



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

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**EXECUTIVE SUMMARY of the RISK ASSESSMENT AND RISK
MANAGEMENT PLAN FOR APPLICATION DIR 054/2004**

INTRODUCTION

The Gene Technology Regulator (the Regulator) has made a decision to issue a licence for dealings involving intentional release of GMOs into the environment, in respect of application DIR 054/2004 from the Commonwealth Scientific and Industrial Research Organisation (CSIRO).

The *Gene Technology Act 2000* (the Act) and the *Gene Technology Regulations 2001* (the Regulations) set out requirements which 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 or 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, and if so, what conditions to impose.

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 the development and use of gene technology.

THE APPLICATION

CSIRO Plant Industry (CSIRO) proposes to conduct a small scale field trial of genetically modified (GM) wheat (*Triticum aestivum* L.) with altered starch characteristics under strictly controlled conditions. The release is proposed to take place at one site covering a maximum total area of 0.25 ha at a research facility in the Australian Capital Territory (ACT) during the winter growing seasons of 2005 and 2006.

CSIRO's aim in conducting the proposed release is to assess the field performance of GM wheat with altered starch characteristics and to generate seed stocks of the modified

wheat lines¹ for further research. The wheat cultivar to be used in this trial, NB1, is a breeding line obtained from the United Kingdom which is not grown commercially in Australia or in the UK.

CSIRO proposes to release six lines of GM wheat that have been modified using a technique called RNA interference (RNAi) to achieve gene silencing (switching off, also known as ‘knock-out’) of particular genes. Gene silencing arises in nature by various naturally occurring mechanisms, as well as through the application of chemical or radiation mutagenesis in conventional plant breeding programs. Here the use of RNAi has enabled the selective targeting of genes that are responsible for producing enzymes involved in the synthesis of starch in the seeds of the GM wheat lines. The sequences in the silencing constructs responsible for tissue specific expression and for knocking out the starch enzyme gene were both derived from wheat.

Starch is an important energy storage compound in plants which can vary in its structural composition and digestibility. In the GM wheats proposed for release, RNAi has been used to silence either starch enzyme (SE) I or SE II in the seeds. The applicant has advised that the modifications have resulted in reduced production of amylopectin starch in the grain of the GM wheat lines, and an increase in the proportion of amylose starch, also known as ‘resistant starch’ as it is digested differently to other starch. Foods made with resistant starch are thought to have properties that are beneficial to human health.

All the GM wheat lines proposed for release also contain the commonly used selectable marker gene neomycin phosphotransferase (*nptII*) from the bacterium *Escherichia coli* that confers resistance to the antibiotic kanamycin. During the development of the GM wheat lines, the marker gene was used in the laboratory for identification and selection of plant tissues in which transformation had occurred and the starch enzyme genes were silenced.

CSIRO proposed a number of containment and inspection measures, in part to limit the possible spread and persistence of the GM wheat lines, and also to ensure the integrity of the trial, including:

- surrounding the 0.25 ha release with a single furrow row of non-GM wheat as a buffer row;
- conducting the release in a pre-existing quarantine facility which encloses the 0.25 ha release site with a rodent, macropod and bird proof fence (~2.0 m high) and netting;
- using bird proof netting across the trial site to discourage birds;
- deploying mouse traps every 10 m inside the fence;
- inspecting the site weekly for volunteers for 12 months after the conclusion of the trial;
- hand-harvesting the GM wheat and non-GM wheat in the buffer row at the end of each winter season; and
- transporting the seed to a facility certified to physical containment level 2 (PC2) in accordance with the OGTR transportation guidelines for threshing and further processing.

¹ The term ‘line’ denotes wheat containing a specific genetic modification derived from a single transformation event.

The applicant proposes to harvest seed some of which will be used in feeding trials on rodents in the laboratory. None of the material harvested from the trial will be used for human food or animal feed and any material not used for further research will be destroyed. This GM wheat would require approval by Food Standards Australia New Zealand (FSANZ) before use for human consumption.

The trial site will be at least 50 m away from natural waterways and an isolation zone of 500 m will be maintained between the trial site and other wheat plants. The trial site is at least 11 km away from other wheat growing areas and the nearest commercial wheat farming is approximately 26 km away.

