Introduction

The content of the clinical trial application (CTA) dossiers to be submitted to Swissmedic can be found in Annex 4 of the Clinical Trials Ordinance (ClinO, SR 810.305).

The present guideline clarifies the requirements for CTA dossiers concerning **clinical trials with medicinal products**.

Application format:

1. All instructions and templates for the submission of a new Clinical Trial Application (CTA) can be found on our webpage: Home > Human medicines > Clinical trials > Clinical trials on medicinal products

2. Use the **FO Submission Form** for the submission of a new Clinical Trial Application. This form contains all 5 possibilities of submissions on clinical trials 1) New CTA, 2) submission to an authorised clinical trial, 3) answer to condition, 4) answer to formal deficiency and 5) answer to further information request.) The form can be downloaded from our webpage. For instructions on this form see <*Quick instruction for use of new submission form*>.

3. Use the **eDoc folder structure** we provide you with on our web page as Zip File for download <*eDoc-file structure (ZIP file)*>.
   For instructions on the filing of the submission package into the E-Doc see <*Instructions for filling the eDoc folder structure*>

   Important:
   - Please note that **the FO Submission Form** has to be filed in the **01FM** folder as a PDF, a scan is not allowed here.
   - The scan of this **signed form** or the **scanned Signature** page of this form has to be filed in the **02FO** folder.

Points to consider:

- **Incomplete submission** dossiers will not be processed. We therefore ask you to ensure that all necessary documentation is provided, in order to avoid queries and delays.

- If any of the documents submitted - such as Investigator's Brochure (IB) or Pharmaceutical Quality Dossier (PQD) - were previously approved by Swissmedic for another clinical trial, cross reference to the other clinical trial should be made in the CTA. Nevertheless, all documents must be submitted again. **Documents modified** since last approval in an other clinical trial should be submitted in **track-change format**.

- **Updated documents becoming available** during the review period by Swissmedic will not be considered as part of the first application and will be evaluated as amendments after study approval. The documents have to be submitted with a new submission form.

- **Parallel submission:**
  For confidentiality reasons documents may be submitted by different providers. E.g. in investigator-initiated trials, the PQD is submitted by the **Drug master File holder** and the rest of the dossier is submitted by the **Sponsor.**
  In such a case the following procedure has to be followed:

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1. The Sponsor submits **Part 1 of the Submission except of** the PQD and GMP documentation. For this, the Sponsor chooses the Submission Form <APPLICATION for a NEW Clinical Trial>.
   "CTA Parallel Submission Part 1" shall be indicated in the reference line of the Cover Letter, and it shall be mention that folder 06 and 07 are empty. The name of the company who will submit the missing PQD has to be indicated in the letter as well.

2. Swissmedic will **answer to the receipt of Part 1** of the dossier with a letter and **asks for the Part 2** of the Dossier to be submitted. The **Case ID** (i.e. 700123) and the **Service number** (i.e. 102987123) will be communicated in this letter.

3. The **Drug master File (DMF) holder shall submit Part 2 of the dossier** with the Submission Form. For this, he chooses < ANSWER to FORMAL DEFICIENCY > in the Form.
   The DMF-Holder shall indicate "**CTA Parallel Submission Part 2**" in the reference line of the **Cover letter** and mention that the GMP documents and PQD to be submitted in folder 06 and 07. The name of the **Sponsor and the Study Code** has to be mentioned to make the reference to the Sponsor Cover Letter.

4. Thereafter the submission is complete and the dossier enters the normal CTA-Process with formal control of the submission followed by **written confirmation of receipt**.

- For investigational medicinal products capable of **emitting ionising radiation** the dossier must include the documents according to ClinO Annex 4 number 5. For category C studies with such products a complete dossier (including hardcopy and electronic copy) must also be submitted to the Radiological Protection Division of the Federal Office of Public Health (FOPH). Both dossiers must be submitted within 7 days.

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Deadlines

In accordance with Art. 33, par. 1 and 2 of the ClinO, Swissmedic shall

- acknowledge receipt of the application within **7 days** and notify the sponsor of any formal deficiencies in the application documents;
- reach a decision **within 30 days** of acknowledgement of receipt of the formally correct application documents.

In accordance with Art. 33, par. 3 of the ClinO, the above mentioned evaluation time may be extended by a maximum of 30 days (i.e. **60 days in total**)

- if a therapeutic product is to be used in persons for the first time
- if a therapeutic product is to be manufactured in a new process.
  Important: this also applies to a new manufacturing process used for a known product.

In accordance with Art. 36, par. 4 of the ClinO, in the case of clinical trials of therapeutic products capable of emitting ionising radiation, Swissmedic shall reach a decision on category C clinical trials **within 60 days** of acknowledgement of receipt of the formally correct application documents.

Contact

Should you have any questions, please contact the secretary's office of the Clinical Trials division, tel. +41 (0)58 462 03 87 or ct.medicinalproducts@swissmedic.ch.

