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

Risk Assessment and Risk Management Plan for

DIR 113

Limited and controlled release of cotton genetically modified for insect resistance and herbicide tolerance

Applicant: Bayer CropScience Pty Ltd

April 2012

PAGE INTENTIONALLY LEFT BLANK

Executive Summary

Introduction

The Gene Technology Regulator (the Regulator) has made a decision to issue a licence in respect of a licence application (DIR 113) from Bayer CropScience Pty Ltd (Bayer). The licence authorises dealings involving the limited and controlled release of genetically modified (GM) cotton into the environment.

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

The decision is based upon a Risk Assessment and Risk Management Plan (RARMP) prepared by the Regulator in accordance with requirements of the legislation. RARMPs apply the *Risk Analysis Framework* and are finalised following consultation with a wide range of experts, agencies and authorities, and the public[1].

The application

Bayer has applied for a licence for dealings involving the intentional release of GM cotton into the environment on a limited scale and under controlled conditions. The GM cotton varieties have been genetically modified for insect resistance and herbicide tolerance. The field trial is authorised to take place at up to six sites per year in the Local Government Areas (LGAs) of Narrabri, NSW, Wyndham-East Kimberly, WA, and Central Highlands, Qld, between May 2012 and May 2015. The maximum area of plantings will be 6 ha in the first year and 36 ha in the second and third years, giving a maximum cumulative area of 78 ha.

The purpose of the trial is to assess the agronomic performance of the GM cotton varieties, and to produce seed for use in further studies or releases (subject to additional approvals). The GM cotton varieties will not be permitted to enter the commercial human or animal food supply chains.

Up to 11 varieties of GM cotton are authorised for release. These cotton varieties contain different combinations of introduced genes conferring insect resistance and introduced genes conferring herbicide tolerance. Some varieties also contain an antibiotic resistance marker gene, which was used to select GM plants during initial development of the plants in the laboratory.

Bayer proposed a number of controls to restrict the spread and persistence of the GM cotton and the introduced genetic materials in the environment that were considered during the evaluation of the application.

Confidential Commercial Information

Details of the genes and other sequences inserted into the GM cotton varieties have been declared Confidential Commercial Information (CCI) under section 185 of the Act. The confidential information was made available to the prescribed experts and agencies that were consulted on the RARMP for this application.

[1] More information on the process for assessment of licence applications to release a genetically modified organism (GMO) into the environment is available from the Office of the Gene Technology Regulator (OGTR) (Free call 1800 181 030 or at <http://www.ogtr.gov.au/>), and in the Regulator's *Risk Analysis Framework* (OGTR 2009) at <http://www.ogtr.gov.au/internet/ogtr/publishing.nsf/Content/riskassessments-1>.

Risk assessment

The risk assessment took into account information in the application (including proposed containment measures), relevant previous approvals and current scientific/technical knowledge. Advice relating to risks to human health and safety and the environment provided in submissions received during consultation on the RARMP was also considered. No new risks to people or the environment were identified from the advice received on the consultation RARMP.

Initially, potential pathways that might lead to harm to people or the environment as a result of gene technology are postulated (risk scenarios), and those that warrant detailed characterisation are determined. This process is described as risk identification.

Six risk scenarios were postulated, including consideration of whether or not expression of the introduced genes could: result in products that are toxic or allergenic to people or other organisms; alter characteristics that may impact on the spread and persistence of the GM cotton; or produce unintended changes in the biochemistry of the GMOs. The opportunity for gene flow to other organisms, and its effects if it were to occur, was also assessed.

A risk is only identified for further assessment when a risk scenario is considered to have some chance of causing harm. Pathways that do not lead to an adverse outcome, or could not reasonably occur, do not advance in the risk assessment process.

The characterisation of the six risk scenarios in relation to both the seriousness and likelihood of harm, in the context of the control measures proposed by the applicant and considering both the short and the long term, did not identify any risks that could be greater than negligible. Therefore, they did not warrant further assessment.

Risks to the health and safety of people, or the environment, from the proposed release of the GM cotton varieties into the environment are assessed to be negligible. Hence, the Regulator considers that the dealings involved in this limited and controlled release do not pose a significant risk to either people or the environment.

Risk management plan

Risk management is used to protect the health and safety of people and to protect the environment by controlling or mitigating risk. The risk management plan evaluates and treats identified risks, evaluates controls and limits proposed by the applicant, and considers general risk management measures. The risk management plan is given effect through licence conditions.

As none of the six risk scenarios characterised in the risk assessment give rise to an identified risk that requires further assessment, the level of risk from the proposed dealings is assessed to be negligible. The Regulator's *Risk Analysis Framework* defines negligible risks as insubstantial, with no present need to invoke actions for their mitigation in the risk management plan. However, conditions have been imposed to restrict the spread and persistence of the GMOs and their genetic material in the environment and to limit the release to the size, locations and duration proposed in the application, as these were important considerations in establishing the context for assessing the risks.

The licence conditions require Bayer to limit the release to a maximum cumulative area of 78 ha at up to six sites per year between May 2012 and May 2015, inclusive. The control measures include containment provisions at the trial sites; preventing the use of GM plant materials in human food or animal feed; destroying GM plant materials not required for further studies; transporting GM plant materials in accordance with the Regulator's transportation guidelines or other specific conditions; and conducting post-harvest monitoring at the trial sites to ensure all GMOs are destroyed.

Conclusions of the RARMP

The risk assessment concluded that this limited and controlled release of up to 11 varieties of GM cotton on a maximum cumulative area of 78 ha over three years in the LGAs of Narrabri, NSW,

Wyndham-East Kimberley, WA, and Central Highlands, Qld, poses negligible risks to the health and safety of people or the environment as a result of gene technology.

The risk management plan concluded that these negligible risks do not require specific risk treatment measures. However, licence conditions have been imposed to limit the release to the size, locations and duration proposed in the application, and to require controls in line with those proposed by the applicant as these were important considerations in establishing the context for assessing the risks.

Table of Contents

Abbreviations

Act	The *Gene Technology Act 2000*
APVMA	Australian Pesticides and Veterinary Medicines Authority
AQIS	Australian Quarantine and Inspection Service
Bayer	Bayer CropScience Pty Ltd
Bt	*Bacillus thuringiensis*
CCI	Confidential Commercial Information
DIR	Dealings involving Intentional Release
DNA	Deoxyribonucleic Acid
FSANZ	Food Standards Australia New Zealand
GM	Genetically Modified
GMO	Genetically Modified Organism
ha	hectare
HGT	Horizontal Gene Transfer
km	kilometre
LGA	Local Government Area
m	metre
NLRD	Notifiable Low Risk Dealing
NSW	New South Wales
OGTR	Office of the Gene Technology Regulator
PC2	Physical Containment level 2
PCR	Polymerase Chain Reaction
Qld	Queensland
RARMP	Risk Assessment and Risk Management Plan
Regulations	Gene Technology Regulations 2001
Regulator	Gene Technology Regulator
T-DNA	Transfer DNA of *Agrobacterium tumefaciens*
the Act	The *Gene Technology Act 2000*
Ti plasmid	Tumour-inducing plasmid of *Agrobacterium tumefaciens*
USA	United States of America
WA	Western Australia

Technical Summary

Introduction

The Gene Technology Regulator (the Regulator) has made a decision to issue a licence in respect of a licence application (DIR 113) from Bayer CropScience Pty Ltd (Bayer). The licence authorises dealings involving the limited and controlled release of genetically modified (GM) cotton into the environment.

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

The decision is based upon a Risk Assessment and Risk Management Plan (RARMP) prepared by the Regulator in accordance with requirements of the legislation. RARMPs apply the *Risk Analysis Framework* and are finalised following consultation with a wide range of experts, agencies and authorities, and the public[2].

The application

Bayer has applied for a licence for dealings involving the intentional release of GM cotton into the environment on a limited scale and under controlled conditions. The GM cotton varieties have been genetically modified for insect resistance and herbicide tolerance. The field trial is authorised to take place at up to six sites per year in the LGAs of Narrabri, NSW, Wyndham-East Kimberly, WA, and Central Highlands, Qld, between May 2012 and May 2015. The maximum area of plantings will be 6 ha in the first year and 36 ha in the second and third years, giving a maximum cumulative area of 78 ha.

The purpose of the trial is to assess the agronomic performance of the GM cotton varieties, and to produce seed for use in further studies or releases (subject to additional approvals). The GM cotton varieties will not be permitted to enter the commercial human or animal food supply chains.

Up to 11 varieties of GM cotton are authorised for release. These cotton varieties contain different combinations of genes conferring insect resistance isolated from the common soil bacterium *Bacillus thuringensis* (Bt), and introduced genes conferring herbicide tolerance. Some varieties also contain an antibiotic resistance marker gene, which was used to select GM plants during initial development of the plants in the laboratory.

The GM cotton lines also contain short regulatory sequences that control expression of the introduced genes. Regulatory sequences were derived from plants (including thale cress), bacteria (*Agrobacterium tumefaciens, Escherichia coli*) or plant viruses.

The GM cotton varieties authorised for release include lines containing a single genetic modification (or 'transformation') event, as well as varieties containing two or more transformation events which have been combined (or 'stacked') by conventional cross-breeding between these lines. All but one of the GM cotton lines containing single transformation events have been previously approved by the Regulator for limited and controlled release in Australia. One GM

[2] More information on the process for assessment of licence applications to release a genetically modified organism (GMO) into the environment is available from the Office of the Gene Technology Regulator (OGTR) (Free call 1800 181 030 or at <http://www.ogtr.gov.au/>), and in the Regulator's *Risk Analysis Framework* (OGTR 2009) at <http://www.ogtr.gov.au/internet/ogtr/publishing.nsf/Content/riskassessments-1>.

cotton line, genetically modified for herbicide tolerance, had not been previously assessed by OGTR but has been approved for release by regulatory authorities in other countries.

Bayer proposed a number of controls to restrict the spread and persistence of the GM cotton varieties and their genetic material into the environment. These controls were considered during the evaluation of the application.

Confidential Commercial Information

Details of the genes and the specific genetic elements (coding and regulatory sequences) inserted into the GM cotton varieties have been declared Confidential Commercial Information (CCI) under section 185 of the Act. The confidential information was made available to the prescribed experts and agencies that were consulted on the RARMP for this application.

Risk assessment

The risk assessment took into account information in the application (including proposed containment measures), relevant previous approvals and current scientific/technical knowledge. Advice relating to risks to human health and safety and the environment provided in submissions received during consultation on the RARMP was also considered. No new risks to people or the environment were identified from the advice received on the consultation RARMP.

A reference document, *The Biology of* Gossypium hirsutum *L. and* Gossypium barbadense *L. (cotton),* was produced to inform the risk assessment process for licence applications involving GM cotton plants. The document is available from the OGTR or from the website <http://www.ogtr.gov.au/internet/ogtr/publishing.nsf/Content/riskassessments-1 >.

Initially, potential pathways that might lead to harm to people or the environment as a result of gene technology are postulated (risk scenarios), and those that warrant detailed characterisation are determined. This process is described as risk identification.

Six risk scenarios were postulated, including consideration of whether or not expression of the introduced genes could: result in products that are toxic or allergenic to people or other organisms; alter characteristics that may impact on the spread and persistence of the GM cotton varieties; or produce unintended changes in the biochemistry of the GMOs. The opportunity for gene flow to other organisms, and its effects if it were to occur, was also assessed.

A risk is only identified for further assessment when a risk scenario is considered to have some chance of causing harm. Pathways that do not lead to an adverse outcome, or could not reasonably occur, do not advance in the risk assessment process.

The characterisation of the six risk scenarios in relation to both the seriousness and likelihood of harm, in the context of the control measures proposed by the applicant and considering both the short and the long term, did not identify any risks that could be greater than negligible. Therefore, they did not warrant further assessment.

The principal reasons for this include:

- widespread presence of the same or homologous genes and proteins in the environment
- toxicity of the proteins encoded by the introduced insect resistance genes is expected to be restricted to target insects and a limited range of related non-target insects
- plant characteristics and abiotic factors limiting the ability of GM or non-GM cotton plants to establish and persist in non-cultivated environments
- limited ability and opportunity for the GM cotton plants to transfer the introduced genes to commercial cotton crops or other cotton plants
- limits on the size, locations and duration of the release proposed by Bayer

- suitability of controls proposed by Bayer to restrict the spread and persistence of the GM cotton plants and their genetic material
- none of the GM plant materials or products will enter commercial human or animal food supply chains.

Risks to the health and safety of people, or the environment, from the proposed release of the GM cotton into the environment are assessed to be negligible.

Risk management plan

Risk management is used to protect the health and safety of people and to protect the environment by controlling or mitigating risk. The risk management plan evaluates and treats identified risks, evaluates controls and limits proposed by the applicant, and considers general risk management measures. The risk management plan is given effect through licence conditions.

As none of the six risk scenarios characterised in the risk assessment give rise to an identified risk that requires further assessment, the level of risk from the proposed dealings is assessed to be negligible. The Regulator's *Risk Analysis Framework* defines negligible risks as insubstantial, with no present need to invoke actions for their mitigation in the risk management plan. However, conditions have been imposed to restrict the spread and persistence of the GMOs and their genetic material in the environment and to limit the release to the size, locations and duration proposed in the application, as these were important considerations in establishing the context for assessing the risks.

Licence conditions

The Regulator has imposed a number of licence conditions, including requirements to:

- limit the release to a total cumulative area of 78 ha in three LGAs between May 2012 and May 2015
- restrict gene flow via pollen from field trial sites using one of the following measures:
  - surround the trial site with a 100 m monitoring zone and maintain a 3 km isolation distance between the site and intentionally planted cotton crops, or
  - surround the trial site by a 20 m pollen trap of non-GM cotton or commercially approved GM cotton, and treating the pollen trap plants in the same way as the GMOs
- harvest and gin all cotton plant material separately from other cotton crops
- clean all equipment used in connection with the cotton plant material
- after harvest, destroy all cotton plant material not required for further analysis or future planting
- after cleaning of sites, apply measures to promote germination of any cotton seeds that may be present in the soil
- after cleaning of sites, monitor for and destroy any GM cotton that may grow for at least 12 months, and until no volunteers are observed for a continuous 6 month period
- transport and store the GM plant material in accordance with the Regulator’s guidelines or other specific conditions
- not allow GM plant material or products to be used for human food or animal feed.

