



26 April 2005

## **EXECUTIVE SUMMARY OF THE RISK ASSESSMENT AND RISK MANAGEMENT PLAN FOR APPLICATION DIR 050/2004**

### **THE DECISION**

On 26 April 2005 the Gene Technology Regulator (the Regulator) issued a licence to the Queensland Government Department of Primary Industries and Fisheries (QDPIF) to conduct a limited and controlled trial of GM BoHV-1 vaccines (the GMOs) in a Physical Containment level 1 (PC1) animal containment facility in Queensland over five years between July 2005 and June 2010.

The *Gene Technology Act 2000* (the Act) and the *Gene Technology Regulations 2001* (the Regulations) set out requirements which the Regulator must follow when considering an application for a licence to intentionally release a genetically modified organism (GMO) into the environment.

For a licence to be issued, the Regulator must be satisfied that the release will not pose any risks to human health and safety or the environment that can not be managed. As part of the evaluation process, Section 51 of the Act requires the Regulator to prepare a risk assessment and risk management plan (RARMP) for each licence application, in consultation with a wide range of expert groups and stakeholders.

Under Section 52 of the Act, the Regulator is required to seek comment on the RARMP from those consulted in its preparation and to invite submissions from the public. Matters raised relating to the protection of human health and safety or the environment are taken into account in finalising the RARMP, which then forms the basis of the Regulator's decision on whether or not to issue a licence, and if so, what conditions to impose.

The Act is designed to operate in a cooperative legislative framework with other regulatory authorities that have complementary responsibilities and specialist expertise. As well as enhancing coordinated decision making, this arrangement avoids duplication. The OGTR liaises closely with other regulators to ensure the identification, evaluation and management of risks that may be associated with the development and use of gene technology.

### **THE APPLICATION**

The Queensland Department of Primary Industries and Fisheries (QDPIF) applied for a licence (application number DIR 050/2004) for the intentional release of up to 19 genetically modified (GM) bovine herpesvirus (BoHV-1) vaccines into the environment, on a limited scale and under controlled conditions. The trial will involve the inoculation of up to 180 cattle in total aged between 4 to 6 months with the approved GM vaccines administered via a nasal drip.

The applicant aims to evaluate of the safety and efficacy of the GM vaccines to protect cattle from primary infection from BoHV-1 and *Bovine viral diarrhoea virus* (BVDV). BoHV-1 can cause infections in both the respiratory and reproductive tracts of cattle, while BVDV is a significant viral disease of cattle in Australia that leads to pneumonia and diarrhoea.

BVDV and BoHV-1 are two of the causative agents of bovine respiratory disease, also known as ‘shipping fever’ which can be initiated as a result of immunosuppression of infected cattle. This can lead to secondary viral or bacterial infections (for example by *Mannheimia haemolytica*) that in turn results in severe pneumonia and death.

The trial will also assess the ability of the vaccines to protect cattle from the development of secondary infections by challenging vaccinated animals with *M. haemolytica* and evaluate the influence of pre-existing immunity to BoHV-1 and BVDV on the efficacy of the vaccines.

The trial will involve groups of cattle being inoculated with the GM vaccines and held in the PC1 animal containment facility for 6-8 weeks. During this time their immune response to the vaccines will be tested. The cattle will shed GM virus for up to 8 days following inoculation and after that time they will be latently infected<sup>1</sup> with the GMOs. Sentinel animals (other cattle, sheep and goats) will be used to investigate the transmission of the virus from infected cattle.

At the end of the test period the cattle will be euthanased in a post-mortem room on site except for 1 or 2 of the groups of cattle that will be moved from the PC1 animal containment facility to designated paddocks on site for a period of 3 weeks before being euthanased. The cattle will be tested to ensure that they are not shedding the GMOs before being placed in the paddocks. During the period in the paddocks data will be collected on the incidence of virus shedding, reactivation and viability in environmental conditions. The carcasses will be stored in refrigeration facilities in the post-mortem room until they are collected and disposed of as clinical waste by incineration in a high-temperature EPA-approved incinerator. Any transport associated with disposal will be in accordance with the OGTR *Guidelines for the transport of GMOs*.

