July 2020
EMA/377885/2015-Rev.2
Veterinary Medicines Division

Validation checklist for initial MAA – pharmaceuticals (applicable to submissions under Article 12(3) of Directive 2001/82)

1. Background on the product

(Invented) Name and procedure number: **INN or common name:**

Indication applied for:

This validation checklist is used by the Agency to validate initial marketing authorisation applications for pharmaceuticals and applicants should use it as a means to review in advance of their submission that standard requirements are fulfilled.

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For the below table, please fill out by referring to the application form one line for each presentation per strength and form. Check consistency with the SPC. This is aimed at having the correct count for the fees.

Pharmaceutical Form (2.2.1 in AF)	**Strength (2.2.1 in AF)**	**Content (concentration) (2.2.1 in AF)**	**Package size (2.2.3 in AF)**
The pharmaceutical form is expressed in accordance with standard terms of the EDQM https://standardterms.edqm.eu/ (user name and password needed, request them from the library/information centre)	*Check that calculation is based on INN, i.e. the base and not the salt/ester etc. The expression of the dosage form is in accordance with http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2010/01/WC500056428.pdf In case of liquid, single/partial use is important for expression of strength --> check section 4.9 of SPC (summary of product characteristics)*	*Mostly for liquids only*	

2. **Summary of Flags to PM** (For internal use only)

3. Background documentation:

Topic	Document
User guide for the electronic application form for a marketing authorisation (veterinary)	http://www.hma.eu/fileadmin/dateien/Veterinary_medicines/CMDv_Website/Procedural_guidance/General_info_on_applications/eSubmission/User_Guide_for_the_electronic_application_form_for_a_marketing_version_3.pdf
Notice To Applicant volume 6B Part 1	https://ec.europa.eu/health/documents/eudralex/vol-6/
EDQM database of TSE/chemical certificates (CEPs)	https://extranet.edqm.eu/publications/recherches_CEP.shtml
In case of doubts regarding a submitted proof of establishment, contact VROS	
Veterinary e-submission guidelines	http://esubmission.ema.europa.eu/tiges/vetesub.htm
Link to the European Pharmacopoeia	http://online.pheur.org/EN/entry.htm
Guideline on Active Substance Master File Procedure	http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000059.jsp&mid=WC0b01ac058002d9ad http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2012/07/WC500129994.pdf
COMMISSION REGULATION (EU) No 37/2010 of 22 December 2009 on pharmacologically active substances and their classification regarding maximum residue limits in foodstuffs of animal origin	http://ec.europa.eu/health/files/mrl/mrl_20101212_consol.pdf
ATCvet codes	https://www.whocc.no/atcvet/atcvet_index/
EDQM standard terms: (It is used to check the dosage form (=pharmaceutical form) and route of administration.)	https://standardterms.edqm.eu/
Process for handling new standard term requests received from applicants in the pre-submission phase (or from other sources, also during any procedure):	If a new term (e.g. pharmaceutical form or unit of measurement) or a request for an update of an already existing term is needed in order to complete the eAF, a request should be submitted through the SPOR Portal - http://spor.ema.europa.eu/rmswi/#/ providing as much supporting documentation as possible (e.g. name of the product concerned, SPC, etc).

Topic	Document
EUTCT: to check the target species	http://eutct.ema.europa.eu/eutct/showAvailableListsDisplay.do?guestuser=true
Ph. Eur.: if the applicant declares that the reference for a substance (active substance or excipient) is the Ph. Eur. , there is a need to check that they use the name in the Ph. Eur and not any other equivalent name.	
ASMF templates for letter of access and submission letter:	https://www.ema.europa.eu/documents/template-form/template-active-substance-master-file-procedure_en.doc

4. Checklist

Definitions:

VSI: Validation Supplementary Information. Information that will be requested by the Agency to the applicant during the validation period and that should be resolved before the start of the procedure, if not indicated otherwise.

Blocking issue: An issue that has been identified during the validation period and that should be resolved before the start of the procedure, otherwise it would prevent validation of the application.

Part 1a: Application Form ***Please ensure that all details given in the application form on product and applicant (incl. address) are consistent throughout the document*** **GENERAL CONSIDERATIONS**		
Has correct version of **Application Form** been used?	Select	*From July 2015, use of the e-application form is mandatory. Check first page of application form against the) latest version. If not request relevant missing/changed parts; suspend validation of these parts until update received: Alternatively, the applicant can provide the correct version of the AF within responses to validation issues plus missing documents.*
Product (Invented) Name: Has submitted name been agreed with the CVMP/Invented Name Check? Is the name the same as indicated in section 2.1.1 and in the Product information.	Select Select	*The invented name should be agreed by CVMP prior submission. However, this is not a validation issue if name not agreed yet. Note: although it is recommended that the invented name is written with the first letter in upper case and the rest as lower cases, it is ultimately the choice of the applicant/ MAH (either upper or lower case), as long as it is written in a consistent format throughout the PI and is consistent with how the invented name will appear on the printed artwork.* *Reference: Compilation of QRD Decisions on stylistic matters – https://www.ema.europa.eu/en/documents/re*

Part 1a: Application Form *Please ensure that all details given in the application form on product and applicant (incl. address) are consistent throughout the document* GENERAL CONSIDERATIONS		
		gulatory-procedural-guideline/compilation-quality-review-documents-decisions-stylistic-matters-product-information_en.pdf
Cover letter:	Select	*For electronic submissions via EMA eSubmission Gateway or Web Client, no hard-copy cover letter is required.*
Declaration on manufacturing sites (attachment to the cover letter) where the applicant confirms that: • The detailed information in relation to the manufacturing sites contained in Part 2/Module 3, is correct in terms of names, addresses and manufacturing activities, and • This information is consistent throughout the dossier, in particular with the corresponding information contained in Part 1 (electronic Application Form, flow-chart in Annex 5.8, QP declaration in Annex 5.19, GMP certificates in Annex 5.9, MIAs or MIAs equivalents in Annex 5.6).	Select	