Other regulatory considerations

Australia's gene technology regulatory system operates as part of an integrated legislative framework that avoids duplication and enhances coordinated decision making. The Regulator is responsible for assessing risks to the health and safety of people and the environment associated with the use of gene technology. However, dealings conducted under a licence issued by the

Regulator may also be subject to regulation by other Australian government agencies that regulate GMOs or GM products, including Food Standards Australia New Zealand (FSANZ), Australian Pesticides and Veterinary Medicines Authority (APVMA), Therapeutic Goods Administration, National Industrial Chemicals Notification and Assessment Scheme and Australian Quarantine Inspection Service (AQIS)[3].

FSANZ is responsible for human food safety assessment and food labelling, including GM food. FSANZ has previously assessed all of the GM cotton lines produced by single transformation events that are proposed for limited and controlled release and has given approval for their use in food. These approvals would also cover the stacked GM cotton varieties produced by conventional cross-breeding between approved lines. However, the applicant will not use materials generated from the GM cotton varieties in the release in human food or in animal feed.

APVMA has regulatory responsibility for agricultural chemicals, including herbicides and insecticidal products, in Australia. Some of the GM cotton varieties proposed for release meet the definition of an agricultural chemical product under the *Agricultural and Veterinary Chemicals Code Act 1994*, due to their production of insecticidal substances, and therefore these plants are subject to regulation by the APVMA. The applicant intends to apply herbicide to the GM cotton lines during the trial, which is also subject to regulation by the APVMA.

A permit from AQIS will be required to enable import of GM cotton seed from the USA.

In addition, dealings authorised by the Regulator may be subject to the operation of State legislation declaring areas to be GM, GM free, or both, for marketing purposes.

Identification of issues to be addressed for future releases

Additional information has been identified that may be required to assess an application for a large scale or commercial release of these GM cotton varieties, or to justify a reduction in containment conditions. This would include:

- additional data on potential increases in toxicity to non-target invertebrates as a result of stacked insect resistance genes
- additional phenotypic characterisation of the GM cotton varieties, in particular of traits which may contribute to weediness
- additional molecular and biochemical characterisation of the GM cotton varieties.

Suitability of the applicant

The Regulator has assessed the suitability of Bayer to hold a DIR licence as required by the Act. Bayer is considered suitable as the Regulator is satisfied that no relevant convictions have been recorded, no licences or permits have been cancelled or suspended under laws relating to the health and safety of people or the environment, and the organisation has the capacity to meet the conditions of the licence.

Conclusions of the RARMP

The risk assessment concluded that this limited and controlled release of up to 11 varieties of GM cotton on a maximum cumulative area of 78 ha over three years in the LGAs of Narrabri, NSW,

[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/internet/ogtr/publishing.nsf/Content/riskassessments-1>.

Wyndham-East Kimberley, WA, and Central Highlands, Qld, poses negligible risks to the health and safety of people or the environment as a result of gene technology.

The risk management plan concluded that these negligible risks do not require specific risk treatment measures. However, licence conditions are imposed to limit the release to the size, locations and duration proposed in the application, and to require controls in line with those proposed by the applicant as these were important considerations in establishing the context for assessing the risks.

Chapter 1 Risk assessment context

Section 1 Background

1. This chapter describes the parameters within which potential risks to the health and safety of people or the environment posed by the proposed release are assessed (Figure 1).

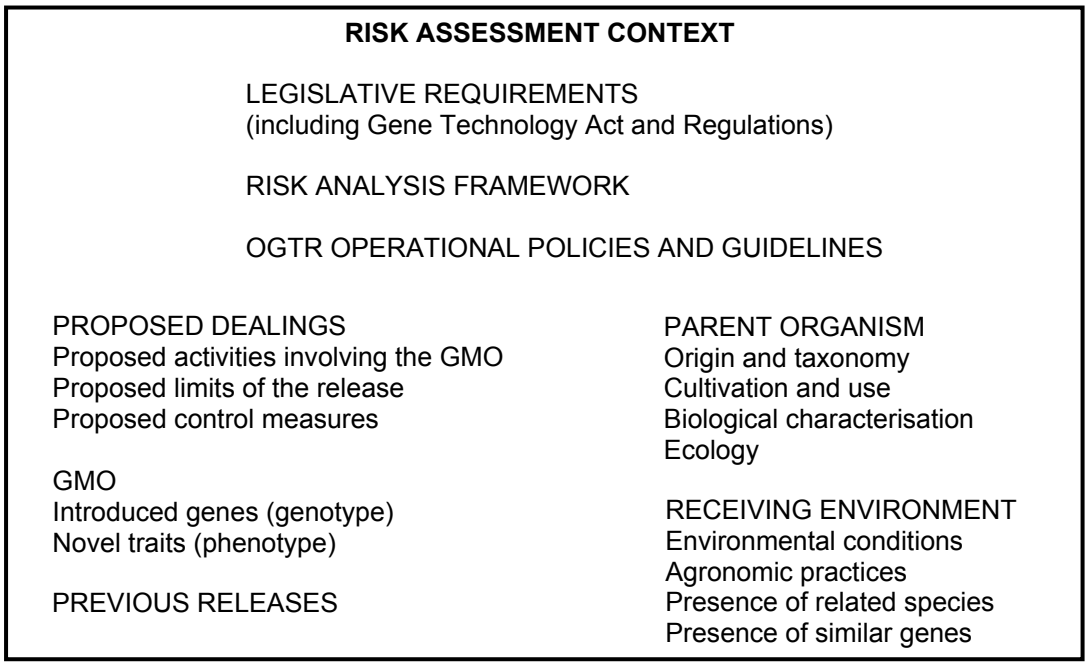

Figure 1. Parameters used to establish the risk assessment context

2. The risk assessment context is developed within the framework of the *Gene Technology Act 2000* (the Act) and Gene Technology Regulations 2001 (the Regulations, Section 2), the *Risk Analysis Framework*, and operational policies and guidelines available at the OGTR website <http://www.ogtr.gov.au>

3. In addition, establishing the risk assessment context for this application includes consideration of:

- the proposed dealings (Section 3)
- the parent organism (Section 4)
- the genetically modified organisms (GMOs), nature and effect of the genetic modification (Section 5)
- the receiving environment (Section 6)
- previous releases of these or other GMOs relevant to this application (Section 7).

Section 2 The legislative requirements

4. Sections 50, 50A and 51 of the Act outline the matters which the Gene Technology Regulator (the Regulator) must take into account, and with whom he must consult, in preparing the Risk Assessment and Risk Management Plans (RARMPs) that form the basis of his decisions on licence applications. In addition, the Regulations outline matters the Regulator must consider when preparing a RARMP.

5. In accordance with section 50A of the Act, the Regulator considered information provided in the application and was satisfied that its principal purpose is to enable the applicant to conduct experiments. In addition, limits on the size, locations and duration of the release and controls have

been proposed by the applicant to restrict the spread and persistence of the GMOs and their genetic material in the environment. Those limits and controls are such that the Regulator considered it appropriate not to seek the advice referred to in subsection 50(3) of the Act. Therefore, this application is considered to be a limited and controlled release.

6. Section 52 of the Act requires the Regulator to seek comment on the RARMP from the States and Territories, the Gene Technology Technical Advisory Committee, Commonwealth authorities or agencies prescribed in the Regulations, the Minister for the Environment, local council(s) considered appropriate, and the public. The advice from the prescribed experts, agencies and authorities and how it was taken into account is summarised in Appendix A. Two submissions were received from the public and their considerations are summarised in Appendix B.

7. Section 52(2)(ba) of the Act requires the Regulator to decide whether one or more of the proposed dealings may pose a 'significant risk' to the health and safety of people or to the environment, which then determines the length of the consultation period as specified in section 52(2)(d). The decision is provided in Section 3 of Chapter 2.

Section 3 The proposed dealings

8. Bayer CropScience Pty Ltd (Bayer) proposes to release up to 11 varieties of GM cotton, which have been genetically modified (GM) for insect resistance and herbicide tolerance, into the environment under limited and controlled conditions.

9. The dealings involved in the proposed intentional release would include:

- conducting experiments with the GMOs
- importing the GMOs
- breeding the GMOs
- propagating, growing, raising or culturing the GMOs
- transporting the GMOs
- disposing of the GMOs
- possession, supply or use of the GMOs for the purposes of any of the above.

10. These dealings are detailed further throughout the remainder of the current Chapter.

11. Details of the genes and the specific genetic elements (coding and regulatory sequences) introduced into the GMOs have been declared Confidential Commercial Information (CCI) under section 185 of the Act. The confidential information was made available to the prescribed experts and agencies that were consulted on the RARMP for this application.

3.1 The proposed activities

12. The applicant has stated that the purpose of the trial is to:

- assess the agronomic performance of the GM cotton varieties
- produce seed for use in further studies or releases (subject to additional approvals).

13. Part of the trial may assess the efficacy of insecticidal proteins against the target pest, *Helicoverpa armigera* (cotton bollworm), under Australian conditions. At the start of flowering, *Helicoverpa armigera* larvae will be introduced into mini-cages enclosing the crop. After completion of bioassays and prior to seed harvest the insects will be destroyed inside the mini-cages.

3.2 The proposed limits of the dealings (size, locations and duration)

14. The applicant proposes to limit the release to six sites per year between May 2012 and May 2015, including summer plantings in the LGAs of Narrabri, NSW, and Central Highlands, Qld, and summer and winter plantings in the Shire of Wyndham-East Kimberly, WA. The maximum area of

plantings would be 1 ha per site in the first year and 6 ha per site in the second and third years, giving a maximum cumulative area of 78 ha. The applicant proposes to limit access to the field sites to trained and authorised personnel.

3.3 The proposed controls to restrict the spread and persistence of the GMOs and their genetic material in the environment

15. The applicant has proposed a number of controls to restrict the spread and persistence of the GM cotton varieties and the introduced genetic material in the environment including:

- locating trial sites at least 50 m away from natural waterways
- separating trial sites from other cotton crops by a 100 m monitoring zone and a 3 km isolation zone or with a 20 m pollen trap of non-GM or commercially released GM cotton
- cleaning all planting and harvesting equipment used at field planting sites of GM material
- harvesting and ginning cotton from the trial separately to other cotton
- cultivating field planting sites after harvest to encourage decomposition or germination of remaining seed
- post-harvest monitoring and destroying any volunteer cotton at field planting sites for at least 12 months
- destroying all plant material from the trial not required for testing or future trials
- transporting the GMOs in accordance with the Regulator's guidelines
- not allowing GM plant material or products to be used for human food or animal feed.

16. These controls, and the limits outlined in Section 3.2, have been taken into account in establishing the risk assessment context (this chapter), and their suitability for containing the proposed release is evaluated in Chapter 3, Section 3.1.1.

Section 4 The parent organism

17. The parent organism is cultivated cotton (*Gossypium hirsutum* L.), which is the most commonly cultivated cotton species worldwide. Cotton is exotic to Australia and is grown as an agricultural crop in New South Wales and in southern and central Queensland, and on a trial basis in northern Queensland, northern Western Australia and in the Northern Territory.

18. Cotton is grown as a source of textile and industrial fibre, cottonseed oil for food use, and cottonseed meal for animal feed. Further detailed information about the parent organism is contained in a reference document, *The Biology of* Gossypium hirsutum *L. and* Gossypium barbadense *L. (cotton),* which was produced to inform the risk assessment process for licence applications involving GM cotton plants (OGTR 2008). The document is available from the OGTR or from the website < http://www.ogtr.gov.au/internet/ogtr/publishing.nsf/Content/riskassessments-1>.

19. All GM cotton events have been backcrossed into the FibreMax 966 genetic background (a commercial variety grown in the USA), and may be crossed into other elite commercial backgrounds.

Section 5 The GMOs, nature and effect of the genetic modification

5.1 Introduction to the GMOs

20. The applicant proposes to release up to 11 varieties of GM cotton containing genes conferring insect resistance and/or herbicide tolerance traits. Some of the GM cotton varieties may also contain an antibiotic resistance selectable marker gene, which was used in the laboratory to select transformed GM plants during early stages of development.

21. The GM cotton varieties also contain short regulatory sequences that control expression of the introduced genes. Regulatory sequences were derived from plants (including thale cress), bacteria (*Agrobacterium tumefaciens, Escherichia coli*) or viruses.

22. The GM cotton varieties proposed for release include lines containing a single genetic modification (or 'transformation') event, as well as varieties containing two or more transformation events which have been combined (or 'stacked') by conventional cross-breeding between these lines. All but one of the GM cotton lines containing single transformation events have been previously approved by the Regulator for limited and controlled release in Australia. One GM cotton line, genetically modified for herbicide tolerance, had not been previously assessed by OGTR but has been approved for release by regulatory authorities in other countries.

23. Additional information relevant to the genetic modifications made to the GMOs is covered by CCI. The confidential information was made available to the prescribed experts and agencies that were consulted on the RARMP for this application.

5.2 The introduced genes and their encoded proteins

24. The genes conferring insect resistance traits to the GM cotton varieties were isolated from the common soil bacterium *Bacillus thuringensis* (Bt). Genes conferring herbicide tolerance were derived from organisms that are widespread in the Australian environment. The antibiotic resistance selectable marker gene was isolated from a commonly occurring bacterium.

25. Additional information relevant to the introduced genes and their encoded proteins is covered by CCI. The confidential information was made available to the prescribed experts and agencies that were consulted on the RARMP for this application.

5.3 Toxicity/allergenicity of the proteins associated with the introduced genes

26. The introduced proteins for insect resistance are derived from *Bacillus thuringensis* (Bt). Bt is found in soil and plant communities worldwide and strains have been isolated from habitats including soil, insects, stored-product dust and deciduous and coniferous leaves (Schnepf et al. 1998 and references therein). Microbial preparations of Bt have been used for decades as a pesticide, being first commercialised as insecticidal products in France in the late 1930s. Several microbial preparations of Bt, containing similar insecticidal proteins to those described in this application, are used in commercial Bt insecticide sprays in Australia (http://apvma.gov.au). There have also been numerous commercial releases of crops genetically modified to express Bt toxins for insect resistance (Sanchis & Bourguet 2008), both in Australia and overseas. On this basis, people and other organisms have a long history of exposure to Bt insecticidal proteins.

27. The World Health Organisation's International Programme on Chemical Safety evaluated the environmental safety of use of Bt as a pest control agent and concluded that, because of the specificity of the mode of action of Bt toxins, Bt products are unlikely to pose any hazard to humans, other vertebrates, or the great majority of non-target invertebrates (International Programme on Chemical Safety 1999). In this report it was noted that Bt has not been reported to cause adverse effects on human health when present in drinking water or food. Two human studies found no observable health effect of an oral dose of 1000 mg of Bt spores per day for 3 or 5 days (McClintock et al. 1995; reviewed by Betz et al. 2000).

