



24 April 2008

**TECHNICAL SUMMARY OF THE RISK ASSESSMENT AND RISK
MANAGEMENT PLAN
FOR
APPLICATION NO. DIR 076/2007
FROM
QUEENSLAND UNIVERSITY OF TECHNOLOGY**

Introduction

The Gene Technology Regulator (the Regulator) has made a decision to issue a licence (DIR 076/2007) to Queensland University of Technology (QUT) for dealings involving the intentional release of genetically modified (GM) banana lines into the Australian 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 Regulator before making a decision whether 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 the *Risk Analysis Framework* and finalised following consultation with a wide range of experts, agencies and authorities and the public¹.

The application

QUT applied for a licence for dealings involving the intentional release of up to 1,290 lines² of banana (*Musa acuminata* cv. Williams) on a limited scale and under controlled conditions. The GM banana lines would be genetically modified for increased levels of pro-vitamin A, vitamin E or iron, or to assess promoter specificity. The trial would take place at one site in the local government area of Cassowary Coast, Queensland on a maximum total area of 1.4 hectares between May 2008 and May 2012.

Up to 390 of the GM banana lines would contain one or two of three different genes that encode proteins involved in pro-vitamin A carotenoid³ synthesis. The *APsy2a* gene derived from the banana cultivar 'Asupina' encodes the protein phytoene synthase which has a primary role in the conversion of geranylgeranyl diphosphate to phytoene. The *PsyB73* gene derived from maize (*Zea mays*) also codes for phytoene synthase. The *CrtI* gene from the bacterium *Erwinia uredovora* encodes the protein carotene desaturase that converts phytoene

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 (Free call 1800 181 030 or at <<http://www.ogtr.gov.au/ir/process.htm>>), and in the Regulator's *Risk Analysis Framework* (OGTR 2007) at <<http://www.ogtr.gov.au/pubform/riskassessments.htm>>.

² The term 'line' is used to denote plants derived from a single plant containing a specific genetic modification made by one transformation event.

³ The three major pro-vitamin A carotenoids are α -carotene, β -carotene and β -cryptoxanthin but in this trial it is expected that β -carotene would be the major end product.

into lycopene and substitutes for two plant desaturases (phytoene desaturase and ξ -carotene desaturase) as well as for carotene isomerase. The expression of these genes, either singly or in a combination, is expected to increase the levels of pro-vitamin A carotenoids in banana tissues.

Up to 360 of the GM banana lines would contain one or two of five different genes that are involved in vitamin E⁴ synthesis. The *vte1*, *vte3* and *vte4* genes are derived from the plant *Arabidopsis thaliana* and each produces a protein (tocopherol cyclase; 2 methyl-6 phytyl-1, 4-benzoquinone methyltransferase; γ – tocopherol methyltransferase respectively) that has a role in tocopherol biosynthesis. The *vte2.1* gene is from maize (*Zea mays*) and its protein product, homogentisic acid phytyltransferase is also important in tocopherol biosynthesis. The gene *HGGT* from rice (*Oryza sativa*) encodes a protein (homogentisic acid geranylgeranyl transferase) that is essential for tocotrienol biosynthesis. Expression of these genes either singly or in a combination is expected to lead to an increased accumulation of vitamin E in banana tissues.

Up to 120 of the GM banana lines would contain one or more of three different genes that are involved in iron accumulation. The *Ferritin* gene from wild soybean (*Glycine soja*) encodes an iron-binding protein (chloroplast ferritin) that has a role in the storage of iron. The *IRT1* gene from the plant *Arabidopsis thaliana* encodes a protein (iron-regulated transporter 1) that affects the uptake of iron from the soil by roots. The *FRO2* gene, also from *Arabidopsis thaliana*, encodes a protein (ferric-chelate reductase) that also has a role in iron uptake by plant roots. The expression of these genes, either singly or in a combination, is expected to lead to enhanced iron levels in banana tissues.

Up to 420 of the GM banana lines would contain the marker/reporter gene *uidA*, derived from the common gut bacterium *Escherichia coli*. It encodes an enzyme β -glucuronidase (GUS) that enables visual identification of plant tissues in which this gene is expressed. GM banana plants containing the *uidA* gene will be used to investigate the level of activity of introduced promoters (regulatory sequences that control the expression of genes) to optimise gene expression in banana fruit.

In addition, all of the GM banana lines would contain the antibiotic resistance selectable marker gene, neomycin phosphotransferase type II (*nptII*). This gene, encoding for the enzyme neomycin phosphotransferase, was derived from *Escherichia coli*, and confers kanamycin or neomycin resistance on the GM plant. The *nptII* gene was used as a selective marker to identify transformed plants during initial development of GM plants in the laboratory.

The purpose of the trial is to conduct proof of concept research involving experiments with the GM banana lines to assess growth, fruit and yield characteristics and analyse the nutrient content of fruit and vegetative parts. A number of promoters are also being tested in order to identify those that achieve best expression of the introduced genes in the fruit. GM bananas produced during the trial will not be used for human food or animal feed.

QUT proposed a number of controls to restrict the dissemination or persistence of the GM banana lines and their genetic materials into the environment. These controls have been considered during the evaluation of the application.

