Australian Government
Department of Health and Aged Care
Office of the Gene Technology Regulator

Updated September 2022

Guidance for conducting human clinical trials involving GMOs

Requirements under the *Gene Technology Act 2000*

This guidance provides basic information to organisations wishing to conduct human clinical trials in Australia with an investigational product (IP) that is, or contains, a genetically modified organism (GMO). Such trials involve dealings with GMOs and these activities are regulated under the *Gene Technology Act 2000* (the GT Act) and the Gene Technology Regulations 2001. This regulatory scheme is administered by the Gene Technology Regulator (the Regulator), who is supported by the Office of the Gene Technology Regulator (OGTR). Conducting dealings without appropriate authorisation under the GT Act is an offence, that is subject to penalties.

The advice in this document is based on current regulatory requirements, which may change in the future with advances in gene technology. To ensure the correct authorisation is obtained, sponsors are encouraged to seek advice from an institutional biosafety committee (IBC) and to discuss the application with the OGTR (ogtr.cdes@health.gov.au) before submission.

Human clinical trials involving most types of GMO require a licence

The introduction of a GMO into a person requires a licence from the Regulator, except where the GMO is a human somatic cell meeting specific criteria, outlined below.

Genetically modified human somatic cells

Introduction of GM human somatic cells, including re-introduction of GM autologous cells into the person from whom they were derived, does not require a licence provided:

- the GM somatic cells **cannot secrete or produce infectious agents** as a result of the genetic modification; and
- if the GM somatic cells were modified using a viral vector, they have been **tested for, and found not to contain**, other viruses likely to recombine with the genetically modified nucleic acid, and the viral vector is **no longer present** in the GM somatic cells.

Dealings with GM somatic cells that meet these requirements are classified as 'exempt'. Exempt dealings are regulated under the GT Act but do not require any specific authorisation from the Regulator; the only requirement is that they must not involve intentional release of GMO into the environment. Once the GM somatic cells are in a person, they cease to be regulated under the GT Act. **If the GM somatic cells do not meet the above criteria, then the clinical trial requires a licence.**

If the GM somatic cells are produced within Australia, the production process must be appropriately authorised under the GT Act.

Activities regulated and not regulated under the GT Act

The GT Act regulates dealings (activities) with GMOs. A GMO is defined as *an organism that has been modified by gene technology*, where an organism is *any biological entity that is viable, or capable of reproduction, or capable of transferring genetic material*. This definition is broad and considered to encompass replication defective viral vectors, as well as nucleic acids that can give rise to infectious agents when introduced into a host cell. Investigational products containing nucleic acids with the potential to replicate within a host cell may also be considered GMOs.

The GT Act does not regulate activities with GM products, which are defined as *a thing (other than a GMO) derived or produced from a GMO*. Examples include purified recombinant proteins and killed vaccines. Human clinical trials of GM products do not require authorisation from the Regulator, provided the IP does not contain the GMO used in manufacturing the GM product in a viable form.

Type of GMO licence required

There are two types of licence, authorising either:

- Dealings involving intentional release (DIR) into the environment; or
- Dealings not involving intentional release (DNIR)

For clinical trials, the Regulator considers that intentional release into the environment occurs when the specific mode of administration results in release of the GMO, e.g., administration using an intranasal spray or nebuliser, or when the GMO may be shed, excreted or otherwise transmitted from trial participants to other people or animals over the course of the study. In these cases, a DIR licence is generally required.

Clinical trials that are DIRs are usually licenced as 'limited and controlled' releases. To qualify as a limited and controlled release, the primary purpose of the work must be to conduct experiments and the application must propose appropriate limits on the release of the GMO and controls to restrict its dissemination or persistence in the environment.

Where it is not expected that the GMO will be released into the environment, a DNIR licence is appropriate. Applications will need to include data that supports this conclusion. Note that the Regulator considers some AAV-based gene therapy treatments as eligible for DNIR licencing. Please contact the OGTR for guidance if your application involves an AAV-based GMO.

