White paper

Structure of NeeS submissions

Regulatory information must be structured in accordance with the Common Technical Document (CTD) standard, which for paper submissions became mandatory in the European Union on 1 July 2003. For NeeS applications the eCTD folder structure is used. The breakdown of the electronic submission should conform with the ICH Granularity Document, and as well the ICH and EU eCTD file naming conventions should be followed. The difference from an eCTD is that the two relevant XML files, the index.xml, and eu-regional.xml for the backbone of Modules 2 to 5 and Module 1 for the EU, respectively and the util folder are not present. So, navigation through a NeeS is based on electronic Tables of Content (TOC) in PDF, bookmarks, and hypertext links.

An example of folder structure:

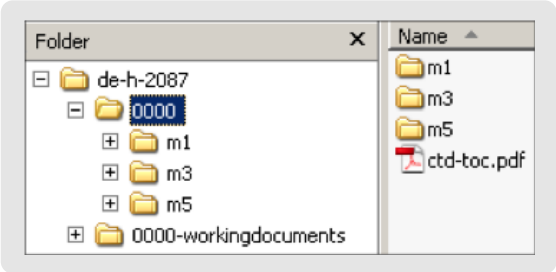

Table of Contents and bookmarks in NeeS

All documents in the NeeS dossier should be referenced from a hyperlinked Table of Contents (TOC). Hyperlinks for each document should always be provided on the first page of the appropriate file.

TOCs always need to be provided by the applicant and should always be submitted in PDF format. In the case of small dossiers (e.g. for certain variations), especially when only one module beside module 1 is concerned, it should be acceptable to only include a main TOC referring directly to the content documents. However, for larger submissions, the main TOC should always be linked to module TOCs, which are then further linked to the documents in each module.

Here is an example of a TOC (created by Nanokinetik TOC Builder):

Nanokinetik NeeS TOC Builder is fully in line with the new validation criteria effective as of 1st December 2012.

For maintenance (variations and renewals) NeeS is the most commonly used format.

For national applications the use of NeeS is preferred, while a large percentage of submissions are still done in a paper only format.

- **Creates hyperlinked Tables of Contents (TOC).**
- **Passes all Pass/Fail and Best Practice criteria.**
- **All created hyperlinks are relative.**
- **All hyperlinks have the 'inherit zoom' level set.**
- **The PDFs for the TOC feature an active 'fast web view.'**
- **Improved navigation aids in the tables of contents: back link.**
- **A customisable header in all TOCs with the company name.**
- **Automatic deletion of 'thumbs.db' files.**

Compliance with the new validation criteria

NeeS TOCs created by Nanokinetik NeeS TOC Builder will pass all the validation criteria for NeeS submissions effective as of 1st December 2012.

The Nanokinetik TOC Builder creates NeeS TOCs within seconds.

Supported product types

This guidance covers the submission of electronic regulatory information for all human and veterinary medicinal products falling within the competence of NCAs in the EEA. This includes prescription and over-the-counter medicines, as well as innovative and generic product submissions. The product types include small molecules, biotech products, herbals, vaccines, homeopathics, and blood products.

Nanokinetik NeeS TOC Builder is very easy to install and use. End users simply like it.

Supported procedures

NeeS covers applications made in community procedures only falling within the competence of NCAs, namely National, Mutual Recognition, and Decentralised. Nees does not cover Centralised procedures.

Supported regulatory activities

The NeeS format applies to all submissions, regardless of size, relating to the authorisation and maintenance of medicinal products including, but not restricted to, new marketing authorisations, variations, renewals, PSURs, and active substance master files.

Some companies don't see the benefit of an eCTD, or even indicate that it takes longer to create an eCTD compared to a NeeS/paper.

Moving to NeeS format applications

A NeeS format application can normally be started with any initial, variation, or renewal MA application. Once the switch to this electronic format is made it is expected that further applications and responses relating to the particular medicinal product will be submitted in NeeS format. There is no requirement to reformat the whole dossier into NeeS format when switching from paper to NeeS format.

Paper requirements

In general, electronic submissions should be accompanied by a signed application form and cover letter. Detailed information on each NCA's specific requirements can be found at the CMDh website, or websites of the individual NCA.

File formats

In general terms, the majority of the documents included in electronic submissions should be in PDF format. Files that might be requested by NCAs in MS Word or RTF format should not be included in the NeeS structure. The Portable Document Format (PDF) is an open, de facto, electronic publishing standard. Although created by Adobe Systems Incorporated, there are several alternative suppliers of PDF software.

Nanokinetik will maintain future releases of NeeS TOC Builder to be fully in line with the latest requirements.

Technical validation of NeeS submissions

The technical validation of a NeeS is a separate activity from the content validation of a submission, and takes place irrespective of the type of the submission. NCAs have adopted a common set of technical validation criteria against which all NeeS can be checked using NeeS review and validation tools. From September 1st 2011, two categories of validation rules apply: "Pass/Fail," and "Best Practice."