Part 1a: Application Form *Please ensure that all details given in the application form on product and applicant (incl. address) are consistent throughout the document*		
Cover page: Is the person authorised to communicate on behalf of the applicant the same as indicated in formatted table and in section 2.4.2 of the application form and is a **letter of authorisation** attached for this person (Annex 5.4)?	Select	*If not, or letter not provided/not correct, request corrected application form/letter.*
Cover page: Is **signatory** on behalf of the applicant either CEO of company, member of management board etc. or a person authorised to communicate on behalf of the applicant, i.e. the designated person as indicated above?	Select	*In case person is different from above ('person authorised to communicate on behalf'.*

Part 1a: Application Form ***Please ensure that all details given in the application form on product and applicant (incl. address) are consistent throughout the document***		
1.1 Eligibility ticked as agreed by CVMP and date correct?	Select	
1.3 Legal basis:	Select	
1.3.7 Article 13c - Informed consent application • The scope of the application is the same as the reference product. • If informed consent is ticked as the legal basis for the application, information on the reference medicinal product is given below (Product invented name, pharmaceutical form(s), strength(s, Marketing authorisation holder, MA Number(s) and Date of authorisation). • Annex 5.2 is ticked in the eAF and the letter of consent from marketing authorisation holder of the authorised (parent) product is attached in Part 1a. • Complete administrative data is provided in the application (including SPC and mock-ups).	Select Select Select Select Select	*If informed consent is not ticked as the legal basis, select N/A.* *Only a complete administrative data must be provided in the application, with consent to use the pharmaceutical, safety, (pre-clinical) and clinical data of the reference product given by the parent MA holder. In this case, there is no need to submit quality, safety and efficacy detailed and critical summaries.* *If the parent product belongs to the same MAH (so called "self-informed" consent), the letter of consent must still be provided - it is not correct when the applicant justifies that this is not applicable.*
1.4 MRL status: Has the applicant provided information for the active substance(s) (pharmaceutical products) or the adjuvant (immunological products)	Select	*Only to be completed when the target species is/are (a) food-producing animal(s) (check target species in section 2.1.4 of the AF).* *For pharmaceutical products information on the active substance(s) has to be included.* *Information can be provided either in the field:* *- "Maximum Residue Limits (MRLS) according to Commission Regulation (EU) No. 37/2010" when the MRL has been established by the European Commission or;* *- "Application for a Maximum Residue Limit has been made to the EMA" when the MRL application has been submitted however MRL(s) has not yet been established.* *Additional substances (excipients) may have been declared on the application form, however are not checked at validation.*
1.4 MRL status: Is the information concerning established MRLs and/or	Select	*There must be an MRL status for each target*

Part 1a: Application Form *Please ensure that all details given in the application form on product and applicant (incl. address) are consistent throughout the document*		
submitted MRL applications correct?		*species (e.g. bovine, porcine, all mammalian species, all food producing species) and/or relevant food commodity (milk, eggs, honey). E.g. if target species is dairy cattle, an MRL for milk is applicable; if target species is laying hens, an MRL for eggs is applicable.*
1.5 Additional requests for consideration: Has the applicant provided documents in support of their request for exceptional circumstances, or market protection or data exclusivity?	Select	
1.5.2 Has **accelerated review** been granted?	Select	*If not ticked, select 'N/a'.*
2.1.3 ATCvet code and pharmacotherapeutic group	Select	*Check correctness on the following link: http://www.whocc.no/atcvet/atcvet_index/ The pharmacotherapeutic group would usually be the 4th group. It is not the name of the substance. Example: Substance: mesulfene ATCvet code: QP53AA01 Pharmacotherapeutic group: Sulfur-containing products. It would be acceptable if both 3rd and 4th groups are stated: ectoparasiticides for topical use incl. insecticides, sulphur-containing products. If an ATC vet code is published by the WHO, but it is not used in the application, a justification should be provided.*
2.1.4 Target species	Select	*Should be in line with product information. If a new target species or a request for an update is needed in order to complete the eAF, a request should be submitted through the SPOR Portal – http://spor.ema.europa.eu/rmswi/#/ providing as much supporting documentation as possible (e.g. name of the product concerned, SPC, etc).*

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2.2.2 Route of administration: In line with Standard Terms?	Select	*Check against standard terms (EDQM). If a new term (e.g. pharmaceutical form or unit of measurement) or a request for an update of an already existing term is needed in order to complete the eAF, a request should be submitted through the SPOR Portal – http://spor.ema.europa.eu/rmswi/#/ providing as much supporting documentation as possible (e.g. name of the product concerned, SPC, etc).*
2.2.3 Container, closure and administration device(s) Are information provided in line with Part 2 and Product Information? Annex 5.17 is ticked in the eAF.	Select	*The container should be selected from the List of Standard Terms published by the EDQM.* *The Annex 5.17 should contain short description (names) of mock-ups or samples / specimens sent or provided with the application.*
2.3 Legal status: Has the applicant proposed a legal status for its medicinal product?	Select	*Applicant to propose i.e.* *- non-prescription* *- restricted* *- special*
2.4.1 Proposed MAH: Is the name and address (if mentioned in the proof of establishment (PoE)) of the proposed MAH exactly the same as in the PoE?	Select	*Annex 5.3 has to be provided and the details should be exactly the same as in section 2.4.1 as far as they are given in the PoE. Ignore section for national/decentralised applicant (should be kept unticked/empty).*
Annex 5.3: Proof of establishment: Does the Annex 5.3 duly establish the applicant as being in the EEA?	Select	*Should not be older than 6 months but can be in any language as long as EN translation is provided.*
2.4.1 Proposed MAH: Is a person identified at the MAH address (for centralised procedure)?	Select	*It can be that the email address is a generic email address. In that case it should be confirmed with the company (can be in the cover letter) that it is a dedicated email address which will reach the allocated person 24h/day.* *If section 2.4.2 is filled in, a personal email address should be included.*

