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

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TECHNICAL SUMMARY OF THE RISK ASSESSMENT AND RISK MANAGEMENT PLAN FOR APPLICATION NO. DIR 101 FROM MONSANTO AUSTRALIA LIMITED

Introduction

The Gene Technology Regulator (the Regulator) has made a decision to issue a licence in respect of application DIR 101 from Monsanto Australia Limited (Monsanto). The licence authorises dealings involving the limited and controlled release of cotton genetically modified (GM) for insect resistance and herbicide tolerance.

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 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

Monsanto has applied for a licence for dealings involving the intentional release of two GM cottons (Bollgard III and Bollgard III/Roundup Ready Flex®) on a limited scale and under controlled conditions. The GM cottons have been genetically modified for insect resistance either alone or in combination with herbicide tolerance. The trial may take place at up to 50 sites per year in up to 34 LGAs in Qld, NSW and WA, on a maximum total area of 1150 ha, between October 2010 and October 2014.

The applicant intends to release two GM cottons. The first, to be known as Bollgard III cotton, contains three insect resistance genes. It is generated by conventionally crossing the commercially released GM Bollgard II® cotton (containing the insect resistance genes *cry1Ac* and *cry2Ab*) with another GM cotton, VIP3A cotton (containing the insect resistance gene *vip3A*). In the second GM cotton, insect resistance is combined with

[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>.

herbicide tolerance by conventionally crossing the GM VIP3A cotton with commercially released GM Bollgard II®/Roundup Ready Flex® cotton (containing the insect resistance genes *cry1Ac* and *cry2Ab* as well as two copies of the herbicide tolerance gene *cp4 esps*). The second GM cotton is to be known as Bollgard III/Roundup Ready Flex® cotton.

In addition to the genes conferring insect resistance and herbicide tolerance, the GM cottons contain antibiotic resistance genes and a reporter gene. The GM cottons proposed for release contain the antibiotic resistance selectable marker genes neomycin phosphotransferase II (*nptII*), 3"(9)-O-aminoglycoside adenyltransferase (*aad*) and hygromycin B phosphotransferase (*aph4*). These genes were originally derived from the common gut bacterium *Escherichia coli*. The *nptII* gene confers resistance to antibiotics such as kanamycin and geneticin, and the *aph4* gene confers resistance to the antibiotic hygromycin. These genes were used only as selective markers during early stages of development of the GM plants in the laboratory. The *aad* gene, which confers resistance to the antibiotics spectinomycin and streptomycin, is linked to a bacterial promoter that does not function in plants so the gene is not expected to be expressed in the GM cotton plants. The GM cottons also contain the β-glucuronidase (*uidA*) gene from *E. coli*, which encodes an enzyme enabling visual identification of plant tissues in which this gene is being expressed.

In addition, the GM cottons contain short regulatory elements used to control expression of the genes. These sequences are derived from plants (including thale cress, pea, petunia and soybean), a soil bacterium (*Agrobacterium tumefaciens*) and plant viruses (Cauliflower mosaic virus and Figwort mosaic virus).

The purpose of the trial is to generate data for future submissions to regulatory agencies, to breed and develop varieties using elite germplasm suitable for use under Australian conditions, and for seed increase. Material from the GM cotton will not be used in human food or animal feed.

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

Risk assessment

The risk assessment took into account information in the application (including proposed containment measures), previous approvals and relevant scientific/technical knowledge. Advice relating to risks to human health and safety and the environment provided in submissions received during consultation on the RARMP has also been 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>.

