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COMMISSION IMPLEMENTING REGULATION (EU) 2021/17

of 8 January 2021

establishing a list of variations not requiring assessment in accordance with Regulation (EU) 2019/6 of the European Parliament and of the Council

(Text with EEA relevance)

(OJ L 7, 11.1.2021, p. 22)

Amended by:

		Official Journal		
		No	page	date
►**M1**	Commission Implementing Regulation (EU) 2023/997 of 23 May 2023	L 136	1	24.5.2023
►**M2**	Commission Implementing Regulation (EU) 2024/916 of 26 March 2024	L 916	1	27.3.2024
►**M3**	Commission Implementing Regulation (EU) 2025/163 of 30 January 2025	L 163	1	31.1.2025
►**M4**	Commission Implementing Regulation (EU) 2026/758 of 1 April 2026	L 758	1	7.4.2026

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COMMISSION IMPLEMENTING REGULATION (EU) 2021/17

of 8 January 2021

establishing a list of variations not requiring assessment in accordance with Regulation (EU) 2019/6 of the European Parliament and of the Council

(Text with EEA relevance)

Article 1

Variations listed in the Annex, which satisfy the requirements applicable to them as set out therein, shall not require assessment.

Article 2

This Regulation shall enter into force on the twentieth day following that of its publication in the *Official Journal of the European Union*.

It shall apply from 28 January 2022.

This Regulation shall be binding in its entirety and directly applicable in all Member States.

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ANNEX

Variations not requiring assessment

	Variation	Requirements The requirements indicated in the line for the main section are valid for each sub-section of the given section. Any additional requirement specified in the sub-section should be read together with the requirements indicated in the main section.	
Number		Conditions	Documents to be provided
A	**Administrative changes**		
▼M3 1	Change in the name or address of:		
a)	— the marketing authorisation holder	The marketing authorisation holder shall remain the same legal entity. The marketing authorisation holder shall already be incorporated in the Union IT systems storing and providing organisational data.	
b)	— a manufacturer or supplier of the active substance, starting material, reagent or intermediate used in the manufacture of the active substance or a quality control testing site (where specified in the dossier) where no European Pharmacopoeia (Ph. Eur.) Certificate of Suitability (CEP) is part of the approved dossier.	The manufacturing or quality control site and all manufacturing operations shall remain the same. The manufacturer or supplier shall already be incorporated in the Union IT systems storing and providing organisational data (not applicable for starting material and reagent manufacturers/suppliers).	
c)	— an active substance master file (ASMF) holder	The manufacturing site and all manufacturing operations shall remain the same. The ASMF holder shall already be incorporated in the Union IT systems storing and providing organisational data.	Updated ‘letter of access’ to the Active Substance Master File.
d)	— a manufacturer of a [novel] excipient (where specified in the dossier)	The manufacturing site and all manufacturing operations shall remain the same.	
e)	— a manufacturer or importer of the finished product (including batch release or quality control testing sites)	The manufacturing or quality control site and all manufacturing operations shall remain the same. The manufacturer or supplier shall already be incorporated in the Union IT systems storing and providing organisational data.	

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	Variation	Requirements The requirements indicated in the line for the main section are valid for each sub-section of the given section. Any additional requirement specified in the sub-section should be read together with the requirements indicated in the main section.	
Number		Conditions	Documents to be provided
2	Change in the (invented) name of the veterinary medicinal product	The acceptability review of the new name by the Agency or the national competent authority, as applicable, shall be finalised and is positive.	
3	Change in name of the active substance or of an excipient	The substance shall remain the same. For veterinary medicinal products for food-producing species, the entry in Regulation (EC) No 470/2009 for this substance shall be amended before implementation of this change.	
4	Change in ATCvet Code	The change shall only be introduced following alteration to the index of the ATCvet Code.	
B	**Changes to the quality part of the dossier**		
▼M3 1	Change in the name or address of a supplier of a packaging component or of a device of the finished product (where mentioned in the dossier):	The supplier shall already be incorporated in the Union IT systems storing and providing organisational data. The manufacturing site shall remain the same.	
▼B 2	Change in the nomenclature [1] of the material for immediate packaging of the finished product	The change shall only be introduced following amendment to the name of the container in the standard terms database on the European Directorate for the Quality of Medicines and HealthCare (EDQM) website.	
3	Deletion of:		Amendment of the relevant section(s) of the dossier.
▼M3 a)	— a manufacturing site for an active substance, intermediate or finished product, packaging site, manufacturer responsible for importation, manufacturer responsible for batch release, site where batch control takes place, or supplier of (1) a starting material for an active substance, (2) a reagent or (3) an excipient (when mentioned in the dossier)	The deletion shall not be due to critical deficiencies concerning manufacturing. There shall at least remain one site or manufacturer, as previously authorised, performing the same function as the one(s) concerned by the deletion. There shall at least remain one site or manufacturer responsible for batch release within the European Union or the European Economic Area.	

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Number	Variation	Requirements The requirements indicated in the line for the main section are valid for each sub-section of the given section. Any additional requirement specified in the sub-section should be read together with the requirements indicated in the main section.	
		Conditions	Documents to be provided
b)	— a manufacturing process for the active substance or the finished product, including an intermediate used in the manufacture of the finished product when an alternative is already approved	The finished product, active substance, intermediates or in-process materials used in the manufacture of the finished product shall still conform to the approved specifications. The deletion shall not be due to critical deficiencies concerning manufacturing.	
c)	— a non-significant in-process test during the manufacture of the active substance (e.g. deletion of an obsolete in-process test)	The change shall not relate to a commitment or to an unexpected event during manufacture. The change shall not concern a critical in-process test and shall not have the potential to affect the identity, quality, purity, potency or physical characteristics of the active substance, starting material, intermediate or reagent used in the manufacturing process of the active substance.	Comparative table of former and new in-process test.
d)	— a non-significant specification parameter (e.g. deletion of an obsolete parameter) of — an active substance; — a starting material; — an intermediate or reagent used in the manufacturing process of the active substance	The change shall not relate to a commitment or to an unexpected event during manufacture. The change shall not concern a critical specification parameter or have the potential to affect the identity, quality, purity, potency or physical characteristics of the active substance, starting material, intermediate or reagent used in the manufacturing process of the active substance.	Comparative table of former and new specifications.
e)	— a test procedure — for the active substance or a starting material, reagent or intermediate of the active substance; — for the immediate packaging of the active substance; — for an excipient or the finished product; — for the immediate packaging of the finished product	An alternative test procedure shall already be authorised by the national competent authority or the Agency and this test procedure has not been added through a variation procedure according to Article 61 of Regulation (EU) 2019/6.	

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	Variation	Requirements The requirements indicated in the line for the main section are valid for each sub-section of the given section. Any additional requirement specified in the sub-section should be read together with the requirements indicated in the main section.	
Number		Conditions	Documents to be provided
f)	— one of the authorised bulk or final containers (including packaging of an active substance) or immediate packaging of the finished product that does not lead to the complete deletion of a strength or pharmaceutical form	Where applicable, the remaining product presentations shall be adequate for the dosing instructions and treatment duration as defined in the summary of product characteristics.	
g)	— a non-significant specification parameter (e.g. deletion of an obsolete parameter) in the specification parameters or limits of the immediate packaging of the active substance or the finished product	The change shall not relate to a commitment or to an unexpected event during manufacture of the immediate packaging material and storage of the active substance or the finished product. The change shall not concern a critical parameter or have the potential to affect the identity or quality of the immediate packaging.	Comparative table of former and new specifications.
h)	— an approved change management protocol related to the active substance or the finished product	The change shall not be the result of an unexpected event or an out of specification result during the implementation of the change(s) described in the protocol.	
▼M3 i)	— a component or components of the flavouring or colouring system	The change shall not have the potential to affect the identity, strength, quality, purity, potency, safety or effectiveness of the finished product. For veterinary medicinal products for oral use, the change does not affect the uptake by target animal species. No change in functional characteristics of the pharmaceutical form, e.g. disintegration time, dissolution profile. Any minor adjustment to the formulation to maintain the total weight shall be made by an excipient which currently makes up a major part of the finished product formulation.	