Content

The dossier must be compiled in the following order:

Inhalt

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Section 00F Fo Submission Form

1. A Clinical Trial Application Part from the FO Submission Form (CTA form) has to be submitted for each CTA.
   Please be aware that JavaScript must be activated in order to complete the form. If JavaScript is not active, important functions of the form will not work and the form will be filled out incorrectly. This can trigger formal deficiencies or requests for further information delaying the evaluation of the CTA.
2. The CTA form must be fully and accurately completed.
3. Only one sponsor may be named.
4. The sponsor must be headquartered or represented in Switzerland (Art. 2 ClinO).
   If the sponsor is abroad, the sponsor representative in Switzerland must be named. Swissmedic will address future correspondence (incl. invoices) to the sponsor representative in Switzerland. For further information regarding sponsor representation in Switzerland, please refer to the Interpretation Guide “Obligations of representatives of foreign sponsors”, available on our website in the section Licenses -> Clinical trials.
   For sponsors headquartered in Switzerland, Swissmedic will address future correspondence and invoices to a single address, i.e. to the named contact address in Switzerland (sponsor or representative).
5. The CTA form must be dated and signed by the sponsor or by the sponsor representative, or by the CRO as per contractual authorisation. Contractual authorisations do not have to be submitted to Swissmedic. Swiss Affiliates of a foreign Sponsor may sign the notification form without contractual authorisation.
6. The complete information has to be entered for each Investigational Medicinal Product (IMP) that will be used in the clinical trial. This also applies to the comparator, the placebo and the Auxiliary Medicinal Product as applicable.
7. Different quantities of active substance per pharmaceutical unit of the same formulation (different strengths) have to be listed as separate IMP.
8. When a product is constituted of several active substances, the information on all active substances must be provided.
9. For investigational medicinal products capable of **emitting ionising radiation** the following form needs to be additionally completed fully and accurately:
   - For category C studies: form for clinical trials of radiopharmaceuticals or radiolabelled compounds (form on FOPH website: www.bag.admin.ch).
     The completed form must be submitted to both Swissmedic and FOPH.
   - For category B studies: form for clinical trials category B with medicinal products capable of emitting ionising radiation (form on Swissmedic website: www.swissmedic.ch > human medicines > Clinical trials on medicinal products > Clinical Trial Application > Forms and Checklists

     The completed form must be submitted to Swissmedic.
10. Import and distribution of investigational medicinal products (IMPs) (see also Swissmedic Journal issue dated 07/2010):
    a. In case the IMP(s) is/are imported from a foreign country and intended to be sent **directly to the Swiss centre(s)** involved in the clinical trial, Swissmedic will grant an authorisation of import based on the information provided in the CTA Form. This authorisation concerns exclusively the IMP(s) used in the clinical trial concerned and is valid only for the duration of the clinical trial. This authorisation of import is given in the

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authorisation letter for the clinical trial.
The same applies for import of auxiliary medicinal products (AxMPs**) used in the clinical trial, based on the information provided in the cover letter.

b. In case of import of the IMP(s) by a **distributor located in Switzerland** (for example a hospital pharmacy or packaging company), this distributor must have the appropriate licences from Swissmedic to import, store and distribute the IMP(s). In case such a company is not in possession of the licences required, the licence(s) need to be applied for. The instructions and forms for such application are available on www.swissmedic.ch (Section Licensing; “Authorisations - > Forms - > Authorisation“). Meanwhile, this company can pursue its activities until the decision with regard to licences has been taken.
The same applies for import of auxiliary medicinal products (AxMPs**) used in the clinical trial, based on the information provided in the cover letter.

c. If substances which are under the control of the **narcotics** law (narcotics like opioids or psychotropics like benzodiazepines) must be imported, an import authorisation according to the narcotics law is required for each import. This authorisation can only be issued by the Narcotics Division of Swissmedic.

d. If substances capable of emitting ionising radiation must be imported, the import for this substance must be covered by the handling licence of the Federal Office of Public Health (FOPH).

**In order to decide whether a product is an IMP or an auxiliary medicinal product (AxMP), please refer to the comprehensive definition in the corresponding EU document “The rules governing medicinal products in the European Union, Volume 10 – Chapter III – *Auxiliary Medicinal Products in Clinical Trials* – Recommendations of the expert group on clinical trials for the implementation of Regulation (EU) No 536/2014 on clinical trials on medicinal products for human use - 28 June 2017” and its appendices.

(This document was previously called Guidance on Investigational Medicinal Products [IMPs] and Non-Investigational Medicinal Products [NIMPs]).