Part 1a: Application Form *Please ensure that all details given in the application form on product and applicant (incl. address) are consistent throughout the document*		
2.4.1 **SME status:** If yes is ticked, is the Qualification as SME in Annex 5.21 still valid? Information provided in the application are the same in Annex 5.21 and in the formatted table.	Select	
2.4.4 **Qualified person for PhV** Is the CV of the qualified person attached in Annex 5.20.	Select	*Name, Address, Telephone number, personalized email address should be included.* *It might be that the email address is in a format such as EUQppv@company.com but in that case it should be confirmed with the company that it is a dedicated email address which will reach the QPPV24h/day.* *If CV of qualified person is missing(no Annex 5.5 nor inclusion in Annex 5.20, issue VSI*
2.5.1.1 Has a person responsible for **product defects and recalls in the EEA** been named along with contact details? (should include at least name / surname, address with postcode and country, 24H tel. # and e-mail address)	Select	*Person has to be located in the EEA.*
2.5.3 **Ph. Eur. Certificate for the active substance(s**) (CEP): If a certificate is claimed to have been issued, has a valid, up-to-date copy been provided in Annex 5.10?	Select	*Check the EDQM certificate database online at https://extranet.edqm.eu/publications/recherches_CEP.shtml* *N.B.: If nothing is ticked, it means that it is not applicable. If Yes is ticked and there is no certificate, then it's a VSI* *Details on CEP-related requirements – please see below in the CEP section at the end of part 2.*
2.5.3 Ph. Eur. Certificate (CEP): If a CEP is used, are the following clearly identified: • Name of the CEP holder • Name of the manufacturer • CEP number • Date of last update	Select	*Check the EDQM certificate database online at https://extranet.edqm.eu/publications/recherches_CEP.shtml* *N.B.: If nothing is ticked, it means that it is not applicable. If Yes is ticked and there is no certificate = VSI* *Check that the CEP and application form are consistent regarding each of the bullet points opposite* *Details on CEP-related requirements – please see below in the CEP section at the end of part 2.*

Part 1a: Application Form *Please ensure that all details given in the application form on product and applicant (incl. address) are consistent throughout the document*		
2.5.3 Active substance master file (ASMF):	Select	*- If the ASMF is not used, select N/A and leave the ASMF-related boxes below blank* *- If presence of the ASMF is indicated in the AF, check if the ASMF from the ASMF holder was provided - If ASMF is indicated and was submitted by the ASFM holder, proceed with the following checks of the application form section 2.5.3 and check of the ASMF itself*
If an ASMF is used, are the following clearly identified in the AF: • Name and address of ASMF holder • Name of manufacturer if different from above • EU ASMF reference number or National (EMEA) ASMF reference number as applicable • Applicant's part version number ASMF submission date and date of last update • The letter of access provided by the ASMF holder to the Applicant should follow the format of Annex 2 of the Guideline on Active Substance Master File Procedure (EMEA/CVMP/134/02) and should be provided in Annex 5.10 of the AF. • Confirmation that changes will be notified (Annex 5.11 provided). It is part of the access letter (Annex 5.10) if the ASMF Guideline template is used. • The ASMF and application form are consistent regarding each of the bullet points above •	Select Select Select Select Select Select Select Select Select	*Name of manufacturer if different from above: Make sure the signature on the letter of access is correct (i.e. if the manufacturer signs ON BEHALF of the ASMF holder, this needs to be appropriately authorised* *Please note that :* *- EU ASMF number: is in place from December 2013. This number is to be allocated if the ASMF assessment worksharing procedure is used. The EU/ASMF/XXXXX will be allocated by PA-BUS (or an NCA, in case of an earlier submission of the ASMF in a national MAA/MAV) upon request by the ASMF Holder, before ASMF submission. The request of the EU ASMF number is not mandatory, but it is mandatory to have EITHER the EU or the National (EMEA) ASMF number.* *- National (EMEA) ASMF number: is in place from 1st September 2013. It is the EMEA number the Agency will allocate to ASMF submitted only centrally and the ASMF assessment worksharing procedure is not used for that ASMF. The EMEA/ASMF/XXXXX will be allocated by PA-BUS upon requested by the ASMF holder, before ASMF submission.* *An ASMF should always be submitted with one of the two (EU or EMEA) numbers.* *Have the letter of access and letter with*

Part 1a: Application Form *Please ensure that all details given in the application form on product and applicant (incl. address) are consistent throughout the document*		
		confirmation regarding notification of any changes been provided (note: can be combined into 1 letter – template of Annex 2)
Further explanations for the validation of the ASMF are below in the checklist at the end of part 2.		
2.6.1 Qualitative and Quantitative composition: Is the information in this section in agreement with the relevant information in Part 2, 2a-qual-quant-partic?	Select	*For liquids, not only concentration per 1 ml needs to be given but also the container size/volume of the product. This can be found either in the AF point 2.2.3 (or 2.2.3.1) or 2.6.1.* *If VSI - Pharmacopoeia terminology should be used.* *This excludes components that are not present in the final dosage form.* *There is no information that can be withheld as confidential in providing a regulatory submission to the Agency. E.g. composition of tablet coating mixtures.*
2.6.1 Qualitative and Quantitative composition: **Cross-check with** in Part 2, 2a-qual-quant-partic Active substance Overages	Select	*Notes:* *- Complete composition to be provided; no information can be confidential – all to be disclosed to the Agency. E.g. for commercially available tablet film-coating mixtures quantitative composition needs to be provided (through confidentiality agreement between the applicant and the mixture manufacturer).* *- For liquids, not only concentration per 1 ml needs to be given but also the container size/volume of the product.* *- Reference to Ph.Eur. for excipients is preferable. If reference to USP/NF or JP is used instead, VSI (but not a blocking issue if not provided with the responses)* *- Overages – extra amount of the active substance or excipients added to compensate for losses*