The GM vaccines will be produced by the insertion of one or more of 19 gene constructs that encode either of the envelope (E) glycoproteins<sup>2</sup> E0 and E2 from BVDV into an existing, conventional BoHV-1 vaccine strain V155. This vaccine has been used in over 2 million feedlot cattle with no adverse effects to human health and safety or to the environment being recorded. Some of the GMOs will also contain the commonly used marker gene green fluorescent protein (GFP) from the jellyfish *Aequorea victoria*. The presence of the gene will be used to distinguish vaccinated animals from naturally infected animals. In a number of the GM vaccines the introduced proteins will be localised both on the surface of the GMOs and on the plasma membrane of infected cattle cells.

The insertion of the gene constructs will lead to the production of new fusion proteins within the GM viruses. It is anticipated that these will act in the same way as other therapeutic vaccines *ie.* when animals are inoculated with the GMOs, the fusion proteins will be recognised as ‘foreign’ by the immune system of the cattle and will consequently stimulate the production of antibodies that will protect the cattle from re-infection by BoHV-1 or BVDV.

The development of the GM vaccines will take place in QDPIF’s certified physical containment level 2 (PC2) laboratory facilities. Initial work has been conducted by QDPIF under the licence DNIR 103/2002 and under GMAC proposal numbers 3091 and 4839. The (non-GM) parent organism, BoHV-1 strain V155, from which the GM vaccines will be derived. While there have been no previous releases of these GM vaccines in Australia, a field trial with a similar vaccine was conducted under the former voluntary system that was

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<sup>1</sup> *Latently infected* - An infection that is not active but can be reactivated by certain stimuli (such as stress).

<sup>2</sup> *Envelope glycoprotein* - a glycosylated protein that is located in the envelope of a virus and that is capable of stimulating an immune response.

overseen by the Genetic Manipulation Advisory Committee (GMAC) (see Chapter 1 of the RARMP). There have been no reports of adverse effects on human health or the environment resulting from this release.

## THE EVALUATION PROCESS

A risk assessment and risk management plan (RARMP) has been prepared in relation to licence application DIR 050/2004 from QDPIF in accordance with the Act, the Regulations and the Regulator's *Risk Analysis Framework*. The framework was originally developed in consultation with the public, State, Territory and Australian government agencies, key stakeholders and the Gene Technology Technical Advisory Committee. It has recently been revised in consultation with the same stakeholders in order to more fully explain the OGTR's risk analysis process and is available at <http://www.ogtr.gov.au/pdf/public/raffinal2.1.pdf>.

The revised framework introduces a *Risk Estimate Matrix* (see below) that is used to assess the combination of likelihood and consequence that leads to an estimate of risks to human health and safety and/or the environment that may be posed by dealings with a GMO<sup>3</sup>.

| RISK ESTIMATE MATRIX |                 |            |            |              |          |
|----------------------|-----------------|------------|------------|--------------|----------|
| LIKELIHOOD           | Highly likely   | Low        | Moderate   | High         | High     |
|                      | Likely          | Negligible | Low        | High         | High     |
|                      | Unlikely        | Negligible | Low        | Moderate     | High     |
|                      | Highly unlikely | Negligible | Negligible | Low          | Moderate |
|                      |                 | Marginal   | Minor      | Intermediate | Major    |
| CONSEQUENCES         |                 |            |            |              |          |

Details of the process that the Regulator must follow, including the prescribed consultation process on the application, and the matters that she must consider in preparing a RARMP, are set out in detail in Appendix 6 of the RARMP. The complete RARMP and a set of 'Questions and Answers' on the application can be obtained from the OGTR by calling 1800 181 030 or from the OGTR's website at [www.ogtr.gov.au](http://www.ogtr.gov.au).

The risk assessment considered information contained in the application (comprising: information required by the Act and the Regulations on the GMO; on the parent organism; the proposed dealings, including proposed containment conditions; and potential impacts on human health and safety and the environment), current scientific knowledge, and submissions received during consultation with expert groups and authorities and the public (issues raised in submissions are summarised in Chapter 2 and Appendix 7 of the RARMP).

Through this process, potential hazards to human health and safety or the environment that may be posed by the release of the GMOs were identified. These have been carefully evaluated to determine whether risks might arise, based on the likelihood of each hazard occurring and the likely impact of the hazard, were it to be realised.