When screening licence applications, the OGTR will consider whether the application type is appropriate for the GMO and the proposed dealings. Assessment of an incorrectly categorised licence application may be delayed while the OGTR seeks more information from the applicant.

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 a licence application the Regulator must consider applicant suitability. As licence holders assume responsibilities and legal obligations imposed by the GT Act, licences are usually issued to organisations with a legal presence in Australia. For human clinical trials, entities likely to be suitable to hold a licence include an Australian product sponsor, the Australian office of an international product sponsor, a local clinical research organisation (CRO), or a clinical trial site conducting a single-site trial.

Licence conditions generally require the licence holder to be accredited under the GT Act. The accreditation process assists the Regulator in determining whether an organisation has the resources and governance in place to enable it to effectively oversee work with GMOs, including for the purpose of deciding whether an applicant is suitable to hold a GMO licence.

If an organisation is not already accredited, it may submit an application for accreditation at the same time as an application for a GMO licence.

> *Note: individual clinical trial sites involved in a multi-site trial do not need to be accredited.*

Institutional Biosafety Committee (IBC) review

Before an organisation can be accredited, it must have established an appropriately constituted IBC, or made a formal arrangement to access one or more IBCs maintained by other accredited organisations. IBCs must include a range of suitable experts and at least one independent person. They provide advice to assist organisations with the identification and management of risks associated with GMO dealings.

To ensure that the information included is complete, GMO licence applications must be reviewed and endorsed by an IBC before submission to the Regulator. The IBC must have appropriate collective technical and scientific expertise to review the application.

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 is available on the OGTR website.

Assessment timeframes

From the date a complete DNIR licence application is received, the Regulator has **90 working days** (about 4½ months) to make a decision.

From the date a complete DIR licence application is received, the Regulator has **150 working days** (about 8 months) to make a decision. 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.

For both types of application, if the Regulator requests further information from the applicant, the days on which the Regulator is waiting for this information may not count towards the assessment timeframe.

No application fees

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

Clinical trial sites

In general, use of OGTR-certified facilities is not required for clinical trials. The Regulator considers the suitability of proposed facilities (or types of facilities) on a case-by-case basis as part of assessing a licence application. This assessment takes into account:

- the nature of the facilities proposed for each planned activity involving GMOs (e.g., transport, storage, preparation, administration, collection and analysis of participant samples likely to contain GMOs, and waste disposal); and
- any relevant standards or guidelines applying to the type of facility (e.g., National Safety and Quality Health Service Standards for care facilities).

A single licence can authorise a clinical trial conducted over multiple sites, and the licence application may be submitted before site selection is complete. However, applicants must be able to identify the types of facility to be used and describe how the work will be managed and conducted. The sites chosen must also be able to comply with all licence conditions imposed. Licence conditions will generally require that before activities with GMOs commence at each clinical trial site, details of the site are notified to the Regulator and a compliance management plan is provided. This plan must include specifics such as key personnel, reporting structures and staff training. If the site has an IBC, it should be consulted about local arrangements for working with GMOs.

Other regulatory authorisations

Clinical trials in Australia are regulated by the Therapeutic Goods Administration (TGA) under the *Therapeutic Goods Act 1989*. Before a clinical trial commences, TGA requirements must be satisfied, including obtaining approval from a Human Research Ethics Committee. The OGTR does not require that regulatory approvals be obtained in any particular order and these processes can run in parallel to OGTR assessment of a licence application.

If the IP is manufactured overseas, you may require an import permit from the Department of Agriculture, Fisheries and Forestry. This will need to be in place before the GMO is first imported into Australia.

Applicants are responsible for ensuring they are aware of and comply with any other Australian regulatory requirements relevant to the proposed clinical trial.

Further information

Additional information is available on the OGTR website, including:

- Types of GMO dealings
- Overview of the approval process
- Apply for a licence to conduct a human clinical trial of a GMO
- Apply for organisation accreditation

If you require further information or clarification, contact the OGTR by email to ogtr.cdes@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.