



**TECHNICAL SUMMARY OF THE RISK ASSESSMENT
AND RISK MANAGEMENT PLAN**
for
APPLICATION NO. DIR 063/2005
from
HEXIMA LTD

INTRODUCTION

The Gene Technology Regulator (the Regulator) has decided to issue a licence (DIR 063/2005) to Hexima Ltd (Hexima) for dealings involving the intentional release of one genetically modified (GM) cotton line into the Australian environment.

The DIR 063/2005 licence permits the limited and controlled release of a GM cotton line with enhanced resistance to certain fungal pathogens. The release is intended to occur on up to three sites of a maximum total area of one hectare during each of the three summer cotton growing seasons of 2006/07, 2007/08 and 2008/09 in the shires of Pittsworth, QLD, and Narrabri or Moree Plains, NSW.

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 063/2005 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 licence conditions that have been imposed.

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.

APPLICATION

Title:	Field trial of GM cotton expressing natural plant genes for fungal resistance*
Applicant:	Hexima Limited
Common name of the parent organism:	Cotton
Scientific name of the parent organism:	<i>Gossypium hirsutum</i> L.
Modified traits:	Fungal resistance, antibiotic resistance
Identity of the genes responsible for the modified traits:	<i>nad1</i> (<i>Nicotiana glauca</i> defensin) gene, from ornamental tobacco (fungal resistance gene); <i>nptII</i> (neomycin phosphotransferase type II) from the bacterium <i>Escherichia coli</i> (antibiotic resistance selectable marker)
Proposed locations:	Up to 3 sites per season in the shires of Pittsworth (QLD), Narrabri and Moree Plains (NSW)
Proposed release size:	Up to one hectare per season over 3 summer cotton growing seasons
Proposed time of release:	2006 - 2009

* The title of the licence application submitted by the applicant is *Assessment of transgenic cotton expressing natural plant genes for fungal control*.

Hexima applied for a licence to release a GM cotton line with enhanced resistance to certain disease causing fungi into the environment². The release of the GM cotton line is intended to take place at up to two sites in the shire of Pittsworth, Queensland (QLD) and one site in the shire of Narrabri or Moree Plains, New South Wales (NSW) on a maximum total area of one hectare during each of the three summer cotton growing seasons of 2006/07, 2007/08 and 2008/09.

The GM cotton line contains the plant defensin gene, *nad1*, derived from *Nicotiana glauca*, ornamental tobacco and an antibiotic resistance marker gene (*nptII*). Some details of the gene construct, including the plasmid map and some of the regulatory sequences, have been declared Confidential Commercial Information (CCI) under section 185 of the Act. This information was made available to the prescribed expert groups that were consulted in the preparation of the risk assessment and risk management plan (RARMP). The information was also considered during the preparation of the RARMP.

The purpose of the trial is to conduct early stage ('proof of concept') research to enable the applicant to assess the extent of enhanced resistance to three fungal diseases and the agronomic performance of the GM cotton line under field conditions; to measure the expression levels of the introduced plant defensin gene and to test for adverse impacts on selected beneficial soil microorganisms. Lint fibres may be tested for quality characteristics. Seed will also be collected for further studies and possible future releases (subject to additional assessments and approvals).

Plant defensins occur naturally in many horticultural and crop plants such as dahlia, tomato, peas and wheat. Their expression can be stimulated by a range of environmental factors, including disease. The *nad1* gene encodes a defensin protein, NAD1, which *in-vitro* inhibits the growth of fungi, including three major fungal pathogens of cotton: *Fusarium oxysporum* f.sp. *vasinfectum*, *Verticillium dahliae* and *Thielaviopsis basicola*, which cause fusarium wilt, verticillium wilt and black root rot, respectively.

No products from the release will be used for human food or animal feed. In addition, the applicant proposed measures to limit the spread and persistence of the GM cotton line into the environment. These were taken into account in establishing the risk assessment context

² Hexima initially requested approval for the release of three GM lines but subsequently amended the application to one only.

for the release and their suitability for limiting the release to the locations, size and duration proposed by the applicant was considered as part of the risk assessment process.

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 on the application (summarised in Appendix B). No further issues were raised in comments received on the consultation version of the RARMP (see Appendix C).

Advice received from a member of the public from consultation on the RARMP and how it was considered is summarised in Appendix D.

In addition, a reference document, *The Biology and Ecology of Cotton (Gossypium hirsutum) in Australia*, was used to provide baseline information on non-GM cotton. The document is available from the OGTR or from the website <<http://www.ogtr.gov.au>>.

The hazard identification process considered the circumstances by which the health and safety of people or the environment may be adversely affected by exposure to the GMO, GM plant materials, GM plant by-products, the introduced genes or products of the introduced genes.

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 24 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 of the RARMP).

		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.

Twenty four events were characterised in the hazard identification process. These 24 events included consideration of whether, or not, expression of the introduced genes could result in

products that are toxic or allergenic to people or other organisms, produce unintended changes in the biochemistry, physiology or ecology of the GM cotton plants, or alter characteristics that may impact on spread and persistence of the GMO. In addition, consideration was given to the opportunity for gene flow to other organisms, and unauthorised activities.

Two of the 24 events characterised in the hazard identification process for the proposed release were identified as requiring further assessment. The potential adverse outcome associated with these events was toxicity to, or growth inhibition of, invertebrates and/or non-target microorganisms. This identified risk was assessed in comparison to the parent organism and other GM cotton lines previously approved for commercial release, in the context of the proposed containment measures and the environmental conditions in the regions where the release will occur. The consequence and likelihood assessments used to derive risk estimates from these two events are summarised in Table 1 (the detailed risk assessments are in Chapter 3).

