

Voluntary Joint pilot between FAMHP, the College, accredited Ethics Committees and sponsors for processing of applications for the authorisation of clinical trials and substantial modifications on medicinal products for human use in accordance with the spirit of the Regulation (EU) No 536/2014 and of the law on CTR

Guidance for participating parties version 4.1, 08.06.2018

DISCLAIMER

The present guidance is a document that could be modified or completed as discussions are still ongoing at European and national level on the implementation of the Clinical Trial Regulation and discussions on the process are also still ongoing between the different instances responsible for the assessment of the CTA dossiers.

The excel file for the letter of intent of sponsors interested to participate to the CTR pilot is to be provided by E-mail to the [new specific E-mail address for the pilot](mailto:CTRpilot@afmps-fagg.be) : CTRpilot@afmps-fagg.be.

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1. Definitions, conventions and abbreviations

ATMP: Advanced Therapy Medicinal Products

Clinical Trial: clinical study as defined in article 2, §2, 2), of the Regulation (EU) No 536/2014.

CESP: Common European Submission Portal – see procedure for submission via CESP in annex III of the present guidance.

CTA: Clinical Trial Application

CTR: Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC

College: an independent organ that coordinates the working of the Ethics Committees and is responsible for their quality assurance. It also acts as single point of contact between Ethics Committees and the FAMHP.

EC: the Ethics Committee as stated in article 2, §2, 11) of the Regulation (EU) No 536/2014.

FAMHP: the federal agency for medicines and health products as defined in the law of 20 July 2006 related to the creation and functioning of the federal agency for medicines and health products.

National contact point: the FAMHP is the national contact point as defined in article 83 of the CTR. This means that for the purpose of the present project, the FAMHP will be the single contact point for the sponsor (for Part I and Part II of the dossier), without prejudice of the organisation between the competent authority and the College at the time all functionalities of the portal will be available.

From a practical point of view, for the sponsor the national contact point will be the following mailbox: CTRpilot@afmps-fagg.be

RMS: Reporting Member State as stated in article 5 of the CTR.

SM: Substantial Modification as stated in article 2, §2, 13) of the Regulation (EU) No 536/2014.

All periods mentioned in the present document are to be understood as **calendar days**.

2. Scope and objectives of the pilot

2.1. Scope

Following the current EU legislation (Directive 2001/20/EC) and the law of 7 May 2004 on experiments on the human person, the authorisation procedures at the FAMHP and the Ethics Committees are currently mostly independent from each other.

This will change when the CTR will come into force as one “single decision” per member state will have to be provided to the EU portal. The assessment of the dossier will have to be performed independently and in parallel by the competent authority and by the Ethics Committee and consolidated as the single decision will have to be reached in a short timeline. Close collaboration between (i) FAMHP and the College and (ii) between the College and the ECs will thus become crucial. This close collaboration between these stakeholders will be even more crucial when Belgium has the role of RMS in the EU clinical trials authorisation process.

Clinical trials that are eligible for the pilot are national submissions of all phases, including ATMP trials.

2.2. Objectives

The purpose of the pilot is to (i) develop processes and procedures for the joint assessment of CTAs and for the compilation of the Assessment Report, (ii) to evaluate them and (iii) to proceed with the adjustments. This will be a learning by doing approach for all parties in the pilot. This is also an opportunity for the FAMHP, the College and the Ethics Committees to test the short timelines for phase I mono-national trials within the framework of the CTR.

The participation in the pilot gives sponsors the opportunity of adjusting and testing their own processes with regard to the timelines and procedures of the CTR.

2.3. Voluntary basis

Sponsors participate in the pilot on a voluntary basis.

The pilot will be conducted with selected initial CTAs.

2.4. Substantial modifications

Substantial modifications related to trials approved in the CTR pilot procedure also have to be submitted following the CTR pilot procedure.

In the spirit of the CTR and as far as possible no substantial modification shall be submitted if the previous one has not been already approved or closed.

2.5. Out of scope

The pilot does not apply to voluntary harmonisation procedures. It is limited to clinical trial applications and substantial modification submissions in Belgium. There will be no interactions with other member states during assessment of multinational clinical trials.

Trials with GMO products submitted following the deliberate release procedure are not accepted in the pilot.

Safety reporting will not be changed by the pilot. This means that the safety reporting documents must not be submitted to the national contact point and that the current rules for submission to the FAMHP, to especially the EC in charge of the evaluation and to the local Ethics Committee(s) have still to be followed. However, after evaluation and consensus, the position might be reviewed.

3. Legal basis

The new law of 7th May 2017 on CTR has been published in the Belgisch Staatsblad/Moniteur Belge on the 22th of May 2017. This law contains article 58 which foresees that for the pilot, Article 11 §§1 to 3 and §7 of the law of 7th May 2004 related to the role of the EC is not valid anymore. The other articles of the law of 7th May 2004 remain applicable, as is the authorisation of the CTA and substantial modifications. Essentially, the pilot follows as expected the **law of 7th May 2004**, but follows the **spirit of CTR and the text of the new Belgian Law of 7 May 2017**, with the selection of the EC by the College and the joint assessment (FAMHP and EC) with the use of the new European templates.

The publication of the new law on clinical trials allowed the start of the CTR pilot.

A set of Royal Decree's is also foreseen (e.g. operational AR of 9th October 2017 published on 10th November 2017, and others that will be published later).

The CTR pilot will also permit to test the joint assessment of phases I mono-national dossiers for which short deadlines are being kept in the text of the new law on CTR.

As one of the principles of the present project is a learning by doing approach, some flexibility will be accepted from all parties involved. The CTA dossiers and SM dossiers will not be automatically rejected if the sponsor cannot answer the questions within the CTR deadlines (12 days). As much as possible, this timeline, as foreseen in the CTR, should be respected but exceeding the time of maximum 20% will be accepted in practice.

This pilot is limited in time. It will not continue after the CTR regulation has come into place.

4. Procedure for sponsor – initial trials

4.1. What if a sponsor wants to propose a dossier for the CTR pilot ? Letter of intent for sponsors.

The appended letter of intent should be submitted by E-mail to the national contact point (CTRpilot@fagg-afmps.be) with the following E-mail title : **CTR pilot – Letter of intent to participate to the CTR pilot procedure – CTA dossier 20xx-xxxxxxx-xx (EudraCT number)**.

The following information should be provided in the intention letter:

- EUDRA-CT number of the clinical trial
- sponsor's trial code as stated when applying for the EUDRA-CT number
- title of the clinical trial
- name and site of the co-ordinating investigator of the clinical trial
- number and addresses of planned trial centres in Belgium if available at the moment of the submission of the letter of intent. Should be provided at the latest at the moment of the confirmation by the sponsor (see below).
- planned submission date for the dossier

The national contact point and the College will decide on a case-by-case basis whether a CTA can be processed in the pilot. The choice of the dossiers will be based on the type of dossier and on the proposed submission date in function of the capacities of the national contact point and the College. As such, no single sponsor is automatically entitled to participate and the decision to include a study in the pilot remains with the national contact point and the College.

