

Comments Concerning Revised Texts Published in Supplement 7.1

Here follows information concerning technical modifications to revised texts adopted by the European Pharmacopoeia Commission at the March 2010 session. This information completes the modifications indicated by lines in the margin. Therefore, the information below is not necessarily exhaustive.

GENERAL TEXTS

2.6.1. Sterility

This chapter has been revised to indicate its status within the context of pharmacopoeial harmonisation, a collaboration between the JP, the USP and the Ph. Eur.

A footnote has been included in the text to refer to chapter 5.8. *Pharmacopoeial harmonisation*. For information, this chapter has reached step 5: Implementation of ICH-Q4B Process (Q4B Annex 8: Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions on Sterility Test General Chapter) and is now interchangeable in the ICH regions.

2.9.1. Disintegration of tablets and capsules

This chapter has been revised to indicate its status within the context of pharmacopoeial harmonisation, a collaboration between the JP, the USP and the Ph. Eur.

A footnote has been included in the text to refer to chapter 5.8. *Pharmacopoeial harmonisation* and to indicate that a specific symbol (♦♦) is used to highlight non-harmonised provisions agreed by the 3 pharmacopoeias.

For information, this chapter has reached Step 5: Implementation of ICH-Q4B Process (Q4B Annex 5: Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions on Disintegration Test General Chapter).

2.9.19. Particulate contamination: sub-visible particles

This chapter has been revised to indicate its status within the context of pharmacopoeial harmonisation, a collaboration between the JP, the USP and the Ph. Eur.

A footnote has been included in the text to refer to chapter 5.8. *Pharmacopoeial harmonisation* and to indicate that a specific symbol (♦♦) is used to highlight non-harmonised provisions agreed by the 3 pharmacopoeias.

For information, this chapter has reached Step 5: Implementation of ICH-Q4B Process (Q4B Annex 3: Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions on Test for Particulate Contamination: Sub-Visible Particles General Chapter).

5.8. Pharmacopoeial harmonisation

The chapter has been revised within the framework of pharmacopoeial harmonisation. Information regarding general chapters 2.6.1, 2.9.1 and 2.9.19 has been added following the publication of ICH Q4B annexes: Annex 8: Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions on Sterility Test General Chapter; Annex 5: Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions on Disintegration Test General Chapter; and Annex 3: Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions on Test for Particulate Contamination: Sub-Visible Particles General Chapter.

DOSAGE FORMS

Ear preparations (0652)

Definition: sterile ear drop solutions that are supplied in a multidose container and which contain a preservative are now marketed. Consequently, the monograph has been revised to take such cases into consideration by adding the

phrase 'unless otherwise justified and authorised' to the corresponding paragraph.

Ear powders: more information on the administration is given in the definition.

HERBAL DRUGS AND HERBAL DRUG PREPARATIONS

Bearberry leaf (1054)

Identification B: illustration of powdered herbal drug introduced and its legend integrated into text of Identification B.

Cascara (0105)

Definition: scientific name updated.

Identification B: illustration of powdered herbal drug introduced and its legend integrated into text of Identification B.

Cinnamon (0387)

Definition: author part of scientific name and part of plant used updated.

Identification B: illustration of powdered herbal drug introduced and its legend integrated into text of Identification B.

Cinnamon bark oil, Ceylon (1501)

Definition: author part of scientific name updated.

Couch grass rhizome (1306)

Identification B: illustration of powdered herbal drug introduced and its legend integrated into text of Identification B.

Fennel, sweet (0825)

Definition: author part of scientific name updated.

Identification B: illustration of powdered herbal drug introduced and its legend integrated into text of Identification B.

Frangula bark (0025)

Identification B: illustration of powdered herbal drug introduced and its legend integrated into text of Identification B.

Identification C: description of detection method corrected.

Lavender flower (1534)

Linseed (0095)

Identification B: illustration of powdered herbal drug introduced and its legend integrated into text of Identification B.

Valerian dry hydroalcoholic extract (1898)

Production: the range of ethanol used for production has been widened to cover all licensed products on the market.

Assay: to harmonise with the monograph *Valerian dry aqueous extract (2400)*, hydroxyvalerenic acid has been included in the calculation of sesquiterpenic acids; the gradient profile has been slightly modified.

Wormwood (1380)

Identification B: illustration of powdered herbal drug introduced and its legend integrated into text of Identification B.

HOMOEOPATHIC PREPARATIONS

Herbal drugs for homoeopathic preparations (2045)

This monograph has been revised to be in line with the monograph *Herbal drugs (1433)* published in Supplement 6.8.

Definition: changes to the terminology used in the individual monographs on herbal drugs for homoeopathic preparations have been stated to clarify the respective scopes.

Pesticides: since the annex to general method 2.8.13. *Pesticide residues* was deleted in Supplement 6.2, reference to this annex has been deleted.

Heavy metals: introduction of limits reflecting current regulatory practice.

Aflatoxins: where relevant, limits for aflatoxins may be provided in individual monographs as is the case for ochratoxin A.

Ochratoxin A: reference is made to the general method on ochratoxin A (2.8.22). Where relevant, limits for ochratoxin A may be provided in individual monographs.

