GENE TECHNOLOGY TECHNICAL ADVISORY COMMITTEE

COMMUNIQUE
No. 8

This is the eighth communique of the Gene Technology Technical Advisory Committee (GTTAC). It covers matters considered at the thirteenth meeting of GTTAC held on 8 and 9 April 2003, as well as matters considered by GTTAC out-of-session in the period from 1 February to 9 April 2003.

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
DNIR 135/2002 Conditionally replicative adenoviruses for neoplastic disease.	The aim of this dealing is to generate adenoviruses that will only replicate in the presence of specific tumour cell proteins. The adenoviruses will be tested for their impact on cell function.	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. In addition, GTTAC advised that the specificity of the vectors should be tested by the applicant and suggested that a new application would be required if the applicant proposed to add non-viral genes into the constructs.
DNIR 144/2002 The role of hyaluronic acid in normal and aberrant stem cell biology.	The aim of this dealing is to analyse the role of hyaluronic acid in leukaemiagenesis by over expressing or inhibiting hyaluronic acid synthase genes in primary human leukaemic cells.	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. GTTAC advised that laboratory guidelines must be followed and that the use of sharp instruments should be avoided where the possibility of accidental inoculation existed. However, when sharps are required, extra care should be taken.
DNIR 156/2002 Gene mediated cell death in ovarian cancer.	The aim of this dealing is to study gene mediated cell death in ovarian cancer by infecting human cancer cells with viral particles containing the Y81 gene. The Y81 protein is hypothesised to slow the growth of the infected cells.	As for DNIR 144/2002.

Application Number and Title	Project Description	GTTAC Comments
DNIR 158/2002 Focal modification of cardiac conduction by gene transfer.	The aim of this dealing is to introduce specific genes into human and animal cells in order to induce electrical conduction between these cells in network.	As for DNIR 144/2002. In addition, GTTAC advised that sheep treated with lentiviral vectors should be kept in a PC2 facility for as long as there is a risk of the animals shedding viable virus. Following this period it would be safe to house the animals in a PC1 facility.
DNIR 160/2002 Metabolic engineering of hyaluronic acid production.	Hyaluronic acid (HA) forms the capsule of some Group A and C Streptococci. The aim of this dealing is to identify and study genes involved in the regulation of HA production in bacterial fermentation processes.	As for DNIR 144/2002. In addition, GTTAC advised that as the GMO included a marker gene that conferred resistance to one of the antibiotics used to treat infection with *Streptococcus*, the applicant should be required to identify alternative antibiotics in case of infection with the GMO.
DNIR 161/2002 Expression of adhesins from bacterial pathogens in non-pathogenic lactic acid bacteria.	The aim of this dealing is to genetically modify non-pathogenic lactic acid bacteria to express adhesin molecules from pathogenic bacteria of risk group 2 or less.	As for DNIR 144/2002. In addition, GTTAC advised that the adhesin molecules could be cloned in *Escherichia coli* in order to amplify the DNA, however they should not be expressed in *E. coli* as this may alter the attachment properties of *E. coli*.
DNIR 166/2002 Retroviral expression cloning to discover new molecules expressed by leukocytes.	The aim of this dealing is to isolate novel gene sequences from leukocytes (white blood cells) to better understand immune function.	As for DNIR 144/2002.

Application Number and Title	Project Description	GTTAC Comments
DNIR 172/2002 *Myxoma virus*/Kunjin replicon vaccine system.	The aim of this dealing is to test the feasibility of a recombinant *Myxoma virus*/Kunjin replicon hybrid as an immuno-contraceptive vaccine in rabbits.	GTTAC advised that the ability of the recombinant virus to infect human cells should be tested by the applicant. GTTAC agreed that, if the virus is rabbit-specific, the risk assessment identifies all the risks associated with the proposed dealings and the measures proposed in the risk management plan are adequate to deal with the identified risks. GTTAC advised that laboratory guidelines must be followed and the use of sharp instruments should be avoided where the possibility of accidental inoculation exists. However, when sharps are required, extra care should be taken.

