

Practical guidance for submission of applications for human medicinal products

Applications for approval of medicinal products should be sent/delivered to the following address:

Postal address

Medical Products Agency
P.O. Box 26
SE-751 03 Uppsala
SWEDEN

Delivery address

Medical Products Agency
Uppsala Science Park
Dag Hammarskjölds väg 42
752 37 Uppsala
SWEDEN

1. Requirements of dossier format and number of copies

As stated in Annex I to Directive 2001/83/EC, implemented through LVFS 2003:7, the Common Technical Document (CTD) format is mandatory for all new applications for approval of human medicinal products. Applicants are requested to adhere to the recommendations formulated in Notice to Applicants Volume 2B (see link below).

1.1. Electronic submissions

Hard media (CD or DVD) should normally be used for the electronic application. The CD/DVD should be appropriately labelled for identification and packed adequately to prevent damage. The applicant is responsible for checking the CD/DVD for viruses and for informing the Medical Products Agency (MPA) of the type of software used for this purpose.

The Cover Letter should state which format is being used (eCTD or NeeS). Please refer to the HMA website for a Cover Letter template (see link below) recommended by the CMDh for MRP/DCP applications and also recommended for national applications to the MPA.

The MPA recommends that Word copies (working documents) are handled outside an eCTD but submitted on the same CD/DVD. All PDF files submitted should preferably be generated from electronic source documents, i.e. easily used for search capabilities and copy and paste functionality into word documents. If some scanned text documents are included in the submission, the MPA strongly encourages the applicant to use good quality OCR software.

One set of CD/DVD should be submitted per application. Each CD or DVD should be properly labelled. Each CD or DVD submitted should include the following label information, clearly presented and printed on the media:

- Format (eCTD or NeeS)
- The name of the applicant
- The product (invented) name(s)
- The International Non-proprietary Name (INN) of the active substance(s)

- The full application number(s) (if known)
- The sequence number(s) of the eCTD submissions contained on the CD/DVD (only for eCTD)
- Number of media units per full set and an indication of the place of the individual CD/DVD within this set (e.g. 1(5), 2(5)...etc.)
- The submission type(s) of each submission contained on the CD/DVD (e.g. Initial Application, Variation Type II)

1.1.1. National Procedure, Mutual Recognition Procedure and Decentralised Procedure

Electronic-only submissions are accepted in eCTD or NeeS format without accompanying papers. However, the Cover Letter and the Application Form has to be submitted in paper with original signatures. A filled “Confirmation of transition to electronic-only submissions” (see link below) has to be submitted the first time an electronic application is submitted for a specific medicinal product. The form should be submitted in paper, attached to the Cover Letter, together with the electronic submission. Please clearly state, in the first section of the Cover Letter, that the application is electronic-only for Sweden.

The criteria for accepting electronic submissions as originals in all procedures are that the current ICH and EU specifications and the EU eCTD or NeeS harmonised guidance are followed. The submissions have to pass the technical validation. Otherwise, paper copies are required. Electronic submissions are not mandatory and paper submissions are still accepted.

Table 1. Electronic only, MRP, DCP, NP

Modules	Electronic format	Paper format
Complete dossier, Module 1-5 <i>If one or more modules are common for multiple strengths/pharmaceutical forms or for duplicate applications it should be clearly explained in the cover letter which parts of the application that are identical and which are not to prevent duplication of assessment.</i>	One set of CD/DVD (eCTD or NeeS) should be submitted per application. If the submission requires more than one CD a DVD is preferred.	Application Form and Cover Letter with original signature.
Module 1.3.1	Word format: For MRP/DCP one copy in English is required. For NP one copy in Swedish is required. Word copies should be handled outside an eCTD or NeeS but submitted on the same	

Modules	Electronic format	Paper format
	CD/DVD.	
Module 2	<p>Word format: One copy is appreciated.</p> <p>Word copies should be handled outside an eCTD or NeeS but submitted on the same CD/DVD.</p>	

1.1.2. Centralised Procedure

Electronic-only submissions are accepted for human medicinal products. A paper copy of the included Cover Letter (original signature is not needed) should also be submitted to the MPA with the hard media to facilitate the identification.

