

PRODUCTION AND RESEARCH USE OF MEDICINAL PRODUCTS CONTAINING GENETICALLY MODIFIED ORGANISMS FROM THE PERSPECTIVE OF THE GENE TECHNOLOGY ACT

Board for Gene Technology

Introduction

Production of medicinal products containing genetically modified organisms (GMO), their preclinical and clinical trials, as well as experimental treatments with GMO medicinal products are covered by the Gene Technology Act (377/1995), if the GMO in question has not yet been approved for marketing in the EU. Depending on the properties of the GMO and the arrangements in the testing, the activities fall either under the scope of regulations on the contained use of GMOs, or those on the deliberate release of GMOs into the environment for any other purpose than for placing on the market (so called field trials).

For such use in Finland, the operator must submit a notification or application to the Board for Gene Technology (GTLK). The notification or the field trial licence must be valid before commencing the use. The timing for submitting the notification or application to GTLK is independent on licence applications submitted to other authorities. If the GMOs are imported to Finland, the appropriate notification or licence must be in effect before transport.

The notification or application procedure under the Gene technology Act is determined on the basis of the following matters:

- 1) The GMO must be a living organism and meet the definition of a genetically modified organism in section 1 of the Government Decree 928/2004. Please note that there are small differences between the GMO definitions in the contained use and deliberate release legislations (for example regarding self-cloning). If the organism to be used does not meet the GMO definition, or it is not able to reproduce or to transfer genetic material, the activity does not fall under the scope of the Gene Technology Act.
- 2) The activities can be considered as **contained use** if the properties of the GMO and the type of use ensure that there is no release of viable GMOs into the environment.¹ In practice, the production and dispensing of GMOs intended for therapeutic purposes is always contained use. During the clinical trial or when administrating the treatment it is required that:

¹ Under the Gene Technology Act (377/1995), contained use means any activity in which organisms are genetically modified or in which genetically modified organisms are cultured, stored, transported, destroyed or disposed of or used in any other way and for which specific containment measures are used to limit their contact with the general population and the environment and to provide a high level of safety for the general population and the environment.

- the health care personnel are not exposed to infection when handling the GMO preparation, and
- having left the contained premises, the human or animal subjects which have received the preparation are (no longer) able to shed GMOs which are capable of replication and/or infectious.

3) If the risk assessment cannot exclude the possibility of reproductive/infectious GMOs being released into the environment, the clinical trial is considered to be **deliberate release**.

We recommend that any operator planning a trial with a GM medicinal product should contact the secretariat of GTLK before preparing their notification/application in order to determine the correct procedure.

If the activities take place in several premises, it must be considered case-by-case, whether all activities can be included in a single notification/application or whether each participating unit should submit a separate notification.

Clinical trials often involve actors at different levels, which means that it must be considered which of them is the designated operator for the notification/application. We recommend that the party best placed to meet the obligations laid down in chapter 3 of the Gene Technology Act should be selected. In most cases, the designated operator is the company, research institute or hospital that actually carries out the trial. Those appointed as responsible persons should be in a contractual relationship with the party designated as the operator.

When processing the notifications and applications, GTLK focuses on the risks that the activities may pose to the environment and third parties. In other words, the Board assesses potential unintended release of GMOs into the environment and risks affecting personnel and other people or animals. The potential adverse effects of the preparation to be used on human or animal subjects or the assessment of the effectiveness of the preparation fall outside the purview of the Board; instead they are assessed by other authorities and ethical committees in their own authorisation procedures. Therefore, the operator should refrain from submitting to the Board unnecessarily extensive or detailed documents regarding the medical aspects of the trial.

Contained use

The notification procedure for contained use depends on the classification of use based on a risk assessment (classes 1-4). The contained use notification must cover all phases of the GMO activities taking place in the units listed in the notification and all premises where GMOs are handled. In other words, the notification must describe the possible production or storage of the medicinal product containing GMOs, its preparation for use and administration to test animals or patients, as well as the treatment of GMO containing waste.

In contained use, the containment level must correspond to the class of use. The requirements concerning this are described in the Annex to the Ministry of Social Affairs and Health Decree 1053/2005. In small-scale production, the requirements laid down in Table 1

of the Annex are usually sufficient. However, in industrial-scale production, the requirements laid down in Table 4 apply. In animal testing, the requirements laid down in Table 3 must be complied with. Certain containment level requirements may be waived in individual cases with the permission of the Board for Gene Technology.

