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**TECHNICAL SUMMARY OF THE RISK ASSESSMENT AND RISK
MANAGEMENT PLAN
FOR
APPLICATION NO. DIR 091
FROM
DOW AGROSCIENCES**

Introduction

The Gene Technology Regulator (the Regulator) has made a decision to issue a licence in respect of licence application (DIR 091) from Dow AgroSciences Australia Ltd (Dow) for a commercial release of genetically modified (GM) cotton.

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 on whether or not to issue a licence to deal with a 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 public¹.

The application

Dow has applied for a licence for dealings involving the intentional release of GM WideStrike™ Insect Protection (WideStrike™) cotton. The applicant proposes that the commercial release would allow WideStrike™ cotton to be grown in all cotton growing areas of Australia south of latitude 22° South and that plant material from the GM cotton be used in the same manner as plant material from non-GM cotton and other commercially approved GM cotton(s), and enter general commerce.

WideStrike™ GM cotton has been genetically modified for resistance to insects. The GM cotton contains the synthetic genes *cryIAc(synpro)* and *cryIF(synpro)*, the sequences of which were originally derived from the common soil bacterium *Bacillus thuringiensis* (Bt). These genes confer resistance to a range of major lepidopteran caterpillar pests of cotton. The two *cry* genes are synthetic genes: the *cryIAc(synpro)* gene is composed of part of the *cryIAc*, *cryICa3* and *cryIAb1* genes from Bt; and *cryIF(synpro)* is composed of parts of the *cryIFa*, *cryICa3* and *cryIAb1* genes. These genes encode the protein toxins CryIAc(synpro) and CryIF(synpro).

In addition to the *cryIAc(synpro)* and *cryIF(synpro)* genes, the GM cotton contains a selectable marker gene (*pat*) from the common soil bacterium *Streptomyces*

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 [the OGTR website](http://www.ogtr.gov.au)), and in the Regulator's *Risk Analysis Framework* (OGTR 2007) at <http://www.ogtr.gov.au/internet/ogtr/publishing.nsf/Content/riskassessments-1>.

viridochromogenes. The *pat* gene confers tolerance to the herbicide glufosinate ammonium. During development of the GM cotton, this marker gene enabled identification and selection of transformed plant tissues. The applicant does not intend glufosinate ammonium to be used on the GM cotton.

Short regulatory sequences that control expression of the introduced genes are also present in the GM cotton. These are derived from a plant, *Zea mays* (corn), and from a common soil bacterium, *Agrobacterium tumefaciens*. Although *A. tumefaciens* is a plant pathogen, the regulatory sequences comprise only a small part of its total genome, and are not in themselves capable of causing disease.

The *cryIAc(synpro)* and *cryIF(synpro)* genes were introduced separately into cotton plant tissue (American cotton cultivar GC510) to generate transformation events 281-24-236 and 3006-210-23, respectively. Each insecticidal gene was introduced in combination with the selectable marker gene, *pat*, providing a means of selection of plant cells expressing the desired modifications. The gene constructs were introduced into the original events by *Agrobacterium*-mediated transformation. This method has been widely used in Australia and overseas for introducing new genes into plants.

The two cotton events expressing the insecticidal genes were combined by conventional breeding to generate the GM cotton proposed for release (WideStrike™ cotton). This GM cotton contains both the *cryIAc(synpro)* and *cryIF(synpro)* genes and two complete copies of the *pat* gene; as well as a small additional fragment of the *pat* gene.

WideStrike™ cotton has been previously approved for field trials in Australia under licences DIR 040/2003 and DIR 044/2003 issued to Dow. There have been no reports of adverse effects on human health and safety or the environment resulting from these releases.

The oil and cotton linters derived from this GM cotton have been approved by Food Standards Australia New Zealand (FSANZ) for use in human food².

Confidential Commercial Information

Some details, including the gene and protein sequences of the introduced synthetic genes and molecular characterisation of WideStrike™ cotton, 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 takes into account information in the application, relevant previous approvals, current scientific knowledge, and advice received from a wide range of experts, agencies and authorities consulted on the preparation of the RARMP and on the consultation RARMP.

A reference document, *The Biology of Gossypium hirsutum and Gossypium barbadense (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>>.

² Insect-protected, glufosinate ammonium-tolerant cotton line MXB-13, Dow AgroSciences, FSANZ Application [A518](#).