▼M3

	Variation	Requirements The requirements indicated in the line for the main section are valid for each sub-section of the given section. Any additional requirement specified in the sub-section should be read together with the requirements indicated in the main section.	
Number		Conditions	Documents to be provided
		Stability studies have been started in line with conditions set out in the relevant guidelines, International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products (ICH/VICH), Ph. Eur. etc., (with indication of batch numbers) and relevant stability parameters have been assessed in at least two pilot scale or industrial scale batches and at least 3 months satisfactory stability data are at the disposal of the applicant and the stability profile is similar to the currently registered situation. Assurance is given that these studies will be finalised and that data will be provided immediately to the competent authorities if outside specifications or potentially outside specifications at the end of the approved shelf life (with proposed action). In addition, where relevant, photo-stability testing shall be performed.	
▼B j)	— a solvent or diluent container from the pack	The pharmaceutical form shall remain unchanged. There shall be appropriate alternative means to obtain the solvent or diluent as required for the safe and effective use.	
k)	— a non-significant in-process test (e.g. deletion of an obsolete test) during the manufacture of the finished product	The change shall not relate to a commitment or to an unexpected event during manufacture. The change shall not concern a critical parameter or have the potential to affect the identity, quality, purity, potency or physical characteristics of the finished product or starting material, intermediate or reagent used in the manufacturing process of the finished product.	Comparative table of former and new in-process tests and limits.

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	Variation	Requirements The requirements indicated in the line for the main section are valid for each sub-section of the given section. Any additional requirement specified in the sub-section should be read together with the requirements indicated in the main section.	
Number		Conditions	Documents to be provided
l)	— details on testing frequency by the finished product manufacturer of an excipient or an active substance or of packaging material for the immediate packaging of an active substance or the finished product, when mentioned in the dossier		
m)	— a non-significant specification parameter (e.g. deletion of an obsolete parameter) in the specification parameters or limits of an excipient	The change shall not relate to a commitment or to an unexpected event during manufacture. The change shall not concern a critical parameter or have the potential to affect the identity, quality, purity, potency or physical characteristics of the excipient.	Comparative table of former and new specification parameters or limits.
n)	— a non-significant specification parameter (e.g. deletion of an obsolete parameter such as odour and taste or identification test for a colouring or flavouring material) in the specification parameters or limits of the finished product	The change shall not relate to a commitment or to an unexpected event during manufacture. The change shall not concern a critical parameter or have the potential to affect the identity, strength, quality, purity, potency or physical characteristics of the finished product.	Comparative table of former and new specification parameters or limits.
o)	— a measuring or administration device	The change shall not affect the delivery, use or safety of the finished product.	
p)	— a non-significant specification parameter (e.g. deletion of an obsolete parameter) of a measuring or administration device	The change shall not relate to a commitment or to an unexpected event during manufacture. The change shall not concern a critical parameter or have the potential to affect the identity or quality of the measuring or administration device.	Comparative table of former and new specifications.
q)	— a test procedure of a measuring or administration device	An alternative test procedure shall already be authorised by the national competent authority or the Agency.	
r)	— pack size(s) of the finished product	The remaining pack-sizes shall be consistent with the posology and treatment duration as approved in the summary of product characteristics.	

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	Variation	Requirements The requirements indicated in the line for the main section are valid for each sub-section of the given section. Any additional requirement specified in the sub-section should be read together with the requirements indicated in the main section.	
Number		Conditions	Documents to be provided
s)	— a supplier of packaging components or devices (when mentioned in the dossier)	The change shall not include the deletion of a packaging component(s) or a device(s).	
t)	— a Ph. Eur. CEP — for an active substance; — for a starting material, reagent or intermediate used in the manufacturing process of the active substance; — for an excipient	At least one manufacturer for the same substance shall remain in the dossier.	
u)	— a Ph. Eur. Transmissible Spongiform Encephalopathy (TSE) CEP — for an active substance; — for a starting material, reagent or intermediate of an active substance; — for an excipient	At least one manufacturer for the same substance shall remain in the dossier.	
v)	— a pharmaceutical form or strength ([2])	Remaining form(s) or strength(s) shall be suitable to allow accurate dosing of the product and treatment duration without the use of multiple presentations (e.g. several pipettes or tablets) or the use of unapproved divided doses (e.g. half tablets that are not already authorised).	
▼M3 4	Change in the manufacturer of a starting material, reagent or intermediate used in the manufacturing process of the active substance or change in the manufacturer of the active substance where no Ph. Eur. CEP is part of the approved dossier:		Amendment of the relevant section(s) of the dossier

▼M3

Number	Variation	Requirements The requirements indicated in the line for the main section are valid for each sub-section of the given section. Any additional requirement specified in the sub-section should be read together with the requirements indicated in the main section.	
		Conditions	Documents to be provided
a)	— change in a manufacturer (including relevant quality control testing sites) that is part of the same pharmaceutical group as the currently approved manufacturer	The change shall not be applicable to a sterile active substance or a biological or immunological substance. The new manufacturer shall already be incorporated in the Union IT-systems storing and providing organisational data. For starting materials and reagents the specifications (including in-process controls, methods of analysis of all materials), shall be identical to those already approved. For intermediates and active substance(s) the specifications (including in process controls, methods of analysis of all materials), method of preparation (including batch size) and detailed route of synthesis shall be identical to those already approved. Where materials of human or animal origin are used in the process, the manufacturer does not use any new supplier for which assessment is required of viral safety or of compliance with the current Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products.	TSE data as appropriate. Batch analysis data for at least two batches (minimum pilot scale). Qualified person (QP) declaration.
b)	— changes to quality control testing arrangements for the active substance: replacement or addition of a site where batch control or testing of the active substance takes place	The change shall not be applicable to a sterile active substance or a biological or immunological substance. The new manufacturer or site shall already be incorporated in the Union IT-system storing and providing organisational data. Method transfer from the former to the new site shall have been successfully completed.	
c)	— introduction of a new site of micronisation for the active substance	The change shall not be applicable to a sterile active substance or a biological or immunological substance. The new manufacturer or site shall already be incorporated in the Union IT-systems storing and providing organisational data. The change shall not provoke an adverse change in physico-chemical properties. The particle size specification for the active substance and the corresponding analytical method shall remain the same.	Batch analysis data for at least two comparative batches (minimum pilot scale). Qualified Person (QP) declaration.

▼M3

Number	Variation	Requirements The requirements indicated in the line for the main section are valid for each sub-section of the given section. Any additional requirement specified in the sub-section should be read together with the requirements indicated in the main section.	
		Conditions	Documents to be provided
d)	— new storage site of Master Cell Bank or Working Cell Banks	No change shall be made to the storage conditions, the shelf-life and the specifications. The new site shall already be incorporated in the Union IT-systems storing and providing organisational data.	

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5	Reduction of re-test period or storage period where no Ph. Eur. CEP covering the retest period is part of the approved dossier	The change shall not be the result of unexpected events arising during manufacture or because of stability concerns.	Amendment of the relevant section(s) of the dossier including specifications and stability confirmation, as appropriate.
6	Change to more restrictive storage conditions:	The change shall not be the result of unexpected events arising during manufacture or because of stability concerns.	Amendment of the relevant section(s) of the dossier including specifications and stability confirmation, as appropriate.
a)	— of the reference standard (when mentioned in the dossier)		
b)	— of the active substance		
7	Change to an approved stability protocol of an active substance (including starting material, reagent or intermediate)	The change shall not be the result of unexpected events arising during manufacture or because of stability concerns. The change shall not have the potential to affect the identity, strength, quality, purity, potency or physical characteristics of the active substance.	Amendment of the relevant section(s) of the dossier including results of appropriate real time stability studies.

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	Variation	Requirements The requirements indicated in the line for the main section are valid for each sub-section of the given section. Any additional requirement specified in the sub-section should be read together with the requirements indicated in the main section.	
Number		Conditions	Documents to be provided
8	Implementation of changes foreseen in an approved change management protocol (CMP) for the active substance	The change shall be in accordance with the approved CMP and the results of studies performed indicate that the predefined acceptance criteria specified in the protocol are met. The implementation of the change shall require no further supportive data to the CMP.	Amendment of the relevant section(s) of the dossier.
▼M3 9	Change in batch size (including batch size ranges) of active substance or intermediate used in the manufacturing process of the active substance:	The change shall not be applicable to a biological or immunological substance. The change shall not adversely affect the reproducibility of the process. Changes to the manufacturing methods shall only be those necessitated by scale-up or downscaling, e.g. use of different-sized equipment.	Amendment of the relevant section(s) of the dossier. Test results of at least two batches in accordance with the specifications for the proposed batch size.
a)	— up to 10-fold increase compared to the originally approved batch size	The change shall not be applicable to a sterile active substance. The active substance and all intermediates, reagents, catalysts or solvents shall still conform to the approved specifications.	
b)	— downscaling down to 10-fold	The change shall not be the result of unexpected events arising during manufacture or because of stability concerns.	
c)	— more than 10-fold increase compared to the originally approved batch size	The change shall not be applicable to a sterile active substance. The intermediates, reagents, catalysts or solvents used in the process shall remain the same. The active substance and all intermediates, reagents, catalysts or solvents shall still conform to the approved specifications. The change shall not provoke an adverse change in qualitative and quantitative impurity profile, or in physico-chemical properties of the active substance. The change shall not refer to the restricted part of an ASMF.	

