Guideline prepared by the Veterinary Harmonisation Group
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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, an evolution of the former TIGes-Vet Sub 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.

At a meeting in July 2007 the HMA recorded the following decision, "In response to a direct request from industry, HMA confirmed that the requirement for authorities to be in a position to accept electronic only submissions by 2009 applied to veterinary as well as to human applications. It should be understood that the investment of resources by the Industry will also depend on progress made by the authorities." This decision meant that authorities had to be able to accept electronic submissions from 1 January 2010 as well as continuing to deal with submissions based on paper. The work will continue to achieve a harmonised way of electronic working by all NCAs.

The final adopted version of the HMA eSubmission Roadmap was endorsed by the EU Telematics Management Board on the 1st of October 2014, and describes the situation of eSubmission in the European Union at that time and the issues that will be addressed in the near future. The roadmap includes a number of initiatives such as dossier formats, portal solutions and application forms.
An annex to this roadmap describes the requirements that have to be fulfilled in order to use and accomplish the following deliverables:

- VNeeS only for New MAA in DCP and CP by Q1 2016
- VNeeS only for all submissions in EU procedures by Q1 2017

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 (i.e. variations and extensions, PSUR submissions, renewal applications and dossiers for referral procedures).
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.

Comment [VHG1]: CR#-VNeeS-0206

2 Procedures for sending electronic information

There are different ways of submitting electronic dossiers to competent authorities, including portals, Eudralink or hard media (CD/DVD), if accepted by authorities. Normally, only one way should be used, to avoid sending multiple copies of the same submission to the authority.

Competent authorities will not accept any hardware (laptops, desktops, etc.) or software from applicants in connection with the submission of information in an electronic format. The electronic information should be directly readable and usable on the competent authorities' hardware (e.g. CD/DVD drive) and software.

Authorities may require provision of a paper cover letter for electronic submissions via hard media, portals or Eudralink. 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 accompany or 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.

2.(a) Portals

It is strongly recommended to use secure portals for the submission of applications. For submissions to national competent authorities (CP or MRP/DCP), the Common European Submission Platform (CESP) can be used for many types of veterinary submissions and is accepted by many authorities, please refer to the CESP website for further details. The EMA eSubmission Gateway/Web Client may be used only for submissions to the EMA in the Centralised Procedure. For further details see the eSubmission website.

2.(b) Eudralink

Eudralink has a size limit for attached files, refer to the EudraLink User Guide for further details. As it is not recommended to split a VNeeS submission, it is unlikely that an e-submission of a complete dossier can be made by this means. If accepted by the competent authority, Eudralink may be used for email communication with the authorities, for submission of smaller applications and responses, and for the exchange of editable versions of the product information (SPC, label, leaflet). Folder-structured submissions via Eudralink have to be submitted as a zip file. Applicants should ensure that the correct e-mail addresses intended for submission via Eudralink are used. When using Eudralink, it is important that the expiry date is set to an appropriate length to ensure that the message can be opened during the procedure.
In addition, all information relating to the submission must be contained within the zipped submission; no formal information should be included in the body of the Eudralink message. A clear reference to the regulatory procedure should appear in the subject line of the message.

2.(c) Hard media (CD/DVD)

Where electronic files are provided on finalised optical media such as CD or DVD, each hard medium on which the e-submission is presented should include at a minimum the following label information:

- Name of the product,
- type of application,
- procedure number (if known in advance by the applicant),
- name of company,
- target species (if necessary to avoid confusion of products),
- version (including date),
- indication as to whether multiple media components are used (and if so, these should be numbered, e.g. 1/2, 2/2),

The information provided, specifically procedure number and version (including date), should allow at any procedural step a unique identification of the submission, that can be referred to by involved competent authorities.

This information should preferably be printed directly onto the hard media as hand-written or self-adhesive labels may compromise the disc or peel-off in time.

Zipped files should not be used when sending CDs or DVDs.

Applicants should provide the electronic submission on the smallest number of media components possible, e.g. if the VNeeS submission spans several CDs, the provision of a DVD is recommended. If more than one media component is needed, the dossier should be split at a logical point within the granularity such that the integrity of the granularity is maintained. Where possible, individual dossier parts (Part 1, Part 2 etc.) should be kept together and not be split over multiple media components.