Advice on containment levels for genetically modified (GM) pathogenic viruses

At the previous GTTAC meeting the Committee agreed to provide further advice on the containment level required for work with particular GM viruses. This involved viral hybrids containing segments of Flaviviruses including HCV, *Murray Valley encephalitis virus*, *Bovine viral diarrhoea virus* and *GBV-C virus*.

The Committee discussed the potential virulence and likely frequency of replication competent virus production of the GMOs.

GTTAC advised the Regulator that:

- With regard to the recombination work conducted in *Escherichia coli*, it is safe for the applicant to undertake this work in a PC2 facility;
- The applicant should provide further data regarding the GMO sequences and frequency of replication competent virus production; and
- The viral replication component of the work should be conducted in a PC3 facility until the requested information can be considered.

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 Cotton

Advice on cotton applications

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

- **Field trials for herbicide tolerant (Roundup Ready® MON 88913) and herbicide tolerant/insect resistant (Roundup Ready® MON 88913 / Bollgard II®) cotton (DIR 035/2002)**

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

  The aims of the proposed field trials are to transfer and establish the MON 88913 trait into elite cotton varieties suitable for use under Australian conditions. Additional aims are to conduct evaluation and gather data on Roundup Ready® 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.

  Roundup Ready® MON 88913 cotton differs from the previous commercially released Roundup Ready® cotton in that it contains two copies of the *cp4 epsps* gene that provides tolerance to glyphosate (the active ingredient in the herbicide Roundup®). Tolerance to glyphosate is prolonged and the applicant has indicated that Roundup® can be applied to control weeds over a longer period of plant growth, giving growers increased flexibility in timing herbicide applications for integrated weed management.

  Roundup Ready® MON 88913/Bollgard II® cotton was produced by conventional breeding of Roundup Ready® MON 88913 cotton with GM Bollgard II® cotton which is resistant to the major caterpillar pests of cotton.

  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 from the release. 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 Confidential Commercial Information (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 this application and advised the Regulator that the following issues should be considered in the preparation of the RARMP:

- The risks posed by DIR 035/2003 are similar to those posed by previous Roundup Ready® and Roundup Ready®/Bollgard II® cotton applications;
- The advice provided in relation to previously assessed GM cottons (Bollgard II® and Roundup Ready® cottons) should be considered in the preparation of the RARMP for DIR 035/2003; and
- The applicant should be asked to provide data on the expression levels of the introduced proteins under Australian field conditions, at the completion of the field trials.

Advice on cotton RARMPs

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

- **Commercial release of INGARD cotton event 531 in Australia (DIR 022/2002)**

The OGTR has received a licence application from Monsanto for the intentional release of INGARD® cotton into the environment in the cotton growing regions of NSW and Qld south of latitude 22º South. Approval would enable the continued commercial release of the GM cotton. Monsanto also proposes the phasing-out of INGARD® cotton over the next two years while Bollgard II® cotton (which was approved for commercial release in September 2002, DIR 012/2002) is phased-in over the same period.

INGARD® cotton is resistant to lepidopteran caterpillar pests that attack cotton. It contains an insecticidal gene, *cry1Ac*, derived from the soil bacterium *Bacillus thuringiensis,* that produces a protein that is toxic to specific insects.

It is intended that the GM cotton plants and their by-products, including cottonseed, be used in the same manner as conventional cotton, including for human food and stockfeed. Cottonseed is processed for oil that is used in a variety of food products and for cotton linters (a type of fibre that does not contain any genetic material) that are used as a cellulose base for several consumer food products. Food Standards Australia New Zealand, FSANZ, (formerly the Australia New Zealand Food Authority, ANZFA) has already approved the use of oil and linters from INGARD® cotton in human food.

The applicant seeks approval for commercial release of the GM cotton in all Australian cotton growing regions south of latitude 22º South, and no limitations on transportation or storage are proposed (see below for further explanation). However, the Australian Pesticides and Veterinary Medicines Authority (APVMA), formerly known as the National Registration Authority, will remain responsible for determining the total planting area of GM cotton each season. The APVMA currently only allows up to 30% of the cotton crop to be planted to GM cotton to guard against the evolution and emergence of resistant insects.