MONOGRAPHS

Cetostearyl alcohol (type A), emulsifying (0801) Cetostearyl alcohol (type B), emulsifying (0802)

Assay of cetostearyl alcohol: since heptadecanol of a purity suitable for CRS purposes is no longer available, another internal standard is now used (1-nonadecanol); a simplified method still using *cetyl alcohol CRS* and *stearyl alcohol CRS* for the quantification of cetostearyl alcohol has been developed.

Chlorambucil (0137)

Identification: IR considered sufficient; 2nd identification deleted as substance not used in pharmacies or hospitals.

Related substances: TLC replaced by 2 LCs in accordance with current policy.

Impurities: section added describing impurities controlled by LC.

Ciprofloxacin hydrochloride (0888)

Related substances: run time extended to allow control of additional late eluting impurities; limit for impurity E increased; wording of limit for unspecified impurities aligned with general monograph *Substances for pharmaceutical use (2034)*.

Citalopram hydrobromide (2288)

Related substances: based on current batch data, impurity F now listed as unspecified impurity and determination of unspecified impurities performed only at 230 nm.

Etoposide (0823)

Characters: substance described as slightly hygroscopic.

Related substances: in accordance with current policy on impurities, the following modifications have been made: relative retentions as well as a suitable CRS for the identification of specified impurities have been introduced; new system suitability criteria focusing on the most critical peak pairs have been introduced; correction factor introduced for impurity O; 4 new impurities (O, P, Q and R) added to the transparency list; according to batch data available, only impurities B, C, D, E, N and O are specified with limits higher than 0.10 per cent.

Heavy metals: test C replaced by test G.

Impurities: section updated.

Flecainide acetate (1324)

Related substances: 1st isocratic step added to gradient; relative retentions of specified impurities and use of *flecainide for system suitability* CRS introduced for peak identification purposes; use of end-capped column prescribed to obtain good elution profile for all impurities; system suitability criterion modified to focus on most critical peak pair; limit for unspecified impurities introduced; disregard limit increased to 0.05 per cent in accordance with general monograph *Substances for pharmaceutical use (2034)*.

Storage: storage in airtight containers prescribed due to hygroscopicity.

Gentamicin sulfate (0331)

Composition, Related substances: revision of the LC tests.

Impurities: impurity C is no longer considered as specified.

Lovastatin (1538)

Related substances: the new specified impurity F has been introduced and qualified at 0.15 per cent, to take account of an additional source of this substance on the European market; the system suitability criterion for resolution has been replaced by a peak-to-valley ratio between the more critical pair of peaks, impurity F and lovastatin.

Nadolol (1789)

Related substances: test solution prepared directly in solvent mixture for stability reasons; CRS mixture for identification of impurities introduced; gradient and column modified to elute all impurities; relative retentions, correction factor and system suitability requirement updated; list of specified impurities and limits modified in view of batch data of substances from current production.

Norfloxacin (1248)

Related substances: a new specified impurity (impurity K) has been introduced and qualified at 0.15 per cent to take into account an additional source of this substance on the European market.

Noscapine (0516)**Noscapine hydrochloride (0515)**

Related substances: the test solution is prepared in methanol as the substance is more stable in this solvent; the injection volume has been decreased and the concentrations of the respective solutions have been adapted accordingly.

Oleyl alcohol (2073)

Refractive index: the acceptance range has been widened because it was found to be too narrow with respect to the results found when analysing current production batches.

Phenobarbital (0201)

Identification C: replacement of chloroform by the less toxic methylene chloride.

Related substances: TLC replaced by LC in accordance with current policy.

Assay: modified in order to avoid the use of pyridine.

Impurities: a section describing the impurities controlled by the LC has been added.

Phenytoin sodium (0521)

Identification: the former identification B has been replaced by a TLC method as identifications B and C alone were insufficient for the 2nd identification series.

Related substances: limit for impurity D has been raised to 0.15 per cent.

Rifaximin (2362)

Impurities: the structure of impurity H has been modified in view of the results of a structure elucidation reported in literature (R. Stradi *et al.*, Structural elucidation of the Rifaximin Ph. Eur. Impurity H, *Journal of Pharmaceutical and Biomedical Analysis* 51 (2010), pp. 858-65).

Sodium cetostearyl sulfate (0847)

Free cetostearyl alcohol, Assay: since heptadecanol of a purity suitable for CRS purposes is no longer available, another internal standard is now used (1-nonadecanol); a simplified method still using *cetyl alcohol* CRS and *stearyl alcohol* CRS for the quantification of cetostearyl alcohol and sodium cetostearyl sulfate has been developed.

Sodium cromoglicate (0562)

Identification B: description of sample preparation deleted in accordance with current policy.

Related substances: TLC replaced by LC in accordance with current policy.

Heavy metals: method C replaced by method F in accordance with current policy.

Assay: dioxan replaced by another less-harmful solvent.

Impurities: section added describing the impurities controlled by LC.

Testosterone enantate (1048)

Specific optical rotation: dioxan replaced by less-toxic anhydrous ethanol; limits adjusted accordingly.

Impurity A: wording harmonised with Free acid test in *Testosterone decanoate (1736)*.

Related substances: TLC and LC revised to detect relevant impurities in view of current production quality; transparency list updated.

Tolnaftate (1158)

Impurity D: symmetry factor outside default range of chapter 2.2.46 defined.

Verapamil hydrochloride (0573)

Related substances: description of column takes account of availability of stationary phases with increased separation capability; limit for unspecified impurities aligned with general monograph *Substances for pharmaceutical use (2034)* and disregard limit increased.