suitable for growing cotton. The GM cotton lines may also be planted on a small scale for evaluation, demonstration, education and research purposes.

Some details of the DNA sequence of the Roundup Ready[®] Flex gene construct have been declared Confidential Commercial Information (CCI) under section 185 of the Act. However, this information was made available to the prescribed expert groups and agencies that were consulted in the preparation of the RARMP.

The GM cotton lines have either one or five introduced genes. Roundup Ready Flex[®] cotton contains two copies of the *cp4 epsps* gene (encoding the CP4 EPSPS protein) from *Agrobacterium* sp. strain CP4. The bacterial CP4 EPSPS protein provides tolerance to glyphosate, the active constituent in Roundup Ready[®] Herbicide.

Roundup Ready[®] cotton, which was approved for commercial release south of latitude 22° South in 2000 and is now widely grown, contains only one copy of the *cp4 epsps* gene. Glyphosate herbicide can only be applied over the top of Roundup Ready[®] cotton plants up to the four-leaf stage of growth (ie prior to flower formation, approximately 3 to 5 weeks after planting) because later applications can lead to yield loss. As Roundup Ready Flex[®] cotton has increased and prolonged expression of the *cp4 epsps* gene, it is tolerant to glyphosate throughout the growing season (approximately 24 to 28 weeks).

Roundup Ready Flex[®]/Bollgard II[®] cotton was produced by conventional crossing of Roundup Ready Flex[®] cotton with Bollgard II[®] cotton (approved for commercial release south of latitude 22° South in 2002 under DIR 012/2002) and contains all the genes

introduced into each of the parent GMOs. This means that the plants contain (in addition to the two copies of the herbicide tolerance gene) the *cry1Ac* and *cry2Ab* genes (encoding the Cry1Ac and Cry2Ab Cystal insecticidal proteins). The insect resistance proteins, Cry1Ac and Cry2Ab, are specifically toxic to caterpillars of some lepidopterans (butterflies and moths), including *Helicoverpa armigera* and *H. punctigera*. These are the two major pests of cotton in Australia.

Roundup Ready Flex[®]/Bollgard II[®] cotton also contains the *nptII* and *aad* antibiotic resistance marker genes (encoding the kanamycin and neomycin resistance protein, and the streptomycin and spectinomycin resistance protein, respectively) and the *uidA* reporter gene (encoding the β -glucuronidase protein). The *aad* gene is not expressed in the GM cotton plants because it is under the control of a bacterial regulatory sequence that is not active in plants. The *uidA* gene enables visual identification of plant material that has incorporated the intended genes.

More detailed information on the GMOs, the introduced genes and their products is provided in Chapter 1.

No specific containment measures have been proposed for the plantings in areas south of latitude 22° South. Monsanto proposes to use the GM cotton plants and their by-products in the same manner as non-GM or other commercially released GM cotton. This would include the sale of seed for commercial planting, use of oil and linters in human food, use of cotton seed in stockfeed, sale of lint, export of seed and unrestricted transport south of latitude 22° South. Monsanto also proposes restricted transport of ginned cotton seed from the release to areas north of latitude 22° South for use as stockfeed.

SECTION 2 RISK ASSESSMENT

The risk assessment considered information contained in the application, previous GM cotton assessments, current scientific knowledge, and issues relating to risks to human health and safety and the environment raised in submissions received during consultation with a wide range of prescribed experts, agencies and authorities, including all local councils in southern Australia, on the application (summarised in Appendix B) and on the RARMP (see Appendix D).

Advice received from the public on the application and from consultation on the RARMP is summarised in Appendices C and E, respectively.

The risk assessment first considered what harm to the health and safety of people or the environment could arise due to gene technology, and how it could happen during this release of GMOs into the environment (hazard identification), in comparison to non-GM and commercially released GM cotton and in the context of the proposed release.

A hazard (source of potential harm) may be an event, substance or organism (OGTR 2005). The hazard identification process resulted in the compilation of a list of 41 events that describe sets of circumstances (events) by which the proposed release could potentially give rise to adverse outcomes.

