Part II Templates

Joint COM/CTFG-HMA/EMA training on the CTR, 9 - 10 March 2021

Katelijne Anciaux

CT College, Belgium

DG GS
Directoraat-generaal Gezondheidszorg
Direction générale Soins de Santé

service public fédéral
SANTE PUBLIQUE,
SECURITE DE LA CHAINE ALIMENTAIRE
ET ENVIRONNEMENT

federale overheidsdienst
VOLKSGEZONDHEID,
VEILIGHEID VAN DE VOEDSELKETEN
EN LEEFMILIEU

.be

Outline

- Overview of the CTA templates
- Who developed the CTA templates?
- Aim and general aspects
- Specific points of attention per CTA template
- Conclusions
- Assessment report Part II template

Overview of CTA templates

	Ref. CTR	
	Article	**Annex I, section**
CV Investigator	7 & 49	M, §65
Declaration of Interest Investigator		M, §66
Sites and facilities suitability	7	N, §67
Recruitment and informed consent procedure	7	D, §17 (z), K, §59 - L, § 62 (a-e)
Compensation for trial participants	7	P, § 70 (subject compensation)

+ a **Guidance document** for sponsors on how to use the templates

to be found on Eudralex Volume 10:
https://ec.europa.eu/health/documents/eudralex/vol-10_en#fragment1

Who developed the CTA templates?

- Prepared by EU WG Harmonization Part II documents:
  - Started 2018
  - Lead: Catherine Blewett (UK), after Brexit Jan 2020: Edit Szepessy (European Commission)
  - Representatives of Ethics committees from NL, SE, BE, SK, GE, FR
  - Final versions were endorsed by the EU CT Expert Group (CTEG, representatives from NCA & Ethics)

Aim and general aspects

- Baseline: develop templates based on the wording in the Regulation / compliant with the CTR
- Where deemed appropriate: include additional fields, endorsed by the member states (CTEG)
- Ethics committees may still request additional information from sponsors
- Member states are advised to implement them (where possible), or to adapt them to the national requirements, and/or to provide guidance to sponsors on how to use them
  - > to support the assessment by the Ethics committee
  - > to support sponsors of CTs in preparing (Part II of) the submission

Aim and general aspects

- Individual Member states may have **national requirements** on the information that is to be provided
- Sponsors should refer to **national guidelines from the member states** when submitting an application in a member state

Overview of CTA templates

	Ref. CTR	
	Article	**Annex I, section**
CV Investigator	7 & 49	M, §65
Declaration of Interest Investigator		M, §66
Sites and facilities suitability	7	N, §67
Recruitment and informed consent procedure	7	D, §17 (z), K, §59 - L, § 62 (a-e)
Compensation for trial participants	7	P, § 70 (subject compensation)

+ a **Guidance document** for sponsors on how to use the templates

to be found on Eudralex Volume 10:
https://ec.europa.eu/health/documents/eudralex/vol-10_en#fragment1

Overview of CTA templates

	Ref. CTR	
	Article	**Annex I, section**
CV Investigator	7 & 49	M, §65
Declaration of Interest Investigator		M, §66
Sites and facilities suitability	7	N, §67
Recruitment and informed consent procedure	7	D, §17 (z), K, §59 - L, § 62 (a-e)
Compensation for trial participants	7	P, § 70 (subject compensation)

+ a **Guidance document** for sponsors on how to use the templates

to be found on Eudralex Volume 10:
https://ec.europa.eu/health/documents/eudralex/vol-10_en#fragment1

CV Investigator & Declaration of Interest Investigator

- Definition of an “Investigator”
  - Principal Investigator : responsible leader of a team of investigators who conduct at a CT site
  - Investigator : responsible for the conduct of a clinical trial at a CT site
- **one** document **per site**

Overview of CTA templates

	Ref. CTR	
	Article	**Annex I, section**
CV Investigator	7 & 49	M, §65
Declaration of Interest Investigator		M, §66
Sites and facilities suitability	7	N, §67
Recruitment and informed consent procedure	7	D, §17 (z), K, §59 - L, § 62 (a-e)
Compensation for trial participants	7	P, § 70 (subject compensation)

+ a **Guidance document** for sponsors on how to use the templates

to be found on Eudralex Volume 10:
https://ec.europa.eu/health/documents/eudralex/vol-10_en#fragment1

CV Investigator

- Annex I, section M, §65

M. SUITABILITY OF THE INVESTIGATOR (INFORMATION PER MEMBER STATE CONCERNED)

65. Description of the qualification of the investigators in a **current curriculum vitae** and other relevant documents shall be submitted.