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Section 01CL Cover Letter

1. This section must contain the cover letter to the Clinical Trial Application (CTA), as well as a copy of any other correspondence with Swissmedic (incl. e-mails) related to this CTA.
2. If for confidentiality reasons, documents are submitted by different providers (e.g. in investigator-initiated trials, the Pharmaceutical Quality Dossier (PQD) is submitted by the Marketing Authorisation Holder (MAH) and the rest of the dossier is submitted by the sponsor), reference to the other provider / company has to be made in the cover letter.
3. For category C studies with investigational medicinal products capable of emitting ionising radiation it must be confirmed that the complete identical dossier was submitted in parallel to the Federal Office of Public Health (FOPH).
4. In case auxiliary medicinal products (AxMPs) are used in the study, information on product(s), marketing approval(s), and import must be provided.
5. The electronic version of the documents (e.g. on a CD) can also be placed in this section
6. Any answer requested **before study approval**, i.e. answers to formal deficiencies, to further information request and to preliminary decisions must be submitted with the FO Submission form by choosing the correct Submission Type see <*Quick instruction for use of new submission form*>. The electronic version of all documents (including cover letter) must be included and filed in the eDoc folder 01CL.
   For information on submission requirements **after study approval** including answers to conditions, please consult our Guideline Amendments and Reporting in Clinical Trials.

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Section 02EC EC Correspondence

1. Information on any applications currently being reviewed by a Research Ethics Committee in Switzerland (**lead EC only**) and any decisions of a REC must be provided (Annex 4 ClinO).

   The information includes:

   a. A copy of the “Research Project Application Form” of the REC

   b. The cover letter sent to the REC

   c. Relevant correspondence between the applicant and the REC providing details on conditions or issues raised.
   Attachments such as protocol, IB, etc. should **not** be submitted.

   d. Approvals with or without conditions received **before** the submission to Swissmedic

2. The authorisation delivered by the REC **after** submission to Swissmedic will be provided to Swissmedic by the REC (Art. 26, para. 4 ClinO).

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Section 03RA Foreign Regulatory Authorities

1. This section applies only to multinational trials.
2. A list of foreign drug RA to which the clinical trial was submitted including details on the approval status (submitted, pending/in review, authorised/authorised with conditions/refused) must be provided.
3. Any decisions of foreign drug RA concerning the clinical trial, including any conditions imposed and the reasons given must be provided (Annex 4 ClinO), as well as relevant information on ongoing applications.
4. It is sufficient to provide information regarding the first 3 European countries (information on VHP if available), and the USA, as applicable at the time-point of submission to Swissmedic.
5. This includes the relevant documents available at the time of submission to Swissmedic. E.g. entire correspondence (**without** submitted attachments such as protocol, IB, etc.) between the applicant and the responsible RA, with details on grounds for non-acceptance (GNAs), conditions or issues, any approvals with or without condition or refusals, and a list of submitted/approved versions of the crucial documents such as protocol, IB, IMPD. Any decision becoming available during the review period should be submitted.
6. If a RA has given its approval, further updates or other correspondence with this RA do not have to be submitted to Swissmedic.

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Section 04P Trial Protocol

1. The final version of the clinical trial protocol must be submitted. This must be the version that has also been submitted to or already approved by the Research Ethics Committee.
2. The protocol must be dated and the pages numbered.
3. The trial protocol must be signed by the sponsor and the investigator prior to the start of the clinical trial (ICH E6 8.2.2). The protocol with the sponsor signature only must be submitted to Swissmedic.
4. If the protocol is signed electronically, the person signing the CTA form takes the responsibility for the validity of the submitted protocol.
5. If the protocol refers to additional documents such as **working instructions** for the personnel designated to perform reconstitution / preparation, these additional documents need to be submitted in this section.
6. Any protocol amendment(s) that are already available must also be submitted with the corresponding sponsor signature. If the protocol amendment(s) is/are signed electronically, the person signing the CTA form takes the responsibility for the validity of the submitted protocol amendment(s).

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Section 05S Safety Documentation

