Federal Institute
for Drugs
and Medical Devices

Step-by-step Guide on e-only Submission at BfArM

Version 2.3
Date: May 10, 2017

Conditions for e-only submissions

- ✓ Electronic submission preferred in eCTD format regardless of whether submission concerns a new application or any post-authorisation regulatory activity.
- ✓ According to transition rules of the HMA eSubmission Roadmap submissions in NeeS format are still possible.
- ✓ Validation in advance according to published EU criteria

Note

A validation report does not have to be provided but should be available on request or in case of different results of the technical validation.

A validation tool is offered free of charge at www.bfarm.de

BfArM assumes that all procedure will follow the e-only conditions and are structured according eCTD (or NeeS) format

Preparations

- ✓ Prior to filing an application, request a processing number, so-called ENR (“Einreichungsnummer”)

  Send an informal letter stating the name and pharmaceutical form of the medicinal product
  by e-mail to

  antragseingang@bfarm.de

  by telefax to

  Bundesinstitut für Arzneimittel und Medizinprodukte,
  Z14.1 - eSubmission

  Kurt-Georg-Kiesinger-Allee 3,

  D-53175 Bonn

  Telefax number: +49 228 207 3681

- ✓ You will receive the requested number of ENRs in due time.

Sending

- ✓ **If using the Common European Submission Platform (CESP), follow the rules published at www.bfarm.de or cesp.hma.eu respectively**
- ✓ If submitting exceptionally CD/DVDs, all initial and subsequent submissions under the rule of “e-only” need to be sent to

Bundesinstitut für Arzneimittel und Medizinprodukte,
Z14.1 - eSubmission

Kurt-Georg-Kiesinger-Allee 3,

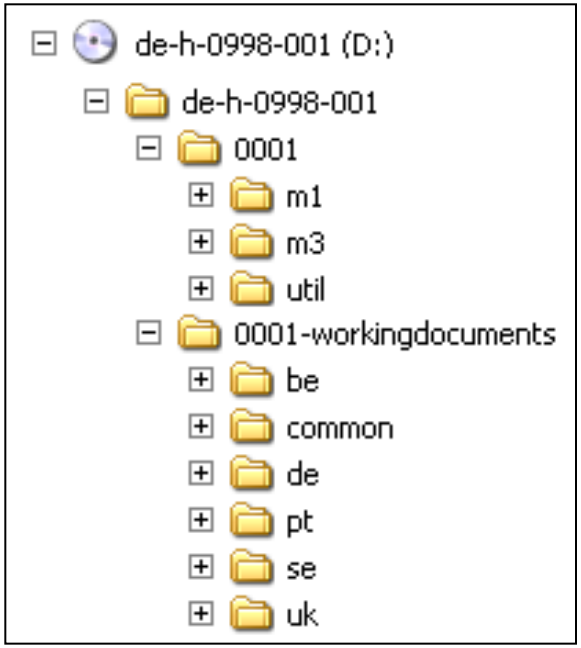
D-53175 Bonn

Telefax number: +49 228 207 3681

Content of the package:
1 set of electronic media (CD / DVD)
Cover letter and tracking table (does not necessarily have to be signed)

Folder structure required

- ✓ Structured in accordance with CTD (NeeS) or completely in accordance with ICH specifications on m2 to m5 and EU specification on m1 (eCTD)
- ✓ Breakdown in conformity with the ICH Granularity Document
- ✓ Root directory named by product name or procedure number
- ✓ Working documents always in a separate folder on root level named <sequence>-workingdocuments (File format should be .doc or .docx)



Note

- ✓ In case of CESP compress your sequence
- ✓ In case of submissions on CD or DVD do not use container files (e.g.zip, rar, 7z)

Rules Confirming Receipt of Submission

- ✓ The HPRA is acting on behalf of BfArM
- ✓ The confirmation of uploaded sequences by HPRA will serve as a confirmation of receipt equivalent to a confirmation you would have received when submitting at BfArM site
- ✓ A renewal application is valid once the upload to HPRA is confirmed
- ✓ The technical validation will still be performed at BfArM and acceptance from technical point of view need to be stated by BfArM
- ✓ Only in case of a positive outcome of the technical validation – if necessary, after the applicant has removed technical deficiencies – the content-related validation starts. The applicant will then receive confirmation that the validation period has started.

