GENE TECHNOLOGY TECHNICAL ADVISORY COMMITTEE

COMMUNIQUE
No. 7

This is the seventh communique of the Gene Technology Technical Advisory Committee (GTTAC). It covers matters considered at the eleventh and twelfth meetings of GTTAC held on 5 December 2002 and 31 January 2003 respectively.

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 002/2001 Gene therapy of hypertension and tumour sensitisation to radiotherapy.	The aim is to develop a new model for gene therapy by treating rats with hypertension (high blood pressure).	GTTAC discussed the early stage vector proposed to be used in this project and suggested that further data should be collected by the applicant on the inability of the viral vector to replicate in human cells. In addition, GTTAC suggested that further information on the gene mutations of interest be requested. GTTAC agreed with the conclusions of the risk assessment and advised that the measures proposed in the risk management plan were adequate to deal with the identified risks.
DNIR 090/2002 Immunocontraception and antigen delivery by recombinant cytomegalovirus.	The aim of this dealing is to genetically modify various cytomegaloviruses (CMVs) to contain reproductive proteins and other proteins. The GMOs will then be tested as immunocontraceptives and as vaccines in a number of animal species.	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 in particular, 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.
DNIR 107/2002 Virus replication and pathogenesis.	This project aims to investigate the function of different viral genes and their role in regulating viral replication and viral pathogenesis.	As for DNIR 090/2002.

Application Number and Title	Project Description	GTTAC Comments
DNIR 108/2002 Targeted gene delivery for vascular and neoplastic disease.	The aim of this dealing is to use targeted gene delivery to investigate pulmonary vascular disease, tumour vasculature and cancer.	As for DNIR 090/2002. In addition, GTTAC advised that there is a very small chance of replication competent virus being produced, however, during recombination the transgene would be lost. Therefore any competent virus produced would be wild type adenovirus which humans are exposed to on a regular basis.
DNIR 109/2002 Signal transduction pathways in human cancers.	The aim of this dealing is to understand the genetic and biochemical changes involved in the development of cancer using human and mouse cells as model systems for human disease.	As for DNIR 090/2002.
DNIR 110/2002 Novel approaches for activation and expansion of genetically engineered T-cells.	The aim of this dealing is to study the anti-tumour activity, expansion and survival of mouse and human genetically modified (GM) primary lymphocytes (T cells) *in vivo*. The GM lymphocytes will be modified to express single chain antibody receptors.	As for DNIR 090/2002.
DNIR 112/2002 Overexpression of diabetes/obesity related genes in cultured cells and animals using recombinant adenovirus.	The aim of this dealing is to study the roles of newly identified genes in the development of diabetes and obesity.	As for DNIR 090/2002.
DNIR 115/2002 Transfection and gene knockout/down of *Plasmodium* and mammalian cell lines.	The researchers propose to use short sequences of dsRNA produced by stable expression vectors to silence the expression of genes in either mammalian cell lines or malaria. They also propose to study the pathogenesis of *Plasmodium berghei* malaria in various mouse knockout models.	As for DNIR 090/2002. In addition, GTTAC agreed that the risks posed by the GMO were less than that of the wild type parasite.

Application Number and Title	Project Description	GTTAC Comments
DNIR 123/2002 Studies on the replication of hepatitis C virus.	The aim of this dealing is to produce a DNA copy of hepatitis C virus (HCV) that contains only the regions of the virus necessary for the virus to replicate. The researchers intend to study HCV replication, as well as design and test antiviral compounds that stop this process.	As for DNIR 090/2002. In addition, GTTAC advised that the risks associated with this proposal were no greater than working with the wild type virus.
DNIR 125/2002 Studies of the replication of hepatitis B virus using recombinant HBV/adenovirus as a delivery system for mammalian cells and studies of HBV and HCV co-infection using HBV/adenovirus and HCV clones.	The aim of this dealing is to study the replication of hepatitis B virus (HBV) by infecting liver cells with HBV using a modified adenovirus containing HBV DNA. HCV genetic material will also be introduced to HBV infected cells to investigate HBV and HCV co-infection.	As for DNIR 090/2002. GTTAC also discussed the possibility of replication competent virus with a broad host range being produced. GTTAC advised that the risk of producing competent virus was low and that this virus would be unable to replicate outside liver cells.
DNIR 126/2002 Molecular regulation of cell lifespan and malignant transformation.	The aim of this dealing is to investigate the molecular regulation of cell lifespan and malignant transformation by genetically modifying mammalian cells with genes of interest.	As for DNIR 090/2002.
DNIR 127/2002 Development of a gene transfer vector for banana.	The aim of this dealing is to develop a gene transfer vector for the banana plant and other plant species.	As for DNIR 090/2002.
DNIR 129/2002 Cloning of genes from potentially toxigenic risk group 2 bacteria.	The aim of this dealing is to analyse genes from a variety of risk group 2 bacteria for commonalities.	As for DNIR 090/2002.
DNIR 130/2002 Use of retroviral and lentiviral gene delivery systems for the expression of HCV proteins in cell culture.	The aim of this dealing is to use retroviruses and lentiviruses to express various HCV proteins. These viruses will be used to study the replication of HCV in cell culture.	As for DNIR 090/2002.

