Technical validation checklist[1] for veterinary electronic submission[2] - Version 3.1

Validation checklist for VNeeS submissions, approved by the Veterinary Harmonisation Group (VHG).

There are two types of criteria: the <u>pass or fail criteria</u> (P/F) and the <u>best practice criteria</u> (BP).

<u>Pass/Fail criteria</u> are validation criteria that can either be passed or failed (see section 1 of the table below). VNeeS submissions that fail to meet one or more of these criteria may be rejected, unless satisfactorily justified in the cover letter, and a replacement submission can be requested by the receiving authority. Any deviations from the P/F requirements of the e-submission guideline, should be discussed with the NCA.

<u>Best practice criteria</u> are criteria which facilitate review. Failing to meet a best practice criterion should never be a reason for technical invalidation. The VNeeS Checker tool supports verification of specific best-practice criteria and includes these in the VNeeS verification report as "warnings", so that applicants can produce VNeeS submissions that are easier to use. These specific BP criteria are listed in section 2 of the table below. Note that the VNeeS guideline includes many more recommendations for best-practices that cannot all be verified by the VNeeS checker.

<u>Mixed VNeeS- and CTD- based submission</u>: If (parts of) the quality documentation of the submission are structured according to CTD, within such a mixed VNeeS- and CTD-based submission specific validation rules apply for location and naming conventions of CTD module top-level folders and module-specific TOCs (see below VNeeS_004, VNeeS_005, VNeeS_008 and VNeeS_009). CTD sub-folders, below m2 and m3, are exempt from CTD folder and file naming convention, i.e. they will not be checked. The folder path criterion (VNeeS_006) shall be established as a Best Practice criterion only, as the path length of a valid module 3 might be slightly longer than 180 characters once integrated into a VNeeS root folder.
Remaining TOC criteria (VNeeS_010 to 012, VNeeS_BP001) apply likewise both to part- and module-specific TOCs.
File-level pass/fail requirements (VNeeS_002 and VNeeS_013 to VNeeS_017) as well as file-level Best Practice criteria (VNeeS_BP002 to VNeeS_BP005) shall apply also to files within CTD-based folders.

---

[1] *Note that this is a maximum list of validation criteria*
[2] *See Guideline on the specifications for provision of an electronic submission (e-submission) for a veterinary medicinal product*
http://esubmission.ema.europa.eu/tiges/vetesub.htm

1) Pass / Fail criteria:

ID	P/F Validation Criterion	Comments on Validation Check
VNeeS_001	**Security settings** No type of security on individual folders	It is not permitted to apply password protection to any folder. All folders must be able to open. If not, then validation failed.
VNeeS_002	**Security settings** No type of security on individual files	Individual files should not be password protected so as to prevent access (i.e. files should be possible to be opened). Additional security settings (e.g. copy-protection due to copyright issues or as used in the electronic application form) are out of scope of the technical validation check.
VNeeS_003	**Virus free**	Ensure that suitable antivirus software is installed that automatically recognises infected files once they are accessed or copied. To avoid false positive results as potential cause of a rejection of a submission a confirmation of the finding may need to be requested from the antivirus software provider.
VNeeS_004	**Folder structure:** Follows folder structure defined in guideline [3]	Any submission that follows the full or parts of the VNeeS folder structure. For these submissions, additional folders which are not specified in the guidance result in validation failure. Issues not resulting in validation failure: - The absence of a 'root' folder for file submissions containing a single concatenated PDF file and the eAF. - Missing level 1, 2 and 3 folders, as empty / not relevant folders should be deleted by the applicant. If during scientific validation it is noticed that folders are missing it will be dealt with at this stage. - Use of different folder structures for dossiers for referral procedures and other submissions not covered by the VNeeS guidance. If for the quality part of the submission (part of) the CTD structure applies, the top-level CTD folders m2 and m3 should be located in the VNeeS root directory.
VNeeS_005	**Folder structure:**	If (part of) the VNeeS structure applies (**VNeeS_004**), naming convention should be observed for all folder names.

---

[3] See: e-VNeeS guideline, Table 1 for pharmaceuticals, Table 2 for biologicals other than immunologicals, Table 3 for immunologicals, and Table 4 for MRL applications, http://esubmission.ema.europa.eu/tiges/vetesub.htm