<sup>3</sup> A *low* risk is considered to be minimal but may invoke actions for mitigation beyond normal practices. A *moderate* risk is considered to be of marked concern that will necessitate actions for mitigation that need to be demonstrated as effective. A *high* risk is considered to be unacceptable unless actions for mitigation are highly feasible and effective. A *negligible* risk is considered to be insubstantial with no present need to invoke actions for mitigation

Identified hazards that warrant consideration relate to:

### **Human health and safety:**

- **transmission of the GMOs to humans due to an altered host range or mode of transmission:** can the GM BoHV-1 be transmitted to and cause disease in humans as a result of the novel gene products that include a host-range determinant from BVDV?
- **toxicity or allergenicity:** could the GM BoHV-1 be harmful to humans as a result of the novel gene products?

### **Environmental safety:**

- **altered viral characteristics:** could the GM BoHV-1 be more virulent<sup>4</sup> or pathogenic<sup>5</sup> to cattle than the unmodified BoHV-1 as a result of the genetic modifications?
- **persistence and spread of the GMOs in the environment:** could the genetic modifications lead to an increased persistence or stability<sup>6</sup> of the GMOs that may in turn lead to an increased ability of the GMOs to spread to other cattle in the environment and have a significant environmental impact?
- **gene transfer to organisms other than humans:** could there be adverse consequences from the potential transfer of the introduced genes to non-GM BoHV-1, closely related viruses, or to other organisms?
- **toxicity or allergenicity of the introduced gene products to cattle:** could the GM BoHV-1 be harmful to cattle as a result of the novel gene products or because of unintended effects?

The Australian Pesticides and Veterinary Medicines Authority (APVMA) has a complementary regulatory role in respect of this application due to its responsibility for veterinary medicine use in Australia, including the registration of vaccines, under the *Agricultural and Veterinary Chemicals Code Act 1994*. Further information about the APVMA's assessment and approval processes is contained in Chapter 1 and Appendix 4 of the RARMP.

For commercial veterinary products, the normal form of approval is through registration. However, the APVMA may also issue permits allowing restricted use of a veterinary medicine for a limited period of time or for a limited area to enable data relevant to the evaluation of applications for registration (e.g. efficacy of the treatment) to be collected. The APVMA can impose conditions on the use of veterinary medicine in registrations and permits.

The APVMA and the OGTR work closely to ensure thorough, coordinated assessments of parallel applications and, wherever possible, that the timing of decisions by both agencies coincides. The applicant has applied to APVMA for a trial permit for the use of the GM vaccines. The trial cannot proceed until both APVMA and OGTR approvals have been granted.

## **CONCLUSIONS OF THE RISK ASSESSMENT**

The Regulator has concluded that the limited release of these GM vaccines under controlled conditions does not pose significant risks to human health and safety and the environment. The risk assessment of each potential hazard identified above is summarised under a separate heading below.

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<sup>4</sup> *Virulence* – the level of disease caused by an organism

<sup>5</sup> *Pathogenicity* – the ability of an organism to cause disease

<sup>6</sup> *Stability of the GMOs* means the ability of the GMOs to remain viable when exposed to the environment.

## **HUMAN HEALTH AND SAFETY**

### **Transmission of the GMOs to humans due to an altered host range or mode of transmission**

BoHV-1 is an animal virus with a host range that extends to animals of the order *Artiodactyla* (cloven hoofed animals) which includes cattle, buffalo and sheep. BoHV-1 does not infect humans and no human diseases associated with BoHV-1 infection have ever been reported. The only BoHV-1 strains that have been isolated in Australia are from the 1.2b subtype. This subtype has only been isolated from cattle and buffalo and does not infect sheep.

The parent organism of the GMOs to be used in this dealing is a BoHV-1.2b subtype (strain V155). It is registered by APVMA and has been used in Australia over the past 5 years as a vaccine ('Rhinogard') against BoHV-1 infection in feedlot cattle. There are no records of any diseases in humans associated with exposure to the V155 vaccine strain. A limited number of people will be exposed to the GMOs by dealing with the GMOs in a laboratory, by inoculating cattle with the GMOs or by handling cattle infected with the GMOs during the trial. The expression of the introduced genes derived from BVDV genes and *Aequoria victoria* in the GMOs will not alter the host range of the GMOs to enable them to infect humans.

The risk estimate of the hazard of transmission of the GMOs to humans has been assessed as negligible.

### **Toxicity or allergenicity of the GMOs**

As discussed above, humans will be exposed to the GMOs only during handling and inoculation of the GMOs or handling of cattle infected with the GMOs. While BoHV-1 cannot infect humans, aerosols containing viral particles could act as potential airborne allergens. The non-GM parent organism has been used as a cattle vaccine over the last five years and there are no reports of any major allergic responses to the parent organism.