A risk is identified when a hazard is considered to have some chance of causing harm to people and/or the environment. Those events that do not lead to an adverse outcome, or could not reasonably occur, do not advance in the risk assessment process. The events that are considered to have the potential to lead to adverse outcomes are assessed further to determine

the seriousness of harm (consequence) that could result and how likely it is that the harm would occur. The level of risk is then estimated using the *Risk Estimate Matrix* (see below and Chapter 2).

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

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.

Eight of the 41 events characterised in the hazard identification process for the proposed release were identified as requiring further assessment. The potential adverse outcomes associated with these events were: toxicity for non-target invertebrates and weediness. These identified risks were assessed in comparison to the parent organism and other GM cotton lines previously approved for commercial release, in the context of the intended agronomic management practices, and the environmental conditions in the regions where the proposed release might occur.

The consequence and likelihood assessments used to derive risk estimates for these eight events are summarised in Table 1 (the detailed risk assessments are in Chapters 3 and 4). More information on the remaining 33 events that were considered not to give rise to an identified risk is provided in Chapter 2.

If a risk is estimated to be higher than negligible, risk treatment measures may be required to protect the health and safety of people or the environment.

Table 1 Summary table for the risk assessment

Potential adverse outcome	Event that may give rise to the adverse outcome	Consequence assessment	Likelihood assessment	Risk estimate	Risk evaluation
Toxicity for non-target invertebrates (see Ch 3)	Event 1 Direct or indirect ingestion of the Cry1Ac and Cry2Ab proteins in combination by non-target invertebrates as a result of this release.	Minor <ul style="list-style-type: none"> The Cry1Ac and Cry2Ab proteins may be toxic to some non-target lepidopteran insects. The Cry1Ac and Cry2Ab proteins may be toxic to some dipteran insects at high concentrations. Field studies have indicated that growing Bollgard II[®] cotton plants does not have any significant effect on the sizes or variety of non-target invertebrate populations in GM cotton fields, as compared to unsprayed non-GM cotton. 	Highly unlikely <ul style="list-style-type: none"> Roundup Ready[®] Flex/ Bollgard II[®] plants are expected to progressively replace the commercially released Roundup Ready[®]/ Bollgard II[®] plants already grown in the release areas. Non-target invertebrates do not appear to be sensitive to the levels of Cry1Ac and Cry2Ab expressed in commercially released Bollgard II[®] plants. The insect resistance of the Roundup Ready Flex[®]/Bollgard II[®] plants has been shown to be similar to that of Bollgard II[®] plants, suggesting that expression levels of the insecticidal proteins are equivalent. 	Negligible	No specific treatment options are required.
Weediness (see Ch 4)	Event 2 Expression of the <i>cp4 epsps</i> gene construct increasing spread and persistence of the GM cotton plants through tolerance to glyphosate	Minor <ul style="list-style-type: none"> Cotton is not a serious weed in southern Australia because of the limited availability of water, nutrients and suitable temperature conditions. Although glyphosate is the most widely used herbicide in Australia today, it is not generally used to control established cotton plants as the herbicide is not effective on cotton beyond the seedling stage (plants are damaged but not killed). Glyphosate tolerant cotton volunteers are effectively controlled by mechanical means or, if still at the seedling stage, by the use of alternative herbicides. 	Highly unlikely <ul style="list-style-type: none"> The proposed release would result in the extensive cultivation of GM cotton plants in current and potential areas south of latitude 22° South that are suitable for growing cotton. Similar commercially approved glyphosate tolerant cotton lines are already extensively cultivated and transported and have not become problematic weeds. Expression of the <i>cp4 epsps</i> gene construct is not expected to alter susceptibility to the environmental conditions that limit the spread and persistence of cotton in southern Australia (particularly limited water availability and frost). The chance of volunteer GM plants establishing as weeds by finding suitable ecological niches would be no greater than for the non-GM parent. 	Negligible	No specific treatment options are required.

