

**Guideline on the specifications for provision of an
electronic submission (e-submission) for a veterinary
medicinal product**

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Introduction

This Guidance Document is intended to assist applicants and regulators with submissions of dossiers in electronic format. It specifies the basic parameters required for an acceptable electronic submission to be known as Veterinary NeeS (VNeeS), the name being inspired by the established NeeS standard for Human medicinal products. The document has been reviewed by the Veterinary Harmonisation Group, which is made up of representatives from National Competent Authorities, the EMA and Industry. All National Competent Authorities and EMA should adopt this guidance as the basis for their acceptance of electronic submissions for marketing authorisations from applicants.

The mandatory implementation of electronic submission has been following the HMA eSubmission roadmap. Electronic submission in the VNeeS format is now mandatory for submissions to EMA as well as for submissions in the Decentralised, Mutual Recognition and National Procedures.

1 Scope

This guidance covers all types of initial applications for marketing authorisation made in the Centralised (CP), Mutual Recognition (MRP), Decentralised (DCP) and National procedures including updates provided during the assessment phase (validation updates and responses to questions).

It applies also to active substance master files (ASMF), MRL applications, and post-authorisation submissions (e.g. variations and dossiers for referral procedures, see section 7.(g)).

For procedures such as requests for Scientific Advice, parallel import or field trial applications, the use of an electronic dossier is feasible in principle, if accepted by the competent authority. The requirements should follow the current guideline, except for the folder structure. For notifications submitted regarding the deliberate release of a Genetically Modified Organism (GMO), it is advisable to confirm acceptance of an e-submission with the concerned national agency.

2 Procedure for submitting the electronic dossier

It is strongly recommended or even mandatory to use secure portals for the submission of applications. For submissions to national competent authorities (MRP/DCP or NP), the [Common European Submission Platform \(CESP\)](#) should be used, please refer to the [CESP website](#) for further details. The EMA eSubmission Gateway/Web Client should always be used for submissions to the EMA (i.e. in the Centralised Procedure and EMA led referral procedures). For further details see the [eSubmission website](#) and also the guidance document "[Dossier requirements for submission](#)".

Authorities may require provision of a paper cover letter for electronic submissions. An electronic version of a cover letter should always be included in the folder "add-info" of the VNeeS submission (PDF preferably generated from text source without a requirement to scan a wet signature).

For authorities requiring an official signature for legal reasons, an originally signed cover letter or application form may follow the electronic submission.

See [CMDv website](#) for further details on NCA requirements. For submissions to the EMA, please refer to the [eSubmission section](#) of the Agency website.

3 Language

In order to facilitate the processing of the application and make the assessment more efficient, the scientific and technical documentation should be submitted in English. Both applicants and authorities should refrain from translations to languages other than English as this makes quality control and validation difficult and less reliable.

4 File Format & Source

All documentation should be submitted using file formats that facilitate both reviews on screen and paper while retaining a similar format.

The portable document format (PDF) is a format which supports the described features. PDF provides an ISO-standardised format (ISO 32000-1:2008), including a long-term archiving format also known as PDF/A (ISO-19005-1:2005, ISO-19005-2:2011 and ISO-19005-3:2012). PDF/A has been accepted as a standard for providing documents in electronic format by the International Conference on Harmonisation (ICH) and is recommended as default file format by the veterinary equivalent (VICH).

The PDF format used for a VNeS-compliant submission should follow the specifications defined in [VICH Guideline 53: Electronic exchange of documents: electronic file format](#). The VNeS specification deviates however from the VICH guideline in terms of file sizes, as it discourages only files sizes larger than 200 MB.

It is noted that VICH Guideline 53 discourages the use of file attachments for any dossier-related content as they can be easily overlooked during compilation / review of documents and may complicate technical validation. As the XML attachment to the eAF form however follows closely defined rules and neither introduces new content nor needs to be subject to VNeS validation criteria, the approach is fully compatible with the VICH concept.

Product information (SPC, label, leaflet) should be submitted in addition to a PDF file in an editable format like Microsoft Word.

5 Requirements for creating PDF files for electronic submission

5.(a) Electronic source documents

To allow functionality such as text searching, copying and pasting into editable formats, PDF documents should be created (rendered) directly from their electronic source documents, except where the applicant has no access to the electronic source document. Such exempted documents are for example

- copies of documents provided by regulatory authorities such as manufacturer's licences, certificates of suitability, manufacturing authorisations,
- copies of documents from other external sources like certificates of analysis,
- any literature references sourced from journals, periodicals and books.

If documents are sourced from a scanned original the only way to create searchable text is using an Optical Character Recognition (OCR) routine. The use of OCR should be considered when preparing key documents of the submission, in particular the main body of text of the critical expert reports, or written summaries of the applicant. Applicants do not have to quality assure the underlying OCR; however, good quality scanned copies should be used for OCR wherever possible, as more accurate text will allow for increased utility by reviewers.

Where only signature pages may need to be scanned, applicants should consider providing signatures on separate pages not containing other information key to the understanding of the submission.

6 Signatures

The applicant has the obligation to ensure a proper certification of the submitted documents. Valid signatures should be available from the applicant and be presented at the request of the authorities. National Competent Authorities should, wherever necessary, accept a signed paper cover letter confirming the correctness of the submitted file(s).

7 Structure of the electronic submission

7.(a) General considerations

The folder structure (granularity) for an electronic submission is based on the Annex II to Regulation (EU) 2019/6 (as amended). This hierarchical structure of folders within a root folder gives, depending on the type of submission, up to three levels of granularity. The complete VNeS folder structure is shown in

- **Table 1 for pharmaceutical products**
- **Table 2 for biological products other than immunological products**
- **Table 3 for immunological products**
- **Table 4 for an MRL application,**
- Table 5 for an Active Substance Master File (ASMF) in VNeS
- Table 6 for a Vaccine Antigen Master File (VAMF)
- Table 7 for mixed VNeS / CTD submissions (CTD quality part)
- Table 8 for mixed VNeS / CTD submissions (ASMF applicant's part in CTD)
- Table 9 for applications for a change in prescription status.

and should be used where applicable to prepare any electronic submission. Only Table 1 to Table 4 (written in bold text above) are used as basis for technical validation of folder structures and folder/file naming. The following tables are showing only existing subsets for specific types of submissions, which are not subject to specific validation rules (except for mixed CTD/VNeS submissions, where additional rules apply for top-level CTD folders m2 and m3 and corresponding TOC files, see also section 7.(b) and section 7.(e)).

