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eSubmission Requirements for Veterinary Medicinal Products and Practical Solutions

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ITEMS

- **The new guideline in Europe**
  - History
  - Current status
- Practical approaches
- Future plans

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The eSubmission guideline in Europe

TIGes Vet Group (Telematics Implementation Group)

- Vet Sub Group for the implementation of eSubmissions for Veterinary Medicinal Products
- Established in 27th July 2006
- Participants: EMA, NCA and Interested Parties (AVC, EGGVP, IFAH Europe)
- Meets 4 x per Year
- Change Control Group (CCG) founded in early 2011 to prepare and propose further changes (react fast on requests and prepare decisions for TIGes Vet Group)

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TIGes Vet Group and CCG

•Guideline Version 1.0
developed within 1 year, published Jan 2008

• **First** Revision of Guideline (**Version 1.0** Rev.1)
published Oct 2009

• **Second** Revision of Guideline (**Version 2.0**)
adopted Feb 2011; published;
came into effect **01 Sep 2011** (6 months term)

•Next update with minor adaptations to be expected soon (**Version 2.1**)

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Objectives

• **Not** follow the approach of Human side

• **V**eterinary **n**on-**e**CTD **eS**ubmission (VneeS)

• Objectives being:

•Keep it easy

•Without sophisticated software packages

• Keep NtA structure

• Get significant benefit from working electronically for both, industry and regulatory authorities

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The guideline - Overview

Media and general requirements

- Media: CD Rom, DVD, Eudralink limited to **80MB** (Zip!)
- Appropriate label: name of product, type of application, procedure number, company, target species, version, numbering if applicable
- Language: English
- If official signature required, signed cover letter or application form may suffice (dependent on NCA)
- Each file <100 MB
- If >1 medium, split at logical point of granularity to maintain integrity

The guideline - Overview

File Format and Source

- Compatible with PDF1.4. No pdf in version <1.3
- Legible with Adobe Reader 5.0 or higher, allowing for text searching, copy & paste.
- Electronic Source: convert directly to .pdf, no scan! Provide separately, if needed
- Paper Source : if needed scan at resolution 300 dpi
- Submission of editable format docs for SPC, leaflet, label in separate folder

The guideline - Overview

- **Paper Format and Fonts**
  - ISO 216:2007 **A4** with sufficient margins
  - Common standard fonts (Arial 11, Times New Roman 12, font colour black, blue font for hyperlinks)
  - Use only characters ‚a' to ‚z', ‚0' to ‚9' and ‚-' as file name
  - Don't use capital letters , SPACE or special characters such as

, . : / \ * ? „ " < > | &

  - Pages to be numbered within a file
  - Pages properly oriented to avoid rotating etc.

The guideline - Overview

- SPC, label, leaflet should be supplied in addtion in editable format, clear identification of purpose, included in separate folder at level of root folder. Clarify purpose, if submitting same docs in different formats.
- Signatures: ensure proper certification of submitted docs. Valid signatures must be present at applicant, presented on request.
- Signed paper cover letter confirming the corrrectness of the submitted file(s) (check with NCA) should suffice with most NCAs

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Requirements – new in Version 2.0

Folder Structure for initial MAA

- Follow Guideline
  - Table 1 (Pharmaceuticals),
  - Table 2 (Immunologicals),
  - Table 3 (MRL)
- Maximum 3 levels of granularity
- Follows NtA Vol 6B, but also additional root folder for editable files; currently difference for VIMP: 4/6 parts
- This structure must be followed: you may delete folders, if not relevant, but you may not create new folders at top hierarchy (included in TOC)

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Requirements – new in Version 2.0

Submission Structure for updates during assessment phase

- Use different root folder names for initial submission and subsequent amendments

→ Include submission date or day of procedure

- Use consistent file naming conventions in subsequent submissions
- But: logical differences in names can be helpful for comparative purposes

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Requirements – new in Version 2.0

Validation updates

•VneeS Checker provided by B/F agencies, available for both, industry and NCAs, checking the pdfs, not the structure (16 items, see http://esubmission.emea.europa.eu/doc/esub%20folder/E-submission%20-%20validation%20checklist-Ver1.0-Feb2011.pdf)

- If invalid in technical validation process → re-create/submit a corr. version of the full appl.
- If invalid in content validation → check with relevant authority if submission of single files or updated VNeeS submission

•GTOC/TOC builder provided by B/F agencies

Requirements – new in Version 2.0

Responses to questions

- Is a stand-alone submission
- No need to send an update of a consolidated initial VNeeS submission
- May consist of actual text of responses as well as amendments to initial dossier
- File main response document in folder “responses” in part 1
- File additional documents in the relevant folders

