Guideline for eSubmission for veterinary medicinal products

Version 1.2

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Federal **A**gency for **M**edicines and **H**ealth **P**roducts
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1. Introduction

In July 2007 the HMA decided that from 01/01/2010 all the national competent authorities (NCA) responsible for the evaluation of applications for marketing authorization for medicines for veterinary had to be able to accept electronic dossier submissions (hereafter called esubmissions).

Nowadays almost all pre- and post-marketing submissions for veterinary medicinal products (VMPs) received by the famhp are submitted in an electronic format, and electronic submission may be mandatory in some EU member states.

The national competent authorities wrote in 2013 an European esubmission roadmap with mandatory VNeeS for new marketing authorisation applications submitted via the centralized procedure(CP) and the decentralized procedure (DCP) by 2016 Q1 and mandatory VNeeS for all procedures by 2017 Q1. The EU esubmission roadmap was presented to HMA in Toledo at the 22nd and 23rd of May 2014 and endorsed. The EU roadmap also foresees mandatory use of the electronic application form (eAF) by 2016 Q1 for all procedures.

Since high quality esubmissions have a lot of advantages for both the applicant and the NCA(s), the famhp tries to facilitate the processing of the applications submitted in correct electronic format.

On European level, the Veterinary Harmonisation Group (VHG) published a guideline on the specifications for provision of an electronic submission for a veterinary medicinal product (http://esubmission.ema.europa.eu/tiges/vetesub.htm). Despite all actions undertaken at national and European level to facilitate the esubmissions a huge variability in the quality of the esubmissions by different applicants is still observed.

The famhp madethe e-submission for pre- and post-authorisation procedures for veterinary medicinal products mandatory from **01/01/2013** onwards. This obligation is applicable on all types of applications related to marketing authorisations for VMPs made in the Mutual Recognition (MRP), Decentralised (DCP) and National procedures (NP) including new applications for marketing authorisation (and also updates provided during the assessment phase, validation corrections and responses to questions) of pre and post-authorisation submissions (variations and extensions, renewal applications and fulfilment of commitments). E-submission is not mandatory but strongly recommended for active substance master files (ASMF) and dossiers submitted for clinical trial applications, medical devices and parallel import applications.

. The VHG published a new version, v2.3 of the VNeeS Guideline, validation criteria and tools, to go into force from October 1st 2015. Applicants are strongly encouraged to provide the validation report in the working documents folder of the submission dossier. New is the concept of pass & fail criteria and best practice criteria. When a dossier fulfils all pass & fail criteria, the validation tool lists the technically valid conclusion on the report. The best practice criteria anticipate the

approved VICH GL 53, the electronic file format (EFF), but as such are currently no reason for rejected. The main raison for the pass & fail criteria and consequently the 'technically valid conclusion' is to work in a harmonised way in Europe. For DCP/MRP procedures, it is foreseen that the validation by the RMS is decisive in Europe and that the CMS use the validation conclusion of the RMS. Applicants are strongly encouraged to submit only technically valid procedures.

In order to assist the applicants with the submission in electronic format and to reduce the variability in the quality of these submissions, a national guidance document for the e-submission was developed by the famhp. To help applicants, an empty folder structure is available (http://www.fagg-afmps.be/nl/DIERGENEESKUNDIG_gebruik/geneesmiddelen/geneesmiddelen/procedures_VHB/esubmission/).

In this view too, the famhp and the ANSES (Agence Nationale de Sécurité Sanitaire – France) worked together to develop a technical validation tool , the "VNeeS Checker", which was released in 2010. This tool can be downloaded free of charge from the website of ANSES and famhp (http://www.fagg-afmps.be/nl/DIERGENEESKUNDIG_gebruik/geneesmiddelen/geneesmiddelen/procedures_VHB/esubmission/).

The applicant is fully responsible for the correctness and completeness of the submitted file within any type of e-dossier submitted to the famhp.

2. Communication channels for eSubmission:

The following communication channels will be allowed for submitting electronic dossiers to the FAHMP:

Dossier size	Communication channels
≤ 5 MB	e-mail, Eudralink, CD-ROM/DVD, CESP
>5 Mb ≤200 MB	Eudralink, CD-ROM/DVD, CESP
> 200 MB	CESP

Starting from the First of July 2013 the famhp encourages to use CESP (Common European Submission platform) for all new applications for marketing authorisation applications.

The use of CESP permits the MAH to submit a dossier in one simple submission. The use of CESP is mandatory if it's not possible to submit a dossier in one simple submission by means of e-mail, Eudralink, CD-ROM or DVD.