Root folder

The name of the top level folder ("root folder") of each VNeS folder structure should allow appropriate identification of the submission.

For reasons of automated identification and technical validation of e-submissions with tools like the VNeS checker¹ each root folder name must start with the letters "root", followed by a specific identification of the submission which can be defined by the applicant. A hyphen ("-") character should be used as separator.

It is recommended to use as specific identification

- the product (invented) name and/or
- the procedure number (if known), and /or
- the submission date or day of procedure, to allow tracking of updates during the procedure

¹ The VNeS Checker is a standard non-commercial, and publically available tool for technical validation of VNeS submissions. For further details please refer to section 9 of this guidance.

For example

root-mydrug
root-mydrug-dk-v-0123-001
root-ema-v-c-0123
root-dk-v-0123-002-1a-003
root-mydrug-ema-v-c-0123-2oct11

Folder "add-info" (additional information)

The folder structure includes a folder called "add-info" located in the root folder.

Working documents for use by assessors, e.g. editable files in Microsoft Word format, should only be submitted as an additional file format which is identical in content to a PDF file that is elsewhere included in the dossier structure. Therefore, any files in MS-Word format should only be saved in the folder "add-info". Examples for such files are SPC and product literature, or the main "responses" (to questions) document; although not mandatory, some NCAs might also wish to receive other documents such as the "critical expert reports" in MS Word format.

Where the applicant still has to fulfil any specific national requirements, related country-specific documents should be provided in this folder. If so, subfolders should be included named with the country code of the country concerned as per Table 10. Documentation of a change in prescription status to be sent to a single member state only should however be placed into the relevant VNeS folders, see section 7.(g) for details.

Any files submitted voluntarily for information only, like user instructions for the reviewer, should also be placed in the folder "add-info". Validation results of tools like the VNeS checker should also be included in that folder.

Files and subfolders in the folder "add-info" are not subject to technical validation. Where previous electronic submissions which had originally been accepted by the receiving authority are included in a later submission, i.e. during a subsequent recognition procedure, authorities should not request an update according to the most recent e-submission format. In such cases the original submissions may be included under "add-info". In any case applicants should ensure that previous submissions include sufficient features for navigation like a hyperlinked table of contents.

Note that except in the case of the above-mentioned documents, administrative information and scientific documentation should not be located in the "add-info" folder, but in the VNeS folders corresponding to the relevant veterinary dossier chapters.

Adaptation of folder structure

For any VNeS submission only folders listed in Table 1 (in case of pharmaceuticals), Table 2 (biologicals other than immunologicals), Table 3 (immunologicals) or Table 4 (in case of MRL submissions) should be used. Other tables do not introduce new VNeS folder definitions but only use a subset of the above folder structures. Including additional (self-defined) folders within the structure of the e-submission is not permitted, except for the folder "add-info" where subfolders could be constructed.

If applicants wish to further separate information within a given folder, this should only be done by clearer guidance in the Table of Contents (e.g. adding additional headings), or by using bookmarks within the appropriate documents (e.g. in order to clearer differentiate between target species, pharmaceutical forms, or lower numbered sections e.g. in the quality or safety dossier).

If there are empty folders in the submission because no data is provided these should be deleted as the folder structure should reflect only what actually is submitted. Corresponding positions in the relevant table of contents (TOC) should also be deleted.

When only little information is presented for a number of folders at the same level of granularity, it is acceptable to include all the information in a single PDF at the higher level of the granularity. This should be indicated in the TOC.

Folder names

Folder names should be in English and where the VNeS structure defined in this guidance is applicable follow exactly the conventions given in Table 1 to Table 9 .

7.(b) Folder structure for initial Marketing Authorisation Application

The folder structure for an electronic submission of an initial application for marketing authorisation is shown in Table 1 for pharmaceutical products, Table 2 for biological products other than immunologicals and Table 3 for immunological products.

The applicant may also optionally submit the chemical, pharmaceutical and biological / microbiological information for the finished product (Part 2) in a Common Technical Document (CTD) structure for human medicinal products for Module 3 and, for reuse of Quality Overall Summaries (QOS) and signed Curriculum Vitae of QOS experts, Module 2 of the CTD. In such cases the dossier contains a "mixed" structure of CTD for the quality part and VNeS for the other dossier parts. Note that the quality part itself may also contain a mixture of VNeS and CTD-structured information, if the Applicant's Part of an ASMF is provided within a CTD folder structure (see section 7.(e) for further details). In each case, a [correlation table](#) should be provided showing which CTD chapter corresponds to which dossier chapter as defined in the Annex II to Regulation (EU) 2019/6 (as amended).

Within such a mixed VNeS- and CTD- structured submission the CTD module folder names should follow the eCTD naming conventions (i.e. "m2" and "m3"). Subfolders in the folder structure beneath should follow the eCTD folder structure requirements, but CTD folder and file naming conventions will not be subject to technical validation.

The top-level CTD folders m2 and m3 should be located in the VNeS root directory. They should contain module-specific TOC files which are named following the eCTD naming conventions, i.e. "m2-toc.pdf" or "m3-toc.pdf" respectively. The GTOC should be hyperlinked to the module-specific TOCs. Only the eCTD folder structure may be used, mixed VNeS / eCTD submission are not acceptable: this means that the eCTD 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 should not be present, so navigation is only based on the electronic TOCs, bookmarks and hypertext links. Applicants therefore should take care that easily readable and fully navigable PDF-based TOCs are available.

If applicants switch to the CTD format, then they should keep it also for next procedures, and it should not be possible to revert to the VNeS format, for example, within variations to the marketing authorisation.