Table 2. Electronic only, CP, Sweden acts as Rapporteur/Co-rapporteur/Peer reviewer

Modules	Electronic format	Paper format
<p>Complete dossier Module 1-5.</p> <p><i>If one or more modules are common for multiple strengths/pharmaceutical forms or for duplicate applications it should be clearly explained in the cover letter which parts of the application that are identical and which are not to prevent duplication of assessment.</i></p>	<p>One set of CD/DVD (eCTD or NeeS) should be submitted per application.</p> <p>If the submission requires more than one CD, a DVD is preferred.</p>	<p>A paper copy of the included Cover Letter (original signature is not needed) should be submitted with the hard media to facilitate the identification.</p>
Module 1.3.1	<p>Word format: If Sweden acts as Rapporteur one copy in English is required.</p> <p>Word copies should be handled outside an eCTD or NeeS but submitted on the same CD/DVD.</p>	
Module 2	<p>Word format: One copy is appreciated.</p> <p>Word copies should be handled outside an eCTD or NeeS but submitted on the same CD/DVD.</p>	

Table 3. Electronic only, CP, Sweden acts as Member State

Modules	Electronic format	Paper format
<p>Complete dossier Module 1-5.</p> <p><i>If one or more modules are common for multiple strengths/pharmaceutical forms or for duplicate applications it should be clearly explained in the cover letter which parts of the application that are identical and which are not to prevent duplication of assessment.</i></p>	<p>One set of CD/DVD (eCTD or NeeS) should be submitted per application.</p> <p>If the submission requires more than one CD, a DVD is preferred.</p>	<p>A paper copy of the included Cover Letter (original signature is not needed) should be submitted with the hard media to facilitate the identification.</p>
<p>Module 2</p>	<p>Word format: One copy is appreciated.</p> <p>Word copies should be handled outside an eCTD or NeeS but submitted on the same CD/DVD.</p>	

1.2. Paper submissions

Electronic submissions are not mandatory and paper submissions are still accepted. For health and safety reasons, the application dossier should be packed in boxes weighing no more than 15 kilos each. All boxes should be numbered and the module number should be stated on the boxes. The box containing the Cover Letter should be easily identified.

It is strongly recommended that the documentation is put in binders with solid backs. The name of the product, the pharmaceutical form, strength and, where applicable, the procedure number should be clearly stated on the spine and front of the binders.

If one or more modules are common for multiple strengths/pharmaceutical forms or for duplicate applications, a reference to these modules in the “first” application should be given in the Cover Letter instead of submitting these copies.

1.2.1. National Procedure, Mutual Recognition Procedure and Decentralised Procedure

Table 4. Paper submission, MRP, DCP, NP

Modules	Paper format	Electronic format
Complete dossier, Module 1-5. <i>If one or more modules are common for multiple strengths/pharmaceutical forms or for duplicate applications, a reference to these modules in the “first” application should be given in the Cover Letter instead of submitting these copies.</i>	One complete original dossier.	One electronic copy of Module 1-5, is appreciated in PDF 1.4 format, preferably in eCTD format. If acceptable NeeS or eCTD format, electronic only submission is recommended. If the submission requires more than one CD a DVD is preferred.
Module 1.3.1		Word format: MRP/DCP: One copy in English is required. NP: One copy in Swedish is required. Word copies should be handled outside an eCTD or NeeS but submitted on the same CD/DVD.
Module 2	One extra paper copy of Module 2.5 and Module 2.7.	Word format: One copy is appreciated. Word copies should be handled outside an eCTD or NeeS but submitted on the same

		CD/DVD.
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2. Duplicate applications

For duplicate applications, there is a specific statement, “Statement for duplicate applications” to fill in and enclose with the application. Please find the template on the MPA website (see link below). A duplicate application is defined by reference to the first application or marketing authorisation as follows:

- same dossier (copy of modules 1, 2, 3, 4 and 5)
- same legal basis according to Directive 2001/83/EC, as amended
- different trade name
- same or different applicant/marketing authorisation holder

In other words, the product name and the Marketing Authorisation Holder are the only things that may differ from the first application referred to.