Several VNeeS submissions for the same medicinal product may be provided on a single media component.

Grouped variations or variations submitted in a worksharing procedure should preferably be submitted on the same media component.

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 ~~will be considered~~ by the veterinary equivalent (VICH).

Comment [VHG2]: CR#-VNeeS-0198

Comment [VHG3]: CR#-VNeeS-0198

The PDF format used for a VNeeS-compliant submission should follow the specifications defined in VICH Guideline 53: Electronic exchange of documents: electronic file format. ~~be legible with Acrobat Reader, version 5.0 or higher. Files should have been created and saved as version PDF 1.4, 1.5, 1.6, or 1.7. No PDF documents should be in version PDF 1.3 or earlier.~~

~~To ensure that PDF files can be accessed efficiently, PDF files should preferably be no larger than 100 MB.~~

Comment [VHG4]: CR#-VNeeS-0198

Product information (SPC, label, leaflet) should be submitted in addition to a PDF file in an editable format like Microsoft Word, normally on the same CD/DVD.

5 Requirements for creating PDF files for electronic submission

~~5.(a) Paper source documents~~

~~PDF documents submitted as scans should be scanned at resolutions that will ensure the pages are legible both on the computer screen and when printed. Not less than 300 dpi gives good results~~

~~without compromising file size for text; higher resolution may be required for graphics. Applicants should ensure that the quality of the renditions is adequate for regulatory review.~~

Comment [VHG5]: CR#-VNeeS-0199

~~5.(b)~~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 detailed and critical summaries, 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.

~~**Fonts for electronic source documents**~~

~~Font point sizes should ensure on-screen readability, for example 11-12 for normal text, 9-10 for tables and 8-10 for footnotes. The recommended font colour is black. The recommended fonts are Arial (11) and Times New Roman (12). Blue font colour can be used for hypertext links.~~

~~Every font used for visible text in the PDF files should be embedded to ensure that those fonts would always be available to the reviewer.~~

~~**Page format and numbering for electronic source documents**~~

~~The print area for pages should fit on ISO 216:2007 A4 sheet of paper with sufficient margins with the exception of the mock-ups for packaging components which may require other formats. Pages should be properly oriented to reduce the effort of rotating pages. Pages within a file should be numbered.~~

Comment [VHG6]: CR#-VNeeS-0199

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 Notice to Applicants Volume 6B as amended by Directive 2009/9/EC[1] (Annex I to Directive 2001/82/EC 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 VNeeS folder structure is shown in Table 1 for pharmaceutical products and Table 2 for immunological products and should be used where applicable to prepare any electronic submission, except for small post-authorisation submissions containing not more than the electronic Application Form (eAF) and a single ("concatenated") PDF file for the documentation to be submitted (see section 7.(f)).

Comment [VHG7]: CR#-VNeeS-0203

Root folder

The name of the top level folder ("root folder") of each VNeeS folder structure should allow appropriate identification of the submission, especially in cases where more than one VNeeS structure is located on a single hard medium.

For reasons of automated identification and technical validation of e-submissions with tools like the VNeeS checker[2] 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), especially if more than one procedure is included on the same CD, and /or
- the submission date or day of procedure, to allow tracking of updates during the procedure

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

[1] ~~The folder structure and naming convention has of necessity been prepared before the publication of the final revised Volume 6B on Presentation and Content of the Dossier based on the new Annex to Directive 2001/82/EC. The folder structure and naming of folders may need revision after publication of Volume 6B.~~

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

questions) document; although not mandatory, some NCAs might also wish to receive other documents such as the “detailed and critical summaries” 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 4.

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 VNeeS 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 repeat-use 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 VNeeS folders corresponding to the relevant veterinary NtA dossier chapters.

Adaptation of folder structure

Where the structure defined in Table 1 to Table 3 applies, including additional folders within the structure of the e-submission is not permitted, with the exception of 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 VNeeS structure defined in this guidance is applicable follow exactly the conventions given in Table 1 for pharmaceutical products, Table 2 for immunological products and Table 3 for MRL applications.

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 and Table 2 for immunological products.