Part 1a: Application Form *Please ensure that all details given in the application form on product and applicant (incl. address) are consistent throughout the document*		
		during manufacture/storage. Generally discouraged – Overfill should not be stated in the Application Form – if it is = to be removed.
2.6.2 Materials of animal origin Cross-check with Part 2, 2c4-bio-origin.	Select	*All material of animal origin should be stated including reagents in the active substance manufacture.*
2.6.2 TSE certificate: If applicant has ticked and given the number of a Ph. Eur. Certificate of suitability, is it/are they duly annexed in 5.12?	Select	*Information on excipients to be consistent with Part 2, 2c4-bio-origin (TSE table A and table B). TSE tables applicable only for materials of animal origin* *In EDQM database, it is better to search for the Certificate number (Certificate of suitability for TSE)* *Check the EDQM certificate database online at https://extranet.edqm.eu/publications/recherches_CEP.shtml* *Lactose is out of the scope of TSE requirements, as TSE transmission was never confirmed through milk. If Lactose is contained in the product, it never has a Certificate, only statement from the manufacturer (appendix to AF 5.12) that it is sourced in the same way as milk for human consumption. However, the option "animal origin susceptible to TSE" still needs to be ticked in the Application Form.*
4.1 Other MAA (for national applications only)	Select	*This section should be left blank for centralised procedures.*
4.3 Multiple applications: If the company is submitting a duplicate/multiple, has the letter of authorisation from the EC been provided?	Select	*Only possible to validate a multiple application in case a letter from EC, with or without conditions to be fulfilled, is attached.*
Annexes: Mock-ups: Is list of mock-ups attached in Annex 5.17 to the application form?	Select	

General Application Form checks		
Is the information on product name, active substance, strength(s) and pharmaceutical form(s) given consistently (and correct) between cover page of the application form, sections 2.1.1, 2.1.2 and 2.2.1 of the application form and PI?	Select	*If No, request corrected application form and/or PI, as appropriate.*
Confirm Product Shared Mailbox, SIAMED, EURS, DREAM Product Folder are consistent with the Product Name given in the Application Form	Select	*EMA internal process*
Are all Annexes as ticked in section '5- Annexed documents' provided?	Select	*Double check with boxes ticked in the individual sections, too. If an Annex is missing issue VSI*

Part 1 – excluding application form		
1b SPC, Labelling and Package Leaflet: Are they provided in EN for all of the applied for forms/strengths? Is Word version of the PI provided (in folder 'add-info')? Is the correct (QRD) format (latest version) used for the product literature? If combined PL, is the justification present?	Select Select Select Select	*Note: If Word version not provided, not a VSI but necessary to be received by day 1 of the procedure.*
1b. Mock-up: Have the mock-ups been provided?		*Mock-up for PL not needed, only labelling (outer and inner)*
In English	Select	*For validation purposes the Agency requests that all applications for a Marketing Authorisation should include the labelling texts in English, together with one English mock-up and one multi-lingual mock-up ('worst case') of the outer and small immediate packaging for each pharmaceutical form in the smallest pack size.*
'Worst case' (e.g. trilingual pack or 3 x EN)	Select	*Even if 3 x EN is provided as the worst-case example, a separate EN mock-up is required as per the row above because this will be the reference mock-up during the assessment.*

Part 1c – Detailed and critical summary reports		
For new applications, statements justifying absence of data or specific parts/sections should be provided in the relevant detailed and critical summary. In case any of these docs need updating, updated expert signatures in Part 1c have to also be provided or updated docs have to be signed. ***<u>For each report a signature of the expert with date</u>, a CV and a declaration of the professional relationship is necessary. Expert does not need to reside within the EEA. If it is obvious from the CV of the expert that he/she is an employee of the applicant, the declaration of his/her professional relationship can be omitted.***		
1c1 Detailed and critical summary report - Quality: • Has the report been provided, together with: • CV of the expert • Declaration of his/her professional relationship to the applicant?	Select Select Select	
1c2 Detailed and critical summary report - Safety and Residues: • Has the report been provided, together with: • CV of the expert • Declaration of his/her professional relationship to the applicant?	Select Select Select	*Separate reports might be provided for safety, residues (not required for non-food producing species) and ERA.* *Short check if the headings of the main subsections (pharmacology, user safety, ERA and residues (for food-producing species only) are present.*
1c3 Detailed and critical summary report - Efficacy: • Has the report been provided, together with: • CV of the expert • Declaration of his/her professional relationship to the applicant?	Select Select Select	*Short check if headings of the main subsections are present (pre-clinical, including target animal safety and clinical)*

PART 2 (Quality)

The following formats for Part 2 (quality) are accepted for veterinary MAA:

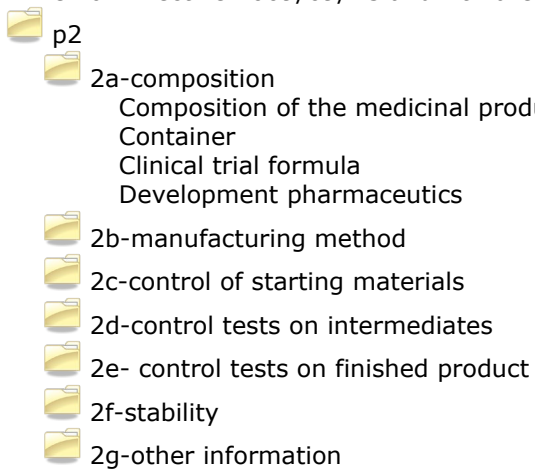
1. According to Annex of Directive 2009/09/EC folder structure: electronic (VNeeS)
2. According to NtA (volume 6B (current version)): electronic (VNeeS)
3. Common Technical document (CTD): electronic (NeeS). Only accepted if previously agreed by the Rapporteurs/CVMP.

