Australian Government
Department of Health
Office of the Gene Technology Regulator

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Requirements under the *Gene Technology Act 2000* for clinical trials in humans involving GMOs – Guidance for clinical trial sponsors

This guidance provides basic information to organisations in Australia wishing to conduct human clinical trials involving an experimental product that is, or contains, a genetically modified organism (GMO). Regulatory requirements are imposed under the *Gene Technology Act 2000* (the GT Act) and the Gene Technology Regulations 2001 (the GT Regulations), which are administered by a statutory office holder, the Gene Technology Regulator (the Regulator), supported by the Office of the Gene Technology Regulator (OGTR). Dealing with a GMO without appropriate authorisation under the GT Act is an offence, and subject to penalties.

Before submitting an application to the Regulator or proceeding with a clinical trial involving a GMO, sponsors are encouraged to discuss the details of their particular case with the OGTR, to ensure that the appropriate authorisation is obtained.

Note that clinical trials must also be conducted in accordance with requirements of the *Therapeutic Goods Act 1989*, administered by the Therapeutic Goods Administration (TGA), which apply to both GMOs and non-GMOs. Clinical trials of therapeutic products that are experimental and under development are regulated through the Clinical Trial Exemption (CTX) scheme or the Clinical Trial Notification (CTN) scheme, and require approval from, and oversight by, a human research ethics committee (HREC). Contact the TGA for further information. Additionally if the product is manufactured overseas, an import permit from the Department of Agriculture and Water Resources will be required.

Types of approvals for GMO clinical trials

The type of approval required depends on the nature of the GMO and on its likely fate once introduced into the trial participant, specifically whether or not the GMOs is expected to be transmitted or shed by trial participants, thereby entering the environment.

GM products that do not contain live GMOs (e.g. a purified recombinant protein)

Purified genetically modified (GM) products that do not contain live GMOs, and which cannot give rise to infectious agents when introduced into host cells, are not regulated under the GT Act. No licence or other authorisation from the Regulator is needed for a clinical trial involving such a GM product. However manufacture of a GM product from a live GMO in Australia is regulated and must be appropriately authorised under the GT Act. Please contact the OGTR for guidance for this situation.

Modified human somatic cells

For a GMO that is a modified human somatic cell, including autologous cells, a clinical trial might be classified as an **exempt dealing** under Schedule 2 of the GT Regulations. To be exempt, the somatic cell must not be capable of producing infectious agents as a result of the genetic modification. Additionally, if the cell was modified using a viral vector, the vector must no longer be present in the cell and the cell must not contain viruses likely to recombine with the introduced genetic material.

Exempt dealings don't require further authorisation from the Regulator; the only requirement under the GT Regulations is that they must not involve intentional release of GMOs into the environment.

Sponsors may seek confirmation from the OGTR that their particular experimental product and protocol meet the requirements for an exempt dealing. The TGA may also require confirmation from the OGTR that this is the case, prior to registration. If the modified somatic cell does not meet these conditions, then a licence is required for the clinical trial (see below).

Clinical trials involving other types of GMOs

A clinical trial involving any other type of GMO requires a licence from the Regulator. The category of licence depends on whether or not the GMO is expected to be shed or excreted from trial participants (i.e. is the GMO likely to be contained in the body of trial participants; or are viable GMOs likely to be shed in body fluids or excreta of trial participants, and thereby released into the environment).

If the GMO is not likely to be shed or excreted, a **Dealing Not involving Intentional Release (DNIR) licence** is required. If the viable GMO has the potential to be shed, excreted or transmitted from trial participants, a **Dealing Involving Intentional Release (DIR) licence** is required.

If in doubt about the appropriate category, sponsors should seek advice from the OGTR prior to preparing an application. When screening applications, the OGTR will consider if the application type is appropriate for the GMO and dealings involved. An incorrectly categorised licence application may be rejected or the assessment delayed while clarification from the applicant is sought.

DNA vaccines

Some DNA vaccines are excluded from regulation under the GT Act, while others are not.

If the vaccine is comprised of naked DNA (i.e. the DNA is not coated in a protein, lipid or other structure) and is incapable of giving rise to infectious agents when introduced into host cells, it is excluded from regulation under the GT Act. Sponsors may seek confirmation from the OGTR that their particular experimental product meets these requirements.

If the DNA vaccine is not naked (e.g. it is encapsulated in a lipid coat or other nanoparticle), it will be subject to regulation under the GT Act, and a licence from the Regulator is required for the clinical trial. If no infectious agents will be produced, a DNIR licence is required. If the DNA vaccine has the potential to give rise to GM infectious agents when administered, then a DIR licence is required.