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	Variation	Requirements The requirements indicated in the line for the main section are valid for each sub-section of the given section. Any additional requirement specified in the sub-section should be read together with the requirements indicated in the main section.	
Number		Conditions	Documents to be provided
10	Change to in-process tests or limits applied during the manufacture of the active substance	The change shall not be a consequence of any commitment from previous assessments to review specification limits. The change shall not result from unexpected events arising during manufacture e.g. new unqualified impurity; change in total impurity limits.	Amendment of the relevant section(s) of the dossier for the new test method, validation and batch data, as appropriate. Comparative table of former and new in-process tests and limits.
a)	— tightening of in-process limits	The change shall be within the range of currently approved limits. The test procedure shall remain the same, or changes in the test procedure shall be minor.	
b)	— addition of a new in-process test and limits	Any new test method shall not concern a novel non-standard technique or a standard technique used in a novel way. The new test method shall not be a biological, immunological or immunochemical method, or a method using a biological reagent for a biological active substance, except if this method is a standard pharmacopoeial microbiological method.	
▼M3 11	Change in the specification parameters or limits of an active substance, starting material, intermediate or reagent used in the manufacturing process of the active substance or of the immediate packaging of the active substance:	The change shall not result from unexpected events arising during manufacture or storage (e.g. new unqualified impurity or change in total impurity). The change shall not be a consequence of any commitment from previous assessments to review specification limits (e.g. made during the procedure for the marketing authorisation application or a variation procedure in accordance with Article 62 of Regulation (EU) 2019/6) unless it has been previously assessed and agreed as part of a follow-up measure in a previous procedure under Regulation (EU) 2019/6.	Amendment of the relevant section(s) of the dossier. Comparative table of former and new specification parameters and limits.
a)	— tightening of specification limits of an active substance, starting material, intermediate or reagent used in the manufacturing process of the active substance for all veterinary medicinal products including products subject to Official Control Authority Batch Release (OCABR);	The test procedure shall remain the same, or changes in the test procedure shall be minor. The change shall be within the range of currently approved limits.	

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Number	Variation	Requirements The requirements indicated in the line for the main section are valid for each sub-section of the given section. Any additional requirement specified in the sub-section should be read together with the requirements indicated in the main section.	
		Conditions	Documents to be provided
▼M3 ———			
c)	— tightening of specification limits of the immediate packaging of the active substance	The test procedure shall remain the same, or changes in the test procedure shall be minor. The change shall be within the range of currently approved limits.	
d)	— addition of a new specification parameter to the specification with its corresponding test method for an active substance, starting material, intermediate or reagent used in the manufacturing process of the active substance	The new test method shall not concern a novel non-standard technique or a standard technique used in a novel way. The new test method shall not be a biological, immunological or immunochemical method, or a method using a biological reagent for a biological active substance, except if this method is a standard pharmacopoeial microbiological method. The change shall not concern a genotoxic impurity. If it involves the final active substance, other than for residual solvents which shall be in line with ICH/VICH limits, any new impurity control shall be in line with the Ph. Eur. or National Pharmacopoeia of a Member State.	Details of any new analytical method and validation data, where relevant. Batch analysis data on two production batches (3 production batches for biologicals, unless otherwise justified) of the relevant substance for all specification parameters. Where appropriate, comparative dissolution profile data for the finished product on at least one pilot batch containing the active substance complying with the current and proposed specification. For herbal veterinary medicinal products, comparative disintegration data may be acceptable. Justification from the marketing authorisation holder (MAH) or ASMF Holder as appropriate of the new specification parameter and the limits.

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Number	Variation	Requirements The requirements indicated in the line for the main section are valid for each sub-section of the given section. Any additional requirement specified in the sub-section should be read together with the requirements indicated in the main section.	
		Conditions	Documents to be provided
▼M3			
e)	— addition of a new specification parameter to the specification with its corresponding test method for the immediate packaging of the active substance	The new test method shall not concern a novel non-standard technique or a standard technique used in a novel way.	Details of any new analytical method and validation data, where relevant. Batch analysis data on two batches of the immediate packaging for all specification parameters. Justification from the marketing authorisation holder or the ASMF Holder, as appropriate, of the new specification parameter and the limits.
12	Minor changes:		
a)	— to an approved test procedure — for active substance or a starting material, reagent or intermediate used in the manufacturing process of the active substance; — for the finished product; — for an excipient	The test method shall not be a biological, immunological or immunochemical method, or a method using a biological reagent (does not include standard pharmacopoeial microbiological methods). Appropriate validation studies shall have been performed in accordance with the relevant guidelines and show that the updated test procedure is at least equivalent to the former test procedure. There shall be no changes of the total impurity limits; no new unqualified impurities shall be detected. The method of analysis shall remain the same (e.g. a change in column length or temperature, but not a different type of column or method).	Amendment of the relevant section(s) of the dossier, including a description of the analytical methodology, a summary of validation data and revised specifications for impurities (if applicable). Comparative validation results, or if justified comparative analysis results showing that the current test and the proposed one are equivalent.

▼M3

	Variation	Requirements The requirements indicated in the line for the main section are valid for each sub-section of the given section. Any additional requirement specified in the sub-section should be read together with the requirements indicated in the main section.	
Number		Conditions	Documents to be provided
b)	— to an approved test procedure — for the immediate packaging of the active substance or the finished product	Appropriate validation studies shall have been performed in accordance with the relevant guidelines and show that the updated test procedure is at least equivalent to the former test procedure. The method of analysis shall remain the same (e.g. a change in column length or temperature, but not a different type of column or method). Any new test method shall not concern a novel non-standard technique or a standard technique used in a novel way.	Amendment of the relevant section(s) of the dossier, including a description of the analytical methodology and a summary of validation data. Comparative validation results or if justified comparative analysis results showing that the current test and the proposed one are equivalent.
c)	— to an approved test procedure for an in-process test — for active substance; — for the finished product	The test method shall not be a biological, immunological or immunochemical method, or a method using a biological reagent for a biological active substance. Appropriate validation studies shall have been performed in accordance with the relevant guidelines and show that the updated test procedure is at least equivalent to the former test procedure. There shall be no changes of the total impurity limits; no new unqualified impurities shall be detected. The method of analysis shall remain the same (e.g. a change in column length or temperature, but not a different type of column or method).	Amendment of the relevant section(s) of the dossier.

▼M3

	Variation	Requirements The requirements indicated in the line for the main section are valid for each sub-section of the given section. Any additional requirement specified in the sub-section should be read together with the requirements indicated in the main section.	
Number		Conditions	Documents to be provided
d)	— in the manufacturing process of an active substance	The change shall not be applicable to a biological or immunological active substance. The change shall not be a change in the geographical source, manufacturing route or production for a herbal veterinary medicinal substance. The change shall not provoke an adverse change in qualitative and quantitative impurity profile or in physico-chemical properties. The synthetic route remains the same, i.e. intermediates remain the same and there are no new reagents, catalysts or solvents used in the process. The specifications of the active substance or intermediates are unchanged. The change shall not refer to the restricted part of an ASMF.	Amendment of the relevant section(s) of the dossier. Batch analysis data (in a comparative tabulated format) of at least two batches (minimum pilot scale) manufactured in accordance with the currently approved and proposed process.
e)	— in synthesis or recovery of a non-pharmacopoeial excipient (when described in the dossier) or a novel excipient	The excipients and all intermediates, reagents, catalysts, solvents or in-process controls shall still conform to the approved specifications (e.g. qualitative and quantitative impurity profile). Adjuvants and preservatives shall be excluded from the scope of this entry. Synthetic routes and specifications shall be identical, and there shall be no change in physico-chemical properties.	Amendment of the relevant section(s) of the dossier for batch data, comparative data, and specification, as appropriate.
f)	— to an in-process limit range for the finished product	The change shall not be the result of unexpected events arising during manufacture or because of stability concerns. The change shall concern an in-process test, which is also part of the finished product specification at release, and the new in-process limit range shall be within the approved release limit.	Amendment of the relevant section(s) of the dossier. Comparative table of former and new in-process limits.