1. A current version of the Investigator's Brochure (IB) must be provided for all Investigational Medicinal Products (IMPs) **without a marketing authorisation** in Switzerland or a country whose GMP control system is recognised as equivalent to the Swiss system* ("GMP-equivalent country").
2. The version submitted should not be older than 18 months and contain a section clearly identified as **reference-safety information (RSI)**. The RSI should fulfil the requirements according to the "Q&A document – Reference Safety Information" dated November 2017 and the RSI cover note dated March 2018 of the Clinical Trial Facilitation Group CTFG (published on the Heads of Medicines Agency HMA – CTFG website (www.hma.eu)).
3. For **first-in-human (FIH) studies**, the complete pre-clinical reports must be joined to the IB as electronic copy (e.g. on a CD).
4. For IMPs **with a current marketing authorisation in Switzerland**, the corresponding Product Information ("Fachinformation", "Information professionnelle") has to be submitted.
5. For IMPs **with a current marketing authorisation in a GMP-equivalent country***, a corresponding Summary of Product Characteristics (SmPC) or Product Information has to be submitted (German, French, Italian, or English).
6. For IMPs with a marketing authorisation in several GMP-equivalent countries having different Product Informations / SmPCs, the sponsor should select the most appropriate Product Information / SmPC as RSI. Justification of the choice of RSI must be provided.
   If the IB is chosen as RSI, the IB has to be submitted in addition to the "Product Information" or SmPC.
7. If the IMP is identified in the protocol only by its active substance and different products with marketing authorisation containing this substance may be used in the trial, only one Product Information/ SmPC must be elected as RSI. Justification of that choice should be provided. A list of the products (name and authorisation number) used at Swiss clinical trial sites must be provided.
8. If an **IMP** with a current marketing authorisation in Switzerland or a GMP-equivalent country* is **not being used in accordance with the terms of** that **authorisation** (e.g. a new route of administration, a new dosage or frequency, a new indication, etc.), an IB specific to that new use should be prepared or a new section should be added to the general IB and submitted in addition to the Product Information / SmPC. The IB should contain separate RSI sections for each indication.
9. For **Investigator Initiated Trials (IITs)**, a scientific summary according to the Guideline ICH-E6 chapter 7 (Investigator's Brochure) may be accepted. In cases where preparation of a formal IB is impractical, the sponsor-investigator should provide, as a substitute, an expanded background information section in the trial protocol containing the minimum current information described in guideline ICH E6.
   Regarding the RSI, if the IMP is used outside the terms of marketing authorisation within the trial and/or if the sponsor does not have access to an IB for the marketed IMP, the Product Information or section 4.8 of the SmPC could be used as RSI, if justified by the sponsor in the clinical trial application cover letter. Otherwise the RSI should always be a clearly separated specific section within the IB as detailed in point 2
10. For an auxiliary medicinal product (AxMP**) authorised in a GMP-equivalent country* the Product Information / SmPC must be submitted. For an unauthorised AxMP, the Investigator's Brochure (IB) must be submitted.

*For information about which countries are considered GMP equivalent, please refer to "List of countries with recognised GMP control systems" on the Swissmedic homepage www.swissmedic.ch > human medicines > Clinical trials on medicinal products > Clinical Trial Application > Guidelines for CTA dossiers submitted

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**In order to decide whether a product is an IMP or an auxiliary medicinal product (AxMP), please refer to the comprehensive definition in the corresponding EU document “The rules governing medicinal products in the European Union, Volume 10 – Chapter III – *Auxiliary Medicinal Products in Clinical Trials* – Recommendations of the expert group on clinical trials for the implementation of Regulation (EU) No 536/2014 on clinical trials on medicinal products for human use - 28 June 2017” and its appendices..
(This document was previously called Guidance on Investigational Medicinal Products [IMPs] and Non-Investigational Medicinal Products [NIMPs]).

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Section 06G GMP Documentation

1. IMP: Submission requirements based on previous assessment status

The following submission requirements are based on the previous assessment status in Switzerland or in a country whose GMP control system is recognised as equivalent to the Swiss system*:

For Investigational Medicinal Products (Drug Product)

a) The IMP **is an unchanged** (including final packaging) **market batch with only a reduced study label added** according to Annex 13 (see section 9.2. of this CTA-Guideline):
   - No documents have to be submitted.

b) The IMP has an MA and has been released for the market, but prior to its use in the clinical trial the IMP is **blinded or modified post-market release**; ; one of the four has to be submitted:
   - Copy of the current valid manufacturing license for all production steps (not older than 3 years) OR
   - GMP certification (not older than 3 years) OR
   - Qualified Persons declaration OR
   - Confirmation document of the authority that the manufacturer complies with PIC/S GMP (i.e. inspection report including Inspection report with a final assessment of GMP status, not older than 3 years).

c) The IMP is **another pharmaceutical form or strength** of a medicinal product which has an MA, and the marketing authorisation holder provides the IMP; one of the four has to be submitted:
   - Copy of the current valid manufacturing license for all production steps (not older than 3 years) OR
   - GMP certification (not older than 3 years) OR
   - Qualified Persons declaration OR
   - Confirmation document of the authority that the manufacturer complies with PIC/S GMP (i.e. inspection report including Inspection report with a final assessment of GMP status, not older than 3 years).

d) The IMP is **not authorised** in Switzerland or a country whose GMP control systems is recognised as equivalent to the Swiss system*; and

   1. The IMP is **manufactured** in Switzerland or a country whose **GMP** control systems is recognised as **equivalent** to the Swiss system*; one of the four has to be submitted:
      - Copy of the current valid manufacturing license for all production steps (not older than 3 years) OR
      - GMP certification (not older than 3 years) OR
      - Qualified Persons declaration OR
      - Confirmation document of the authority that the manufacturer complies with PIC/S GMP (i.e. inspection report including Inspection report with a final assessment of GMP status, not older than 3 years).
   2. The IMP is **manufactured** in a country whose **GMP** control systems is **not** recognised as **equivalent** to the Swiss system*; the following has to be submitted:

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- **GMP-Certificate** (not older than 3 years) of the authority of the not recognised* country of origin
- **In addition** one of the three from a recognised country has to be submitted
  a) GMP certification (not older than 3 years) OR
  b) Confirmation document of the authority that the manufacturer complies with PIC/S GMP (i.e. inspection report including Inspection report with a final assessment of GMP status, not older than 3 years) OR
  c) Audit report or Qualified Persons declaration on GMP compliance IMP based on audit (not older than 3 years).

e) **In addition**, the following document has to be submitted for an IMP (Drug Product) as applicable:

Copy of the import authorisation in case the IMP is not imported directly to the trial site.