In case the dossier is accepted within the pilot an acceptance E-mail containing a CTR pilot number will be sent to the sponsor by the national contact point.

After this, any communication between sponsor and the national contact point must at least contain the following title: **CTR pilot number : XXX – CTA 20XX-XXXXXX-XX**

Should it not be possible to process the CTA within the pilot, the national contact point will inform the sponsor as soon as possible. In this case the sponsor can submit the dossier in accordance to the current legislation. However, **the content of the dossier, as prepared according to the requirements of the CTR, will be accepted** even if the review process of the dossier will be performed in accordance with the Directive 2001/20/EC.

4.2. Practical procedure

4.2.1. Submission of the CTA

The national contact point (CTRpilot@afmps-fagg.be) and the sponsor will stay in close contact in order to refine the submission date if necessary.

For a submission of a CTA dossier following the CTR pilot process, the “Guidance for submission of clinical trial applications, substantial amendment notifications and end of trial declarations to the R&D division”, also published on 15th May 2018, will not be applicable. This present guidance provides the details of the requirements for submission of the dossiers for the pilot CTR procedure.

The submission dossier (structure and contents) must comply with the requirements of annex I of the CTR. The Regulation provides the option of separately submitting the documentations for Part I and Part II. However, it has been decided that the sponsor cannot make use of this option in the course of the pilot. Part I and Part II packages have to be submitted together at the same moment to the national contact point.

For the sake of a swift processing of the dossier it is asked to the sponsor to submit the CTA package by Eudralink¹ or by CESP² until 30th September 2018.

From 1st October 2018, only submissions through CESP will be accepted as CESP has been selected as unique way of submission to harmonize the way the different type of dossiers are submitted in the R&D division of the FAMHP.

During a transition period (until 30 September 2018) submission of CTR pilot dossiers will be accepted by either Eudralink or by CESP, but not both.

At the time of the submission the cover letter must point out that participation in the pilot has been confirmed and must contain the pilot number. The cover letter must be provided hand signed and scanned in the Eudralink/CESP submission.

All communications (additional information, responses to questions, ...) from the sponsor during the procedure are to be sent by E-mail and/or Eudralink/CESP to the national contact point (CTRpilot@afmps-fagg.be).

4.2.2. Payment of the fee for an initial dossier

No fee is currently due for the submission of a CTA initial dossier in the CTR pilot (nor to the agency, nor to the evaluating Ethics Committee).

¹ Eudralink : the expiry date of each Eudralink package in this pilot will be set to its maximum of 90 days. See also : <https://eudralink.ema.europa.eu/EudraLink-User-Guide.pdf>.

² CESP : (Common European Submission Portal). See procedure for submission via CESP in annex III of the present guidance.

4.2.3. Validation phase

The validation of the dossier (Part I & Part II) is performed by the national contact point.

Timelines of the CTR apply for the validation phase, while timelines of the law of 7 May 2004 (28 days or 15 days) apply once the T0 is given for the start of the procedure. However as far as possible, timelines for validation will be kept short.

At the end of the **validation phase** which will last a maximum of **10 days (except for phases I mono-national trials for which the validation phase will last a maximum of 5 days)**, the sponsor will receive a notice of validation (beginning of assessment) from the national contact point. An operational calendar with a clear overview of the different timelines will be part of this notification to the sponsor.

If the validation shows that deficiencies are present or that relevant documentation is missing, leading to the CTA itself not being valid, the sponsor is granted a **10-day** period to remove the deficiencies. The corresponding response by the sponsor (Eudralink/CESP if possible) is to be sent to the national contact point.

The national contact point evaluates the supplemented documentation **within 5 days** after receipt of the comments or the amended application dossier. If the national contact point comes to the conclusion that the documentation regarding Part I and/or Part II is still not valid despite the supplement or if the sponsor neglects timely submission of the supplement, the FAMHP informs the sponsor that the CTA can no longer be processed within the pilot.

Upon successful validation, the national contact point sends the trial dossier to the College by means of an Eudralink.

It is to be noted that the EC will have access to the entire submission dossier Part I with the exception of the quality documentation.

4.2.4. Assessment phase

After successful validation, the CTA is assessed by the FAMHP and the Ethics Committee.

The assessment regarding the aspects covered by Part I of the CTA is performed in parallel by the FAMHP and the Ethics Committee selected by the College. The aspects covered by Part II are assessed by the Ethics Committee.

During the assessment procedure of Part I of the dossier, if the CTA dossier is not directly granted a positive assessment, the sponsor will receive a list of questions and/or requests for additional information from the national contact point.

Contents covered by the Part II of the CTA pursuant to the CTR are assessed in parallel by the Ethics Committee. Questions and/or requests for additional information regarding these aspects are sent to the sponsor by the national contact point at the same time with the list of questions related to Part I of the dossier.

Informed Consent Forms (ICFs) are reviewed by the EC in one language. The correct translation into all other languages remains the responsibility of the sponsor. Comments/remarks on the ICF could be provided by the EC into one of the language versions of the PDF document. In this case, the commented PDF will be added as an annex to the RFI letter and these comments/remarks have to be taken into account by the sponsor when providing the answers to the questions. However, the sponsor remains responsible for the translation of the updated ICF into the other ICF's languages.

In the case of a deficiency letter, the sponsor is called upon to remedy the deficiencies noted or to supply the requested information within **12 days at the most** in order to comply with the deadlines specified in the CTR. As before, the answer here should also be as a single response sent by E-mail (Eudralink/CESP if possible) to the national contact point (CTRpilot@afmps-fagg.be).

In case a question of the deficiency letter should be unclear it is recommended to contact the national contact point by E-mail.

As only one round of questions is foreseen in the CTR, it is recommended to formulate answers in a clear unambiguous way and check their completeness before sending them to the national contact point.

4.2.5. Approval

After evaluation of the sponsor's response to questions related to Part I and Part II of the dossier by the FAMHP and the Ethics Committee, the NCP compiles their final decisions on the basis of the Assessment Reports on Part I and Part II of the CTA. The final and unique conclusion is provided to the sponsor by the national contact point.

If the CTA is "Authorised", the clinical trial can be started immediately.

If the CTA is "Authorized subject to conditions", the clinical trial can be started after fulfilment of the conditions by the sponsor. The approval letter is sent at the time of the conditional approval. When all conditions are met an E-mail is sent by the NCP to the sponsor to indicate that the trial is fully approved and may start. No additional approval letter is sent.