▼M3

	Variation	Requirements The requirements indicated in the line for the main section are valid for each sub-section of the given section. Any additional requirement specified in the sub-section should be read together with the requirements indicated in the main section.	
Number		Conditions	Documents to be provided
g)	— to an approved change management protocol of the active substance that does not change the strategy defined in the protocol	The intermediates, reagents, catalysts or solvents used in the process shall remain the same. The active substance and all intermediates, reagents, catalysts or solvents shall still conform to the approved specifications. There shall be no adverse change in qualitative and quantitative impurity profile or in physico-chemical properties. The change shall not refer to the restricted part of an ASMF. The changes shall be within the range of currently approved limits. In case of biological veterinary medicinal products, this change shall be only possible if comparability is not required. Changes in the geographical source, manufacturing route or production of a herbal substance or herbal preparation of a herbal veterinary medicinal product shall be excluded.	Amendment of the relevant section(s) of the dossier.
h)	— to production equipment (when described in the dossier) including processes related to the equipment	The change shall not result in any changes or modifications of the production process or quality of the product.	Amendment of the relevant section(s) of the dossier.
i)	to an approved test procedure — of a measuring or administration device	Appropriate validation studies shall have been performed in accordance with the relevant guidelines and show that the updated test procedure is at least equivalent to the former test procedure. The method of analysis shall remain the same.	Amendment of the relevant section(s) of the dossier, including a description of the analytical methodology and a summary of validation data. Comparative validation results or if justified comparative analysis results showing that the current test and the proposed one are equivalent.

▼M3

Number	Variation	Requirements The requirements indicated in the line for the main section are valid for each sub-section of the given section. Any additional requirement specified in the sub-section should be read together with the requirements indicated in the main section.	
		Conditions	Documents to be provided
j)	— in the manufacturing process of the finished product, including an intermediate used in the manufacture of the finished product	The change relates only to an immediate release solid oral dosage form/ oral solution and the veterinary medicinal product concerned is not a biological/immunological or herbal veterinary medicinal product. The manufacturing steps remain the same. The finished product / intermediates / in-process materials used in the manufacture of the finished product shall still conform to the approved specifications. No adverse change in qualitative and quantitative impurity profile or in physico-chemical properties. The new process shall lead to an identica product regarding all aspects of quality, safety and efficacy. Relevant stability studies in accordance with the relevant guidelines shall have been started with at least one pilot scale or industrial scale batch and at least 3 months stability data shall be at the disposal of the applicant.	Amendment of the relevant section(s) of the dossier. For solid dosage forms: dissolution profile data of one representative production batch and comparative data of the last three batches from the previous process; data on the next two full production batches shall be available on request or reported if outside specification (with proposed action). Justification for not submitting a new bioequivalence study in accordance with the relevant guidance on Bioavailability/Bioequivalence. Batch analysis data (in a comparative tabulated format) on a minimum of one batch manufactured in accordance to both the currently approved and the proposed process.
13	Changes to a test procedure (including replacement or addition):	The active substance/finished product shall not be biological or immunological. Appropriate validation studies have been performed in accordance with the relevant guidelines and show that the updated test procedure is at least equivalent to the former test procedure. The new test method shall not concern a novel non-standard technique or a standard technique used in a novel way.	Amendment of the relevant section(s) of the dossier and comparative validation data, as appropriate. In the absence of comparative validation data, if justified, comparative analysis results showing that the current test and the proposed one are equivalent. This requirement is not applicable in case of an addition of a new test procedure.
a)	— for a reagent used in the manufacturing process of the active substance but which does not have a significant effect on the overall quality of the active substance	There shall be no changes to the total impurity limits; no new unqualified impurities shall be detected. The method of analysis shall remain the same (e.g. a change in column length or temperature, but not a different type of column or method).	

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Number	Variation	Requirements The requirements indicated in the line for the main section are valid for each sub-section of the given section. Any additional requirement specified in the sub-section should be read together with the requirements indicated in the main section.	
		Conditions	Documents to be provided
b)	— for the immediate packaging of the active substance		
14	Change in qualitative or quantitative composition of the immediate packaging for the active substance	Sterile, liquid, biological or immunological active substances shall be excluded. The new packaging material shall be at least equivalent to the approved material in respect of its relevant properties. Relevant stability studies have been started under VICH conditions and relevant stability parameters have been assessed in at least two pilot scale or industrial scale batches and at least 3 months satisfactory stability data are at the disposal of the applicant at time of implementation. However, if the proposed packaging is more resistant than the existing packaging, the 3 months' stability data do not yet have to be available. These studies shall be finalised and the data shall be provided immediately to the competent authorities if outside specifications or potentially outside specifications at the end of the shelf-life/retest period (with proposed action).	Amendment of the relevant section(s) of the dossier. Appropriate data on the new packaging (e.g. comparative data on permeability, e.g. for O_2, CO_2 moisture), including a confirmation that the material complies with relevant pharmacopoeial requirements or Union legislation on plastic materials and objects in contact with foodstuffs. Where appropriate, proof shall be provided that no interaction between the content and the packaging material occurs (e.g. no migration of components of the proposed material into the content and no loss of components of the product into the pack). Comparative table of former and new immediate packaging specifications, permeability data and interaction data, as appropriate.
15	Addition of or change to a calendar package for a pack size already registered in the dossier	The primary packaging material shall remain the same.	

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	Variation	Requirements The requirements indicated in the line for the main section are valid for each sub-section of the given section. Any additional requirement specified in the sub-section should be read together with the requirements indicated in the main section.	
Number		Conditions	Documents to be provided
16	Change or addition of imprints, bossing or other markings including replacement, or addition of inks used for product marking of the finished product	The change shall not affect the delivery, use or safety of the finished product. The finished product release and shelf life specifications shall not have been changed except for appearance. The ink shall comply with the relevant pharmaceutical legislation. The change shall not relate to a scored tablet that is intended to be divided into equal doses.	Amendment of the relevant section(s) of the dossier.
17	Change in the shape or dimensions of the pharmaceutical form for immediate release tablets, capsules, suppositories and pessaries	The dissolution profile of the product shall remain unchanged. For herbal medicinal products, where dissolution testing may not be feasible the new disintegration time of the product shall be comparable to the former one. The release and end of shelf-life specifications of the product shall not have been changed. The qualitative or quantitative composition and mean mass shall remain unchanged. The change shall not relate to a scored tablet that is intended to be divided into equal doses.	Amendment of the relevant section(s) of the dossier.
▼M3 18	Change(s) in the composition (excipients) of the finished product:	The change shall not be applicable to a biological or immunological veterinary medicinal product. The change shall not have the potential to affect the identity, strength, quality, purity, potency, physical characteristics, safety or effectiveness of the finished product. Any minor adjustment to the formulation to maintain the total weight shall be made by an excipient which currently makes up a major part of the finished product formulation. The change shall not affect the functional characteristics of the pharmaceutical form (e.g. disintegration time, dissolution profile). Stability studies shall have been started under International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products (VICH) conditions; relevant stability parameters shall have been assessed in at least two pilot scale or industrial scale batches, and at least three months satisfactory stability data shall be at the disposal of the applicant. The stability profile shall be similar to the currently registered situation. In addition, where relevant, photo-stability testing shall be performed.	Amendment of the relevant section(s) of the dossier including stability confirmation.

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	Variation	Requirements The requirements indicated in the line for the main section are valid for each sub-section of the given section. Any additional requirement specified in the sub-section should be read together with the requirements indicated in the main section.	
Number		Conditions	Documents to be provided
a)	— increase or reduction of a component or components of the flavouring or colouring system	Quantitative change(s) shall not exceed +/- 10 % of the existing concentration of the component. The finished product specification shall only have been updated in respect of appearance, odour or taste and, if relevant, deletion of an identification test. For veterinary medicinal products for oral use, the change shall not negatively affect the uptake by target animal species.	
b)	— any minor adjustment of the quantitative composition of the finished product with respect to excipients	Quantitative change(s) shall not exceed +/- 10 % of the existing concentration of the component. Where relevant, the dissolution profile of the changed product shall be determined on a minimum of two pilot scale batches and shall be comparable to the former one. No significant differences regarding comparability shall occur. For herbal veterinary medicinal products, where dissolution testing may not be feasible, the disintegration time of the changed product shall be comparable to the former one. The change shall not be the result of stability issues and shall not result in potential safety concerns, e.g. differentiation between strengths.	

