GENE TECHNOLOGY TECHNICAL ADVISORY COMMITTEE

COMMUNIQUE

This is the fourth communique of the Gene Technology Technical Advisory Committee (GTTAC). It covers matters considered at the sixth and seventh meetings of GTTAC held on 30 May 2002 (teleconference) and 27 June 2002 respectively.

GTTAC is a statutory advisory committee to the Gene Technology 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 all applications for licences to conduct dealings with GMOs and comment on the Risk Assessment and Risk Management Plan (RARMP) that is prepared in respect of each application.

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 on those applications and RARMPs.

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

RARMPs for licence applications for Dealings involving the Intentional Release of genetically modified organisms (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 the document.

1. Dealings Not Involving the Intentional Release of Genetically Modified Organisms

1.1 Input to the preparation of, and advice on, RARMPS for DNIRs (in numerical order of receipt)

Meningococcal Virulence Genes (DNIR 025)

GTTAC considered an application from the University of Western Australia for a licence to characterise the function and expression levels of virulence genes of the human bacterial pathogen *Neisseria meningitidis.* GTTAC noted that the OGTR had requested advice from the applicant on the necessity of testing laboratory workers for the presence of the organism. GTTAC accepted that throat swabs would be more likely to identify naturally acquired, as distinct from laboratory acquired, infection and that the risk of acquiring meningococci in laboratories is rare.

GTTAC agreed that the risk assessment identifies 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.

The Mechanisms of Establishing and Maintaining Immunological Memory (DNIR 026)

GTTAC considered an application from the Ludwig Institute for Cancer Research for a licence to investigate the development and maintenance of cytotoxic T lymphocyte (CTL) immunological memory against influenza virus proteins. GTTAC discussed the potential risks posed to laboratory workers by this dealing and agreed that standard PC2 requirements, in conjunction with the use of protective clothing would be adequate to ensure worker safety. GTTAC noted that the applicant had stated that all personnel involved with the dealing would be vaccinated against vaccinia virus.

GTTAC agreed that the risk assessment identifies 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.

Whooping Cough Vaccine IV (DNIR 027)
Whooping Cough Vaccine V (DNIR 028)

GTTAC considered two applications from the University of Southern Queensland. The aim of DNIR 027 is to create a safe non-invasive whooping cough vaccine which will neutralise consequences of the major toxin of *Bordetella pertussis*. The aim of DNIR 028 is to study *Bordetella pertussis* genes which are important in developing immune responses and protection from infection in mice. GTTAC discussed a number of technical issues in relation to these applications but noted that they did not impact on the safety of the proposal.

GTTAC agreed that the risk assessment identifies all the risks associated with the proposed dealing and that the measures proposed in the risk management plan are adequate to deal with the identified risks.

A Drug Screen for Anti-viral Compounds (DNIR 029 & DNIR 030)

GTTAC considered an application from the Australian National University (in conjunction with Biotron Limited) for a licence to screen compounds for their ability to inhibit the human immunodeficiency virus (type 1) budding process. GTTAC noted that the applicant proposed to use standard vectors and methods which were well understood and documented.

GTTAC agreed that the risk assessment identifies 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 vivo analysis of modified myxoma virus for immunocontraception and vaccine development (DNIR 032 & DNIR 034)

GTTAC considered applications from the Commonwealth Scientific and Industrial Research Organisation (CSIRO) and the Australian National University for licences to produce and test recombinant myxoma viruses that could be used in the development of immunocontraceptives and/or vaccines. GTTAC noted that the applicant had stated that expression of the rabbit cytokine IL4 had been shown to increase the virulence of the virus

and requested that the OGTR contact the applicant to provide further information about the proposed use of IL4 in the dealing.

GTTAC further noted that the successful development of this contraceptive could lead to it being used to help control rabbits in the Australian environment. This led to the identification of a number of issues that would need to be addressed in a possible future application for intentional release of the GMO, including the need for controls to prevent the international spread of biological control agents to places where rabbits are native.

GTTAC agreed that the risk assessment identifies all the risks associated with the proposed dealing and that measures proposed in the risk assessment and risk management plan are adequate to deal with the identified risks. However, GTTAC requested that the applicant should be requested to provide further information on the use of the rabbit cytokine IL4 in the dealing.

Mechanisms by which CD44 variant exon 6 promotes disease progression in acute leukemia (DNIR 033)

GTTAC considered an application from the Western Sydney Area Health Service for a licence to investigate the effect of the protein CD44H on the proliferation and survival of leukemic cells in culture and in mice. GTTAC discussed the dangers posed to laboratory workers by this dealing and agreed that standard PC2 requirements, in conjunction with accepted laboratory practices, were sufficient to ensure worker safety.

