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## **GENE TECHNOLOGY TECHNICAL ADVISORY COMMITTEE**

# **COMMUNIQUE No. 10**

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*This is the tenth communique of the Gene Technology Technical Advisory Committee (GTTAC). It covers matters considered at the sixteenth and seventeenth meeting of GTTAC, held on 18 September 2003 and 28 October 2003 respectively, as well as matters considered by GTTAC out-of-session in the period from 25 July to 28 October 2003.*

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GTTAC is a statutory advisory committee to the Gene Technology Regulator (the Regulator) and the Gene Technology Ministerial Council. All Committee members and expert advisers hold office on a part-time basis.

The Regulator receives input from GTTAC on applications for licences to conduct dealings with genetically modified organisms (GMOs), as well as comments on the Risk Assessment and Risk Management Plan (RARMP) that is prepared for each of these applications.

The purpose of this Communique is to provide a brief overview of the applications and RARMPs considered by GTTAC and the advice the Committee has provided to the Regulator with regard to those applications and RARMPs.

The Communique also provides an overview of any other major issues discussed by GTTAC.

### **Dealings Not Involving the Intentional Release of Genetically Modified Organisms**

Dealings Not Involving the Intentional Release of GMOs (DNIRs) are dealings that are usually undertaken within a certified facility (so that the organism is physically contained) and where the personnel involved in the dealing have been assessed as having adequate training and experience for the task. These are typically laboratory-based projects.

**Applications and RARMPs for the following DNIRs were assessed:**

Application Number and Title	Project Description	GTTAC Comments
<p><b>DNIR 233/2003</b> Mutation of an infectious clone of BIV R29.</p> <p><b>DNIR 234/2003</b> Transcomplementation of <i>vif</i> deleted BIV with bovine lentivirus.</p> <p><b>DNIR 235/2003</b> Use of an infectious clone of BIV R29.</p>	<p>The aim of these dealings is to investigate the role of accessory genes in <i>Bovine immunodeficiency virus</i> (BIV) by creating point mutations in these genes which result in either a deletion or truncation of the proteins they encode.</p> <p>In addition the applicant aims to determine whether there is functional homology between certain proteins from BIV and the related Jembrana disease virus, and to use an infectious clone of BIV as a standard in molecular biological tests.</p>	<p>These applications were considered together.</p> <p>GTTAC agreed that the risk assessment identified all the risks associated with the proposed dealings and that the measures proposed in the risk management plan are adequate to deal with the identified risks.</p> <p>However, the Committee suggested that the risk of the formation of novel recombinant viruses be considered in more detail.</p>
<p><b>DNIR 238/2003</b> Mutational analysis of the Australian strain of <i>Porcine circovirus</i> type 1.</p> <p><b>DNIR 239/2003</b> Production of an infectious clone from the Australian strain of <i>Porcine circovirus</i> type 1.</p> <p><b>DNIR 240/2003</b> Mutational analysis of the Australian strain of <i>Porcine circovirus</i> type 2.</p> <p><b>DNIR 241/2003</b> Production of an infectious clone from the Australian strain of <i>Porcine circovirus</i> type 2.</p>	<p>The aim of these dealings is to investigate the importance of particular coding regions, conserved motifs and domains in the genomes of both <i>Porcine circovirus</i> type 1 (PCV-1) and PCV-2 by creating mutations in these genes.</p> <p>In addition the applicant aims to clone full-length genomes of PCV-1 and PCV-2 to be used in further studies and as standards in diagnostic techniques.</p>	<p>These applications were considered together.</p> <p>GTTAC agreed that the risk assessment identified the risks associated with the proposed dealings and that the measures proposed in the risk management plan are adequate to deal with the identified risks.</p> <p>However the Committee suggested that further information regarding the genes being used should be sought from the applicant and added to the RARMP. They also suggested that more detail be included in the RARMP about the possible risk to operators from the GM viruses.</p>