No parallel submission channels will be allowed, applicants need to choose one of the options listed in the table above.

Compressed files

Folder-structured submissions that are sent via e-mail/Eudralink/CESP need to be compressed. Cesp only accepts zipped submissions. This provides an extra security check. When the applicants zips, a checksum is incorporated in the zip. When the NCA unzips the submission, the unzip software will recalculate the checksum and verify wioth the checksum inside the zip. When these are identical, one concludes that the digital transfert, from applicant to NCA went without any communication errors and that the transfert is complete.

Signatures:

on the cover letter:

Each submitted dossier needs to be foreseen of a handwritten signature (signed and printed/scanned cover letter) when submitted by mail/Eudralink/CD-ROM/DVD/CESP.

On the application form:

A signature on the application form is required for all dossiers. The type of signature on the application form (qualified, embedded, scanned) is open and will not lead to a rejection of the file.

A. submissions by CESP

CESP (Common European Submission Platform) is an electronic platform allowing companies to submit applications relating to veterinary medicinal products following the national procedure, MRP, DCP and CP concerning medicinal products in a safe, quick and simple way.

CESP can be approached via http://cesp.hma.eu. On the website all practical information (e.g. FAQs, trainingsvideos) can be found, and a user account can be created,

A “self-service model for user management” has been selected. This means that any company can assign it’s own “company administrator”, who will manage and maintain the user accounts for the other employees within that company.

In order to start the registration of the “company administrator”, a form is to be completed via the Registration-link on the website.

Questions concerning the registration, the technical set-up and the connection can be handled via cesp@hma.eu.

The type of applications that can be submitted via veterinary CESP to the famhp are the following:

- Initial Marketing Authorisation Application
- Variation Type IA
- Variation Type IB
- Variation Type II
- Extension application
- Renewal application
- Transfer of a marketing authorisation

- National variations
- Authorisation for temporary use

If you ticked a regulatory activity which does not appear in the list here above, the CESP submission will not be accepted by the famhp. In that case you will receive an email (via a noreply address) explaining that you need to re-submit the concerned dossier if you wishes to continue that submission.
For each of the accepted regulatory activities, one has to indicate the subtype (initial, answer to question during validation, during procedure, closing documents) , if applicable. This allows the famhp to dispatch automatically all subtypes to the proper staff.

famhp

In order to guarantee a correct and efficient transfer of your dossier, the famhp advices you to limit the size of the dossier to 2 GB. If this seems not possible, please contact the concerned division.

Be sure that the submission is transferred First, followed by the delivery form (xml), and not the other way around! You always need to transfer one dossier at a time followed by it's delivery file (xml), before starting the transfer of the second submission. Moreover, once the CESP mail for the first submission is received, delete all files on the CESP file directory (the one on the CESP server), before initiating the transfer of the second submission.

Currently, when applicants use for the CP the EMA gateway, they also have to send the submission to the NCA. For this submission, Cesp is highly recommended.

B. E-mail

For NP, DCP, MRP dossier submission, as well as any type of correspondence related to the dossiers (for example national translations of the SPC, labelling and leaflet submitted in the closing phase), emails up to a size of 5,00 MB will be allowed. Please compress the file(s) using the zip format.

The general e-mail addresses for electronic dossier submission are:

For all new applications for marketing authorisations (MA), line extensions and repeat use procedures: pre.authorisation.v@fagg-afmps.be

For all variations, renewals: post.authorisation.v@fagg-afmps.be

These e-mail addresses are not applicable for the submission of Periodic Safety Update Reports (PSURs) irrespective from a renewal application. The general e-mail address for electronic PSUR submission is: psurv@fagg-afmps.be.

Following rules concerning the e-mail format must be respected:

1. The **mail subject** should read: (all fields should be separated by "-")
    1. type of procedure (MRP, DCP, NP – grouping, WS (worksharing), MRP-like)
    2. type of documents : initial (initial application), ATQ (answers to questions), closing (documents for national closing phase)
    3. the (proposed) name of the VMP in Belgium
    4. dossier ID (except for initial applications for national MA[1])

examples of mail subject
MRP-ATQ-Wonderpil-BE/V/1234/001/II/002
NP-initial-Newdrug

2. The following information should be stated on top of the **body of the mail :**
    1. type of procedure (MRP, DCP, NP – grouping, WS (worksharing), MRP-like)
    2. type of documents : initial (initial application), ATQ (answers to questions), closing (documents for national closing phase)
    3. Type of dossier (type IA, IB, II anv (analytical type II variation), II clv (clinical type II variation), II phvig (update DDPS), REN (renewal), NA (new authorisation), EXT (extension), RUP (Repeat Use Procedure)