For Active Pharmaceutical Ingredients (Drug Substances) used for the production of IMPs

The IMP is **not authorised** in Switzerland or a country whose GMP control systems is recognised as equivalent to the Swiss system*; and

1. The Drug Substance is **used in a Drug Product, which is authorised** in Switzerland or a country whose **GMP** control systems is recognised as **equivalent** to the Swiss system* and the Drug Substance from the same marketing authorisation holder and manufacturer is used in the IMP; the following has to be submitted:
   - Confirmation of the marketing authorisation holder that the Drug Substance used in the IMP was manufactured under the marketing authorisation of the authorised Drug Product.
2. The IMP is **manufactured** in Switzerland or a country whose **GMP** control systems is recognised as **equivalent** to the Swiss system*; one of the four has to be submitted:
   - Copy of the current valid manufacturing license for all production steps (not older than 3 years) OR
   - GMP certification (not older than 3 years) OR
   - Confirmation document of the authority that the manufacturer complies with PIC/S GMP (i.e. inspection report including Inspection report with a final assessment of GMP status, not older than 3 years) OR
   - Audit report or Qualified Persons declaration on GMP compliance of IMP based on audit (not older than 3 years).

   In case no documents are available for manufacturers of certain countries, a confirmation of the regulatory authority of this country has to be submitted, confirming that the regulatory authority is not providing certificates for the respective production step.
3. The IMP is **manufactured** in a country whose **GMP** control systems is **not** recognised as **equivalent** to the Swiss system*; the following has to be submitted:
   - **GMP-Certificate** (not older than 3 years) of the authority of the not recognised* country of origin.
   - **In addition** one of the three from a recognised* country has to be submitted
     a) GMP certification (not older than 3 years) OR

b) Confirmation document of the authority that the manufacturer complies with PIC/S GMP (i.e. inspection report including Inspection report with a final assessment of GMP status, not older than 3 years) OR

c) Audit report or Qualified Persons declaration on GMP compliance of IMP based on audit (not older than 3 years)

In case no documents are available for manufacturers of certain countries, a confirmation of the regulatory authority of this country has to be submitted, confirming that the regulatory authority is not providing certificates for the respective production step.

2. Certificates of Analysis

Certificate of analysis must be submitted only in exceptional cases, where impurities are not justified or unexpected impurities are detected.

3. Auxiliary Medicinal Products (AxMPs)

The AxMPs** should be mentioned in the cover letter (see section 1).

No proof of GMP documentation has to be submitted for authorised AxMPs.

If the AxMP does not have a marketing authorisation, documents shall be submitted according to chapter 1 in this section 8.

4. Investigational Medicinal Products (IMP) to be reconstituted before use

No copy of the manufacturing license is to be submitted, **if**

a) after shipment to study site the IMP **only** has to be reconstituted **or only** has to be reconstituted and subsequently blinded for administration

AND

b) no further manufacturing step according to the Therapeutic Product Act (HMG/LPTh/LATer°) and the Medicinal Products Authorisation Ordinance (AMBV/OAMéd/OAMed°°) is performed at the study site

AND

c) the procedure is patient specific and not for a group of individuals (no batch blinding)

Instead, the following has to be submitted:

Working instructions for the personnel designated to perform this reconstitution / preparation, or the reference to this instruction if provided in another document of the CTA-Dossier.

These working instructions can be provided either in the study protocol or in an independent document bearing a document name, version and version date.

Important:

It is the responsibility of the sponsor to ensure that the designated personnel is properly trained for reconstitution/preparation tasks, that the training is documented, and that IMP accountability and traceability are guaranteed.

*For information about which countries are considered GMP equivalent, please refer to “List of countries with recognised GMP control systems” on the Swissmedic homepage www.swissmedic.ch > human medicines > Clinical trials on medicinal products > Clinical Trial Application > Guidelines for CTA dossiers submitted

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**In order to decide whether a product is an IMP or an auxiliary medicinal product (AxMP), please refer to the comprehensive definition in the corresponding EU document “The rules governing medicinal products in the European Union, Volume 10 – Chapter III – *Auxiliary Medicinal Products in Clinical Trials* – Recommendations of the expert group on clinical trials for the implementation of Regulation (EU) No 536/2014 on clinical trials on medicinal products for human use - 28 June 2017” and its appendices.
(This document was previously called Guidance on Investigational Medicinal Products [IMPs] and Non-Investigational Medicinal Products [NIMPs]).