Please refer to Table 7 as an example of a mixed VNeS and CTD submission.

7.(c) Use of summary reports in MRL dossier

Summary reports (obligatory Detailed and Critical Summaries or DACS) should be saved into p2 for safety and p3 for residues (see Table 4).

7.(d) Submission structure for updates during assessment phase

The initial submission and subsequent amendments during the assessment phase should use different root folder names to allow efficient tracking of submissions, e.g. by including the submission date or day of procedure.

Though applicants are strongly encouraged to use in subsequent submissions consistent file naming conventions there is no requirement to exactly preserve file names during life cycle changes; in fact, logical differences in file names can be helpful during review when both files are open simultaneously for comparative or other purposes.

Validation updates

As a consequence of the technical or regulatory validation process there may be the need for updates of the VNeS submission.

Normally, a corrected version of the full application has to be re-submitted if the submission is technically invalid.

If there is a need to update the dossier due to the content validation, the applicant should liaise with the relevant authority whether these documents could be submitted as single documents, or sending an updated VNeS submission is required. Single files should be properly named so it is easily understood what is submitted.

Responses to Questions

In response to questions on the initial submission the applicant submits document(s) containing the actual text of the responses as well as amendments to the initial dossier.

If the response submission contains more than a single file, the main response document(s) should be located in the folder "responses" in Part 1. Any additional documents submitted with the responses should be assigned to the relevant folders, as specified in Table 1 to Table 9. The response submission is a stand-alone submission; it is thus not required to send an update of the initial VNeS submission consolidated with the responses.

Where new or updated documents are required, easy navigation to the new or updated documents should be ensured.

7.(e) Active Substance Master Files

The VNeS folder structure applies also to the Active Substance Master File (ASMF) procedure. For an initial ASMF (containing Applicant's Part and Restricted Part) the relevant VNeS folders are detailed in Table 5.

The master file holder may also optionally submit the ASMF within a CTD folder structure (also using the eCTD v.3.2.2 format²). In this case, a [correlation table](#) should be provided showing which CTD chapter corresponds to which veterinary dossier chapter as defined in the Annex II to Regulation (EU) 2019/6 (as amended). The name given to the root folder is the decision of the ASMF holder but should uniquely identify the ASMF, preferably by the EMEA/EU ASMF reference number or the name of active substance and name of the ASMF holder.

The Restricted Part should be provided by the ASMF holder together with the Applicant's Part. It could be provided either as a separate folder, structured in accordance with the example above, or incorporated in the same structure, but then by using the suffix "rp" and "ap" respectively in each file name for clarification.

Where the Applicant's Part is provided within a CTD folder structure the same requirements apply as for initial submissions using a mixed VNeS- and CTD-structured submission (see chapter 7(b)). In case

² The acceptability of eCTD for ASMF submissions will be revisited after implementation of eCTD version 4.

of referring to multiple ASMFs separate m2 and m3 folders should be used. In this case the module folder name needs to be extended by a hyphen and a variable folder name component, e.g. "m3-substance1" and "m3-substance2". See Table 8 as an example of a mixed VNeS- and CTD structured submission where the Applicant's Part is provided within a CTD folder structure.

In the corresponding marketing authorisation application dossier, the documents in the Applicant's Part of the ASMF(s) should be assigned to the relevant folders and subfolders as specified in Table 1 in this guidance, and clearly named for identification, in particular if more than one ASMF is used.

7.(f) Platform Technology Masterfile

Content and thus folder structure of a Platform Technology Masterfile (PTMF) may vary depending on the type of platform. Applicants should refer to the general structure for immunologicals and select the relevant headings on a case-by-case basis.

7.(g) Submission structure for post-authorisation submissions

Variations

All files should be assigned, wherever possible, to the relevant folder as specified in Table 1 to Table 3, e.g. for quality variations primarily the folders within Part 1 (e.g. for application forms, updated product literature) and Part 2 'Quality Documentation'. Empty folders in the submission should be deleted so that the structure reflects only what actually is submitted.

For grouped variations or worksharing procedures, a single submission structure (i.e. one root folder) should be used. If these submissions are product specific, the product-specific documentation should be provided in separate files and applicants should ensure that file names or TOCs allow easy identification of the related products.

SPC harmonisation

In an SPC harmonisation procedure according to Section 4 of Regulation (EU) 2019/6 the dossier submitted for the examination phase for the reference veterinary medicinal product should include next to the relevant information to be provided in Part 1 of the dossier all appropriate existing data to support any aspects of the proposed harmonised SPC that go beyond the 'common denominator SPC'.

For such submissions thus the same folder structure as for the initial MAA applies, depending on the product type in scope of the actual procedure (see Table 1 for pharmaceuticals, Table 2 for biologicals other than immunologicals or table 3 for immunologicals). Empty folders in the submission should be deleted so that the structure reflects only what actually is submitted.

For further details please refer to [CMDv best practice guides](#).

Application for a change in prescription status

Documentation of an application for change in prescription status (OTC application) for an MRP/DCP product which is relevant to a single (Concerned) Member State only, should not be placed into the "add-info" folder but into the relevant VNeS folders. However, for all country-specific files the country code of the country concerned should appear in the file name as per Table 10.

Supporting, administrative and scientific documentation for the OTC switch should be placed in the VNeS folders specified in Table 9 (example for a pharmaceutical product and biological product other than an immunological product).

For applications related to an immunological product corresponding folders should be used (specifically "3b-preclin" for an updated User Risk Assessment).

Other post authorisation submissions

For other post authorisation submissions such as dossiers for referral procedures the folder structure as defined in Table 1 to Table 3 may not be applicable. When consisting of more than a single file, the applicant should use for such submissions any appropriate folder structure that facilitates the review.