[1] This national procedure number will be available at time of receipt of the dossier only

4. The (proposed) name of the medicinal product in Belgium + pharmaceutical form and (proposed) target species
5. dossier ID (except for initial applications for national MA)
6. Pharmacotherapeutic group the product belongs to (IVMP, antibiotic, NSAID, antiparasitic, other)

example:

MRP-grouping

Closing

Variation IB, variation IA

Wonderpil1

BE/V/1234/001/IB/002- BE/V/1234/001/IA/003

NSAID

3. The content of the cover letter should be copied in the body of the mail.

4. Folder-structured submissions that are sent via e-mail/Eudralink need to be compressed. Only compressed files in ZIP format will be accepted.

5. Do not use any password protection

C. EUDRALINK:

NP, DCP, MRP dossiers as well as any type of correspondence related to the dossiers can be submitted by using Eudralink.

Eudralink should not be used for submissions without attachments.

This solution is a secure solution and allows to submit larger files (up to 200 MB).

Dispatch the EudraLink to following e-mail address:

For all new applications for marketing authorisations (MA), line extensions and repeat use procedures: pre.authorisation.v@fagg-afmps.be

For all variations, renewals: post.authorisation.v@fagg-afmps.be

These e-mail addresses are not applicable for the submission of Periodic Safety Update Reports (PSURs) not submitted as a part of a renewal. The general e-mail address for electronic PSUR submission is: psurv@fagg-afmps.be.

Attachments sent by Eudralink should be submitted in one single compressed file ("zipped").Always use the **90 day** expiry date, do not use password protection!

Following rules concerning the Eurdralink format must be respected:

1. The **Eudralink subject** should read: (all fields should be separated by "-")
    1. type of procedure (MRP, DCP, NP – grouping, WS (worksharing), MRP-like)
    2. type of documents : initial (initial application), ATQ (answers to questions), closing (documents for national closing phase)
    3. the (proposed) name of the VMP in Belgium
    4. dossier ID (except for initial applications for national MA[1])

2. The following information should be stated on top of the **body of the Eudralink :**
    1. type of procedure (MRP, DCP, NP – grouping, WS (worksharing), MRP-like)
    2. type of documents : initial (initial application), ATQ (answers to questions), closing (documents for national closing phase)
    3. Type of dossier (type IA, IB, II anv (analytical type II variation), II clv (clinical type II variation), II phvig (update DDPS), REN (renewal), NA (new authorisation), EXT (extension), RUP (Repeat Use Procedure)

4. The (proposed) name of the medicinal product in Belgium + pharmaceutical form and (proposed) target species
5. dossier ID (except for initial applications for national MA)
6. Pharmacotherapeutic group the product belongs to (IVMP, antibiotic, NSAID, antiparasitic, other)

3. The content of the cover letter should be copied in the body of the Eudralink message. The Eudralink information in the body of the message must match the information in the cover letter. When there are differences, the information in the cover letter takes precedent.

4. Folder-structured submissions that are sent via e-mail/Eudralink need to be compressed. only compressed files in ZIP format will be accepted.

5. Do not use any password protection

D. CD-ROM/DVD:

When the size of the dossier exceeds 5.00 Mb and is lower than 200 MB submission via mail is not supported, but Eudralink is still an option. When the size of the electronic dossier exceeds the size of 200 MB, the applicant needs to submit the dossier on a CD-ROM or DVD which needs to be shipped to the famhp (for DVDs all standards are accepted).

Please use following correspondence address:

Federal Agency for Medicines and Health Products

DG Pre Authorisation

Veterinary Division

Eurostation II

Place Victor Horta 40/40

1060 Brussels

Belgium

Pay attention to the following:

1. Please provide the signed cover letter, shipped along with the CD-ROM/DVD. Mention the number of media components included in the package.

2. Do not use any password protection. In line with the 'Guideline on the specifications for provision of an electronic submission for a veterinary medicinal Product' of the VHG, 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.