There have been no previous releases of these GM wheat lines in Australia. The lines were originally developed in certified contained laboratory and glasshouse facilities within the provisions of the Act, under Notifiable Low Risk Dealing (NLRD) 770/2003. However, under the former voluntary system that was overseen by the Genetic Manipulation Advisory Committee (GMAC) five field releases of similar and other types of GM wheat were approved (see Chapter 1 of the risk assessment and risk management plan). There have been no reports of adverse effects on human health or the environment resulting from these releases.

In accordance with the provisions of section 185 of the *Gene Technology Act 2000* (the Act), CSIRO sought and received approval for details of the gene constructs, gene sequence information and the precise identity of the silenced genes to be declared as Confidential Commercial Information (CCI). While the Regulator was satisfied that the public interest in the release as proposed did not outweigh the prejudice that disclosure would cause the applicant, the CCI was made available to the various prescribed expert groups that were consulted on the preparation of the RARMP for this application.

THE EVALUATION PROCESS

A risk assessment and risk management plan (RARMP) has been prepared in relation to licence application DIR 054/2004 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.

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 and a review document 'The Biology and Ecology of Bread Wheat (*Triticum aestivum*) in Australia' (produced to further inform the risk analysis) and a set of 'Questions and Answers' on the evaluation of the application can be obtained from the OGTR by calling 1800 181 030 or from the OGTR's website at www.ogtr.gov.au.

The risk assessment considered information contained in the application (comprising: information required by the Act and the Regulations on the GMO; on the parent organism; the proposed dealings, including proposed containment conditions; and potential impacts on human health and safety and the environment), current scientific knowledge, and submissions received during consultation with expert groups and authorities and the public (issues raised in submissions are summarised in Chapter 2 and Appendix 7 of the RARMP).

Through this process, potential hazards were identified to human health and safety or the environment that may be posed by the GM wheat lines proposed for release. These

have been carefully 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 wheat plants be more toxic or allergenic to humans than non-GM wheat plants, or harmful to other organisms as a result of the novel gene products or because of unintended effects resulting from the introduced genetic elements or gene silencing?
- **weediness:** could the genetic modifications be harmful to the environment by increasing the potential for these wheat plants to establish as problematic weeds? and
- **transfer of introduced genes to other organisms:** could there be adverse consequences from potential transfer of the introduced gene/genetic materials to non-GM wheat crops, naturalised wheat or to other organisms?

CONCLUSIONS OF THE RISK ASSESSMENT

The Regulator has concluded that the proposed limited and controlled release of these GM wheat lines on 0.25 hectares over two seasons will not pose significant risks to human health and safety and the environment. The risk assessment of each potential hazard identified above is summarised under a separate heading below.

Toxicity or allergenicity to humans and other organisms

As this is an early stage ‘proof of concept’ trial, the GM wheat lines proposed for release have not been tested for acute toxicity. None of the gene sequences introduced into the GM wheat are derived from or similar to known toxin or allergen genes. The genetic modification results in highly specific knock-out of the starch enzymes (SEs). The resulting reduced expression of starch enzymes leads to high levels of amylose starch in the grain. However, this is not expected to have any impact on toxicity or allergenicity compared to non-GM wheat.

Allergies to non-GM wheat grains and pollen are fairly common in the general population but wheat grains are not considered toxic. The only functional protein added to the GM wheat is the NPTII enzyme. The level of occupational exposure to this introduced protein through working with the GM wheat is likely to be very low. There have been no reports of toxic or allergenic effects from previous releases of other GMOs containing the *nptII* gene. Exposure to the GM wheat would be limited because the proposed release is limited in scale and licence conditions have been imposed to limit unintended exposure to the GMOs (refer to key licence conditions below).

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

Weediness

The domestication of *Triticum aestivum* L. into what we now know as bread wheat resulted in the loss of most of the characteristics that contribute to successful weediness, such as competitive ability and seed heads that shatter at maturity. It is unlikely that the genetic modifications in the GM wheat lines would increase any of these traits compared to the parent plant.

The risk of the GM wheat lines establishing as weeds in the release area proposed by the applicant is also considered to be very low due to the very small scale of the release and the proposed containment measures. The Regulator has imposed measures to minimise the spread and persistence of the GMOs in the environment, including the use of an isolation zone, distance from natural waterways and other wheat crops, and post-harvest monitoring of the site (refer to key licence conditions below).