7.(h) Indexing

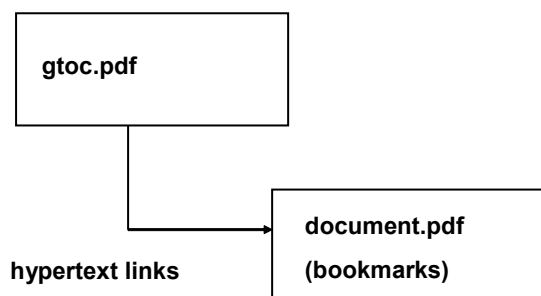
The electronic submission must include a general table of contents (GTOC) in the root directory. A part-specific table of contents (TOC) in the top level folder of each part of the dossier is strongly encouraged as this improves the navigation within the dossier.

The GTOC should be a complete index to the whole dossier either referring directly to content documents or via the part-specific TOCs, while the TOC for each part of the dossier should be a complete index for that part of the dossier. Files being present in the folder "add-info" should not be included in the GTOC or TOCs.

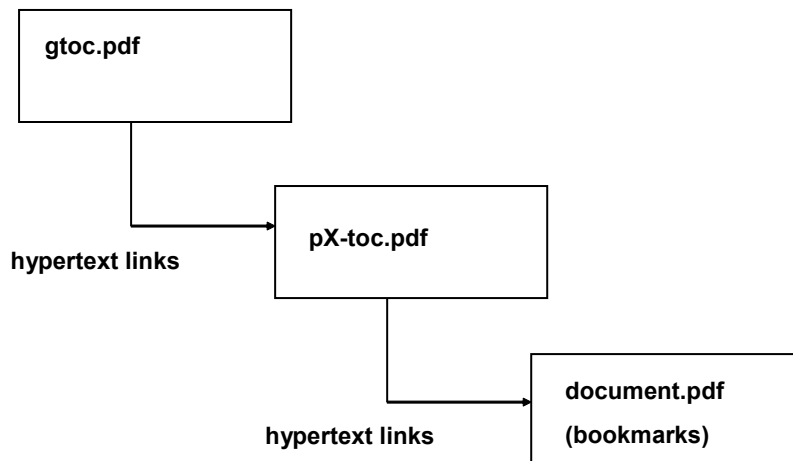
Hypertext links in GTOC or TOCs are essential for efficient navigation through any larger submission. Therefore, all documents in the submission should be referenced in a GTOC or TOC using a hyperlink. The general TOC should always be hyperlinked to any part-specific TOCs. Hyperlinks to the documents in each dossier part should be present either in the GTOC or the part-specific TOCs. Hyperlinks should only be made to documents within the same VNeS submission and not to external sources.

The diagrams below illustrate the recommended use of features for navigation. Alternative methods (like use of bookmarks in the (G)TOCs or hyperlinks between specific documents, e.g. from reports to annexes) can be used if they assure equivalent efficiency of navigation, but these features may not be supported by the VNeS checker.

Navigation via GTOC only:



Navigation via GTOC and part-specific TOCs:



File naming conventions for the table of contents should be followed to allow automated validation tools like the VNeS checker to easily identify and check GTOC and TOCs, including the functionality of inserted hyperlinks.

The GTOC should be named "*gtoc.pdf*". The files containing the part-specific TOCs should be named "*p1-toc.pdf*", "*p2-toc.pdf*", "*p3-toc.pdf*" and "*p4-toc.pdf*".

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, named "*p3e-toc.pdf*".

TOCs should follow the structure of Annex II to Regulation (EU) 2019/6, as amended, and the description of each hyperlinked document should easily allow identifying the contents of the file. In case applicants are using an automated TOC builder, the text of the TOC entry might just be the file name of the hyperlinked document. In such case applicants should put more emphasis on using descriptive file names. If the names of the files are not self-explanatory, the TOC needs to be edited manually e.g. by using commercially available PDF-editing software.

Further guidance on (G)TOC is provided in a separate document published on the veterinary section of the EU [eSubmission website](#).

7.(i) Files

Size and number

A submission is a collection of documents and each document should preferably be provided as a separate file. If more than one PDF is provided in any section, discrete studies or reports should not be split between PDF files unless necessary. If splitting is necessary due to large file size (> 200 MB), it should be done at a sensible point to facilitate the review (i.e. do not split in the middle of a paragraph but rather between the text and the annexes for instance). Please note, that the file size limit for product information documents to be uploaded to the Union Product database (UPD) is 2 MB only.

Naming

The name of the files should be in English. They should be descriptive and unambiguous especially if more than one PDF is included in a particular section. Any information that may help identify the contents of the file is encouraged to be included in the file name.

Preferably the file name should include the part of the dossier where the document is located. In these cases file names should be based on the naming convention for dossier parts used in the folder structure as defined in Table 1 to Table 9.

In case applicants are using an automated TOC builder, the text of the TOC entry might just be the file name of the hyperlinked document. In such case applicants should put more emphasis on using descriptive file names.

However, excessively long file names should be avoided. The length of a path including file name, and extension should not exceed 180 characters.

Examples of valid file names are:

application-form.pdf
p1c2-cers-safety.pdf
part-2e3-ident-assay-excip.pdf
p3a2-report-no-12345.pdf
part-3a6-era.pdf

If one document has to be split over more than one PDF because its file size is too large, then the files should be numbered as “1ofx”, “2ofx” for example:

carcinogenicity-rat-1of4.pdf

Where possible, applicants are strongly encouraged to use in subsequent submissions naming conventions consistent with the naming used in the initial submission.

Study reports and/or other literature will usually accompany the information provided in the dossier. These can be provided as individual PDF files or as a single PDF containing a number of studies. In general providing each study as a single PDF file is preferred. PDF files which are required in more than one section of the dossier need not be submitted more than once, although the file(s) can be submitted in each section in which they are required. If a file is only to be submitted once but referenced a number of times then a simple cross-reference or a hyperlink to the section of the dossier where the files can be found is necessary.

Files should have the proper extension (e.g. PDF).

The file name should not contain any 'special' characters; only alphanumeric characters (characters a-z, digits 0-9) and hyphens are allowed. Use of upper case characters would not lead to invalidation, nonetheless for product information documents only lower case should be used (see below).