GTTAC advised the Regulator that they endorsed the risk assessment and management plan for DIR 022/2002 but suggested clarification of the licence conditions relating to:

- The control of volunteer plants after feeding stock with cottonseed.
- The research on the distribution of feral cotton populations in Queensland.

- **Seed increase and efficacy studies in Northern Australia of transgenic cotton expressing a new insecticidal protein gene – extension of DIR 017/2002 (DIR 025/2002)**

CSIRO has applied for a licence for the limited and controlled release (field trial) into the environment of GM cotton containing an insecticidal gene (*vip3A*).

Details of the gene construct and the regulatory sequences (promoters), including the plasmid map, have been declared as Confidential Commercial Information (CCI). However this information was made available to GTTAC and the other prescribed expert authorities that were consulted on the preparation of the RARMP.

The main aim of the proposed release is to evaluate the agronomic performance of cotton lines modified to express a new insecticidal protein (VIP3A) that is toxic to lepidopteran caterpillar pests. The lines also contain an antibiotic resistance marker gene (*hph*). The release would also be used to produce seed for future releases in an ongoing breeding program (which would be subject to further approvals).

CSIRO proposes to carry out a limited and controlled release on three sites, in the shire of Wyndham-East Kimberley, over a total area of 3 hectares. 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 from the release. Lint does not contain genetic material or protein.

GTTAC advised the Regulator that they agreed with the conclusions of the risk assessment and noted that:

- Gene flow to native cotton species does not need to be managed as there is very little potential for this to occur;
- The licence conditions should specify a minimum width for pollen traps;
- The licence conditions should be clarified to explain how the stability of proteins in the soil will be evaluated if these proteins are already in the soil from indigenous populations of *Bacillus thuringensis*; and
- The level and frequency of reporting required should be reviewed.

Advice on Canola

GTTAC considered the RARMP prepared in response to the following application concerning the release of transgenic canola in Australia.

- **Commercial release of InVigor® canola (*Brassica napus*) for use in the Australian cropping system (DIR 021/2002)**

  The OGTR has received an application from Bayer CropScience Pty Ltd (Bayer) for the commercial release of GM canola into the environment.

  Bayer are seeking regulatory approval for seven similar GM 'lines' of canola which have all been trialed previously in Australia under limited and controlled conditions. Although Bayer only intends to commercialise two lines in Australia, the applicant is seeking approval for all seven GM canola lines to achieve consistency with existing overseas regulatory approvals.

  Oil derived from all seven canola lines has been approved for use in human food in Australia by Food Standards Australia New Zealand. The GM canola from the proposed release would be used as oil in human food, or in animal feed, in the same way as conventional (non-GM) canola.

  The hybrid canola seed, which Bayer seeks to commercialise in Australia as InVigor® canola, is produced with a novel hybrid generation system based on two genetically modified 'parent' lines of canola: a male sterile (MS) line that contains a male sterility gene (*barnase*), and a fertility restorer (RF) line containing a fertility restorer gene (*barstar*). The progeny are expected to have enhanced agronomic performance, otherwise known as 'hybrid vigour'.

  All seven GM canola lines include a gene that confers tolerance to the herbicide glufosinate ammonium. The herbicide tolerance serves as a dominant marker for the introduced traits during breeding and hybrid seed production. It may also be used for the control of weeds in the canola crop, although glufosinate ammonium is not currently registered for use in broad-acre cropping in Australia. Bayer is seeking registration of glufosinate ammonium for use on InVigor® canola under the trade name Liberty® through the APVMA.

  Four of the GM canola lines contain a gene that provides a 'marker' for antibiotic resistance in plants. This gene is used to identify and select modified plants during the development stage.

  In accordance with section 184 of the Act, Bayer has sought approval to enable detailed technical information on precise gene constructs and molecular characterisation data to be declared 'Confidential Commercial Information'. However, this information was made available to GTTAC and other prescribed expert authorities that were consulted on the preparation of the RARMP.