If the CTA is "Refused", the clinical trial cannot be started.

5. Procedure for sponsors - Substantial Modifications

5.1. Submission of a substantial modification regarding a clinical trial approved in the CTR pilot

Substantial modifications (SM) regarding clinical trials that were approved in the CTR pilot procedure will also need to be submitted following the CTR pilot procedure.

Upon submission, the SM cover letter and any other communication should clearly state: **CTR pilot number : XXX – CTA 20XX-XXXXXX-XX – SM n°XX**

The submission dossier must comply with the requirements of annex II of the CTR.

5.2. Payment of the fee for a substantial modification

No fee is currently due for the submission of a CTA substantial modification in the CTR pilot (nor to the agency, nor to the evaluating Ethics Committee).

5.3. Validation phase

The validation of the substantial modification is performed by the national contact point.

Timelines of the CTR apply for the validation phase, while timelines of the law of 7 May 2004 (28 days or 15 days) apply once the T0 is given for the start of the procedure. However as far as possible, timelines for validation will be kept short.

At the end of the **validation phase** which will last a maximum of **6 days (except for phase I mono-national trials for which the validation phase will last a maximum of 5 days)**, the sponsor will receive a notice of validation (beginning of assessment) from the national contact point. An operational calendar with a clear overview of the different timelines will be part of this notification to the sponsor.

If the validation shows that deficiencies are present or that relevant documentation is missing, leading to the SM itself not being valid, the sponsor is granted a **10-day** period to remove the deficiencies. The corresponding response by the sponsor is to be sent to the national contact point (CTRpilot@afmps-fagg.be).

The national contact point evaluates the supplemented documentation **within 5 days** after receipt of the comments or the amended SM dossier.

5.4. Assessment phase

After successful validation, the SM is assessed by the FAMHP and in principle the Ethics Committee that was responsible for the assessment of the initial dossier.

The assessment regarding the aspects covered by Part I of the CTA is performed in parallel by the FAMHP and the EC with the exception of the modifications related to the quality part of the dossier which are only assessed by the FAMHP. The aspects covered by Part II are assessed by the EC.

It is to be noted that the EC will have access to the submission dossier for substantial modification on Part I (excepted quality documentation) even if "A.3 Notification for an opinion to the Ethics Committee" was not ticked in the EU application form. The EC will decide on case by case basis if an EC evaluation (and thus an EC approval) is needed.

During the assessment procedure of Part I of the dossier, if the SM dossier is not directly granted a positive assessment, the sponsor will receive a list of questions and/or requests for additional information from the national contact point.

SM contents covered by the Part II of the CTA pursuant to the CTR are assessed in parallel by the Ethics Committee. Questions and/or requests for additional information regarding these aspects are sent to the sponsor by the national contact point at the same time with the list of questions related to Part I of the SM dossier.

If the substantial modification is related to an update of the Inform Consent Form (ICF), the ICF is reviewed by the EC in only one language. The correct translation into all other languages remains the responsibility of the sponsor. Comments/remarks on the ICF could be provided by the EC into one of the language versions of the PDF document. In this case, the commented PDF will be added as an annex to the RFI letter and these comments/remarks have to be taken into account by the sponsor when providing the answers to the questions. However, the sponsor remains responsible for the translation of the updated ICF into the other ICF's languages.

In the case of a RFI letter, the sponsor is called upon to remedy the deficiencies noted or to supply the requested information within **12 days at the most** in order to comply with the deadlines specified in the CTR. As before, the answer here should also be as a single response sent by E-mail (Eudralink/CESP if possible) to the national contact point (CTRpilot@afmps-fagg.be).

In case a question of the deficiency letter should be unclear it is recommended to contact the national contact point by E-mail.

As only one round of questions is foreseen in the CTR, it is recommended to formulate answers in a clear unambiguous way and check their completeness before sending them to the national contact point.

5.5. Approval

After evaluation of the sponsor's response to questions related to Part I and Part II of the SM dossier by the FAMHP and the EC, the NCP compiles their final decisions on the basis of the Assessment Reports on Part I and Part II of the SM. The final and unique conclusion is provided to the sponsor by the national contact point.

If the SM is "Authorised", the substantial modification can be implemented.

If the SM is "Authorized subject to conditions", the substantial modification can be implemented after fulfilment of the conditions by the sponsor. The approval letter is sent at the time of the conditional approval. When all conditions are met an E-mail is sent by the NCP to the sponsor to indicate that the trial is fully approved and may start. No additional approval letter is sent.

If the SM is "Refused", the substantial modification cannot be implemented.

6. Survey

The national contact point will organise a survey to all the stakeholders (sponsor, FAMHP, College and EC) to collect comments, lessons learned, suggestions on the pilot process to obtain a joint conclusion with recommendations and adaptations where required.

7. Annex I – Timetables for the CTR pilot process

7.1. National initial dossier (other than phase I mono-national trial)

Maximum duration of the process: 28 days (timeline as foreseen in the law of 7 May 2004) + 10 days for validation + max. 15 additional days if questions during validation + max. 12 days if list(s) of questions during assessment => max. 65 days

Step	DAY
Confirmation of receipt to Sponsor/beginning of validation	Date submission = T0 - 10
Notification of the validation status to the sponsor: <ul style="list-style-type: none"> - Dossier complete => beginning of assessment - Dossier still not complete after max. 15 additional days (10 for the sponsor to answer the request for additional info + 5 for the national contact point to verify if the dossier is complete after answer from the sponsor) => dossier refused 	T0 (+ max. 10 + max. 5 if validation questions)
Compiled assessment report for Part I and assessment for Part II available : <ul style="list-style-type: none"> ⇒ Direct approval at T28 at the latest if no questions from FAMHP or EC ⇒ List(s) of questions provided by the national contact point to the sponsor 	T23
Response on questions by sponsor due by (maximum 12 days clock stop if list of questions)	T23 (+ max. 12 days)
Review of the answers by FAMHP and/or Ethics Committee and final coordinated decision sent by the national competent authority by	T28

For an ATMP clinical trial, 30 days (as foreseen by the law of 7 May 2004) will be added to the 28 days legal delay. These 30 days will be added to the assessment period of 23 days.