Transfer of introduced genes to other organisms

Wheat is predominantly self-pollinating with rates of out-crossing to other cultivated wheat plants of less than 5% between adjacent rows. Wheat pollen is relatively heavy compared to grass pollen and does not remain viable for long periods (under field conditions, up to 30 minutes) and its dispersal is wind, rather than insect mediated. Because wheat is primarily self-pollinating and pollen movement is mediated by wind, an isolation zone is a more suitable measure than a pollen trap to prevent pollen escape from the release site.

Gene transfer from the GM wheat lines to other wheat plants (including wheat crops and naturalised wheat) or to weedy wheat relatives is unlikely to occur during the proposed trial due to isolation from other wheat and sexually compatible plants. The GM wheat lines proposed for release are derived from parental cultivar NB1 and the applicant has observed that this cultivar is strongly self-pollinating. NB1 is a cultivar from the UK and the floral characteristics of the GM wheat lines in this parental background under Australian field conditions are unknown at this stage. However, it is expected that the out-crossing frequency under Australian conditions will be very low.

Wheat can cross-pollinate with a number of species both within the genus *Triticum* and related genera such as *Aegilops*, *Elytrigia*, *Hordeum*, *triticale* and *Secale*. Out-crossing to these species will not occur as these plants will not be present near the trial. Licence conditions have been imposed to minimise the risk of transfer of the introduced genes to plants outside the release site including the use of an isolation zone (refer to key licence conditions below).

The risk of transfer of the introduced genes to other organisms is negligible because of genetic incompatibility. Even if such transfer occurred, it would be unlikely to pose any risk 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 Conclusion of the Risk Assessment, above). The applicant proposed a number of containment measures, in part to contain the GMOs during the trial, and in part to maintain its integrity. The Regulator considered these proposals in selecting the licence conditions that have been imposed to implement the risk management measures that will minimise the potential exposure of humans and other organisms, and limit the likelihood of spread and persistence of the GMOs or the introduced genetic materials in the environment. The key licence conditions are outlined below.

Toxicity or allergenicity to humans and other organisms

Licence conditions have been imposed requiring the applicant to:

- prevent the GMOs and products derived from the GMOs entering the human food supply;
- prevent GM wheat products being used as animal feed;

- limit the scale and duration of the release;
- limit exposure to humans and other animals;
- destroy all GM wheat material not required for possible future trials or research;
- securely transport and store the GM wheat materials and seeds; and
- report any adverse effects to the Regulator.

Weediness

Licence conditions have been imposed requiring the applicant to:

- limit the scale and duration of the release;
- locate the release site at least 50 m from natural waterways;
- exclude large animals from the site;
- take measures to minimise rodent numbers, including mowing a 10 m monitoring zone around the trial site;
- securely transport and store the GM wheat material and seeds;
- clean the release site after harvest and equipment used at the site; and
- monitor the release site and a 10 m monitoring zone after harvest and destroy volunteers for at least 24 months.

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 wheat lines with a 500 m isolation zone in which no other wheat or sexually compatible plants are planted;
- monitor the release site and a 10 m monitoring zone after harvest and destroy volunteers for at least 24 months; and
- clean the release site after harvest and equipment used at the site.

General conditions

Any licence issued by the Regulator also contains a number of general conditions that 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 and safety or to the environment.

Chapter 2 of the RARMP provides a tabulated summary of assessment conclusions and corresponding management conditions. Full details of the imposed 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, 'proof of concept' trial over two seasons. Hence, no research conditions have been imposed in the licence. However, the following information would be required from future applications, particularly to assess requests for larger scale releases of these GM wheat lines.

- the precise copy number, the stability of the insertions in the GM wheat, the heritability of the trait and the specificity of the expression of the RNAi construct under the control of the Bx17 HMWG promoter;
- agronomic characteristics of the GM wheats that relate to weediness; and
- any unintended or secondary effects resulting from the genetic modification.

It should be noted that provision of the above data during the proposed release are not required to ensure the management of risks to human health and safety and the environment from the proposed release. The risk management measures summarised in Chapter 2, Table 4 and given effect by the licence conditions, will achieve this purpose

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 unforeseen problems.

FURTHER INFORMATION

Detailed information on the evaluation of the application, including the licence conditions, is available in the RARMP document for this application and a set of Questions and Answers on licence decision of this application. These can be obtained from the website of the Office of the Gene Technology Regulator (www.ogtr.gov.au), or by calling 1800 181 030 (please quote application number DIR 054/2004).