If the GMOs could be shed from the patient after the procedure, the potential adverse effects arising from shedding must be prevented with containment and protective measures. In such cases, particular attention must be paid to situations in which exposure to third parties or the environment may occur and whether the exposure can be particularly harmful to certain groups, such as pregnant women or immunocompromised persons.

Class 1 or 2 contained use does not require a written decision from the Board for Gene Technology. Class 1 use may be started as soon as the notification referred to in section 14 of the Gene Technology Act has been submitted to the Board. If a Class 1 clinical trial will be conducted in previously notified premises, no new notification is required as long as the record-keeping procedure is followed. However, the risk assessment referred to in section 8 of the Act must be submitted to the Board before commencing the new trial.

Class 2 use may be started 45 days from the submission of the notification, if the contained use premises have not been previously approved for containment level 2 use. As regards class 2, the operator has the possibility to request a written decision from GTLK.

Class 3 use always requires an application and decision on approval by GTLK before the use can be commenced.

The contained use notification must be written in Finnish or Swedish. Only if the persons in charge and their deputies are not able to use either Finnish or Swedish, can the notification be submitted in English.

For the notification form for contained use and for more detailed instructions on the notification procedure, please visit the website of GTLK (geenitekniikanlautakunta.fi).

Field trial (deliberate release for any other purpose than for placing on the market)

Provisions on the deliberate release into the environment for any other purpose than for placing on the market (field trials) are stipulated in Chapter 5 of the Gene Technology Act. The Decree of the Ministry of Social Affairs and Health on the Deliberate Release of Genetically Modified Organisms (1105/2019) contains more detailed provisions on the contents of a field trial application, risk assessment and reporting of the results. The national legislation is based on the Directive 2001/18/EC and the Commission and Council decisions supplementing it. Operators planning field trials should familiarise themselves with the contents of these provisions.

Activities that involve placing of a product on the market cannot be considered as field trials. Marketing means that the GMO product is made available to third parties, whether in return for payment or free of charge.

GTLK must issue its decision within 120 days of receiving the application. The waiting period for any additional information requested by the Board is not included. Therefore, it is recommended that the operator submits their application to the Board at least 4-5 months before the intended start of the field trial.

A public consultation lasting 30 days is held on every field trial application submitted in Finland with the exception of certain specific cases defined by law. The public is informed of the arrival of the field trial application on the website of the Board for Gene Technology, and the application documents (excluding confidential information) are published there. The summary of the application will also be published on the European Commission's website.

An application concerning genetically modified microorganisms must contain the following documents:

- 1) a technical document i.e. the application form available at the website, written in Finnish or Swedish and containing the information required under chapter 3 sections 6-12 of the Decree (1105/2019) of the Ministry of Social Affairs and Health on the Deliberate Release of Genetically Modified Organisms;
- 2) a risk assessment document written in Finnish or Swedish that meets the requirements laid down in chapter 7 of the Decree;
- 3) an English summary of the application (B-SNIF) that the operator submits through the electronic submission platform ESFC. More info on this procedure is provided in the [Commission website](#) and the [ESFC Guidance](#).

It is essential that the operator clearly indicates which information in the application they would like to keep confidential, as laid down in sections 32 and 32a of the Gene Technology Act. Please note that the Act specifically lists information that cannot be considered confidential. All the confidential information should be provided in a separate annex, so that the rest of the application can be made publicly accessible.

The field trial may be started only after GTLK has issued a written permit for it. Every trial is subject to mandatory reporting and possible post-monitoring requirements, which are defined in the terms and conditions of the permit.

All above-mentioned statutes are available in the section “Legislation” of the GTLK website: <https://geenitekniikanlautakunta.fi/en/legislation>.

Guidance on the authorisation procedures for ATMP products containing GMOs (https://health.ec.europa.eu/medicinal-products/advanced-therapies_en) and summaries of all field trial applications in the European Union are also available on the Commission's website. (https://webgate.ec.europa.eu/fip/GMO_Registers/).

For more information, contact the Board secretariat: gtlk@gov.fi