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	Variation	Requirements The requirements indicated in the line for the main section are valid for each sub-section of the given section. Any additional requirement specified in the sub-section should be read together with the requirements indicated in the main section.	
Number		Conditions	Documents to be provided
c)	— addition or replacement of a component or components of the flavouring or colouring system	The finished product specification has only been updated in respect of appearance/odour/taste and if relevant, deletion of an identification test. Any new proposed components shall comply with the relevant applicable Regulations. A new component shall not include the use of materials of human or animal origin. Where applicable, the change does not affect the differentiation between strengths and does not have a negative impact on taste acceptability. For veterinary medicinal products for oral use, the change does not affect the uptake by target animal species. For veterinary medicinal products for food-producing species, the component or components of the flavouring or colouring system shall be allowed in accordance with Regulation (EC) No° 470/2009 and the acts adopted on the basis thereof before implementation of this change. The change shall not be the result of stability issues and shall not result in potential safety concerns (e.g. differentiation between strengths).	Either a Ph. Eur. Certificate of Suitability for any new component of animal origin susceptible to TSE risk or where applicable, documentary evidence that the specific source of the TSE risk material has been previously assessed by the competent authority and shown to comply with the scope of the current Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathies via Human and Veterinary Medicinal Products. The following information shall be included for each such material: name of manufacturer, species and tissues from which the material is a derivative, country of origin of the source animals and its use. Data to demonstrate that the new excipient does not interfere with the finished product specification test methods, if appropriate.

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19	Change in coating weight of oral dosage forms or change in weight of capsule shells for a solid oral pharmaceutical form	The change shall not be the result of stability issues and shall not result in potential safety concerns (e.g. differentiation between strengths). For veterinary medicinal products for oral use, the coating shall not be a critical factor for the release mechanism and the change shall not affect the uptake by target animal species. The finished product specification shall only be updated in respect of weight and dimensions, if applicable. The dissolution profile of the changed product shall be determined on a minimum of two pilot scale batches and shall be comparable to the former one. For herbal medicinal products, where dissolution testing may not be feasible, the disintegration time of the changed product shall be comparable to the former one.	

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	Variation	Requirements The requirements indicated in the line for the main section are valid for each sub-section of the given section. Any additional requirement specified in the sub-section should be read together with the requirements indicated in the main section.	
Number		Conditions	Documents to be provided
		Relevant stability studies shall have been started under VICH conditions and relevant stability parameters shall have been assessed in at least two pilot scale or industrial scale batches and at least three months satisfactory stability data shall be at the disposal of the applicant at time of implementation.	Amendment of the relevant section(s) of the dossier including stability confirmation.
20	Replacement or addition of a primary packaging site of a non-sterile finished product	The change shall not be applicable to a biological or immunological medicinal product. The primary packaging site shall already be introduced in the Union IT systems storing and providing organisational data. The site shall be appropriately authorised to manufacture the pharmaceutical form or product concerned and satisfactorily inspected. The validation scheme shall be available or validation of the manufacture at the new site has been successfully carried out according to the current protocol with at least three production scale batches, as appropriate. If the manufacturing site and the primary packaging site are different, conditions of transport and bulk storage shall be specified and validated.	Amendment of the relevant section(s) of the dossier.
21	Replacement or addition of a secondary packaging site of a finished product	The secondary packaging site shall already be introduced in the Union IT systems storing and providing organisational data. The site shall be appropriately authorised to manufacture the pharmaceutical form or product concerned and satisfactorily inspected.	Amendment of the relevant section(s) of the dossier.
22	Change to importer, batch control arrangements and quality testing (replacement or addition of a site) for a finished product	The site shall be already introduced in the Union IT systems storing and providing organisational data. The site shall be appropriately authorised and satisfactorily inspected. The change shall not be applicable to a biological or immunological medicinal product. Method transfer from the former to the new site shall have been successfully completed.	

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Number	Variation	Requirements The requirements indicated in the line for the main section are valid for each sub-section of the given section. Any additional requirement specified in the sub-section should be read together with the requirements indicated in the main section.	
		Conditions	Documents to be provided
23	Replacement or addition of a manufacturer of a finished product responsible for importation	The site shall already be introduced in the Union IT systems storing and providing organisational data. The site shall be appropriately authorised and satisfactorily inspected	
▼M1 24	Replacement or addition of a manufacturer responsible for:	The manufacturer or the site shall already be introduced in the Union IT systems storing and providing organisational data. The site shall be appropriately authorised and satisfactorily inspected.	Amendment of the relevant section(s) of the dossier, including revised product information, as appropriate. Qualified person (QP) declaration.
a)	— batch release including batch control or testing of a sterile or non-sterile finished product	The change shall not be applicable to a biological or immunological medicinal product. Method transfer from the former to the new site shall have been successfully completed.	
b)	— batch release not including batch control or testing of a sterile or non-sterile finished product	At least one batch control/testing site remains within the EEA or in a country where an operational and suitably scoped GMP mutual recognition agreement (MRA) exists between the country concerned and the EU, that is able to carry out product testing for the purpose of batch release within the EEA.	
▼B 25	Change in the packaging material of bulk product (intermediate product) not in contact with the bulk product formulation (including replacement or addition)	The manufacturing steps shall remain the same. The finished product, intermediates or in-process controls used in the manufacture of the finished product shall still conform to the approved specifications. The secondary packaging shall not play a functional role on the stability of the bulk product, or if it does, it shall not be less protective than the approved one.	Amendment of the relevant section(s) of the dossier.

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	Variation	Requirements The requirements indicated in the line for the main section are valid for each sub-section of the given section. Any additional requirement specified in the sub-section should be read together with the requirements indicated in the main section.	
Number		Conditions	Documents to be provided
26	Change in the batch size (including batch size ranges) of the finished product:	The change shall not be applicable to a biological or immunological medicinal product. The change shall not be the result of unexpected events arising during manufacture or because of stability concerns. The change shall not affect reproducibility or consistency of the product. The changes to the manufacturing method or to the in-process controls shall be only those necessitated by the change in batch-size, e.g. use of different sized equipment. A validation scheme shall be available or a validation of the manufacture shall have been successfully carried out according to the current protocol with at least three batches of the new batch size in accordance with the relevant guidelines.	Amendment of the relevant section(s) of the dossier. Where relevant, the batch numbers, corresponding batch size, the manufacturing date of batches ([3]) used in the validation study and the validation data or the validation protocol (scheme) shall be provided.
a)	— up to 10-fold increase compared to the originally approved batch size of an immediate release oral pharmaceutical forms or of a non-sterile liquid based pharmaceutical form	The batch size shall be within the 10-fold range of the batch size foreseen when the marketing authorisation was granted.	
b)	— up to 10-fold increase compared to the originally approved batch size for the pharmaceutical form medicinal gas	The batch size shall be within the 10-fold range of the batch size foreseen when the marketing authorisation was granted.	
c)	— downscaling down to 10-fold compared to the originally approved batch size of an immediate release oral pharmaceutical forms or to non-sterile liquid based pharmaceutical form	The batch size shall be within the 10-fold range of the batch size foreseen when the marketing authorisation was granted.	
d)	— downscaling down to 10-fold (for the pharmaceutical form medicinal gas	The batch size shall be within the 10-fold range of the batch size foreseen when the marketing authorisation was granted.	
e)	— more than 10-fold increase compared to the originally approved batch size for an immediate release, solid oral pharmaceutical form		3 months stability data for at least one pilot batch under VICH condition.

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	Variation	Requirements The requirements indicated in the line for the main section are valid for each sub-section of the given section. Any additional requirement specified in the sub-section should be read together with the requirements indicated in the main section.	
Number		Conditions	Documents to be provided
27	Change to in-process tests or limits applied during the manufacture of the finished product:	The change shall not relate to a commitment or to an unexpected event during manufacture. The change shall not have the potential to affect the identity, strength, quality, purity, potency or physical characteristics of the finished product, intermediates or in-process materials.	Comparative table of former and new in-process tests or limits.
a)	— tightening of in-process limits	The change shall be within the range of currently approved limits. The test procedure shall remain the same, or changes in the test procedure shall be minor.	Amendment of the relevant section(s) of the dossier.
▼M3 b)	— addition of a new in-process test and limits	Any new test method shall not concern a novel non-standard technique or a standard technique used in a novel way. The new test method shall not be a biological, immunological or immunochemical method, or a method using a biological reagent for a biological active substance, except if this method is a standard pharmacopoeial microbiological method.	Amendment of the relevant section(s) of the dossier for method and validation data, where relevant, batch data and relevant comparative data.
▼B 28	Change in the specification parameters or limits of an excipient	The change shall not be a consequence of any commitment from previous assessments to review specification limits (e.g. made during the procedure for the marketing authorisation application or a variation procedure according to Article 62 of Regulation (EU) 2019/6). The change shall not be a result of unexpected events arising during manufacture, e.g. new unqualified impurity or change in total impurity limits.	
a)	— tightening of specification limits	The change shall be within the range of currently approved limits. The test procedure shall remain the same, or changes in the test procedure shall be minor.	

