

## Introduction

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

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

### Application format:

- **One hard copy** of the documents must be placed in a folder with the colour indicated on the homepage [www.swissmedic.ch/clinicaltrials](http://www.swissmedic.ch/clinicaltrials) > Clinical trials on medicinal products. Please note that for logistical reasons, the folder colour changes each year.
- The folder must be equipped with a 20-tab file divider.
- The documents must be filed in the sequence shown in the list below. Documents should be inserted in sections 1-10, and sections 11-20 will be needed for Swissmedic purposes.
- In addition, **a copy** of all documents, including cover letter, has to be submitted **in electronic form** e.g. **on a CD**.  
The electronic files shall be organised in folders with numbers corresponding to the file sections listed below. In order to identify the documents the files should be named with a reasonable filename.
- Do not compile the electronic copies into zip-files.
- 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).

### 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 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.

For confidentiality reasons, documents may be submitted by different providers. E.g. in investigator-initiated trials, the PQD is submitted by the Marketing Authorisation Holder (MAH) and the rest of the dossier is submitted by the sponsor. In such a case, all documents have to be submitted within 7 days. The cover letters must include the reference to the other part of the dossier. If a dossier is still incomplete after 7 days, the already submitted documents will be sent back to the sender.

### 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](mailto:ct.medicinalproducts@swissmedic.ch).

### Content

The dossier must be compiled in the following order:

<a href="#">File section 1</a>	Cover letter to the Clinical Trial Application and related correspondence
<a href="#">File section 2</a>	Clinical Trial Application Form
<a href="#">File section 3</a>	Authorisation of Research Ethics Committee (REC) and/or correspondence with REC
<a href="#">File section 4</a>	Approvals of foreign drug Regulatory Authorities (RA) and/or correspondence with other RAs
<a href="#">File section 5</a>	Clinical trial protocol
<a href="#">File section 6</a>	Investigator's Brochure, Product information or Summary of Product Characteristics for unchanged products with Marketing Authorisation
<a href="#">File section 7</a>	Pharmaceutical quality documentation of Investigational Medicinal Product (e.g. IMPD)
<a href="#">File section 8</a>	Proof of compliance of Good Manufacturing Practice (GMP)
<a href="#">File section 9</a>	Trial product labels
<a href="#">File section 10</a>	Other documents

**Section 1 Cover letter to the Clinical Trial Application and related correspondence**

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 a cover letter. The electronic version of all documents (including cover letter) must be included. 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 2 Clinical Trial Application Form

1. A Clinical Trial Application 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 and the placebo, as applicable.
7. Different quantities of active substance per pharmaceutical unit of the same formulation (different strengths) can be listed together in the same section related to that 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](http://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/clinicaltrials](http://www.swissmedic.ch/clinicaltrials)).  
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 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](http://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. In case **immunological products, blood and blood products** must be imported, it is necessary to file an additional application for authorisation of import for each shipment. Further important information can be found on [www.swissmedic.ch](http://www.swissmedic.ch) (Section Licensing; "Blood and blood components").
- d. 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.
- e. If substances capable of emitting ionising radiation must be imported, an authorisation of import and transport is additionally needed from 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 3 Authorisation of Research Ethics Committee (REC) and/or correspondence with REC**

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 4 Approvals of foreign drug Regulatory Authorities (RA) and/or correspondence with other RAs**

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 5 Clinical 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 6 Investigator's Brochure (according to Guideline ICH-E6, chapter 7), Product information or Summary of Product Characteristics for unchanged products with marketing authorisation**

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](http://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 any other information for healthcare professionals, e.g. "Fachinformation") 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.  
If the IB is chosen as RSI, the IB has to be submitted in addition to the "Product Information" or SmPC.  
Justification of the choice of RSI must be provided.
7. If the IMP is identified in the protocol only by its active substance, the sponsor must elect one Product Information/ SmPC as equivalent to the IB for all medicinal products that contain that active substance and are used at any clinical trial site. Justification of that choice should 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 and be submitted in addition to the "Product Information" / SmPC. Alternatively, the "Product Information" / SmPC should be complemented with a summary of relevant nonclinical and clinical data that support the use of the IMP in that clinical trial.
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.
10. For **auxiliary medicinal products (AxMPs\*\*)** the document used as RSI must be submitted. For AxMPs without marketing authorisation in Switzerland or in a GMP-equivalent country\*, this document should be the Investigator's Brochure (IB). For AxMPs with marketing authorisation in Switzerland or a GMP-equivalent country, the corresponding Summary of Product Characteristics (SmPC) or "Product Information" should be submitted (German, French, Italian, or English).

\*For information about which countries are considered GMP equivalent, please refer to “List of countries considered as GMP equivalent in Switzerland” on the Swissmedic homepage [www.swissmedic.ch/licensing](http://www.swissmedic.ch/licensing) > 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 7    Pharmaceutical quality documentation (PQD) of Investigational Medicinal Product (IMP) (Art. 19 and 32 ClinO)**

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 **PQD** or IMPD shall comply with the following:
  - I. The document has a document title, version date and sequential pagination ascending from the first to the last page.
  - II. In case the PQD or IMPD is not in line with point I above, an overview-of the PQD or IMPD (**Overview-PQD**) must be submitted in addition to the main PQD or IMPD. This **Overview-PQD** must provide a table listing all sections of the PQD/IMPD, showing the numbers and titles and the version dates of each section of the PQD or IMPD. The Overview-PQD must have a document title and version date.
- 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 CTA. 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.