If publicly announced by the competent authority, 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 using the format for Non-eCTD electronic Submissions (NeeS) for human medicinal products for Module 3 or, where Quality Overall Summaries

are reused, Module 2 of the CTD. In this case, a correlation table should be provided showing which CTD chapter corresponds to which veterinary NtA chapter. An overview of CTD format acceptance by Member States is published by the CMDv under Frequently asked questions (Question 123).

Within such a mixed NtA- and CTD- structured VNeeS 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 NeeS / 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 VNeeS root directory. They should contain module-specific TOC files which are named following the NeeS naming conventions, i.e. "m2-toc.pdf" or "m3-toc.pdf" respectively. The GTOC should be hyperlinked to the module-specific TOCs.

Comment [VHG8]: CR#-VNeeS-0195

Only the NeeS / eCTD folder structure may be used, mixed VNeeS / 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.

Comment [VHG9]: CR#-VNeeS-0197

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

Summary reports (obligatory Detailed and Critical Summaries or DACS) should be saved into p1, and the textual summaries are optional (see Table 3).

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 VNeeS 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 VNeeS 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 3. The response submission

is a stand-alone submission; it is thus not required to send an update of the initial VNeeS 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 VNeeS 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 VNeeS folders are:

- 1a-admin-info: Letter of access or other administrative documents as applicable
- 1c1-qual: Detailed and critical summary document
- 2c1-act-sub
- 2f1-act-sub (if applicable)

If agreed by the competent authority, the master file holder may also optionally submit the ASMF within a CTD folder structure, e.g. using the NeeS or eCTD format. In this case, a correlation table should be provided showing which CTD chapter corresponds to which veterinary NtA chapter. An overview of CTD format acceptance by Member States is published by the CMDv under Frequently asked questions (Question 123).

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 on the same CD/DVD as 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 NtA- and CTD-structured VNeeS (see chapter 7(b)). In case 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 variable component followed by a hyphen and a variable folder name component, e.g. "m3-substance1" and "m3-substance2".

Comment [VHG10]: CR#-VNeeS-0196

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 and Table 2 in this guidance, and clearly named for identification, in particular if more than one ASMF is used.

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

Variations / Extensions

In case of submissions with a small number of documents, e.g. type IA variations, the documentation provided in addition to the electronic application form (eAF)[3] may be presented as a single ("concatenated") bookmarked PDF file (typically not more than 50 pages or 10 merged documents).

In case of submissions containing more than the eAF plus a single concatenated PDF file, all files should be assigned, wherever possible, to the relevant folder as specified in Table 1 and Table 2, e.g.

[3] It is technically not possible to merge the eAF with another PDF file.

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) may be used in case the documentation is completely identical for all products. If these submissions are product specific, one submission structure per product should be provided. The same rationale applies for small submission where instead of a folder structure only a single concatenated PDF file and the eAF are provided.

Renewals

For renewal applications all files should be assigned to the relevant VNeeS folders as specified in Table 1 and Table 2:

- 1a-admin-info: renewal application form including all annexes, declaration of TSE status,
- 1b-spc-pl: SPC, labelling and package leaflet,
- 1c1-dacs: pharmacovigilance documents (PSUR, bridging report),
- 1c1-dacs\effic: efficacy expert statement,
- 1c1-dacs\qual: quality expert statement including attachments,
- 1c1-dacs\saf: safety expert statement.

Empty folders in the submission should be deleted so that the structure reflects only what actually is submitted.

Other post authorisation submissions

For other post authorisation submissions such as PSUR submissions, or 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.(g) 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.
If more than one media component is needed (e.g. several DVDs), TOCs must be provided. In this case, the GTOC should be present only on the first hard medium; part-specific TOCs must be available on the media component where the files covering that part of the dossier are located.

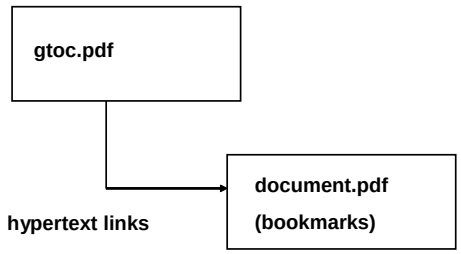
In case of very small submissions consisting of only the eAF and a single concatenated PDF file, no separate GTOC or TOC files need to be created.

