European Commission

Public Health

EudraLex - Volume 10 - Clinical trials guidelines

Volume 10 of the publication "The rules governing medicinal products in the European Union" contains guidance documents applying to clinical trials.

A number of documents in Volume 10 are being revised and updated to bring them in line with the changes required by the Clinical Trials Regulation (EU) No 536/2014. Additionally, new documents were prepared to cover new aspects introduced by the same Regulation.

In order to make a distinction between documents applicable to clinical trials authorised under Directive 2001/20/EC (i.e. the current applicable documents) and documents relevant to clinical trials authorised under Regulation (EU) No 536/2014, these documents will be listed in two separate pages on the Eudralex Volume 10 website.

Until the Clinical Trials Regulation becomes applicable sponsors should follow the documents relevant to the Clinical Trials Directive.

During the transitional period, which will last for a period of 3 years starting from when the Regulation becomes applicable, both sets of documents will apply accordingly and should be referred to respectively according to the legislation under which the Clinical trial is conducted.

At the end of the transitional period all clinical trials shall be conducted under the Regulation and should follow only the set of documents applicable to the Regulation.

Although it is not mandatory, stakeholders are encouraged to take already into consideration a number of aspects that are outlined in the new or updated documents published in the page dedicated to the Clinical Trial Regulation and apply them to those clinical trials authorised under the Directive, to the extent possible and in compatibility with the legal framework of the Directive.

Set of documents applicable to clinical trials authorised under Regulation EU No 536/2014

Recommendations to sponsors on managing the impact of the war in Ukraine on clinical trials

The Clinical Trials Coordination Group (an HMA working group of experts in the classification, assessment and oversight of clinical trials from National Agencies) has published a set of recommendations focusing on the transfer of trial participants from centres in Ukraine to centres in the EU/EEA *(https://www.hma.eu/fileadmin/dateien/HMA_joint/00-_About_HMA/03-Working_Groups/CTCG/2022_04_CTCG_recommendation_to_sponsors_on_managing_the_impact_of_the_war_in_Ukraine_on_clinical_trials.pdf)* within the same multinational clinical trial.

Guidance on the management of clinical trials during COVID-19 pandemic

Guidance document EN ••• (UPDATED VERSION v5 - 10 February 2022)
Slides of the webinar about the Guidance on the management of clinical trials during the COVID-19 pandemic EN •••
Webinar about the Guidance on the management of clinical trials during the COVID-19 pandemic EN •••

Chapter I - Application and application documents

- Part II application document templates
  - Compensation for trial participants - Template: PDF EN •••/Word EN •••
  - Harmonisation guidance: PDF EN •••
  - Investigator Curriculum Vitae template: PDF EN •••/Word EN •••
  - Declaration of interest template: PDF EN •••/Word EN •••
  - Site suitability form: PDF EN •••/Word EN •••
  - Informed consent and patient recruitment procedure template: PDF EN •••/Word EN •••
  - Compliance with applicable rules for biological samples: PDF *(/document/download/bd1f95f2-93a2-4877-8c20-45f150949aa4_en?filename=mp_compliance-app-rules-bio_en.pdf)* EN •••/Word *(/document/download/29ba64b6-8057-4e39-b09b-8ad356a8f5ca_en?filename=mp_compliance-app-rules-bio_en.docx)* EN •••

Chapter II - Safety reporting

- ICH guideline E2F - Note for guidance on development safety update reports (September 2010)

For more guidance on safety reporting please refer to the Q&A document on the Clinical Trials Regulation in Chapter V

Chapter III – Quality

- Template for the qualified person's declaration equivalence to EU GMP for Investigational Medicinal Products manufactured in third countries : PDF version EN - Word version EN (may 2013)
- Detailed Commission guideline of 8 December 2017 on the good manufacturing practice for investigational medicinal products pursuant to the second paragraph of the Article 63(1) of Regulation (EU) No 536/2014 EN
- Template for IMP batch release (applicable as from the date of entry into application of Regulation (EU) No 536/2014 on Clinical Trials) EN
- Union Basic Format for Manufacturer's Authorisation (June 2013)
- Guideline on the requirements to the chemical and pharmaceutical quality documentation concerning investigational medicinal products in clinical trials (revision 2 – January 2022) *(/document/download/257ad13a-c480-4c34-82df-1760ad1d5f68_en?filename=mp_eudralex_guideline-chemical_en_1.pdf)* EN
- Guideline on the requirements for quality documentation concerning biological investigational medicinal products in clinical trials (Revision 2 - January 2022) *(/document/download/bd71e2e7-4df1-491a-8775-c6483a97f749_en?filename=mp_eudralex_guideline-quality_en_0.pdf)* EN
- Auxiliary medicinal products in clinical trials EN (rev. 2, June 2017)