<p><b>DNIR 250/2003</b> Cellular interactions between HBV and HCV.</p>	<p>The aim of this dealing is to investigate the effect that <i>Hepatitis B virus</i> (HBV) replication has on <i>Hepatitis C virus</i> (HCV) replication, cell growth, cell viability and cellular gene expression by transfecting hepatocyte cells containing a HCV replicon (a truncated, non-infectious HCV genome) with plasmids containing the HBV genome.</p>	<p>GTTAC agreed that the risk assessment identified all the risks associated with the proposed dealings and that the measures proposed in the risk management plan are adequate to deal with the identified risks.</p>
<p><b>DNIR 254/2003</b> Evaluation of the effects of apoptosis and necrosis on tumour antigen presentation and anti-tumour response.</p>	<p>The aim of this dealing is to determine whether induction of different types of cell death mechanisms in tumours can increase the immune response to these tumours.</p>	<p>As for DNIR 250/2003.</p>
<p><b>DNIR 256/2003</b> Genetics of <i>Clostridium perfringens</i> pathogenesis.</p>	<p>The aim of this dealing is to investigate the role of specific, defined toxin proteins in the pathogenesis of <i>C. perfringens</i>.</p>	<p>As for DNIR 250/2003.  In addition GTTAC recommended that masks and goggles be used by operators when handling infected animals and that a Class II biosafety cabinet be used for performing necroscopies.</p>
<p><b>DNIR 259/2003</b> Study of plant-virus interactions using fluorescence-tagged viruses.</p>	<p>The aim of this dealing is to study the function of viral genes in virus movement and host interaction in resistant and susceptible plants.</p>	<p>As for DNIR 250/2003.</p>
<p><b>DNIR 260/2003</b> Use of adenovirus and adeno-associated virus gene delivery systems for the expression of HCV proteins.</p>	<p>Recombinant adenovirus and adenovirus-associated viruses carrying <i>Hepatitis C virus</i> (HCV) genes will be used to produce HCV proteins in cell cultures and mice to study the structure and function of the proteins as well produce HCV protein for immune studies.</p>	<p>As for DNIR 250/2003.</p>
<p><b>DNIR 261/2003</b> Novel gene delivery vector.</p>	<p>The aim of this dealing is to develop a novel drug delivery vector that combines drug biosynthesis and targeted delivery.</p>	<p>As for DNIR 250/2003.</p>

<p><b>DNIR 269/2003</b> Characterisation of genes involved in hematopoietic stem cell growth and regulation.</p>	<p>The aim of this project is to examine the role of known and novel genes in human blood cell growth with the purpose of learning more about normal blood cell development and what goes wrong in this process to cause leukaemia.</p>	<p>As for DNIR 250/2003.</p>
<p><b>DNIR 270/2003</b> Retroviral and adenoviral mediated gene transfer into murine mammary cells and breast cancer cell lines.</p>	<p>The aim of this dealing is to elucidate the role of mammalian genes in mammary cell growth, proliferation, apoptosis, differentiation and oncogenesis.</p>	<p>As for DNIR 250/2003.</p>

## Dealings Involving the Intentional Release of Genetically Modified Organisms

Dealings Involving the Intentional Release of GMOs (DIRs) are dealings that are undertaken outside of a contained facility. DIRs involve the limited and controlled release (field trial) of a GMO or a commercial (general) release of a GMO.

RARMPs for licence applications for DIRs are released for public comment as part of the consultation process for these applications. Information on how to obtain copies of applications and RARMPs for DIRs is provided at the end of this document.

### Advice on Clover

GTTAC considered the following application concerning the release of transgenic clover in Australia and provided advice on issues to be considered in the preparation of the associated RARMP.

- **Field trial – Field evaluation of white clover transformed to resist infection by *Alfalfa Mosaic virus* and *Clover yellow vein virus* (DIR 042/2003)**

The OGTR has prepared a RARMP for an application from the Commonwealth Scientific and Industrial Research Organisation (CSIRO) for the limited and controlled release of GM white clover that has been modified to resist infection by *Alfalfa mosaic virus* (AMV) and *Clover yellow vein virus* (CYVV). CSIRO proposes to conduct field trials on one site in New South Wales (NSW), over a total area of 2 hectares.

The aim of the proposed release is the field evaluation of GM white clover to determine the maintenance of resistance to AMV and CYVV that was observed in the plants grown in the glasshouse. The GM white clover plants contain coat protein genes from AMV and/or CYVV, which reduces the susceptibility of the clover plants to AMV and CYVV, respectively. CSIRO proposes evaluation of four types of GM white clover.

GTTAC discussed this application and advised the Regulator that the following issues should be considered in the preparation of the RARMP:

- The experiments involving GM white clover expressing CYVV coat protein genes should not be allowed to proceed;
- The risks posed by the AMV resistant GM white clover are similar to those posed by previous white clover applications PR-64, PR-64X, PR-64X2 and PR-67;
- The applicant should be requested to provide data to clarify whether white clover is present in the area surrounding the trial site;
- The applicant should also be requested to provide information on the risks related to the distance of the trial site from the Murray River; and
- The applicant should be asked to remove the seeds produced at the trial site.

