Medicinal Products for Human Use - BELGIUM

Competent authority

Contact Details

Contact Name 1

Federal Agency for Medicines and Health Products (FAMHP) / Agence Fédérale des Médicaments et des Produits de santé (AFMPS) / Federal Agentschap voor Geneesmiddelen en Gezondheidsproducten (FAGG)

Contact Name 2

Research and Development division (R&D division)

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Email Department

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Address

Eurostation II - Victor Horta Place 40/40

ZIP/City

1060 Brussels

Country

Belgium (BE)

Web address

http://www.fagg-afmps.be/en/famhp/

Additional Information

Belgian Center for Pharamcovigilance for medicines for Human use (BCPH): vig@fagg-afmps.be

The FAMHP- AFMPS-FAGG acts on behalf of the minister as competent authority.

Trial Authorisation / Registration / Notification

Regulatory and ethics bodies involved in approval process

Competent Authority/-ies (CA)
Ethics committee(s)
Agency for data protection

CA - Submission for authorisation mandatory for

Clinical IMP trials

CA - Registration/ notification without approval required for

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CA - Submission required to

National CA

Specific Competent Authority for ATMP trials in place

No

Additional Information

NB! Specific provisions apply for non-commercial experiments as specified in Chapter XIX Art 31 Law 7 May 2004 (e.g. waiver of application and remuneration fees).

Submission of Application

Responsible for study submission

Sponsor

Entitled to study submission

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Prerequisites for submission

–

Guidance on submission of application

Detailed guidance for Clinical Trial submission is provided on the FAMHP site (section: Human medicines > Medicines > Medicines > Research & Development > Clinical trials) in the following documents:
1) Detailed Guidance CT1: Detailed guidance for the request for authorisation of a CT on a medicinal product for human use
2) Circular 575 + annexes: Application for clinical trials and submissions of substantial amendments.

Applicable national legal framework/ Reference

Chapter IX Art 12 (1) Law 7 May 2004

Submission Format

Format option(s)

Full electronic file and a hard-copy cover letter

Preferred format

–

Guidance on submission format available

Yes

Guidance on submission format

Circular letter no 575 + annexes provides guidance on submission format and required documentation of the application.

Language of Submission

Language(s) of application

Dutch
French
German
English

Preferred language of application

English

English accepted

–

Documents mandatory to be in official national language

–

Additional Information

The document for patient consent must be written in the language of the patients (French, Dutch or German).

Submission Fees

Fees for trial submission mandatory

Yes

Fees

Each Clinical Trial Application (CTA) must be accompanied by payment of a fee.

The fees applicable in 2015 are provided in Circular 616 and are as follows:

• Complete new application file: € 3672,23.-
• Substantial amendment: € 604,63.-
• Annual Safety report: € 655,02.-

Waiver for academic (non-commercial) studies possible

Yes

Official guidance on required fees

Circular letter 616: provides the current fees for 2015
A circular letter with the exact amounts and specificities is published each year and is available on the FAMHP website in section: Human medicines > Medicines > Herbal medicinal products > Research and Development > Clinical trials

Additional Information

NB: No fees are charged for non-commercial, academic studies (pursuant to Chapter XIX Art 31 (5) Law 7 May 2004).

Timelines Authorisation

General timespan (max nr days)

15 (for monocentric Phase I trials)
28

Mode of approval (General)

Tacit (Silent)

ATMP/GMO trials (max nr days)

+ 30
(up to 90 days if the Belgian Biosafety Advisory Council has to be asked for advice)

Mode of approval (ATMP/GMO trials)

–

External expert advice required (max nr days)

–

Xenogeneic cell therapy (max nr days)

No time limit

Mode of approval (Xenogeneic cell therapy)

–

Clock-stop possible if complementary information requested

Yes

Timespan counted from

–

Additional Information

The order of submission to the EC and CA is not defined. The trial cannot start until both instances have given a positive reaction.

