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Overview of procedures for submitting an application for clinical trials with GMO-medicinal products for human and veterinary use in Belgium

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Overview of procedures for submitting an application for clinical trials with GMO-medicinal products for human and veterinary use in Belgium

Overall, a clinical trial can only be conducted in Belgium if it satisfies several regulatory/advisory requirements. More details about the Belgian law and its implementation decisions as well as about procedures and application content are available on the web site of the Federal Agency for Medicines and Health Products (FAMHP), chapter clinical trials for human medicines (in English - in Dutch - in French) and for veterinary medicines (in Dutch or in French).

When the Investigational Medicinal Product (IMP) used in a clinical trial is based on a **'genetically modified organism' (GMO)** [1] the clinical trial can only be conducted in Belgium if it also complies with the legislative provisions on biosafety regarding deliberate release of GMOs in the environment and/or contained use of GMOs.

This means that **clinical trials** using GMOs or involving medicinal products containing GMOs have to comply with the Belgian regional regulations on contained use of GMOs and/or pathogenic organisms (Flemish Region - Brussels-Capital Region - Walloon Region) which implement Directive 2009/41/EC (in English - in Dutch - in French) when the full trial or some activities related to the trial, like preparation and administration of the study medication, conservation of study drug… are performed in a 'contained use' facility (e.g. laboratories, hospital rooms or veterinary facilities). The contained use authorization is given by the Regional Competent Authorities, based on a scientific advice given by the SBB[3]. In case the clinical trial cannot be conducted in authorized 'contained use[2]' facilities, it has to comply with Directive 2001/18/EC 'on the deliberate release of GMOs into the environment' (in English - in Dutch - in French) (transposed in the Belgian law by the **Royal Decree of 21 February 2005** (in Dutch and French)) and the authorization is given by the Federal Competent Authority, based on a scientific advice given by the Biosafety Advisory Council[4]

When the clinical trial is covered by the legislation on 'contained use' and there is a risk of possible release of the GMO in the environment a notification under 'deliberate release' will be required, in the opposite case (no risk of release) a '**contained use only**' procedure is sufficient.

Formal advice on the acceptability and conditions under which a human or veterinary clinical trial can be considered eligible or not for the 'contained use only' procedure will be given by the competent authority at the federal level (FAMHP) as a scientific-technical advice based on preliminary information provided by the applicant. Such advice will be given together with the SBB (e.g. on demand of the applicant or upon recommendation of the FAMHP and SBB) depending on the specific nature of the questions for which formal advice is requested prior to Clinical trial application (CTA) submission (i.e. through a joint scientific-technical advice request). All practical information and guidance on how to submit a request for (joint) national scientific-technical advice at the FAMHP can be found on the following website (human medicines: in English - in Dutch - in French; veterinary medicines: In English - in Dutch - in French).

Note:

A 'contained use' authorization is given for a defined 'contained use' activity on a defined site (or facility) for several years . An activity can not only cover a particular protocol but also a whole program of clinical trials, (e.g. phase II and III protocols using one type of vector with one transgene of interest in a determined therapeutic area, etc.) which can be considered equal with regard to biosafety aspects.

A 'deliberate release' authorization can cover a particular gene therapy clinical trial conducted in different sites but also a whole program of clinical trials.

Overview of procedures for submitting an application for clinical trials with GMO-medicinal products for human and veterinary use

(1) An application by the sponsor to the Competent Authority at the federal level (FAMHP)
(2) An application by the principal investigator to the Ethics Committee

More details about the Belgian law and its implementation decisions as well as about procedures and application content are available on the web site of the Federal Agency for Medicines and Health Products (FAMHP)
Links: clinical trials for human medicines and for veterinary medicines (Dutch or French)

Is the clinical trial planned in authorized 'contained use[2]' facilities (e.g. laboratories, hospital rooms or veterinary facilities) ?

Yes ↓

Is there any possible release of the GMO in the environment (GM medication taken at home or risk of shedding, spreading,…) that cannot be avoided by proper management procedures or working practices?

No[§;*] ↓

Yes[§] →

No ↓

(3) An authorization is needed in the frame of the Royal Decree of 21 February 2005 governing the deliberate release of GMOs into the environment (transposing Directive 2001/18/EC (in English - in Dutch - in French).

The competent authority will forward a copy of the dossier to the Belgian Biosafety Advisory Council (BAC) for advice; this dossier will be reviewed by the BAC which transmits its advice to the competent authority at the federal and regional level.

Links: *GMO medicinal products ; application content 'deliberate release'*

(4) A "contained use" authorization is (also) needed in the frame Belgian regional regulations on contained use of GMOs and/or pathogenic organisms

A notification of the clinical trial by each participating "contained use" facility according to the "contained use" procedures is requested. ***It is recommended to complete the biosafety dossier with the clinical trial protocol to provide extra information for proper risk assessment.***

Links: *website: contained use of GMOs and pathogens ;*
'contained use' procedure (Flemish Region - Brussels-Capital Region – Walloon Region)

§. Formal advice on the acceptability and conditions under which a clinical trial can be considered eligible or not for the 'contained use only' procedure can be given by the competent authority at the federal level (FAMHP) as a scientific-technical advice based on preliminary information provided by the applicant.

* Even if a "contained use only" procedure is allowed, the notifier can always decide to go for an additional 'deliberate release' notification

Note: "contained use" and "deliberated release" procedures can run in parallel but "deliberate release" authorization is mandatory before authorization under contained use.

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[1] means an organism, with the exception of human beings, in which the genetic material has been altered in a way that does not occur naturally by mating and/ or natural recombination (Directive 2001/18/EC)

[2] 'contained use' means any activity in which micro-organisms are genetically modified or in which such GMMs are cultured, stored, transported, destroyed, disposed of or used in any other way, and for which specific containment measures are used to limit their contact with, and to provide a high level of safety for, the general population and the environment (Directive 2009/41/EC). e.g. laboratories, veterinary facilities or a hospital rooms.

[3] SBB or Biosafety and Biotechnology Unit a multidisciplinary group of scientists (mostly postgraduates) performing scientific expertise in the field of biosafety. As part of a Federal scientific Institute, the SBB holds an independent position with regard to expertise in Biosafety, accessible to any public or private organization. Upon request, one can appeal to the SBB expertise for public information and education, technology demonstration or discussion forums. The SBB is also technical expert for the competent authorities. As centre of expertise in Biosafety, the SBB advises the Federal and Regional competent authorities about biosafety-related contained use matters

[4] The Biosafety Advisory Council is one of the two pillars (with the Biosafety and Biotechnology Unit - SBB) of the common scientific evaluation system that has been set up in Belgium to advise the competent authorities about the safety of activities involving genetically modified organisms (GMOs) and/or pathogens, including genetic and ecological aspects related to biodiversity. The Council consists of representatives of the Regional and Federal authorities. It is assisted by experts in its scientific work. The secretariat of the Council is ensured by the SBB. http://www.bio-council.be/