7.2. National initial phase I mono-national dossier

Maximum duration of the process: 15 days (timeline as foreseen in the law of 7 May 2004) + 5 days for validation (+ max. 15 additional days if questions during validation) + max. 12 days if list(s) of questions during assessment => max. 47 days

Step	DAY
Confirmation of receipt to Sponsor (dossier + payment)/beginning of validation	Date submission = T0 - 5
Notification of the validation status to the sponsor: <ul style="list-style-type: none"> - Dossier complete => beginning of assessment - Dossier still not complete after max. 15 additional days (10 for the sponsor to answer the request for additional info + 5 for the national contact point to verify if the dossier is complete after answer from the sponsor). => dossier refused 	T0 (+ max. 10 + max. 5 if validation questions)
Compiled assessment report for Part I and assessment for Part II available : <ul style="list-style-type: none"> ⇒ Direct approval at T15 at the latest if no questions from FAMHP or EC ⇒ List(s) of questions provided by the national contact point to the sponsor 	T10
Response on questions by sponsor due by (maximum 12 days clock stop if list of questions)	T10 (+ max. 12 days)
Review of the answers by FAMHP and/or Ethics Committee and final coordinated decision sent by the national competent authority by	T15

For an ATMP clinical trial, 30 days (as foreseen by the law of 7 May 2004) will be added to the 15 days legal delay. These 30 days will be added to the assessment period of 10 days.

7.3. National Substantial Modification (other than phase I mono-national trial)

Maximum duration of the process: 28 days (timeline as foreseen in the law of 7 May 2004) + 6 days for validation (+ max. 10 + max. 5 days if questions during validation)+ max. 12 additional days if list of questions => max. 61 days

Step	DAY
Confirmation of receipt to Sponsor (dossier + payment)/beginning of validation	Date submission = T0 - 6
Notification of the validation status to the sponsor: <ul style="list-style-type: none"> - Dossier complete => beginning of assessment - Dossier still not complete after max. 15 additional days (10 for the sponsor to answer the request for additional info + 5 for the national contact point to verify if the dossier is complete after answer from the sponsor). => dossier refused 	T0 (+ max. 10 + max. 5 if questions during validation)
Compiled assessment report for Part I and/or assessment for Part II available (depending from the scope of the substantial amendment) : <ul style="list-style-type: none"> ⇒ Direct approval at T28 at the latest if no questions from FAMHP or EC ⇒ List(s) of questions provided by the national contact point to the sponsor 	T23
Response on questions by sponsor due by (Clock stop of maximum 12 days if list of questions)	T23 (+ max. 12 days)
Review of the answers by FAMHP and/or Ethics Committee and final coordinated decision sent by the national competent authority by	T28

7.4. National Substantial Modification for a phase I mono-national trial

Maximum duration of process: 15 days (timeline as foreseen in the law of 7 May 2004) + 5 days for validation (+ max. 10 + max. 5 days if questions during validation) + max. 12 additional days if list of questions => max. 47 days

Step	DAY
Confirmation of receipt to Sponsor (dossier + payment)/beginning of validation	Submission date = T0 - 5
Notification of the validation status to the sponsor: <ul style="list-style-type: none"> - Dossier complete => beginning of assessment - Dossier still not complete after max. 15 additional days (10 for the sponsor to answer the request for additional info + 5 for the national contact point to verify if the dossier is complete after answer from the sponsor). => dossier refused 	T0 (+ max. 10 + max. 5 if validation questions)
Compiled assessment report for Part I and/or assessment for Part II available (depending from the scope of the substantial amendment) : <ul style="list-style-type: none"> ⇒ Direct approval at T15 at the latest if no questions from FAMHP or EC ⇒ List(s) of questions provided by the national contact point to the sponsor 	T10
Response on questions by sponsor due by (clock stop of maximum 12 days if list of questions)	T10 (+ max. 12 days)
Review of the answers by FAMHP and/or Ethics Committee and final coordinated decision sent by the national competent authority by	T15

8. Annex II – Dossier structure as per regulation 536

8.1. Initial application

During the course of the pilot, Part I and Part II packages have to be submitted together.

8.1.1 [Please use a folder structure with Part I and Part II](#)



Name ^	Date modified	Type
part I	14/12/2016 15:19	File folder
part II	14/12/2016 15:19	File folder

A zip-file with the structured folders with the available templates (written statement of the sites and Investigator's CV) is available on our website next to the present guidance.

8.1.2 [Consider to apply the following folder structure – an empty folder structure can be provided.](#)

APPLICATION DOSSIER FOR THE INITIAL APPLICATION

Part I

A. Fulfilment of INTRODUCTION AND GENERAL PRINCIPLES

B. COVER LETTER

C. EU APPLICATION FORM

D. PROTOCOL

E. INVESTIGATORS BROCHURE (IB)

F. DOCUMENTATION RELATING TO COMPLIANCE WITH GOOD MANUFACTURING PRACTICE (GMP) FOR THE INVESTIGATIONAL MEDICINAL PRODUCT

G. INVESTIGATIONAL MEDICINAL PRODUCT DOSSIER (IMPD)

1.1. Data relating to the investigational medicinal product

1.2. Simplified IMPD by referring to other documentation

1.3. IMPD in cases of placebo

H. AUXILIARY MEDICINAL PRODUCT DOSSIER

I. SCIENTIFIC ADVICE AND PAEDIATRIC INVESTIGATION PLAN (PIP)

J. CONTENT OF THE LABELLING OF THE INVESTIGATIONAL MEDICINAL PRODUCTS

Part II (INFORMATION PER MEMBER STATE CONCERNED)

K. RECRUITMENT ARRANGEMENTS

L. SUBJECT INFORMATION, INFORMED CONSENT FORM AND INFORMED CONSENT PROCEDURE

M. SUITABILITY OF THE INVESTIGATOR

N. SUITABILITY OF THE FACILITIES

O. PROOF OF INSURANCE COVER OR INDEMNIFICATION

P. FINANCIAL AND OTHER ARRANGEMENTS

R. PROOF THAT DATA WILL BE PROCESSED IN COMPLIANCE WITH UNION LAW ON DATA PROTECTION

8.1.3. [File format](#)

Please apply the PDF file format except for the EudraCT application form, which in addition to the PDF format, must be in XML format.

Some requirements for the preparation of these PDF files:

1. The files must allow "copy/paste" and other changes. If the source file is no longer available, the applicant can provide a scanned copy. However he must provide readable documents.
2. Certificates, licenses, authorizations and other documents with a signature must be scanned.
3. The layout should be as clear as possible. If possible a detailed table of contents must be included in order to find quickly specific sections of text.
4. Files should not be locked by a password.
5. Each part of the application dossier for clinical trial should be a separate file.
6. The names of these files must follow the syntax described below.
7. The PDF version of the European application form must be saved twice: a first part corresponding to the entire form and the second part with only the signed page that has been scanned. The same principle applies to the European substantial amendment notification form.

8.1.4. [Filenames](#)

Please consider to use **descriptive filenames**. To name the different files we ask you to respect a defined syntax: pilot number and EudraCT number first, followed by the file name in English (see list below):

Example:

PilotXXX_xxxx-xxxxxx-xx_Name of file.pdf

Pilot 999_2010-090094-00_Cover-Letter.pdf

Special cases:

1) To name the scanned pages of the documents with signatures we ask you to add "signature" in the name.