In case of questions to the applicant: One clock-stop of maximum one month for supplementary information is possible

Amendments/ Substantial Amendments (SA)	**Notification mandatory for** – **Authorisation mandatory for** Any substantial amendments **Responsible for submission of SA** Sponsor **Timeline for approval of SA (max nr days)** 28 15 (for monocentric Phase I trials) **Guidance on submission of SA** Further details on submission of amendments are specified in Circular 575 + annexes: 'Application for clinical trials and submissions of substantial amendments' (available on the FAMHP website in section: Human medicines > Medicines > Herbal medicinal products > Research and Development > Clinical trials) **Applicable national legal framework/ Reference** Chapter X Art 19 Law 7 May 2004
Safety Reporting	**Responsible for AE reporting to CA** Sponsor **Sponsor must declare reportable events to** Competent Authority Relevant EC(s) **Reportable AEs** SAE (Serious Adverse Event) SUSAR (Suspected Unexpected Serious Adverse Reaction) **SUSAR being life-thereatening or leading to death must be reported** Within a max of 7d upon first knowledge (+ 8d for additional information) **All other SUSARs** Within a max of 15d upon first knowledge **SAE /SADE must be reported** – **National standard reporting form available** – **Reporting format - Options** – **Preferred format** – **Provision of Annual safety report mandatory** Yes **Annual safety report shall be provided by sponsor to** National CA Relevant EC(s)

Guidance on AE reporting procedure available

Yes

Guidance on AE reporting procedure

Details on submission procedures are given in Circular n° 593 and Circular n° 586, provided on the FAMHP website in section: Human medicines > Medicines > Medicines > Research & Development > Clinical trials

Applicable national legal framework/ Reference

Chapter XV + XVI, Art 27 +28 Law 7 May 2004

Additional Information

The Belgian Centre for Pharmacovigilance for medicines for Human use (BCPH), that is part of the FAMHP, is responsible for the coordination of the different tasks related to pharmacovigilance.

Investigator shall report SAE to

Sponsor

Reporting timeline

Immediately

End of Trial

End of trial declaration mandatory for

All clinical trials requiring authorisation by CA

Responsible for End of trial declaration

Sponsor

Regular Termination - Declaration timespan (max nr days)

90

Timespan counted from

–

Early/premature Termination - Declaration timespan (max nr days)

15

Reasons for early termination shall be clearly stated

Yes

Applicable national legal framework/ Reference

Chapter XI Art 21 Law 7 May 2004

Ethics committee

Contact Details

Contact Name 1

Recognized local Ethics Committees (currently 24)

Contact Name 2

List and contact details provided on FAMHP- AFMPS-FAGG website

Web address

http://www.fagg-afmps.be/en/human_use/medicines/medicines/research_development/ethic_committee/

Ethical Review – General

Submission for Ethical review mandatory for

Clinical IMP trials
Clinical ATMP trials

Submission to CA and EC to be performed in the following order

In parallel
Sequentially (in any order)
Order of submission not defined

Additional Information

Circular 619 (08/04/2015) (french version): Provides a list of Ethics Committees having full accreditation status according to the law dated 7th May 2004 related to experiments on human people.

Regulatory and ethics bodies involved in approval process

Competent Authority/-ies (CA)
Ethics committee(s)
Agency for data protection

Single-Centre Studies - Ethical Review

Ethical approval (favourable opinion) to be obtained from

Local EC linked to the trial site

Additional Information

The opinion has to be issued by an EC with full accreditation status (Apr 2014- Apr 2018: n=24 - Status 2015)

If the EC linked to the site has not been awarded full accreditation, but only partial accreditation status, the sponsor of the research project designates a committee with the required status to be authorized to issue a single opinion.
The EC with partial accreditation, linked to the site where the study will be conducted, should issue an opinion on the competencies of the researcher, the appropriateness of the facility and the adequacy and completeness of the patient information materials.

Multi-Centre Studies - Ethical Review

Ethical approval (favourable opinion) required from

Lead EC (authorised to issue a single opinion)

Submission of application required to

Lead EC + All concerned local ECs for site-specific assessment

Additional Information

The formal opinion should be issued by one of the ECs with full accreditation status (see Circular).

The situation in the hierarchy (Academic Hospital ECs authorised to issue a single opinion > Non- Academic Hospital ECs authorised to issue a single opinion > Hospital ECs not authorised to issue a single opinion) will guide the sponsor in his choice of the leading EC (LEC) to issue the single opinion for the multi-centre research project.