Any previous **training** in the principles of **good clinical practice** or **experience** obtained from work with **clinical trials** and patient care shall be described.

CV Investigator

- Suitability must be proven for **one (principal) investigator per site**
  - Qualifications of the **other investigators**, **other personnel** is covered in the **Site suitability declaration**
- Experience given should be **relevant**:
  - regarding time: preceding 10 years as a maximum
  - regarding role as principal investigator
- **National legislation** might be different regarding:
  - For whom the CV should be provided (only PI or also other investigators)
  - Whether CV should be signed or not, or type of signature (electronic, wet ink)

Overview of CTA templates

	Ref. CTR	
	Article	**Annex I, section**
CV Investigator	7 & 49	M, §65
Declaration of Interest Investigator		M, §66
Sites and facilities suitability	7	N, §67
Recruitment and informed consent procedure	7	D, §17 (z), K, §59 - L, § 62 (a-e)
Compensation for trial participants	7	P, § 70 (subject compensation)

+ a **Guidance document** for sponsors on how to use the templates

to be found on Eudralex Volume 10:
https://ec.europa.eu/health/documents/eudralex/vol-10_en#fragment1

Declaration of Interest of Investigator

- Annex I, section M, §66

M. SUITABILITY OF THE INVESTIGATOR (INFORMATION PER MEMBER STATE CONCERNED)

66. Any **conditions**, such as economic interests and institutional affiliations, **that might influence the impartiality of the investigators** shall be presented.

Declaration of Interest of Investigator

- Documentation on Impartiality must be given for **one (principal) investigator per site**
  - To address impartiality of the **other investigators and other personnel,** is covered in the **Site suitability declaration**
- National legislation might be different regarding:
  - For whom the DOI should be provided (only PI or also other investigators)
  - Type of Signature : wet ink or electronic

Overview of CTA templates

	Ref. CTR	
	Article	**Annex I, section**
CV Investigator	7 & 49	M, §65
Declaration of Interest Investigator		M, §66
Sites and facilities suitability	**7**	**N, §67**
Recruitment and informed consent procedure	7	D, §17 (z), K, §59 - L, § 62 (a-e)
Compensation for trial participants	7	P, § 70 (subject compensation)

+ a **Guidance document** for sponsors on how to use the templates

to be found on Eudralex Volume 10:
https://ec.europa.eu/health/documents/eudralex/vol-10_en#fragment1

Sites and facilities suitability

- Annex I, section N, §67

N. SUITABILITY OF THE FACILITIES (INFORMATION PER MEMBER STATE CONCERNED)

67. A duly justified written statement on the **suitability of the clinical trial sites** adapted to the nature and use of the investigational medicinal product and including

a description of

the suitability of facilities,
equipment,
human resources and description of expertise,

issued by the head of the clinic/institution at the clinical trial site or by some other responsible

person, according to the system in the Member State concerned, shall be submitted.

Sites and facilities suitability

- **One** document **per site:**
  - When information of the template is already available elsewhere in the CTA,

    a **reference** may be added
- **National legislation** might be different regarding:
  - Information to be provided (if no national guidelines, it should be completed in full)
  - Type of Signature : wet ink or electronic

Overview of CTA templates

	Ref. CTR	
	Article	**Annex I, section**
CV Investigator	7 & 49	M, §65
Declaration of Interest Investigator		M, §66
Sites and facilities suitability	7	N, §67
Recruitment and informed consent procedure	7	D, §17 (z), K, §59 - L, § 62 (a-e)
Compensation for trial participants	7	P, § 70 (subject compensation)

+ a **Guidance document** for sponsors on how to use the templates

to be found on Eudralex Volume 10:
https://ec.europa.eu/health/documents/eudralex/vol-10_en#fragment1

Recruitment and Informed Consent Procedure

- Protocol (in Annex I)

D. PROTOCOL

17. The protocol shall at least include:

(z) a detailed description of the **recruitment and informed consent procedure**, especially when subjects are incapable of giving informed consent;

Recruitment and Informed Consent Procedure

- Recruitment arrangements (in Annex I)

K. RECRUITMENT ARRANGEMENTS (INFORMATION PER MEMBER STATE CONCERNED)

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.