28. Inhalation and ingestion of Bt is not known to cause allergic reactions (International Programme on Chemical Safety 1999). A survey of farm workers who picked or packed vegetables that had been treated with Bt sprays (Bernstein et al. 1999) indicated that occupational exposure to Bt products could lead to induction of IgE and IgG antibodies. However, there were no reports of occupationally related clinical allergic disease arising from this immunological reaction in any of the workers. The USA Environmental Protection Agency has investigated several claims of dermal allergic reactions attributed to Bt microbial products, and determined that the reactions were not due to Bt itself or any of its insecticidal proteins. The reported reactions were determined to be due to

non-insecticidal proteins produced during fermentation or to added formulation ingredients (EPA 2001).

29. Toxicity studies have been conducted on the proteins encoded by each of the introduced genes in the GMOs. All of the proteins were found to be non-toxic towards model vertebrate species.

30. Bioinformatic analysis may assist in the risk assessment process by predicting the allergenic potential of a protein based on similarity to known allergens. The results of such analyses are not definitive and are used to identify those proteins requiring more rigorous testing (Goodman et al. 2008). The applicant compared the predicted amino acid sequences of the proteins encoded by each of the introduced genes to a database of known allergens, and found that none of the proteins to be expressed in the GM cotton varieties has sequence or structure homology to any known allergen.

31. Food Standards Australia New Zealand (FSANZ) has previously assessed all of the GM cotton lines produced by single transformation events that are proposed for release and has approved them as safe for use in food. These approvals would also cover the stacked GM cotton varieties produced by conventional cross-breeding between approved lines.

32. Additional information relevant to toxicity or allergenicity of the GMOs is covered by CCI. The confidential information was made available to the prescribed experts and agencies that were consulted on the RARMP for this application.

5.4 The regulatory sequences

33. Promoters are DNA sequences that are required in order to allow RNA polymerase to bind and initiate correct gene transcription. Also required for gene expression in plants is a transcription termination region, including a polyadenylation signal. Other regulatory sequences, such as introns and protein targeting sequences, may contribute to the expression pattern of a given gene.

34. The introduced regulatory sequences of the GM cotton varieties are derived from plants (including thale cress), common soil and gut bacteria (*Agrobacterium tumefaciens* and *Escherichia coli*, respectively) or plant viruses. Although some of the regulatory sequences are derived from plant pathogens (*A. tumefaciens,* plant viruses), or an opportunistic pathogen of humans and animals (*E. coli*), the regulatory sequences comprise only a small part of the total genome, and are not in themselves capable of causing disease.

35. Additional information relevant to the introduced regulatory sequences is covered by CCI. The confidential information was made available to the prescribed experts and agencies that were consulted on the RARMP for this application.

5.5 Method of genetic modification

36. *Agrobacterium tumefaciens*-mediated transformation was used to generate the genetic modifications in the proposed release. *A. tumefaciens* is a soil bacterium that causes gall formation on a wide range of plant species. The gall is induced by transfer of hormone-producing genes from the bacterial cell into the plant genome. The genes are carried on an extrachromosomal, circular DNA molecule found within the bacterial cell called a Tumour-inducing (Ti) plasmid. During the infection process, only a section of the Ti plasmid known as the Transfer DNA (T-DNA) is transferred to the plant. Molecular biologists have studied the infection and T-DNA transfer process of *A. tumefaciens* for many years and have used this natural process to facilitate genetic modification of plants. Well-characterised *A. tumefaciens* Ti plasmids have been produced that lack the genes responsible for tumour formation (disarmed plasmids) and instead enable genes of interest to be inserted between the T-DNA border sequences. When used to infect plants, *A. tumefaciens* cells carrying such plasmids cannot produce a tumour but will transfer the T-DNA sequence carrying the genes of interest into the plant cell where they stably integrate into the plant genome (Bevan 1984; Klee & Rogers 1989).

37. In addition to transfer of the T-DNA sequence, recent publications have shown that small segments of flanking Ti plasmid sequence and *A. tumefaciens* chromosomal sequence may be

transferred into the plant genome at a low frequency during the transformation process (Smith 1998; Ulker et al. 2008). However, *A. tumefaciens*-mediated plant transformation has been used extensively in Australia and overseas and is not known to adversely affect human health and safety or the environment.

5.6 Characterisation of the GMOs

38. All of the GM cotton lines containing single transformation events are well characterised, as described below. There is no stability, molecular or phenotypic characterisation data available for some of the stacked GM cotton varieties in which two or more transformation events have been combined by conventional cross-breeding.

5.6.1 Stability and molecular characterisation

39. All plasmid constructs used for generation of the GM cotton lines have been fully sequenced. Southern blot analysis and polymerase chain reaction (PCR) amplification confirmed the presence of the inserted genes in the GM cotton lines and found that no sequences from the *A. tumefaciens* vector were inserted. Southern blot analysis determined that each line contains either 1 or 2 copies of the inserted genes. The inserted genes have been maintained as dominant Mendelian traits over a number of generations of self-crosses and back-crosses (information supplied by applicant).

40. The exact location of the inserted genes within the cotton genome is not known. *A. tumefaciens* inserts genetic material into plant genomic DNA via illegitimate recombination, which can potentially result in insertion of the introduced genes anywhere in the host genome.

5.6.2 Characterisation of the phenotype of the GM cotton varieties

41. Some of the introduced genes in the GM cotton varieties are expected to provide resistance against herbivory by target insect species. These GM cotton plants will therefore sustain less pest damage than unsprayed non-GM plants, and may exhibit improved retention of fruiting structures. Some of the introduced genes are expected to provide post-emergence tolerance to specific herbicides. The purpose of the proposed trial is to evaluate the agronomic performance of the GM cotton varieties and to assess the efficacy of the insecticidal proteins against *Helicoverpa armigera*.

42. The GM cotton lines containing single transformation events are end products of breeding programs in which plant lines with poor agronomic performance were discarded. Field trials of these GM cotton lines in Australia or other countries have not identified secondary effects resulting in agronomic penalties as a result of the genetic modifications. The GM cotton lines have performed in a similar manner to non-GM cotton varieties.

Section 6 The receiving environment

43. The receiving environment forms part of the context in which the risks associated with dealings involving the GMOs are assessed. This includes: any relevant biotic/abiotic properties of the geographic regions where the release would occur; intended agricultural practices, including those that may be altered in relation to normal practices; other relevant GMOs already released; and any particularly vulnerable or susceptible entities that may be specifically affected by the proposed release (OGTR 2009).

6.1 Relevant abiotic factors

44. The abiotic factors relevant to the growth and distribution of commercial cotton in Australia are discussed in *The Biology of* Gossypium hirsutum *L. and* Gossypium barbadense *L. (cotton)* (OGTR 2008). To summarise, factors restricting where cotton can be grown in Australia are water availability (ie irrigation or rainfall), soil suitability and, most importantly, temperature. Cotton seedlings may be killed by frost, and a minimum of 180 frost-free days of uniformly high temperatures (averaging 21-22°C) are required for crop growth. Growth and development of cotton plants below 12°C is minimal and a long, hot growing season is crucial for achieving good yields.

45. The size, locations and duration of the proposed limited and controlled release are outlined in Section 3.2. The proposed dealings involve planting GM cotton in established farmlands in the LGAs of Narrabri, NSW, Wyndham-East Kimberley, WA, and Central Highlands, Qld. Rainfall and temperature statistics representative of these planting areas are given in Table 1.

Table 1 Temperature and rainfall data representative of proposed release sites*

LGA	Weather station	Mean temperature (ºC)				Mean monthly rainfall (mm)	
		Summer max.	Summer min.	Winter max.	Winter min.	Summer	Winter
Shire of Wyndham-East Kimberley	Kimberley Research Station	36.3	24.6	31.5	15.1	185.3	2.8
Narrabri Shire	Narrabri West PO	33.3	18.7	18.8	4.5	74.0	45.2
Central Highlands Region	Emerald PO	34.1	21.0	23.3	7.8	98.0	27.8

*Data were taken from the Australian Bureau of Meteorology website < http://www.bom.gov.au/climate/data/>. Temperature and rainfall data are an average of at least 40 years of records. Summer entries are averages of monthly data from December to February, and winter entries are averages of monthly data from June to August.

6.2 Relevant biotic factors

46. The biotic factors pertaining to the growth and distribution of commercial cotton in Australia are discussed in *The Biology of* Gossypium hirsutum *L. and* Gossypium barbadense *L. (cotton)* (OGTR 2008). In addition, the following points are of particular relevance to this release:

- Narrabri Shire and the Central Highlands Region are commercial cotton growing regions, whereas cotton is an experimental or occasional small-scale crop in the Shire of Wyndham-East Kimberley
- Insect resistant and/or herbicide tolerant GM cottons constitute the majority of Australia's cotton crops (see Chapter 1, Section 6.4).

47. Invertebrates, vertebrates and microorganisms are expected to be exposed to the introduced genes, their encoded proteins and end products.

6.3 Relevant agricultural practices

48. The limits and controls of the release are outlined in Section 3.2 and 3.3 of this Chapter. With regard to the agricultural practices, the GMOs proposed for field release would be planted with a standard cone seeder and grown following standard cotton agricultural protocols. Herbicides applied to the GM cotton fields would include the herbicides to which the GMOs are tolerant and other herbicides commonly used in commercial cotton cultivation. Part of the trial may assess the efficacy of the introduced insecticidal proteins against the target pest, *Helicoverpa armigera* (cotton bollworm), under Australian conditions. Introduced infestations of *Helicoverpa armigera* larvae would be contained inside mini-cages and destroyed prior to harvest.

6.4 Presence of related plants in the receiving environment

49. Commercial cotton cultivation is established in the Narrabri and Central Highlands regions. Experimental cotton crops have been grown for over a decade in the Ord River Irrigation area in the shire of Wyndham-East Kimberley.

50. Data on the commercial cultivation of cotton in Australia are discussed in *The Biology of* Gossypium hirsutum *L. and* Gossypium barbadense *L. (cotton)* document (OGTR 2008). Cotton commercially grown in Australia is predominantly *G. hirsutum* species.

51. Herbicide tolerant and/or insect resistant GM cotton plants are used widely in commercial cotton production. Over 95% of Australia's cotton growers planted GM cotton in the 2007/08 season (Cotton Australia website, www.cottonaustralia.com.au). For a list of relevant approvals for commercial releases of GM cottons in Australia, see Section 7.1.

52. In southern Australia, ephemeral populations of cotton may be present outside of cultivation. Cultivated cotton can persist as a perennial plant in tropical areas and small populations of naturalised cotton (*G. hirsutum* and *G. barbadense*) exist in northern Australia, particularly in areas associated with a prolonged supply of fresh water (Hnatiuk 1990). The majority of naturalised cotton populations occur in the Northern Territory and eastern Queensland (Australian Virtual Herbarium, <http://www.chah.gov.au/avh/>).

53. There are 17 native species of *Gossypium* in Australia, most of which can be found in the Northern Territory and the north of Western Australia (OGTR 2008). *G. australe* is the most widely distributed species, occurring from the east to west coast of northern Australia (Australian Virtual Herbarium, <http://www.chah.gov.au/avh/>). The native *Gossypium* species prefer well-drained sandy loams and are rarely found on heavy clay soils favoured by cultivated cotton (OGTR 2008). Generally, they are found in native vegetation and not in disturbed/modified habitats such as agricultural areas (Groves et al. 2002).

54. Well established genetic incompatibility prevents crossing of native cotton species with cultivated cotton in the natural environment (discussed in OGTR 2008).

6.5 Presence of the introduced genes or similar genes and encoded proteins in the environment

55. The introduced genes for insect resistance were originally isolated from Bt. Bt is a common natural soil bacterium in Australia. For several decades, the use of microbial Bt formulations in products for insect control has resulted in occupational exposures of agricultural workers (e.g. inhalation of sprays), smaller-scale exposure in domestic gardens, and dietary exposure through consumption of Bt-treated fruit and vegetables. For a decade, commercial GM cotton plants containing Bt genes have also contributed to the levels of Bt genes in agricultural areas of Australia. For these reasons, Bt insecticidal genes and their encoded proteins are ubiquitous in the Australian environment.

56. The introduced genes for herbicide tolerance were derived from organisms that are widespread in the Australian environment. The antibiotic resistance selectable marker gene was isolated from a common bacterium.

57. Additional information relevant to the presence of the herbicide tolerance and antibiotic resistance genes in the environment is covered by CCI. The confidential information was made available to the prescribed experts and agencies that were consulted on the RARMP for this application.

Section 7 Australian and international approvals

7.1 Australian approvals of GM cotton

7.1.1 Previous releases approved by Genetic Manipulation Advisory Committee or the Regulator

58. All but one of the GM cotton lines containing single transformation events that are proposed for limited and controlled release in this application have been previously approved for limited and controlled release in Australia. One of the GM cotton lines, genetically modified for herbicide tolerance, had not been previously assessed by the Regulator.

59. Previous approvals for commercial release of other cotton varieties genetically modified for insect resistance and/or herbicide tolerance are:

- insect resistant INGARD® *G. hirsutum* (DIR 022/2002; withdrawn from the market in 2004 in favour of Bollgard II® *G. hirsutum*)
- glyphosate tolerant Roundup Ready® *G. hirsutum* (DIR 023/2002 and DIR 066/2006; withdrawn from the market in 2009 in favour of Roundup Ready Flex® *G. hirsutum*)

- glyphosate tolerant / insect resistant Roundup Ready®/INGARD® *G. hirsutum* (DIR 023/2002; withdrawn from the market in favour of Bollgard II®/Roundup Ready® *G. hirsutum*)
- insect resistant Bollgard II® *G. hirsutum* (DIR 012/2002 and DIR 066/2006)
- insect resistant / glyphosate tolerant Bollgard II®/Roundup Ready® *G. hirsutum* (DIR 012/2002 and DIR 066/2006; withdrawn from the market in 2009 in favour of Bollgard II®/Roundup Ready Flex® *G. hirsutum*)
- glyphosate tolerant Roundup Ready Flex® *G. hirsutum* (DIR 059/2005 and DIR 066/2006)
- glyphosate tolerant / insect resistant Roundup Ready Flex®/Bollgard II® *G. hirsutum* (DIR 059/2005 and DIR 066/2006)
- glufosinate ammonium tolerant LibertyLink® *G. hirsutum* (DIR 062/2005)
- glufosinate ammonium tolerant / insect resistant LibertyLink®/Bollgard II® *G. hirsutum* (DIR 062/2005)
- insect resistant / glufosinate ammonium tolerant WideStrike™ cotton (DIR 091).

