Medicinal Products for Human Use - LUXEMBOURG

Competent authority

Contact Details	**Contact Name 1** Ministry of Health **Contact Name 2** Division of Pharmacy and Drugs - Division de la Pharmacie et des Médicaments DPM **Contact Name 3** Sécretariat Médicaments à usage humain: **Phone** +352 247-85592 / 96 **Fax** +352 24795615 **Email General** info@ms.etat.lu **Address** Allée Marconi - Villa Louvigny **ZIP/City** 2120 Luxembourg **Country** Luxembourg (LU) **Web address** http://www.ms.etat.lu **Additional Information** No local / regional CA.
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 Clinical ATMP trials **CA - Registration/ notification without approval required for** – **CA - Submission required to** National CA **Applicable national legal framework/ Reference** Art 8 modified RGD 30 May 2005

Submission of Application	**Responsible for study submission** Sponsor **Entitled to study submission** – **Prerequisites for submission** –
Submission Format	**Format option(s)** – **Preferred format** – **Standard application form available** Yes **Standard application form** EU Standard CT application form **Standard application form - Additional information** No national document available.
Language of Submission	**Language(s) of application** French English **Preferred language of application** – **English accepted** Partly, not for all documents **Documents mandatory to be in official national language** Informed consent form and patient information sheet in German and French.
Submission Fees	**Fees for trial submission mandatory** Yes **Fees** Since January 2015: Fees for initial submission: 1000€ Substantial amendment: 1000€ **Waiver for academic (non-commercial) studies possible** No
Timelines Authorisation	**General timespan (max nr days)** 60 **Mode of approval (General)** Tacit (Silent) **ATMP/GMO trials (max nr days)** 90 **Mode of approval (ATMP/GMO trials)** Explicit

	External expert advice required (max nr days) 180 **Xenogeneic cell therapy (max nr days)** No time limit **Mode of approval (Xenogeneic cell therapy)** – **Timespan counted from** Date of submission of valid application **Applicable national legal framework/ Reference** Art 8 modified RGD 2005
Amendments/ Substantial Amendments (SA)	**Notification mandatory for** All clinical trials requiring authorisation by CA **Authorisation mandatory for** – **Responsible for submission of SA** Sponsor **Standard notification form** EU Standard Amendment Notification form **Timeline for approval of SA (max nr days)** 35 **Applicable national legal framework/ Reference** Art 9 modified RGD 30 May 2005 **Additional Information** Timelines of approval counted from the date of receipt of the proposed amendment. Implicit approval if no reasoned objections raised by CA.
Safety Reporting	**Responsible for AE reporting to CA** Sponsor **Sponsor must declare reportable events to** – **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 7d upon first knowledge (+ 8d for additional information) **SAE /SADE must be reported** –

National standard reporting form available

No specific document

Reporting format - Options

Email to CA (domestic SUSARs) + Online Portal (domestic + foreign SUSARs)

Preferred format

–

Online Safety Reporting Portal

EMA EudraVigilance CT Module (EVCTM) for reporting of domestic and foreign SUSARs

Provision of Annual safety report mandatory

Yes

Annual safety report shall be provided by sponsor to

National CA (via e-mail AND CD) or preferably via CESP (http://cesp.hma.eu/Home)

Applicable national legal framework/ Reference

Art 16 modified RGD 30 May 2005

Additional Information

Domestic SUSARs (same protocol & other protocols with same IMP): via e-mail AND to Eudravigilance
Foreign SUSARs (same protocol & other protocols with same IMP) Eudravigilance
6 monthly SUSARs line listing: via e-mail
Email CA for safety reporting: jacqueline.genoux-hames(at)ms.etat.lu

Investigator shall report SAE to

–

Reporting timeline

–

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

Standard Declaration form

EU Standard End of trial Declaration form

	Applicable national legal framework/ Reference Art 9(c) modified RGD 30 May 2005
Additional Information & Specifics	**Additional Information** Note: Submission fees are mandatory since January 2015!