Recruitment and Informed Consent Procedure

- Informed Consent Procedure (in Annex I)

L. SUBJECT INFORMATION, INFORMED CONSENT FORM AND INFORMED CONSENT PROCEDURE (INFORMATION PER MEMBER STATE CONCERNED)

62. A description of **procedures relating to informed consent** for **all subjects**, and in particular:

(a) in clinical trials with **minors or incapacitated subjects**, the procedures to obtain informed consent from the legally designated representatives, and the involvement of the minor or incapacitated subject shall be described;

(b) if a procedure with consent witnessed by an **impartial witness** is to be used, relevant information on the reason for using an impartial witness, on the selection of the impartial witness and on the procedure for obtaining informed consent shall be provided;

(c) in the case of clinical trials in **emergency situations** as referred to in Article 35, the procedure for obtaining the **informed consent** of the subject or the legally designated representative to continue the clinical trial shall be described;

(d) in the case of clinical trials in **emergency situations** as referred to in Article 35, the description of the procedures followed to **identify the urgency** of the situation and to document it;

(e) in the case of clinical trials where their methodology requires that **groups of subjects** rather than individual subjects are allocated to receive different investigational medicinal products, as referred to in Article 30, and where, as a consequence simplified means for obtaining informed consent will be used, the simplified means shall be described.

Recruitment and Informed Consent Procedure

- **How** to use the template?
  - Use template and refer to it in protocol

  OR

  - In protocol: describe general (minimal) information (valid for all member states) and use the template to describe member state specific info

- **Additional info** to be submitted:
  - Recruitment advertisement materials (if applicable)
  - All info given to participant, consent documents:
    - Incl. e-consent procedures (if applicable)
    - Impartial witness: not being able to write physically or due to illiteracy

Overview of CTA templates

	Ref. CTR	
	Article	**Annex I, section**
CV Investigator	7 & 49	M, §65
Declaration of Interest Investigator		M, §66
Sites and facilities suitability	7	N, §67
Recruitment and informed consent procedure	7	D, §17 (z), K, §59 - L, § 62 (a-e)
Compensation for trial participants	7	P, § 70 (subject compensation)

+ a **Guidance document** for sponsors on how to use the templates

to be found on Eudralex Volume 10:
https://ec.europa.eu/health/documents/eudralex/vol-10_en#fragment1

Compensation for trial participants

- Annex I, section P, §70

P. FINANCIAL AND OTHER ARRANGEMENTS (INFORMATION PER MEMBER STATE CONCERNED)

70. Information on financial transactions and **compensation paid to subjects** and investigator/site for participating in the clinical trial shall be submitted.

Compensation for trial participants

- **All** compensation (**monetary & non-monetary**)
  paid to trial participants & persons supporting the participant.
  It may concern compensation for
  - Costs
  - Loss of earnings
  - Discomfort and suffering
  - If applicable: mention the conditions to the payment
- Compensation should **not lead to undue influence**
- **Patient** trials:
  - Some members states do not accept monetary compensations for participation.
  - Incapacitated adults, minors, breast-feeding women: no incentive or financial inducement is accepted (except compensation of expenses or loss of earnings), a small token of appreciation needs to be allowed by the EC (Q&A 9.1.).

Compensation for trial participants

- **Additional info** to be submitted:
  - Other financial agreements between sponsor and investigator (Annex I, P §70-71)

Conclusions - CTA templates

- Templates are **compliant with CTR**
- Member states / Ethics committees may request **additional information**
- **Member states are advised**
  - to implement the templates, and
  - to provide guidelines to sponsors to clarify national requirements
  - (if applicable) to provide own (slightly) adapted versions to sponsors

Assessment report Part II - template

- E.g. Article 7, §2

Each Member State concerned shall complete its assessment ... and submit, through the EU portal, **Part II of the assessment report**, including its conclusion, to the sponsor.

Assessment report Part II - template

- Assessment report (Part I and) Part II must be submitted via the EU Portal
- Template for Assessment report Part II will be available in CTIS
  - It is not mandatory to use the template
- Member states are advised
  - to use as much as possible the template and
  - adapt it to national requirements and procedures

Assessment report Part II - template

Assessment report Part II

1) ADMINISTRATIVE INFORMATION

EU trial number	
Title of the study	
Name of sponsors	
IMPs (repeat for PR1, PR2.....)	**Substance (name/ code):** **Marketing authorization status (MA number, MS where authorized etc):** **Modified in relation to MA:**

Has Part I been submitted prior to the submission of Part II?	Yes ☐ No ☐
If Yes	
Is there already a conclusion on part I?	Yes ☐ No ☐
Is the CT already approved in any member state?	Yes ☐ No ☐

Version; draft or final

2) GENERAL INFORMATION

Is the CT a low-interventional trial?[1]	Yes ☐ No ☐
First in man ☐, Phase I ☐, II ☐, III ☐, IV ☐ NA ☐	
Is the CT a cluster trial[2]	Yes ☐ No ☐
Is the CT intended to be performed in more than one member states?	Yes ☐ No ☐

Assessment report Part II - template

Content