Potential adverse outcome	Event that may give rise to the adverse outcome	Consequence assessment	Likelihood assessment	Risk estimate	Risk evaluation
	<p>Event 3 Expression of the <i>cp4 epsps</i>, <i>cry1Ac</i> and <i>cry2Ab</i> genes in combination increasing spread and persistence of the GM cotton plants through tolerance to glyphosate and reduced lepidopteran herbivory</p>	<p>Minor</p> <ul style="list-style-type: none"> • Cotton is not a serious weed in southern Australia because of the limited availability of water, nutrients and suitable temperature conditions. • Lepidopteran herbivory is not an important limiting factor on the spread and persistence of cotton in southern Australia. • The herbicide tolerance and insecticidal genes operate through independent, unrelated biochemical mechanisms and there is no evidence of any interaction. 	<p>Highly unlikely</p> <ul style="list-style-type: none"> • The proposed release would result in the extensive cultivation of GM cotton plants in current and potential areas south of latitude 22° South that are suitable for growing cotton. • Similar commercially approved GM cotton plants containing the <i>cp4 epsps</i>, <i>cry1Ac</i> and <i>cry2Ab</i> genes in combination are already extensively cultivated and transported and have not become problematic weeds. • Expression of the <i>cp4 epsps</i>, <i>cry1Ac</i> and <i>cry2Ab</i> genes in combination is not expected to alter susceptibility to the environmental conditions that limit the spread and persistence of cotton in southern Australia (particularly limited water availability and frost). • The chance of volunteer GM plants establishing as weeds by finding suitable ecological niches would be no greater than for the non-GM parent. 	Negligible	No specific treatment options are required.
	<p>Event 4 Dispersal of GM seed during transport or storage north of latitude 22° South</p>	<p>Minor</p> <ul style="list-style-type: none"> • Although protection from lepidopteran insect herbivory may provide some selective advantage in northern Australia, current weed management practices would be able to control cotton volunteers around storage areas and on roadsides. • The use of glyphosate to control weeds on roadsides would be ineffective on established cotton plants (whether GM or non-GM) and other means are required to control these plants. • Glyphosate tolerant cotton volunteers are 	<p>Unlikely</p> <ul style="list-style-type: none"> • The applicant intends to apply the industry standard of transporting ginned cotton seed in covered containers/vehicles. • Seed from similar GM cotton plants containing the same introduced genes have been similarly transported to areas north of latitude 22° South for stockfeed since 2000 and have not become problematic weeds. • Any incident involving spillage of GM cotton seed in northern Australia can be readily controlled through cleaning of the site of the spill. • Expression of the introduced genes is not expected to alter susceptibility to the environmental conditions that limit the establishment 	Low	Treatment options proposed to minimise dissemination of seed from the GM cotton lines, and spread and persistence of GM cotton plants in areas north of latitude 22° South.

Potential adverse outcome	Event that may give rise to the adverse outcome	Consequence assessment	Likelihood assessment	Risk estimate	Risk evaluation
		susceptible to other forms of chemical and mechanical control.	<p>and persistence of cotton in northern Australia (eg plant competition, fire, herbivory by non-lepidopteran insects and variable availability of water and nutrients).</p> <ul style="list-style-type: none"> • Surveys of transport routes indicate that survival of cotton volunteers is limited to disturbed environments. • Cotton volunteers around storage areas are easily controlled and those on roadsides are generally controlled by plant competition and roadside management practices (slashing). 		
	<p>Event 5 Dispersal of seed via use of GM cotton seed as stockfeed in areas north of latitude 22° South</p>	<p>Minor</p> <ul style="list-style-type: none"> • Protection from lepidopteran insect herbivory may provide some selective advantage in northern Australia. • Glyphosate tolerant cotton volunteers are effectively controlled by mechanical means or, if still at the seedling stage, by the use of alternative herbicides. 	<p>Unlikely</p> <ul style="list-style-type: none"> • Seed from similar GM cotton lines containing the same introduced genes has been used as stockfeed in northern Australia since 2000 and these GM cotton lines have not become problematic weeds. • Surveys of the incidence of cotton volunteers in areas where stock is fed cotton seed indicate that cotton volunteers are not problematic. • Animal trampling and grazing are known to limit spread and persistence of cotton plants in areas where stock is fed cotton seed or where stock grazes after being fed cotton seed. 	Low	Treatment options proposed to minimise dissemination of seed from the GM cotton lines, and spread and persistence of GM cotton plants in areas north of latitude 22° South.