Specific file naming conventions apply to

- (G)TOCs (see above) and to
- product information documents which will be uploaded into the Union Product database (UPD). Please refer to the Annex 2 from the chapter 2 of the Implementation Guide on veterinary medicines product data in the UPD ([VET EU IG](#)) for obtaining detailed information on the specifications that apply to naming convention for product information documents.

Bookmarks and hyperlinks (outside the GTOC or TOC)

Navigation is significantly enhanced by appropriate use of bookmarks and hyperlinks in PDF files. The inclusion of bookmarks / hyperlinks into PDF files aids in the navigation around the document content. Hyperlinks in key documents of the submission (e.g. critical expert reports, written summaries of the applicant or main response documents) to related files like references, or appendices are helpful and greatly improve navigation efficiency through a VNeS submission. Especially in case of single PDF files containing several references, bookmarks should be included for efficient navigation.

8 Security

It is not permitted to apply password protection to the submitted files. Authorities are obliged to have properly secured systems that guarantee the documentation is accessed only by authorized persons. Applicants have the right to get the assurance that the appropriate level of security is applied.

9 Technical validation

In order to be accepted as valid, an electronic VNeS submission has to comply with the common set of technical pass/fail criteria defined in the 'Technical validation checklist for veterinary electronic submission' as published on the veterinary section of the EU [eSubmission website](#).

The pass/fail criteria included in this checklist above should be considered as a maximum set of criteria. Authorities should not enlarge the list as this will result in a non-unified approach to the validation.

Submissions that fail to comply with these technical validation criteria may be rejected and a replacement submission can be requested by the receiving authority (if necessary).

As literature files may not be able to comply with specific technical requirements, these files can be exempted from such criteria, if the prefix "lit-" is added to their file name. Please refer to the 'Technical validation checklist for veterinary electronic submission' for further details.

VNeS submissions can be checked against the technical validation criteria using for instance the VNeS checker tool. The VNeS Checker tool should be used as point of reference for technical validity of a submission by competent authorities. It is available for free download e.g. via the veterinary section of the EU [eSubmission website](#). The tool will be updated in line with revisions to this guideline. Before sending a VNeS submission, applicants should technically validate it with a validation tool and can use the VNeS checker tool for that purpose. Validation results provided by the validation tool should be placed in the "add-info" folder of the submission. Applicant should take care that when running a validation tool, the correct type of VNeS folder structure is selected (i.e. for pharmaceutical products, immunological products or MRL applications).

10 Glossary

eAF: electronic Application Form

ERA: Environmental risk assessment

GMO: Genetically modified organism

GTOC: General Table of Contents. The GTOC should be a complete index to the whole dossier.

ICH: International Conference on Harmonisation

ISO: International Organization for Standardization

MB: Megabyte; unit of information storage or computer storage

PDF: Portable Document Format

PDF/A: ISO-standardized version of PDF suitable for long-term archiving of electronic documents

RMS: Referentials Management Service - lists of terms (controlled vocabularies)

SPC: Summary of Product Characteristic

SPOR: Substance, product, organisation and referential master data services

TOC: Table of Contents. The TOC should be a complete index for that part of the dossier.

URA: User risk assessment

UPD: Union Product Database

VICH: International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products.

VNeeS: Veterinary NeeS (the name being inspired by the earlier used term NeeS, Non-eCTD electronic Submissions for Human medicinal products), an electronic application prepared using standard software and which follows the structure set out in this guidance.

TABLE 1: Folder structure and Standard files for an electronic application for a pharmaceutical product















 root-<mydrug>	(Submission-specific root folder - see section 7.(a) for naming conventions)
 gtoc.pdf	(General Table of Contents)
 add-info	(Additional information)
 p1	(Country code as per Table 10) (Part 1- Summary of the dossier)
 cc	
 p1-toc.pdf	(Table of Contents Part 1)
 1a-admin-info	(Administrative information)
 1b-spc-pl	(SPC, Labelling and Package Leaflet)
 1c-cers	(Critical expert reports)
 1c1-qual	(Critical expert report on the quality documentation)
 1c2-saf	(Critical expert report on the safety documentation)
 1c3-effic	(Critical expert report on the efficacy documentation)
 1-responses	(Responses to questions)
 p2	(Part 2 - Quality documentation)
 p2-toc.pdf	(Table of Contents Part 2)
 2a-prod-descr	(Product description)
 2b-manuf	(Description of the manufacturing method)
 2c-contr-start-mat	(Production and control of starting materials)
 2c1-act-sub	(Active substances)
 2c2-excip	(Excipients)
 2c3-cont-clos-sys	(Packaging (container-closure systems))
 2c4-bio-origin	(Substances of biological origin)
 2d-contr-intermed	(Control tests carried out on isolated intermediates during the manufacturing process)
 2e-tests-fin-prod	(Control tests on the finished product)
 2f-stab	(Stability tests)
 2f1-act-sub	(Active substances)
 2f2-fin-prod	(Finished product)
 2g-other-info	(Other information)
 p3	(Part 3 – Safety documentation)
 p3-toc.pdf	(Table of Contents Part 3)
 3a-saf	(Safety tests)
 3a1-ident	(Precise identification of the product and of its active substance(s))
 3a2-pharmacol	(Pharmacology)
 3a3-tox	(Toxicology)
 3a4-other	(Other requirements)
 3a5-ura	(User safety)
 3a6-era	(Environmental risk assessment)
 3b-resid	(Residue tests)
 3b1-ident	(Identification of the product)
 3b2-metab-resid	(Depletion of residues)
 3b3-resid-analyt-met	(Residue analytical method)
 p4	(Part 4 – Efficacy documentation)
 p4-toc.pdf	(Table of Contents Part 4)
 4a-preclin	(Pre-clinical studies)
 4a1-pharmacol	(Pharmacology)
 4a2-resist	(Development of resistance and related risk in animals)
 4a3-dose-determ	(Dose determination and confirmation)
 4a4-tas	(Tolerance in the target animal species)
 4b-clin	(Clinical trials)