More information on the remaining 22 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. However, all risks were estimated to be negligible for this release.

Table 1 Summary table for the risk assessment

Event that may give rise to toxicity for, or growth inhibition of, invertebrates and/or non-target microorganisms	Consequence assessment	Likelihood assessment	Risk estimate	Risk evaluation
Event 1 Contact with or ingestion of GM cotton plant materials containing NAD1 protein by invertebrates.	Minor <ul style="list-style-type: none"> The NAD1 protein may be toxic to certain insects. 	Highly unlikely <ul style="list-style-type: none"> Limited exposure of insects to the NAD1 protein expected due to the small size and short duration of the proposed release. Low expression of the protein would further limit the level of exposure. Agronomic practices proposed by the applicant, specifically insecticide use, are expected to have a greater impact on invertebrate survival than the expression of the NAD1 protein in the GM cotton plants. 	Negligible	No specific risk treatment options are required, however, some conditions have been imposed to limit the release in time and space.
Event 2 Contact with NAD1 protein by non-target microorganisms.	Minor <ul style="list-style-type: none"> The NAD1 protein may be toxic to some non-target microorganisms (neutral, beneficial or pathogenic). 	Highly unlikely <ul style="list-style-type: none"> Limited exposure of non-target microorganisms to the NAD1 protein expected due to the small size and short duration of the proposed release. Low expression of the protein would further limit the level of exposure. 	Negligible	No specific risk treatment options are required, however, some conditions have been imposed to limit the release in time and space.

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 two events that might lead to risk to the health and safety of people or the environment. The risk estimates for the adverse outcome associated with those two events are **negligible**, ie insubstantial with no present need to invoke actions for their mitigation. Therefore, no risk treatment measures for the identified risk have been imposed.

However, containment and disposal measures have been imposed to restrict the release to the locations, size and duration requested by the applicant, as these were important parameters in establishing the context for assessing the risks.

Licence conditions to manage this limited and controlled release

A number of licence conditions have been imposed to limit and control the release, including requirements to:

- surround each release site with a pollen trap of non-GM cotton
- locate the release sites at least 50 m away from natural waterways
- harvest cotton seed from the release separately from any other crop
- prohibit the use of cotton seed and other materials from the release in human food or animal feed
- destroy any plant materials remaining at the sites and clean the sites and any equipment used on the sites
- inspect the sites following harvest and cleaning, any areas used to clean equipment and any irrigation channels associated with the release
- destroy any volunteer plants prior to flowering
- conduct regular inspections of the release sites and other areas following harvest for at least 12 months and until six consecutive months have passed without any volunteer cotton plants.

The Regulator has issued guidelines and policies for the transport, supply and storage of GMOs (*Guidelines for the transport of GMOs, June 2001*; *Policy on transport and supply of GMOs, July 2005*). Licence conditions based on these guidelines and policies have also been imposed to control possession, use or disposal of the GMO for the purposes of, or in the course of, the authorised dealings.

Other regulatory considerations

Australia's gene technology regulatory system operates as part of an integrated legislative framework (OGTR 2005). Other agencies that also regulate GMOs or GM products include FSANZ (Food Standards Australia New Zealand), APVMA (Australian Pesticides and Veterinary Medicines Authority), Therapeutic Goods Administration (TGA), National Industrial Chemicals Notification and Assessment Scheme (NICNAS), National Health and Medical Research Council (NHMRC) and Australian Quarantine and Inspection Service

(AQIS). Dealings conducted under any licence issued by the Regulator may also be subject to regulation by one or more of these agencies³.

The GM cotton line proposed for release meets the definition of an agricultural chemical product under the *Agricultural and Veterinary Chemicals Code Act 1994*, due to its production of a fungal growth-inhibiting substance, and therefore it is subject to regulation by the APVMA. Currently, APVMA is assessing a research permit application from Hexima for the proposed release. The Regulator has liaised closely with APVMA to ensure the thorough and coordinated assessment of these parallel applications.

No products from the release will be permitted for use in human food (or animal feed). Therefore, at this stage, no application has been made to FSANZ.

Identification of issues to be addressed for future releases

The risk assessment identified additional information that may be required to assess an application for a large scale release of this GM cotton line or to justify a reduction in the containment conditions, including:

- data on expression levels of the plant defensin NAD1 in the GM cotton line (in whole plants, leaves, pollen, stems, roots, seeds and bolls) and data on root exudation of NAD1
- the mode of action of NAD1
- characterisation of the potential toxicity of NAD1 and the GM cotton line to vertebrates (including people)
- *in-vitro* experiments or field studies addressing the effect of NAD1 on species of invertebrates and non-target microorganisms such as mycorrhiza fungi and *Rhizobium* spp.
- agronomic characteristics indicative of weediness
- any effects resulting from stacking of the *nad1* gene with other introduced traits in commercially released GM cotton plants such as herbicide tolerance and insect resistance.

CONCLUSIONS OF THE RARMP

The risk assessment concludes that this limited and controlled release of a GM cotton line with enhanced resistance to certain fungal pathogens in the shires of Pittsworth, QLD, and Narrabri or Moree Plains, NSW, poses negligible risks to the health and safety of people and the environment posed by or as a result of gene technology.

The risk management plan concludes that these negligible risks do not require specific risk treatment measures. However, licence conditions have been imposed to limit the release to the proposed locations, size and duration requested by the applicant.

³ More information on Australia's integrated regulatory framework for gene technology is contained in the *Risk Analysis Framework* available from the Office of the Gene Technology Regulator (OGTR). Free call 1800 181 030 or at <<http://www.ogtr.gov.au/pdf/public/raffinal2.2.pdf>>.