The LEC reviews the experiment and issues a single opinion on the trial protocol considering all the aspects of the trial. The other “non-leading” ECs (n-LEC) send remarks to the LEC on the following aspects of the trial: suitability of investigator, suitability of facilities, Informed consent form.

Submission of Application

Responsible for study submission

Principal Investigator
Sponsor (EC selection)

Entitled to study submission

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Prerequisites for submission / approval

–

Additional Information

Multi-centre trials: Submission to the Lead EC and non -Lead EC has to take place in parallel.

Submission Format

Format option(s)

Depends on the EC concerned

Preferred format

–

Standard application form available

No

Additional Information

No details provided.

Language of Submission

Language(s) of application

Dutch
French

Preferred language of application

–

English accepted

Yes

Documents mandatory to be in official national language

–

Submission Fees

Fees for Ethical review mandatory

Depends on request

Waiver for academic (non-commercial) studies possible

Yes

Fees for Ethical review

Research ECs charge fees for trials with a commercial sponsor as fixed by the Royal Decree of 15 July 2004, but they are subject to an indexation each year (e.g. in 2015: fixed fees given as follows + 25 % approximately):

1. Interventional studies:
• Initial evaluation: single opinion committee: €1000.-; other committees: €300.- (local advice only).
• Amendments: €250.- to the EC that gave the single advice.
2. Non-interventional studies:
• Initial evaluation: single opinion committee. €400; other committees: €100 (local advice only).
• Amendments: €100 to the EC that gave the single advice.

No fees for non-commercial, academic trials are charged.

Applicable national legal framework/ Reference

Royal Decree of 15 July 2004

Additional Information

Moreover, the committees receive each year a certain amount of money from the CA : 75 % of the fees paid by commercial sponsors to the CA should be redistributed to the EC. This redistribution is done on the basis of the number of trial protocols evaluated by each committee- further details on the particular procedure is provided in the latest circular “Pending payments for ethics committees”, available on the FAMHP website in section Ethics committee.

Timelines Ethical Review	**General timespan for single-centre studies (max nr days)** 28 15 (for monocentric Phase I trials) **General timespan for multi-centre studies (max nr days)** 28 **ATMP/GMO trials (max nr days)** + 30 (up to 90 days if the Belgian Biosafety Advisory Council has to be asked for advice) **External expert advice required: Timespan (max nr days)** – **Xenogeneic cell therapy: Timespan (max nr days)** No time limit **Clock-stop possible if complementary information requested** Yes **Timespan counted from** – **Applicable national legal framework/ Reference** Chapter VIII Art 11 Law 7 May 2004 **Additional Information** The ethics committee has to give a written reply and submits a copy to the CA. ad multi-centre trials: Lead -EC delivers opinion within 20 days to local ECs of participating sites, local ECs have 5 days to respond to Lead -EC, Lead-EC has 3 days to issue final single opinion to investigator.
Amendments/ Substantial Amendments (SA)	**Ethical review mandatory for** Any substantial amendments (concerning investigator, trial site, informed consent) **Responsible for notification of SA** Investigator **Timeline Ethical review of SA (max nr days)** – **Guidance on submission of SA** Circular letter 575 provides guidance on the submission and characterization of amendments to the EC (available on the FAMPH website in section: Human medicines > Medicines > Herbal medicinal products > Research and Development > Clinical trials) **Applicable national legal framework/ Reference** Chapter X Art 19 Law 7 May 2004 **Additional Information** The investigator must notify the EC concerned on the content and reasons of any substantial amendments planned
Safety Reporting	**Reportable AEs** SAE (Serious Adverse Event) SUSAR (Suspected Unexpected Serious Adverse Reaction) occurring in the respective country

	Investigator shall report SAE to Sponsor **Reporting timeline** Immediately **Responsible for AE reporting to relevant EC(s)** Sponsor **SUSAR being life-thereatening or leading to death must be reported** Within a max of 7d upon first knowledge (+ 8d for additional information) **All other SUSAR must be reported** Within a max of 15d upon first knowledge **SAE/SADE must be reported** – **National Standard Reporting form available** – **Reporting format - Options** – **Preferred reporting format** – **Provision of Annual safety report mandatory** Yes
End of Trial	**End of trial Declaration mandatory** Yes **Responsible for End of trial Declaration** Sponsor **Regular Termination - Declaration timespan (max nr days)** 90 **Timespan counted from** – **Early/premature Termination - Declaration timespan (max nr days)** 15 **Reasons for early termination shall be clearly stated** Yes **Applicable national legal framework/ Reference** Chapter XI Art 21 Law 7 May 2004
Additional Information & Specifics	**Additional Information** The Belgian Advisory committee on Bioethics and Ordre de Médecins provide useful information regarding ethical aspects and general issues. .