TABLE 2: Folder structure and Standard files for an electronic application for a biological product other than immunological















































 root-<mydrug>	(Submission-specific root folder - see section 7.(a) for naming conventions)
 gtoc.pdf	(General Table of Contents)
 add-info	(Additional information)
 p1	(Country code as per Table 10) (Part 1- Summary of the dossier)
 cc	(Table of Contents Part 1)
 p1-toc.pdf	(Administrative information)
 1a-admin-info	(SPC, Labelling and Package Leaflet)
 1b-spc-pl	(Critical expert reports)
 1c-cers	(Critical expert report on the quality documentation)
 1c1-qual	(Critical expert report on the safety documentation)
 1c2-saf	(Critical expert report on the efficacy documentation)
 1c3-effic	(Responses to questions)
 1-responses	(Part 2 - Quality documentation)
 p2	(Table of Contents Part 2)
 p2-toc.pdf	(Product description)
 2a-prod-descr	(Description of the manufacturing method)
 2b-manuf	(Production and control of starting materials)
 2c-contr-start-mat	(Starting materials listed in pharmacopoeias)
 2c1-start-mat-in-ph	
 2c2-start-mat-not-in-ph	(Starting materials not listed in a pharmacopoeia)
 2d-contr-intermed	(Control tests during the manufacturing process)
 2e-tests-fin-prod	(Control tests on the finished product)
 2f-batch-consist	(Batch to batch consistency)
 2g-stab	(Stability tests)
 2h-other-info	(Other information)
 p3	(Part 3 – Safety documentation)
 p3-toc.pdf	(Table of Contents Part 3)
 3a-saf	(Safety tests)
 3a1-ident	(Precise identification of the product and of its active substance(s))
 3a2-pharmacol	(Pharmacology)
 3a3-tox	(Toxicology)
 3a4-other	(Other requirements)
 3a5-ura	(User safety)
 3a6-era	(Environmental risk assessment)
 3b-resid	(Residue tests)
 3b1-ident	(Identification of the product)
 3b2-metab-resid	(Depletion of residues)
 3b3-resid-analyt-met	(Residue analytical method)
 p4	(Part 4 – Efficacy documentation)
 p4-toc.pdf	(Table of Contents Part 4)
 4a-preclin	(Pre-clinical studies)
 4a1-pharmacol	(Pharmacology)
 4a2-resist	(Development of resistance and related risk in animals)
 4a3-dose-determ	(Dose determination and confirmation)
 4a4-tas	(Tolerance in the target animal species)
 4b-clin	(Clinical trials)

TABLE 3: Folder structure and Standard files for an electronic application for an immunological product








































 root-<mydrug>	(Submission-specific root folder - see section 7.(a)0 for naming conventions)
 gtoc.pdf	(General Table of Contents)
 add-info	(Additional information)
 p1	(country code as per Table 10) (Part 1- Summary of the dossier) (Table of Contents Part 1)
 p1-toc.pdf	(Table of Contents Part 1)
 1a-admin-info	(Administrative information)
 1b-spc-pl	(SPC, Labelling and Package Leaflet)
 1c-cers	(Critical expert reports)
 1c1-qual	(Critical expert report on the quality documentation)
 1c2-saf	(Critical expert report on the safety documentation)
 1c3-ffic	(Critical expert report on the efficacy documentation)
 1-responses	(Responses to questions)
 p2	(Part 2 - quality documentation) (Table of Contents Part 2)
 p2-toc.pdf	(Table of Contents Part 2)
 2a-prod-descr	(Product description)
 2b-manuf	(Description of the manufacturing method)
 2c-contr-start-mat	(Production and control of starting materials)
 2c1-start-mat-in-ph	(Starting materials listed in pharmacopoeias)
 2c2-start-mat-not-in-ph	(Starting materials not listed in a pharmacopoeia)
 2d-contr-manuf	(Control tests during the manufacturing process)
 2e-tests-fin-prod	(Control tests on the finished product)
 2f-batch-consist	(Batch-to-batch consistency)
 2g-stab	(Stability tests)
 2h-other-info	(Other information)
 p3	(Part 3 – Safety documentation) (Table of Contents Part 3)
 p3-toc.pdf	(Table of Contents Part 3)
 3a-gen-requ	(General requirements)
 3b-preclin	(Pre-clinical studies)
 3c-clin	(Clinical trials)
 3d-era	(Environmental risk assessment)
 3e-gmo	(Assessment required for VMPs containing or consisting of GMOs)
 p3e-toc.pdf	(Table of Contents Part 3E)
 3e-annexes	(Annexes)
 3f-resid	(Residue tests to be included in the pre-clinical studies)
 p4	(Part 4 – Efficacy documentation) (Table of Contents Part 4)
 p4-toc.pdf	(Table of Contents Part 4)
 4a-gen-requ	(General requirements)
 4b-preclin	(Pre-clinical studies)
 4c-clin	(Clinical trials)

TABLE 4: Folder structure and Standard files for an electronic MRL application




























 root-<mydrugsubstance>	<i>(Submission-specific root folder - see section 7.(a) for naming conventions)</i>
 gtoc.pdf	<i>(General Table of Contents)</i>
 add-info	<i>(Additional information)</i>
 p1	<i>(Part 1 – Administrative data and summary of the dossier)</i>
 p1-toc.pdf	<i>(Table of Contents Part 1)</i>
 1-admin-info-summary	<i>(Administrative information and summary of evaluation proposed by applicant/requestor)</i>
 1-responses	<i>(Response to list of questions)</i>
 p2	<i>(Part 2 – Safety file)</i>
 p2-toc.pdf	<i>(Table of Contents Part 2)</i>
 2a-dacs-saf	<i>(Detailed and Critical Summary (DACS) for safety)</i>
 2b-ident	<i>(Precise identification of the substance concerned by the application)</i>
 2c-pharmacol	<i>(Pharmacology)</i>
 2d-tox	<i>(Toxicology)</i>
 2e-other	<i>(Other effects (immunotoxicity, microbiological properties of residues, observations in humans)</i>
 p3	<i>(Acceptable Daily Intake or alternative limit)</i>
 2f-adi	<i>(Part 3 – Residue file)</i>
 p3-toc.pdf	<i>(Table of Contents Part 3)</i>
 3a-dacs-resid	<i>(Detailed and Critical Summary (DACS) for residues)</i>
 3b-metab-resid	<i>(Metabolism and residue kinetics)</i>
 3c-monit-expos	<i>(Monitoring and exposure data, if relevant)</i>
 3d-resid-analyt-met	<i>(Residue analytical method)</i>
 p4	<i>(Part 4 – Risk management considerations)</i>
 p4-toc.pdf	<i>(Table of Contents Part 4)</i>
 4a-other-factors	<i>(Other legitimate factors)</i>
 4b-other-rm	<i>(Other relevant risk management considerations)</i>
 4c-mrls	<i>(Elaboration of MRLs)</i>
 4d-extrapolation	<i>(Considerations on possible extrapolation of MRLs)</i>