## Advice on Cotton

GTTAC considered the RARMPs prepared in response to the following applications concerning the release of transgenic cotton in Australia.

- **The evaluation of transgenic cotton plants expressing the *vip* gene (DIR 034/2003)**

The OGTR has prepared a RARMP for an application from Syngenta Seeds Pty Ltd (Syngenta) for the limited and controlled release of GM insecticidal cotton into the environment. Syngenta proposes to conduct trials on 30 sites covering a total area of 10 hectares, over two years, in the cotton growing regions of NSW and Queensland (Qld).

The main aim of the proposed release is to assess the agronomic performance and efficacy of the insecticidal activity of the new lines in all the major cotton growing areas of Australia.

The GM cotton proposed for release is a backcross of an insecticidal cotton, described by Syngenta as COT102, into three elite Australian cotton cultivars. Limited and controlled field trials of COT102 have been previously approved in Australia under PR-151, DIR 017/2002 and DIR 025/2002.

The GM cotton contains an insecticidal gene (*vip3A*), derived from a common soil bacterium, which encodes an insecticidal protein (VIP3A) that is toxic to lepidopteran caterpillar pests of cotton. It also contains a bacterial gene *hph*, conferring resistance to hygromycin, an antibiotic that was used as a selectable marker in the initial laboratory stages of developing the GM cotton.

None of the cotton plants from the proposed release, or their by-products, will be used for human food or animal feed. The applicant proposes to sell the lint for use in clothing and upholstery. Lint does not contain genetic material or protein.

Details of the plasmid map, including the gene construct containing the insecticidal *vip3A* gene, and the regulatory sequences (promoters), have been declared Confidential Commercial Information (CCI) under section 185 of the *Gene Technology Act* (the Act). However, this information has been made available to GTTAC and other prescribed expert authorities that are being consulted on the preparation of the RARMP.

GTTAC discussed the RARMP prepared for this application and advised the Regulator that:

- The Committee agrees with the assessment made by the OGTR on the risk of toxicity, allergenicity, weediness and gene transfer;
- The Committee agrees with the proposed licence conditions;
- The applicant should be requested to provide further data and information on the toxicity of the GMO to non-target organisms and the biochemical pathways involving VIP3A protein; and
- The Committee recommends that research should be commissioned to investigate potential risks of the GMO to Australian species of non-target insects.

- **Field trials of Roundup Ready cotton MON 88913 (DIR 035/2003)**

The OGTR has prepared a RARMP for an application from Monsanto Australia Limited (Monsanto) for the limited and controlled release of GM herbicide tolerant cotton (Roundup Ready<sup>®</sup> MON 88913) and herbicide tolerant/insect resistant cotton (Roundup Ready<sup>®</sup> MON 88913 /Bollgard II<sup>®</sup>). Monsanto proposes to conduct trials on 50 sites covering a total of 954 hectares, over three years, in the cotton NSW, Qld, NT, and WA.

Roundup Ready<sup>®</sup> MON 88913 cotton differs from the previous commercially released Roundup Ready<sup>®</sup> cotton in that it contains two copies of the *cp4 epsps* gene that provides tolerance to glyphosate (the active ingredient in the herbicide Roundup<sup>®</sup>). The applicant anticipates that this will enable Roundup<sup>®</sup> to be applied to control weeds over a longer period of plant growth, giving growers increased flexibility in timing herbicide applications for integrated weed management.

The proposed field trials aim to transfer and establish the MON 88913 trait into elite cotton varieties and to evaluate the GM cottons' agronomic performance in Australian agricultural conditions. Additional aims are to conduct evaluation and gather data on Roundup Ready<sup>®</sup> MON 88913 levels of CP4 EPSPS protein expression, tolerance to glyphosate, seed composition, weed control effectiveness and glyphosate residue levels for future large scale or commercial releases, which would require separate approvals.

None of the cotton plants from the release, or their by-products, would be used for animal and human food. However, the applicant proposes to sell lint. Lint does not contain genetic material or protein. Transport of the GM material would be in accordance with the transport guidelines issued by the Regulator.