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.

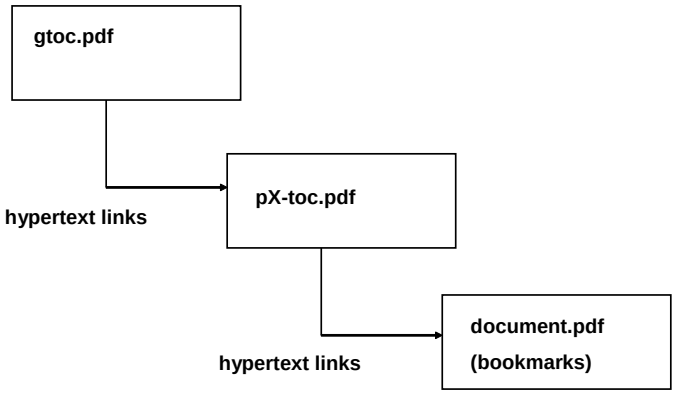
Hyperlinks should only be made to documents within the same VNeeS submission and not to external sources.

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 VNeeS 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 VNeeS 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 the Annex I to Directive 2001/82/EC, 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.(h) Files

Size and number

~~The number of files should reflect the size of the dossier. Individual files should not be larger than 100 MB.~~

Comment [VHG11]: CR#-VNeeS-0200

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, 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).

Comment [VHG12]: CR#-VNeeS-0200

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 3.
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-dacs-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 ~~is~~ large~~r than 100 MB,~~ then the files should be numbered as “1ofx”, “2ofx” for example:

Comment [VHG13]: CR#-VNeeS-0200

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.

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. detailed and critical summaries, 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 VNeeS submission.
Especially in case of submissions consisting of only the eAF and a single concatenated PDF file, without separate GTOC or TOC files, or single PDF files containing several references, bookmarks should be included for efficient navigation.

8 Security

It is not permitted to apply password protection to either the media carrying the files or the files themselves. As with paper dossiers, 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.

~~It has to be recognised that some documents, such as references taken from journals and other publications, may not be able to be stripped of all security settings (e.g. preventing the copying of text from the article) without violating copyright rules. These files must then be exempt from a validation criterion regarding security settings.~~

Comment [VHG14]: CR#-VNeeS-0201

9 Technical validation

In order to be accepted as valid, an electronic VNeeS 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). Such replacement submissions can be requested for all types of submissions including Type IA notifications that fail to comply with VNeeS technical validation criteria.
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.

VNeeS submissions can be checked against the technical validation criteria using for instance the VNeeS checker tool. The VNeeS 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 VNeeS submission, applicants should technically validate it with a validation tool and can use the VNeeS 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 VNeeS folder structure is selected (i.e. for pharmaceutical products, immunological products or MRL applications).

10 Glossary

CD: "Compact Disc"; an optical disc that contains data accessible by a computer.

dpi: dot per inch; measure of printing resolution (number of individual dots of ink a printer or toner can produce within a linear one-inch (2.54 cm) space).

DVD: "Digital Versatile Disc" or "Digital Video Disc"; optical disc storage media format that can be used for data storage, with a capacity 8 times higher (single layer, single sided) than the CD.

eAF: electronic Application Form

ERA: Environmental risk assessment

EUDRALINK: system designed to enable files to be sent securely over the Internet via a user-friendly Web interface, available to the EMA, Member State competent authorities, Industrial Pharmaceutical Companies, Members of Working Parties / Committees and Experts.

GMO: Genetically modified organism

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

Hard medium: Any type of physical media used for storage and transfer of electronic data (e.g. optical media like CDs or DVDs) in contrast to a purely electronic transfer e.g. via Eudralink or any web portal.

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

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SmPC/SPC: Summary of Product Characteristic

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

URA: User risk assessment

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

VNeeS: Veterinary NeeS (the name being inspired by the established NeeS standard for Human medicinal products), an electronic application prepared using standard software and which follows the structure set out in Table 1 to Table 3.