Example: Pilot999_2010-090094-00_Application_Form_Signature.pdf

2) In case the document refers to a particular medicinal product (investigational medicinal product or authorized medicinal product) we ask you to add the name of this medicinal product in the filename.

Example: EudraCT Number-Manufacturing-Authorisation-Name of the medicinal product.pdf

PART I

File/Document	Name	Annex I Regulation No 536/2014	References
B. Cover Letter	Cover-Letter.pdf	B	Pilot number
C. EU application Form	Application-form.pdf	C	EU Application Form (the current EU Application Form should be used during the pilot as a new CTR Application Form is not yet available)
D. Protocol	Protocol.pdf	D D 24.	See also ICH E6 GCP The protocol shall be accompanied by a synopsis of the protocol, provided as a separate document. The first act of recruitment (e.g. advertising) should be specified.
E. Investigator's Brochure	Investigators_Brochure.pdf	E	See also ICH E6 GCP
F. Documentation relating to GMP for the IMP <ul style="list-style-type: none"> • Copy of the manufacturing authorisation • Certification by the Qualified Person • ... 	<ul style="list-style-type: none"> • Manufacturing-Authorisation.pdf • QP-Declaration.pdf • ... 	F	GMP certificates not accepted, only GMP manufacturing authorisations EU template strongly recommended for QP declaration
G. Investigational Medicinal Product Dossier	Impd.pdf	G	See also Eudralex volume 10 chapter III for content and Common Technical Document (CTD) format. GLP statement has to be part of the IMPD (see: point 44. Of annex I of the CTR and http://www.hma.eu/fileadmin/dateien/Human_Medicines/01-About_HMA/Working_G

			roups/CTFG/QAs_document_on_GLP_-_2017.pdf
G. Simplified Investigational Medicinal Product Dossier	Simplified-Impd	G	See CTR (annex I points 50 to 53) to see cases when a simplified IMPD is accepted
G. Summary of product characteristics	Smpc.pdf	G	If applicable
H. Auxiliary Medicinal product Dossier	Ampd.pdf	H	AMPD or SmPC if applicable
I. Copy of the summary of scientific advice	Scientific-Advice.pdf	I 56	If applicable
I. Copy on the agreement on the PIP	PIP.pdf	I 57	If applicable
J. Content of the labelling	Labels.pdf	J	Example of the planned label in accordance with annex 13 of the GMP

Remark: Section A. of Part I "Fulfilment of Introduction and General Principles" may be left empty if no specific information as foreseen in annex I point A. of the Regulation 536/2014 is available.

PART II (no specific cover letter for Part II)

File/Document	Name	Annex I Regulation No 536/2014	References
K. Recruitment arrangements, unless described in the protocol	Recruitment-arrangements.pdf	K 59	Stand-alone document or reference to the applicable section of the protocol has to be provided.
K. Advertising material	Advertising-material-name.pdf	K 60	If applicable.
L. Subject (and legally designated representative) information and informed consent ICF, questionnaires, participation card, diaries or other patient documents	ICF-language-target group.pdf	L 61&63	Use of the existing template strongly recommended. New version of the template ICF for interventional trials in adults foreseen Q4 2018. To be submitted in all languages that will be used in Belgium. Sponsor is responsible for appropriate translations. The EC only reviews the ICFs in one language.
L. Informed consent Procedure	ICF-procedure.pdf	L 62	A stand-alone document or a reference to the applicable section of the protocol has to be provided.
M. List of the planned sites, name and position of PI and planned number of subjects at the sites	Planning.pdf	M 64	Has to be provided.
M. CV and declaration of interest of the principal investigator of each site.	CV-name.pdf & DOI-name.pdf	M 65&66	<u>CV</u> : diplomas have to be listed. GCP training should be documented (in the CV or by a GCP certificate) Proposed template (not mandatory): TransCelerate template (available in the

			<p>structure zip file on the FAMHP website)</p> <p><u>Declaration of interest:</u> The FAMHP recommends to use the following form https://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM048310.pdf</p> <p>With the following explanation https://www.ecfr.gov/cgi-bin/text-idx?SID=c6ab674f8ec325be440c8b408bc55e4a&mc=true&node=pt21.1.54&rgn=div5</p>
N. Statement on the suitability of the sites	Suitability-statement-namesite.pdf	N	<p>Most recent version of the written statement issued by the site.</p> <p>Template available in the structure zip file in on the FAMHP website.</p> <p>It is advised to contact the sites as soon as possible when identified in order to have the written statements ready at the time of submission</p>
O. Proof of insurance cover or indemnification	Proof of Insurance Cover.pdf	O	<p>Certificate with specification of the amount insured and reference to the Belgian law of 7 May 2004, art. 29 §1 (No fault insurance).</p>
P. Brief description of the financing of the CT	Financing.pdf	P 69	If applicable

<p>P. Information on financial transactions and compensation paid to subjects and investigator/site</p>	<p>Budget-namesite.pdf</p>	<p>P 70</p>	<p>Draft version of the contract with (draft) amounts is currently accepted.</p> <p>It is advised to contact as soon as possible the CTCs of the concerned sites in order to gain time in the evaluation of the financial agreements.</p>
<p>P. Description of any other agreement</p>	<p>Agreement-namesite.pdf</p>	<p>P 71</p>	<p>Clinical trial agreements and others with relation to the trial if applicable.</p>
<p>R. Statement that data will be collected and processed in accordance with the General Data Protection Regulation (GDPR)</p>	<p>Data-Protection-Statement.pdf</p>	<p>R</p>	<p>A stand-alone document (statement) has to be provided.</p>

8.2. SUBSTANTIAL MODIFICATIONS

The following folder structure should be applied and sections A to G should be provided upon submission of the substantial modification – an empty folder structure can be provided.

Please note that during the CTR pilot, the submission of a substantial modification should be made separately for the trial(s) in the pilot and the trials approved within the current process. After implementation of the CTR, the same substantial modification can be submitted again for all trials concerned.

Substantial modifications that are currently submitted for EC only, mainly correspond to Part II of the dossier structure within CTR. These substantial modifications also need to be submitted to the national contact point who will distribute them to the College and subsequently to the EC.

Non-substantial modifications should not be submitted, but should be added to the documentation for the next substantial modification.

A zip-file with the structured empty folders is available on our website next to the present guidance.