**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
  
- b) The IMP has an MA and **is an unchanged** (including final packaging) **market batch, but is used after it has been blinded or modified in another way**; the following has to be submitted:
  - Drug Product part including appendices
  
- 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.  
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.

**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 considered as GMP equivalent in Switzerland” on the Swissmedic homepage [www.swissmedic.ch/licensing](http://www.swissmedic.ch/licensing) > 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..  
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**Section 8 Proof of compliance Good Manufacturing Practice (GMP)**

**1. IMP: Submission requirements based on previous assessment status**

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\*:

- a) The IMP is an **unchanged** (including final packaging) **market batch**:
  - No documents have to be submitted.
- b) The IMP is an **unchanged** (including final packaging) **market batch but is used after it has been blinded or modified in another way**; the following has to be submitted:
  - Copy of the current valid manufacturing license (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; the following has to be submitted:
  - Copy of the current valid manufacturing license (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\*; the following applies:
  1. The IMP is **manufactured** in Switzerland or a country whose **GMP** control systems is recognised as **equivalent** to the Swiss system\*; the following has to be submitted:
    - Copy of the current valid manufacturing license (not older than 3 years), OR
  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:
    - **GMP-Certificate** (not older than 3 years) of the authority of the not recognised\* country of origin
    - **Confirmation** of a “Fachtechnisch verantwortliche Person” (FvP) in Switzerland or a qualified person (QP, or Responsible Person = RP) in a recognised country\*. This document shall confirm that the manufacturing site works in **compliance with a GMP system** equivalent to the countries listed in “List of countries considered as GMP-equivalent in Switzerland”\*, or that each production batch has undergone all relevant analyses, tests or checks, necessary to confirm this quality.
    - And, in addition, one of the three documents:
      - a. **GMP-Certificate** (not older than 3 years) of a recognised\* authority, OR
      - b. **Inspection report** (not older than 3 years) of a recognised\* authority including GMP-evaluation, OR
      - c. **Copy of the audit reports** (not older than 3 years) of a company of a recognised\* country.
    - Certification of **GMP status for biological substances** (if applicable)
- e) In addition, the following document have to be submitted as applicable:
  - Viral safety studies
  - TSE Certificates
  - Copy of the import authorisation in case the IMP is not imported directly to the trial site.

## 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 authorised (cantonal law) and 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 considered as GMP equivalent in Switzerland" on the Swissmedic homepage [www.swissmedic.ch/licensing](http://www.swissmedic.ch/licensing) > 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..

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° 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 medicinali / SR 812.212.1

## Section 9 Trial product 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/identifier (incl. placebo, if applicable) and strength/potency
  - b) "For clinical trial 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" (except when the product is for use in trials where the product is not taken home by subjects)
  - h) Name of sponsor or principal investigator or CRO (global Sponsor is acceptable)
  - i) Storage requirements
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. Labels must not contain foreign phone/fax numbers, but details of main contact **in Switzerland**. These can be provided alternatively e.g. on a patient card or a leaflet given to the patient with the study medication.
5. For IMPs emitting ionising radiation, labels must also comply with art. 46 of the Radiological Protection Ordinance (SR 814.501).
6. A copy of the identification labels must be submitted for both primary and secondary packaging (outer and inner packaging).
7. 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.
8. 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 – 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:



- 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 considered as GMP equivalent in Switzerland” on the Swissmedic homepage [www.swissmedic.ch/licensing](http://www.swissmedic.ch/licensing) > 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 medicinali / SR 812.212.1

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## Section 10 Other or additional documents

Any other trial related documents that could be relevant for the review of the clinical trial application by Swissmedic may be submitted (e.g. scientific advice of a Competent Authority).

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### Change history

Version	Valid and binding as of:	Modified without version change	Description, comments (by author)	Author's initials
6.0	01.06.2018		<b>Inclusion of additional information in requirements for reference safety information and for auxiliary medicinal products AxMPs, clarifications</b>	hch
05	15.10.17		<b>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.</b>	hch
04	12.05.17		<b>Clarifications for submission requirement</b>	hch, jaf
		13.01.17	Information on certificates of analysis in section 8 moved to point 2	hch
03	01.01.17		<b>EU-harmonised submission requirements for quality and GMP documentation, added information on import of NIMPs and on requirements for reconstitution of IMPs, included clarifications</b>	hch, gav, jaf
02	08.04.16		<b>Addition of information on requirement for submission of pre-clinical reports and of documentation for non-authorised NIMPs emitting ionising radiation Minor corrections</b>	hch
		22.03.16	Language corrected	sel
01	25.01.16		<b>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</b>	hch
17	30.04.15		<b>Inclusion of information concerning radiopharmaceuticals / deadlines / clarifications concerning reference safety information / clarifications concerning contact details on labels / correction in 8.1</b>	hch
16	27.11.14		<b>Clarifications for submission requirements</b>	hch
		30.07.14	New change history inserted in the document, dropdown field inserted in the header	wis