Study specific Requirements

Sponsor	**Sponsor - Definition (pursuant to national law)** The sponsor who is an individual, company or organisation takes responsibility for the initiation, management and /or financing of a clinical trial. (Definition pursuant to Art 2(21) Law 7 May 2004) Several tasks can be delegated by the sponsor to the (coordinating) investigator by contract, but not the legal responsibility.
Study Participants - Informed Consent (IC)	**Standard IC form (ICF) available** Yes **Standard IC form (ICF)** For the purpose of simplification, harmonization and better information to the patient, Belgian ECs developed 4 different validated templates for informed consent (see Circular n° 604) 1. A basic model for interventional clinical trials on adults capable of autonomy, 2. A specific introduction for the inclusion of a participant with consent of a legal representative, 3. A specific introduction for the inclusion of a participant in an emergency situation, 4. A basic model for non-interventional studies on adults. All four templates can be downloaded at the FAMHP website under section: Human medicines > Research & Development > Ethic Committee >Templates for informed consent. **Standard ICF - Additional Information** The templates for informed consent have been published in August 2013, they will be re-evaluated after an evaluation period in the presence of all Ethics Committees with a complete recognition. **IC is regulated by law** Yes **Informed Consent - Definition/ Requirements** Participants must give their free and informed consent before the commencement of a trial (according to the provisions specified in Chapter III Art 6 of Law 7 May 2004) **Applicable national legal framework/ Reference** Chapter III Art 6 of Law 7 May 2004
Study Participants - Vulnerable Population	**Minors / Children - Studies allowed** Yes Special provisions apply **Legal framework/Reference (Minors/Children)** Chapter IV Art 7 of Law 7 May 2004 **Incapacitated persons - Studies allowed** Yes Special provisions apply **Legal framework / Reference (Incapacitated persons)** Chapter V Art 8 Law 7 May 2004 **Emergency situations - Studies allowed** Yes Special provisions apply **Emergency situation without prior consent of patient or proxy - Studies allowed** Yes Special provisions apply

Conditions allowing trial participation in emergency setting without prior consent

1° the experiment relates directly to a clinical condition from which the subject, whose consent cannot be obtained due to emergency, suffers and which is life threatening or which can lead to serious and permanent injuries; the experiment is essential to validate data obtained in experiments on individuals capable to give informed consent or by other research methods;
2° the experiment has been designed to minimize pain, discomfort, fear and any other foreseeable risk in relation to the disease and developmental stage; both the risk threshold and the degree of distress shall be specially defined and constantly monitored;
3° the risks taken by the subject....are not disproportionate in relation to the benefit expected for that individual;
4° the positive opinion on the protocol is given by an ethics committee...;
5° no incentives or financial inducements are given with the exception of compensation;
6° the investigator shall respect the requirements referred to in Article 6 with regard to the subject as soon the individual regains the capacity to consent, or with regard to his representative, as referred to in Articles 7, 1° and 8, 1°, as soon as it is possible to contact him.

Legal framework / Reference (Emergency Situation)

Chapter VI Art 9 Law 7 May 2004

Pregnant or breastfeeding women - Studies allowed

No national legal framework available

Specific provisions

There are no explicit provisions for pregnant or lactating women mentioned in Law 7/2004.

Study Participants - Recruitment & Trial Outcome

Mandatory to inform participant of clinical trial outcome

Yes

Data Protection

Notification to DP Authority/ Ombudsmann is mandatory

Yes

Specific notification timelines before operations start

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Language of notification

Official National Language(s)

Notification format

Paper hardcopy
Electronically

Notification fee required

Yes

Fee

25€ (electronically), 125€ (paper version)

Guidance on notification requirements available

Yes

Guidance on notification requirements

Further details on the declaration procedure are provided on the Commission’s website in section “Privacy topics” (in French or Dutch only).