Details of the gene construct, including the plasmid map, some of the regulatory sequences and preliminary protein expression data, have been declared CCI under section 185 of the Act. However, this information has been made available to GTTAC and other prescribed expert authorities that are being consulted on the preparation of the RARMP.

GTTAC discussed the RARMP prepared for this application and advised the Regulator that:

- The Committee agrees with the assessment made by the OGTR on the risk of toxicity, allergenicity, weediness and gene transfer; and
- The Committee agrees with the proposed licence conditions.

- **Breeding and pre-commercial evaluation of transgenic cotton expressing a vegetative insecticidal protein (VIP) gene and a herbicide tolerance gene – continuation of DIR 017/2003 and DIR 025/2003 (DIR 036/2003)**

The OGTR has prepared a RARMP for an application from the CSIRO for a licence for the limited and controlled release of GM cotton into the environment. CSIRO proposes to release the transgenic cotton on 16 sites within existing cotton growing regions in Qld and NSW, covering a total area of less than 45 hectares per growing season for three seasons.

The three insecticidal GM cotton lines proposed for release, COT200, COT102, and COT102xLL25, express vegetative insecticidal protein (VIP) from the *vip* gene. This protein is different to the other insecticidal proteins present in the GM insecticidal cottons being trialled or grown commercially in Australia. In addition to the *vip* gene, COT102 contains an antibiotic resistance gene and COT102xLL25 contains an antibiotic resistance gene and a herbicide tolerance gene.

The proposed trial is part of an ongoing breeding program to develop lines suitable for commercial development. The main aim of the proposed release is to evaluate the agronomic performance of cotton lines modified to express a new insecticidal protein that is toxic to lepidopteran caterpillar pests of cotton. The release would also allow the assessment of the efficacy of the insecticidal protein, the combining of the insecticidal and herbicide tolerance traits by crossing different GM lines (containing insecticidal and herbicide tolerant traits), and production of seed for future releases, subject to future approvals.

None of the cotton plants from the release, or their by-products, would be used for animal feed or human food. However, the applicant proposes to sell lint from the release. Lint does not contain genetic material or protein.

Details of the gene construct, including the plasmid map and regulatory sequences for the COT200, COT102 and LL25 events, have been declared as CCI. CSIRO has sought approval for details of the gene construct, including the plasmid map and regulatory sequences of the COT102xLL25 line, to be declared CCI. CCI information is made available to GTTAC and other prescribed expert authorities that are being consulted on the preparation of the RARMP.

GTTAC discussed the RARMP for this application and advised the Regulator that:

- The Committee agrees with the assessment made by the OGTR on the risk of toxicity, allergenicity, weediness and gene transfer; and
  - The Committee agrees with the proposed licence conditions.
- **Breeding and pre-commercial evaluation of transgenic cotton expressing tolerance to the herbicide glufosinate ammonium – continuation of DIR 015/2003 (DIR 038/2003)**

The OGTR has prepared a RARMP for an application from CSIRO for a licence for the limited and controlled release of GM cotton into the environment. CSIRO is proposing to release this transgenic cotton on 16 sites, in NSW and Qld, over a total area of 45 hectares per year over three growing seasons.

The aim of the proposed release is breeding and pre-commercial field evaluation of GM herbicide tolerant Liberty® cotton. The release would also be used for demonstration purposes.

Liberty® cotton is tolerant to the herbicide glufosinate ammonium (also called phosphinothricin), the active constituent of herbicides Basta® and Liberty® (hence the name Liberty® cotton). It is expected that use of Liberty® cotton plants will allow more effective weed control in cotton crops by allowing the crop to be sprayed with glufosinate ammonium to kill problem weeds without damaging the crop itself.

None of the cotton plants from the release, or their by-products, would be used for animal feed or human food. However, the applicant is proposing to sell lint, which does not contain any genetic material, from the GM cotton plants and the conventional cotton plants in the surrounding pollen trap.

CSIRO has requested that details of the gene construct, including the plasmid map and regulatory sequences, be declared as CCI under section 185 of the Act. However, this information has been made available to GTTAC and other prescribed expert authorities that are being consulted on the preparation of the RARMP.

GTTAC discussed the RARMP prepared for this application and advised the Regulator that:

- The Committee agrees with the assessment made by the OGTR on the risk of toxicity, allergenicity, weediness and gene transfer; and
- The Committee agrees with the proposed licence conditions.