60. In addition, a number of limited and controlled releases of similar GMOs have been approved. To date, the Regulator has not received any reports of adverse effects caused by these authorised releases.

61. Information on all DIR assessments and approvals by the Regulator can be found on the OGTR website < http://www.ogtr.gov.au/internet/ogtr/publishing.nsf/Content/ir-1>. Information on which assessments and approvals are relevant to the GMOs proposed for release in this application is covered by CCI. The confidential information was made available to the prescribed experts and agencies that were consulted on the RARMP for this application.

7.1.2 Approvals by other government agencies

62. Australia's gene technology regulatory system operates as part of an integrated legislative framework that avoids duplication and enhances coordinated decision making. The Regulator is responsible for assessing risks to the health and safety of people and the environment associated with the use of gene technology. However, dealings conducted under a licence issued by the Regulator may also be subject to regulation by other Australian government agencies that regulate GMOs or GM products, including Food Standards Australia New Zealand (FSANZ), Australian Pesticides and Veterinary Medicines Authority (APVMA), Therapeutic Goods Administration, National Industrial Chemicals Notification and Assessment Scheme and Australian Quarantine Inspection Service (AQIS)[4].

63. FSANZ is responsible for human food safety assessment and food labelling, including GM food. FSANZ has previously assessed all of the GM cotton lines produced by single transformation events that are proposed for limited and controlled release and has given approval for their use in food. These approvals would also cover the stacked GM cotton varieties produced by conventional cross-breeding between approved lines. However, the applicant will not use materials generated from the GM cotton varieties in the release in human food or in animal feed.

64. APVMA has regulatory responsibility for agricultural chemicals, including herbicides and insecticidal products, in Australia. Some of the varieties of GM cotton proposed for release meet the definition of an agricultural chemical product under the *Agricultural and Veterinary Chemicals*

[4] 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/internet/ogtr/publishing.nsf/Content/riskassessments-1>.

Code Act 1994, due to their production of insecticidal substances, and therefore these plants are subject to regulation by the APVMA. The applicant intends to apply herbicide to the GM cotton fields during the trial, which is also subject to regulation by the APVMA.

65. A permit from AQIS will be required to enable import of GM cotton seed from the USA.

66. In addition, dealings authorised by the Regulator may be subject to the operation of State legislation declaring areas to be GM, GM free, or both, for marketing purposes.

67. Additional information relevant to approvals of GM cotton by other Australian government agencies is covered by CCI. The confidential information was made available to the prescribed experts and agencies that were consulted on the RARMP for this application.

7.2 International approvals of GM cotton

68. All of the GM cotton lines containing single transformation events that are proposed for limited and controlled release in this application have been approved for release and have undergone field trials in other countries.

69. Additional information relevant to international approvals of GM cotton is covered by CCI. The confidential information was made available to the prescribed experts and agencies that were consulted on the RARMP for this application.

Chapter 2 Risk assessment

Section 1 Introduction

70. The risk assessment identifies and characterises risks to the health and safety of people or to the environment from dealings with GMOs, posed by or as the result of gene technology (Figure 2). Risks are identified within the context established for the risk assessment (see Chapter 1), taking into account current scientific and technical knowledge. A consideration of uncertainty, in particular knowledge gaps, occurs throughout the risk assessment process.

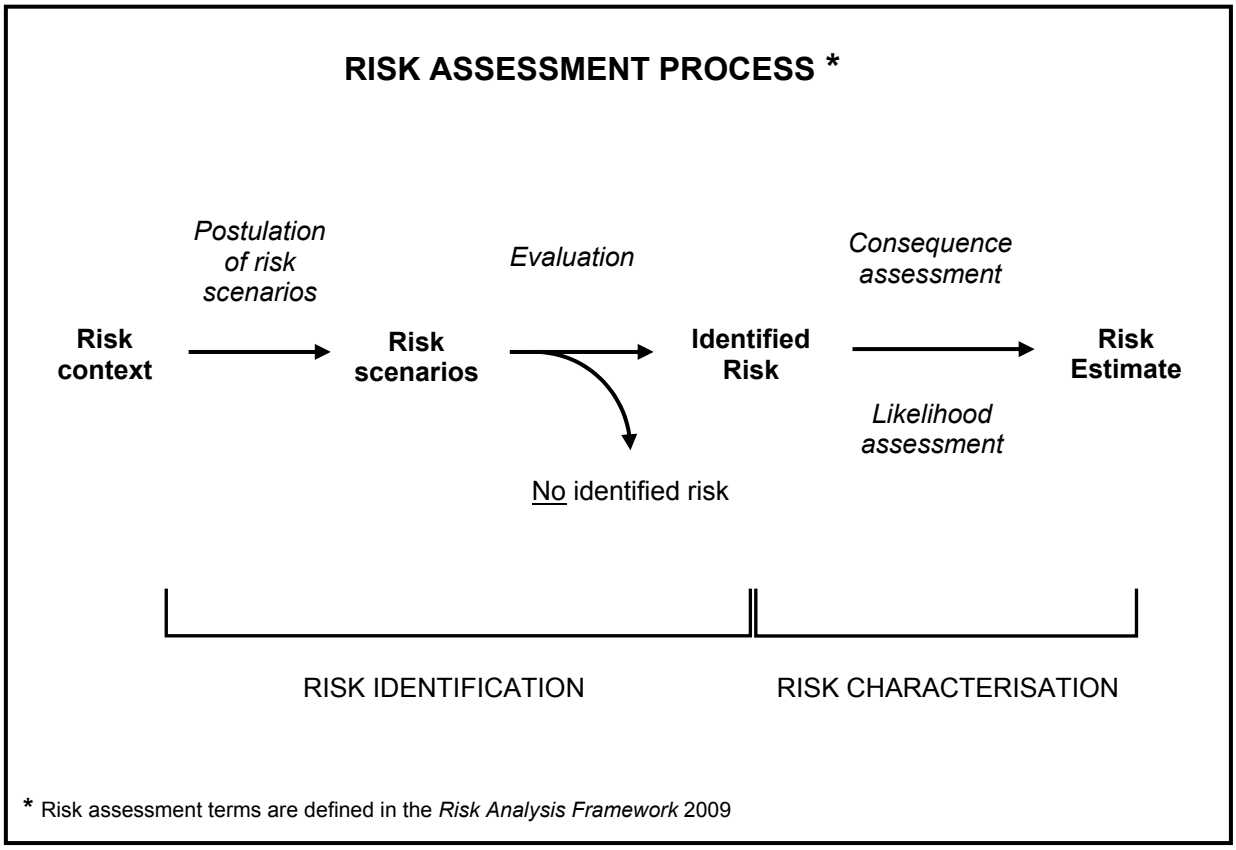

Figure 2. The risk assessment process.

71. Initially, risk identification considers a wide range of circumstances whereby the GMO, or the introduced genetic material, could come into contact with people or the environment. Consideration of these circumstances leads to postulating plausible causal or exposure pathways that may give rise to harm for people or the environment from dealings with a GMO (risk scenarios).

72. Each risk scenario is evaluated to identify those risks that warrant detailed characterisation. A risk is only identified for further assessment when a risk scenario is considered to have some reasonable chance of causing harm in either the short or long term. Pathways that do not lead to harm, or could not plausibly occur, do not advance in the risk assessment process.

73. A number of risk identification techniques are used by the Regulator and staff of the OGTR, including checklists, brainstorming, commonsense, reported international experience and consultation (OGTR 2009). In conjunction with these techniques, risk scenarios postulated in previous RARMPs prepared for licence applications of the same and similar GMOs are also considered.

74. Identified risks (*i.e.* those identified for further assessment) are characterised in terms of the potential seriousness of harm (Consequence assessment) and the likelihood of harm (Likelihood assessment). The level of risk is then estimated from a combination of the Consequence and Likelihood assessments.

Section 2 Risk Identification

75. The following factors are taken into account when postulating relevant risk scenarios:

- the proposed dealings, which may be to conduct experiments, develop, produce, breed, propagate, grow, import, transport or dispose of the GMOs, use the GMOs in the course of manufacture of a thing that is not the GMO, and the possession, supply and use of the GMOs in the course of any of these dealings.
- the proposed limits
- the proposed controls
- characteristics of the parent organism(s)
- routes of exposure to the GMOs, the introduced gene(s) and gene product(s)
- potential effects of the introduced gene(s) and gene product(s) expressed in the GMOs
- potential exposure to the introduced gene(s) and gene product(s) from other sources in the environment
- the environment at the site(s) of release
- agronomic management practices for the GMOs.

76. Six risk scenarios were postulated and evaluated. These are summarised in Table 2, where circumstances that share a number of common features are grouped together in broader risk categories. In the context of the control measures proposed by the applicant, and considering both the short and long term, none of the risk scenarios were identified as a risk that could be greater than negligible. Therefore, they did not warrant further detailed assessment. More detail of the evaluation of these scenarios is provided later in this section.

77. All of the introduced gene regulatory sequences, such as gene promoters, gene terminators and untranslated leader sequences, operate in the same manner as do regulatory elements endogenous to cotton plants. Any potential for adverse impacts from the introduced regulatory elements are considered equivalent to and no greater than those from endogenous regulatory elements of cotton. Therefore the potential effects will not be further assessed for this application.

78. The potential for horizontal gene transfer (HGT) and any possible adverse outcomes has been reviewed in literature (Keese 2008) as well as assessed in many previous RARMPs. HGT was most recently considered in the RARMP for DIR 108, while HGT was considered for GM cotton genetically modified for insect resistance and herbicide tolerance in DIR 101. These RARMPs are available at <http://www.ogtr.gov.au/internet/ogtr/publishing.nsf/Content/ir-1> or by contacting the OGTR. No risk from HGT was identified due to the rarity of these events, and because the genes are already present in the environment and available for transfer via demonstrated natural mechanisms. This is also the case for the genes proposed for release in the GM cotton in this application so this risk category will not be assessed further.

Table 2 Summary of risk scenarios from dealings with cotton genetically modified for insect resistance and herbicide tolerance

Risk category	Risk scenario		Identified risk?	Reason
	Pathway that may give rise to harm	Potential harm		
Section 2.1 Production of a substance toxic or allergenic to people or toxic to other organisms	1. Exposure of people or other vertebrates to GM plant material containing the proteins encoded by the introduced genes	Allergic reactions in people or toxicity in people and other vertebrates	No	• The introduced genes, or homologues, and their encoded proteins are widespread in the environment and are unlikely to be toxic or allergenic to people or toxic to other vertebrates. • None of the GM cotton material proposed for release will be used in human food or animal feed. • The limited scale, and other proposed

				limits and controls, further reduce exposure of people and other vertebrates to products of the introduced genes.
	2. Exposure of invertebrates and soil organisms to GM plant material containing the proteins encoded by the introduced genes	Toxicity to non-target invertebrates or soil organisms	No	• The introduced genes, or homologues, and their encoded proteins are widespread in the environment. • The toxicity of the proteins encoded by the individual insect resistance genes and any combination effects are expected to be confined to target insects and a limited range of related non-target insects that are sensitive to Bt sprays. • The limited scale reduces exposure of invertebrates and soil organisms to the products of the introduced genes.
Section 2.2 Weediness of GM cotton plants in the environment	3. Expression of the introduced genes increases the weediness of the GMOs	Weediness; allergic reactions in people or toxicity in people and other organisms	No	• The proposed limits and controls for the release would minimise persistence of GMOs at the trial sites or dispersal of reproductive material beyond the sites. • Cultivated cotton is not considered to be weedy and insect resistance, herbicide tolerance and/or antibiotic resistance are unlikely to increase weediness as abiotic factors limit the spread and persistence of cotton in Australia.
Section 2.3 Vertical transfer of genes or genetic elements to sexually compatible plants	4. Expression of the introduced genes in cotton plants that are not part of the trial	Weediness; allergic reactions in people or toxicity in people and other organisms	No	• Cotton is predominately self-pollinating and outcrossing is limited. • The applicant proposed a number of controls, including surrounding trial fields with a 20 m pollen trap or 3 km isolation zone, which would minimise gene flow via pollen. • Risk scenarios 1 – 3 did not constitute risks warranting further assessment.
Section 2.4 Unintended changes in biochemistry, physiology or ecology	5. Changes to biochemistry, physiology or ecology of the GM cotton plants resulting from expression, or random insertion, of the introduced genes	Weediness; allergic reactions in people or toxicity in people and other organisms	No	• Unintended, adverse effects, if any, would be minimised by the proposed limits and controls. • Unexpected characteristics were not observed in the GM cotton lines produced by single transformation events in earlier trials.
Section 2.5 Unauthorised activities	6. Use of the GMOs outside the licence conditions (non-compliance)	Potential adverse outcomes mentioned in Sections 2.1 to 2.4	No	• The Act provides for substantial penalties for non-compliance and unauthorised dealings with GMOs and also requires consideration of the suitability of the applicant to hold a licence prior to the issuing of a licence by the Regulator

2.1 Production of a substance toxic or allergenic to people or toxic to other organisms

79. Toxicity is the adverse effect(s) of exposure to a dose of a substance as a result of direct cellular or tissue injury, or through the inhibition of normal physiological processes (Felsot 2000).

80. Allergenicity is the potential of a substance, including proteins, to elicit an immunological reaction following its ingestion, dermal contact or inhalation, which may lead to tissue inflammation and organ dysfunction (Arts et al. 2006).

Risk scenario 1 Exposure of people or other vertebrates to GM plant materials containing the proteins encoded by the introduced genes

81. The proteins expressed from the introduced genes for insect resistance, herbicide tolerance and antibiotic resistance could be toxic or allergenic for people, or toxic for other vertebrates. If humans or other vertebrates were exposed to the expressed proteins in GM plant materials, this might give rise to detrimental biochemical or physiological effects on the health of these people or other vertebrates.

82. In the context of the proposed dealings, both of the following requirements would have to be met for GM cotton to have any increased toxic or allergenic effect:

- the genetic modifications would have to result in production of toxic or allergenic proteins or compounds not present in commercially grown cotton varieties, or increased levels of toxins naturally present in cotton, and
- humans or other vertebrates would have to be exposed to the GM cotton plants through contact, ingestion or inhalation.