Requirements – new in Version 2.0

Folder Structure for Active Substance Master File

Restricted part:

- 1a-administrative-information
- 1c1-quality
- 2c1-active-substances
- 2f1-active-substances

CTD folder structure may be allowed after agreement with relevant authority (also initiative by VICH Quality Working party)

Applicant’s part:

- To be provided on the same CD/DVD as restricted part
- Either as separate folder structured as above
- or incorporated with files using suffix “rp” and “ap” in the file name

Requirements – new in Version 2.0

Variations/ Extensions

Small submissions

- as single bookmarked pdf file

Larger submissions

- More than one pdf file
- Assigned to the relevant folder as specified in the Guideline Tables 1-3, if applicable
- Delete empty folders

Grouped variations or worksharing procedures

- One single file or a single submission structure if documentation is completely identical for all products
- Otherwise one file per product or one submission structure per product

Requirements – new in Version 2.0

Other post authorisation submissions

PSUR submissions, Renewals, Dossiers for referral procedures

→ Applicant should use any appropriate folder structure that facilitates the review

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- **Practical approaches**
- Future plans

Practical approaches

Equipment

- ✓ Windows Explorer to create folder structure
- ✓ Software to create editable docs (e.g. Word)
- ✓ Software to create suitable pdfs (e.g. Acrobat)
- ✓ Recommended: large screen or two screens for efficient work
- ✓ Use relevant versions of TOC Builder and Vnees Checker

Practical approaches

How to create suitable files for eSubmission:

- Try some suitable file names and decide on an internal convention for naming of all relevant documents
- Work with templates of documents (e.g. Word) to assure correct format/features of such documents (e.g. fonts, index, paginating, bookmarks, copy&paste, searchable)
- Make sure that external writers are aware of the requirements

Practical approaches

How to create suitable files for eSubmission:

- Requirements for electronic files are different from paper version
- Everyone creating documents for submission is involved, not only Reg Aff department
- Creating suitable eSubmission files starts with creating a suitable MS-Word-Document

Practical approaches

Software:

- Requirements are relatively easy to implement using current software (e.g. Explorer, MS Word, Adobe Acrobat), although special expertise may help to implement specific requirements
- Vendor solutions available, hopefully soon one adapted to veterinary medicine

Practical considerations

The change to eSubmission:

- Some NCAs produce already enormous pressure on industry to submit electronically
- There is the point of no (difficult) return (per product): If you start to submit electronically, further submissions for this product need to be electronically.

⇨ Therefore plan well before submitting electronically

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- **Future plans**

Future plans

HMA roadmap 2011-2015 to have eSubmission only

Therefore Objective:

- Development of stable, simple, cost effective system
  - Gain experience
  - Harmonise and adapt for practical needs
  - Adapt NtA and VneeS structures
  - Keep up to date with further developments

Future plans: Readiness of NCAs

http://www.hma.eu/uploads/media/Vet_sector_-_electronic_only_readiness_2011-for_publication_rev__6.pdf

Future plans

TIGes Roadmap 2011-16 currently drafted:

- Headed by regulators, supported by industry
- Support applicants in using it to facilitate implementation
- Provide tools (e.g. VneeS checker and TOC Builder)
- Harmonisation of requirements, adaptation of guideline where needed (6 months advance notice)
- Major update of guideline to be announced 2 years in advance (to allow for Software adaptation)
- Electronic Application Form (eAF) currently developed
- Central portal/eSignature (eID: www.eid-stork.eu)

Summary

- Guideline on the specifications for provisions of an electronic submission (eSubmission) for VMP in place
- Version 2.0 in place and to be used from 1SEP11, Version 2.1 to be published soon
- Adapt source documents to allow to fulfill specifications
- If change to eSubmission, no return to paper
- TOC builder and Vnees Checker useful tools (free)
- Objective of HMA to change completely to eSubmission
- If questions, ask CCG/TIGes Vet Group via IFAH, EGGVP or AVC or us

References

eSubmission Guideline

Validation Checklist

Template for folder structure

'http://esubmission.emea.europa.eu/tiges/vetesub.htm'

VNees Checker 2.0 Validation Tool for free download

available on website of Belgian Agency FAGG-AFMPS and French Agency ANMV

http://www.fagg-afmps.be/en/veterinary_use/medicines/medicines/MA_procedures/esubmission/ '
http://www.anmv.anses.fr/en_anmv/vneeschecker/info.asp

VNeeS Toc Builder for free download

http://users.telenet.be/neestool/

Thank you: Questions …

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