During discussion of this application GTTAC noted that replication-incompetent retroviruses had been in use for many years and that the history of their use should be well documented. Consideration could therefore be given to having these applications considered in-house by the OGTR. GTTAC further noted that consideration should also be given to including them in a category similar to notifiable low risk dealings when the Gene Technology Regulations 2001 are next reviewed.

GTTAC agreed that the risk assessment identifies all the risks associated with the proposed dealing and that the measures proposed in the risk assessment and risk management plan are adequate to deal with the identified risks.

A replicon-based vaccine for Hepatitis C Virus (DNIR 035)

GTTAC considered an application from the Macfarlane Burnet Centre for Medical Research for a licence to develop a vaccine for Hepatitis C virus (HCV) using a recombinant vaccinia virus. GTTAC discussed a number of technical issues in relation to these applications but noted that they did not impact on the safety of the proposal.

GTTAC agreed that the risk assessment identifies all the risks associated with the proposed dealing and that the measures proposed in the risk assessment and risk management plan are adequate to deal with the identified risks.

A cell culture system for Hepatitis C Virus (DNIR 036)
Replication of GB-Virus and related Chimeras (DNIR 037)

The Macfarlane Burnet Centre for Medical Research has applied for licences to (1) develop a mammalian cell culture system to study Hepatitis C virus (HCV) using recombinant baculoviruses; and (2) to develop a mammalian cell culture system to study HCV using chimerics of HCV and GB viruses. GTTAC noted that while an appropriate facility and procedures were proposed for the dealing, operators should nevertheless be made aware of the potential of chimeric viruses to become more virulent.

GTTAC agreed that the risk assessment identifies all the risks associated with the proposed dealing and that the measures proposed in the risk assessment and risk management plan are adequate to deal with the identified risks.

In vivo testing of immuno-contraceptive effects and species specificity of a recombinant murine cytomegalovirus (MCMV) expressing mouse ZP3 (DNIR 043)

The CSIRO has applied for a licence to test the efficacy and safety of a recombinant murine cytomegalovirus (MCMV) containing a mouse reproductive protein as an immuno-contraceptive in domestic mice and a number of native and exotic rodent species. GTTAC noted that the applicant had made a statement about the ZP3 protein and its ability to alter the host range of the virus that should be supported by further evidence. It did not, however, impinge on the safety of the dealing.

GTTAC agreed that the risk assessment identifies all the risks associated with the proposed dealing and that the measures proposed in the risk assessment and risk management plan are adequate to deal with the identified risks. GTTAC requested that the applicant be asked provide further evidence in support of the statement that the ZP3 protein is unlikely to alter the host range of the virus.

2. Dealings Involving the Intentional Release of Genetically Modified Organisms

2.1 Advice on Oilseed Poppy (*Papavier somniferum*) (DIR 018 and DIR 007)

GTTAC considered two applications concerning the trialing of oilseed poppy in Australia. The CSIRO (DIR 018) has applied for a limited release of GM oilseed poppies on one site over 0.21 hectares in Tasmania. The aim of this proposed release is to determine the effect of a range of genetic modifications on alkaloid metabolism in *Papavier somniferum* under field conditions.

The second application, submitted by the Department of Agriculture Western Australia (DIR 007), is for the limited and controlled release of an oilseed poppy which has been genetically modified by the introduction of a modified gene involved in the alkaloid production pathway, and a gene conferring resistance to the antibiotic hygromycin. The purpose of the proposed release is to identify whether the alkaloid production of oilseed

poppy is altered by the introduction of the genetic modifications. The proposed trial will be carried out on one site in Western Australia covering a total area of 0.2 hectares.

After an extensive discussion of the characteristics of oilseed poppy and the measures proposed to limit the ability of the plant to persist in the environment, GTTAC agreed with the main conclusions of the risk assessment and risk management plan for DIR 007. GTTAC provided the following advice/recommendations to the Regulator with regard to the risk assessment and risk management plan for DIR 007 and the licence application for DIR 018.

Pre harvest

. Although the tight controls on poppy cultivation mean that it is difficult to identify any hazards associated with pollen flow, the isolation zone should remain as 500 metres, as per previous releases for GM oilseed poppy under the Genetic Manipulation Advisory Committee. More data is required to support any reduction in size of the isolation zone.

. Any crop not sexually compatible with oilseed poppy can be grown in the isolation zone provided it does not interfere with monitoring of the GMO and the sighting of volunteers.