The GMOs will differ from the parent organism by the presence of introduced BVDV proteins or GFP on the surface of the GMOs. Cattle handlers would already be exposed to the BVDV proteins as infection of cattle by BVDV is common. There are no reports of any toxicity or allergenicity to humans from exposure to BVDV. GFP is not considered to be toxic or allergenic to humans. Therefore the risk associated with the toxicity and allergenicity of the GMOs to humans has been estimated as negligible.

The applicant does not intend to use any material from animals inoculated with the GMOs for human or animal consumption.

## **ENVIRONMENTAL SAFETY**

### **Altered viral characteristics**

Changes in viral characteristics such as host range, mode of transmission, virulence and pathogenicity potentially leading to an increased disease burden were considered as hazards to environmental safety. As discussed above, the host range and mode of transmission of the GMOs is not expected to change relative to the parent organism as a result of the expression of introduced BVDV and GFP proteins on the surface of the GMOs.

The virulence of the GMOs is not expected to increase compared to the parent organism. This is because the parent organism, V155, is attenuated<sup>7</sup> relative to other BoHV-1.2b strains.

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<sup>7</sup> *Attenuated* – decreased in fitness (ability to infect, spread and cause disease) relative to another virus

Also, experiments with GMOs that produce the E2 glycoprotein have shown that the virulence of the GM viruses is decreased because the ability of the virus to enter host cells is decreased. Neither GFP nor E0, which will also be expressed in the GMOs, are virulence determinants and are therefore unlikely to increase the virulence of the GMOs.

Expression of the shortened E0 protein may increase the pathogenicity of the GMOs that express this protein. This is because a specific region of the protein may encode a functional enzyme (RNase)<sup>8</sup> that can kill the infected cells. However, in the event that the shortened E0 protein could kill infected cells, this would be no different to the effect observed following infection of cells with the parent organism. Therefore, there is unlikely to be any environmental impact from an increase in pathogenicity of the GMOs that express the shortened E0 protein.

The risk estimate of the hazard to the environment associated with altered viral characteristics has been assessed as negligible.

### **Persistence and spread of the GMOs**

The ability of enveloped viruses such as BoHV-1 to survive in the environment decreases as temperature increases and the lipid envelope is sensitive to environmental factors such as UV light, temperature and moisture. Persistence of the GMOs in the environment could be increased by stabilising the outer envelope. However, the expression of foreign proteins on the surface of the GMOs may decrease the ability of the recombinant viruses to survive in the environment by altering the composition of the viral envelope.

Wild type BoHV-1 persist within cattle by establishing a latent infection in which only the viral nucleic acid is maintained and is localised to nerve cells. During a latent infection with BoHV-1, the only viral gene expressed is one that enables the virus to remain latent within the nerve cells. Because none of the introduced genes that will be expressed in the GMOs encode proteins that are involved in the maintenance of latency, there is not expected to be an increase in viral persistence within animals infected with the GMOs.

Reactivation of the virus would lead to shedding of the GMOs into the environment and the possible spread of the GMOs to other cattle not involved in the trial which may then be moved off-site. Although the cattle that will be moved from the PC1 animal containment facility to test for viral reactivation, are unlikely to be subjected to the level of stress required for reactivation, such as prolonged transport or exposure to immunosuppressive chemicals, viral reactivation is possible. However, any risks posed by the spread of the GMOs beyond the trial site will be managed by ensuring that no cattle infected with the GMOs are moved off site.

The risk estimate of viral reactivation and subsequent spread of the GMOs has been assessed as low. No susceptible animals that are not included in the dealing will be permitted on the site until the results of the trial have been assessed by the Regulator.

### **Transfer of introduced genes to other organisms**

In order to transfer genes to other organisms the GMOs must be able to infect the host cell, the viral nucleic acid must be present in the same area of the cell as the other organism and in general there must be a sufficient amount of homology<sup>9</sup> between the nucleic acids of both organisms.

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<sup>8</sup> *RNase* – ribonuclease, an enzyme that degrades ribonucleic acid (RNA)

<sup>9</sup> *Homology* – Degree of similarity

The host range of the GMOs is unlikely to be different to that of the parent organism because the introduced proteins that will be expressed on the surface of the viruses are not sufficient on their own to change the host range. Hence, they will only be able to infect the same species as the parent organism ie. cattle and buffalo. This will be confirmed by *in vitro* tests of the ability of the GMOs to infect cell lines of other species prior to vaccination and the use of sentinel animals (sheep and goats) within the PC1 animal containment facility.

