

# Medicinal Products Containing GMOs -Clinical Trials/Studies

## Introduction

According to the Czech legislation on medicinal products, applicants for authorisation to conduct a clinical trial/study involving products containing genetically modified organisms (GMOs) are required to obtain an authorisation for the use of GMOs as specified by the Act No. 78/2004, on the Use of Genetically Modified Organisms and Genetic Products. Such authorisation, issued by the Ministry of the Environment, should either be attached to the documentation on making application to the State Institute for Drug Control (SUKL) for a clinical trial authorisation, or submitted subsequently, however, no later than three days prior to the final outcome of the SUKL assessment process. Should the applicant fail to submit authorisation for the GMOs use by the end of clinical trial assessment process, the application for clinical trial authorisation shall be refused.

- SUKL website on clinical trials: <http://www.sukl.cz/>

## Legislative Framework on GMOs

The Czech Act No. 78/2004, on the Use of Genetically Modified Organisms and Genetic Products, as amended, covers the contained use, deliberate release of GMOs into the environment and placing on the market of GMOs as such or in products, including the export and import thereof. The Act transposes the EU Directives 2001/18/EC, 90/210/EEC and 98/81/EC and complies with the Cartagena Protocol on Biosafety.

Formats of notifications for the use of GMOs, procedure of risk assessment and other requirements are laid down in the implementing Decree No. 209/2004, on Detailed Conditions for the Use of Genetically Modified Organisms and Genetic Products.

- Ministry of the Environment website on GMOs:  
[http://www.mzp.cz/en/environmental\\_risks](http://www.mzp.cz/en/environmental_risks)
- Legislation on GMOs (incl. English translations and format for notifications):  
Acts, Regulations & Guidelines - <http://www.mzp.cz/biosafety>

## State Administration on GMOs

The Competent Authority receiving the notifications and regulating the use of GMOs in the Czech Republic is the Ministry of the Environment (Competent Authority under the EU Directives 2001/18/EC and 90/219/EEC). It co-operates with the Ministry of Health regarding risks for human health and with the Ministry of Agriculture as to agricultural risk, animal health, crops and feeds. The Czech Commission for the Use of Genetically Modified Organisms and Genetic Products serves as the expert advisory body to the Ministry of the Environment. Members of the Commission are representatives of administrative authorities, scientists and representatives of NGOs. The main task of the Commission is the environmental risk assessment of the notified GMOs. The Czech Environmental Inspectorate is the Competent Authority on state supervision of the use of GMOs which co-operates with other state supervision bodies in this respect.

## Authorisation Procedure for the Use of GMOs

**The administrative procedure for authorisation of the use of GMOs is considerably different in case of deliberate release (under the EU Directive 2001/18/EC, Part B: more complicated, takes at least 90 days) and in case of contained use (under the EU Directive 90/219/EEC as amended by 98/81/EC: easier procedure, short).**

As the first step, the company planning the study must decide which path to take, based on the way and conditions of application of the product to humans, metabolism of the product, nature of the GMO, etc. The reason for the chosen procedure has to be described in detail in the notification dossier.

The environmental risk assessment is required as a part of the notification, so it should be provided by the notifier. In case of contained use, the risk assessment results in determination of a risk category (class) of the GMO use which is crucial for the authorisation procedure and for the requirements regarding the contained space.

The notification has to be submitted to the Ministry of the Environment, Department of Environmental Risks, **in Czech language**, both in printed and electronic forms (e-mail or CD ROM). The format of the dossier is prescribed by the Annex 1, Part A of the Decree (the format is also available as a Word document on the Ministry of the Environment – part GMO website). Description of the contained space forms an important part of the notification and consists of the description of the specific hospital / laboratory facilities, where the trial will take place, and the description of the handling of the product – transport, preparation for application, disposal of the unused suspension etc. In case that the dossier includes some documents in English (Annexes to the Risk Assessment

e.g. toxicological studies) a summary of each such document must be provided in the Czech language.

**Important: A separate notification has to be submitted by each institution (hospital) that will participate in the clinical study. Each subject (legal person) that will handle the GM product has to be authorised including the company importing and distributing the product! According to the Czech legislation, authorisation for the use of GMOs may only be granted to a legal person or a natural person authorised to run a business. This means that only a company (affiliate) registered in the Czech Republic is entitled to submit a notification.**

The notifier can refer to data included in other notification of the same study (e. g. hospital can refer to the risk assessment data provided by the producer in its notification).

To prepare the dossier in Czech and for communication with the Czech Authorities during the authorisation process we recommend the notifier to hire a Czech expert as a **professional consultant**. (The professional consultant is required by the Act 78/2004.) The Ministry of the Environment cannot recommend any specific person, but it is advisable to contact the institutions, which are already authorised for the contained use of GMOs. One person could be a professional consultant for all institutions carrying out the clinical trial.