⁴ The term Vitamin E refers to a family of molecules comprising 4 tocopherols and 4 tocotrienols

Risk assessment

The risk assessment took into account information contained in the application, relevant previous approvals, current scientific knowledge, and advice relating to risks to human health and safety and the environment provided in submissions received during consultation on the RARMP. The feedback received from prescribed experts, agencies and authorities (summarised in Appendix B of the RARMP) and the public (summarised in Appendix C of the RARMP) led to the identification of an additional hazard that was examined in the finalised RARMP (Event 8, Section 2.6, Chapter 2) but was not considered to give rise to an identified risk to human health and safety and/or the environment that required further analysis.

A reference document on the parent organism, *The Biology of Musa L.(banana)*, was produced to inform the risk assessment process for licence applications involving GM banana plants. The document is available from the OGTR or from the website <http://www.ogtr.gov.au>.

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 of GMOs due to gene technology, and how it could happen, in comparison to the non-GM parent organism and in the context of the proposed receiving environment.

Nine events, including one identified in the consultation process, were considered whereby the proposed dealings might give rise to harm to people or the environment. 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 plants; or produce unintended changes in their biochemistry or physiology. The opportunity for gene flow to other organisms and its effects if this occurred was 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 characterisation of the nine events in relation to both the magnitude and probability of harm, in the context of the control measures proposed by the applicant, did not give rise to any identified risks that required further assessment. The principle reasons for this include:

- ♦ limits on the size and duration of the release proposed by QUT;
- ♦ suitability of controls proposed by QUT to restrict the dissemination or persistence of the GM banana plants and their genetic material;
- ♦ limited capacity of the GM banana lines to spread and persist outside the areas proposed for release;
- ♦ limited ability and opportunity for the GM banana lines to transfer the introduced genes to commercial banana crops or other sexually related species;
- ♦ none of the GM plant materials or products will be used in human food or animal feed;
- ♦ widespread presence of the same or similar proteins encoded by, and end products produced as a result of the activity of, the introduced genes in the environment and lack of known toxicity or evidence of harm from them.

Therefore, any risks of harm to the health and safety of people, or the environment, from the proposed release of the GM banana lines into the environment are 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.

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. As none of the nine events characterised in the risk assessment are considered to give rise to an identified risk that requires further assessment, the level of risk is considered 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, a range of measures have been imposed to limit the release to the size, location and duration requested by the applicant, as these were an important part of establishing the context for assessing the risks.

Licence conditions to manage this limited and controlled release

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

- ◆ conduct the release on a total area of up to 1.4 ha at one site in the local government area of Cassowary Coast (Queensland) between May 2008 and May 2012.
- ◆ remove and destroy all male/hermaphrodite flowers on the inflorescences unless they are required for experimental analysis;
- ◆ cover any male/hermaphrodite flowers left on the inflorescences;
- ◆ cover fruit bunches;
- ◆ remove and destroy all fruit not required for experimental analysis;
- ◆ destroy any plant waste containing meristematic tissue;
- ◆ clean all equipment used in cultivation practices;
- ◆ not permit any materials from the release to be used in human food or animal feed; and
- ◆ at the end of the trial, destroy all plant materials not required for further analysis.

The Regulator has issued guidelines and policies for the transport, supply and storage of GMOs (*Guidelines for the transport of GMOs, July 2007; Policy on transport and supply of GMOs, July 2005*). Licence conditions based on these guidelines and policies have also been proposed to control possession, use or disposal of the GMOs for the purposes of, or in the course of, the authorised dealings.

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. Dealings

conducted under a licence issued by the Regulator may also be subject to regulation by other agencies that also regulate GMOs or GM products including 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)⁵.

FSANZ is responsible for human food safety assessment, including GM food. As the trial involves proof of concept research, the applicant does not intend any material from the GM banana lines proposed for release to be used in human food. Accordingly, the applicant has not applied to FSANZ to evaluate any of the GM banana lines. FSANZ approval would need to be obtained before they could be used in human food in Australia.

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 any of these GM banana lines that may be selected for further development, or to justify a reduction in containment conditions. This would include:

- ♦ characterisation of the introduced genetic material in the plants, including copy number and genotypic stability;
- ♦ additional data on the potential toxicity of plant materials from the GM banana lines;
- ♦ additional data on the allergenicity of proteins encoded by the introduced genes for enhanced nutrition; and
- ♦ characteristics indicative of weediness including measurement of altered reproductive capacity; tolerance to environmental stresses; and disease susceptibility.

Suitability of the applicant

The Regulator determined, at the commencement of the assessment process for this application, that QUT is suitable to hold a DIR licence under the requirements of section 58 of the Act. The Regulator is satisfied that QUT remains suitable as no relevant convictions have been recorded, no licences or permits have been cancelled or suspended under OGTR legislation relating to the health and safety of people or the environment, and the organisation has confirmed its ability to comply with the licence conditions.

Conclusions of the RARMP

The risk assessment concludes that this limited and controlled release of up to 1,290 GM banana lines on a maximum total area of 1.4 ha over four years in the Queensland local government area of Cassowary Coast poses **negligible** risks to the health and safety of people or the environment as a result of gene technology.

The risk management plan concludes that these negligible risks do not require specific risk treatment measures. However, licence conditions have been imposed to limit the release to the

⁵ 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/pubform/riskassessments.htm>>.

size, location and duration requested by the applicant as these were important considerations in establishing the context for assessing the risks.