83. Non-GM cotton produces natural toxins for defence against herbivory including gossypol and cycloprenoid fatty acids (OGTR 2008). The proposed genetic modifications are not expected to affect the level of these toxins produced.

84. Although no toxicity studies have been performed on plant material from the GM cotton varieties, toxicity studies have been carried out on all of the proteins encoded by the introduced genes (Chapter 1, Section 5.3) and the proteins were found to be non-toxic towards model vertebrate species. The introduced genes were isolated from naturally occurring organisms that are widespread and prevalent in the Australian environment (Chapter 1, Section 6.5), so people and animals are regularly exposed to proteins similar to those encoded by these genes. No information was found to suggest that the proteins encoded by the introduced genes are toxic or allergenic to people or toxic to other vertebrates (Chapter 1, Section 5.3).

85. FSANZ has approved food derived from all of the GM cotton lines produced by single transformation events as safe for human consumption. This approval would include products derived from stacked GM cotton varieties produced by conventional cross-breeding of these lines. There is no indication that any combination of the multiple proteins encoded by the various introduced genes would lead to an increase in the potential for toxicity or allergenicity to humans and other organisms that were unaffected by the individual proteins. Unintended effects of the proposed release are discussed in risk scenario 5.

86. The proposed limits and controls of the trial (Chapter 1, Sections 3.2 and 3.3) would minimise the likelihood of exposure of people and other vertebrates to GM plant materials. There is little potential for human ingestion of the GM cotton, as no GM plant material will be used for human food as part of this release. Similarly, livestock would not be intentionally exposed as the GM plant material will not be used as animal feed. Cotton pollen is large, sticky, and generally not dispersed by wind (OGTR 2008). The applicant proposes that access to the trial sites, and thus potential contact with or inhalation of GM plant materials, would be limited to trained and authorised staff.

87. After harvest, the applicant proposes to destroy all GM cotton materials produced, apart from some seeds and plant samples for research purposes and further plantings. These measures would minimise exposure to the GM plant material. The short duration (2012-2015) and small size (up to 36 ha per year) of the trial would also limit the potential for exposure to the GM plant material.

88. ***Conclusion***: The potential for allergic reactions in people or toxicity in people or other vertebrates as a result of exposure to GM plant materials containing the proteins encoded by the introduced genes, in the context of the limits and controls proposed by the applicant and considering both the short and long term, is not identified as a risk that could be greater than negligible. Therefore, it does not warrant further assessment.

Risk scenario 2 Exposure of invertebrates and soil organisms to GM plant material containing the proteins encoded by the introduced genes

89. The proteins expressed from the introduced genes for insect resistance, herbicide tolerance and antibiotic resistance could be toxic for certain invertebrates or soil organisms. If non-target invertebrates or soil organisms were exposed to the expressed proteins through direct ingestion of the GM plant materials, indirect ingestion through the food chain, or contact with root exudates or dead plant material in the soil, this might give rise to detrimental biochemical or physiological effects on the health of these non-target invertebrates or soil organisms.

90. The introduced herbicide resistance genes and antibiotic resistance marker gene are isolated from organisms that are widespread in the Australian environment (Chapter 1, Section 6.5). There is no data to suggest that any of the proteins encoded by these genes are toxic to invertebrates or soil organisms.

91. The purpose of the introduced Bt genes is to provide resistance to insect herbivory. The encoded insect resistance proteins are known to be toxic to a range of insect pests of cotton, including the major Australian pest *Helicoverpa armigera*, as well as other target pests. The toxicity of these proteins towards insect pests that ingest cultivated cotton is not considered to be an adverse outcome but rather the intent of the genetic modification. However, non-target species such as predators of targeted pests, pollinator species and beneficial soil organisms may also be exposed to the expressed proteins.

92. Oral toxicity studies suggest that each of the individual Bt insect resistance proteins in the GMOs is non-toxic to a wide range of non-target invertebrates (Chapter 1, Section 5.3). The toxicity of the Bt insect resistance proteins is due to specific interactions with insect mid-gut receptor molecules (Chapter 1, Section 5.3). The proteins are therefore toxic only to organisms that both:

- ingest significant doses of intact proteins, and
- produce susceptible mid-gut receptor molecules.

93. It is possible that additive or synergistic effects could occur between the different Bt insecticidal proteins, increasing the toxic effect and/or range of insects beyond those sensitive to any one of the insect resistance proteins alone. It is not expected that the range of susceptible insects would increase beyond the insect families sensitive to the commercial Bt insecticidal sprays approved by APVMA (http://apvma.gov.au), which contain Bt strains that express similar combinations of insect resistance proteins. Microbial Bt products have been assessed as unlikely to pose any hazard to the great majority of non-target invertebrates (International Programme on Chemical Safety 1999). However, some uncertainty exists in the area of potential additive or synergistic effects between Bt toxins isolated from different Bt strains due to data gaps.

94. Native Bt bacteria that express combinations of insect resistance proteins are widespread in the Australian agricultural and natural environments (Chapter 1, Section 6.5).

95. The short duration (2012-2015) and small size (up to 36 ha per year) of the release would limit the potential for exposure of invertebrates or soil organisms to the GM plant material.

96. ***Conclusion***: The potential for toxicity to non-target invertebrates or soil organisms as a result of exposure to GM plant materials containing the proteins encoded by the introduced genes, in the context of the limits and controls proposed by the applicant and considering both the short and long term, is not identified as a risk that could be greater than negligible. Therefore, it does not warrant further assessment.

2.2 Weediness of the GM cotton plants in the environment

97. This section addresses the question of whether or not the proposed dealings with the GMOs may lead to harm to human health and safety or to the environment as a result of an increased potential for weediness due to the genetic modifications.

98. All plants have the potential to lead to harm in certain environments. Harms that may arise from a certain plant species in a particular environment include:

- adverse effects on the health of people and/or animals
- reduction in the establishment, yield and/or quality of desired plants
- restriction in the physical movement of people, animals, vehicles, machinery and/or water
- adverse effects on environmental health, such as adverse changes to strata levels, nutrient levels, fire regime, soil salinity, soil stability, or by providing food and/or shelter to pests, pathogens and/or diseases (National Weed Prioritisation Working Group 2006).

99. For the purpose of this document, plant species causing significant levels of one or more of these harms are called 'weeds'. A plant species may be weedy in one or more land uses, such as dryland cropping or nature conservation.

100. Characteristics that influence the spread (dispersal of the plant or its genetic material) and persistence (establishment, survival and reproduction) of a plant species impact on the degree of its invasiveness. These characteristics include the ability to establish in competition with other plants, to tolerate standard weed management practices, to reproduce quickly, prolifically and asexually as well as sexually, and to be dispersed over long distances by natural and/or human means (National Weed Prioritisation Working Group 2006). The degree of invasiveness of a plant species in a particular environment gives an indication of the likelihood of its weediness in that environment. In addition to local experience, a history of weediness overseas can be used as an indicator for weediness in Australia (Pheloung et al. 1999).

101. Baseline information on the potential weediness of non-GM cotton plants is given in *The Biology of* Gossypium hirsutum *L. and* Gossypium barbadense *L. (cotton)* (OGTR 2008). In summary, cotton does not possess any of the characteristics associated with problematic weeds, and the spread and persistence of cotton are limited by a number of biotic and abiotic factors, especially cold stress in southern Australia and water stress in non-irrigated environments throughout almost all of Australia. Cotton has been grown for centuries throughout the world without any reports that it is a serious weed, and it is likewise not considered to be a serious weed in Australia (Groves et al. 2003).

Risk scenario 3 Expression of the introduced genes increases the weediness of the GMOs

102. In the context of the proposed dealings, in order for the GM cotton plants to become weedy in the environment both of the following conditions would need to be met:

- GM cotton plants are present outside the limits (locations and/or duration) of the trial; and
- GM cotton plants are able to establish populations that cause harms associated with weediness.

Presence of GM cotton plants outside the trial limits

103. GM cotton plants could be present outside the trial limits due to survival at the trial sites after completion of the trial duration, or due to dispersal of reproductive plant material outside the site locations during or after the trial.

104. After completion of the trial, it is possible that whole GM plants could survive in the trial sites, or ratoon plants could regrow from post-harvest stubble, or new volunteer plants could grow from seeds fallen in the trial fields. The applicant proposes a number of control measures to prevent these eventualities, including: destruction of all plant materials not required for further analysis or future planting, cultivating field planting sites after harvest to encourage decomposition or germination of remaining seed, post harvest monitoring of each trial site for at least twelve months and until the site has been clear of volunteers for six months, and to destroy any volunteers found prior to flowering. It is not expected that genetic modifications for the traits of insect resistance,

herbicide tolerance or antibiotic resistance would increase the ability of the GMOs to survive these standard control measures.

105. Potential dispersal of reproductive GM plant material outside the site boundaries would be limited to seed or pollen, as cotton does not reproduce vegetatively under natural conditions (OGTR 2008). Gene flow via pollen is discussed in risk scenario 4. As the introduced genes of the GMOs are not related to seed production and dispersal traits, these characteristics are not expected to be altered in the varieties of GM cotton proposed for release compared to non-GM or commercially released GM cotton varieties.

106. In the field, seed cotton is present as large lint-covered bolls. Wild mammals and birds generally avoid feeding on cotton plants, in particular finding the seed unpalatable because of its high gossypol content, and therefore wild animals do not disperse bolls any great distance from the cotton fields (OGTR 2008). GM cotton seeds produced in this trial will not be used as stock feed, so would not be dispersed by stock.

107. Cotton bolls are large, heavy and remain attached to the plant (OGTR 2008), so they are not normally transported by wind or by runoff after rainfall or irrigation. Extremes of weather may cause dispersal of plant parts. The applicant proposes that release sites will be located at least 50 m away from natural waterways to prevent dispersal in the event of flooding.

108. Dispersal of seeds by authorised people entering the trial sites would be minimised by cleaning of all equipment used at the trial sites, including clothing. The applicant proposes to transport any plant material according to the Regulator's transport guidelines. Spillage of GM seed during transport to and from the release sites would be rare and could be readily controlled through cleaning and monitoring of the site of the spill.

GM cotton plants are able to establish populations that cause harms associated with weediness

109. Non-GM or commercially released GM cotton seed is abundant in the environment through distribution pathways including residual seed bank in growing fields, roadside seed spills and dispersal through use as stock feed. Despite this, feral cotton populations are sparse and ephemeral (OGTR 2008) in all current cotton growing regions of Australia. The only regions of Australia in which small naturalised cotton populations are known to have established are disturbed areas of the wet tropics of northern Australia. Modelling of climactic factors limiting cotton persistence indicate that cotton has naturalisation potential only in the coastal regions of north-east Australia (Rogers et al. 2007), which are over two hundred kilometres away from any of the proposed trial sites.

110. The expression of the introduced genes for insect resistance, herbicide tolerance, or antibiotic resistance traits are not expected to increase cotton survival in unfavourable climactic conditions such as cold stress or dry stress. In the unlikely event that GM cotton plants were present outside the trial limits, their ability to spread and persist would be restricted in the same way as non-GM cotton plants. Cotton persistence is expected to be limited by cold stress for the proposed field trial sites in Narrabri LGA, and limited by water availability in all three of the proposed LGAs. Small and ephemeral feral GM cotton populations would be unlikely to cause harms associated with weediness such as reducing establishment of desired plants, restricting physical movement, or adversely affecting environmental health.

111. Even small and ephemeral feral GM cotton populations could cause adverse effects to human or animal health through toxicity. However, toxicity of the introduced proteins of the GMOs was discussed in risk scenarios 1 and 2. It is unlikely that the GMOs would have higher toxicity than non-GM cotton, except towards a limited range of insects, many of which are agricultural pests.

112. ***Conclusion:*** The potential for harm due to expression of the introduced genes increasing the weediness of the GMOs, in the context of the limits and controls proposed by the applicant and considering both the short and long term, is not identified as a risk that could be greater than negligible. Therefore, it does not warrant further assessment.

2.3 Vertical transfer of genes or genetic elements to sexually compatible plants

113. Vertical gene flow is the transfer of genetic information from an individual organism to its progeny by conventional heredity mechanisms, both asexual and sexual. In flowering plants, pollen dispersal is the main mode of gene flow (Waines & Hegde 2003). For GM crops, vertical gene flow could therefore occur via successful cross-pollination between the crop and neighbouring crops, plants, related weeds or native plants (Glover 2002).

114. It should be noted that vertical gene flow *per se* is not considered an adverse outcome, but may be a link in a chain of events that may lead to an adverse outcome. For an increased potential for adverse effects to arise as a result of gene flow of the introduced genetic elements from the GM cotton varieties to sexually compatible plants, both of the following steps must occur:

- transfer of the introduced genetic elements to sexually compatible plants
- increased potential for adverse effects, such as allergenicity, toxicity or weediness of the recipient plants, due to expression of the introduced gene(s).

115. Baseline information on vertical gene transfer associated with non-GM cotton plants is provided in *The Biology of* Gossypium hirsutum *L. and* Gossypium barbadense *L. (cotton)* (OGTR 2008). In summary, cotton is predominantly self-pollinating and outcrossing is rare, although cross-pollination can occur at low levels over short distances. The only sexually compatible species present in Australia that could receive genes from the GM cotton are *G. hirsutum* and *G. barbadense* (including both cultivated GM and non-GM cotton, and naturalised cotton).

116. Most of the Australian *Gossypium* species have limited distributions and occur at considerable geographic distances from cultivated cotton fields. Furthermore, there is well established genetic incompatibility between native *Gossypium* species and cultivated cotton; the likelihood of fertile hybrids occurring between cultivated cotton and native *Gossypium* species is very low (summarised in OGTR 2008). Therefore, these species are not considered further.

Risk scenario 4 Expression of the introduced genes in cotton plants that are not part of the trial

117. If the introduced genes for insect resistance, herbicide tolerance or antibiotic resistance were transferred and expressed in cotton plants that are not part of the trial, the resulting plants could have increased toxicity or allergenicity to people, toxicity to other organisms, or weediness potential.

118. Pollen dispersal characteristics are not expected to be altered in the varieties of GM cotton proposed for release compared to non-GM or commercially released GM cotton varieties. As discussed in the *The Biology of* Gossypium hirsutum *L. and* Gossypium barbadense *L. (cotton)* (OGTR 2008) cotton is predominantly self-pollinating, with pollen that is large, sticky and heavy and generally not dispersed by wind. Cotton gene flow studies consistently show that outcrossing is localised around the pollen source and decreases rapidly with distance.