In case of contained use classified as the **first risk category** (lowest risk), the Ministry of the Environment has 30 days to assess the notification and to confirm the authorisation for the use of GMOs. For the **second category** this time limit is 45 days. During this period the Ministry and the Czech Commission for the Use of Genetically Modified Organisms and Genetic Products review the risk assessment and the proper classification of the use. The Ministry is entitled within this time limit to ask additional information from the notifier and/or to require him/her to modify the conditions of the use described in the notification.

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Activities within **class 3 and class 4 of contained use** or **deliberate release** may only commence on the basis of written consent/permission for the contained use issued by the Ministry of the Environment, and only within the scope and under conditions defined. The administrative procedure for granting a consent for contained use is prescribed by the Article 5 of the Act on the Use of Genetically Modified Organisms and Genetic Products and is similar to the procedure for authorisation of deliberate release of GMOs under part B of the Directive 2001/18/EC:

(1) Notification is submitted by the applicant to the Ministry of the Environment (MoE), Department of Environmental Risks, in Czech language, in 4 printed copies and at the same time in electronic form (e-mail or CD ROM). The format of the dossier is prescribed by the Annex 1, Part B to the Decree No. 209/2004 for contained use and the Annex 2, Parts A and B for deliberate release.

(2) Ministry assesses completeness of the notification. If the dossier meets all the requirements pursuant to the Act, the Ministry forwards copies of it to the Ministry of Agriculture and to the Ministry of Health, and at the same time makes the summary of the notification available to the public on the internet and in the municipality of the intended contained use or deliberate release location. The notification, especially the risk assessment, is also reviewed by the Czech Commission for the Use of Genetically Modified Organisms and Genetic Products.

(3) Ministries concerned and the Czech Commission send to the Ministry of the Environment their opinions regarding the notification, including the request for additional information, if appropriate, within 30 days of receiving the dossier. Consequently, the MoE may ask additional information from the notifier. The MoE forwards any received additional information to the Ministries concerned and to the Czech Commission. If the applicant fails to provide the requested information within the set time-period (30 days), the Ministry suspends the administrative procedure.

(4) Everybody may send his/her opinion to the MoE or make comments within 30 days of publication of the summary of the notification. In case of some negative opinion/comment from the public, in which results of environmental risk assessment are doubted or an objection to insufficient protection of the health and the environment is raised, the Ministry of the Environment is obliged to arrange public hearing prior to making a decision.

(5) MoE shall take a decision on the notification within 90 days of receiving the dossier. For the purpose of calculating this time-period, any period of time for completing the notification by the notifier upon request for additional information and the period during which public hearing is organised are not taken into account. However, the public consultation cannot extend the 90 days period by more than 30 days.

(6) When making the decision, the MoE is obliged to consider the opinions of the Ministries concerned and of the Czech Commission together with the results from the public consultation. The MoE can lay down in its decision special conditions for the contained use.

(7) Final decision is made available to the public after its entry into force on the internet and in the municipality of the contained use location.

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The notifier has to pay **an administrative fee** of the CZK 2 000 (approx. 70 EUR) for issuing authorisation for the class 3 and class 4 of contained use, or of the CZK 20 000 (approx. 700 EUR) for deliberate release. The Ministry calls on the notifier to pay the fee shortly before issuing the consent. No fee is paid when the notification is rejected or withdrawn.

### **Confidentiality and Information for Public**

The notifier may indicate certain data in the notification as confidential business information, provided he/she is in the position to give verifiable justification that disclosure of such information might harm his/her competitive position.

Following information cannot be indicated as confidential business information:

- General description of the genetically modified organism
- Identity of the notifier
- Location of the facility and the risk category of contained use, the requirements for the contained space and protective measures for the risk category of the contained use involved
- Risk assessment
- Emergency response plan.

The information indicated as confidential business information is only accessible to:

- State authorities referred in the Act
- Czech Commission for the Use of Genetically Modified Organisms and Genetic Products
- Laboratories carrying out the detection of GMOs for the Ministry of the Environment and the Czech Environmental Inspectorate under contract
- Relevant authorities of other EU Member States
- European Commission.

In case of the first and second risk category of contained use, the Ministry of the Environment makes available only the basic data to the public on the internet: Name and address of the authorised user, GMO(s) used, date of the authorisation and the general emergency response plan.

Public consultation could be a part of the approval process in cases of class 3 and class 4 of contained uses (see above).