3. Do not send parts of dossiers by email/Eudralink and parts on CD-ROM/DVD.

The CD-ROM/DVD should be presented with at a minimum the following label information:

1. type of procedure (MRP, DCP, NP – grouping, WS (worksharing), MRP-like)
2. type of documents : initial (initial application), ATQ (answers to questions), closing (documents for VMP in Belgium)
3. the (proposed) name of the VMP in Belgium
4. dossier ID (except for initial applications for national MA[1])

The CD-ROM/DVD box should be presented with at a minimum the following information:

1. type of procedure (MRP, DCP, NP – grouping, WS (worksharing), MRP-like)
2. type of documents : initial (initial application), ATQ (answers to questions), closing (documents for national closing phase)
3. Type of dossier (type IA, IB, II anv (analytical type II variation), II clv (clinical type II variation), II phvig (update DDPS), REN (renewal), NA (new [2]authorisation), EXT (extension), RUP (Repeat Use Procedure)
4. The (proposed) name of the medicinal product in Belgium + pharmaceutical form and (proposed) target species
5. dossier ID (except for initial applications for national MA)
6. Pharmacotherapeutic group the product belongs to (IVMP, antibiotic, NSAID, antiparasitic, other)

[1] This national procedure number will be available at time of receipt of the dossier only

3. Acceptable file formats & structure for e-Submission

The VHG published a guideline on the specifications for provision of an electronic submission for a veterinary medicinal product (http://esubmission.ema.europa.eu/tiges/vetesub.htm). Esubmissions submitted to the famhp should be fully compliant with the validation criteria.

FAMHP**If one of the mandatory criteria scores is not obtained for your dossier and the conclusion of the validation tool is 'technically invalid', the dossier may be rejected. In that case, the dossier needs to be resubmitted to the famhp. From 1/10/2015 onwards, an administrative fee will be charged in the case of a technical invalidation**.

4. Technical validation

The VHG has developed a technical validation checklist with the common set of criteria a VNeeS submission has to comply with in order to be "valid". This checklist is published on the EU veterinary eSubmission website : http://esubmission.ema.europa.eu/tiges/vetesub.htm.

Based on this checklist the famhp and the ANSES worked together to develop a technical validation tool , the "VNeeS Checker". This tool can be downloaded free of charge from the website of ANSES and famhp:
http://www.fagg-afmps.be/en/veterinary_use/medicines/medicines/MA_procedures/esubmission/

The "VNeeS Checker" verifies in the compliance of a MA dossier based on respect of a set of pass & fail and best practice criteria defined in the European guideline.
The tool is straightforward to install and to use, allowing with a few clicks to define the technical quality of a dossier and to produce a report that can be instantly displayed and saved as an HTML file. A light version is also available on the website of the famhp. This light version can be downloaded on an external device.

The use of a checker before submission will be mandatory from 1/7/2013 on. By using a checker before submission, the applicant can anticipate on a technical invalidation of the dossier.

The validation report generated by the VNeeS checker should be placed in the folder "add-info" of the folder structure.

5. Glossary

Please find below a list of abbreviations and key words used in this Guidelines document:

Key word or abbreviation	Explanation or definition
AMM	Autorisation de Mise sur le Marché (national Marketing autorisation document)
ANSES	Agence Nationale de Sécurité Sanitaire – France
CESP	Common European Submission Platform
CVMP	Committee on Veterinary Medicinal Products of the EMA
CTD	Common Technical Document (Document standard developed by ICH and supported by EMA)
DCP	Decentralised Procedure
eCTD	The electronic CTD
eAF	Electronic application form
EFF	VICH Guideline 53, the electronic file format (EFF)
EMA	European Medicines Agency (www.ema.europa.eu)
EUDRALINK	System developed by EMA for secure electronic transfer of files
FAMHP	Federal Agency for Medicines and Health Products
GTOC	General Table Of Contents
HMA	Head of Medicines Agencies
IVMP	Immunological Veterinary Medicinal Product
MRP	Mutual Recognition Procedure
NCA	National Competent Authority
VNeeS	Veterinary Non-eCTD electronic Submission
NP	National Procedure
PDF	Portable Document Format
PIL	Patient Information Leaflet
PSUR	Periodic Safety Update Report
RUP	Repeat Use Procedure
SPC	Summary of Products Characteristics
TIGes	Telematic Implementation Group
TOC	Table Of Content
VICH	The International Conference on Harmonisation of Technical Requirements for Registration of Veterinary Products is a unique project that brings together the

	regulatory authorities of Europe, Japan and the United States and experts from the pharmaceutical industry in the three regions to discuss scientific and technical aspects of product registration.
VHG	Veterinary Harmonisation Group
VMP	Veterinary Medicinal Product
WS	Worksharing

6. Document History

Date	Author	Version	Comments
12/12/2012	Dries Minne,	1.0	First version for publication
01/07/2013	Dries Minne	1.1	Inclusion of CESP
01/06/2015	Pieter Vankeerberghen	1.2	Adaptation to version 2.3 VNeeS guideline

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