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

Eight risk scenarios were postulated. This included consideration of whether or not expression of the introduced genes could: result in products that are toxic or allergenic to

people or other organisms; alter characteristics that may impact on the spread and persistence of the GM cottons; or produce unintended changes in the biochemistry of the GMO. 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 eight risk scenarios in relation to both the seriousness and likelihood of harm, in the context of the control measures proposed by the applicant, did not identify risks that required further assessment. The principal reasons for this include:

- limits on the size, locations and duration of the release proposed by Monsanto
- suitability of controls proposed by Monsanto to restrict the spread and persistence of the GM cotton plants and their genetic material
- widespread presence of the same genes or sequences in the environment
- toxicity of the proteins encoded by the introduced insect resistance genes is expected to be limited to certain insects in the order Lepidoptera
- the GMOs are produced by conventional breeding of other GM cottons which have previously been assessed as posing negligible risks
- limited ability and opportunity for the GM cotton plants to transfer the introduced genes to commercial cotton crops or other cotton plants
- none of the GM plant materials or products would be used in human food or animal feed as part of the release.

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**. 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 proposed licence conditions.

As none of the eight 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 are imposed to restrict the spread and persistence of the GMOs and their genetic material in the environment and to limit the proposed release to the size, locations and duration requested by the applicant, 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 cumulative total area of 1150 ha between October 2010 and October 2014 in up to 34 LGAs in Qld, NSW and WA

- locate the field trial sites at least 50 m away from natural waterways
- restrict gene flow via pollen from field trial sites by surrounding the trial site with:
  - a 100 m monitoring zone and a 3 km isolation distance between the site and other cotton crops, or
  - a 20 m pollen trap of non-GM cotton or commercially approved GM cotton
- remove and/or destroy any cotton plants growing in the monitoring zone prior to flowering
- restrict gene flow via pollen from the glasshouses by:
  - implementing an insect control program within the glasshouses, or
  - maintaining a distance of at least 3 km from the nearest cotton crop
- harvest and gin all cotton from the trial separately from other cotton
- remove and/or destroy all cotton plant materials from the trial site and adjacent areas (eg pollen trap, equipment cleaning areas) after harvest, except for materials required for research or further planting
- after harvest, 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 the GM plant materials in accordance with Regulator's transportation guidelines, unless otherwise specified for particular circumstances
- restrict access to the trial sites to authorised personnel only
- not permit the use of GM plant material or products to be used for human food or animal feed.

The sale of lint is permitted.

Other regulatory considerations

Australia's gene technology regulatory system operates as an integrated legislative framework involving the Regulator and other regulatory agencies that avoids duplication and enhances coordinated decision making. Other agencies that also regulate GMOs or GM products include Food Standard Australia New Zealand (FSANZ), Australian Pesticides and Veterinary Medicines Authority (APVMA), Therapeutic Goods Administration (TGA), National Industrial Chemicals Notification and Assessment Scheme (NICNAS) and Australian Quarantine Inspection Service (AQIS)[2].

APVMA has regulatory responsibility for agricultural chemicals, including herbicides and insecticidal products, in Australia. The GM cottons 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 cottons during the trial, which is also subject to regulation by the APVMA.

[2] 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>.

FSANZ is responsible for human food safety assessment and food labelling, including GM food. FSANZ has previously given approval for the use in food of cotton seed oil and linters derived from the GM parent cottons, ie Bollgard II®, Roundup Ready Flex® and VIP3 GM cottons. However, the applicant does not intend to use materials from the GM cottons generated in the proposed release in human food.

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 cottons, or to justify a reduction in containment conditions. This would include:

- additional data on the potential toxicity of Vip3A in combination with the proteins encoded by the other introduced insect resistance genes to non-target invertebrates
- phenotypic characterisation of the GM cottons, in particular of traits which may contribute to weediness, persistence, and ability to disperse in the environment
- data on the effects on non-target insects and weediness potential of Bollgard III or Bollgard III/Roundup Ready Flex® combined with insect resistant WideStrike™ cotton.

Suitability of the applicant

The Regulator is satisfied that Monsanto is suitable to hold a DIR licence as 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 proposed limited and controlled release of the two GM cottons (Bollgard III and Bollgard III/Roundup Ready Flex®) on a maximum total cumulative area of 1150 ha in up to 34 LGAs in Qld, NSW and WA between October 2010 and October 2014, 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 by the applicant, 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.