APPLICATION DOSSIER FOR SUBSTANTIAL MODIFICATIONS

- A. Fulfilment of INTRODUCTION AND GENERAL PRINCIPLES
- B. COVER LETTER
- C. MODIFICATION APPLICATION FORM
- D. DESCRIPTION OF THE MODIFICATION
- E. SUPPORTING INFORMATION
- F. UPDATE OF EU APPLICATION FORM

8.2.1. [File format](#)

Please apply the PDF file format except for the initial EudraCT application form, which should also be provided in the XML format.

Some requirements for the preparation of these PDF files:

1. The files must allow "copy/paste" and other changes. If the source file is no longer available, the applicant can provide a scanned copy. However he must provide readable documents.
2. Certificates, licenses, authorizations and other documents with a signature must be scanned.
3. The layout should be as clear as possible. If possible a detailed table of contents must be included in order to find quickly specific sections of text.
4. Files should not be locked by a password.
5. Each part of the application dossier for the substantial modification should be a separate file.
6. The names of these files must follow the syntax described below
7. The PDF version of the Modification Application Form must be saved twice: a first part corresponding to the entire form and the second part with only the signed page that has been scanned.

8. An extract from the amended documents or the amended document itself showing previous and new wording in track changes, as well as the extract/document only showing the new wording must be provided. A summary of changes must also be provided. If the summary of changes and the track changes version(s) of the updated documents are not present, this will be a validation question.

9. Regarding modifications to the Reference Safety Information:

In view of the update of the CTFG - Q&A document on RSI, published on:

http://www.hma.eu/fileadmin/dateien/Human_Medicines/01-About_HMA/Working_Groups/CTFG/2017_11_CTFG_Question_and_Answer_on_Reference_Safety_Information_2017.pdf , the sponsor should fully comply with the Q&A during the IB updates that follow this publication.

8.2.2. [Filenames](#)

Please consider to use **descriptive filenames**. To name the different files we ask you to respect a defined syntax: EudraCT number first, followed by the file name in English (see list below):

Example:

PilotXXX_SMX_xx-xxxxxx-xx__Name of file. pdf

Pilot999_SM1_2010-090094-00_Cover-Letter. Pdf

Please assure that the complete filenames are not longer than 200 characters (folder names included)

Special cases:

1) To name the scanned pages of the documents with signatures we ask you to add "signature" in the name.

Example: Pilot999_SM1_2010-090094-00_Application-Form-Signature. pdf

2) In case the document refers to a particular medicinal product (investigational medicinal product or authorized medicinal product) we ask you to add the name of this medicinal product in the filename.

Example: Pilot999_SM1_xxxx-xxxxxx-xx__Manufacturing-Authorisation_Name of the medicinal product.pdf

Document	Name	Annex II Regulation No 536/2014	References
B. Cover Letter	Cover-Letter.pdf	B	Pilot number
C. Modification Application Form	Modification-Application-Form.pdf	C	Modification Application Form (the current Substantial Amendment Notification Form should be used during the pilot as a new CTR Modification Application Form is not yet available)
D. Description of the modification	e.g. Protocol-edition-date.pdf Protocol-edition-date-TC version.pdf Investigators-Brochure-edition-date.pdf Investigators-Brochure-edition-date-TC version.pdf Impd-edition-date.pdf Impd-edition-date-TC version.pdf Summary-of-changes.pdf ICF-language-target group-edition-date.pdf ICF-language-target group-edition-date-TC version.pdf ...	D	See ICH E6 GCP/EudraLex volume 10 Track changes version(s) must be provided! A summary of changes must be provided! Use of the existing template strongly recommended – possible update in 2017 To be submitted in all languages that will be used in Belgium.
E. Supporting information	e.g. Benefit-Risk.pdf, Justification-of changes.pdf...	E	
F. Update of the EU Application Form	Application-form.pdf	F	Revised version of the EU Application Form (with changes clearly highlighted)

Remark: Section A. "Fulfilment of Introduction and General Principles" may be left empty if no specific information as foreseen in annex II point A. of the Regulation 536/2014 is available.

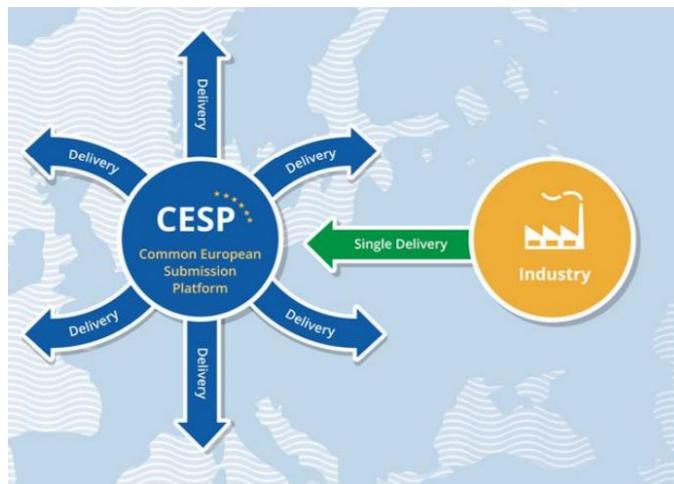
9. Annex III - E-submission through the Common European Portal (CESP)

The Common European Submission Portal is a simple and secure mechanism for the exchange of submission information between applicants and competent authorities in Europe.

CESP is a secure web platform developed by HPRA (Ireland) under the supervision of the Heads of Medicines of Agencies.

The main advantages of this portal include:

- A multipurpose delivery system, can be used for any type of digital information transfer
- Tracking system
- Automatic notification by the application
- Simple, fast, efficient delivery system for information.
- Allows easier, faster submission updates / responses to agency information requests
- Provide a secure method of communicating with the Regulatory Agencies via one platform
- Reduce the burden for both Industry and Regulators of submitting/handling applications on CD-ROM and DVD



9.1. For which application CESP must be used ?

Clinical trials (medicines)	Initial application for a clinical trial
	Substantial amendment for a clinical trial
	ASR/DSUR submission
	Urgent safety measure
	Temporary halt notification
	End of trial declaration
	CTR Pilot – initial application for a clinical trial
	CTR Pilot – Substantial modification for a clinical trial
Clinical investigations (medical devices)	Initial application for a clinical investigation
	Serious Adverse Events Notification
	Notification of end of clinical investigation / performance study
Unmet Medical Needs	Initial application for a CUP/MNP
	Periodic Reevaluation for a CUP/MNP
	Substantial Amendment for a CUP/MNP
Clinical trials, clinical investigations and Unmet Medical Needs	Approval of the ethics committee

When using CESP, please do not send the same dossier via other ways to the agency.

9.2. How to submit an application through CESP?

9.2.1. Account and connection

Link to the website : <https://cesportal.hma.eu/Account/Login>

If you don't already get an account, select "register" or follow this link <https://cesportal.hma.eu/delivery/create>

HMA Common European Submission Portal

Home Announcements FAQs General Information Contacts Terms & Conditions Register

Welcome to the Common European Submission Portal

This system provides a simple and secure mechanism for exchange of information between applicants and regulatory agencies.

