KLH-19 version 3

Requirements on authorisation of clinical trials on medicinal products – data required for the pharmaceutical part of the documentation

This guideline supersedes the KLH-19 guideline, version 2, effective from September 11, 2024.

This guideline specifies the requirements for the quality part of the documentation submitted with the application for authorisation of a clinical trial. The guideline is issued on the basis of and in accordance with the provisions of Sections 51 and 56 of Act No. 378/2007 Coll., on Pharmaceuticals and on Amendments to Some Related Acts (Act on Pharmaceuticals), as amended.

This guideline serves as a recommendation.

Requirements for Quality Data

Investigational medicinal product is a pharmaceutical form of an active substance, i.e., a drug product or a product obtained by technological processing of only excipients (placebo), which is tested or used as a reference in a clinical trial. Investigational medicinal product may also be an already authorised medicinal product which is used or modified (with respect to formulation or packaging) in a way different from the authorised form, or when used for an unauthorised indication, or when used to gain further information about the authorised form.

The requirements for quality documentation are therefore the same for both tested and comparator products. Data on the placebo are also submitted, if used in the study.

In those cases where a medicinal product not authorised in the Czech Republic is to be used in a clinical trial as a standard, relief, or rescue medication, it is necessary to submit quality data in the same extent as those for investigational medicinal products.

At present, clinical trials are conducted in compliance with Directive 2001/20/EC or Regulation (EU) no. 536/2014 of the European Parliament and of the Council. A request for a new clinical trial application can only be submitted under Regulation No. 536/2014, however, clinical trials authorised in the past under the Directive 2001/20/EC must either be completed or transitioned by 30th January 2025. For more details, it is recommended to follow the website of the European Commission and of the State Institute for Drug Control (SÚKL).

The quality dossier which is to be submitted with the application for a clinical trial, should follow the CTD format. For information on the structure of the documentation and on the content of individual sections see: ICH Official web site : ICH

The quality part of the dossier corresponds to Module 3. This template is common for all types of medicinal products. It is therefore necessary to adapt the content of the documentation to the specific type of the product. Nevertheless, this template should be followed during assembling of the documentation and if any part of the dossier is omitted, such omission should be justified.

1. Medicinal Products Obtained through Chemical Synthesis

The extent of the required information is defined by the current effective version of the European Medicines Agency (EMA) guideline "Requirements to the Chemical and Pharmaceutical Quality Documentation Concerning Investigational Medicinal Products in Clinical Trials" (CHMP/QWP/545525/2017) as published on EMA´s website („home/human regulatory/research and development/scientific guidelines/quality guidelines/specific types of products").

(https://www.ema.europa.eu/en/requirements-chemical-pharmaceutical-quality-documentation-concerning-investigational-medicinal-products-clinical-trials-scientific-guideline)

2. Medicinal Products of Biological/Biotechnological Origin

The extent of the required information is defined by the current effective version of the EMA guideline "Requirements for quality documentation concerning biological investigational medicinal products in clinical trials" (CHMP/BWP/534898/2008), as published on the EMA´s website („home/human regulatory/ research

and development/scientific guidelines/quality guidelines/biologicals/finished product/ investigational medicinal products“).

(https://www.ema.europa.eu/en/requirements-quality-documentation-concerning-biological-investigational-medicinal-products-clinical-trials-scientific-guideline)

If the product contains a raw material obtained from human blood or its components, the submitted documentation must meet the requirements defined by SÚKL Guideline REG-60 “Requirements for the Marketing Authorisation of Medicinal Products Manufactured Using Materials Derived from Human Blood or Blood Components”, published on SÚKL´s website under the Guidelines and Forms section. These products must also meet the requirements of the current effective guidelines for blood derivatives listed on the EMA website (e.g. “Guideline on plasma-derived medicinal products” (EMA/CHMP/BWP/706271/2010)) and must be in accordance with the European Pharmacopoeia (Ph.Eur.). It is also necessary to submit documents in accordance with the Act on Pharmaceuticals and the Decree on Human Blood (i.e. Decree No. 143/2008 Coll. on the determination of detailed requirements for ensuring the quality and safety of human blood and its components, as amended).

EMA guidelines: Biologicals: active substance | European Medicines Agency (europa.eu)

3. Advanced Therapy Medicinal Products

The required extent of information is defined by the current effective version of the EMA “Guideline on quality, non-clinical and clinical requirements for investigational advanced therapy medicinal products in clinical trials” (EMA/CAT/852602/2018) as published on the EMA´s website (https://www.ema.europa.eu/en/guideline-quality-non-clinical-clinical-requirements-investigational-advanced-therapy-medicinal). Where human tissues and cells or human blood and its components are the starting material for manufacture, their donation, procurement, and testing should follow the Directive 2004/23/EC or Directive 2002/98/EC, as applicable.

SÚKL recommends following the relevant guidance on the EMA´s website dedicated to ATMP (“home/human regulatory/research and development/advanced therapy medicines/scientific guidelines”).

(https://www.ema.europa.eu/en/human-regulatory/research-development/advanced-therapies/guidelines-relevant-advanced-therapy-medicinal-products)

4. Radiopharmaceutical Products

According to Act No. 378/2007 Coll., on Pharmaceuticals and on Amendments to Some Related Acts (Act on Pharmaceuticals), as amended, radiopharmaceuticals are medicinal products which, when ready for use, contain one or more radionuclides (radioactive isotopes) integrated for medicinal purposes. Furthermore, the Act on Pharmaceuticals defines radionuclide generators, kits, and radionuclide precursors.

The requirements related to the documentation for radiopharmaceutical products are summarised in the current effective version of the EMA guideline “Requirements to the Chemical and Pharmaceutical Quality Documentation Concerning Investigational Medicinal Products in Clinical Trials”, (CHMP/QWP/545525/2017), as published on the EMA´s website („home/human regulatory/research and development/scientific guidelines/quality guidelines/specific types of products“).

(https://www.ema.europa.eu/en/requirements-chemical-pharmaceutical-quality-documentation-concerning-investigational-medicinal-products-clinical-trials-scientific-guideline)

The aforementioned products must also meet the requirements defined by the European Pharmacopoeia (Ph. Eur.).

Where radiopharmaceuticals not authorised according to the Act on Pharmaceuticals are to be used, SÚKL shall request an opinion from the State Office for Nuclear Safety (SÚJB) as specified under Section 56, paragraph 3 of the Act on Pharmaceuticals. In accordance with valid legislation, SÚKL may request this opinion from the sponsor.

SÚJB contact address for request for opinion:

Státní úřad pro jadernou bezpečnost

odbor usměrňování expozic

Senovážné nám. 9

110 00 Praha 1

5. Other Required Documents

Good manufacturing practice (GMP) documents have to be submitted for all manufacturing, testing, packaging, labelling, certification, and import sites. The requirements related to these documents are summarised in the relevant European legislation (e.g. in the Regulation (EU) no. 536/2014 of the European Parliament and of the Council) and in the current version of SÚKL´s Guideline KLH-12.

For the purposes of a clinical trial, all investigational medicinal products have to be labelled in the Czech language.

The requirements for labelling of investigational medicinal products to be used in clinical trials authorised under Directive 2001/20/EC are summarised in SÚKL´s guideline VYR-32 Annex 13 version 1 (translation of "The Rules Governing Medicinal Products in the European Union, Volume 4, EU Guidelines to Good Manufacturing Practice, Annex 13, Investigational Medicinal Products").

For clinical trials authorised under Regulation (EU) no. 536/2014 of the European Parliament and of the Council, the labelling requirements are summarised in chapter X and in Annex VI.