Obtaining a GMO licence

Who can apply for a licence

The GT Act does not restrict who can apply for a licence, however in considering licence applications the Regulator must consider applicant suitability. Licence holders assume certain responsibilities and legal obligations imposed by the GT Act and the Regulator, so licences are usually issued to organisations operating in Australia, such as universities, hospitals or companies. Generally, licence conditions also require the licence holder to be accredited under the GT Act. If an organisation is not already accredited, it is possible to submit an application for accreditation at the same time as an application for a GMO licence. Licence applications must be endorsed by an Institutional Biosafety Committee (IBC) prior to being submitted to OGTR, and IBCs are usually associated with accredited organisations (see below). An application can be endorsed by the IBC of another organisation when the submitting organisation does not have its own IBC. The IBC must have appropriate collective technical and scientific expertise to review the application.

Accreditation and Institutional Biosafety Committees (IBCs)

The process of accreditation assists the Regulator in assessing if the organisation has the resources and the internal processes in place to enable it to effectively oversee work with GMOs, including for the purpose of deciding whether an applicant for a GMO licence is suitable to hold a licence.

Before an organisation can be accredited, it must have established, or have access to, an appropriately constituted Institutional Biosafety Committee (IBC). IBCs are required to comprise a range of suitable experts and at least one independent person.

IBCs provide a quality assurance mechanism, providing advice to assist organisations with the identification and management of the risks associated with GMO dealings, including containment of GMOs. IBCs provide evaluation of low-risk contained dealings that do not require case-by-case consideration by the Regulator (Notifiable Low Risk Dealings), and review GMO licence applications prior to submission to the Regulator to confirm that the information included is complete.

More information about accreditation and IBCs can be found in the *Explanatory Information on the Guidelines for Accreditation of Organisations* and in the Accreditation Guidelines themselves. A list of accredited organisations can also be found on the OGTR website.

When to apply & assessment timeframes

Before a clinical trial can proceed, it must be appropriately authorised under both the *Gene Technology Act 2000* and the *Therapeutic Goods Act 1989*. Each approval process is independent, and can run in parallel. An application for a GMO licence for a clinical trial can be submitted to the OGTR at the same time as seeking approval from an HREC and the TGA (if required).

GMO licence applications must be endorsed by an Institutional Biosafety Committee before being submitted to the OGTR. Once submitted, applications are screened for completeness, and may be rejected if information is lacking.

For **DNIR applications the Regulator has 90 working days** (about 4 ½ months) from the date a completed application is received to make a decision. If the Regulator requests further information from the applicant, days on which the Regulator is unable to proceed while waiting for this information do not count for the purpose of this timeframe.

For **DIR applications the Regulator generally has 150 working days** (about 8 months) to make a decision. As for DNIRs, days on which the Regulator is unable to proceed while waiting for requested information do not count towards this timeframe. However, a longer timeframe will apply if the Regulator finds that the proposed dealings may pose significant risks to people or the environment, or if the DIR application does not qualify as a 'limited and controlled release' application. To qualify as limited and controlled, the application must propose appropriate limits and controls and the primary purpose must be to conduct experiments (see the link below for Overview of the application process).

No application fees

Currently there is no fee associated with applications under the *Gene Technology Act 2000*.

Where can a clinical trial be conducted

While many activities with GMOs are required to be conducted in appropriate physical containment facilities certified by the Regulator, it may not be practicable for clinical trials to be conducted in such certified facilities. The Regulator considers the suitability of proposed facilities for clinical trials as part of the assessment of licence applications.

Generally, standard clinical or hospital facilities, accredited to the National Safety and Quality Health Service (NSQHS) Standards, will be appropriate for administration of the GMO (experimental product). Requirements for collection and analysis of patient samples that are likely to contain the

GMO should also be considered when preparing a GMO licence application, as this activity would also be subject to regulation under the GT Act, and licence conditions may apply. The nature of proposed facilities for all activities involving GMOs should be described in a GMO licence application. This should include indicating any relevant standards and guidelines that apply to particular facilities, such as those under the NSQHS or the National Pathology Accreditation Advisory Council, as this will assist in evaluation of the application.

Further information

Additional information can be found on the OGTR website, including:

- Overview of application process
- Application forms
- Accreditation
- GMO Record

If you require any additional information or clarification, please contact the OGTR by email to ogtr@health.gov.au or free call 1 800 181 030.

DISCLAIMER

The purpose of this document is to provide practical and operational information to organisations and researchers engaged in the relevant field. The information in this document does not constitute legal advice on the interpretation of the *Gene Technology Act 2000*, or other applicable laws. Individuals and organisations should obtain their own legal advice on these matters from an appropriately qualified Australian legal practitioner.