119. The applicant has proposed a number of measures to restrict the potential for gene transfer via pollen flow to sexually compatible plants (Chapter 1, Section 3.2 and 3.3). These include surrounding the trial sites with either a 20 m pollen trap or a 3 km exclusion zone (within which intentional planting of cotton is not allowed). Either of these measures is expected to prevent transport of pollen to nearby cotton crops by pollinators during the course of the trial. Provisions are made to monitor for volunteer cotton plants and to destroy any volunteers prior to flowering. Limits on the number of sites (up to 6 per year) and duration (3 years) of the trial would further reduce the likelihood of vertical gene transfer occurring.

120. As discussed in risk scenarios 1 and 2, the proteins encoded by the introduced genes are unlikely to be allergenic to people or toxic to people or organisms, except for toxicity towards certain target invertebrates and toxicity to a limited range of related non-target invertebrates. As discussed in risk scenario 3, the proteins encoded by the introduced genes are unlikely to increase

weediness, as the spread and persistence of cotton plants is primarily limited by abiotic factors. These risk assessments would not change if the introduced genes were expressed in cotton plants that are not part of the trial.

121. Previously approved commercial GM cotton varieties (Section 7.1.1) may be planted in the vicinity of the trial sites. If crossing occurred between the GM cotton varieties proposed for release and some of the commercial GM cotton varieties which express different Bt insecticidal proteins, this could result in cotton plants containing a new combination of stacked insect resistance genes. This could potentially increase the toxic effect and/or range of susceptible insects relative to either of the individual parent GM plants and is an area of uncertainty due to data gaps.

122. If a pollen trap is used to control pollen flow in the proposed trial, the cotton plants in the pollen trap may be non-GM cotton or GM cotton approved under commercial licences DIR 062/2005 or DIR 066/2006. Additional discussion of potential stacking of introduced genes by cross-pollination between the GMOs and pollen trap plants is covered by CCI. The confidential information was made available to the prescribed experts and agencies that were consulted on the RARMP for this application. The applicant proposes that pollen trap plants will be handled, controlled and monitored post-harvest in the same way as the GMOs.

123. ***Conclusion:*** The potential for increased allergenicity in people, toxicity in people and other organisms, or increased weediness due to the expression of the introduced genes in cotton plants that are not part of the trial as a result of gene transfer, in the context of the limits and controls proposed by the applicant and considering both the short and long term, is not identified as a risk that could be greater than negligible. Therefore, it does not warrant further assessment.

2.4 Unintended changes in biochemistry, physiology or ecology

124. All methods of plant breeding can induce unanticipated changes in plants (Haslberger 2003). Gene technology has the potential to cause unintended effects that may include:

- producing a gene product that affects multiple traits
- altered expression of an unrelated gene at the site of insertion of new genetic material
- altered expression of an unrelated gene distant to the site of insertion, for example, due to the encoded protein of an introduced gene changing chromatin structure, affecting methylation patterns, or modulating signal transduction and transcription
- increased metabolic burden associated with high level expression of an introduced gene
- novel traits arising from interactions of the protein encoded by an introduced gene product with endogenous non-target molecules
- secondary effects arising from altered substrate or product levels in a biochemical pathway incorporating the protein encoded by an introduced gene.

Risk scenario 5 Changes to biochemistry, physiology or ecology of the GM cotton plants resulting from expression or random insertion of the introduced genes

125. Unintended pleiotropic (collateral) effects of the genes introduced into the GM cotton varieties might result in adverse outcomes such as production of novel toxins or allergens or higher levels of endogenous toxins or allergens; increased weediness; altered pest or disease burden; or reduced nutritional value as compared to the parent organism.

126. The outcome of random insertion of introduced genes is impossible to predict. However, unintended changes that occur as a result of gene insertions are rarely advantageous to the organism (Kurland et al. 2003), so are unlikely to increase spread or persistence of the GM plants.

127. Accumulated experience with genetic modification of plants indicates that, as for conventional (non-GM) breeding programs, the process has little potential for unexpected outcomes that are not detected and eliminated during the early stage of selecting plants with new properties (Bradford et al. 2005). The applicant states that large numbers of GM breeding lines have been tested for the

desired agronomic and GM traits and only the best performing lines were selected for further development. The GM cotton lines produced by single transformation events have been extensively tested in field trials, in Australia and other countries, and no unintended secondary effects have been observed.

128. The applicant proposes to measure the agronomic performance of the stacked GM cotton varieties during this limited and controlled release, and any unintended effects resulting in agronomic penalties are likely to be detected during the trial. The biochemical composition (levels of toxins and nutrients) of the GM cotton plant material, particularly the stacked GMOs, is an area of uncertainty due to data gaps.

129. Adverse effects, if any, arising due to inadvertent changes in biochemistry, physiology or ecology will be minimised by the proposed limits and controls outlined in Chapter 1, Sections 3.2 and 3.3. In particular, the small scale and short duration of the trial would limit the potential for adverse effects. Humans and livestock would not be intentionally exposed to the GM plant material as the GM cotton will not be used as food or animal feed as part of the release.

130. ***Conclusion:*** The potential for an adverse outcome as a result of inadvertent changes in biochemistry, physiology or ecology is not identified as a risk that could be greater than negligible. Therefore, it does not warrant further assessment.

2.5 Unauthorised activities

Risk scenario 6 Use of the GMOs outside the licence conditions (non-compliance)

131. Non-compliance with the conditions imposed by the licence could lead to spread and persistence of the GM cotton plants outside of the release areas and/or increased exposure of people and other organisms to GM material. The adverse outcomes that this risk scenario could cause are the same as those discussed in the sections above. The Act provides for substantial penalties for non-compliance and unauthorised dealings with GMOs. The Act also requires that the Regulator has regard for the suitability of the applicant to hold a licence prior to the issuing of a licence. These legislative provisions are considered sufficient to minimise risks from unauthorised activities.

132. ***Conclusion:*** The potential for an adverse outcome as a result of unauthorised activities is not identified as a risk that could be greater than negligible. Therefore, it does not warrant further assessment.

Section 3 Risk estimate process and assessment of significant risk

133. The risk assessment begins with postulation of potential pathways that might lead to harm to the health and safety of people or the environment during the proposed release of GMOs due to gene technology, and how it could happen, in comparison to the parent organism and within the context of the receiving environment.

134. Six risk scenarios were identified whereby the proposed dealings might give rise to harm to people or the environment. This included consideration of whether expression of the introduced genes could: result in products that are toxic or allergenic to people or other organisms; alter characteristics that may impact on the spread and persistence of the GM plants; or produce unintended changes in their biochemistry or physiology. The opportunity for gene flow to other organisms and its effects if it occurred were also assessed.

135. A risk is only identified when a risk scenario is considered to have some chance of causing harm. Risk scenarios that do not lead to harm, or could not reasonably occur, do not represent an identified risk and do not advance any further in the risk assessment process.

136. The characterisation of the six risk scenarios in relation to both the seriousness and likelihood of harm, in the context of the limits and controls proposed by the applicant and considering both the short and the long term, did not give rise to any identified risks that warranted further assessment. The principal reasons for this include:

- widespread presence of the same or homologous genes and proteins in the environment
- toxicity of the proteins encoded by the introduced insect resistance genes is expected to be restricted to target insects and a limited range of related non-target insects
- plant characteristics and abiotic factors limiting the ability of GM or non-GM cotton plants to establish and persist in non-cultivated environments
- limited ability and opportunity for the GM cotton plants to transfer the introduced genes to commercial cotton crops or other cotton plants
- limits on the size, locations and duration of the release proposed by Bayer
- suitability of controls proposed by Bayer to restrict the spread and persistence of the GM cotton plants and their genetic material
- none of the GM plant materials or products will enter commercial human or animal food supply chains.

137. Therefore, any risks to the health and safety of people, or the environment, from the proposed release of the GM cotton plants into the environment is considered to be negligible. Hence, the Regulator considers that the dealings involved in this proposed release do not pose a significant risk to either people or the environment.

Section 4 Uncertainty

138. Uncertainty is an intrinsic property of risk and is present in all aspects of risk analysis, including risk assessment, risk management and risk communication. Both dimensions of risk (consequence and likelihood) are always uncertain to some degree.

139. Uncertainty in risk assessments can arise from incomplete knowledge or inherent biological variability[5]. For field trials, because they involve the conduct of research, some knowledge gaps are inevitable. This is one reason they are required to be conducted under specific limits and controls to restrict the spread and persistence of the GMOs and their genetic material in the environment, rather than necessarily to treat an identified risk.

140. For DIR 113, the primary purpose of which is to undertake research, uncertainty is noted particularly in relation to the characterisation of:

- Risk scenario 2, regarding potential increases in toxicity to non-target invertebrates as a result of the combination of the introduced insect resistance genes
- Risk scenario 4, regarding potential increases in toxicity to non-target invertebrates and/or weediness as a result of gene transfer to commercially approved GM cotton varieties leading to expression of new combinations of stacked insect resistance genes.
- Risk scenario 5, associated with the potential for any unintended effects as a result of changes to biochemistry, physiology or ecology of the GM cotton plants, particularly levels of toxins and nutrients.

141. Additional data, including information to address these uncertainties, may be required to assess possible future applications for a larger scale trial, reduced containment conditions, or the commercial release of these GM cotton varieties if they are selected for further development.

142. Chapter 3, Section 4 discusses information that may be required for future releases.

[5] A more detailed discussion is contained in the Regulator's *Risk Analysis Framework* available at <http://www.ogtr.gov.au/internet/ogtr/publishing.nsf/Content/riskassessments-1> or via Free call 1800 181 030.

Chapter 3 Risk management plan

Section 1 Background

143. Risk management is used to protect the health and safety of people and to protect the environment by controlling or mitigating risk. The risk management plan evaluates and treats identified risks, evaluates controls and limits proposed by the applicant, and considers general risk management measures. The risk management plan informs the Regulator's decision-making process and is given effect through licence conditions.

144. Under section 56 of the Act, the Regulator must not issue a licence unless satisfied that any risks posed by the dealings proposed to be authorised by the licence are able to be managed in a way that protects the health and safety of people and the environment.

145. All licences are subject to three conditions prescribed in the Act. Section 63 of the Act requires that each licence holder inform relevant people of their obligations under the licence. The other statutory conditions allow the Regulator to maintain oversight of licensed dealings: section 64 requires the licence holder to provide access to premises to OGTR inspectors and section 65 requires the licence holder to report any information about risks or unintended effects of the dealing to the Regulator on becoming aware of them. Matters related to the ongoing suitability of the licence holder are also required to be reported to the Regulator.

146. The licence is also subject to any conditions imposed by the Regulator. Examples of the matters to which conditions may relate are listed in section 62 of the Act. Licence conditions can be imposed to limit and control the scope of the dealings. In addition, the Regulator has extensive powers to monitor compliance with licence conditions under section 152 of the Act.

Section 2 Risk treatment measures for identified risks

147. The risk assessment of risk scenarios listed in Chapter 2 concluded that there are negligible risks to people and the environment from the proposed trial of GM cotton. These risk scenarios were considered in the context of the scale of the proposed release (a maximum cumulative area of 78 ha on up to six sites per year between May 2012 and May 2015), the proposed containment measures (Chapter 1, Section 3), and the receiving environment (Chapter 1, Section 6), and considering both the short and the long term. The *Risk Analysis Framework* (OGTR 2009), which guides the risk assessment and risk management process, defines negligible risks as insubstantial with no present need to invoke actions for their mitigation. Therefore, no conditions are imposed to treat these negligible risks.

Section 3 General risk management

148. Licence conditions have been imposed to restrict the spread and persistence of the GMOs and their genetic material in the environment and limit the release to the size, locations and duration proposed in the application. Both of these considerations were important in establishing the context for the risk assessment and in reaching the conclusion that the risks posed to people and environment are negligible. The conditions are detailed in the licence and summarised in this Chapter.

3.1 Licence conditions to limit and control the release

3.1.1 Consideration of limits and controls proposed by Bayer

149. Sections 3.2 and 3.3 of Chapter 1 provide details of the limits and controls proposed by Bayer in their application. These are discussed in the six risk scenarios characterised for the proposed release in Chapter 2. Many of these proposed control measures are considered standard GM cotton licence conditions and have been imposed by the Regulator in previous DIR licences. The appropriateness of these controls is considered further below.

150. The release would be limited to up to 6 sites per year in the LGAs of Narrabri, NSW, Wyndham-East Kimberley, WA, and Central Highlands, Qld. The duration of the release would be limited to three years and the maximum cumulative area of the release would be 78 ha. Only staff with appropriate training would be allowed to deal with the GMOs. GM plant material will not be permitted to enter commercial human or animal food supply chains. These measures will minimise the potential exposure of humans and other organisms to the GMOs (risk scenarios 1 and 2) and the potential for the GM cotton to be dispersed outside the trial limits (risk scenario 3).

151. Each site would be surrounded by a 20 m wide pollen trap or a 3 km exclusion zone, the latter in combination with a 100 m monitoring zone, to restrict gene flow from the GM cottons. As discussed in the *The Biology of* Gossypium hirsutum *L. and* Gossypium barbadense *L. (cotton)* (OGTR 2008), cotton is predominantly self-pollinating, with the highest level of outcrossing occurring between adjacent rows. Outcrossing is rare beyond 20 m (Llewellyn et al. 2007), and a 20 m pollen trap of non-GM cotton or GM cotton approved under commercial licences DIR 062/2005 and DIR 066/2006 would minimise gene transfer to sexually compatible plants outside the trial (risk scenario 4).

152. As an alternative to a 20 m pollen trap, a 3 km exclusion zone in combination with a 100 m monitoring zone immediately surrounding a trial site was proposed. The exclusion zone would be free of intentionally planted (GM and non-GM) cotton. The monitoring zone would be inspected every 30 days while the cotton plants are being grown at the trial site and kept free of flowering cotton plants. In the RARMP prepared for DIR 081/2007, the literature regarding outcrossing rates over heterogenous terrain was reviewed. In addition, the suitability of the combination of these controls was assessed and found acceptable to restrict vertical gene transfer from GM cotton trial sites to other (GM and non-GM) cotton.

153. The applicant has proposed to locate the trial sites more than 50 m from the nearest waterway which would minimise the chance of viable plant material being washed away from the site. This is a standard DIR licence condition. In addition, licence conditions have been imposed requiring immediate notification of any extreme weather conditions affecting the site during the proposed release, and cleaning of areas where GM plant material has been dispersed. These measures will minimise likelihood for the GM cotton to be dispersed outside the release sites (risk scenario 3).