The risk assessment begins with a hazard identification process, to consider what harm to the health and safety of people or the environment could arise during this release and how it could happen, in comparison to the non-GM parent organism and in the context of the proposed receiving environment. The receiving environment includes commercially approved GM cotton lines currently grown in Australia. In taking into account a potential risk, the Regulator must consider the probability and potential impact of an adverse outcome over the foreseeable future.

Fourteen events were identified whereby the proposed dealings might give rise to harm to people or the environment. The risk assessment 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 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.

A risk is only identified when a hazard is considered to have some chance of causing harm. Events that do not lead to an adverse outcome, or could not reasonably occur, do not represent an identified risk and do not advance any further in the risk assessment process. The events that are considered to have the potential to lead to adverse outcomes are assessed further to determine the seriousness of harm (consequence) that could result and how likely it is that the harm would occur. The level of risk is then estimated using the Risk Estimate Matrix (see below and Chapter 2).

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

Figure 1 The OGTR Risk Estimate Matrix (OGTR 2007)

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

The characterisation of the fourteen events in relation to both the magnitude and probability of harm, in the context of the control measures proposed by the applicant, gave rise to three identified risks that required further assessment to determine their level of harm to people or the environment.

The consequence and likelihood assessments used to derive risk estimates for the three Identified Risks are summarised in Table 1 (the detailed risk assessments are in Chapters 3 and 4 of the RARMP). More information on the remaining events that were considered not to give rise to an identified risk is provided in Chapter 2. If a risk is estimated to be higher than negligible, risk treatment measures may be required to protect the health and safety of people or the environment.

Table 1 Summary table for the risk assessment

Potential adverse outcome	Event that may give rise to the adverse outcome	Consequence assessment	Likelihood assessment	Risk estimate	Risk treatment required?
Toxicity to non-target invertebrates (see Chapter 3)	Identified Risk 1 Direct or indirect ingestion of the introduced Cry1Ac(synpro) and Cry1F(synpro) proteins by non-target invertebrates.	Minor <ul style="list-style-type: none"> Non-target dietary toxicity studies suggest Cry1Ac(synpro) and Cry1F(synpro) proteins are toxic or growth inhibitory only to a limited range of insects, including the specified target insects. A field study suggests that growing WideStrike™ cotton plants has no significant effect on non-target invertebrate populations when compared to unsprayed non-GM cotton. Non-GM cotton is sprayed with insecticides which impact on non-target insects. 	Unlikely <ul style="list-style-type: none"> Exposure to the GM cotton lines and the Cry proteins would occur mostly to those non-target invertebrates directly/indirectly consuming the GM cotton within the cotton field. Non-target invertebrates appear insensitive to the levels of Cry1Ac(synpro) and Cry1F(synpro) proteins expressed in the WideStrike™ plants. 	Low	No , however PRR conditions are imposed.
Weediness (see Chapter 4)	Identified risk 2 Expression of the introduced genes for insect resistance improving the survival of GM cotton plants and leading to increased spread and persistence north of latitude 22° South.	Minor <ul style="list-style-type: none"> The expressed genes for insect resistance are not expected to impact on health of humans, other vertebrates or microorganisms. The expression of <i>cry</i> genes will not extend the range of GM cotton compared to non-GM cotton. 	Unlikely <ul style="list-style-type: none"> WideStrike™ cotton will not be grown north of latitude 22° South. WideStrike™ cotton volunteers can be effectively controlled by mechanical means, or if still at the seedling stage by the use of herbicides. The chance of GM volunteer plants arising from unintended seed dispersal finding suitable ecological niches and establishing as weeds would be no greater than for non-GM cotton. The expressed genes for insect resistance would only confer a selective advantage in areas where insect predation limits cotton. 	Low	Yes PRR conditions are imposed.
	Identified risk 3 Expression of the introduced <i>cry</i> genes in other insect resistant GM cotton plants as a result of gene transfer leading to increased spread and persistence.	Minor <ul style="list-style-type: none"> The expressed genes for insect resistance are not expected to impact on health of humans, other vertebrates or microorganisms. The expression of <i>cry</i> genes will not extend the range of GM cotton compared to non-GM cotton. Although the effects of combining the <i>cry</i> genes from WideStrike™ and Bollgard® cotton could provide unexpected protection from herbivory, if GM cotton were to spread and persist it is expected to have a limited impact on native vegetation and this would only occur in areas with suitable environmental conditions. 	Highly unlikely <ul style="list-style-type: none"> Cotton is primarily self-pollinating and gene transfer to other insect resistant GM cotton plants would only occur over short distances and at low frequencies. The GM cotton will not be grown north of latitude 22° South. The chance of GM volunteer plants arising from seed dispersal finding suitable conditions to establish as weeds may be no greater than for non-GM cotton plants. Although reduced lepidopteran insect herbivory may offer a small competitive advantage, abiotic and biotic factors are likely to be more important in limiting the spread and persistence of cotton, especially in southern Australia. Insect resistant cotton volunteers can be effectively controlled by mechanical means, or if still at the seedling stage by the use of herbicides. 	Negligible	No

Risk management

The risk management process builds upon the risk assessment to determine whether measures are required in order to protect people and/or the environment.

