



EXECUTIVE SUMMARY
of
THE RISK ASSESSMENT AND RISK MANAGEMENT PLAN
for
APPLICATION NO. DIR 049/2004
from
CSIRO

INTRODUCTION

The *Gene Technology Act 2000* (the Act) and the *Gene Technology Regulations 2001* (the Regulations) set out requirements which the Gene Technology Regulator (the Regulator) must follow when considering an application for a licence to intentionally release a genetically modified organism (GMO) into the environment.

For a licence to be issued, the Regulator must be satisfied that the release will not pose any risks to human health and safety and the environment that can not be managed. As part of the evaluation process, Section 51 of the Act requires the Regulator to prepare a risk assessment and risk management plan (RARMP) for each licence application, in consultation with a wide range of expert groups and stakeholders.

Under Section 52 of the Act, the Regulator is required to seek comment on the RARMP from those consulted in its preparation and to invite submissions from the public. Matters raised relating to the protection of human health and safety or the environment are taken into account in finalising the RARMP, which then forms the basis of the Regulator's decision on whether, or not, to issue a licence.

The Act is designed to operate in a cooperative legislative framework with other regulatory authorities that have complementary responsibilities and specialist expertise. As well as enhancing coordinated decision making, this arrangement avoids duplication. The OGTR liaises closely with other regulators to ensure the identification, evaluation and management of risks that may be associated with development and use of gene technology.

The Regulator has made a decision to issue a licence in respect of application DIR 049/2004 from CSIRO.

THE APPLICATION

CSIRO has applied for a licence (application number DIR 049/2004) for the intentional release, under limited and controlled conditions, of 60 genetically modified (GM) cotton lines¹. CSIRO proposes to conduct a small field trial over two summer growing seasons (between October 2004 and May 2006) on one site covering a total area of 0.1 hectares in each season in New South Wales. The aim of the proposed release is to assess the efficacy of a new promoter, compared to a commonly used promoter, in controlling the expression of the *uidA* reporter gene under field conditions. This new promoter is a candidate for controlling the expression of potential

¹ The term "line" has been used throughout this RARMP to denote cotton containing a specific genetic modification derived from a single transformation event.

commercially useful introduced traits in cotton. The GM cotton lines proposed for release are for research purposes only and are not suitable for commercial development.

Promoters are short regulatory sequences that control the expression of genes that they are linked to. They control the location, timing and level of expression of the gene and thus where, when and how much of the protein it encodes is produced. The promoters under evaluation in this field trial are linked to the *uidA* reporter gene from *Escherichia coli* (a common gut bacterium) that encodes the enzyme² β -glucuronidase (GUS). GM tissues expressing GUS turn an easily visible blue colour when treated with a simple biochemical stain. Thus the strength and distribution of the blue colour in the plant tissues after staining will provide an indication of the activity of the promoters being evaluated. Therefore, expression of the GUS enzyme is for research purposes only and no trait of commercial interest has been introduced.

In 30 of the GM cotton lines, the expression of the *uidA* reporter gene is being controlled by a new promoter, the Rubisco small subunit (*rbcS*) promoter, which is derived from cotton itself. This promoter normally controls the expression of a Rubisco small subunit gene that encodes a subunit of the ribulose-1,5-bisphosphate carboxylase/oxygenase (Rubisco) enzyme that is involved in the photosynthetic pathway in plant green tissues. It is expected that this promoter from cotton will direct the expression of the *uidA* reporter gene in the photosynthetic green tissues of the GM cotton plants throughout the life of the plants.

In the other 30 GM cotton lines, the expression of the *uidA* reporter gene is being controlled by the 35S promoter, derived from Cauliflower mosaic virus, that is commonly used to control the expression of introduced genes in GM plants. It is expected that this will direct the expression of the *uidA* reporter gene in most tissues of the GM cotton plants, as has been shown in previous releases of other GM cottons containing the 35S promoter.

All of the GM cotton lines also contain an antibiotic resistance gene (*nptII*) from *E. coli* (a common gut bacterium), a selectable marker which confers resistance to the antibiotics kanamycin and neomycin. This marker gene was used in the laboratory during the development of the GMOs for identification and selection of plant tissues in which the *uidA* reporter gene was also present. Due to the genetic modification process used to develop the GM cotton lines containing the introduced *rbcS* promoter, these lines also contain a second antibiotic resistance gene (*hph*) from *E. coli* that confers resistance to the antibiotic hygromycin B. None of the antibiotics are currently in clinical use in Australia.