Chapter IV – Inspections

- Guidance for the conduct of good clinical practice inspections (August 2017) EN
- Annex I – to guidance for the conduct of good clinical practice inspections – investigator site (September 2017) EN
- Annex II – to guidance for the conduct of good clinical practice inspections – clinical laboratories (August 2017) EN
- Annex III – to guidance for the conduct of good clinical practice inspections – computer systems (March 2018) EN
- Annex IV – to guidance for the conduct of good clinical practice inspections – sponsor and CRO (August 2017) EN
- Annex VI – to guidance for the conduct of good clinical practice inspections – record keeping and archiving of documents (June 2017) EN
- Annex VII – to guidance for the conduct of good clinical practice inspections – bioanalytical part, pharmacokinetic and statistical analyses of bioequivalence trials (June 2017) EN
- Guidance for the preparation of good clinical practice inspections (August 2017) EN
- Guidance for the preparation of good clinical practice inspection reports and communication of inspection findings (June 2017) EN
- Guidance for coordination of GCP inspections requested in the context of marketing authorisation applications for mutual recognition and decentralised procedures and cooperation between Member States (March 2018) EN

Note: The revision of Annex V on inspections of phase I unit, has been put on hold until finalisation of the "Guideline on strategies to identify and mitigate risks for first-in-human and early clinical trials with investigational medicinal products" now published on the EMA website. An updated version of the document will be provided in due course.

Chapter V - Additional documents

- Accelerating clinical trials in the EU (ACT EU) - Delivering an EU clinical trials transformation initiative *(https://ec.europa.eu/health/document/download/8a2858a2-c825-4439-8e16-d7d8892f5607_en)* EN
- Questions and Answers Document - Regulation (EU) 536/2014 – Version 6.1 (May 2022) EN
  Please note that certain Q&As and a section of this document are still being discussed within the expert group on clinical trials and are therefore not yet included. Updated versions of the document will be published progressively.
- Q&A on Complex clinical trials (May 2022) *(https://ec.europa.eu/health/document/download/644db849-052e-42f6-8619-8bba9c7b974e_en?filename=medicinal_qa_complex_clinical-trials_en.pdf)* EN
  This document has been developed in close collaboration between the European Medicines Agency, the Clinical Trials Coordination Group and the Clinical Trial Expert Group. It was endorsed by those groups and by the ACT EU Steering Group.
- Q&A on the interface between Regulation (EU) 536/2014 on clinical trials for medicinal products for human use (CTR) and Regulation (EU) 2017/746 *(https://ec.europa.eu/health/document/download/59abcc81-fd32-4546-a340-24c8fad4e2ac_en?filename=mdcg_2022-10_en.pdf)* EN
  This document has been developed and endorsed by the Medical Device Coordination Group (MDCG) and the Clinical Trial Expert Group (CTEG).
- Question and Answers on the interplay between the Clinical Trials Regulation and the General Data Protection Regulation (April 2019) EN
  This document is applicable under the Clinical Trials Regulation except for question 11 which explains the current situation under the Clinical Trials Directive.
- Guideline on strategies to identify and mitigate risks for first-in-human and early clinical trials with investigational medicinal products - EMEA/CHMP/SWP/28367/07 Rev. 1 (July 2017)
- Guideline for good clinical practice - ICH E6(R2) - EMA/CHMP/ICH/135/1995 (2016)
- Risk proportionate approaches in clinical trials EN (April 2017)
- Summaries of Clinical Trial Results for Laypersons EN (version 2 - February 2018)
- Good Lay Summary Practice Guidance EN
- Ethical considerations for clinical trials on medicinal products conducted with minors EN
- Detailed guidelines on good clinical practice specific to advanced therapy medicinal products – (*Update currently ongoing*)
- Recommendation on the content of the trial master file and archiving – (*Update currently ongoing*)
- List of national contact points EN

Chapter VI – Legislation

Regulation (EU) No 536/2014 EN 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

Commission Implementing Regulation (EU) 2017/556 EN of 24 March 2017 on detailed arrangements for the good clinical practice inspection procedures pursuant to Regulation (EU) No 536/2014 of the European Parliament and of the Council