ID	P/F Validation Criterion	Comments on Validation Check
	Follows names defined in guideline [4]	If for the quality part of the submission (part of) the CTD structure applies (VNeeS_004), naming conventions should be observed for module 2 and 3 folder names. These folder names have a fixed component ("m2" and "m3") optionally followed by a hyphen and a variable folder name component, e.g. "m3-substance1").
VNeeS_006	**Folder Path Length:** Total length does not exceed 180 characters	Path starting from the "root" folder and including all folder names, file name and file name extension (e.g. "root-mydrug\p1\1a-admin-info\applicationform.pdf"). If (parts of) the quality documentation is structured according to CTD, the folder path criterion (VNeeS_006) shall be established as a Best Practice criterion only, as the path length of a valid module 3 might be slightly longer than 180 characters once integrated into a VNeeS root folder. While the "add-info" folder in general is exempt from technical validation, the same logic applies to Subsequent Recognition Procedures where path length of submissions integrated into the "add-info" folder may become longer than 180 characters. Therefore, also in this case the path criterion (VNeeS_006) shall be established as a Best Practice criterion.
VNeeS_007	**General Table of Contents (GTOC):** A General TOC file is situated within the root folder of the VNeeS structure	General table of contents (GTOC) is present in the root directory **(LEVEL 1)**. In case of very small submissions consisting of only a single concatenated PDF file and the eAF, no separate GTOC needs to be created.
VNeeS_008	**Table of Contents (TOC):** A TOC file is situated within the correct folder for each part of the dossier	If a TOC is present it is located in the top level folder of each dossier part **(LEVEL 2)**. In case of immunological products, the contents of Part 3E 'Assessment for products containing or consisting of GMOs' may be covered by a separate TOC for this subpart **(LEVEL 3)**. In case of mixed VNeeS/CTD-structured submissions any module-specific TOC is likewise located in the top level folder of each dossier module **(LEVEL 2)**.
VNeeS_009	**Table of Contents:** Naming convention	Naming convention for general table of contents (GTOC): *gtoc.pdf* Naming convention for TOC in the top level folder of each part: *p1-toc.pdf, p2-toc.pdf, p3-toc.pdf and p4-toc.pdf*

[4] See: VNeeS guideline, Table 1 for pharmaceuticals, Table 2 biologicals other than immunologicals, Table 3 for for immunologicals and Table 4 for MRL applications.

ID	P/F Validation Criterion	Comments on Validation Check
		TOC in Part3E of immunological products: ***p3e-toc.pdf*** In case of mixed VNeeS/CTD-structured submissions naming conventions for TOCs in the top level folder of module 2 and module 3 are **m2-toc.pdf** and **m3-toc.pdf**. Only files following this naming convention can be checked by the VNeeS checker tool.
VNeeS_010	**Table of Contents:** The GTOC should be a complete index to the whole dossier either referring directly to content documents or via the part-specific TOCs	The GTOC should be a complete index of the whole dossier, either directly to individual files or to the part-specific TOCs. In case both GTOC and the part-specific TOCs are hyperlinked in parallel to all indexed documents, this will <u>not</u> invalidate the submission. There should not be any hyperlinks to documents in the "add-info" folder.
VNeeS_011	**Table of Contents:** GTOC and TOC include navigation features for efficient electronic navigation	The GTOC should use hyperlinks directly to documents or to part-specific TOCs. The GTOC should be hyperlinked to any part-specific TOCs. TOCs of each part provide hyperlinks to all indexed documents. [5] In case both GTOC and the part-specific TOCs are hyperlinked in parallel to all indexed documents, this will not invalidate the submission. There should not be any hyperlinks to documents in the "add-info" folder. For documents which are referred to in multiple dossier sections but physically submitted in one folder only, multiple hyperlinks to the same folder position are allowed. Therefore, additional hyperlinks to a file from different TOCs, pointing to a folder not within the same dossier part of that TOC, will <u>not</u> lead to validation failure.

---

[5] Alternative methods (such as the use of bookmarks within one document or hyperlinks between specific documents, e.g. from reports to annexes) can be used, if they assure equivalent efficiency of navigation, but these may not be supported by the VNeeS checker.

ID	P/F Validation Criterion	Comments on Validation Check
VNeeS_012	**Table of Contents:** Hyperlinks in the GTOC and TOC are functional	Hyperlinks must be relative, and functional. In the GTOC/TOC this should be observed for all hyperlinks. Hyperlinks should only be made to documents inside the same VNeeS submission and not to external sources. All hyperlinks and bookmarks between two PDFs must be configured as specified in ISO 32000-1:2008. Consult the PDF specifications as in ISO 32000-1:2008 for section 7.11.2 on how the paths need to be written in PDF. The paths cannot contain back slashes, only forward slashes. Please note, not all PDF tools correctly display the path for the link with forward slashes, thus the presence of a backslash in a link as displayed in a PDF viewer or editor does not necessarily mean that the link is NOT according to the ISO specifications. Therefore, tests for backslashes must be performed in VNeeS validation software. This criterion is important because links that are not according to section 7.11.2.3 may not work on certain devices, such as non-Windows operating systems or tablets.
VNeeS_013	**File format:** File format is PDF	PDF format for all normally visible files (with exception of any files in the folder "add-info" which are out of scope of technical validation). File names should have the proper extension (i.e. ".pdf" or ".PDF").
VNeeS_014	**File format:** Files have been created and saved as PDF 1.4, 1.5, 1.6, or PDF 1.7	For PDF files with apparent versions of 1.3 or earlier, the version information should be taken from the first eight characters from the first line of the header in the file. For versions 1.4 and higher, the version should be taken from the document catalogue dictionary, if present. If both the header information and the catalogue information are present, then the document catalogue dictionary information takes precedent, see PDF 32000-1:2008 specification, chapter 7.5.2 for further details. This test is important to ensure that PDF files can be correctly opened and read by assessors.