The MPA has experienced that some applications have for example different batch release sites or package sizes, even if applied for as duplicates. In these cases, the applications should be handled as non-duplicates and invoiced accordingly. So please, make sure that the applications comply with the above stated criteria before submitting them as duplicates.

Furthermore, since all applications for approval of marketing authorisation have to fulfil the requirements in the new legislation (see the European Commission website), this also applies to duplicate applications. Therefore, the documentation for the first application referred to has to be in line with the new legislation before a duplicate application can be submitted. To update the first application, a Type II variation (other, updated documentation to new legislation) should normally be submitted.

In order to comply with the current legislation, as amended 2006-05-01, the dossier has to be updated with the following documents:

- Pharmacovigilance system (Module 1.8.1)
- Risk-management plan (Module 1.8.2)
- Consultation with target patient groups for the package leaflet (Module 1.3.4)
- Proposed implementation of Braille on the packaging (Module 1.3.6)
- Environmental risk assessment (Module 1.6)
- QP declaration concerning GMP compliance of manufacturing of the active substance

3. Product samples

As stated in the Notice to Applicants, an application for a Marketing Authorisation in Sweden should be accompanied by a sample of the finished product (one package per medicinal product/strength/pharmaceutical form). The sample should preferably be the product in its intended package. The purpose of the sample is not to perform any laboratory analyses or to evaluate the labelling but rather to assure user friendly packages. There are, however, some exemptions to this requirement.

Placebo samples rather than drug containing samples *should* be submitted:

- if the drug substance is classified as a narcotic substance in Sweden
- if the drug substance is cytostatic or otherwise particularly toxic

Placebo samples rather than drug containing samples *may* be submitted:

- if the originators patent is still in force and prohibit samples containing the drug to be sent
- if the price of the drug substance is particularly high

If justified, an empty sample of the package can be sufficient, for example if the filled package is very large. Finished product, active substance and impurities should be available on request for analysis purposes.

4. Contact information

If, for some reason, the requirements stated above cannot be fulfilled or if you have any other questions related to new applications, please contact the MPA by e-mail to the New Application Group at the unit for Registration and Information Management (NAG@mpa.se).

If you have questions on electronic submissions, please contact the MPA by e-mail to eSubmission@mpa.se

5. Related links

Dossier format

Please refer to the Notice to Applicants Volume 2B for further guidance:

http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol2_en.htm

Product Information (SmPC, Package Leaflet and Labelling)

Please refer to the EMEA website for templates:

<http://www.emea.europa.eu/htms/human/grd/grdtemplate.htm>

Cover Letter

Please refer to the CMDh website for template:

<http://hma.eu/219.html>

Duplicate applications

Please refer to the MPA website for “Statement for duplicate applications”:

<http://www.lakemedelsverket.se/upload/Om%20LV/blanketter/Word/Statement%20for%20duplicate%20applications.doc>

Electronic submissions to the MPA

Please refer to the MPA website for more information regarding electronic submissions:

<http://www.lakemedelsverket.se/english/product/Medicinal-products/Electronic-submissions-to-the-MPA/>

Please refer to the MPA website for “Confirmation of transition to electronic-only submissions”:

[http://www.lakemedelsverket.se/upload/Confirmation%20of%20transition%20to%20electronic-only%20submissions%20\(2\).doc](http://www.lakemedelsverket.se/upload/Confirmation%20of%20transition%20to%20electronic-only%20submissions%20(2).doc)