The purpose of the system is to:

- Provide a secure method of communicating with the Regulatory Agencies via one platform
- Allow submission of an application once to reach all required Agencies
- Reduce the burden for both Industry and Regulators of submitting/handling applications on CD-ROM and DVD

Login

Username

Password [Forgot password?](#)

[Log in](#) [Register](#)

Latest Updates

Contact	DE(PEI)	28-SEP-2017
Contact	GR(EDF)	29-JUN-2016
Contact	SK(SUKL)	21-JUN-2016
Contact	LV(ZVA)	03-JUL-2017
Contact	CZ(SUKL)	12-JAN-2018
Contact	LT(NMVRVI)	03-JAN-2017
Contact	UK(MHRA)	22-FEB-2017
Contact	PT	07-FEB-2018
Contact	ES	19-DEC-2016
Contact	LT(VVKT)	27-APR-2016

9.2.2. E-submission

First create a delivery file: A new delivery file has to be made for each submission.

The screenshot shows the HMA Common European Submission Portal interface. The left sidebar contains a navigation menu with the following items: Dashboard, New Delivery File (circled in red), Web Upload, Deliveries, Support, Training, Reports, Announcements, Contacts, General Information, FAQs, and Terms & Conditions. The main content area is titled 'New Delivery File' and features a four-step progress indicator (Step 1, Step 2, Step 3, Step 4). Below the progress indicator are several form fields:

- Company *: Test Company
- Area *: Human Medicines
- Regulatory Activity *: Authorisation for temporary use
- Sub Activity *: H001 Not Applicable
- Zip File Type *: 7-Zip
- Comment: (empty text area)

A red-bordered box on the right side of the form contains the following instructions:

1. Select New Delivery File
2. Select Human Medicines or Medical Devices following the object of your submission

A 'Next >' button is located at the bottom right of the form.

- Dashboard
- New Delivery File
- Web Upload
- Deliveries
- Support
- Training
- Reports
- Announcements
- Contacts
- General Information
- FAQs
- Terms & Conditions

New Delivery File

Step 1
Step 2
Step 3
Step 4

Company *

Area *

Regulatory Activity *

Sub Activity *

Zip File Type *

Comment

3. Select :

Clinical trial for the following related submission :

- Initial application for a clinical trial
- Substantial amendment for a clinical trial
- CTR Pilot – initial application for a clinical trial
- CTR Pilot – Substantial modification for a clinical trial
- Urgent safety measure
- Temporary halt notification
- End of trial declaration

Development Safety Update Report :

- ASR/DSUR submission

Authorization for temporary use for the following related submission :

- Initial application for a CUP/MNP
- Periodic Reevaluation for a CUP/MNP
- Substantial Amendment for a CUP/MNP

Medical device for the following related submission :

- Initial application for a clinical investigation
- Substantial amendment for a clinical investigation / performance study
- Notification of end of clinical investigation / performance study

HMA Common European Submission Portal

Dashboard
New Delivery File
Web Upload
Deliveries
Support
Training
Reports
Announcements
Contacts
General Information
FAQs
Terms & Conditions

New Delivery File

Step 1 Step 2 Step 3 Step 4

Company *
Test Company

Area *
Human Medicines

Regulatory Activity *
Clinical Trial

Sub Activity *
H001 Not Applicable

Zip File Type *
7-Zip

Comment

Next >

Select **Sub-Activity** following the procedure step

- Not applicable
- Initial
- Answers to question during validation
- Answers to question during procedure
- Closing Documents

Select the **Zip File Type**

HMA Common European Submission Portal

Dashboard
New Delivery File
Web Upload
Deliveries
Support
Training
Reports
Announcements
Contacts
General Information
FAQs
Terms & Conditions

New Delivery File

Step 1 Step 2 Step 3 Step 4

Company *
Test Company

Area *
Human Medicines

Regulatory Activity *
Clinical Trial

Sub Activity *
H001 Not Applicable

Zip File Type *
7-Zip

Comment

Next >

Indicate here any comment on the process.
e.g. for CTR Pilot: please indicate CTR Pilot

HMA Common European Submission Portal

Dashboard
New Delivery File
Web Upload
Deliveries
Support
Training
Reports
Announcements
Contacts
General Information
FAQs
Terms & Conditions

New Delivery File

Step 1 Step 2 Step 3 Step 4

Procedure Type *
National

Submission Type *
Other eSubmission Type

Technically Validated *
 Yes
 No

< Previous Next >

Choose 'National' as **Procedure type** and 'Other eSubmission Type' as **Submission type** for all related processes.

Should always be 'no' for all related processes.

HMA Common European Submission Portal

Dashboard

- New Delivery File
- Web Upload
- Deliveries
- Support
- Training
- Reports
- Announcements
- Contacts
- General Information
- FAQs
- Terms & Conditions

New Delivery File

Step 1 Step 2 Step 3 Step 4

National Agency (mouseover flag for National Requirements) *

 AT	 BE	 HR	 CY	 CZ(SUKL)
 DK	 EE	 FI	 FR(ANSM)	 DE(BfArM)
 DE(PEI)	 GR(EOF)	 HU(OGYEI)	 IS	 IE
 IT(AIFA)	 LV(ZVA)	 LT(VKLT)	 LU	 MT
 NL	 NO	 PL(URPL)	 PT	 RO(ANMDM)
 SK(SUKL)	 SI(JAZMP)	 ES	 SE	 UK(MHRA)
 EU				

Choose Belgium – famhp to send your submission

HMA Common European Submission Portal

Dashboard

- New Delivery File
- Web Upload
- Deliveries
- Support
- Training
- Reports
- Announcements
- Contacts
- General Information
- FAQs
- Terms & Conditions

New Delivery File

Step 1 Step 2 Step 3 Step 4

Additional Email Addresses

Email

Add Row Delete Row

Product(s)

Agency	MAA Number	Product Name
Select Country		

Add Product Delete Product

Product Details Filename

You can enter the filename of the Products Details File you will be submitting instead of listing the products above

< Previous Submit

- Dashboard
- New Delivery File
- Web Upload
- Deliveries
- Support
- Training
- Reports
- Announcements
- Contacts
- General Information
- FAQs
- Terms & Conditions

Delivery File Download

IMPORTANT NOTICE: Please check for any national requirements for electronic submissions, refer to the [contacts page](#) for agency specific information.