154. The applicant has proposed that the GM cotton would be harvested and ginned separately from other cotton crops to prevent mixing. All equipment used in connection with cultivating the GM cotton will be cleaned on site prior to removal. An additional licence condition has been imposed requiring that any gin used for the GM cotton must be cleaned immediately following its use and before any other cotton crop is ginned. These measures are expected to limit the potential exposure of humans and other vertebrates to the GMOs (risk scenario 1) and the potential for the GM cotton to be dispersed outside the release sites (risk scenario 3).

155. After the GM cottons have been harvested, the applicant has proposed to destroy all remaining plant material not required for further testing, and to clean the sites and all equipment used. As discussed in the *The Biology of* Gossypium hirsutum *L. and* Gossypium barbadense *L. (cotton)* (OGTR 2008), cotton seeds have low dormancy levels and do not generally form a viable seed bank. However, dormancy can be induced in cotton seeds by low soil temperature and/or soil moisture. The applicant proposes at least one post-harvest cultivation (followed by an irrigation event) of the trial sites and pollen traps to promote cotton seed germination and minimise the persistence of a GM cotton seed bank. A licence condition has been imposed requiring this cultivation to occur in the spring or summer following the harvest, so that soil temperature will be suitable for cotton seed germination. The licence requires that each trial site would be monitored post-harvest at least every two months for a minimum of twelve months and until the site has been clear of volunteers for at least six months. These measures will limit the persistence of the GM cotton in the environment (risk scenario 3).

156. The applicant has stated that any plant material taken off-site for experimental analysis will be transported according to the Regulator's *Guidelines for the Transport, Storage and Disposal of GMOs* (http://www.ogtr.gov.au/internet/ogtr/publishing.nsf/Content/transport-guide-1). These are standard protocols for the handling of GMOs to minimise exposure of people and other organisms to the GMOs (risk scenarios 1 and 2), dispersal into the environment (risk scenario 3), and gene transfer (risk scenario 4).

3.1.2 Summary of measures imposed by the Regulator to limit and control the release

157. A number of licence conditions have been imposed to limit and control the proposed release, based on the above considerations. These include requirements to:

- limit the release to a total cumulative area of 78 ha in three LGAs between May 2012 and May 2015.
- restrict gene flow via pollen from field trial sites using one of the following measures:
  - surround the trial site with a 100 m monitoring zone and maintain a 3 km isolation distance between the site and intentionally planted cotton crops, or
  - surround the trial site by a 20 m pollen trap of non-GM cotton or commercially approved GM cotton, and treating the pollen trap plants in the same way as the GMOs
- harvest and gin all cotton plant material separately from other cotton crops
- clean all equipment used in connection with the cotton plant material
- after harvest, destroy all cotton plant material not required for further analysis or future planting
- after cleaning of sites, apply measures to promote germination of any cotton seeds that may be present in the soil
- after cleaning of sites, monitor for and destroy any GM cotton that may grow for at least 12 months, and until no volunteers are observed for a continuous 6 month period
- transport and store the GM plant material in accordance with the Regulator's guidelines or other specific conditions
- not allow GM plant material or products to be used for human food or animal feed.

158. Research with the GMOs or GM plant material may be conducted in certified physical containment facilities as Notifiable Low Risk Dealings (NLRD) in accordance with all applicable requirements of the *Gene Technology Regulations 2001*, and therefore this activity is not covered in the licence.

3.2 Other risk management considerations

159. All DIR licences issued by the Regulator contain a number of conditions that relate to general risk management. These include conditions relating to:

- applicant suitability
- contingency plans
- identification of the persons or classes of persons covered by the licence
- reporting structures
- a requirement that the licence holder allows access to the trial sites and other places for the purpose of monitoring or auditing.

3.2.1 Applicant suitability

160. In making a decision whether or not to issue a licence, the Regulator must have regard to the suitability of the applicant to hold a licence. Under section 58 of the Act, matters that the Regulator must take into account include:

- any relevant convictions of the applicant (both individuals and the body corporate)
- any revocation or suspension of a relevant licence or permit held by the applicant under a law of the Commonwealth, a State or a foreign country
- the capacity of the applicant to meet the conditions of the licence.

161. On the basis of information submitted by the applicant and records held by the OGTR, the Regulator considers Bayer suitable to hold a licence.

162. The licence includes a requirement for the licence holder to inform the Regulator of any circumstances that would affect their suitability or their capacity to meet the conditions of the licence.

163. Bayer must continue to have access to a properly constituted Institutional Biosafety Committee and be an accredited organisation under the Act.

3.2.2 Contingency plan

164. Bayer is required to submit a contingency plan to the Regulator within 30 days of the issue date of the licence. This plan must detail measures to be undertaken in the event of any unintended presence of the GM cotton outside of the permitted areas.

165. Bayer is also required to provide a method to the Regulator for the reliable detection of the presence of the GMOs and the introduced genetic materials in a recipient organism. This instrument is required within 30 days of the issue date of the licence.

3.2.3 Identification of the persons or classes of persons covered by the licence

166. The persons covered by the licence are the licence holder and employees, agents or contractors of the licence holder and other persons who are, or have been, engaged or otherwise authorised by the licence holder to undertake any activity in connection with the dealings authorised by the licence. Prior to growing the GMOs, Bayer is also required to provide a list of people and organisations who will be covered, or the function or position where names are not known at the time.

3.2.4 Reporting requirements

167. The licence obliges the licence holder to immediately report any of the following to the Regulator:

- any additional information regarding risks to the health and safety of people or the environment associated with the trial
- any contraventions of the licence by persons covered by the licence
- any unintended effects of the trial.

168. A number of written notices are also required under the licence that assist the Regulator in designing and implementing a monitoring program for all licensed dealings. The notices include:

- locations of trial sites
- expected and actual dates of planting
- details of areas planted to the GMOs
- expected dates of flowering
- expected and actual dates of harvest and cleaning after harvest
- details of inspection activities.

3.2.5 Monitoring for Compliance

169. The Act stipulates, as a condition of every licence, that a person who is authorised by the licence to deal with a GMO, and who is required to comply with a condition of the licence, must

allow inspectors and other persons authorised by the Regulator to enter premises where a dealing is being undertaken for the purpose of monitoring or auditing the dealing. Post-release monitoring continues until the Regulator is satisfied that all the GMOs resulting from the authorised dealings have been removed from the release site.

170. If monitoring activities identify changes in the risks associated with the authorised dealings, the Regulator may also vary licence conditions, or if necessary, suspend or cancel the licence.

171. In cases of non-compliance with licence conditions, the Regulator may instigate an investigation to determine the nature and extent of non-compliance. The Act provides for criminal sanctions of large fines and/or imprisonment for failing to abide by the legislation, conditions of the licence or directions from the Regulator, especially where significant damage to health and safety of people or the environment could result.

Section 4 Issues to be addressed for future releases

172. Additional information has been identified that may be required to assess an application for a large scale or commercial release of these GM cotton varieties, or to justify a reduction in containment conditions. This includes:

- additional data on potential increases in toxicity to non-target invertebrates as a result of stacked insect resistance genes
- additional phenotypic characterisation of the GM cotton varieties, in particular of traits which may contribute to weediness
- additional molecular and biochemical characterisation of the GM cotton varieties.

Section 5 Conclusions of the RARMP

173. The risk assessment concluded that this limited and controlled release of up to 11 varieties of GM cotton on a maximum cumulative area of 78 ha over three years in the LGAs of Narrabri, NSW, Wyndham-East Kimberley, WA, and Central Highlands, Qld, poses negligible risks to the health and safety of people or the environment as a result of gene technology.

174. The risk management plan concluded that these negligible risks do not require specific risk treatment measures. However, licence conditions have been imposed to limit the release to the size, locations and duration proposed in the application, and to require controls in line with those proposed by the applicant, as these were important considerations in establishing the context for assessing the risks.

References

Arts, J., Mommers, C., de Heer, C. (2006). Dose-response relationships and threshold levels in skin and respiratory allergy. *Critical review in Toxicology* **36**: 219-251

Bernstein, I.L., Bernstein, J.A., Miller, M., Tierzieva, S., Bernstein, D.I., Lummus, Z., Selgrade, M.K., Doerfler, D.L., Seligy, V.L. (1999). Immune responses in farm workers after exposure to *Bacillus thuringiensis* pesticides. *Environmental Health Perspectives* **107**: 575-582

Betz, F.S., Hammond, B.G., Fuchs, R.L. (2000). Safety and advantages of *Bacillus thuringiensis*-protected plants to control insect pests. *Regulatory Toxicology and Pharmacology* **32**: 156-173

Bevan, M. (1984). Binary *Agrobacterium* vectors for plant transformation. *Nucleic Acids Research* **12**: 8711-8721

Bradford, K.J., van Deynze, A., Gutterson, N., Parrot, W., Strauss, S.H. (2005). Regulating transgenic crops sensibly: lessons from plant breeding, biotechnology and genomics. *Nature Biotechnology* **23**: 439-444

EPA (2001). Biopesticides registration action document: *Bacillus thuringiensis* plant-incorporated protectants. US EPA

Felsot, A.S. (2000). Insecticidal genes. Part 2: Human health hoopla. *Agrichemical & Environmental News* **168**: 1-7

Glover, J. (2002). Gene flow study: Implications for the release of genetically modified crops in Australia. Bureau of Rural Sciences, Australia, available online at http://adl.brs.gov.au/brsShop/data/12860_gene_flow_report.pdf

Goodman, R.E., Vieths, S., Sampson, H.A., Hill, D., Ebisawa, M., Taylor, S.L., van Ree, R. (2008). Allergenicity assessment of genetically modified crops - what makes sense? *Nature Biotechnology* **26**: 73-81

Groves, R.H., Hosking, J.R., Batianoff, G.N., Cooke, D.A., Cowie, I.D., Johnson, R.W., Keighery, G.J., Lepschi, B.J., Mitchell, A.A., Moerkerk, M., Randall, R.P., Rozefelds, A.C., Walsh, N.G., Waterhouse, B.M. (2003). *Weed categories for natural and agricultural ecosystem management.* Bureau of Rural Sciences Canberra, available online at affashop.gov.au/PdfFiles/PC12781.pdf

Groves, R.H., Hosking, J.R., Cooke, D.A., Johnson, R.W., Lepschi, B.J., Mitchell, A.A., Moerkerk, M., Randall, R.P., Rozefelds, A.C., and Waterhouse, B.M. (2002). The naturalised non-native flora of Australia: its categorisation and threat to agricultural ecosystems. Unpublished report to Agriculture, Fisheries and Forestry Australia by the CRC for Weed Management Systems.

Haslberger, A.G. (2003). Codex guidelines for GM foods include the analysis of unintended effects. *Nature Biotechnology* **21**: 739-741

Hnatiuk, R.J. (1990). *Census of Australian vascular plants.* Australian Government Publishing Service Canberra.

International Programme on Chemical Safety (1999). Environmental Health Criteria 217: *Bacillus thuringiensis*. Report No. E, United Nations Environment Programme; International Labour Organisation; World Health Organization

Keese, P. (2008). Risks from GMOs due to horizontal gene transfer. *Environ Biosafety Res* **7**: 123-149

Klee, H.J., Rogers, S.G. (1989). Plant gene vectors and genetic transformation: plant transformation systems based on the use of *Agrobacterium tumefaciens*. *Cell Culture and Somatic Cell Genetics of Plants* **6**: 1-23

Kurland, C.G., Canback, B., Berg, O.G. (2003). Horizontal gene transfer: a critical view. *Proceedings of the National Academy of Science of the United States of America* **100**: 9658-9662

Llewellyn, D.J., Tyson, C., Constable, G.A., Duggan, B., Beale, S., Steel, P. (2007). Containment of regulated genetically modified cotton in the field. *Agriculture, Ecosystems & Environment* **121**: 419-429

McClintock, J.T., Schaffer, C.R., Sjoblad, R.D. (1995). A comparative review of the mammalian toxicity of *Bacillus thuringiensis*-based pesticides. *Pesticide Science* **45**: 95-105

National Weed Prioritisation Working Group (2006). National post-border weed risk management protocol. Handbook HB 294:2006, Standards Australia, Standards New Zealand and the Cooperative Research Centre for Australian Weed Management.

OGTR (2008). The Biology of *Gossypium hirsutum* L. and *Gossypium barbadense* L. (cotton). Document prepared by the Office of the Gene Technology Regulator, Canberra, Australia, available online at http://www.ogtr.gov.au/internet/ogtr/publishing.nsf/Content/riskassessments-1

OGTR (2009). *Risk Analysis Framework.* Version 3, Document produced by the Australian Government Office of the Gene Technology Regulator, available online from http://www.ogtr.gov.au/internet/ogtr/publishing.nsf/Content/riskassessments-1

Pheloung, P.C., Williams, P.A., Halloy, S.R. (1999). A weed risk assessment model for use as a biosecurity tool evaluating plant introductions. *Journal of Environmental Management* **57**: 239-251

Rogers, D.J., Reid, R.E., Rogers, J.J., Addison, S.J. (2007). Prediction of the naturalisation potential and weediness risk of transgenic cotton in Australia. *Agriculture, Ecosystems & Environment* **119**: 177-189

Sanchis, V., Bourguet, D. (2008). Bacillus thuringiensis: applications in agriculture and insect resistance anagement. A review. *Agron Sustain Dev* **28**: 11-20

Schnepf, E., Crickmore, N., Van Rie, J., Lereclus, D., Baum, J., Feitelson, J., Zeigler, D.R., Dean, D.H. (1998). *Bacillus thuringiensis* and its pesticidal crystal proteins. *Microbiology and Molecular Biology Reviews* **62**: 775-806

Smith, N. (1998). More T-DNA than meets the eye. *Trends in Plant Science* **3**: 85

Ulker, B., Li, Y., Rosso, M.G., Logemann, E., Somssich, I.E., Weisshaar, B. (2008). T-DNA-mediated transfer of *Agrobacterium tumefaciens* chromosomal DNA into plants. *Nature Biotechnology* **26**: 1015-1017

Waines, J.G., Hegde, S.G. (2003). Intraspecific gene flow in bread wheat as affected by reproductive biology and pollination ecology of wheat flowers. *Crop Science* **43**: 451-463

Appendix A Summary of issues raised in submissions received from prescribed experts, agencies and authorities[6] on the consultation RARMP for DIR 113

The Regulator received several submissions from prescribed experts, agencies and authorities on the consultation RARMP. All issues raised in submissions that related to risks to the health and safety of people and the environment were considered in the context of the currently available scientific evidence and were used in finalising the RARMP that formed the basis of the Regulator's decision to issue the licence. Advice received is summarised below.