TABLE 5: Folder structure and Standard files for an electronic application for an Active Substance Master File (ASMF) in VNeS
















 root-<mydrug>	<i>(Submission-specific root folder - see section 7.(a) for naming conventions)</i>
 gtoc.pdf	<i>(General Table of Contents)</i>
 add-info	<i>(Additional information)</i>
 p1	<i>(Part 1- Summary of the dossier)</i>
 p1-toc.pdf	<i>(Table of Contents Part 1)</i>
 1a-admin-info	<i>(Administrative information: Letter of access or other administrative documents as applicable)</i>
 1c-cers	<i>(Critical expert reports)</i>
 1c1-qual	<i>(Critical expert report on the quality documentation)</i>
 1-responses	<i>(Responses to questions)</i>
 p2	<i>(Part 2 - Quality documentation)</i>
 p2-toc.pdf	<i>(Table of Contents Part 2)</i>
 2c-contr-start-mat	<i>(Production and control of starting materials)</i>
 2c1-act-sub	<i>(Active substances)</i>
 2f-stab	<i>(Stability tests, if applicable)</i>
 2f1-act-sub	<i>(Active substances)</i>

TABLE 6: Folder structure and Standard files for an electronic application for a Vaccine Antigen Master File (VAMF)



















 root-<mydrug>	<i>(Submission-specific root folder - see section 7.(a) for naming conventions)</i>
 gtoc.pdf	<i>(General Table of Contents)</i>
 add-info	<i>(Additional information)</i>
 p1	<i>(Part 1- Summary of the dossier)</i>
 p1-toc.pdf	<i>(Table of Contents Part 1)</i>
 1a-admin-info	<i>(Administrative information)</i>
 1-responses	<i>(Responses to questions)</i>
 p2	<i>(Part 2 - Quality documentation)</i>
 p2-toc.pdf	<i>(Table of Contents Part 2)</i>
 2a-prod-descr	<i>(Product description)</i>
 2b-manuf	<i>(Description of the manufacturing method)</i>
 2c-contr-start-mat	<i>(Production and control of starting materials)</i>
 2c1-start-mat-in-ph	<i>(Starting materials listed in pharmacopoeias)</i>
 2c2-start-mat-not-in-ph	<i>(Starting materials not listed in a pharmacopoeia)</i>
 2d-contr-manuf	<i>(Control tests during the manufacturing process)</i>
 2f-batch-consist	<i>(Batch-to-batch consistency)</i>
 2g-stab	<i>(Stability)</i>
 2h-other-info	<i>(Other information)</i>

TABLE 7: Example of Folder structure and Standard files for a mixed VNeS / CTD submissions (CTD quality part)

Note: Grey shaded part not subject to technical validation. Not all CTD subfolders are shown.


















































 root-<mydrug>		<i>(Submission-specific root folder - see section 7.(a) for naming conventions)</i>
 gtoc.pdf		<i>(General Table of Contents)</i>
 add-info		<i>(Additional information)</i>
 m2	 cc	<i>(Country code as per Table 10)</i>
	 m2-toc.pdf	<i>(Table of Contents Module 2)</i>
 m3	 23-qos	<i>(Quality Overall Summary)</i>
	 m3-toc.pdf	<i>(Table of Contents Module 3)</i>
	 32-body-data	<i>(Body of Data)</i>
	 32a-app	<i>(Appendices)</i>
	 [...]	<i>[further CTD subfolders]</i>
	 32p-drug-prod	<i>(Drug Product)</i>
	 [...]	<i>[further CTD subfolders]</i>
	 32r-reg-info	<i>(Regional Information)</i>
	 [...]	<i>[further optional CTD subfolders]</i>
	 32s-drug-sub	<i>(Drug Substance)</i>
	 [...]	<i>[further CTD subfolders]</i>
	 33-lit-ref	<i>(Literature References)</i>
	 [...]	<i>[further optional CTD subfolders]</i>
 p1	 p1-toc.pdf	<i>(Table of Contents Part 1)</i>
	 1a-admin-info	<i>(Administrative information)</i>
	 1b-spc-pl	<i>(SPC, Labelling and Package Leaflet)</i>
	 1c-cers	<i>(Critical expert reports)</i>
	 1c2-saf	<i>(Critical expert report on the safety documentation)</i>
	 1c3-effic	<i>(Critical expert report on the efficacy documentation)</i>
	 1-responses	<i>(Responses to questions)</i>
 p3	 p3-toc.pdf	<i>(Table of Contents Part 3)</i>
	 3a-saf	<i>(Safety tests)</i>
	 3a1-ident	<i>(Precise identification of the product and of its active substance(s))</i>
	 3a2-pharmacol	<i>(Pharmacology)</i>
	 3a3-tox	<i>(Toxicology)</i>
	 3a4-other	<i>(Other requirements)</i>
	 3a5-ura	<i>(User safety)</i>
	 3a6-era	<i>(Environmental risk assessment)</i>
	 3b-resid	<i>(Residue tests)</i>
	 3b1-ident	<i>(Identification of the product)</i>
	 3b2-metab-resid	<i>(Depletion of residues)</i>
	 3b3-resid-analyt-met	<i>(Residue analytical method)</i>
 p4		<i>(Part 4 – Efficacy documentation)</i>
	 p4-toc.pdf	<i>(Table of Contents Part 4)</i>
	 4a-preclin	<i>(Pre-clinical studies)</i>
	 4a1-pharmacol	<i>(Pharmacology)</i>
	 4a2-resist	<i>(Development of resistance and related risk in animals)</i>
	 4a3-dose-determ	<i>(Dose determination and confirmation)</i>
	 4a4-tas	<i>(Tolerance in the target animal species)</i>
	 4b-clin	<i>(Clinical trials)</i>