Application Number and Title	Project Description	GTTAC Comments
DNIR 132/2002 Whooping cough vaccine VI.	The aim of this dealing is to develop a genetically engineered non-toxic whooping cough vaccine.	As for DNIR 090/2002. In addition, GTTAC advised that it was not necessary for the applicant to check for reversions of the two point mutations used to create the vaccine strain, as either of the mutations is capable of eliminating pathogenic activity in the GMO on its own.
DNIR 133/2002 *Pasteurella multocida* Type A genes and gene products.	The aim of this dealing is to study the role of various genes and gene products in the pathogenesis of *Pasteurella multocida*.	As for DNIR 090/2002.
DNIR 134/2002 Mechanisms of immunity to salmonellosis.	The aim of this dealing is to characterise the immunoregulating factors produced by mice vaccinated with two attenuated strains of *Salmonella typhimurium*.	As for DNIR 090/2002.
DNIR 139/2002 Recombinant canine herpesvirus as vaccine vector.	The aim of this dealing is to construct a recombinant canine herpesvirus to be used as a vaccine vector.	As for DNIR 090/2002. In addition, GTTAC agreed that the virus is very species specific and that the genetic modifications are likely to attenuate the virus. GTTAC discussed the potential effect of an unintentional release of the GMO and agreed that the likelihood of the virus spreading among foxes in the wild was very low.

Advice on containment levels for genetically modified pathogenic viruses

GTTAC was asked for advice on the containment level required for work with particular GM viruses. The GMOs included vaccinia virus recombinants carrying HCV antigens, as well as viral hybrids containing segments of Flaviviruses including HCV, Murray Valley encephalitis virus, Bovine viral diarrhoea virus and GBV-C virus.

GTTAC discussed the risks involved with this work and determined that, because the RNA polymerase gene had been removed from each of the GMOs, the GM viruses would be unable to replicate.

GTTAC advised the Regulator that further information regarding this application should be sent to three Committee members for further consideration.

DNIR licence for the importation of corn as stockfeed

Due to the current drought, an application has been received requesting approval to import corn as stockfeed from the U.S., a proportion of which may be GM. GTTAC advised the Regulator that the RARMP addressed all risks associated with the importation of GM corn.

Revision of the DNIR application form

GTTAC reviewed the draft revision of the DNIR application form prepared by the Office of the Gene Technology Regulator (OGTR). Members provided feedback on the new format and revised questions. The new application form is due for release early in 2003.

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 Papaya

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

- **Field trial for evaluation of genetically modified papaya to delay fruit ripening and to test the expression of the introduced genes (DIR 026/2002)**

  An application has been received from the University of Queensland for a licence for the intentional release of GM papaya (*Carica papaya* L, cultivar 'Solo') plants into the environment. Approval would enable the continued limited and controlled release (field trial) of GM papaya approved under the former voluntary system, as well as for several new lines of GM papaya.

  The applicant proposes to study up to 300 individual papaya plants at one site, over a total area of 1.7 hectares in the Shire of Redlands (Qld).

The release involves growing several lines of papaya plants that have been modified to delay fruit ripening by down-regulation of a plant hormone, ethylene, or by modifying the ethylene receptor molecule. Some plants have also been modified to express a reporter gene that can be used to identify the plants with genetic modifications.

The GM papaya plants contain either:

- additional copies of *capacs 1* or *capacs 2* genes from papaya, which are associated with the biosynthesis of ethylene; or
- the *etr1-1* gene encoding the modified ethylene receptor protein from the plant *Arabidopsis thaliana*.

One type of GM papaya contains a reporter gene (GUS) to aid selection of the GMO in the laboratory.