Abbreviations: **Bt**: *Bacillus thuringiensis*; **CCI**: Confidential Commercial Information; **DIR**: Dealings involving Intentional Release; **GM**: Genetically Modified; **GMO**: Genetically Modified Organism; **OGTR**: Office of the Gene Technology Regulator; **RARMP**: Risk Assessment and Risk Management Plan.

Summary of issues raised	Comments
Agrees with the overall conclusions of the RARMP.	Noted.
Suggests that the technical summary of the RARMP (in addition to the licence conditions) should explicitly state that cotton used in the pollen trap must be treated in the same way as GM cotton.	The Technical Summary has been modified to include this point.
Agrees that this dealing does not represent a risk to human health and the environment.	Noted.
Suggests that the OGTR should consider including a requirement for licence holders to document any observed unusual incidents that occur during the trial.	Licence condition 19 requires the licence holder to inform the Regulator if the licence holder becomes aware of any unintended effects of the dealings authorised by the licence.
Suggests that the OGTR should consider analysing the identified / unidentified risks that eventuated from previously approved DIR licences and publishing the results.	The risk assessment process for this release considered risk assessments and monitoring reports from previous DIR licences involving similar GM traits.
Given the previous releases approved by the Regulator, along with the scale and the purpose of the proposed release, considers that the proposed licence conditions are appropriate.	Noted.
Suggests that the field trial be used as an opportunity to acquire further data which reduces apparent uncertainty around potential toxicity to non-target species, especially in the case of 'stacked' traits.	In Chapter 3, Section 4, of the RARMP it is stated that additional data on potential increases in toxicity to non-target invertebrates as a result of stacked insect resistance genes may be required to assess a large-scale or commercial release of the GM cotton varieties. OGTR has advised the licence holder that they should consider how this data could be collected.
The evidence supplied indicates that the proposed containment measures are adequate to minimise the risk of spread of the GMOs.	Noted.
Suggests that landholders adjoining the trial site be advised of this application and the control processes	In Chapter 2 of the RARMP, Risk Scenarios 3 and 4 consider the likelihood of spread and persistence of the GMOs beyond

[6] Gene Technology Technical Advisory Committee, State and Territory Governments, Australian Government agencies, LGAs and the Minister for the Environment.

Summary of issues raised	Comments
involved.	the trial sites, or of interbreeding with cotton plants outside the trial sites. In the context of the limits and controls imposed by the licence conditions, these scenarios are assessed as posing negligible risks. Therefore, the Regulator has not imposed an additional licence condition requiring notification of landholders adjoining the trial sites. However Bayer and/or the site landholder may choose to inform adjacent landholders.
Satisfied with the conclusions of the draft RARMP. Considers that the proposed licence conditions would minimise the risk of gene transfer, weediness and toxicity to organisms to an acceptable level.	Noted.
Points out that cotton has demonstrated long term survival in northern Australia and is classified as a minor to moderate weed, requiring control in a small number of locations. Cold stress is presented in the RARMP as an abiotic factor which could limit cotton weediness potential; however, this is unlikely to be a relevant factor in the north of Western Australia. In this area, it is possible that insect predation is a factor limiting cotton survival, and it is plausible that the genetic modifications for insect resistance may increase the weediness potential of the GM cotton. While it is agreed that the limited nature of the trial and the proposed controls will reduce the risks, it is recommended that the applicant should collect data on potential fitness advantages for these GM cotton varieties, particularly information about the effects of gene stacking on their potential weediness in suitable non-agricultural environments. This data would inform the risk assessment should the applicant seek approval for any larger scale or commercial release application of these GM cotton varieties.	The RARMP states that the abiotic factors limiting cotton survival in Australia are cold stress, dry stress and soil suitability. Although the north of Western Australia would be warm enough to allow cotton persistence, none of the field trial sites are consistently wet enough to allow cotton persistence. A sentence has been added to Risk Scenario 3 in Chapter 2 of the RARMP to emphasise this point. In the context of the locations, limits and controls of the current release, the potential persistence of these GM cotton varieties is considered to be limited by abiotic factors, and therefore modifications for insect resistance are not expected to increase weediness potential. However, in the future the applicant may seek approval to release these GM cotton varieties in high rainfall areas of north-eastern Australia, where cotton has demonstrated naturalisation potential. The part of the RARMP which lists issues to be addressed for further releases (Chapter 3, Section 4) has been modified to include additional phenotypic characterisation of the GM cotton varieties, in particular of traits which may contribute to weediness. OGTR has advised the licence holder that they should consider how this data could be collected.
Suggests that to properly assess the risks posed by a commercial release of these cotton types, information would be required on the Australian insect toxicity range. The insect host ranges of the introduced Bt toxins are not fully described in the RARMP. Recommends that data about toxicity effects on Australian non-target species be collected from the trial.	Available information on the relevant Bt proteins toxicity ranges has been summarised in brief in the CCI Attachment to the RARMP. The toxicity information has not been discussed in detail as this was not necessary for the purposes of risk assessment for the current limited and controlled release. In Chapter 3, Section 4, of the RARMP it is stated that additional data on potential increases in toxicity to non-target invertebrates as a result of stacked insect resistance genes may be required to assess a large-scale or commercial release of the GM cotton varieties. OGTR has advised the licence holder that they should consider how this data could be collected.
There is some inconsistency in the use of the terms “type”, “variety” and “line” in the RARMP. If these terms are interchangeable, it is recommended that one of them should be used consistently. Otherwise, the definition of each term should be made explicit.	The term “line” is used to mean GM cotton containing a single transformation event, and is defined at its first appearance. The general terms “type” and “variety” are interchangeable, and the RARMP has been modified to use only the term “variety”.

Appendix B Summary of issues raised in submissions received from the public on the consultation RARMP for DIR 113

The Regulator received two submissions from the public on the consultation RARMP. These submissions are summarised in the table below. Issues raised relating to human health and safety and the environment were considered in the context of currently available scientific evidence in finalising the RARMP that formed the basis of the Regulator's decision to issue the licence.

View (general tone): n = neutral; x = do not support; y = support

Issues raised: AR: Antibiotic resistance genes; **AS**: Applicant suitability; **E**: Environment; **F**: GM food; **HS**: human safety; **PC**: Public consultation; **RA**: Risk analysis; **U**: Uncertainty; **W**: Weediness

Other abbreviations: Act: *Gene Technology Act 2000*; **CCI**: Confidential Commercial Information; **DIR**: Dealings involving Intentional Release; **GM**: Genetically Modified; **GMO**: Genetically Modified Organism; **OGTR**: Office of the Gene Technology Regulator; **RARMP**: Risk Assessment and Risk Management Plan.

Type: IB: Industry body; **NGO**: Non-government organisation.

Sub. No:	Type	View	Issue	Summary of issues raised	Comment
1	IB	y	RA	Supports the RARMP for DIR 113 and believes that the proposed trial poses negligible risk to human health and safety or the environment.	Noted.
			HS	Asserts that GM insect resistant and herbicide tolerant crops have improved occupational health of agricultural workers by reducing exposure to insecticide sprays during hand hoeing.	Benefits of gene technology are outside the matters to which the Regulator may have regard when deciding whether or not to issue a licence.
			E	Commercial GM cottons have reduced environmental insecticide and herbicide residues due to the reduction in the use of insecticides by 80-90% and residual herbicides by over 30%. The commercial GM cottons also have reduced tillage requirements leading to improved soil conservation practices.	Benefits of gene technology are outside the matters to which the Regulator may have regard when deciding whether or not to issue a licence.
			RA, PC	Appreciates the rigorous scientific assessment and public consultation process.	Noted.
2	NGO	x	AS	Asserts that the applicant is unsuitable to hold GM licences, due to convictions for offences against laws of foreign countries, and failure to report these offences to the OGTR as required by	The applicant for licence DIR 113 is Bayer CropScience Pty Ltd, an Australian proprietary company limited by shares. The Regulator has assessed the suitability of Bayer CropScience Pty Ltd to hold a DIR licence as required by the

Sub. No:	Type	View	Issue	Summary of issues raised	Comment
				the Act. Contends that Bayer CropScience Pty Ltd in Australia is a business under the control of a parent company, Bayer CropScience AG, on the grounds that: a. the Bayer CropScience AG website states that Germany is the location of "Global Bayer CropScience Headquarters", and b. In order to demonstrate financial suitability to hold a GM licence, Bayer CropScience Pty Ltd submitted a financial report for the global Bayer Group as part of its licence application. Provides a list of criminal fines and civil damages levied against Bayer Group companies in the USA and Switzerland.	Act. The company is considered suitable as the Regulator is satisfied that no relevant convictions have been recorded, no licences or permits have been cancelled or suspended under laws relating to the health and safety of people or the environment, and the organisation has the capacity to meet the conditions of the licence. Bayer CropScience Pty Ltd has submitted a financial report pertaining to its own operations.
			PC	Asserts that the applicant's CCI claims are unjustified. The application concerns approved plant varieties that have been conventionally crossed and stacked with others, and there is no case for hiding such details. In particular, information about approvals by regulatory agencies and published references must be in the public domain. Failure to disclose which selectable markers are used prevents members of the public to fairly and fully exercise their right to comment on the application. Recommends that the OGTR review its CCI approval and exercise its discretion in favour of the public's right to know.	The CCI application received from Bayer CropScience Pty Ltd was considered in accordance with the requirements of the Act. Information that could reveal CCI has not been included in the publicly released RARMP. CCI is available to the OGTR, prescribed experts and Commonwealth and State government agencies for the purposes of risk assessment.
			RA	Asserts that Bayer's application fails to satisfy the OGTR's Risk Analysis Framework requirements due to inadequate data provided in the application form. The application is also based on old and outdated evidence. Points out that the RARMP does not cite the recent study: Aris *et al*., 2011, Maternal and fetal exposure to pesticides associated to genetically modified foods in Eastern Townships of Quebec, Canada	The RARMP for this release considered both information provided by the applicant and the currently available scientific information (including many recent as well as relevant older publications and reports). During the risk assessment process additional information was requested from and provided by the applicant. In the context of the limits and controls imposed by the licence, the RARMP concluded that risks to human health and the environment are negligible. The Aris *et al*. paper relates to food safety which is the regulatory responsibility of FSANZ. FSANZ have responded to this paper via a fact sheet published on the FSANZ website. GM cotton material from the current release

Sub. No:	Type	View	Issue	Summary of issues raised	Comment
					will not be permitted to enter human food or animal feed.
			AR	Points out that technologies exist for removal of antibiotic resistance marker genes to generate marker-free plants. Recommends that the OGTR require that antibiotic resistance marker genes be completely removed from all potential commercial GM food crops, in the interests of human and animal health.	The antibiotic resistance marker gene present in some of the GM cotton varieties has been considered in detail by the OGTR, by other Australian regulatory agencies, by regulatory agencies in other countries and by international bodies, and has not been found to pose a risk to people or the environment. No adverse effects from its use in field trials or commercial release of GMOs have been recorded in Australia or elsewhere. Nonetheless, GM cotton material from the current small-scale trial will not be permitted to enter human food or animal feed.
			RA, W, U	Recommends that the OGTR require trials to be designed so that robust data will be available towards the precautionary assessment of any subsequent applications. In particular, recommends that the applicant be required to manage these trials so as to gather data about potential weediness.	Section 4 of Chapter 3 of the RARMP lists additional information that may be required to assess a large scale or commercial release of the GM cotton varieties. The list includes additional phenotypic characterisation of the GM cotton varieties, in particular of traits which may contribute to weediness. OGTR has advised the licence holder that they should consider how this data could be collected. If insufficient data is presented in a future application, the application may not be accepted, more data may be required from the applicant, risk treatment measures imposed or a licence refused.
			F	Notes that Bayer's application states 'Highly processed edible oils contain virtually no protein, indicating a minimal allergenic potential of cottonseed oil for human consumption', which contradicts FSANZ's view that processed vegetable oils contain no DNA or protein. Recommends that the OGTR initiates a review on the regulatory assumptions that are not supported by the evidence. Suggests that all GM foods that contain any novel DNA or protein should be labelled as such.	No GM cotton materials or products from the current trial will be permitted to enter human food or animal feed. Bayer's application cites clinical trials demonstrating the absence of both water-soluble allergens and clinical allergy observations. Food safety and food labelling are the responsibility of FSANZ.
			RA, F	Asserts that the RARMP is selective in its citations of evidence and considers only likely scenarios and never worst case scenarios. Asserts that the OGTR's dominant assumption is that ingested DNA and protein do not survive digestion, based	RARMPs are prepared using the risk analysis model and terminology as described in the Regulator's Risk Analysis Framework (RAF), which is based on the internationally recognised Australia-New Zealand Standard on Risk Management (AS/NZS ISO

Sub. No:	Type	View	Issue	Summary of issues raised	Comment
				on research using simulated gastric juices. Points out that the OGTR does not cite the study: Netherwood *et al.*, 2004, "Assessing the survival of transgenic plant DNA in the human gastrointestinal tract".	31000:2009). Risks are assessed within the risk assessment context, and a risk is only identified for further assessment when a risk scenario is considered to have some reasonable chance of causing harm. Pathways that do not lead to harm, or could not plausibly occur, do not advance in the risk assessment process. The assessment of potential toxicity in the RARMP (Risk Scenario 1, Chapter 2) for DIR 113 is based primarily on direct toxicity tests in animals and humans. The fact that all introduced genes and proteins in the GM cotton varieties are also widely present in the environment in non-GM organisms which are likely to form part of the human diet and cause no known toxicity, along with testing demonstrating that the introduced DNA and proteins are largely digested in the gastrointestinal tract (supported by the Netherwood *et al* paper, among many others) are used as supplementary evidence for the risk assessment. Risk Scenario 1 of the RARMP concludes that the potential for toxicity in people as a result of exposure to the GM cotton, in the context of the limits and controls imposed by the licence, poses negligible risk.
			U	Recommends that trait stability determination, the number and position of all transgenic inserts, and complete molecular and phenotypic characterisation of all GMOs proposed for release be required prior to licencing. Recommends that GMOs with stacked traits should be the subject of separate applications to the OGTR due to the lack of characterisation. Asserts that application deficiencies were ignored and that the application should be rejected.	Uncertainty is an intrinsic property of risk assessments. In the context of the limited scale of the release and the proposed control measures, and acknowledging knowledge gaps, the dealings proposed were assessed to pose negligible risk to people or the environment.