While other cattle may only be kept on site, subject to testing that demonstrates that the GMOs are unable to be transmitted over short distances, there are no buffalo within infective range of the trial site. Therefore, gene transfer is only likely between the genome of the GMOs and cattle involved in the trial and between the GMOs and that of other viruses that may be circulating in cattle involved in the trial.

Gene transfer between the GMOs and the genome of infected cattle is unlikely to occur because there is insufficient homology between the two genomes to enable gene transfer to occur and no selective advantage is likely to be gained by either host or virus following gene transfer.

The risk estimate for gene transfer between the GMOs and unmodified strains of BoHV-1 and BVDV that may be circulating in the environment was also considered. This has been assessed as negligible because the introduced genes would not confer a selective advantage on BVDV.

Gene transfer between the GMOs and wild type circulating strains of BoHV is possible. However, the risk is assessed as being negligible because cross-interference<sup>10</sup> is likely to prevent the entry and replication of related herpesviruses into cells that are already infected with another herpesvirus.

### **Toxicity and allergenicity of the introduced proteins to cattle**

As discussed above, the host range of the GMOs is unlikely to be different to that of the parent organism. Therefore, the risks associated with toxicity and allergenicity of the introduced proteins are only applicable to cattle and not to any other organism.

The parent organism has been used as a vaccine in feedlot cattle for over five years with no adverse effects, including toxicity or allergenicity, being reported. The virus from which some of the introduced genes have been derived, BVDV, is a common pathogen of cattle. A simultaneous infection of cattle with BoHV-1 and BVDV is common in field conditions. This means that expression of the introduced BVDV genes in conjunction with those of the parent organism is consistent with natural viral infection and is highly unlikely to result in toxicity to vaccinated animals.

GFP has been reported as toxic when expressed at high levels in tissue culture cells. However, these reports are outweighed by other studies which show that expression of GFP has neither toxic nor allergenic effects. Furthermore, when used as a dietary supplement in animals, GFP was found to be neither toxic nor allergenic.

The risk estimate of the hazards of toxicity or allergenicity to cattle from the introduced proteins has been assessed as negligible.

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<sup>10</sup> *Cross-interference* – A mechanism whereby the infection of a cell with a virus interferes or prevents infection of the same cell with a closely related virus.

## **THE RISK MANAGEMENT PLAN (KEY LICENCE CONDITIONS)**

As part of the evaluation process for this licence application, a risk management plan has been developed based on the risk estimate derived from the risk assessment process summarised above. This plan is given effect by the licence conditions. Chapter 2 of the risk assessment and risk management plan provides a tabulated summary of assessment conclusions and corresponding management conditions. Full details of the proposed licence conditions are provided in Appendix 5.

The key licence conditions are outlined below.

### **Transmission of the GMOs to humans due to an altered host range or mode of transmission:**

No conditions have been imposed in relation to the hazard of altered viral characteristics, as the risk estimate has been assessed as negligible.

### **Toxicity or allergenicity of the GMOs to humans**

No conditions have been imposed to manage the hazards of toxicity and allergenicity of the GMOs to humans, as the risk estimate has been assessed as negligible.

### **Altered viral characteristics**

No conditions have been imposed in relation to the hazard of altered viral characteristics, as the risk estimate has been assessed as negligible.

### **Toxicity to non-host organisms**

No conditions have been imposed in relation to the hazard of toxicity to non-host organisms, as the risk estimate has been assessed as negligible.

### **Gene transfer to organisms other than humans**

No conditions have been imposed in relation to the hazard of gene transfer to organisms other than humans, as the risk estimate has been assessed as negligible.

### **Persistence and spread of the GMOs**

The risk to the environment from the persistence and spread of the GMOs has been estimated as being low. Therefore, licence conditions have been proposed which require the applicant to:

- limit the scale of the release;
- conduct the dealing involving inoculation of the cattle with the GMOs in a PC1 animal containment facility;
- hold the cattle in the PC1 animal containment facility until at least 14 days after inoculation with the GMOs;
- restrict access to the facility to authorised persons;
- minimise spread of the GMOs by workers by the use of personal protective equipment such as overalls, gloves and boots and, for those workers inoculating the animals, face-masks;
- decontaminate the trial pens within the PC1 animal containment facility daily for 10 days after inoculation with the GMOs and after each group of infected animals is removed from the facility;

- decontaminate equipment used at the release site;
- treat waste material to inactivate the virus;
- monitor cattle in paddocks for signs of viral reactivation prior to being euthanased; and
- test all cattle in the facility not involved in the dealing for antibodies to the GM BoHV-1 before removal and if positive, euthanase on site.