Commission Delegated Regulation (EU) 2017/1569 EN (for linguistic versions, click here EN) of 23 May 2017 supplementing Regulation (EU) 536/2014 of the European Parliament and of the Council by specifying principles and guidelines for good manufacturing practice for investigational medicinal

products for human use and arrangements for inspections (applicable as from the date of entry into application of Regulation (EU) No 536/2014 on Clinical Trials)

Commission Implementing Regulation (EU) 2022/20 EN ••• of 7 January 2022 laying down rules for the application of Regulation (EU) No 536/2014 of the European Parliament and of the Council as regards setting up the rules and procedures for the cooperation of the Member States in safety assessment of clinical trials (Text with EEA relevance)

Set of documents applicable to clinical trials authorised under Directive 2001/20/EC

Joint EC/EMA/HMA technical notice to sponsors regarding continuous compliance with the EU legislation for clinical trials following the withdrawal of the United Kingdom from the EU EN •••

General information EN ••• (July 2006)

Chapter I - Application and application form

- Detailed guidance for the request for authorisation of a clinical trial on a medicinal product for human use to the competent authorities, notification of substantial amendments and declaration of the end of the trial EN •••.
  - Annex 1 revised : PDF version EN ••• - Word version EN ••• (revision 4 of November 2009 ; updated on 22 of November 2019). EudraCT Version 8.0 uses the Revision 4 dated November 2009 of the Clinical Trials Application Form (updated on November 22, 2019). For more information please refer to the EudraCT website.
  - Substantial Amendment Notification Form : PDF version EN ••• - Word version EN ••• (revision 3 of June 2010)
  - Declaration of the End of Trial Form : PDF version EN ••• - Word version EN ••• (revision 19 of June 2019)
- Detailed guidance on the application format and documentation to be submitted in an application for an Ethics Committee opinion on the clinical trial on medicinal products for human use EN ••• (revision 1 of February 2006)
- Detailed guidance on the European clinical trials database (EUDRACT Database) EN ••• (revision of April 2004)

Chapter II - Safety reporting

- Detailed guidance on the collection, verification and presentation of adverse event/reaction reports arising from clinical trials on medicinal products for human use ("CT-3") EN •••
- ICH guideline E2F - Note for guidance on development safety update reports (September 2010)

Chapter III - Quality of the investigational medicinal product

- Template for the qualified person's declaration equivalence to EU GMP for Investigational Medicinal Products manufactured in third countries : PDF version EN ••• - Word version EN ••• (may 2013)
- Good manufacturing practice for investigational medicinal products
  - Good manufacturing practices for manufacture of investigational medicinal products EN ••• (February 2010)
  - Detailed Commission guideline of 8 December 2017 on the good manufacturing practice for investigational medicinal products pursuant to the second paragraph of the Article 63(1) of Regulation (EU) No 536/2014 EN ••• (applicable as from the date of entry into application of Regulation (EU) No 536/2014 on Clinical Trials)
  - Template for IMP batch release (applicable as from the date of entry into application of Regulation (EU) No 536/2014 on Clinical Trials) EN •••
- Union Basic Format for Manufacturer's Authorisation EN ••• (October 2014)
- Guideline on the requirements to the chemical and pharmaceutical quality documentation concerning investigational medicinal products in clinical trials EN •••
- Guideline on the requirements for quality documentation concerning biological investigational medicinal products in clinical trials EN ••• (September 2018)
- Guidance on Investigational Medicinal Products (IMPs) and "non investigational medicinal products" (NIMPs) EN ••• (rev. 1, March 2011)