Important note: Please check the document "Exceptions to the VNeeS format" for latest information of acceptance of other formats.

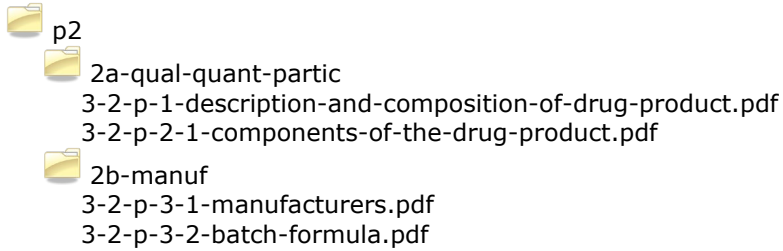
Also note that these formats might be combined and this would be acceptable.

Examples of combined structures:

1. Annex of Directive 2009/09/EC and NtA are mixed:



2. NtA or Annex of Directive 2009/09/EC folder structure but the documents within the folders are provided in CTD format.



Option 1: According to Annex of Directive 2009/09/EC folder structure: electronic (VNeeS)

Part 2 – Quality ***Check for either documents in the appropriate indent or a justification for absence has been provided in the quality overview -> If neither is present => VSI.*** ***The purpose of Part 2 validation is to check presence or absence of documents.***		
Part 2 ToC	Select	*Should be in P2 folder but outside any of the subfolders within P2. (this is also checked by the VNeeS checker)*
2.A. Qualitative and quantitative particulars of the constituents		*It is acceptable not to create one folder per subsection (i.e. 2a1, 2a2, 2a3, 2a4) It can be all included in the same document.* *The information in this section should be consistent with section 2.6.1 of the application form.*
2.A.1. Qualitative particulars	Select	
2.A.2. Usual terminology	Select	
2.A.3. Quantitative particulars	Select	
2.A.4. Development pharmaceutics	Select	
2.B. Description of the manufacturing method	Select	
2.C. Control of starting materials		
2.C.1.1. Active substance(s)	Select	
2.C.1.2. Excipients	Select	
2.C.1.3. Container-closure system	Select	
2.C.1.4. Substances of biological origin	Select	*Tables A, B and C to be included here, if applicable. If there are no substances of animal origin the tables do not need to be included. The information here should be consistent with section 2.6.2 of the application form.*
2.D. Control tests carried out at intermediate stages of the manufacturing process	Select	

Part 2 – Quality *Check for either documents in the appropriate indent or a justification for absence has been provided in the quality overview -> If neither is present => VSI.* ***The purpose of Part 2 validation is to check presence or absence of documents.***		
2.E. Tests on the finished product	Select	
2.F. Stability test		
2.F.1. Active substance(s)	Select	
2.F.2. Finished product	Select	
2.G. Other information	Select	*Can contain information related to the quality of the veterinary medicinal product but not covered in the previous sections.*

Option 2: According to NtA (volume 6B): electronic.

Part 2 – Quality ***Check for either documents in the appropriate indent or a justification for absence has been provided in the quality overview -> If neither is present => VSI.*** ***The purpose of Part 2 validation is to check presence or absence of documents.***		
Part 2 ToC	Select	*Should be in P2 folder but outside any of the subfolders within P2.*
2.A. Qualitative and quantitative particulars of the constituents		*It is acceptable not to create one folder per subsection (i.e. 2a1, 2a2, 2a3, 2a4) It can be all included in the same document.* *The information in this section should be consistent with section 2.6.1 of the application form.*
Composition of the medicinal product	Select	
Container	Select	
Clinical trial formula	Select	
Development pharmaceutics	Select	
2B Description of the manufacturing method		
Manufacturing formula	Select	
Manufacturing process	Select	
Validation of the process	Select	
2C Control of starting materials	Select	
Active substance	Select	
Excipients	Select	
Container closure system	Select	
2D Specific measures concerning the prevention of the transmission of animal spongiform encephalopathies	Select	*Tables A, B and C to be included here, if applicable. If there are no substances of animal origin the tables do not need to be included. The information here should be consistent with section 2.6.2 of the application form.*
2E Control tests on intermediate products	Select	

Part 2 – Quality ***Check for either documents in the appropriate indent or a justification for absence has been provided in the quality overview -> If neither is present => VSI.*** ***The purpose of Part 2 validation is to check presence or absence of documents.***		
2F Control tests of finished product	Select	
2G Stability		
Active substance	Select	
Finished product	Select	
2H Genetically modified organisms	Select	
2Q Other information	Select	

Option 3: According to Common Technical document (CTD) structure

A correlation table indicating the correspondence between CTD sections and NtA or Dir 2009/09 structure should be provided.
If not = VSI

