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

In general, 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 website of the Federal Agency for Medicines and Health Products (FAMHP), chapter clinical trials for human medicines and for veterinary medicines (Dutch or French).

When the Investigational Medicinal Product (IMP) used in a clinical trial is based on a ‘genetically modified organism’ (GMO) the clinical trial can only be conducted in Belgium if it also complies with the legislative provisions on biosafety regarding deliberate release of GMO’s in the environment and/or contained use of GMOs and the protection of workers exposed to biological agents at work.

This means that clinical trials using genetically modified organisms or involving medicinal products containing GMOs have 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)) when the clinical trial cannot be conducted in authorized ‘contained use’ facilities (e.g. laboratories, hospital rooms or veterinary facilities). In the case 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, the clinical trial has to comply with the Belgian regional regulations on contained use of GMO’s and/or pathogen organisms (Flemish Region - Brussels-Capital Region - Walloon Region) which implement Directive 2009/41/EC (in English - in Dutch - in French) and the notifier is obliged to send additionally a ‘contained use’ dossier to the technical expert of the SBB.

When the clinical trial is covered by the legislation on ‘contained use’ and there is no risk of possible release of the GMO in the environment a notification under ‘deliberate release’ will not be required and a ‘contained use only’ procedure is sufficient. The decision on whether or not to accept a clinical trial under ‘contained use only’ procedure is taken on a case-by-case basis by the competent authority at the federal level (FAMHP), based on preliminary information provided by the notifier and after consultation of the SBB and Agency.

Note:

A ‘contained use’ authorization is given for a defined ‘contained use’ activity on a defined site (or facility) for several years (e.g. 5 years). An operation/activity can not only cover a particular protocol but also a whole program of clinical trials.

A ‘deliberate release’ authorization can cover a particular gene therapy clinical trial conducted in different sites but also a whole program of clinical trials. This program may integrate several protocols of the same kind (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.
Overview of procedures for submitting an application for clinical trials with GMO\(^1\)-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?

Yes\(^8\)

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; ‘deliberate release’ procedure

No\(^\$\star\)

(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)

\(^\$\) A case by case decision by the competent authority at the federal level based on preliminary information provided by the notifier and after consultation with the SBB and Agency. This decision does not exempt to apply a dossier under the scope of the Belgian regional regulations on contained use of GMO’s and/or pathogen organisms.

\(^\$\star\) 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.
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: Biosafety and Biotechnology Unit, technical expert for the competent authorities