When uploading your submission with either the sFTP client or the web based file transfer system :

1. Download the delivery file to your local PC, by selecting the "Download XML file" button.
2. Do not rename or modify the delivery file.
3. Ensure that there are no other files or folders in the root of the remote server
4. Upload you submission zip file to the remote server, ensuring that is its fully uploaded before going to the next step.
5. Upload your delivery file to the remote server.
6. The submission will then be delivered and you will receive confirmation emails of delivery.
7. Ensure that the emails from cesp@hma.eu are not blocked or sent to your junk mail.

Download Delivery File

You must download the xml file and upload this with your files to submit the application (see next steps).

9.2.3. Upload your files (i.e. the dossier) on CESP

1. Select **Web upload**

The screenshot displays the HMA Common European Submission Portal dashboard. The left sidebar contains navigation options: Dashboard, New Delivery File, Web Upload, Deliveries, Support, Training, Reports, Announcements, Contacts, General Information, FAQs, and Terms & Conditions. The 'Web Upload' option is highlighted with a red arrow. The main content area features four summary cards: Deliveries Uploaded (0), Deliveries Complete (0), Data Uploaded (0.00 MB), and Data Delivered (0.00 MB). Below these is a chart titled 'DELIVERIES COMPLETED BY WEEK' with a legend for years 2014-2018. At the bottom, a section titled 'CESP REAL-TIME INFORMATION: YEAR TO DATE' shows four summary cards for the current year: Deliveries Uploaded (0), Deliveries Complete (0), Data Uploaded (0 MB), and Data Delivered (0 MB).



Two ways to upload files :

- Select "file" and "upload", select your file that you want to upload.
- You can also directly select your file from your windows explorer, and slip it up to the webpage.

You can create several folders for each application

The details over the transfers :

- Completed upload
- Upload in progress
- Pending upload

Very Important: First upload your dossier – as a zip. When the zip is fully uploaded, then upload your delivery file previously downloaded (i.e. the file ending with xml). Also important – do not include a zip inside the zip as cesp does not allow this.



You will find the uploaded files in your folder :

- CESP_Submission_XXXXX.xml : the delivery information, downloaded previously from CESP. It is different for each applications. It has thus to be systematically done for each application (whatever it is).
- "name of your file.zip" : the content of your application in zip format.

NB :

- Reminder: first upload your dossier in ZIP format on the website. When fully uploaded, then add the XML file.
- No further action is requested, the portal will send it to the selected agency and send you an e-mail regarding the notification. You can check it in the "deliveries" section on CESP.

9.3. Training and support

- An On Demand Training module is available to all CESP users. This contains the Latest Video Guides and Training documentation.
- Support : the CESP Group shall provide support in respect of the Portal to authorised users during normal working hours on Monday to Friday (other than public holidays). Contact details for accessing CESP Group support are available on the Portal.
- FAQ is available for your common questions regarding the system :

<https://cespportal.hma.eu/Public/FAQs>

10. Annex IV: Important points for the preparation of the CTR pilot dossier and Q&A

10.1. Important points for the preparation of the CTR pilot dossier

- In the tables presented from page 20 to page 27 of the present document, the column “References” gives some guidance on the way to complete each file of the provided empty structure of the pilot submission dossier. This column “References” has been updated in the present version of the guidance for sponsors, based on the most frequent questions received from the sponsors who already participated to the pilot.
- Protocol:
 - ⇒ following Helsinki declaration art.34 Post trial provisions : “In advance of a clinical trial, sponsors, researchers and host country governments should make provisions for post-trial access for all participants who still need an intervention identified as beneficial in the trial”. As far as possible this should be foreseen in the protocol.
 - ⇒ the first act of recruitment (e.g. advertising) should be specified in the protocol as according to the clinical regulation 536/2014 it defines the official start of the trial.
- Written statements from the sites on their suitability (section N. of Part II, see template in the annexed empty file) are crucial documents for the completeness of the submission dossier as only 1 EC (independent of the participating sites) will evaluate the application dossier. It is thus important to contact the sites as soon as possible in order to obtain these documents in due time for the submission.
- The following templates are available in the annexed empty structure for submission:
 - => Curriculum Vitae of the principal investigator (section M. of Part II). It is not mandatory to use the TransCelerate CV template. Any CV containing the same information would be accepted.
 - => Written statement of the site (section N. of Part II). It is not obligatory to use the template provided as written statement. However, this is strongly recommended as it has been discussed and agreed among ECs that are volunteers to participate to the CTR pilot.
- In the Zipped empty structure the names of the folders have been shortened so that final folder names are not too long. Issues can be encountered at the extraction of a zip-file when the full path length is too long. When sending the submission dossier via Eudralink or CESP, please make sure the files are comprised at the level of the folders Part I & Part II to avoid the presence of unnecessary levels in the dossier.

- Insurance: it is important to refer to art.29 §1 of the law of 7 May 2004 (related to the no fault insurance) in the proof of insurance document.
- The DSMB charter must be part of the submission dossier if a DSMB (Data Safety Monitoring Board) is foreseen for the trial (unless this will be part of the RFI – Request For Information).

10.2. Questions and answers

1) Timelines ?

Short timelines (annex I page 16 of the present guidance) will apply for all phase I trials even if multicentric in Belgium as only one independent EC will assess the dossier.

For ATMP trials an additional period of 30 days will be added to the normal timeline (28 + 30 for phase II, III or IV ATMP trials and 15 + 30 for phase I ATMP trial).

2) Which folders of the zipped empty structure can be left empty ?

Folders A, H and I of Part I are only to be completed if applicable. All folders of Part II have to be completed, either with documentation or a statement or a reference to the protocol (e.g. a reference to the protocol can be accepted in folder K. and L. but a statement from the sponsor has to be provided in folder R.)

3) Fee ?

No fee has to be paid for the submission of a CTA initial dossier or a substantial modification in the CTR pilot, neither to the FAMHP nor to the EC. Folder Q. has been deleted from Part II in the zipped empty structure.

4) How should the synopsis of the protocol be submitted ?

It should be submitted as a separate document.

5) Local ECs?

The submission dossier will be provided for information to the local ECs by the College. The sponsor only provides the submission dossier to the national contact point. The College will also communicate the final decision to the local ECs for information.

6) Safety reporting?

It is not performed via the national contact point but directly to each concerned as usual and following the rules of the CT3 (Detailed guidance on the collection, verification and presentation of adverse event/reaction reports arising from clinical trials on medicinal products for human use) and circular letters 586 and 593 available on the FAMHP website.

7) What is awaited as recruitment procedure (section K.) ?

Reference is made to Regulation 536/2014 : Page 62. K 59. Unless described in the protocol, a separate document shall describe in detail the procedures for inclusion of subjects and shall provide a clear indication of what the first act of recruitment is.

8) For whom is the CV and DOI to be provided in the clinical team?

The CV and DOI are only to be provided for the principal investigator of each site.