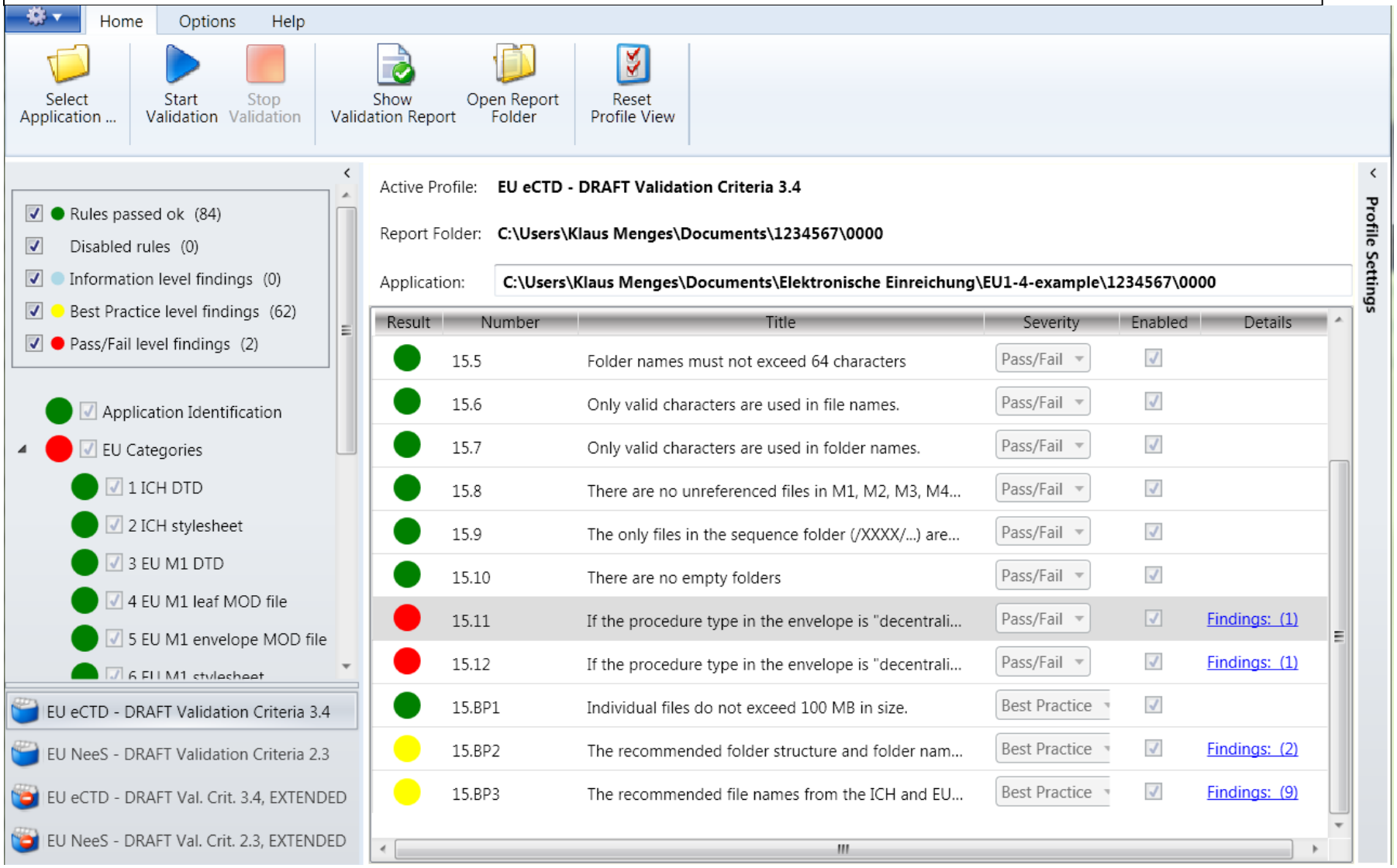
Use of “BfArM eValidator”