Ethics committee

Contact Details	**Contact Name 1** Comité National d'Éthique de Recherche (CNER)/ National Research Ethics Committee (NREC) **Phone** +352 26 970879 **Fax** +352 26 970870 **Address** 1a-b- rue Thomas Edison **ZIP/City** 1445 Strassen **Country** Luxembourg (LU) **E-Mail** contact@cner.lu **Web address** http://www.cner.lu **Additional Information** No local EC
Ethical Review – General	**Submission for Ethical review mandatory for** – **Submission to CA and EC to be performed in the following order** – **Additional Information** Clinical trials on IMP must be submitted to the EC for ethical review according to Art 6 modified RGD 30 May 2005 and Art 25 Hospital Act of 28th August 1998 (fr) **Regulatory and ethics bodies involved in approval process** –
Single-Centre Studies - Ethical Review	**Ethical approval (favourable opinion) to be obtained from** Central EC **Additional Information** The national EC (CNER/NREC) provides a single opinion which is valid for all the country's investigational sites
Multi-Centre Studies - Ethical Review	**Ethical approval (favourable opinion) required from** National EC

	Submission of application required to – **Additional Information** The national EC (CNER/NREC) provides a single opinion which is valid for all the country's investigational sites
Submission of Application	**Responsible for study submission** Principal Investigator **Entitled to study submission** – **Prerequisites for submission / approval** – **Additional Information** The PI shall orally, and shortly, present the study at the next CNER meeting.
Submission Format	**Format option(s)** Paper hardcopy Electronically **Preferred format** 14 copies (paper) + electronic version of documents on CD-Rom or USB key. **Standard application form available** Yes **Standard application form** "Fiche synthétique pour la soumission d'un projet d'étude au CNER" **Guidance on submission format** Standard form and accompanying documentation to be submitted to CNER are provided on the CNER website in section Procedures>Submission for a new Study
Language of Submission	**Language(s) of application** French English **Preferred language of application** – **English accepted** Cover letter in French or English **Documents mandatory to be in official national language** Informed consent form and patient information sheet in German and French.
Submission Fees	**Fees for Ethical review mandatory** Yes **Waiver for academic (non-commercial) studies possible** Yes

	Fees for Ethical review Fees for Ethical review: Trials with commercial sponsor: € 1000.- (+VAT17%) Academic Study: € 500.- (+VAT17%) Substantial Amendment: € 250.- (+VAT17%) Amendments to MNPs (Medical Need Program) and CUPs (Compassionate Use Program): € 250.- (+VAT17%) **Official guidance on required fees** Current fees and related payment information is provided on CNER website in section Fees.
Timelines Ethical Review	**General timespan for single-centre studies (max nr days)** 60 **General timespan for multi-centre studies (max nr days)** 60 **ATMP/GMO trials (max nr days)** 90 **External expert advice required: Timespan (max nr days)** 180 **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** Art 6 modified RGD 30 May 2005 **Additional Information** NB: There are submission deadlines for initial applications: at the latest three weeks before the date of the next CNER meeting (every 2nd month). The exact meeting dates and their respective submission deadlines are provided on the CNER website. Copies of the opinion issued by the EC are sent to the CA and the National Data Protection Authority.
Amendments/ Substantial Amendments (SA)	**Ethical review mandatory for** Any substantial amendments affecting the safety of participants, changing the interpretation of the scientific pieces, etc) **Responsible for notification of SA** Sponsor **Standard notification form available** No **Timeline Ethical review of SA (max nr days)** 35

Guidance on submission of SA

Notification Format: in paper + electronically
14 copies of a summary of the amendments made + 14 copies of new full version + electronic version (CD-Rom or USB key)
Further guidance and examples of substantial versus non- substantial amendments are provided on the CNER website in section Procedures > Submission of a substantial amendment

Applicable national legal framework/ Reference

Art 9 modified RGD 30 May 2005

Safety Reporting

Reportable AEs

SAE + SUSARs from Luxembourg trial sites

Investigator shall report SAE to

Sponsor + EC (all SAEs having lead to death)

Reporting timeline

–

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

–

Sponsor is obliged to notify all investigators of SAE/ SADE occurrence

Yes

National Standard Reporting form available

No

Reporting format - Options

Email

Preferred reporting format

Email

Provision of Annual safety report mandatory

Yes

Guidance on AE reporting procedure

All documents to be sent electronically to: contact(at)cner.lu
Annual study report (regarding study progress and safety aspects: Modèle rapport annual CNER (template available).