Potential adverse outcome	Event that may give rise to the adverse outcome	Consequence assessment	Likelihood assessment	Risk estimate	Risk evaluation
	<p>Event 6 Dispersal of GM seed via flooding north of latitude 22° South</p>	<p>Marginal</p> <ul style="list-style-type: none"> • Protection from lepidopteran insect herbivory may provide some selective advantage in northern Australia. • Glyphosate tolerant cotton volunteers are effectively controlled by mechanical means or, if still at the seedling stage, by the use of alternative herbicides. 	<p>Unlikely</p> <ul style="list-style-type: none"> • Similar GM cotton lines containing the same introduced genes have been commercially grown and transported in southern Australia, and their seed used as stockfeed in northern Australia, since 2000 and have not become problematic weeds. • Although habitats close to waterways may be favourable for cotton establishment, expression of the introduced genes is not expected to alter susceptibility to the environmental factors (eg plant competition, fire or herbivory by non-lepidopteran insects) that will limit the establishment and persistence of cotton plants in these or other areas where seed may be dispersed to during flooding. 	Negligible	No specific treatment options are required.
	<p>Event 7 Expression of the <i>cp4 epsps</i> gene construct in other <i>G. hirsutum</i> or <i>G. barbadense</i> cotton plants (including commercially released GM cotton lines) providing glyphosate tolerance</p>	<p>Minor</p> <ul style="list-style-type: none"> • Although transfer of the <i>cp4 epsps</i> gene construct to similar commercially released GM cotton plants could result in plants containing three copies of the <i>cp4 epsps</i> gene, this would not alter the limited effectiveness of glyphosate in controlling cotton plants beyond the seedling stage. • The expression of the <i>cp4 epsps</i> gene construct is not expected to alter susceptibility to the environmental conditions that limit the spread and persistence of cotton in southern Australia (particularly limited water availability and frost). 	<p>Highly unlikely</p> <ul style="list-style-type: none"> • Cotton is primarily in-breeding and gene transfer to other cotton plants is expected to occur in close proximity and at low frequencies. • If transfer of the <i>cp4 epsps</i> gene construct to other cotton plants occurred, the likelihood of it causing weediness in these plants is expected to be the same as for the GM cotton plants. 	Negligible	No specific treatment options are required.

Potential adverse outcome	Event that may give rise to the adverse outcome	Consequence assessment	Likelihood assessment	Risk estimate	Risk evaluation
	<p>Event 8 Expression of the <i>cp4 epsps</i>, <i>cry1Ac</i> and <i>cry2Ab</i> genes in combination in other <i>G. hirsutum</i> or <i>G. barbadense</i> cotton plants (including commercially released GM cotton lines) providing glyphosate tolerance and reducing lepidopteran herbivory</p>	<p>Minor</p> <ul style="list-style-type: none"> • Crossing of Roundup Ready Flex[®]/Bollgard II[®] plants with similar commercially released GM cotton plants could result in plants containing three copies of the <i>cp4 epsps</i> gene (assessed in event 7). • The expression of the <i>cp4 epsps</i>, <i>cry1Ac</i> and <i>cry2Ab</i> genes in combination is not expected to alter susceptibility to the environmental conditions that limit the spread and persistence of cotton in southern Australia (particularly limited water availability and frost). 	<p>Highly unlikely</p> <ul style="list-style-type: none"> • Cotton is primarily in-breeding and gene transfer to other cotton plants is expected to occur in close proximity and at low frequencies. • If transfer of the <i>cp4 epsps</i>, <i>cry1Ac</i> and <i>cry2Ab</i> genes in combination to other cotton plants occurred, the likelihood of it causing weediness in these plants is expected to be the same as for the GM cotton plants. 	Negligible	No specific treatment options are required.

SECTION 3 RISK MANAGEMENT

A risk management plan builds upon the risk assessment to consider whether any action is required to mitigate the identified risks, and what can be done to protect the health and safety of people and the environment.