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

- In order to minimise the risk of outcrossing, the male flowers of the GM plants should be removed and non-GM male plants grown to facilitate pollination.
- The netting enclosure proposed by the applicant would be adequate to prevent pollen dispersal, so long as the enclosure is 'sealed' to ground level.
- The enclosed area used for this trial should be monitored every 3 months for 12 months following harvest.
- Further information should be sought on whether seeds are shed by the GM plants.
- If the applicant proceeds with the viral work at a later date, further advice should be sought on the viral work proposed as the virus used could potentially affect cucurbits, possibly including those in the wild.
- Further information from the applicant on the polygalacturonase (PGA) promoter should be requested.
- The proposed dealing posed no significant risk to human health and safety, or the environment.

Advice on Pineapple

GTTAC considered the following two applications concerning the release of transgenic pineapple in Australia and provided advice on issues to be considered in the preparation of the associated RARMPs.

- **Field test of pineapple plants modified to control flowering (DIR 027/2002)**

An application has been received from the University of Queensland for a licence to continue the limited and controlled release (field trial) of GM pineapple (*Ananas comosus,* now called *Ananas comosus* var. *comosus*) first planted in 1999 under the former voluntary system. The University of Queensland is proposing to continue the trial on one site in the Shire of Redlands (Qld), over a total area of 0.1 hectares.

The aim of the proposed release is to test pineapple plants that have been modified to control flowering. Another aim of the release is to assess the activity of different regulatory sequences under field conditions.

The GM pineapple plants have been modified by insertion of a truncated copy of the pineapple ACC (1-aminocyclopropane-1-carboxylate) synthase (*ACACS3*) gene to 'silence' the existing gene in the pineapple. ACC synthase is a key enzyme in the pathway that leads to formation of ethylene in plants and has a role in natural flowering.

Other GM pineapple plants have been modified by insertion of a reporter gene (*uidA*), which allows assessment of the activity of different regulatory sequences under field conditions.

All of the GM pineapples also contain a selectable marker gene (S*uRB*) conferring resistance to ALS inhibitors, including sulfonylurea herbicide, which is used to select transgenic plants in the laboratory.

Short regulatory sequences that control expression of the introduced genes are also present in the GM pineapples. Although some of these sequences are derived from plant pathogens like cauliflower mosaic virus and *Agrobacterium tumefaciens*, the regulatory sequences comprise only a small part of the pathogen's total genome and are not in themselves capable of causing disease.

None of the pineapple plants from the trial, or their by-products, will be used for human food, animal feed or therapeutics.

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

- The application posed no risk to human health and safety or the environment.
- Army worm moths do not pose a risk and therefore guard rows are not required.
- A six to seven month monitoring period would be adequate.
- Either incineration or burial would be adequate for disposal of the GM plants.
- The applicant should be asked to fence the trial site.
- Only the release site needs to be monitored post-harvest.

- **Field trial of pineapple plants modified for blackheart reduction and to delay flowering (DIR 028/2002)**

An application has been received from the Queensland Department of Primary Industries for a licence to continue the limited and controlled release (field trial) of GM pineapple (*Ananas comosus,* now called *Ananas comosus* var. *comosus*) first planted in 2001 under the former voluntary system. The applicant is proposing to continue the trial on one site in the Shire of Redlands (Qld) and one site in the Shire of Maroochy, (Qld), over a total area of 0.12 hectares. [NB - *Following the meeting the applicant requested that the total trial area be increased to 0.22 hectares*.]

The aims of the proposed release are to conduct an evaluation of pineapple plants that have been modified for blackheart reduction and/or to control flowering, as well as to assess the activity of different regulatory sequences under field conditions.

The GMOs covered by this proposal contain one of the following modifications:

- A truncated copy of the pineapple *PPO2* gene to reduce the expression of the PPO enzyme, believed to be responsible for tissue discolouration (blackheart) in pineapples.
- A truncated copy of the pineapple *ACACS2* which 'silences' the existing gene for natural flowering in the pineapple.

- A truncated copy of the pineapple *PPO2* and *ACACS2* gene to 'silence' the existing genes for blackheart and flowering in the pineapple.
- The *uidA* gene (a marker gene) used to assess the activity of different regulatory sequences under field conditions.

All GM pineapple plants contain a selectable marker gene (*nptII*) conferring antibiotic resistance used to select GMOs containing the modified DNA. The GM plants also contain the non-expressed bacterial genes *bla* (ampicillin resistance), *aad* (streptomycin and spectinomycin) and *LacZ* (ß galactosidase).