Related information is available on CNER/NREC website in section Procedures > Follow-up procedures

Applicable national legal framework/ Reference

Art 15 & 16 modified RGD 30 May 2005

Additional Information

If clinical trial on experimental medicine (other required documents):
• 6-monthly SUSARs line listing
• DSUR

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

Standard Declaration form available

No

Applicable national legal framework/ Reference

Art 9(c) modified RGD 30 May 2005

Additional Information

The Clinical / Final study report + publications if any have to be sent to the EC

Study specific Requirements

Study Participants - Informed Consent (IC)

Standard IC form (ICF) available

Yes

Standard ICF - Additional Information

Templates for informed consent forms (available in French, German and English) are provided on the CNER/NREC website in section Procedures > Submission of a new study

IC is regulated by law

Yes

Informed Consent - Definition/ Requirements

“A decision, which must be written, dated and signed, to take part in a clinical trial, taken freely after being duly informed of the nature, significance, implications and risks and appropriately documented, by any person capable of giving consent or, where the person is not capable of giving consent, by his or her legal representative; if the person concerned is unable to write, oral consent in the presence of at least one witness may be given in exceptional cases, as provided for in national legislation."

Applicable national legal framework/ Reference

Art 2(j) modified RGD 30 May 2005
Art 3-5 modified RGD 30 May 2005

	Additional Information Further requirements on granting consent, in particular regarding vulnerable populations are specified in Art 3-5 modified RGD 30 May 2005.
Study Participants - Vulnerable Population	**Minors / Children - Studies allowed** Witnessed oral consent **Specific provision** Clinical trials involving minors are possible under special provisions **Legal framework/Reference (Minors/Children)** Art 4 modified RGD 30 May 2005 **Incapacitated persons - Studies allowed** – **Specific provisions** Clinical trials involving incapacitated adults are possible under special provisions **Legal framework / Reference (Incapacitated persons)** Art 5 modified RGD 30 May 2005 **Emergency situations - Studies allowed** – **Emergency situation without prior consent of patient or proxy - Studies allowed** – **Conditions allowing trial participation in emergency setting without prior consent** Clinical trials involving subjects incapable of granting consent themselves are only permitted if the legal representative signs the consent form. **Legal framework / Reference (Emergency Situation)** Art 5 (a) modified RGD 30 May 2005 **Pregnant or breastfeeding women - Studies allowed** – **Specific provisions** Not referenced in national law
Study Participants - Compensation & Reimbursement	**Reimbursement for study participants** Not specified **Compensation is limited to/provided for** Not specified **Additional Information** No specific requirements referenced in national law.
Data Protection	**Notification to DP Authority/ Ombudsmann is mandatory** Yes **Approval/ authorisation required** Not specified

Specific notification timelines before operations start

–

Language of notification

–

Notification format

–

Guidance on notification requirements

Generally, research projects involving human subjects also have to be notified to or authorized by the National Data Protection Commission (CNPD).
The EC is in contact with the CNPD.

CNPD Notification:
Notification form (in french or German) is available on the CNPD website in section 'Formulaires': "Notification prealable/ Formulaire notification prealable"

CNPD Authorisation:
Obligation to prior authorisation and related requirements are specified in Art 14 of the national Data Protection Act modified law 02/08/2002 (en))/ Loi modifiée du 2 août 2002 (fr).
No standard form available: procedure to find on the website.

Data Protection Authority/ Agency - Contact Details

National Data Protection Commission (CNPD)

Phone

(+352) 26 10 60-1

Fax

(+352) 26 10 60-29

Web address

http://www.cnpd.public.lu/en/

Address

1, avenue du Rock'n'Roll

ZIP/City

4361 Esch-sur-Alzette

Country

Luxembourg (LU)

Additional Information

Related acts and regulations are provided on the CNPD website in section Home > Legislation > National legislation

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

–

Insurance

Liability insurance or alternative arrangements for damages mandatory for

Investigator(s)
Sponsor
Study participants

Responsible for covering insurance

Sponsor
Investigator

Applicable national legal framework/ Reference

Art 3 (1f) of modified RGD 30 May 2005
Art 25 of Hospital Act of 28th August 1998 (fr)

Additional Information

Provisions for insurance or indemnity to cover the liability of the investigator and sponsor are mandatory.
According to Art 25 of Hospital Act of 28th August 1998 (fr) the sponsor / investigator shall subscribe an insurance covering his responsibility as well as the responsibility of all the persons involved.
The study insurance covers the risks encountered by the patients during their participation in the trial. In case of malpractice and non-conformity to the protocol, the insurance might of course turn against the physician. It is the responsibility of the physicians in Luxembourg to have a liability insurance and to check whether it covers malpractice or not.

