

Certification of Substances Division

IMPLEMENTATION OF THE EUROPEAN PHARMACOPOEIA SUPPLEMENT 6.3

Dear Sir or Madam,

Supplement 6.3 of the European Pharmacopoeia, including a number of revised monographs, will be implemented on 1 January 2009.

You hold a certificate or an application for certificate of suitability for a substance for which a revised monograph has been published (section 'REVISED TEXTS', see enclosed list). It is your responsibility to update specifications and test procedures for concerned pharmaceutical substances in order to implement the new version or any corrected text of the monograph in due time. You should proceed as follows:

- Amendments to the monograph (e.g. preparation of a reference solution, deletion of an identification test, ...) that do not require you to submit additional documents : Substances concerned by such amendments are annotated in the attached list with a '1'. A reply to this letter is not necessary.
- Amendments to the monograph that, as laid down in Resolution AP-CSP (07) 1, require updating of the Certification file to demonstrate whether, the substance complies with the new requirements of the monograph; the extent of information to be provided depends on the actual changes/modifications in the sections "Production" or "Tests": Updated substance specifications referring to the revised monograph and certificates of analysis of 2 batches based on new instructions should be submitted which is annotated in the attached list with a '2'.

Where further supporting documentation is necessary to cover the impurity profile of your substance, this is annotated in the attached list with a '3'. In this case, the documents requested as mentioned under '2' should also be provided and completed with chromatograms, cross-validation with in-house methods, comparison of impurity profile with the transparency list etc.

If the requested information has already been presented this should be indicated in your reply.

In cases '2' and '3' you are expected to reply to this request and provide the supporting documents within three months.

Upon receipt, the updated documentation will be reviewed and you will be informed of the outcome of the evaluation.

Failure to reply to this request and to comply with the above requirements may lead to the suspension of the concerned granted certificate/s, or to delay the on-going evaluation process of the concerned application.

This procedure is free of charge, unless you submit, at the same time, a request for revision or renewal of the concerned certificate of suitability, when granted.

Yours faithfully,

Certification of Substances Division

Enclosure: List of revised texts of the European Pharmacopoeia Supplement 6.3 for implementation 1 January 2009 and their classification.

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EDQM – Certification of Substances Division

	Case No 1	Case No 2	Case No 3
Aluminium phosphate gel (2166) *	X		
Amphotericin B (1292)			X
Aprotinin (0580)			X
Aprotinin concentrated solution (0579)			X
Ascorbic acid (0253)			X
Beclometasone dipropionate, anhydrous (0654)			X
Betamethasone valerate (0811)			X
Calcium folinate (0978)	X		
Calcium gluconate (0172) *	X		
Calcium gluconate for injection (0979) *	X		
Calcium stearate (0882) *	X		
Cellulose, microcrystalline (0316) *	X		
Chondroitin sulphate sodium (2064) *	X		
Cisplatin (0599)			X
Croscarmellose sodium (0985) *	X		
Crospovidone (0892)		X	
Dextran 1 for injection (1506) *	X		
Dextran 40 for injection (0999) *	X		
Dextran 60 for injection (1000) *	X		
Dextran 70 for injection (1001) *	X		
Ferrous gluconate (0493) *	X		
Galactose (1215) *	X		
Gelatin (0330) *	X		
Lactulose (1230) *	X		
Lactulose, liquid (0924) *	X		
Magnesium oxide, heavy (0041)		X	

	Case No 1	Case No 2	Case No 3
Magnesium stearate (0229) *	X		
Mannitol (0559) *	X		
Mefenamic acid (1240)			X
Methotrexate (0560)	X		
Mianserin hydrochloride (0846)			X
Nicotine (1452)			X
Nicotine resinate (1792)			X
Omega-3-acid ethyl esters 60 (2063)	X		
Omega-3-acid triglycerides (1352)	X		
Oxaliplatin (2017)	X		
Oxymetazoline hydrochloride (0943)			X
Paclitaxel (1794) *	X		
Pancreas powder (0350) *	X		
Pravastatin sodium (2059)			X
Sodium ascorbate (1791)			X
Sodium hyaluronate (1472) *	X		
Sorbitol (0435) *	X		
Sumatriptan succinate (1573)	X		
Tryptophan (1272)	X		

*** Within this monograph, the Microbial contamination test has been revised:**

The implementation of the internationally harmonised chapters 2.6.12, 2.6.13 and 5.1.4 required the revision of the acceptance criteria and the style used in Supplement 6.3 of Ph. Eur.

The general chapters “Microbiological examination of non-sterile products – Microbial enumeration tests” (2.6.12) and “Microbiological examination of non-sterile products – Tests for specified micro-organisms” (2.6.13) presents 2 sets of tests. The 2 sets of tests are considered to be equivalent. Either set of tests can be used until 31 December 2008. As of 1 January 2009 the 2nd set of tests is to be used as the Ph. Eur. reference method.

For CEP applications, notifications, including an updated specification for all products concerned, will not be requested. However, when submitting a quality related variation application for another reason it is recommended to include the updated specification (with the implemented harmonised acceptance criteria/method).