Short regulatory sequences that control expression of the introduced genes are also present in the GM pineapples.

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

- The proposal poses no risk to human health and safety or to the environment.
- The use of the antibiotic resistance genes had been discussed by GTTAC previously and had been found to be of no risk to human health and safety and the environment.
- Advice given for DIR 027/2002 would also be applicable to DIR 028/2002.

Advice on Cotton

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.

- **Defining sustainable production systems for transgenic cotton (INGARD®, Bollgard II® and Bollgard II®/Roundup Ready®) in the Kimberley region of Western Australia (DIR 029/2002)**

An application has been received from the Department of Agriculture, Western Australia for a licence for the intentional release of GM insecticidal (INGARD® and Bollgard II®) and insecticidal/herbicide tolerant (Bollgard II®/Roundup Ready®) cotton (*Gossypium hirsutum* L) into the environment. The applicant proposes to carry out a limited and controlled release (field trial) at 10 sites, over 82 hectares in Kununurra and Broome in Western Australia.

INGARD® and Bollgard II® cotton are resistant to the lepidopteran caterpillar pests that attack cotton. They contain one or two insecticidal genes, respectively, that produce proteins that are toxic to specific insects. Bollgard II®/Roundup Ready® cotton also contains a gene for tolerance to the herbicide glyphosate (Roundup®).

On 23 September 2002, Bollgard II® cotton and Bollgard II®/Roundup Ready® cotton were approved for commercial release (licence number DIR 012/2002). However, the release was restricted to south of latitude 22º South, because of continuing concerns about the potential weediness of the insecticidal cotton in tropical areas, as well as the potential for out-crossing to naturalised cotton in these areas. Therefore, field trials to gather additional data on these issues must be conducted under limited and controlled conditions.

The proposed release aims to assess the performance of the GM cotton varieties in the Kimberley environment and will compare the effectiveness of conventional insecticide and Bt resistance. Effects of the GMOs on the type and abundance of pest and beneficial insects, as well as the potential development of insects resistant to the insecticidal activity of the GM cotton will be studied. In addition, the applicant will measure the refuge value of alternative crops to Bt insecticidal resistance management in the northern tropical environment.

None of the cotton plants from this release, or their by-products, will be used for human food, however the applicant proposes to sell some of the GM cottonseed as stockfeed after it has been rendered non-viable. It is also proposed that lint from the release be sold commercially. Lint does not contain genetic material or protein.

GTTAC discussed this application and advised the Regulator that the following issues should be considered when preparing the RARMP:

- The application is similar, and poses risks similar to, DIR applications 005/2001, 006/2001, 008/2001, 009/2001 and 012/2001.
- The advice provided for DIR applications 005/2001, 006/2001, 008/2001, 009/2001 and 012/2001 would also apply to this application.

Advice on Carnation

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

- **Ongoing commercial release of colour modified carnations (extension of deemed licence GR-2) (DIR 030/2002)**

  An application has been received from Florigene for a licence for the ongoing commercial release of GM carnations (*Dianthus caryophyllus)*. The current application is an extension of a general release of colour modified carnations that was approved in 1995 under the former voluntary system.

  The present application is for a licence to deal with any transgenic carnation line produced after transformation with either of two binary vectors, pCGP1470 or pCGP1991.

  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. The GM carnations in this application contain the genes coding for the enzymes flavonoid 3', 5' hydroxylase (F3'5'H) and dihydroflavonol reductase (DFR) which allow production of delphinidins. The delphinidins are responsible for the blue spectrum of colours in flowers.

  The GM carnations also contain a selectable marker conferring resistance to sulfonylurea herbicides, as well as regulatory sequences designed to enhance expression of the inserted genes.

  GTTAC discussed this application and advised the Regulator that the proposed dealings posed no risks to human health and safety, or to the environment.

Advice on Grapevine

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

- **Field trial of genetically modified grapevines – evaluation of berry colour, sugar composition, flower and fruit development and gene flow study (DIR 031/2002)**

  An application has been received from the Commonwealth Scientific and Industrial Research Organisation (CSIRO) for a licence for the intentional release of GM grapevines (*Vitis vinifera* L) into the environment. Approval would enable the continued limited and controlled release (field trial) of GM grapevines, approved under the former voluntary system, on one site in Mildura Rural City Council, Victoria, over a total area of 0.38 hectares.

  The aims of the proposal are to evaluate the field performance of GM grapevines containing additional copies of various grapevine genes which are modified to improve berry colour, sugar composition, flowering and fruit quality. The applicant also proposes to monitor pollen flow using GM grapevine containing green fluorescent protein (GFP).