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	Variation	Requirements The requirements indicated in the line for the main section are valid for each sub-section of the given section. Any additional requirement specified in the sub-section should be read together with the requirements indicated in the main section.	
Number		Conditions	Documents to be provided
b)	— addition of a new specification parameter to the specification with its corresponding test method	Any new test method shall not concern a novel non-standard technique or a standard technique used in a novel way. The new test method shall not be a biological, immunological or immunochemical method, or a method using a biological reagent for a biological active substance, except if this method is a standard pharmacopoeial microbiological method. The change shall not concern a genotoxic impurity.	Amendment of the relevant section(s) of the dossier for method and validation, batch data and relevant comparative data.
29	Change in source of an excipient or reagent with TSE risk from material with TSE risk to vegetable or synthetic origin	The excipient, finished product release and end of shelf life specifications shall remain the same. The change shall not concern an excipient or reagent used in the manufacture of a biological or immunological active substance or in a biological or immunological medicinal product.	Amendment of the relevant section(s) of the dossier. Declaration from the manufacturer or the marketing authorisation holder of the material that it is purely of vegetable or synthetic origin.
30	Change in the specification parameters or limits of the finished product:	The change shall not be a consequence of any commitment from previous assessments to review specification limits (e.g. made during the procedure for the marketing authorisation application or a variation procedure according to Article 62 of Regulation (EU) 2019/6), unless the supporting documentation has already been assessed and approved within the context of another procedure under Regulation (EU) 2019/6. The change shall not result from unexpected events arising during manufacture, e.g. new unqualified impurity or change in total impurity limits.	Amendment of the relevant section(s) of the dossier. Comparative table of former and new specification parameters and limits.
a)	— tightening of specification limits	The change shall be within the range of currently approved limits. The test procedure shall remain the same, or changes in the test procedure shall be minor.	
b)	— tightening of specification limits for finished products subject to Official Control Authority Batch Release	The change shall be within the range of currently approved limits. The test procedure shall remain the same, or changes in the test procedure shall be minor.	

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	Variation	Requirements The requirements indicated in the line for the main section are valid for each sub-section of the given section. Any additional requirement specified in the sub-section should be read together with the requirements indicated in the main section.	
Number		Conditions	Documents to be provided
c)	— addition of a new specification parameter to the specification with its corresponding test method	Any new test method shall not concern a novel non-standard technique or a standard technique used in a novel way. The test method shall not be a biological, immunological or immunochemical method, or a method using a biological reagent for a biological active substance except if this method is a standard pharmacopoeial microbiological method. The change shall not concern any impurities (including genotoxic) or dissolution.	Amendment of the relevant section(s) of the dossier for method and validation, batch data and relevant comparative data.
d)	— update of the dossier to comply with the provisions of an updated general monograph of the Ph. Eur. for the finished product	The change shall be within the range of currently approved limits. The test procedure shall remain the same, or changes in the test procedure shall be minor. The change shall not concern any impurities (including genotoxic) or dissolution.	
31	Uniformity of dosage units is introduced to replace the currently registered method	The change shall follow changes to the Ph. Eur. Standard 2.9.5. Uniformity of mass or Ph. Eur. Standard 2.9.6 Uniformity of content.	Amendment of the relevant section(s) of the dossier. Comparative table of former and new specification parameters and limits.
32	Change in the specification parameters or limits of the finished product to describe more accurately the appearance of the product	The change shall not be a result of any unexpected events arising during manufacture or testing of the finished product.	Amendment of the relevant section(s) of the dossier. Comparative table of former and new specification parameters and limits.

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	Variation	Requirements The requirements indicated in the line for the main section are valid for each sub-section of the given section. Any additional requirement specified in the sub-section should be read together with the requirements indicated in the main section.	
Number		Conditions	Documents to be provided
33	Change in test procedure for the finished product to comply with Ph. Eur.:	The change shall not concern changes of the total impurity limits; no new unqualified impurities shall be detected. The method of analysis shall remain the same (e.g. a change in column length or temperature, but not a different type of column or method). The test method shall not be a biological, immunological or immunochemical method, or a method using a biological reagent for a biological active substance, except if this method is a standard pharmacopoeial microbiological method.	Amendment of the relevant section(s) of the dossier.
a)	— update of the test procedure to comply with the updated general monograph in the Ph. Eur.		
b)	— update of the test procedure to reflect compliance with the Ph. Eur. and remove reference to the outdated internal test method and test method number		
34	Change in qualitative and quantitative composition of the immediate packaging for a solid pharmaceutical form for a finished product	For solid pharmaceutical forms, the change shall only concern the same packaging or container type (e.g. blister to blister). The finished product shall not be sterile. The change shall not affect the delivery, use, safety or stability of the finished product. Relevant stability studies shall have been started under VICH conditions and relevant stability parameters shall have been assessed in at least two pilot scale or industrial scale batches and at least three months satisfactory stability data shall be at the disposal of the applicant at time of implementation. However, if the new packaging is more resistant than the existing packaging, the three months' stability data do not yet have to be available. The new packaging material shall be at least equivalent to the approved material in respect of its relevant properties.	Amendment of the relevant section(s) of the dossier. Comparative table of former and new immediate packaging specifications, permeability data and interaction data, as appropriate.

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	Variation	Requirements The requirements indicated in the line for the main section are valid for each sub-section of the given section. Any additional requirement specified in the sub-section should be read together with the requirements indicated in the main section.	
Number		Conditions	Documents to be provided
35	Change in the specification parameters or limits of the immediate packaging of the finished product:	The changes shall not be a consequence of any commitment from previous assessments to review specification limits (e.g. made during the procedure for the marketing authorisation application or a variation procedure according to Article 62 of Regulation (EU) 2019/6) unless the supporting documentation has already been assessed and approved within the context of another procedure under Regulation (EU) 2019/6. The change shall not result from unexpected events arising during manufacture.	Comparative table of former and new specifications or limits.
a)	— tightening of specification limits	The change shall be within the range of currently approved limits. The test procedure shall remain the same, or changes in the test procedure shall be minor.	
b)	— addition of a new specification parameter to the specification with its corresponding test method	Any new test method shall not concern a novel non-standard technique or a standard technique used in a novel way.	Amendment of the relevant section(s) of the dossier for method and validation and batch data, as appropriate.
36	Change in test procedure for the immediate packaging of the finished product (including replacement or addition)	The change shall not be applicable to a biological or immunological medicinal product. Appropriate validation studies shall have been performed in accordance with the relevant guidelines and show that the updated test procedure is at least equivalent to the former test procedure. Any new test method shall not concern a novel non-standard technique or a standard technique used in a novel way.	Amendment of the relevant section(s) of the dossier for method and validation and batch data, as appropriate.

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	Variation	Requirements The requirements indicated in the line for the main section are valid for each sub-section of the given section. Any additional requirement specified in the sub-section should be read together with the requirements indicated in the main section.	
Number		Conditions	Documents to be provided
37	Change in shape or dimensions of the container or closure (immediate packaging) of a non-sterile finished product	The change shall not concern a part of the packaging material, which affects the delivery, use, safety or stability of the finished product. The change shall not concern the qualitative or quantitative composition of the container. In case of a change in the headspace or a change in the surface/volume ratio, stability studies in accordance with the relevant guidelines shall have been started, relevant stability parameters shall have been assessed in at least two pilot scale or industrial scale batches, and at least three months stability data shall be at the disposal of the applicant.	Amendment of the relevant section(s) of the dossier.
38	Change in pack size (number of units e.g. tablets, ampoules, etc. in a pack) within the range of the currently approved pack size ([3])	The new pack size shall be consistent with the posology and treatment duration as approved in the Summary of Product Characteristics. The primary packaging material shall remain the same.	
39	Change in any part of the primary packaging material not in contact with the finished product formulation (such as change of colour due to different plastic used for flip-off caps, colour code rings on ampoules or change of needle shield)	The change shall not concern a part of the packaging material that affects the delivery, use, safety or stability of the finished product.	Amendment of the relevant section(s) of the dossier.
40	Replacement or addition of a supplier of packaging components or devices (when mentioned in the dossier)	The qualitative and quantitative composition of the packaging components or device and design specifications shall remain the same. The change shall not have the potential to affect the identity, quality or purity of the packaging component or devices.	Amendment of the relevant section(s) of the dossier.