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. Low risks are defined as minimal but may invoke actions for mitigation beyond normal practices. The level of risk to human health and safety and the environment for twelve of the fourteen events assessed was estimated as negligible. Therefore, no specific risk treatment measures are imposed in relation to these. The risk estimate for the two remaining events was low. The Regulator has proposed several licence conditions that would treat the low risk of spread and persistence of the GM cotton in northern Australia. The Regulator has also imposed licence conditions under post-release review (PRR).

Licence conditions

The licence contains a number of general conditions relating to ongoing licence holder suitability, auditing and monitoring, and reporting requirements which include an obligation to report any unintended effects. There are also general conditions to ensure ongoing oversight of the release.

The Regulator has also imposed several specific licence conditions including requirements to:

- transport whole GM cotton seed in covered vehicles in areas north of latitude 22° South
- in areas north of latitude 22° South, only feed GM cotton seed to livestock inside stockyards, feedlots or dairies
- inform people of the specific conditions referred to in the above dot points
- survey areas where livestock are fed GM cotton seed north of latitude 22° South, in order to determine the incidence of volunteer plants in these areas
- undertake confirmatory research to collect further information on potential effects on key non-target invertebrates.

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 Standards Australia New Zealand (FSANZ), the Australian Pesticides and Veterinary Medicines Authority (APVMA), Therapeutic Goods Administration (TGA), National Industrial Chemicals Notification and Assessment Scheme (NICNAS) and Australian Quarantine and Inspection Service (AQIS)³. Dealings conducted under a licence issued by the Regulator may also be subject to regulation by one or more of these agencies.

³ More information on Australia's integrated regulatory framework for gene technology is contained in the Risk Analysis Framework available from the OGTR (free call 1800 181 030 or at [the OGTR website](#)).

FSANZ is responsible for human food safety assessment, including GM food. FSANZ has approved the use of linters and cotton seed oil from WideStrike™ cotton for use in human food.

The APVMA has regulatory responsibility for agricultural chemicals, including herbicides and insecticidal products, in Australia. The GM cotton proposed for release meets the definition of an agricultural chemical product under the *Agricultural and Veterinary Chemicals Code Act 1994*, due to its production of insecticidal substances. Therefore, these plants are also subject to regulation by the APVMA. The APVMA is currently assessing an application from Dow for WideStrike™ cotton.

Although the GM cotton has also been modified to be tolerant to glufosinate ammonium, the applicant does not intend this herbicide to be used on the cotton and therefore is not seeking approval for this from the APVMA.

The Regulator is liaising closely with the APVMA during the assessment of the application pertaining to this commercial release of GM WideStrike™ cotton.

An AQIS permit has been granted to allow the importation of seed.

Identification of issues to be addressed for future releases

Additional information has been identified that may be required to assess an application for reduced containment measures for the commercial release of WideStrike™ cotton north of latitude 22° South. This would include:

- characteristics, type and abundance of beneficial/non-target invertebrates in crops of the GM cotton grown north of latitude 22° South
- information on the potential for WideStrike™ cotton to have increased survival in the natural environment compared to other commercial GM and non-GM cottons as a result of the introduced genes for insect resistance
- information on any potential synergistic effects of the introduced genetic material when stacked with Bollgard II® cotton [either as individual genes or in combination].

The applicant would be encouraged to work with the Regulator in the design of experiments to address these issues, and would require an additional authorisation from the Regulator to undertake plantings of GM WideStrike™ cotton north of latitude 22° South.

Conclusions of the RARMP

The risk assessment concludes that this commercial release of WideStrike™ cotton to be grown in areas south of latitude 22° South, and the entry of products derived from the GM cotton into general commerce Australia wide, poses **negligible** risks to the health and safety of people, and **negligible to low** risks to the environment as a result of gene technology.

The risk management plan concludes that one of the low risks requires specific risk treatment measures. General licence conditions are imposed to ensure that there is ongoing oversight of the release.