The risk assessment considered eight events that might lead to a risk to the environment. The risk estimates for the adverse outcomes associated with six events are **negligible** (ie insubstantial with no present need to invoke actions for their mitigation). The risk estimates for the remaining two events are **low** (ie minimal but may invoke actions for mitigation beyond normal practices).

3.1 Risk treatment measures for identified risks

The risks of the following two events that may lead to the GM cotton lines exhibiting greater weediness than non-GM cotton or other GM cotton lines previously approved for commercial release were estimated as **low**:

- dispersal of GM seed during transport or storage north of latitude 22° South
- dispersal of seed via use of GM cotton seed as stockfeed in areas north of latitude 22° South.

Therefore, risk treatment measures have been imposed to minimise dissemination of GM cotton seed, and spread and persistence of GM cotton plants, in areas north of latitude 22° South.

The following licence conditions have been imposed:

- transport of GM cotton seed to areas north of latitude 22° South must only be conducted in covered vehicles
- requirement to label the consignments of GM seed with contact phone numbers to call in case of spillage or misdirection
- the licence holder is required to inform people who transport the GM seed to areas north of latitude 22° South of the conditions associated with shipments
- north of latitude 22° South, GM cotton seed is only allowed to be fed to stock inside stockyards, feedlots or dairies
- the licence holder is required to provide information about cotton volunteers and their control to end-users of cotton seed north of latitude 22° South.

3.2 Other regulatory considerations

In July 2003, the Australian Pesticides and Veterinary Medicines Authority (APVMA) registered the use of the insecticidal proteins produced by the *cry1Ac* and *cry2Ab* genes in GM Bollgard II[®] cotton as insecticidal products. This registration also covers the Roundup Ready Flex[®]/Bollgard II[®] GM cotton line, including a requirement to implement the insect resistance management plan developed for Bollgard II[®] cotton by the Transgenic and Insect Management Strategy Committee to maintain the efficacy of the product.

Accordingly, when the possibility of insects developing resistance to the Cry1Ac and Cry2Ab proteins as a result of this proposed release was considered in the risk assessment (see Section 2.10.1), no chance of harm to the environment was identified. Hence no conditions have been imposed in relation to management of insecticide resistance.

The use of Roundup Ready[®] Herbicide on the GM cotton lines proposed for release is also subject to regulation by the APVMA. Roundup Ready[®] Herbicide is currently registered for the use on Roundup Ready[®] cotton up to the four-leaf stage of growth. Monsanto requires APVMA approval of its application to vary the registration to allow the herbicide to be applied to Roundup Ready Flex[®] lines (including application after the four-leaf stage) to undertake the commercial release of these GM cotton lines. As the APVMA generally imposes conditions on the use pattern of herbicides, there will be restrictions on the number of applications that can be made and on the spraying window (ie up to what stage of crop growth herbicide applications can be made) eg in order to limit resistance development and comply with residue limits.

Accordingly, when the possibility of the use of glyphosate on the GM cotton lines resulting in changes in the weed spectrum (Section 2.9.2) or the development of herbicide resistant weeds (Section 2.10.3) as a result of this release was considered, no chance of harm was identified and no additional conditions have been imposed.

Food Standards Australia and New Zealand (FSANZ) is responsible for food safety standards. FSANZ previously approved food (oil and linters) derived from Roundup Ready[®] cotton and Bollgard II[®] cotton. Roundup Ready Flex[®] cotton has recently received similar approval.

These assessments have been conducted in parallel and involved mandated consultation between the agencies. This ensures the exchange of information, sharing of expertise and coordinated decision making.

SECTION 4 CONCLUSIONS OF THE RARMP

The risk assessment concludes that this commercial release of herbicide tolerant and herbicide tolerant/insect resistant GM cotton lines poses **low to negligible** risks to the health and safety of people and the environment as a result of gene technology.

The risk management plan concludes that the negligible risks do not require specific risk treatment measures. However, licence conditions have been imposed to treat the low risks to the environment which relate to the use of GM cotton seed as stockfeed in northern Australia. Therefore, conditions have been imposed to minimise spread and persistence of the GMOs in areas north of latitude 22° South.