  Several types of GM grapevines are proposed for release. The GMO's will contain one of the following modifications:
  - The *gus* reporter gene from *Escherichia coli* which enables the visual identification of plant tissues expressing the transgene.
  - Additional copies of the *ppo* gene, derived from grapevine, coding for the enzyme polyphenol oxidase. The modified *ppo* gene derived from grapevine has been introduced to test silencing of the natural copy of the *ppo* gene, thereby reducing browning in GM sultanas.
  - Modified *sh4* gene from grapevine, designed to improve flower and fruit characters, which are beneficial to the grape industry.
  - Additional copies of a *ufgt* gene encoding for UDP glucose flavonoid 3-O-glucosyl transferase from grapevine which is involved in flowering.
  - The modified *dfr* gene from grapevine which is designed to down-regulate the expression of the enzyme dihydroflavonol reductase, to alter the production of anthocyanin or tannin which are important for the stabilisation of colour during wine making and for wine mouthfeel.
  - The modified *inv* gene designed to down-regulate the invertase enzyme, which breaks down sucrose into fructose and glucose. This is expected to maintain sucrose levels in the grape berries.
  - The *gfp* reporter gene isolated from jellyfish (*Aequorea victoria*), encoding for GFP that enables the visual identification of plant tissues expressing the transgene.

  Most of the above GMOs contain an antibiotic resistance gene, *nptII*, except for one group that contains *hph*. These genes are used as selectable markers in the initial laboratory stages to select grapevine plants containing the modified genes. All of the GMOs also contain short regulatory sequences that control expression of the inserted genes.

  None of the grapevine plants from the release, or their by-products, would be sold as animal or human food.

GTTAC discussed this application and advised the Regulator that the following issues should be considered when preparing the RARMP:

- The applicant should be asked to ensure all *Agrobacterium* are removed from the GM plants before release.
- The applicant should be asked to construct a fence around the enclosure to exclude small mammals from the trial site.
- The applicant should be asked to manage the site to control volunteers.
- A large isolation zone is not required, given that the fruit will be bagged.
- Any potential effect of the genetic modifications on other plant functions, which may have potentially adverse consequences to human health, should be considered.
- The applicant should be advised to notify Food Standards Australia New Zealand prior to conducting taste testing of sultanas and wine derived from GM fruit.

Advice on Canola

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

- **Field trial – seed increase and field evaluation of herbicide tolerant hybrid canola (DIR 032/2002)**

  An application has been received from Bayer CropScience Pty Ltd (Bayer) for a licence for the limited and controlled release (field trial) of GM canola (*Brassica napus* L) into the environment. The aim of the proposed release is to allow seed increase of promising canola lines that are herbicide tolerant hybrids (to produce seeds for future trials) and for ongoing evaluation trials planned for Canada and Australia. The proposed release would occur at 4 sites in 4 different locations per year for 3 years. The total area of land to be used is 16 ha per year in Victoria, South Australia and New South Wales.

  Bayer has developed a novel breeding system, based on GM male sterile (MS) and fertility restorer (RF) lines to emulate the natural phenomenon of hybrid vigour.

  The MS *barnase* gene is derived from the bacterium *Bacillus amyloliquefaciens*. The enzyme encoded by this gene prevents pollen production, thus conferring male sterility. The RF *barstar* gene is also derived from *B. amyloliquefaciens* and encodes a protein that inhibits the Barnase enzyme produced in the MS line. Crosses of the MS line with the RF line ensure the production of fertile hybrids. It is this resultant hybrid seed that is employed in agricultural production.

  The MS and RF lines have also been modified to confer tolerance to a herbicide. The herbicide tolerance trait may be used to control weeds in the canola crop. Bayer has sought to have the origin and identity of the herbicide tolerance gene and regulatory sequences declared as Confidential Commercial Information (CCI) under s185 of the *Gene Technology Act 2000.* However, this information was made available to GTTAC and other prescribed expert authorities that were consulted on the preparation of the RARMP.

  The GM canola also contains regulatory sequences that control the expression of the inserted genes.

None of the GM plants or their by-products will be used for human or animal consumption, or as therapeutics.

GTTAC discussed this application and advised the Regulator that the licence conditions imposed for previous canola trials should be considered in the preparation of the RARMP.