° HMG/LPTh/LATer = Heilmittelgesetz / Loi sur les produits thérapeutiques / Legge sugli agenti terapeutici / SR 812.21

°° AMBV/OAMéd/OAMed = Arzneimittel-Bewilligungsverordnung / Ordonnance sur les autorisations dans le domaine des médicaments / Ordinanza sull'autorizzazione dei medicamenti / SR 812.212.1

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Section 07Q Quality Documentation

The manufacturing, handling and storage conditions of the trial product(s) must comply with Good Manufacturing Practice (GMP) according to PIC/S (Pharmaceutical Inspection Conventions / Cooperation Scheme) and Eudralex Volume 4 including Annex 13.

Investigational medicinal products (IMPs)** are test product(s), comparator(s) or placebo(s).

1. Formal aspects of the document:

a) The document has to be structured as described in the **Guidance on Pharmaceutical Quality Dossier** (BW101_10_006e_AA Guidance Pharmaceutical Quality Dossier) provided on the Swissmedic homepage, using the suggested section numbers and titles.
Swissmedic accepts a **European IMPD** (Investigational Medicinal Product Dossier) as **Pharmaceutical Quality Dossier (PQD)**. If an IMPD is submitted, only the quality part (Drug Substance and Drug Product) of this document shall be provided.

b) The following formats of the **PQD** or IMPD are accepted:

I. Simplified IMPDs
II. One-Document IMPDs
III. 3m-Structure IMPDs (in accordance with the e-CDT structure)

Depending on the Structure of the IMPD the corresponding eDoc –Folder has to be chosen.

71_sIMPD	Simplified IMPDs
72_one_doc	One-Document IMPDs
73_3m	3m-Structure IMPDs (in accordance with the e-CDT structure)

Fill in the documents into the eDoc Structure and delete the folders which are not used. Do not submit empty folders. A Table of Content (TOC) has to be submitted where it is requested.

c) **Data presented** in the PQD should be provided **under the headings and arranged in the order** given in the Guidance on Pharmaceutical Quality Dossier (BW101_10_006e_AA Guidance Pharmaceutical Quality Dossier). This document structure is to be followed regardless whether the compiler of the document is the **sponsor-investigator, the hospital pharmacy, the contract manufacturer or the pharmaceutical company**. In case independent or separate documents or working instructions are the basis of the quality documentation, all these documents have to be compiled into one PQD under the respective headings and according to the given structure. Not applicable sections (headings) must be clearly described as not applicable with the mention “NA”.
Another form of documentation cannot be accepted.

d) If an IMP has a previously approved CTA in Switzerland, **cross reference** to the other clinical trial should be made in the FO Submission Form (CTA form). For this you have to provide the **IMP-ID** (IMP Identifier number, depicted in the approval letter of the clinical trial. i.e. 1023), which will be allocated to each IMP submitted after 13.09.2021. Nevertheless, as no full electronic submission is possible, the quality documentation has to be submitted in paper form and on CD as described below:

I. If **no new data** are provided as compared to the previous CTA, a clean version of the same PQD or IMPD has to be submitted
II. If **new data** are provided, a **track change version and/or summary of changes** to the PQD or IMPD version of the previously approved CTA has to be submitted. The summary of changes shall list all sections changed and give the reason for each change, thus providing transparency on the development of the quality data of the IMP.

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2. IMP: Submission requirements based on previous assessment status concerning a marketing authorisation

The following submission requirements are based on the previous assessment status in **Switzerland or a country whose GMP control systems is recognised as equivalent to the Swiss system***. For category B studies reference can only be made to products on Swiss market.

a) The IMP has a marketing authorisation (MA) and **is an unchanged** (including final packaging) **market batch**:

- No documents have to be submitted for an unchanged market product authorised in Switzerland
- For an unchanged IMP with marketing authorisation in a country whose GMP control system is recognised as equivalent to the Swiss system*, the Summary of Product Characteristics (SmPC) or Product Information from the country of origin must be submitted

b) The IMP has an MA and has been released for the market, but prior to its use in the clinical trial the IMP is **blinded or modified post-market release**; the following has to be sumitted:

- Summary of Product Characteristics (SmPC) or Product Information of the country of origin.
- Simplified PQD including Drug Product part and appendices if necessary, depicting all changes to the marketed product.

c) The IMP is **another pharmaceutical form or strength** of a medicinal product which has an MA, and the marketing authorisation holder provides the IMP; the following has to be submitted:

- Drug Product part including appendices
  - A simplified PQD or IMPD providing the differences with the PQD or IMPD of the product authorised in the country of reference.
  - A summary table accompanying the simplified PQD or IMPD, summarising the modifications made in each sub-section (Drug Product part) and Appendices as compared to the PQD or IMPD of the product authorised in the country of reference.
    In addition, it must be clear from the summary that there is no difference in the Drug Substance part.

d) The **IMP has no MA**, but the **Drug substance** of this IMP **is part of a product with MA;** the following has to be submitted:

1. If the IMP is supplied from **the same manufacturer**
   - Country of reference of the authorised product
   - Drug Product part including appendices
     - A simplified PQD or IMPD providing the differences with the PQD or IMPD of the product authorised in the country of reference.
     - A summary table accompanying the simplified PQD or IMPD, summarising the modifications made in each sub-section (Drug Product part) and Appendices as compared to the PQD or IMPD of the product authorised in the country of reference.

