B.III CEP/TSE/MONOGRAPHS

B. III.1 Submission of a new or updated Ph. Eur. certificate of suitability or deletion of Ph. Eur. certificate of suitability: For an active substance For a starting material/reagent/intermediate used in the manufacturing process of the active substance For an excipient	Conditions to be fulfilled	Documentation to be supplied	Procedure type
a) European Pharmacopoeial Certificate of Suitability to the relevant Ph. Eur. Monograph.			
1. New certificate from an already approved manufacturer	1, 2, 3, 4, 5, 8, 11	1, 2, 3, 4, 5	IA_{IN}
2. Updated certificate from an already approved manufacturer (no new manufacturing site)	1, 2, 3, 4, 8	1, 2, 3, 4,	IA
3. New certificate from a new manufacturer (replacement or addition)	1, 2, 3, 4, 5, 8, 11	1, 2, 3, 4, 5	IA_{IN}
4. Updated certificate from an already approved manufacturer (includes new manufacturing site)	1, 2, 3, 4, 8	1, 2, 3, 4, 5	IA_{IN}
5. Deletion of certificates (in case multiple certificates exist per material)	10	3	IA
6. New certificate for a non sterile active substance that is to be used in a sterile medicinal product, where water is used in the last steps of the synthesis and the material is not claimed to be endotoxin free		1, 2, 3, 4, 5, 6	IB
b) European Pharmacopoeial TSE Certificate of suitability for an active substance/starting material/reagent/ intermediate/or excipient			
1. New certificate for an active substance from a new or an already approved manufacturer	3, 5, 6, 11	1, 2, 3, 4, 5	IA_{IN}
2. New certificate for a starting material/reagent/ intermediate/or excipient from a new or an already approved manufacturer	3, 6, 9	1, 2, 3, 4, 5	IA
3. Updated certificate from an already approved manufacturer	7, 9	1, 2, 3, 4, 5	IA
4. Deletion of certificates (in case multiple certificates exist per material)	10	3	IA

	5. New/updated certificate from an already-approved/new manufacturer using materials of human or animal origin for which an assessment of the risk with respect to potential contamination with adventitious agents is required			II

Conditions

1.	The finished product release and end of shelf life specifications remain the same.
2.	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.
3.	The manufacturing process of the active substance, starting material/reagent/intermediate does not include the use of materials of human or animal origin for which an assessment of viral safety data is required.
4.	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.
5.	The active substance/starting material/reagent/intermediate/excipient is not sterile.
6.	The substance is not included in a veterinary medicinal product for use in animal species susceptible to TSE.
7.	For veterinary medicinal products: there has been no change in the source of material.
8.	For herbal active substances: the manufacturing route, physical form, extraction solvent and drug extract ratio (DER) should remain the same.
9	If Gelatin is to be used in a medicinal product that is for parenteral use, if manufactured from bones, it should **only** be manufactured in compliance country requirements as stated in the Note for Guidance for minimising the risk transmitting animal spongiform encephalopathy (EMA/410/01 current revision).
10.	At least one manufacturer for the same substance remains in the dossier.
11.	If the active substance is a not a sterile substance but is to be used in a sterile medicinal product then according to the CEP it must not use water during the last steps of the synthesis or if it does the active substance must also be claimed to be free from bacterial endotoxins.

Documentation

1.	Copy of the proposed Ph. Eur. Certificate of Suitability.
2.	In case of an addition of a manufacturing site, the variation application form should clearly outline the "present" and "proposed" manufacturers as listed in section 2.5 of the application form for marketing authorisation.

Administrator
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Documentation ... [14]

Administrator
Supprimé: Copy of the current (updated) Ph. Eur. Certificate of Suitability.

Administrator
Mis en forme: CM3

Administrator
Supprimé: In case of an addition of a manufacturing site, the variation application form should clearly outline the "present" and "proposed" manufacturers as listed in section 2.5 of the (Part IA) application form.

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3.	Amendment of the relevant section(s) of the dossier (presented in the EU-CTD format.
4.	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 should 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. For the Centralised Procedure, this information should be included in an updated TSE table A (and B, if relevant).
5.	Where applicable, for active substance - a declaration by the Qualified Person (QP) of each of the manufacturing authorisation holders listed in the application where the active substance is used as a starting material and a declaration by the QP of each of the manufacturing authorisation holders listed in the application as responsible for batch release. These declarations should state that the active substance manufacturer(s) referred to in the application operate in compliance with the detailed guidelines on good manufacturing practice for starting materials. A single declaration may be acceptable under certain circumstances - see the note under variation no. B.II.b.1. The manufacture of intermediates also require a QP declaration, while as far as any updates to certificates for active substances and intermediates are concerned, a QP declaration is only required if, compared to the previously registered version of the certificate, there is a change to the actual listed manufacturing sites.
6.	Suitable evidence to confirm that the water used in the final steps of the synthesis of the active substance complies with NfG on quality of water for pharmaceutical use (CPMP/QWP/158/01 Rev or EMEA/CVMP/115/01 Rev).

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B.III.2 Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State	**Conditions to be fulfilled**	**Documentation to be supplied**	**Procedure type**
a) Change of specification(s) of a former non EU Pharmacopoeial substance to fully comply with the Ph. Eur. or with a national pharmacopoeia of a Member State			
1. Active substance	**1, 2, 3, 4, 5**	**1, 2, 3, 4, 5**	**IA_{IN}**
2. Excipient/active substance starting material	**1, 2,4**	**1, 2, 3, 4, 5**	**IA**
b) Change to comply with an update of the relevant monograph of the Ph. Eur. or national pharmacopoeia of a Member State	**1, 2, 4, 5**	**1, 2, 3, 4, 5**	**IA**
c) Change in specifications from a national pharmacopoeia of a Member State to the Ph. Eur.	**1, 4, 5**	**1, 2, 3, 4, 5**	**IA**

Conditions

1.	The change is made exclusively to fully comply with the pharmacopoeia. All the tests in the