### **Risk Assessment**

The risk assessment must be carried out or at least verified by a professional consultant (an expert) of the notifier/user and is submitted by the notifier/user to the Ministry of the Environment as a part of the notification and consequently every 5 years or in case of new information concerning the risks of the use. The notifier/user is obliged to keep records on the risk assessment for at least 10 years from the date of its submission and provide it on request to the competent authorities referred to in the Act.

The result of the risk assessment of contained use is the assignment of such use to one of the four risk categories (classes) defined in the Annex to the Act on the Use of Genetically Modified Organisms and Genetic Products. If the risk assessment has not resulted in the definite assignment of the contained use to a certain class, it is required to carry out such use under the requirements for the higher class. The risk assessment and the classification of contained use provided by the user/notifier are in each case reviewed by the Czech Commission for the Use of Genetically Modified Organisms and Genetic Products as an expert advisory body to the Ministry of the Environment. The assessment and its revisions are based on all available information, references, experience and comparison with relevant non-modified organisms (national and international classification of micro-organisms).

### **Accident and Emergency Plans**

An emergency response plan is defined in the Act on the Use of Genetically Modified Organisms and Genetic Products as a document describing activities and measures carried out in the event of an accident. The detailed requirements for an emergency response plan are laid down by the implementing Decree No. 209/2004.

The emergency response plan has to be submitted to the Ministry of the Environment as a part of the notification for contained use or deliberate release and consequently by the authorised user every 5 years or in a case of new information concerning the risks of the GMOs use. The notifier is obliged to submit the emergency response plan prior to commencement of the use of genetically modified organisms and in the above mentioned cases also to the municipalities where the contained use is to take place, to the fire rescue brigade, to the regional authority and on request also to any persons that may be directly affected by an accident.

The MoE makes the information on emergency response plan available to the public. The scope of such information is laid down by the implementing Decree.

### **Labelling**

The authorisation holder is obliged to ensure proper **labelling**: Packaging of the genetically modified organism must have a visible label clearly stating “genetically modified organism”, in Czech “geneticky modifikovaný organismus” or “this product contains a genetically modified organism” or “this product contains a genetically modified organisms”, in Czech “tento výrobek obsahuje geneticky modifikovaný organismus” or “tento výrobek obsahuje geneticky modifikované organismy”. This text has to appear also in the accompanying documents during the transport. Any further requirements for the labelling laid down in the authorisation decision must be observed.

### **Waste Disposal**

Description of waste management for each facility using GMOs is required in the notification. The key step in disposal of waste from contained use of GMOs is the inactivation of any viable organisms in the waste.

## Import and Export

Only genetically modified organisms or genetic products authorised for **placing on the market** in the EU may be imported or exported to and from the Czech Republic.

Furthermore, the **person authorised for contained use** may import or export GMO to which this authorisation applies, provided that they are exclusively intended for contained use.

The **person authorised for deliberate release** under part B of the Directive 2001/18/EC may import or export genetically modified organisms to which the authorisation applies, provided that they are exclusively intended for the approved deliberate release.

The authorised person that intends to import or to export genetically modified organisms for contained use or deliberate release (see above) is obliged to inform the Ministry of the Environment on the species and amount of genetically modified organisms that will be imported or exported and on the supposed place of entry to or exit from the territory of the Czech Republic, at the latest 5 days before effecting the import or export.

The authorisation holder is obliged to ensure proper **labelling**: Packaging of the genetically modified organism or genetic product must have a visible label clearly stating “genetically modified organism”, in Czech “geneticky modifikovaný organismus” or “this product contains a genetically modified organism” or “this product contains genetically modified organisms”, in Czech “tento výrobek obsahuje geneticky modifikovaný organismus” or “tento výrobek obsahuje geneticky modifikované organismy”. This text has to appear also in the accompanying documents during the transport. Any further requirements for the labelling laid down in the authorisation decision must be observed.

Detailed requirements for import and export documentation etc. are defined in § 25 of the Act 78/2004.

Transboundary movements within the EU (e.g. from France to the Czech Republic) are not considered as export or import. Any transport has to be described in the notification (packaging, way of transport, emergency measures etc.)

The **Cartagena Protocol on Biosafety** is focusing specifically on transboundary movements of living modified organisms (viable GMOs). The Czech Republic as well as the European Union are Parties to the Protocol.

National Biosafety Clearing House of the Czech Republic has been established as an information-exchange system under the Cartagena Protocol where the following information are available:

- Final decisions regarding import to the Czech Republic or release of living modified organisms
- Existing laws, regulations and guidelines
- Summaries of risk assessment or environmental assessment of genetically modified organisms generated by regulatory process, including relevant information on genetic products where appropriate.

Information on GMOs -website of the Ministry of the Environment (legislation, authorisations, guidelines, formats)

<http://www.mzp.cz/en/gmo>

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