None of the cotton plants from the release, or their by-products, will be used for animal feed or human food, and seed not required for possible future trials (subject to approval) or research will be destroyed. Following hand-harvesting of selected GM material for research purposes, the applicant proposes that plant materials remaining at the site will be slashed and incorporated into the soil by cultivation. Any regrowth will be destroyed. Seed cotton from the pollen trap will be harvested by a commercial harvester and burnt on the site. The GMOs and material from the GMOs will be transported in accordance with the OGTR guidelines.

There have been no previous releases of GM cotton lines containing the *rbcS* promoter in Australia. However, licences for the intentional release of GM cottons containing various combinations of the 35S promoter and/or the introduced genes (*uidA*, *nptII* and *hph*) have been issued under the current regulatory system (DIRs 005/2001, 006/2001, 008/2001, 009/2001, 012/2001, 017/2002, 022/2002, 023/2002, 025/2002, 034/2003, and 036/2003). There have been no reports of adverse effects on human health or the environment resulting from these releases.

² Enzymes are proteins which catalyse specific biochemical reactions.

THE EVALUATION PROCESS

A RARMP has been prepared in relation to licence application DIR 049/2004 from CSIRO in accordance with the Act, the Regulations and the Risk Analysis Framework. This framework was developed as part of the establishment of the regulatory arrangements in consultation with the public, State, Territory and Australian government agencies, key stakeholders and the Gene Technology Technical Advisory Committee, and is available at www.ogtr.gov.au/pdf/public/raffinal.pdf.

Details of the process that the Regulator must follow, including the prescribed consultation process on the application, and the matters that she must consider in preparing a RARMP, are set out in Appendix 6 of the RARMP. The complete RARMP can be obtained from the OGTR by contacting the Office on 1800 181 030 or from the OGTR's website at www.ogtr.gov.au.

The risk assessment considered information contained in the application (including information required by the Act and the Regulations on the GMO, the parent organism, the proposed dealings and on potential impacts on human health and safety and the environment), current scientific knowledge, and submissions received during consultation with expert groups and authorities.

Through this process, potential hazards to human health and safety or the environment that may be posed by the proposed release of the 60 GM cotton lines were identified. These have been evaluated to determine whether risks might arise, based on the likelihood of each hazard occurring and the likely impact of each hazard, were it to be realised.

The identified potential hazards relate to:

- **toxicity and allergenicity to humans and other organisms:** could these GM cottons be more toxic or allergenic than non-GM cotton to humans or harmful to other organisms as a result of the introduction of the new genetic material?
- **weediness:** could the genetic modifications be harmful to the environment by increasing the potential for these GM cottons to establish as problem weeds? and
- **transfer of introduced genes to other organisms:** could there be adverse consequences from potential transfer of the introduced genes to non-GM cotton crops, feral or native cottons, or to other organisms?

CONCLUSIONS OF THE RISK ASSESSMENT

The Regulator has concluded that the proposed limited and controlled release of the 60 GM cotton lines will not pose significant risks to human health and safety and the environment as a result of the genetic modification. The Regulator has imposed licence conditions to minimise potential exposure of humans and other organisms to the GM cottons and to limit the spread and persistence of the GMOs and the introduced genetic material in the environment. The assessment of each potential hazard identified above is summarised under a separate heading below.

Toxicity or allergenicity to humans and other organisms

The 60 GM cotton lines are unlikely to prove more toxic or allergenic to humans than conventional cotton. Cotton pollen is unlikely to be an airborne allergen and exposure to the introduced proteins through working with the GM cottons is expected to be very low. Humans are already exposed to the proteins produced from the introduced genes, as these proteins are naturally produced by the bacterium *E. coli* and are therefore already present in the environment. A number of other organisms contain similar genes that confer resistance to the same antibiotics or encode GUS proteins and are widespread in the environment. None of the introduced proteins are known to be

toxins or allergens and there have been no reports of toxic or allergenic effects from previous releases of GM cotton lines containing the same introduced genes derived from the same bacterium. The proposed release is limited in scale and licence conditions have been imposed to limit unintended exposure to the GMOs.

The applicant does not intend to use any material produced in the proposed release in human food or animal feed, or to sell lint or linters for processing, thus limiting potential exposure. Food Standards Australia New Zealand (FSANZ) is responsible for human food safety assessment, and FSANZ approval would be needed before products from these GM cottons could be used in human food.

Weediness

The germination and persistence of both GM and non-GM cottons in Australia are limited by the availability of adequate soil moisture, nutrients, herbivory (vertebrate and invertebrate), fire, plant competition and/or frost. It is highly unlikely that the genetic modifications would affect the response of the GM cottons to these variables and, thereby, alter the weediness of the GM cottons. Other GM cottons containing the same introduced proteins, grown commercially or under limited and controlled conditions in Australia, have not become problematic weeds.