TABLE 8: Example of a folder structure for mixed VNeS / CTD submissions (ASMF applicant's part in CTD, referring to two separate ASMFs)

Note: Grey shaded part not subject to technical validation. Not all subfolders are shown.



















































 root-<mydrug>	(Submission-specific root folder - see section 7.(a) for naming conventions)
 gtoc.pdf	(General Table of Contents)
 add-info	(Additional information)
 cc	(Country code as per Table 10)
 m2-substance1	(CTD Module 2 - CTD Summaries)
 m2-toc.pdf	(Table of Contents Module 2)
 23-qos	(Quality Overall Summary)
 m2-substance2	(CTD Module 2 - CTD Summaries)
 m2-toc.pdf	(Table of Contents Module 2)
 23-qos	(Quality Overall Summary)
 m3-substance1	(CTD Module 3: Quality)
 m3-toc.pdf	(Table of Contents Module 3)
 32-body-data	(Body of Data)
 32s-drug-sub	(Drug Substance)
 [...]	[further CTD subfolders]
 m3-substance2	(CTD Module 3: Quality)
 m3-toc.pdf	(Table of Contents Module 3)
 32-body-data	(Body of Data)
 32s-drug-sub	(Drug Substance)
 [...]	[further CTD subfolders]
 p1	(Part 1- Summary of the dossier)
 p1-toc.pdf	(Table of Contents Part 1)
 1a-admin-info	(Administrative information)
 1b-spc-pl	(SPC, Labelling and Package Leaflet)
 1c-cers	(Critical expert reports)
 1c1-qual	(Critical expert report on the quality documentation)
 1c2-saf	(Critical expert report on the safety documentation)
 1c3-effic	(Critical expert report on the efficacy documentation)
 1-responses	(Responses to questions)
 p2	(Part 2 - Quality documentation)
 p2-toc.pdf	(Table of Contents Part 2)
 2a-prod-descr	(Product description)
 2b-manuf	(Description of the manufacturing method)
 2c-contr-start-mat	(Production and control of starting materials)
 2c1-act-sub	(Active substances – data not covered by ASMF)
 2c2-excip	(Excipients)
 2c3-cont-clos-sys	(Packaging (container-closure systems))
 2c4-bio-origin	(Substances of biological origin)
 2d-contr-intermed	(Control tests carried out on isolated intermediates during the manufacturing process)
 2e-tests-fin-prod	(Control tests on the finished product)
 2f-stab	(Stability tests)
 2f1-act-sub	(Active substances)
 2f2-fin-prod	(Finished product)
 2g-other-info	(Other information)
 p3	(Part 3 – Safety documentation)
 p3-toc.pdf	(Table of Contents Part 3)
 [...]	[further VNeS subfolders]
 p4	(Part 4 – Efficacy documentation)
 p4-toc.pdf	(Table of Contents Part 4)
 [...]	[further VNeS subfolders]

TABLE 9: Folder structure and Standard files for an electronic application for a change in prescription status

Example is given for a pharmaceutical product or a biological product other than immunological. For applications related to an immunological product, corresponding folders should be used (specifically “3b-preclin” for an updated User Risk Assessment).






















 root-<mydrug>	<i>(Submission-specific root folder - see section 7.(a) for naming conventions)</i>
 gtoc.pdf	<i>(General Table of Contents)</i>
 add-info	<i>(Additional information)</i>
 p1	<i>(Country code as per Table 10)</i>
 cc	<i>(Part 1- Summary of the dossier)</i>
 p1-toc.pdf	<i>(Table of Contents Part 1)</i>
 1a-admin-info	<i>(Administrative information: eAF and administrative appendices)</i>
 1b-spc-pl	<i>(SPC, Labelling and Package Leaflet: updated product information)</i>
 1c-cers	<i>(Critical expert reports: include pharmacovigilance documents at this folder level)</i>
 1c2-saf	<i>(Revised / addendum to Critical Expert Report on the safety documentation)</i>
 1c3-effic	<i>(revised / addendum to Critical Expert Report on the efficacy documentation)</i>
 1-responses	<i>(Responses to questions)</i>
 p3	<i>(Part 3 – Safety documentation)</i>
 p3-toc.pdf	<i>(Table of Contents Part 3)</i>
 3a-saf	<i>(Safety tests)</i>
 [...]	<i>[safety studies and literature (subfolder depending on file content)]</i>
 3a5-ura	<i>(Updated User Risk Assessment)</i>
 [...]	<i>[safety studies and literature (subfolder depending on file content)]</i>
 p4	<i>(Part 4 – Efficacy documentation)</i>
 p4-toc.pdf	<i>(Table of Contents Part 4)</i>
 [...]	<i>[pre-/clinical studies and literature (subfolder depending on file content)]</i>

TABLE 10: Recommended country codes for country-specific folders when a file is submitted to only one country

at	Austria
be	Belgium
bg	Bulgaria
cy	Cyprus
cz	Czech Republic
de	Germany
dk	Denmark
ee	Estonia
el	Greece
es	Spain
fi	Finland
fr	France
hr	Croatia
hu	Hungary
ie	Ireland
is	Iceland
it	Italy
li	Liechtenstein
lt	Lithuania
lu	Luxembourg
lv	Latvia
mt	Malta
nl	Netherlands
no	Norway
pl	Poland
pt	Portugal
ro	Romania
se	Sweden
si	Slovenia
sk	Slovakia
xi	United Kingdom (Northern Ireland)