Data Protection Authority/ Agency - Contact Details

The Commission for the Protection of Privacy (CPP)

Contact Name 2

“The Privacy Commission”

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E-Mail

commission@privacycommission.be

Web address

https://www.privacycommission.be/en

Address

Rue de la Presse 35

ZIP/City

1000 Brussels

Country

Belgium (BE)

Additional Information

Clinical Trials must comply with data protection rules as specified in the Belgian Data Protection Act and its implementing Royal Decrees provided on the CPP website.

Legal framework (on safeguarding the collection, handling, recording, keeping and/or processing of any clinical trial related data and patient files)

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Insurance

Liability insurance or alternative arrangements for damages mandatory for

Study participants

Responsible for covering insurance

Sponsor

Applicable national legal framework/ Reference

Chapter XVII Art 29 Law 7 May 2004

Additional Information

A no fault liability insurance for participants is mandatory.

National legislation

General Information: Applicable Legislation & Conventions

Official website providing relevant national legislation available

Yes

Official website providing relevant national legislation

A comprehensive overview on the applicable legal texts (laws, Royal decrees, Circulars) including corresponding links is provided on the FAMPH website in section: Human medicines > Medicines > Herbal medicinal products > Research and Development > Clinical trials (Legal texts).

Clinical Trials on IMPs in Humans	**Applicable national regulations** Transposition of (CT) Directive 2001/20/EC Other **Transposition of (CT) Directive 2001/20/EC (or comparable national legal framework)** Law of 7 May 2004 relating to experiments on human people (Loi relative aux expérimentations sur la personne humaine). This law (“Law 7 May 2004”) is the transposition of the Directive 2001/20/EC into national legislation, but also applies to any other research, such as gene therapy. It has been modified several times and is only available in French and Dutch. **Applicable to ATMP/ GMO trials** Yes **Transposition of (GCP) Directive 2005/28/EC** – **Other applicable regulations/ implementing provisions (Acts, laws, decrees, ordinances, circulars, etc)** Other applicable legal texts (laws, Royal decrees, Circulars) including corresponding links is provided on the FAMPH website in section: Human medicines > Medicines > Medicines > Research & Development > Clinical trials (Legal texts)
Gene Therapy	**Specific requirements** Yes **Applicable legal framework** (1) The Law of 7 May 2004 concerning experiments on humans (Loi relative aux expérimentations sur la personne humaine/Wet inzake experimenten op de menselijke person) (see: Law of 7 May 2004, French version (consolidated version) and unofficial translation: Law of 7 May 2004, English version). Art. 13 § 3 and § 4, Art. 11 § 10 and § 11 and Articles 17 and 18 contain special provisions regarding gene therapy. (2) As a matter of principle Good Manufacturing Practice (GMP) is required for the manufacture of medicinal products for human use. The EC-GMP-Guideline covers this issue. **Additional Information** Due to the fact that gene therapy medicinal products are covered by the Law of 7 May 2004, the legal procedure is generally the same as for medicinal products for human use. Any specific requirements are indicated in the applicable sections.
Data Protection	**Legal framework (on safeguarding the collection, handling, recording, keeping and/or processing of any clinical trial related data and patient files)** National Data Protection Act **National DP act** Law of 8 December 1992 on Privacy Protection in relation to the Processing of Personal Data (“The Privacy Act”). **Implementing decrees / ordinances** The Privacy Act and its implementing Royal Decrees are provided in various languages on the website of the Privacy Commission in section Legislation and Standards.

Definition

IMP/IMP Study	**IMP - Definition available in national law** Yes

IMP - Definition

The investigational medicinal product is a pharmaceutical form of an active substance or placebo being tested or used as a reference in a clinical trial, including products already with a marketing authorisation but used or assembled (formulated or packaged) in a way different from the authorised form, or when used for an unauthorised indication, or when used to gain further information about the authorised form.
(pursuant to Art 2 (19) Law 7 May 2004)