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	Variation	Requirements The requirements indicated in the line for the main section are valid for each sub-section of the given section. Any additional requirement specified in the sub-section should be read together with the requirements indicated in the main section.	
Number		Conditions	Documents to be provided
41	Change in the shelf-life or to an approved stability protocol of the finished product:	The change shall not be the result of unexpected events arising during manufacture or because of stability concerns.	Amendment of the relevant section(s) of the dossier.
a)	— reduction of the shelf life of the finished product as packaged for sale, after first opening or after dilution or reconstitution		
b)	— change to an approved stability protocol	The change shall not have the potential to affect the identity, strength, quality, purity, potency or physical characteristics of the finished product. The change shall not concern a widening of the acceptance criteria in the parameters tested, a removal of stability indicating parameters or a reduction in the frequency of testing.	
42	Implementation in practice of changes already foreseen in an approved change management protocol (CMP) for the finished product	The change shall be in accordance with the approved CMP and the results of studies performed indicate that the predefined acceptance criteria specified in the protocol are meet. The implementation of the change shall require no further supportive data to the CMP.	
43	Editorial changes to part 2 of the dossier if inclusion in an upcoming procedure concerning part 2 is not possible		Comparative table of the changes to the dossier.

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	Variation	Requirements The requirements indicated in the line for the main section are valid for each sub-section of the given section. Any additional requirement specified in the sub-section should be read together with the requirements indicated in the main section.	
Number		Conditions	Documents to be provided
▼M3 44	Submission of a Ph. Eur. CEP for: — active substance; — starting material, reagent or intermediate used in the manufacturing process of the active substance; — excipient	The finished product release and end of shelf life specifications shall remain the same. Unchanged (excluding tightening) additional (to Ph. Eur.) specifications for impurities (excluding residual solvents, provided they are in compliance with ICH/VICH) and product specific requirements (e.g. particle size profiles, polymorphic form), if applicable. For active substance only, it will be tested immediately prior to use if no retest period is included in the Ph. Eur. Certificate of Suitability or if data to support a retest period is not already provided in the dossier. For a herbal substance or a herbal preparation, the manufacturing route, physical form, extraction solvent and drug extract ratio (DER) shall remain the same. The manufacturer shall already be approved and incorporated in the Union IT systems storing and providing organisational data (not applicable for starting material, reagent and excipient manufacturers/ suppliers).	Amendment of the relevant section(s) of the dossier, including a copy of the updated Ph. Eur. CEP and QP declaration, as appropriate.
a)	Updated certificate	The manufacturing process of the active substance, starting material, reagent, intermediate or excipient shall not include the use of material from human or animal origin, or if it does, any information in relation to material from human or animal origin shall remain unchanged. If the active substance is not a sterile substance but is to be used in a sterile veterinary medicinal product, in accordance with the CEP, the manufacturing process shall not include the use of water during the last steps of the synthesis, or if it does, the quality of water used in the last step of the synthesis shall be unchanged compared to the previous version of the CEP submitted.	

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	Variation	Requirements The requirements indicated in the line for the main section are valid for each sub-section of the given section. Any additional requirement specified in the sub-section should be read together with the requirements indicated in the main section.	
Number		Conditions	Documents to be provided
b)	New certificate	The manufacturing process of the active substance, starting material, reagent, intermediate or excipient shall not include the use of material from human or animal origin. The active substance/starting material/reagent/intermediate/excipient is not sterile. If the active substance is not a sterile substance but is to be used in a sterile veterinary medicinal product, in accordance with the CEP the manufacturing process shall not include the use of water during the last steps of the synthesis, or if it does, the active substance shall be free from bacterial endotoxins.	
———			
46	Submission of an updated Ph. Eur. TSE CEP of an already approved manufacturer for: — active substance; — starting material, reagent, intermediate used in the manufacturing process of the active substance; — excipient	There has been no change in the source of material. The viral risk assessment is unchanged. If gelatine manufactured from bones is to be used in a veterinary medicinal product for parenteral use, it shall only be manufactured in compliance with the relevant requirements. The manufacturer shall already be approved and incorporated in the Union IT systems storing and providing organisational data (not applicable for starting material, reagent and excipient manufacturers/suppliers).	Amendment of the relevant section(s) of the dossier, including a copy of the updated Ph. Eur. CEP and QP declaration, as appropriate. Where applicable, a document providing information of any materials falling within the scope of the Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products including those which are used in the manufacture of the active substance/excipient. The following information shall be included for each such material: Name of manufacturer, species and tissues from which the material is a derivative, country of origin of the source animals and its use. That information shall be included in an updated TSE table A (and B, if relevant).

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	Variation	Requirements The requirements indicated in the line for the main section are valid for each sub-section of the given section. Any additional requirement specified in the sub-section should be read together with the requirements indicated in the main section.	
Number		Conditions	Documents to be provided
47	Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State:	The change shall be made exclusively to fully comply with the pharmacopoeia. All the tests in the specification shall correspond to the pharmacopoeial standard after the change, except any additional tests. Additional validation of a new or changed pharmacopoeial method shall not be required. For a herbal substance or a herbal preparation the manufacturing route, physical form, extraction solvent and drug extract ratio (DER) shall remain the same.	Amendment of the relevant section(s) of the dossier ([4]). Comparative table of the former and new specifications, if applicable.
a)	— change of specification(s) of a former non EU Pharmacopoeial active substance, excipient or active substance starting material to fully comply with the Ph. Eur. or with a national pharmacopoeia of a Member State	Additional specifications to the pharmacopoeia for product specific properties shall be unchanged (e.g. particle size profiles, polymorphic form, bioassays or aggregates). The change shall not concern significant changes in qualitative and quantitative impurities profile unless the specifications are tightened.	Batch data and data demonstrating the suitability of the monograph to control the substance.

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Number	Variation	Requirements The requirements indicated in the line for the main section are valid for each sub-section of the given section. Any additional requirement specified in the sub-section should be read together with the requirements indicated in the main section.	
		Conditions	Documents to be provided
b)	— change to comply with an update of the relevant monograph of the Ph. Eur. or national pharmacopoeia of a Member State	Additional specifications to the pharmacopoeia for product specific properties shall be unchanged (e.g. particle size profiles, polymorphic form, bioassays or aggregates).	
c)	— change in specifications from a national pharmacopoeia of a Member State to the Ph. Eur.		Amendment of the relevant section(s) of the dossier, including batch data and data demonstrating the suitability of the monograph to control the substance.
d)	— to reflect compliance with the Ph. Eur. by removing reference to the internal test method and test method number		
48	Addition or replacement of a measuring or administration device which is not an integrated part of the primary packaging	The change shall not affect the delivery, use, safety or stability of the finished product. The change shall be only applicable to a device with CE marking. The new measuring or administration device shall accurately deliver the required dose for the product concerned in line with the approved posology, and results of such studies shall be available. The new device shall be compatible with the veterinary medicinal product. The change shall not lead to substantial amendments of the product information.	Amendment of the relevant section(s) of the dossier.

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	Variation	Requirements The requirements indicated in the line for the main section are valid for each sub-section of the given section. Any additional requirement specified in the sub-section should be read together with the requirements indicated in the main section.	
Number		Conditions	Documents to be provided
49	Change in specification parameters or limits of a measuring or administration device:	The change shall not be a consequence of any commitment from previous assessments to review specification limits (e.g. made during the procedure for the marketing authorisation application or a variation procedure according to Article 62 of Regulation (EU) 2019/6) unless it has been previously assessed and agreed as part of a follow-up measure in a previous procedure under Regulation (EU) 2019/6. The change shall not be the result of unexpected events arising during manufacture.	Amendment of the relevant section(s) of the dossier. Comparative table of former and new specification parameters and limits.
a)	— tightening of specification limits	The change shall be within the range of currently approved limits. The test procedure shall remain the same, or changes in the test procedure shall be minor.	
b)	— addition of a new specification parameter to the specification with its corresponding test method	Any new test method shall not concern a novel non-standard technique or a standard technique used in a novel way.	Amendment of the relevant section(s) of the dossier for method and validation and batch data.
50	Change in test procedure (including replacement or addition) of a measuring or administration device	Appropriate validation studies shall have been performed in accordance with the relevant guidelines and show that the updated test procedure is at least equivalent to the former test procedure. Any new test method shall not concern a novel non-standard technique or a standard technique used in a novel way.	Amendment of the relevant section(s) of the dossier for method and validation and batch data.
51	Update of the quality dossier intended to implement the outcome of a Union interest referral procedure according to Article 83 of Regulation (EU) 2019/6:	This change shall only be applicable when no new or additional data is required for an assessment.	Amendment of the relevant section(s) of the dossier.