. Natural waterways can exist in the isolation zone at a minimum distance of 50 meters from the release site.

. The GMO and fencing should be covered with a bird net to prevent access to birds and animals.

Post Harvest

. The release site should be monitored for a minimum of 3 years as long as the final 12 months are free of volunteers. If not, monitoring should continue until the site has been free of volunteers for 12 months.

. The release site should be lightly cultivated at least 3 times at 3 week intervals during poppy growing season in the first 2 years of monitoring.

. Pasture can be grown at the release site after harvest of the GMO. Grazing animals on pasture at the release site is acceptable as the oilseed poppy is likely to be at the seedling stage and will not be toxic.

. Seed disposal should be done with burning and not deep burial.

. Non-seed material can be disposed of by burial.

Other advice for DIR 018

. The information provided in the application is generally sufficient for risk assessment.

. In addition, the following risks or potential risks should be assessed in relation to the application:

- The impact of recently introduced bumble bees in Tasmania on insect-mediated pollination in oilseed poppy.
- Information on seed dormancy of oilseed poppy available in the literature.

2.2 Advice on Canola (*Brassica napus*) (DIR 010 and DIR 011)

GTTAC considered two risk assessment and risk management plans prepared by the Regulator with respect to the trialing of canola in Australia.

Aventis CropScience Pty Ltd has applied for a licence for the limited and controlled release of genetically modified InVigor® canola into the environment. The male sterility line of the modified canola contains the *barnase* gene conferring male sterility and the fertility restorer line contains the *barstar* gene, which inhibits the enzyme produced in the male sterile line. Crossing of the male sterile line with the fertility restorer line results in hybrids which are fertile. Both the male sterile and fertility restorer lines of the modified canola contain the *bar* gene involved in conferring tolerance to the herbicide glufosinate ammonium.

The purpose of the proposed release by Aventis CropScience Pty Ltd is to evaluate the agronomic performance of the modified canola and to produce seed for future releases both here (subject to further licence applications) in Australian conditions and overseas. The proposed release would be carried out over three years covering a total of 318 hectares of GM canola on 90 different sites, comprising 106 hectares at 30 sites in each year.

Monsanto Australia Ltd has applied for a licence for the limited and controlled release of genetically modified Roundup Ready® canola into the environment. Roundup Ready® canola is tolerant to glyphosate, the active constituent of the proprietary herbicide Roundup®. Roundup Ready® canola has been genetically modified by the introduction of two genes, the CP4 EPSPS and *gox* genes that confer tolerance to the herbicide glyphosate.

The purpose of the proposed release by Monsanto Australia Ltd is to continue development and evaluation of potential commercial lines of genetically modified Roundup Ready® canola, including seed production in preparation for possible commercial release (subject to future licence applications). The proposed release would be carried out on a total area of 34 hectares over 26 sites in winter 2002.

After an extensive discussion of the characteristics of canola and the measures proposed to limit the ability of the plant to persist in the environment, GTTAC provided the following advice/recommendations to the Regulator.

> GTTAC agrees with the main conclusions of the risk assessment and the proposed risk management plan with respect to glufosinate-ammonium and glyphosate tolerant GM canola and the conclusions regarding the potential for gene flow, and the possible impacts of gene flow (and introgression) to related Brassicacious weeds; and the weediness of canola in natural habitats, particularly when the use of glyphosate is considered.
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> GTTAC agrees that the proposed control measures are adequate for this limited and controlled release of GM canola and that no additional isolation from other GM canola trials is required.
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> GTTAC further advises that:
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> (a) For most winter trial releases of GM canola the minimum isolation zone required was 400 metres rather 1 kilometre. A 1 kilometre isolation zone was introduced by

GMAC in relation to summer trial releases of GM canola. Based on the Rieger, M. et al *Pollen Mediated Movement of Herbicide Resistance between Commercial Canola Fields* (2002) data, a one kilometre isolation distance would be unlikely to result in any greater reduction in outcrossing than a 400 metre isolation distance.

(b) The RARMP and the OGTR document *The biology and ecology of canola (Brassica napus)* should be amended to incorporate consideration of the disturbance of natural habitats.

(c) The collection of further information on the efficacy of pollen traps would be beneficial, but the scale of study required to obtain statistically significant data might be practically difficult to achieve.

Enquiries and Risk Assessment and Risk Management Plans

For all enquiries and to obtain copies of Risk Assessment and Risk Management Plans for dealings involving the intentional release of GMOs into the environment please phone the OGTR on 1800 181 030. The Plans are also available electronically from our website at http://www.ogtr.gov.au/publications/riskassessments.htm

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