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In addition, it must be clear from the summary that there is no difference in the Drug Substance part.

- If the differences as compared to the market product concern **only** secondary packaging and labelling, the confirmation from the MA-Holder that the product, including primary packaging, is produced according to MA may be provided instead of a simplified PQD or IMPD together with a list of the manufacturers involved in secondary packaging and labelling. This confirmation has to be signed by the "Fachtechnisch verantwortliche Person"/"Responsible technique" in Switzerland or a qualified person (QP, or Responsible Person = RP).

2. If the IMP is supplied by **another manufacturer**:
   - ➢ Drug Substance part and Drug Product part and Appendices.

e) If the IMP is **NOT authorised** in Switzerland or a country whose GMP control systems is recognised as equivalent to the Swiss system*, the following documents have to be submitted:
   - ➢ Drug Substance part and Drug Product part and Appendices

f) **Appendices to the IMPD** – according to Guidance on Pharmaceutical Quality Dossier (BW101_10_006e_AA Guidance Pharmaceutical Quality Dossier) - have to be submitted as applicable

Remark: In certain cases, additional information on the quality of the IMP maybe requested by the Reviewer.

3. Placebo

For placebo the Drug Product part of the Pharmaceutical Quality Dossier including appendices has to be submitted: These data and information can be provided in a separate document or included in the "Pharmaceutical Quality Dossier" of the active IMP.

4. Auxiliary Medicinal Products (AxMPs)

The AxMPs** should be mentioned in the cover letter (see section 1).

For AxMPs, data on the pharmaceutical quality must be submitted as required for IMPs and explained in chapter 2 in this section 7.

*For information about which countries are considered GMP equivalent, please refer to "List of countries with recognised GMP control systems" on the Swissmedic homepage www.swissmedic.ch > human medicines > Clinical trials on medicinal products > Clinical Trial Application > Guidelines for CTA dossiers submitted

**In order to decide whether a product is an IMP or an auxiliary medicinal product (AxMP), please refer to the comprehensive definition in the corresponding EU document "The rules governing medicinal products in the European Union, Volume 10 – Chapter III – *Auxiliary Medicinal Products in Clinical Trials* – Recommendations of the expert group on clinical trials for the implementation of Regulation (EU) No 536/2014 on clinical trials on medicinal products for human use - 28 June 2017" and its appendices.
(This document was previously called Guidance on Investigational Medicinal Products [IMPs] and Non-Investigational Medicinal Products [NIMPs]).

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Section 08LA Labels

For clinical trials of **Category B and C, examples** of the IMP labels to be used for the final product must be provided.

1. The identification labels for the trial products must comply with the requirements of Annex 13 of the " EUDRALEX Volume 4 - Medicinal Products for Human and Veterinary Use: Good Manufacturing Practice". The following elements are essential:
    a) IMP name (incl. placebo, if applicable) dose form and strength of the product
    b) "For clinical trial use only"
    c) Number or name of the clinical trial
    d) Batch number
    e) Expiry date or retest date
    f) Patient number or randomisation number
    g) "Keep out of reach of children" (if IMP administered by the patient himself)
    h) Name of sponsor or principal investigator or CRO (global Sponsor is acceptable)
    i) Storage conditions

    These parameters have to be clearly identifiable. Parameters which are not self-explaining or which are not depicted on the label, but are are compiled in a unique identifier, because Interactive Randomisation Technology is involved,have to be presented by listing them and providing the missing information. The following has to be obvious for the assessor:

    - Which number or sign is the unique identifier
    - Which of the mandatory parameter are connected with the unique identifier
    - Which is the Sponsor Study code
2. The identification labels for the **IMP purchased directly from the market** must comply with the requirements of Annex 13 of the " EUDRALEX Volume 4 - Medicinal Products for Human and Veterinary Use: Good Manufacturing Practice". The following elements are essential:
    a) Number or name of the clinical trial
    b) Patient number or randomisation number
    c) Name of sponsor or principal investigator or CRO
3. The identification labels must be available in the appropriate Swiss national language. The identification labels may be provided in English if the trial product is administered directly by the investigator to the trial subject at the trial centre.
4. For IMPs emitting ionising radiation, labels must also comply with art. 46 of the Radiological Protection Ordinance (SR 814.501).
5. A copy of the identification labels must be submitted for both primary and secondary packaging (outer and inner packaging).
6. For auxiliary medicinal products (AxMPs**) authorised in Switzerland or in a GMP-equivalent country* with packaging in the appropriate Swiss national language, no study-specific labels have to be submitted. Otherwise, labels must be submitted according to points 1 and 3-6 in this section 9.
7. If an IMP, after it has been shipped to the study site, **only** has to be reconstituted **or only** has to be reconstituted and subsequently blinded for administration – i.e. no further manufacturing step according to the Therapeutic Product Act (HMG/LPTh/LATer°) and the Medicinal Products Authorisation Ordinance (AMBV/OAMéd/OAMed°°) is performed at the study site –