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	Variation	Requirements The requirements indicated in the line for the main section are valid for each sub-section of the given section. Any additional requirement specified in the sub-section should be read together with the requirements indicated in the main section.	
Number		Conditions	Documents to be provided
a)	— the finished product is covered by the defined scope of the procedure		
b)	— the finished product is not covered by the defined scope of the procedure but the change(s) implements the outcome of the procedure		
C	**Changes to the safety, efficacy and pharmacovigilance part of the dossier**		
1	Change(s) in the name or address or contact details of a qualified person for pharmacovigilance (QPPV)		
2	Change(s) in the Summary of Product Characteristics (SPC), labelling or package leaflet intended to implement the outcome of a Union interest referral procedure according to Article 83 of Regulation (EU) 2019/6	The veterinary medicinal product shall be covered by the defined scope of the referral. This change shall only be applicable when no new or additional data is required for an assessment. The proposed Summary of Product Characteristics, Labelling and Package Leaflet shall be identical for the concerned sections to that annexed to the Commission Decision on the referral procedure for the reference medicinal product.	
3	Change(s) in the SPC, labelling or package leaflet of a generic or hybrid medicinal product following assessment of the same change(s) for the reference product	This change shall only be applicable when no new or additional data is required for an assessment. The proposed changes to Summary of Product Characteristics, Labelling and Package Leaflet shall be identical to those changes approved for the reference medicinal product. The reference product shall be approved in the Member State concerned.	

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	Variation	Requirements The requirements indicated in the line for the main section are valid for each sub-section of the given section. Any additional requirement specified in the sub-section should be read together with the requirements indicated in the main section.	
Number		Conditions	Documents to be provided
▼M3 4	Change(s) in the SPC, labelling or package leaflet intended to implement the outcome of a procedure or recommendation from the competent authority or the Agency concerning risk management measures in pharmacovigilance related to veterinary medicinal products	This change shall only be applicable when no new or additional data is required for an assessment. The proposed changes to Summary of Product Characteristics, Labelling and Package Leaflet shall be identical to wording agreed by the competent authority or the Agency.	Reference to the agreement/assessment of the competent authority or the Agency.
▼B 5	Change in the pharmacovigilance system master file (PSMF) location		
6	Introduction of a summary of the PSMF or changes to the summary of the PSMF not already covered elsewhere in this Annex		Summary of pharmacovigilance system master file according to Article 8(1)(c) of Regulation (EU) 2019/6.
▼M3 7	Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the risk management plan	The wording shall be limited to that agreed by the competent authority or the Agency.	Reference to the agreement/assessment of the competent authority or the Agency.
▼B 8	Implementation of changes in the SPC not already covered elsewhere in this Annex	This change shall only be applicable when no new or additional data is required for an assessment. The changes shall not affect the quality, safety or efficacy of the product. Changes shall be minor in nature and shall be consistent with the information currently included in the SPC.	
9	Editorial changes to SPC, package leaflet or labelling if inclusion in an upcoming procedure is not possible	The changes shall not affect the quality, safety or efficacy of the medicinal product.	

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	Variation	Requirements The requirements indicated in the line for the main section are valid for each sub-section of the given section. Any additional requirement specified in the sub-section should be read together with the requirements indicated in the main section.	
Number		Conditions	Documents to be provided
10	Changes to the labelling or the package leaflet which shall not be connected with the SPC:		
▼M4 a)	— administrative information concerning the holder's representative or the distributor(s) ([7])		
▼B b)	— other changes	Changes shall be minor in nature and shall be consistent with the information included in the SPC. The change shall not include the introduction of new batch release sites. Changes shall not be promotional in nature and shall not have a negative impact on the legibility of the product information.	
c)	— inclusion of traceability stickers in or on product carton	Addition shall not have a negative impact on the legibility of the product information.	
▼M3 d)	— replacement of information on the immediate or outer packaging by an abbreviation or pictogram (including initial addition) — replacement of an existing abbreviation or pictogram on the immediate or outer packaging that is not compliant with Commission Implementing Regulation (EU) 2024/875 ([5]) by another abbreviation or pictogram	The new abbreviation or pictogram is included in Annex I or Annex II to Implementing Regulation (EU) 2024/875. The addition does not have a negative impact on the readability of the labelling.	
▼M2 e)	Alignment of the labelling of the immediate packaging with the requirements laid down in Article 12 of Regulation (EU) 2019/6	The packaging qualifies as a small immediate packaging unit under Commission Implementing Regulation (EU) 2024/878 adopting uniform rules on the size of small immediate packaging units of veterinary medicinal products as referred to in Article 12 of Regulation (EU) 2019/6 of the European Parliament and of the Council (OJ L, 2024/878, 22.3.2024, ELI: http://data.europa.eu/eli/reg_impl/2024/878/oj).	

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	Variation	Requirements The requirements indicated in the line for the main section are valid for each sub-section of the given section. Any additional requirement specified in the sub-section should be read together with the requirements indicated in the main section.	
Number		Conditions	Documents to be provided
▼M3 f)	Alignment of the product information with the requirements laid down in article 9 of Commission Delegated Regulation (EU) 2024/1159 ([6])	This change shall only be applicable when no new or additional data is required for an assessment.	
▼B D	**Changes to the vaccine antigen master file (VAMF) part of the dossier**		
▼M3 1	Change in the name or address of the VAMF certificate holder for biological products	The VAMF certificate holder shall remain the same legal entity.	Amendment of the relevant section(s) of the dossier, as appropriate.
▼B 2	Inclusion of an already certified VAMF in the marketing authorisation dossier of a veterinary medicinal product. (VAMF 2*nd* step procedure)	Changes shall not affect the properties of the finished product.	Amendment of the relevant section(s) of the dossier.

([1]) As per EDQM standard terms the system of names and terms published by the EDQM for marketing authorisation applications.
([2]) In cases where a given pharmaceutical form or strength has received an individual marketing authorisation which is separate to the marketing authorisation for other pharmaceutical forms or strengths of the same product, the deletion of the former will not be a variation but the withdrawal of the marketing authorisation.
([3]) In cases where a given pack size has received an individual marketing authorisation which is separate to the marketing authorisation for other pack sizes of the same product, the change of the former will not be a variation according to Article 61, but a variation according to Article 62 of Regulation (EU) 2019/6.
([4]) There is no need to notify the competent authorities of an updated monograph of the European pharmacopoeia or a national pharmacopoeia of a Member State in the case that reference is made to the 'current edition' in the dossier of an authorised medicinal product. Applicants are reminded that compliance with the updated monograph should be implemented within six months. If implementation does not occur within 6 months from the publication date, this variation applies.
([5]) Commission Implementing Regulation (EU) 2024/875 of 21 March 2024 adopting a list of abbreviations and pictograms common throughout the Union to be used on the packaging of veterinary medicinal products for the purposes of Article 10(2) and Article 11(3) of Regulation (EU) 2019/6 of the European Parliament and of the Council (OJ L, 2024/875, 22.3.2024, ELI: http://data.europa.eu/eli/reg_impl/2024/875/oj).
([6]) Commission Delegated Regulation (EU) 2024/1159 of 7 February 2024 supplementing Regulation (EU) 2019/6 of the European Parliament and of the Council by laying down rules on appropriate measures to ensure the effective and safe use of veterinary medicinal products authorised and prescribed for oral administration via routes other than medicated feed and administered by the animal keeper to food-producing animals (OJ L, 2024/1159, 19.4.2024, ELI: http://data.europa.eu/eli/reg_del/2024/1159/oj).
([7]) The reference to a change in the administrative information of the distributor(s) applies only in those cases where the competent authority has allowed, in accordance with Regulation (EU) 2019/6, the inclusion of the information on the distributor(s).