### **Toxicity and allergenicity of the introduced gene products to cattle**

No conditions have been imposed in relation to the hazard of toxicity to non-host organisms, as the risk estimate has been assessed as negligible.

### **General conditions**

Every licence issued by the Regulator also contains a number of general conditions, which are also relevant to risk management. These include, for example:

- identification of the persons or classes of person covered by the licence;
- a requirement that the applicant allows access to the release site by the Regulator, or persons authorised by the Regulator, for the purpose of monitoring or auditing; and
- a requirement to inform the Regulator if the applicant becomes aware of any additional information about risks to human health or safety or to the environment.

### **Research requirements**

The licence conditions include the requirement that the applicant collect and provide the Regulator with the following information to validate the conclusions of the risk assessment:

- the presence, if any, of antibodies to BoHV-1 or GM BoHV-1 in workers who inoculate the trial animals and/or handle the inoculated cattle;
- the ability of the GMOs to infect, replicate in and express introduced genes on the surface of cell lines from a variety of mammals including humans, sheep, goats, rabbits, mice and monkeys *in vitro*;
- transmission of the GMOs to sentinel animals<sup>11</sup> including cattle and other ruminants such as sheep or goats during the trial;
- any reactivation of the virus in trial animals following release from the PC1 animal containment facility into holding paddocks;
- the persistence and stability of the GMOs in field conditions in experiments carried out within the PC1 animal containment facility; and
- residual levels of introduced proteins in different animal tissues such as muscle, kidney, liver and central nervous system.

### **Identification of issues to be addressed for future releases**

The proposed limited and controlled release is a small scale, single site trial over five years.

Additional information would therefore be required to assess future applications for releases of GM BoHV-1, particularly for larger scale releases of GM BoHV-1, and before approvals for commercial release could be contemplated. Data would need to be provided on:

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<sup>11</sup> *Sentinel animals* – animals that are used to test the host range or mode of transmission of the GMOs

- the expression levels, localisation and distribution of viral or introduced gene products upon reactivation of the virus from cattle by treatment with corticosteroids such as dexamethasone; and
- molecular characterisation of the introduced genetic material.

### **Monitoring and enforcement of compliance by the OGTR**

As well as the legislative capacity to enforce compliance with licence conditions, the Regulator has additional options for risk management. The Regulator can direct a licence holder to take any steps the Regulator deems necessary to protect the health and safety of people or the environment. The OGTR also independently monitors releases that the Regulator has authorised. At least 20% of all field trial sites will be inspected each year, in accordance with a monitoring and compliance strategy based on risk profiling (which takes into account biological, seasonal, geographical and ecological risk factors), to determine whether licence holders are complying with the licence conditions, or whether there are any unintended effects.

### **FURTHER INFORMATION**

Detailed information on the evaluation of the application, including the proposed licence conditions, is available in the risk assessment and risk management plan document for this application, which can be obtained from the website of the Office of the Gene Technology Regulator ([www.ogtr.gov.au](http://www.ogtr.gov.au)), or by calling 1800 181 030 (please quote application number DIR 050/2004).

Copies of the licence application, the RARMP and the licence can be obtained from the OGTR. Please quote application number DIR 050/2004. The RARMP and licence can also be accessed at the OGTR website.

If you have any questions about the application or the evaluation process, please contact the OGTR at:

**The Office of the Gene Technology Regulator**  
**PO Box 100 WODEN ACT 2606**  
**Tel: 1800181030**  
**Fax: 0262714202**  
**Email: [ogtr@health.gov.au](mailto:ogtr@health.gov.au)**  
**Website: [www.ogtr.gov.au](http://www.ogtr.gov.au)**

**Please note that issues such as food labelling, the use of agricultural chemicals and veterinary medicines, and marketability and trade implications do NOT fall within the scope of the evaluations conducted under the Act as these are the responsibility of other agencies and authorities.**

Information about the use and safety of veterinary medicines is available from the Australian Pesticides and Veterinary Medicines Authority (APVMA, [www.apvma.gov.au](http://www.apvma.gov.au)).