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and the IMP is thereafter transferred to a final container which is different from the one labelled according to the example submitted in the CTA, then the following applies:

It is in the responsibility of the sponsor to instruct the personnel designated to perform this reconstitution / preparation to label the final container in order to provide the following information:

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a. Number or name of the clinical trial
b. IMP name/identifier and strength/potency and or placebo
c. Patient number or randomisation number
d. If needed: Date/time of reconstitution
e. Use-up date/time
f. Storage requirements

*For information about which countries are considered GMP equivalent, please refer to “List of countries with recognised GMP control systems” on the Swissmedic homepage www.swissmedic.ch > human medicines > Clinical trials on medicinal products > Clinical Trial Application > Guidelines for CTA dossiers submitted

**In order to decide whether a product is an IMP or an auxiliary medicinal product (AxMP), please refer to the comprehensive definition in the corresponding EU document “The rules governing medicinal products in the European Union, Volume 10 – Chapter III – *Auxiliary Medicinal Products in Clinical Trials* – Recommendations of the expert group on clinical trials for the implementation of Regulation (EU) No 536/2014 on clinical trials on medicinal products for human use - 28 June 2017” and its appendices..
(This document was previously called Guidance on Investigational Medicinal Products [IMPs] and Non-Investigational Medicinal Products [NIMPs]).

° HMG/LPTh/LATer = Heilmittelgesetz / Loi sur les produits thérapeutiques / Legge sugli agenti terapeutici / SR 812.21

°° AMBV/OAMéd/OAMed = Arzneimittel-Bewilligungsverordnung / Ordonnance sur les autorisations dans le domaine des médicaments / Ordinanza sull'autorizzazione dei medicamenti / SR 812.212.1

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Section 09PM Pharmacy Manual

Pharmacy Manuals containing instructions for the pharmacist on dilution, preparation or storage of the IMP shall be submitted. This Document is important to underline the compliance with the storage and handling conditions written in the IMPD. If not already submitted with the initial Submission Package the Pharmacy Manual may be requested by the assessor during the clinical study assessment.

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Section 19 Toxicology Reports

Toxicology reports have to be submitted for each IMP which is firstly applied to human.

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Change history

Version	Valid and binding as of:	Description, comments	Author's initials
10.0	**24.09.2021**	**Parallel submission Part**	**gav**
9.0	**09.09.2021**	**Corrections on formal aspects with respect to "**New VO form and new format for authorisation applications plus changes/ notifications/ reports regarding clinical trials with medicinal products as of 13 September 2021"	**gav**
8.0	**17.01.2020**	**Revised section 8, clarifications, correction of links**	**hch**
7.0	**01.01.2019**	**Deletion of requirement for special import licence for immunological products, blood and blood products due to revised AMBV/OAMéd/OAMed** **Clarifications regarding RSI, AxMP, PQD submission for market batches** **Corrections and administrative changes**	**hch**
6.0	**01.06.2018**	**Inclusion of additional information in requirements for reference safety information and for auxiliary medicinal products AxMPs, clarifications**	**hch**
05	**15.10.2017**	**Change of terminology from "non-investigational medicinal product NIMP" to "auxiliary medicinal product AxMP" in accordance with Eudralex Vol. 10 Chapter III - Auxiliary Medicinal Products in Clinical Trials and clarifications concerning protocol signature and manufacturing licenses.**	**hch**
04	**12.05.2017**	**Clarifications for submission requirement**	**hch, jaf**
	13.01.2017	Information on certificates of analysis in section 8 moved to point 2	hch
03	**01.01.2017**	**EU-harmonised submission requirements for quality and GMP documentation, added information on import of NIMPs and on requirements for reconstitution of IMPs, included clarifications**	**hch, gav, jaf**
02	**08.04.2016**	**Addition of information on requirement for submission of pre-clinical reports and of documentation for non-authorised NIMPs emitting ionising radiation** **Minor corrections**	**hch**
	22.03.2016	Language corrected	sel
01	**25.01.2016**	**QM ident. changed** **old: BW101_10_001e_AL_Guideline_Clinical_Trial_Application_Dossier** **new: BW101_10_004e_AA_Guideline_Clinical_Trial_Application_Dossier** **Minor modifications in submission requirements, clarifications and corrections**	**hch**
17	**30.04.2015**	**Inclusion of information concerning radiopharmaceuticals / deadlines / clarifications concerning reference safety information / clarifications concerning contact details on labels / correction in 8.1**	**hch**
16	**27.11.2014**	**Clarifications for submission requirements**	**hch**
	30.07.2014	New change history inserted in the document, dropdown field inserted in the header	wis

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