Quality Assurance/ Quality Control (QA/QC)

Monitoring

Not specified

Audit by sponsor

Not specified

Standard Operating Procedures (SOPs)

Not specified

Additional Information

Related obligations are not specified in national law.

Archiving & Data Management

Study documents must be kept at least (in years)

5

Applicable national legal framework/ Reference

RGD 30/05/2005

Additional Information

Essential documents are kept by the Investigator and the sponsor for at least 5 years after the end of the study. The documents are kept longer if required by applicable requirements or agreement between Investigator and sponsor.

National legislation

General Information: Applicable Legislation & Conventions

Official website providing relevant national legislation available

Yes

Official website providing relevant national legislation

http://www.ms.public.lu/fr/legislation/medicaments/index.html

Official governmental legal database available

Yes

Official governmental legal database

http://www.legilux.public.lu

Additional Information

Legislations applicable to medicinal products are provided on the MoH website in section Législation > Médicaments

Clinical Trials on IMPs in Humans	**Applicable national regulations** General Act(s) on Medical/Clinical Research in Humans Transposition of (CT) Directive 2001/20/EC **Transposition of (CT) Directive 2001/20/EC (or comparable national legal framework)** Grand Ducal Regulation of 30th May 2005 on clinical trials of drugs for human use ("Modified RGD 30 May 2005") / RGD du 30 mai 2005 relatif à l'application de bonnes pratiques cliniques dans la conduite d'essais cliniques de médicaments à usage humain **Transposition of (GCP) Directive 2005/28/EC** – **Other applicable regulations/ implementing provisions (Acts, laws, decrees, ordinances, circulars, etc)** Other national legal texts are also applicable in the context of clinical trials and other types of studies: (1) Hospital Act of 28th August 1998 (fr)/ Code de la Santé - 11 Hôpitaux - A - Dispositions Générales Article 25 states that no trial, study or experimentation can be done on a human being with the aim of furthering knowledge in the fields of biological and medical sciences if the project has not firstly been submitted to the approval of a research ethics committee (2) Medical Deontology Code (fr), approved by the Ministerial Decree of 1st March 2013/ Arrêté ministériel du 1er mars 2013 approuvant le Code de déontologie médicale (2005); Chapter 5 (Art 76-79) on human experimentation, in particular, states that any study protocol, whether it is done in a hospital context or not must have been authorized. The trial can only start after the delivery of a positive opinion from the research ethics committee and after the implicit or explicit approval of the health Minister, in agreement with the legal and regulatory requirements that are to be applied in the matter. **Additional Information** NB: Modified RGD 30 May 2005 does not apply to non-interventional trials!
Radiation & Radiotherapy	**Use of radiation or radioactive compounds - Specific requirements** Yes **Applicable legal framework** Specific regulations must be considered if ionising radiation is involved (MoH Website in section Accueil > Législation > Protection radiologique dans les applications médicales) **Additional Information** The Division of Radioprotection of the MoH deals with all questions regarding protection from radiation.
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 Other legislation covering DP related issues **National DP act** National Data Protection Act modified law 02/08/2002 (en)/ Loi modifiée du 2 août 2002 (fr) **Other applicable regulations (covering DP related issues)** Act of Data Protection and electronic communication 2005 (en)

Definition

IMP/IMP Study

IMP - Definition available in national law

Yes

IMP - Definition

IMP – Definition according to Art 2(d) modified RGD 30 May 2005:
„principe actif sous forme pharmaceutique ou placebo expérimenté ou utilisé comme référence dans un essai clinique, y compris les produits bénéficiant déjà d'une autorisation de mise sur le marché, mais utilisés ou formulés (présentation ou conditionnement) différemment de la forme autorisée, ou utilisés pour une indication non autorisée ou en vue d'obtenir de plus amples informations sur la forme autorisée;"

IMP Study - Definition available in national law

Yes

IMP Study - Definition

Clinical trial (including single-centre, multicentre and multinational trials) – Definition according to Art 2(a) modified RGD 30 May 2005
„toute investigation menée chez l'homme, afin de déterminer ou de confirmer les effets cliniques, pharmacologiques et/ou les autres effets pharmacodynamiques d'un ou de plusieurs médicaments expérimentaux, et/ou de mettre en évidence tout effet indésirable d'un ou de plusieurs médicaments expérimentaux, et/ou d'étudier l'absorption, la distribution, le métabolisme et l'élimination d'un ou de plusieurs médicaments expérimentaux, dans le but de s'assurer de leur innocuité et/ou efficacité"