Part 2 – Quality *Check for either documents in the appropriate indent or a justification for absence has been provided in the quality overview -> If neither is present => VSI.* *The purpose of Part 2 validation is to check presence or absence of documents.*		
3.2.S Drug Substance		
3.2.S.1 General Information		
3.2.S.1.1 Nomenclature	Select	
3.2.S.1.2 Structure	Select	
3.2.S.1.3 General properties	Select	
3.2.S.2 Manufacture		
3.2.S.2.1 Manufacturer(s)	Select	
3.2.S.2.2 Description of manufacturing process and process controls	Select	
3.2.S.2.3 Control of materials	Select	
3.2.S.2.4 Controls of critical steps and intermediates	Select	
3.2.S.2.5 Process validation and/or evaluation	Select	*For chemicals, process validation is only applicable to sterile active substances; otherwise N/A.*
3.2.S.2.6 Manufacturing process development	Select	
3.2.S.3 Characterisation		
3.2.S.3.1 Elucidation of structure and other characteristics	Select	
3.2.S.3.2 Impurities	Select	
3.2.S.4 Control of drug substance		
3.2.S.4.1 Specification	Select	
3.2.S.4.2 Analytical procedures	Select	*In 3.2.S.4.2 and 3.2.S.4.3 – for pharmacopoeial methods, reference to Ph.Eur. is sufficient.*

Part 2 – Quality ***Check for either documents in the appropriate indent or a justification for absence has been provided in the quality overview -> If neither is present => VSI.*** ***The purpose of Part 2 validation is to check presence or absence of documents.***		
3.2.S.4.3 Validation of analytical procedures	Select	*Full validation reports of all methods (excluding Ph.Eur. methods) should be provided. Validation summary is not sufficient.*
3.2.S.4.4 Batch analyses	Select	
3.2.S.4.5 Justification of specification	Select	
3.2.S.5 Reference Standards or Materials	Select	*Includes batch results/analysis (table) or certificate of analysis for the reference standard batch*
3.2.S.6 Container Closure System	Select	
3.2.S.7 Stability		
3.2.S.7.1 Stability Summary and Conclusions	Select	
3.2.S.7.2 Post-approval stability protocol	Select	
3.2.S.7.3 Stability data	Select	
3.2.P Drug product		
3.2.P.1 Description and composition of the drug product		*Should be consistent with section 2.6.1 of the Application Form.*
3.2.P.2 Pharmaceutical Development	Select	*Note: it is possible that no subfolders for the sections below can be found. It might be all in one document.*
3.2.P.2.1 Components of the drug product	Select	
3.2.P.2.1.1 Drug substance	Select	
3.2.P.2.1.2 Excipients	Select	
3.2.P.2.2 Drug product	Select	
3.2.P.2.2.1 Formulation developments	Select	
3.2.P.2.2.2 Overages	Select	
3.2.P.2.2.3 Physicochemical & biological properties	Select	

Part 2 – Quality ***Check for either documents in the appropriate indent or a justification for absence has been provided in the quality overview -> If neither is present => VSI.*** ***The purpose of Part 2 validation is to check presence or absence of documents.***		
3.2.P.2.3 Manufacturing process development	Select	
3.2.P.2.4 Container closure system	Select	
3.2.P.2.5 Microbiological attributes	Select	
3.2.P.2.6 Compatibility	Select	
3.2.P.3 Manufacture		
3.2.P.3.1 Manufacturer(s)	Select	
3.2.P.3.2 Batch formula	Select	
3.2.P.3.3 Description of Manufacturing Process and Process Controls	Select	
3.2.P.3.4 Controls of critical steps and intermediates	Select	
3.2.P.3.5 Process validation and / or evaluation	Select	*Either process validation is described or reference is made to Module 3.2.R, where validation scheme is provided.*
3.2.P.4 Control of excipients		
3.2.P.4.1 Specifications	Select	*Reference to the Ph.Eur. is sufficient. If an excipient is tested according to Ph.Eur., modules 3.2.P.4.2, 3.2.P.4.3 and 3.2.P.4.4 are N/A.*
3.2.P.4.2 Analytical procedures	Select	
3.2.P.4.3 Validation of analytical procedures	Select	
3.2.P.4.4 Justification of specifications	Select	
3.2.P.4.5 Excipients of human or animal origin	Select	*Should be consistent with consistent with 2.6.2 of the AF and Mod. 3.2.P.4.5*
3.2.P.4.6 Novel excipients	Select	
3.2.P.5 Control of drug product		
3.2.P.5.1 Specification(s)	Select	
3.2.P.5.2 Analytical procedures	Select	*In 3.2.P.5.2 and 3.2.P.5.3 – for pharmacopoeial methods, reference to Ph.Eur. is sufficient.*

Part 2 – Quality ***Check for either documents in the appropriate indent or a justification for absence has been provided in the quality overview -> If neither is present => VSI.*** ***The purpose of Part 2 validation is to check presence or absence of documents.***		
3.2.P.5.3 Validation of Analytical Procedures	Select	*Full validation reports of all methods (excluding Ph.Eur. methods) should be provided. Validation summary is not sufficient.*
3.2.P.5.4 Batch analyses	Select	*If there are more strengths of the product (same dosage form), batch analysis results should be presented for each strength. If any strength is missing – VSI*
3.2.P.5.5 Characterisation of impurities	Select	
3.2.P.5.6 Justification of specification(s)	Select	
3.2.P.6 Reference Standards or Materials	Select	*Reference to module 3.2.S.5 is sufficient.*
3.2.P.7 Container Closure System	Select	
3.2.P.8 Stability		
3.2.P.8.1 Summary and conclusion	Select	*Shelf-life should be proposed in 3.2.P.8.1, including in-use shelf-life (after dilution, reconstitution or first opening), if applicable. Storage conditions need to be defined. The shelf-life should be the same in Module 3.2.P.8.1 and Application Form 2.2.3.*
3.2.P.8.2 Post-approval protocol and stability commitment	Select	
3.2.P.8.3 Stability data	Select	
3.2.A Appendices		
3.2.A.1 Facilities and Equipment	Select	*Only applicable to biologicals. No check required for Pharmaceuticals Applications.*
3.2.A.2 Adventitious Agents Safety Evaluation	Select	*In most cases only applicable to biologicals. If there are materials with TSE risk, information will be included here as well (identical to 3.2.P.4.5 and 3.2.R – TSE tables).*
3.2.A.3 Excipients	Select	