Advice on Sugarcane

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

- **Agronomic assessment of transgenic sugarcane engineered with reporter genes (DIR 019/2002)**

  An application has been received from the Bureau of Sugar Experiment Stations (BSES) for a licence for the limited and controlled release (field trial) of GM sugarcane (*Saccharum* hybrid) on one site over a total area of 0.7 ha in the Cairns district of Queensland. The applicant proposes to conduct extensive evaluation and comparison of 60 GM sugarcane lines produced by either a new tissue culture process or by a standard tissue culture process.

  The GM sugarcane would contain three new genes:
  - The *gfp* gene, derived from jellyfish (*Aequorea victoria*), which encodes a reporter protein that acts as a marker to distinguish between GM and unmodified plants.
  - The *nptII* gene, derived from the bacterial Tn5 transposon, which encodes resistance to the antibiotics kanamycin and neomycin and is therefore useful for selecting GM plants in the laboratory.
  - The *bla* gene, derived from the bacterium *Escherichia coli*, which encodes ampicillin resistance. This gene is not expressed in the GM sugarcane and was used to select for bacteria containing the desired genes, in the laboratory, prior to the production of the GM plants.

  Short regulatory sequences that are required to control the expression of the genes are also present in the GM sugarcane.

  None of the GM sugarcane from the trial, or its by-products, would be used as human food or animal feed.

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

  - The likelihood of adverse impacts on human or other species as a result of toxicity or allergenicity of the GM sugarcane is extremely low.
  - Evidence from toxicological and allergenicity studies, together with the low level of expression of the introduced proteins, suggests that the GM sugarcane will not be more toxic or allergenic than conventional sugarcane.
  - The risk of the GM sugarcane establishing and causing harm in the environment is low.
  - Sugarcane itself is not a problematic weed and the introduced genes do not increase the weediness potential of the plants.
  - The likelihood of dispersal of GM sugarcane, through vegetative material, from the release site is extremely low.
  - Expression of NPT II is not likely to have any adverse effect on the rhizosphere.

- Transfer of genes to other sugarcane crops, naturalised sugarcane populations or weedy relatives will be managed by harvesting the sugarcane before flowering.
- The applicant should be asked to prevent public access to the trial site.

Advice on Cholera Vaccine

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

- **Orochol© vaccine (DIR 033/2002)**

  An application has been received from CSL Limited for a licence for the continued commercial release of live GM cholera vaccine (Orochol®). The proposal was previously approved under the former voluntary system.

  Cholera is a disease with an extremely low incidence in Australia. In the last ten years, an average of four cases have been reported annually from across Australia, with the exception of Tasmania, where there has been no reported cases. The majority of these cases involved people who had entered or returned to Australia from other countries.

  Orochol® is a self-administered prescription medicine to immunise people against cholera. Following extensive evaluation of its safety, quality and efficacy, the vaccine was registered as a prescription medicine under the *Therapeutic Goods Act 1989* in April 2000. Since this time, over 60,000 doses have been distributed nationally.

  Orochol® vaccine contains the live bacterium *Vibrio cholerae*. Native cholera bacteria produce a toxin containing 2 subunits, A and B. The GM vaccine strain has been produced by deleting most of the toxic A-subunit gene (*ctx*A) and inserting a mercury resistance operon (*mer*) into the haemolysin gene (*hly*A). The non-active B-subunit of the cholera molecule is still synthesised but it does not cause disease.

  GTTAC discussed this application and advised the Regulator that this proposal posed no risks to human health and safety or to the environment.

Organisms that are not genetically modified organisms

GTTAC was asked for advice on the interpretation of Item 1 of Schedule 1 of the Gene Technology Regulations (the regulations) which reads:

'A mutant organism in which the mutational event did not involve the introduction of any foreign nucleic acid (that is, non-homologous DNA, usually from another species).'

The Committee was asked whether this Item was intended to include organisms created by the introduction of foreign DNA, followed by the subsequent deletion of the foreign DNA along with a gene of interest, resulting in the GM end product containing no foreign DNA.

An applicant had requested advice on whether an attenuated fowlpox vaccine created in the above manner should be classified as a GMO.

GTTAC discussed this issue and concluded that such organisms (missing a copy of a gene) occurred spontaneously in nature and therefore posed no greater risk than the wild type organism.

GTTAC advised the Regulator that:

- Attenuated fowlpox vaccine does not pose a risk to human health or the environment as a result of the genetic modification.
- Item 1 of Schedule 1 of the regulations could be modified as follows: 'A mutant organism which does not contain any foreign nucleic acid (that is, non-homologous DNA, usually from another species)'.

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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