- **Field evaluation of high-oleic (HO) cotton (DIR 039/2003)**

The OGTR has prepared a RARMP for an application from CSIRO for a licence for the limited and controlled release of GM cotton into the environment. CSIRO is proposing to release two transgenic cotton lines on 2 hectares at one site at the Australian Cotton Research Centre Narrabri, NSW.

The main aims of the proposed release are to conduct agronomic evaluation of the GM cotton lines and to test for maintenance of the HO phenotype under field conditions.

Oil from GM HO cottonseed is expected to have a greater stability than other seed oils. This may enable direct use in frying or for margarine hard stock, without the need for hydrogenation that current oils require.

None of the cotton plants from the release, or their by-products, will be used for animal or human consumption. The applicant is proposing to sell lint from non-GM cotton used as pollen trap rows surrounding the release site, but not from the release. Lint does not contain genetic material or protein.

GTTAC discussed the RARMP prepared for this application and advised the Regulator that:

- The Committee agrees with the assessment made by the OGTR on the risk of toxicity, allergenicity, weediness and gene transfer; and
- The Committee agrees with the proposed licence conditions.

- **Agronomic assessment and seed increase of transgenic cotton expressing insect tolerance genes from *Bacillus thuringiensis* (DIR 040/2003)**

The OGTR has prepared a RARMP for an application from Dow AgroSciences Australia Limited (Dow AgroSciences) for a licence for the intentional release of GM insect resistant / herbicide tolerant cotton into the environment, on a limited scale and under controlled conditions on two sites covering a total area of 0.04 hectares in NSW.

There have been no previous releases of this particular variety of GM cotton in Australia. The main aim of the proposed release is to evaluate the agronomic performance and insecticidal efficacy of a cotton line modified to express two insecticidal proteins (Cry1Ac and Cry1Fa) that are toxic to lepidopteran caterpillar pests of cotton. This line also contains a marker gene (*pat*) which confers tolerance to the herbicide glufosinate ammonium. Seed would also be retained for potential future releases, which would require further licence applications and separate assessment processes.

None of the cotton plants from the release, or their by-products, would be used for animal or human food.

Some specific Dow AgroSciences documents, which contain some details of the gene construction, gene sequence information and molecular characterisation of the GMO, have been declared as CCI under section 185 of the Act. However, this information has been made available to GTTAC and other prescribed expert authorities that are being consulted on the preparation of the RARMP.

GTTAC discussed the RARMP prepared for this application and advised the Regulator that:

- The Committee agrees with the assessment made by the OGTR on the risk of toxicity, allergenicity, weediness and gene transfer; and
- The Committee agrees with the proposed licence conditions.

## Advice on Lupins

GTTAC considered the following application concerning the release of transgenic lupins in Australia and provided advice on issues to be considered in the preparation of the associated RARMP.

- **Preliminary agronomic assessment of high sulphur lupin (DIR 043/2003)**

The OGTR has received an application from the University of Western Australia proposing to conduct a single field trial at one site, over a single year, covering a total area of 0.5 hectares.

The aim of the proposed release is to determine the agronomic performance of two high sulfur lupin lines and their F<sub>1</sub> progeny and to compare this with the non-transgenic cultivar Kalya, from which they were derived. The applicant also proposes to harvest and store seed from the trial for sulfur analysis.

The high sulfur lupin contains the sunflower seed albumen (*ssa*) gene derived from the sunflower (*Helianthus annuus* L.) and associated regulatory sequences from pea (*Pisum sativum*). The effect of the modification is to increase methionine and cysteine content in the seed. These are nutritionally important amino acids especially in stockfeeds.

GTTAC advised the Regulator that:

- The risks posed by the genetically modified high sulphur lupins are similar to those posed by previous lupin applications PR-49, PR-49X, PR-49X(2) and PR-49X(3); and
- The applicant should be requested to provide a protocol for cleaning the harvesting machinery.

## **Presentations**

The Committee received and discussed presentations on the following topics:

- The Precautionary Principle
- Evolved Glyphosate Resistance
- Antibiotic Resistance Genes in GMOs in Australia

## **Enquiries and Risk Assessment and Risk Management Plans**

For all enquiries and to obtain copies of applications or RARMPs for dealings involving the intentional release of GMOs into the environment, please phone the OGTR Free-call hotline on 1800 181 030. The RARMPs are also available electronically from our website at <http://www.ogtr.gov.au/publications/riskassessments.htm>

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