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)*
cc	*(Country code as per Table 4))*
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-dacs	*(Detailed and Critical Summaries (DACS))*
1c1-qual	*(DACS on the quality documentation)*
1c2-saf-resid	*(DACS on the safety and residues documentation)*
1c3-effic	*(DACS on the efficacy documentation)*
1-responses	*(Responses to questions)*
p2	*(Part 2 - quality documentation)*
p2-toc.pdf	*(Table of Contents Part 2)*
2a-qual-quant-partic	*(Qualitative and quantitative particulars of the constituents)*
2b-manuf	*(Description of the manufacturing method)*
2c-contr-start-mat	*(Control of starting materials)*
2c1-act-sub	*(Active substances)*
2c2-excip	*(Excipients)*
2c3-cont-clos-sys	*(Container-closure systems)*
2c4-bio-origin	*(Substances of biological origin)*
2d-contr-intermed	*(Control tests carried out at intermediate stages of the production process)*
2e-tests-fin-prod	*(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 and residues tests)*
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	*(Precise identification of the product concerned by the application)*
3b2-metab-resid	*(Metabolism and residue kinetics)*
3b3-resid-analyt-met	*(Residue analytical method)*
p4	*(Part 4 – Pre-clinical and clinical trials)*
p4-toc.pdf	*(Table of Contents Part 4)*
4a-preclin	*(Pre-clinical trials)*
4a1-pharmacol	*(Pharmacology)*
4a2-resist	*(Development of resistance)*
4a3-tas	*(Tolerance in the target animal species)*
4b-clin	*(Clinical trials)*

TABLE 2: Folder structure and Standard files for an electronic application for an immunological product[4]

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 4)*
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-dacs	*(Detailed and Critical Summaries (DACS))*
1c1-qual	*(DACS on the quality documentation)*
1c2-saf	*(DACS on the safety documentation)*
1c3-effic	*(DACS on the efficacy documentation)*
1-responses	*(Responses to questions)*
p2	*(Part 2 - quality documentation)*
p2-toc.pdf	*(Table of Contents Part 2)*
2a-qual-quant-partic	*(Qualitative and quantitative particulars of the constituents)*
2b-manuf	*(Description of the manufacturing method)*
2c-prod-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 tests)*
p3-toc.pdf	*(Table of Contents Part 3)*
3a-gen-requ	*(General requirements)*
3b-lab-tests	*(Laboratory tests)*
3c-field-stud	*(Field studies)*
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)*
p4	*(Part 4 – Efficacy tests)*
p4-toc.pdf	*(Table of Contents Part 4)*
4a-gen-requ	*(General requirements)*
4b-lab-trials	*(Laboratory trials)*
4c-field-trials	*(Field trials)*

[4] Immunological dossiers may also be presented with two additional folders in the root directory (LEVEL 1), named "p5" and "p6".

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

root-<mydrugsubstance>	*(Submission-specific root folder - see section 7.(a) for naming conventions)*
gtoc.pdf	*(General Table of Contents)*
add-info	*(Additional information)*
p1	*(Part 1 – Administrative data and summary of the dossier)*
p1-toc.pdf	*(Table of Contents Part 1)*
1a-admin-info	*(Administrative information)*
1b-dacs	*(Detailed and Critical Summaries (DACS))*
1b1-dacs-saf	*(DACS on safety documentation)*
1b2-dacs-resid	*(DACS on residues documentation)*
1-responses	*(Response to list of questions)*
p2	*(Part 2 – Safety file)*
p2-toc.pdf	*(Table of Contents Part 2)*
2a-sum-saf	*(Summary of safety documentation (optional))*
2b-ident	*(Precise identification of the substance concerned by the application)*
2c-pharmacol	*(Pharmacology)*
2d-tox	*(Toxicology)*
2e-other	*(Other effects (immunotoxicity, microbiological properties of residues, observations in humans)*
2f-adi	*(Acceptable Daily Intake or alternative limit)*
p3	*(Part 3 – Residue file)*
p3-toc.pdf	*(Table of Contents Part 3)*
3a-sum-resid	*(Summary of residues documentation (optional))*
3b-ident	*(Precise identification of the substance concerned by the application)*
3c-metab-resid	*(Metabolism and residue kinetics)*
3d-monit-expos	*(Monitoring and exposure data, if relevant and available)*
3e-resid-analyt-met	*(Residue analytical method)*

TABLE 4: 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
uk	United Kingdom