However this is the first proposed field trial of these GM cottons and there may be unintended or secondary effects resulting from the genetic modification that could alter their potential for weediness under field conditions.

The applicant has not observed any unintended or secondary effects in the GM cotton lines grown under glasshouse conditions and reports that the growth characteristics of the GM cotton lines are the same as for conventional cotton.

Therefore the risk of the GM cottons establishing as problematic weeds in the proposed release area is considered very low and not likely to be greater than that of non-GM cotton. Licence conditions have been imposed to minimise the spread and persistence of these GM cottons in the environment (refer to key licence conditions below).

Transfer of introduced genes to other organisms

Some gene transfer from the GM cottons to other cultivated cottons would be likely under uncontrolled conditions, although the overall frequency of out-crossing would be low as cotton is primarily self-pollinating. Transfer of introduced genes to other cultivated cotton would pose the same very low risk posed by the GM cottons themselves. Licence conditions have been imposed to minimise the risk of transfer of the introduced genes to plants outside the release site (refer to key licence conditions below).

The risk of transfer of the introduced genes to feral/naturalised cotton is negligible due to geographic isolation. The risk of transferring the introduced genes to native cotton is also negligible because of geographic isolation and genetic incompatibility. Similarly, the likelihood of transfer of the introduced genes to other organisms is negligible because of well established genetic incompatibility. Even if such transfer occurred, it would be unlikely to pose any hazard to human health and safety and the environment.

THE RISK MANAGEMENT PLAN (KEY LICENCE CONDITIONS)

As part of the evaluation process for this licence application, a risk management plan has been developed to address the risks identified (refer to Conclusions of the Risk Assessment, above). This

plan has been given effect by the licence conditions imposed. The key licence conditions are outlined below.

Toxicity or allergenicity to humans and other organisms

Licence conditions have been imposed which require the applicant to:

- prevent entry of the GMOs and products derived from the GMOs into the human food supply;
- prevent GM cottonseed being used as stockfeed;
- limit the scale and duration of the release;
- destroy all GM materials not required for possible future trials or research;
- securely transport and store the GMOs; and
- report adverse effects.

Weediness

Licence conditions have been imposed which require the applicant to:

- limit the scale and duration of the release;
- prevent cottonseed being used as stockfeed;
- surround the GM cottons by a 20 m pollen trap of non-GM cotton;
- prevent the GM cottons being grown within 50 metres of a natural waterway;
- securely transport and store the GM cottons;
- clean the release site after harvest and equipment used at the site; and
- monitor the release site after harvest and destroy volunteers.

Transfer of introduced genes to other organisms

Licence conditions have been imposed which require the applicant to:

- limit the scale and duration of the release;
- surround the GM cottons by a 20 m pollen trap of non-GM cotton;
- securely transport and store the GM cottons;
- clean the release site after harvest and equipment used at the site; and
- monitor the release site after harvest and destroy volunteers.

General conditions

Any licence issued by the Regulator also contains a number of general conditions, which are also relevant to risk management. These include, for example:

- identification of the persons or classes of persons covered by the licence;
- a requirement that the applicant allows access to the release site by the Regulator, or persons authorised by the Regulator, for the purpose of monitoring or auditing; and
- a requirement to inform the Regulator if the applicant becomes aware of any additional information about risks to human health or safety or to the environment.

Chapter 2 of the risk assessment and risk management plan provides a tabulated summary of assessment conclusions and corresponding management conditions. Full details of the licence conditions are provided in Appendix 5.

Identification of issues to be addressed for future releases

The proposed limited and controlled release is a small scale, single-site ‘proof of concept’ trial over two cotton growing seasons to test the efficacy of the *rbcS* promoter from cotton under field conditions. If the applicant makes an application for any future use of the *rbcS* promoter to control the expression of potential commercially useful introduced traits in any GMOs, data would be required to be collected on:

- the level of expression of the introduced genes and encoded proteins, and the plant tissues in which they are being expressed, by the *rbcS* promoter under Australian field conditions;
- stability of the introduced genes and modified traits under Australian field conditions;
- genetic segregation and molecular characterisation of the introduced genetic materials;
- agronomic characteristics relating to fitness; and
- unintended effects of the genetic modification.

Monitoring and enforcement of compliance by the OGTR

As well as the legislative capacity to enforce compliance with licence conditions, the Regulator has additional options for risk management. The Regulator can direct a licence holder to take any steps the Regulator deems necessary to protect the health and safety of people or the environment. The OGTR also independently monitors releases that the Regulator has authorised. At least 20% of all field trial sites will be inspected each year, in accordance with a monitoring and compliance strategy based on risk profiling (which takes into account biological, seasonal, geographical and ecological risk factors) to determine whether licence holders are complying with the licence conditions, or whether there are any unintended effects.