Chapter IV - Inspections

- Guidance for the preparation of GCP inspections EN ••• (June 2008)
- Recommendation on inspection procedures for the verification of good clinical practice compliance EN ••• (July 2006)
- Guidance for the conduct of GCP inspections EN ••• (June 2008)
- Annex I to Guidance for the conduct of GCP inspections - Investigator site EN ••• (June 2008)
- Annex II to Guidance for the conduct of GCP inspection - Clinical laboratories EN ••• (June 2008)
- Annex III to Guidance for the conduct of GCP inspections - Computer systems EN ••• (June 2008)
- Annex IV to Guidance for the conduct of GCP inspections - Sponsor and CRO EN ••• (June 2008)
- Annex V to Guidance for the conduct of GCP inspections - Phase I Units EN ••• (November 2008)
- Annex VI to Guidance for the conduct of GCP inspections - Record keeping and archiving of documents EN ••• (March 2010)
- Annex VII to Guidance for the conduct of GCP inspections - Bioanalytical part, Pharmacokinetic and Statistical Analyses of Bioequivalence Trials EN ••• (November 2008)
- Guidance for coordination of GCP inspections and co-operation between GCP inspectors, the reference and concerned Member States and CMD(h), in the context of the evaluation of the GCP compliance of marketing authorization applications for mutual recognition and decentralized procedures EN ••• (June 2009)
- Guidance for exchange of GCP Inspection Reports according to Article 15(2) of Directive 2001/20/EC EN ••• (revision 1 - May 2009)
- Guidance for the communication on GCP inspections and findings EN ••• (June 2008)
- Procedure for standardisation of GCP inspection entries in EudraCT EN ••• (November 2008)
- Guidance for the preparation of Good Clinical Practice inspection reports EN ••• (June 2008)
- Recommendations on the qualifications of inspectors verifying compliance in clinical trials with the provisions of Good Clinical Practice EN ••• (July 2006)

Chapter V - Additional information

- Guideline on strategies to identify and mitigate risks for first-in-human and early clinical trials with investigational medicinal products - EMEA/CHMP/SWP/28367/07 Rev. 1 (July 2017)
- Guideline for good clinical practice - ICH E6(R2) - EMA/CHMP/ICH/135/1995 (2016)
- Guidelines on Good Clinical Practice specific to Advanced Therapy Medicinal Products EN •••(2019)
- Recommendation on the content of the trial master file and archiving EN ••• (July 2006)
- "Questions & Answers" Document - Version 11.0 EN ••• (May 2013)
- Ethical considerations for clinical trials on medicinal products conducted with the paediatric population:
  - Original version EN ••• (2008)
- Guideline 2008/C168/02 on the data fields from the European clinical trials database (EudraCT) that may be included in the European database on Medicinal Products EN •••
- List of fields contained in the "EudraCT" clinical trials database to be made public, in accordance with Article 57(2) of Regulation (EC) No 726/2004 and its implementing guideline 2008/C168/02 EN ••• (June 2019)
- Guideline 2009/C28/01 on the information concerning paediatric clinical trials to be entered into the EU Database on Clinical Trials (EudraCT) and on the information to be made public by the European Medicines Agency (EMA), in accordance with Article 41 of Regulation (EC) No 1901/2006 EN •••
- List of fields to be made public from EudraCT for Paediatric Clinical Trials in accordance with Article 41 of Regulation (EC) No 1901/2006 and its implementing guideline 2009/C28/01 EN ••• (June 2019)
- Guidance on posting and publication of result-related information on clinical trials in relation to the implementation of Article 57(2) of Regulation (EC) No 726/2004 and Article 41(2) of Regulation (EC) No 1901/2006 EN •••
- Technical guidance on the format of the data fields of result-related information on clinical trials submitted in accordance with Article 57(2) of Regulation (EC) No 726/2004 and Article 41(2) of Regulation (EC) No 1901/2006 EN ••• (January 2013)
- EudraCT - List of additional fields contained in EudraCT (reasons for negative opinions of the Ethics Committee) EN ••• (November 2010)

Chapter VI - Legislation

- Directive 2001/20/EC OF the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use EN •••
- Commission Directive 2005/28/EC of 8 April 2005 laying down principles and detailed guidelines for good clinical practice as regards investigational medicinal products for human use, as well as the requirements for authorisation of the manufacturing or importation of such products EN •••
- Commission Directive 2003/94/EC of 8 October 2003 laying down the principles and guidelines of good manufacturing practice in respect of medicinal products for human use and investigational medicinal products for human use (OJ L 262, 14.10.2003, p. 22-26) EN •••

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News announcement | 30 May 2022

Questions and Answers Document – Regulation (EU) 536/2014 – Version 6.1, May 2022 *(/latest-updates/questions-and-answers-document-regulation-eu-5362014-version-61-may-2022-2022-05-30_en)*

News announcement | 25 May 2022

Q&A on the interface between Regulation (EU) 536/2014 on clinical trials for medicinal products for human use (CTR) and Regulation (EU) 2017/746 *(/latest-updates/qa-interface-between-regulation-eu-5362014-clinical-trials-medicinal-products-human-use-ctr-and-2022-05-25_en)*

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