Part 2 – Quality ***Check for either documents in the appropriate indent or a justification for absence has been provided in the quality overview -> If neither is present => VSI.*** ***The purpose of Part 2 validation is to check presence or absence of documents.***		
3.2.R Regional information (for EU) Process validation scheme for the drug product Medical device information Certificate(s) of suitability (CEPs) Table A (materials of animal origin - TSE) Table B (other material of animal origin) Table C (albumin and other human tissue derived materials)	Select	*Process validation: if included in 3.2.P.3.5 only, it's acceptable.* *TSE tables A, B, C – to be filled in if any materials of human/animal origin were used – consistent with 2.6.2 of the AF and Mod. 3.2.P.4.5.* *Lactose should be in table B.* *If no such materials were used, the tables don't have to be included.*

ASMF	Select	*When ASMF procedure is not used, complete active substance information is in Part 2 or Module 3, as applicable.* *– If the ASMF is not used, select N/A and leave the ASMF-related boxes below blank* *– Presence of the ASMF is indicated in the AF 2.5.3. If the ASMF option is ticked but the ASMF is missing (not submitted) = VSI and blocking issue.* *– Applicant's part in the ASMF submission must be the same (incl. version and date) as the Applicant's part submitted by the applicant in the dossier for the product.*
To be provided by the ASMF holder: • ASMF dossier (Applicant's part, Restricted part, Quality Overall Summary (if CTD format) or Detailed and Critical Summary (if NtA or Dir 2009/09 format), and Expert's *curriculum vitae*); • Applicant's Part and Restricted Part are clearly identified in all documents forming part of the ASMF data, by splitting the documents into Open/closed subfolders (AP/RP folders) • Letter of Access (Annex 2 of the Guideline on Active Substance Master File Procedure (EMEA/CVMP/134/02)); • Submission Letter and Administrative Details (Annex 3 of the Guideline on Active Substance Master File Procedure (EMEA/CVMP/134/02)) is	Select Select Select Select	*Note: the EMEA/ASMF/xxxxx or EU/ASMF/xxxx reference number should be included in the following documents:* *• Letter of Access (Annex 2 of the ASMF Guideline);* *• Submission Letter and Administrative Details (Annex 3 of the ASMF Guideline) – no section should be deleted, if a section is not applicable, it should be left blank.* *If not included = VSI*

provided and contains all sections as in the template; • A commitment to inform the applicant and the EMA of any change in the ASMF to be provided either as a separate letter or within the Letter of Access (Annex 2 of the ASMF Guideline). • The ASMF follows either the VNeeS (NtA or Dir 2009/09) structure or CTD (human Common Technical Document) structure	Select Select	*Check the version history in section 4 of Submission Letter – does it make sense (i.e. are they submitting the latest version)? Procedure numbers in section 4 should be actual procedures (eg, variations if applicable), not just product numbers.* *The technical structure of the ASMF must follow either VNeeS or CTD format as per the latest Guideline on eSubmission for Veterinary products*
To be provided by the Applicant: • Copy of the Letter of Access (Annex 2 of the ASMF Guideline); • Copy of the complete current version of the Applicant's Part of the ASMF or its revised sections, as applicable, in the relevant part of the dossier; • The Applicant's Part of the Applicant is identical to the Applicant's Part of the ASMF holder (check it's the same version and the same cover page details) • Copy of the commitment from the ASMF holder to inform the applicant and the EMA of any change in the ASMF to be provided either as a separate letter or within the Letter of Access (Annex 2 of the ASMF Guideline).	Select Select Select Select	*Letter of Access to be included in annex 5.10 of the application form.* *Commitment from ASMF holder to be included in annex 5.11 of the application form if it's not part of the Letter of Access.* *Note: the EMEA/ASMF/xxxxx or EU/ASMF/xxxx reference number should be included in the following documents:* *• MAA application form (in the field of the National ASMF reference number or EU ASMF reference Number as appropriate) or variation application form (in the Present and Proposed field);* *• Letter of Access (Annex 2 of the ASMF Guideline).* *If not included = VSI*
ASMF – Restricted Part (RP) contents		*The ASMF contains commercially confidential information not disclosed to the applicant. If some of the sections are missing in the ASMF but are present in the dossier for the MAA (Applicant Part (AP)) (the ASMF holder does not consider it confidential), it is fine – the information must be at least in one place in the dossier (i.e. MAA + ASMF).*