ID	P/F Validation Criterion	Comments on Validation Check
VNeeS_015	**File names:** No prohibited characters used	The file name should not contain any 'special' characters; only alphanumeric characters (characters a-z, digits 0-9) and hyphens are allowed. Use of <u>upper case characters</u> would not lead to invalidation.
VNeeS_016	**Files:** The submission does not contain corrupted files	This check can be achieved by opening a PDF file in software which is compliant to ISO 32000-1:2008; if the file opens without error, the PDF file is considered to be conformant. Absence of detection of conformance means corrupted PDF.
VNeeS_017	**File format:** Presence of hidden files	In a file system specific files or folders do not display by default. Such hidden files like Microsoft Office temporary files (~$filename.doc) or MS Windows hidden files (e.g. thumbs.db) may appear also in a folder structure to be submitted. These files must be deleted to avoid unintended transfer of such files and the information contained. To see all protected system files that are usually hidden from view, advanced file and folder settings in the MS Windows Control Panel need to be adapted accordingly. Technical validation with the VNeeS checker tool will usually detect such hidden files. Note however that files in the "add-info" folder are not subject to validation, and that access to dossier files after final validation may create again new temporary files.

Based upon the full compliance of the P/F criteria above (except VNeeS_003), the VNeeS checker tool provides a conclusion (i.e. technically valid or technically invalid) on top of the report. This conclusion is to be used together with the output of the updated virus scan to have the final conclusion.

2) Best Practice criteria

ID	BP Criterion	Comments on Verification Check
VNeeS_BP001	**Table of Contents (TOC):** A TOC file is present for each part of the dossier	The applicant must provide a complete index to the whole dossier either referring directly to content documents in a GTOC or via additional part-specific TOCs. The presence of part-specific TOCs as such is no P/F criterion.
VNeeS_BP002	**Individual file size** File size of a single file should be limited to 200 MB	Large files are more difficult to handle by users/reviewers and may impose practical limitations with downloads from common repositories.

ID	BP Criterion	Comments on Verification Check
VNeeS_BP003	**Mechanisms used for making inter-document hyperlinks** Only GotoR actions allowed between PDF documents	Hyperlinks should neither be made with JavaScript code in the PDF nor with executable file launches. Instead, inter-document hyperlinks should always be provided as specified in ISO 32000-1:2008, section 12.6.4.3 "Remote Go-To Actions" (GoToR), i.e. as an action to jump to a page view of another ("remote") PDF file. Use of executable file launches would currently not lead to invalidation but lead to a warning by the VNeeS checker tool, as such types of hyperlinks may raise IT security concerns or may be lost during archiving processes (conversion to PDF/A). This criterion is both valid for hyperlinks from tables of contents as for hyperlinks between other PDF's in the dossier. Uniform Resource Identifier (URI) actions are exceptionally allowed.
VNeeS_BP004	**Font embedding** Every font used for visible text should be embedded within the PDF file	Literature files can be exempted from this criterion, if the prefix "lit-" is added to their file name. The eAF, owing to technical reasons, does not support font embedding. Therefore the related warning is to be ignored for this file. Only embedding of the subset of characters actually used in a given font is required. Embedding complete fonts needlessly increases the size of the PDF file. Invisible fonts used in scanned documents for creating searchable text by an Optical Character Recognition (OCR) routine may be embedded but are exempted from a best practice requirement. Note that the VNeeS checker does list all unembedded fonts. This warning therefore can be ignored for files where in exceptional cases OCR had been used. Please note that all embedded fonts must also be legally embeddable, i.e. licence agreements must allow unlimited embedding into the PDF file, either fully or as a subset, for the purpose of printing or viewing the document. Subsetting and use of commonly used fonts is recommended from a copyright perspective. However, the VNeeS checker cannot verify whether fonts are also legally embeddable. The test is skipped for PDF/A-compliant files as these files already fulfill this criterion. The VNeeS checker verifies PDF/A compliance by checking the PDF/A metadata (pdfaid entries).
VNeeS_BP005	**File format:**	PDF files that conform to [ISO-19005-1:2005], [ISO-19005-2:2011] or [ISO-19005-3:2012] are accepted. The minimum PDF/A conformance level, i.e. Level B conformance (PDF/A-1b, PDF/A-2b or PDF/A-3b) is sufficient.

ID	BP Criterion	Comments on Verification Check
	PDF files have been created and saved as PDF/A-conforming files.	The VNeeS checker verifies PDF/A compliance by checking the PDF/A metadata (pdfaid entries). The eAF, owing to technical reasons, is not in conformance with the PDF/A standard. Therefore the related warning is to be ignored for this file.