  GTTAC discussed the RARMP for this application and advised the Regulator as follows:

  - The Committee agrees with the assessment made by the OGTR on risk of toxicity, allergenicity, weediness and gene transfer. There is no risk to human health and safety above those presented by conventional canola, and that while the probability of gene transfer to other canola plants was high, the overall rate of outcrossing would be very low and the impact of this would be negligible; and

- The Committee agrees with the proposed licence conditions, however advised that consideration should be given to:
  - clarifying licence condition Part 2, Section 2.2.2 which requires the applicant to report adverse impacts to human health and safety and the environment.; and
  - the means of collecting data on the area planted to each GMO, as required by licence condition Part 2, Section 2.2.3 as it would be preferable to collect this information independently rather than via the applicant.

Advice on Carnation

GTTAC considered the RARMP prepared in response to the following application concerning the release of transgenic carnations in Australia.

- **Commercial release of colour modified carnation (continuation of deemed licence GR2) (DIR 030/2002)**

  An application has been received from Florigene for a licence for the ongoing commercial release of GM carnations (*Dianthus caryophyllus)*. The general release of colour modified carnations (GR-2) was authorised in 1995 under the former voluntary system by the Genetic Manipulation Advisory Committee (GMAC). Florigene propose to release four transgenic lines that were approved previously by GMAC.

  The carnations have been modified to produce violet, mauve, or purple coloured flowers. Non-GM carnations lack the part of the anthocyanin biosynthetic pathway that is responsible for the production of delphinidins, which produce the blue spectrum of colours in flowers. The GM carnations in this application contain the genes coding for the two key enzymes in this pathway: flavonoid 3', 5' hydroxylase (F3'5'H) and dihydroflavonol reductase (DFR).

  The GM carnations also contain a selectable marker conferring resistance to acetolactate synthase (ALS) inhibiting herbicides, as well as regulatory sequences designed to enhance expression of the inserted genes.

  GTTAC discussed the RARMP for this application and advised the Regulator as follows:

  - The Committee agrees with the assessment made by the OGTR that, in regard to toxicity, allergenicity, weediness and gene transfer, the risks posed to human health and safety or to the environment are no greater than those posed by non-GM carnations;
  - The Committee agrees with the proposed licence conditions; and
  - GM carnations may be a suitable candidate for the GM Register.

Advice on Post-Harvest Monitoring Conditions

In accordance with Section 190 of the *Gene Technology Act 2000* (the Act), 'deemed' licences were issued for limited and controlled releases (field trials) of GMOs under the previous voluntary system, prior to the commencement of the Act on 21 June 2001. Deemed licences are only in effect for the transition period and therefore, in the absence of a licence from the Regulator, these deemed licences will expire on 20 June 2003.

Where only post-harvest monitoring of trial sites will continue past 21 June 2003, applicants have not been asked to submit an application for a DIR licence under the new regulatory system. Instead, the conditions for post-harvest monitoring of the trial sites will be attached to other relevant DIR licences held by the same organisation.

GTTAC was asked for advice on the post-harvest monitoring conditions for fourteen deemed licences currently in the post-harvest phase.

GTTAC discussed the proposed post-harvest monitoring conditions and advised the Regulator as follows:

- Conditions relating to cultivation should be made more specific.
- If volunteer plants were seen at the end of a specified monitoring period then further post-harvest monitoring should be required;
- Bi-monthly monitoring would be appropriate for GM white clover, subclover, field peas, and lupins;
- GM *Brassica* species should be treated as in recent canola applications; and
- References to isolation distances and insect proof screens should be removed from the post-harvest monitoring conditions as these applied to the trial phase.

Review of the Gene Technology Regulations

OGTR representatives explained the process required for the amendment of the *Gene Technology Regulations 2001* (the Regulations), which is scheduled to begin later in 2003. The Committee discussed the way in which they could most efficiently provide advice to the Regulator on any proposed amendments of a scientific nature.

GTTAC advised the Regulator that:

- Prior to GTTAC's review of the proposed amendments, the Institutional Biosafety Committees should be invited to submit proposed changes to the Regulations.
- A one or two-day face-to-face meeting should be organised to allow GTTAC to provide advice on the proposed changes.

Presentations

At the April meeting of GTTAC the Committee received and discussed presentations on the following topics:

- Horizontal gene flow
- Defective viral vectors
- Plant viral trangenes

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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