		In the MAA (Applicant's part), either limited information or only reference to the Restricted Part (RP) is made for the contents of the sections below. Both options are fine. *If any confidential information is missing, separate VSI to ASMF holder will be sent.* *For different versions of the AP (between ASMF and MAA) or any part (as whole) missing – VSI to the applicant as normal.* *If CTD, a correlation table indicating the correspondence between CTD sections and NtA or Dir 2009/09 structure should be provided by the ASMF holder. If not = VSI*
3.2.S.2.2 Description of Manufacturing Process and Process controls (if CTD) Within part 2C1 if NtA or Dir 2009/09	Select	*A brief description of the manufacturing process might be included in the applicant's part.*
3.2.S.2.3 Control of materials Within part 2C1 if NtA or Dir 2009/09	Select	
3.2.S.2.4 Control of critical steps and intermediates Within part 2C1 if NtA or Dir 2009/09	Select	
3.2.S.2.5 Process validation and/or Evaluation Within part 2C1 if NtA or Dir 2009/09	Select	*Only applicable for sterile products*
3.2.S.2.6 Manufacturing Process Development Within part 2C1 if NtA or Dir 2009/09	Select	
Following documents present either in the RP or in the AP of the dossier		*Note: It is mandatory to have them at least in one part of the dossier (restricted or open), otherwise = VSI*
3.2.S.3.2 Impurities Within part 2C1 if NtA or Dir 2009/09	Select	
3.2.S.4.5 Justification of specifications Within part 2C1 if NtA or Dir 2009/09	Select	

CEP – certificate of suitability of the European Pharmacopoeia FOR THE ACTIVE SUBSTANCE (chemical and microbiological quality)	Select	*Information on the active substance can be in some cases replaced by a CEP for the active substance. This certificate guarantees quality of the active substance as the Ph.Eur. quality.*
Location of the CEP in the dossier	Select	*Annex 5.10 and one of the following:* *Part 2C1: control of starting materials (active substance). If NtA or Annex of Directive 2009/09 formats used.* *3.2.S: if CTD.* *Reference to Annex 5.10 within the dossier sections above is also acceptable.* *Note: if CEP is used annex 5.11 of the application form should be provided.*
Validity of the CEP	Select	*- Check the EDQM database here for validity of the CEP: https://extranet.edqm.eu/publications/recherches_CEP.shtml* *- Check version number (consistent with the EDQM database)*
Content of the CEP:		
Additional methods/limits	Select	*Additional limits/methods (e.g. additional impurities, residual solvents) – description appended to the CEP. These are presented in the form of annexes and should be appended to the CEP. The CEP gives the information on how many lines the CEP has and how many annexes (if any) and how many pages each of these annexes have.*
Re-test period	Select	*Mentioned in CEP – no action* *Not mentioned – stability data of the active substance must be submitted:* • *Part 2f1 (if Dir 2009/09 structure)* • *Part 2g (if NtA)* • *modules 3.2.S.7.1, 3.2.S.7.2 and 3.2.S.7.3 (if CTD)*
Declaration of access	Select	*It should be completed and signed and/or stamped by the CEP holder.*
Parts of Part 2 or Module 3.2.S not covered by a CEP	Select	• *Manufacturers: to be provided in:* *2c1, if NtA or Dir 2009/9 structure* *3.2.S.2.1, if CTD.*

		• *Nomenclature:* *If CTD: 3.2.S.1.1 – Nomenclature* *Reference to CEP in the above-mentioned cases is not sufficient* *Note: CEPs issued on and after 15 July 2013 information on the manufacturers (quality control/in process testing sites, intermediate manufacturers, milling and sterilisation sites) will be appended to the granted CEP.* *For CEPs granted before 15 July 2013, this information will not be appended to the CEP and should be included in Part 2 or Module 3.2.S.2.1, as applicable.*

Part 3 – Safety and Residues ***Check that documents/cross-reference/justification for absence have been provided in the appropriate indent -> If none present => VSI.***		
Part 3A Safety		
Table of contents present, clearly indicating cross-references to part 4 (if applicable)	Select	
1 Precise identification of the product and of its active substances	Select	
2 Pharmacology		
2.1 Pharmacodynamics	Select	
2.2. Pharmacokinetics	Select	
3 Toxicology		
3.1 Single-Dose Toxicity	Select	
3.2 Repeat-Dose Toxicity	Select	
3.3 Tolerance in the target species	Select	
3.4 Reproductive toxicity including teratogenicity	Select	

Part 3 – Safety and Residues *Check that documents/cross-reference/justification for absence have been provided in the appropriate indent -> If none present => VSI.*		
3.4.1. Study of the effects on reproduction	Select	
3.4.2. Study of developmental toxicity	Select	
3.5 Genotoxicity	Select	
3.6 Carcinogenicity	Select	
3.7. Exceptions	Select	
4 Other requirements	Select	*For antibiotics, lack of this section is a validation issue.*
5 User safety	Select	
6 Environmental risk assessment		
6.1. Environmental risk assessment of veterinary medicinal products not containing or consisting of genetically modified organisms	Select	
6.2. Environmental risk assessment for veterinary medicinal products containing or consisting of genetically modified organisms	Select	*Only applicable to GMO products*
Part 3B Residues	Select	*Only applicable to food-producing species*
1. - Identification of the product	Select	
2. - Metabolism and residue kinetics	Select	
2.1. Pharmacokinetics (absorption, distribution, metabolism, excretion)	Select	
2.2. Depletion of residues	Select	

Part 3 – Safety and Residues *Check that documents/cross-reference/justification for absence have been provided in the appropriate indent -> If none present => VSI.*		
3. - Residue analytical method	Select	

Part 4 –Efficacy *Check that documents/cross-reference/justification for absence have been provided in the appropriate indent -> If none present => VSI.*		
Table of contents present, clearly indicating cross-references to part 3 (if applicable)	Select	
Part 4.1 Pre-clinical Documentation		
A. Pharmacology	Select	
A.1 Pharmacodynamics (for each target species)	Select	
A.2 Development resistance *(if applicable)*	Select	
A.3 Pharmacokinetics (for each target species)	Select	
Bioequivalence study (*if required)*	Select	
B. Tolerance in the target species	Select	
Part 4.2 Clinical Documentation		
Dose determination (for each target species)	Select	
Dose confirmation (for each target species)	Select	
Field studies (for each target species, indication and pharmaceutical form)	Select	