- ✓ Before sending, check your submission according to the published EU criteria for eCTD or NeeS, respectively
- ✓ You can download and use the “BfArM eValidator” free of cost

Note

- ✓ Make sure that there are no errors, warnings will be ignored

“BfArM eValidator” Screenshot



Technical validation

- ✓ Advance use of the BfArM eValidator (or any other Validation Tool) is highly recommended
- ✓ Internal check with eValidator of each submission at least if BfArM is RMS
- ✓ In case of deficiencies you will receive our validation report as feedback:
  - Errors will lead to rejection of a submission
  - You may be advised of warnings but they will be ignored for further processing

Most Frequent Problems Using CESP

Data transmission

- ✓ Re-use of an old CESP delivery number
- ✓ Wrong order of upload

Metadata

- ✓ Incomplete European procedure number
- ✓ Incorrect regulatory activity ID, e.g. variation type II instead of Response to question (variation)
- ✓ Missing national procedure number, i.e. ENR in case of BfArM

Content

- ✓ Only eCTD and NeeS sequences, educational material, PSURs, and ASMF are supported and processed
- ✓ No draft versions or unstructured compilations will be processed

PDF file requirements

Portable Document Format (PDF)

- ✓ No restriction of accessing the content of PDF files
- ✓ Generated from electronic (text) source documents
- ✓ Module 2 **always** from an electronic source document
- ✓ Scanned images for certain documents only
- ✓ Scanned documents 300 dpi recommended
- ✓ PDF version 1.4 to 1.7 can be used as well as PDF/A-1 or A-2

Change to Electronic Format

- ✓ **Switch** from paper **to NeeS or eCTD**
  at any phase of the life cycle of a medicinal product, but always before or after a regulatory activity, never inbetween
- ✓ **Switch** from paper or NeeS **to eCTD**
  at any phase of the life cycle of a medicinal product, but always before or after a regulatory activity and start with real sequencing then
- ✓ A baseline – preferably for Module 3 – can be submitted at any time. Although not required, a **baseline is highly recommended**

Note

- ✓ Once changed to eCTD this format needs to be maintained or in case of NeeS be “up-graded” only

Baseline when switching to eCTD

- ✓ As published, all available and currently valid files should be included according to CTD structure. You have to submit this electronic baseline even BfArM received the data in another configuration already (submission type “none”, submission unit type “reformat“).
- ✓ In case the baseline will be built from scratch it is recommended to include all m3 files and m2 files. For practical reasons m1 files, e.g. cover letter, tracking table, application form and annexes, expert statements and risk management plan are also a considerable minimum (submission type “none”, submission unit type “reformat“).
- ✓ In case no electronic files are available you can start with eCTD as well. The sequence number will be 0000 anyway (submission type depends from type of regulatory activity).
- ✓ There is no need to re-submit working documents.

Submission of product information texts

When which format via which channel?

- ✓ Initial submission
  - ✓ Will be part of the dossier (module 1.3.1) and need to be PDF-files
  - ✓ Additional working documents as DOC- or DOCX-files in the folder <workingdocuments> at the same level as the sequence
- ✓ During the assessment phase (will include check of national text versions in case of Type1A/B variations as well)
  - ✓ Will be part of the dossier (module 1.3.1) and need to be PDF-files
  - ✓ Additional working dosumenrts as DOC- or DOCX-files in the folder <workingdocuments> at the same level as the sequence. It will be possible to exchange draft versions between process management and pharmaceutical company via e-mail or EudraLink outside eCTD life cycle.
- ✓ After end of procedure (in case of MAA and Type2 variations)
  - ✓ All translations of the product information texts into German should be submitted as a DOC- or DOCX-file using the national template „Bescheidmaske“ and sent to the attention of translations@bfarm.de.
- ✓ After national authorisation
  - ✓ The authorised text version need to be submitted as „clean version“ in PDF-format using AMG-EV e-mail procedure „Freigabe“.

Contact

Federal Institute for Drugs and Medical Devices
Kurt-Georg-Kiesinger-Allee 3
D-53175 Bonn

Contact
info-esubmission@bfarm.de

or

Dr. Klaus Menges
klaus.menges@bfarm.de
www.bfarm.de
Tel. +49 (0)228 99 307-3458