

Comments concerning texts published in Supplement 11.6

Brief descriptions of the modifications that have been made to new, revised and corrected texts adopted by the European Pharmacopoeia Commission at the November session and published in Supplement 11.6 are provided below. Please note that these descriptions are not provided systematically for new and corrected texts, but are instead provided on a case-by-case basis. This information is reproduced in the Knowledge database under View history.

All revised, corrected or deleted parts of a text published in the online version of the European Pharmacopoeia are now indicated by change marks in the form of triangles. For reasons of readability, these triangles are not shown in the print version, but users will still be able to determine if a text has been corrected or revised from the version date indicated above the title of the monograph and, if applicable, by 'corrected X.X', indicating publication of a corrected version in Supplement X.X.

GENERAL CHAPTERS

2.2.46. Chromatographic separation techniques

Adjustment of chromatographic conditions (isocratic and gradient elution): clarification of the requirement for internal diameter.

2.6.12. Microbiological examination of non-sterile products: microbial enumeration tests

Results and interpretation: clarification of the reading procedure to be performed when verifying the suitability of the membrane filtration method.

3.1.14. Materials based on plasticised poly(vinyl chloride) for containers for aqueous solutions for intravenous infusion

Additives: addition of an explanatory note on the sunset date for the use of plastic additive 01 in immediate packaging materials for medicinal products.

Plastic additive 01: clarification of the approach for the Identification and Tests sections.

5.22. Names of herbal drugs used in traditional Chinese medicine

Table updated to include 2 new monographs.

GENERAL MONOGRAPHS

Allergen products (1063)

Tests. Individual allergens: an instruction to use a Ph. Eur. analytical procedure, when available, has been added.

Labelling: a recommendation to include the individual allergen content on labels when an individual allergen-specific reference standard and a Ph. Eur. analytical procedure are available has been added. It is considered that providing information on the individual allergen content is beneficial for the allergen field and would allow for more transparency on the content of these products, since their efficacy and safety are affected both by the individual allergen content, in addition to the other allergens and product formulations.

Editorial modifications have been made throughout the text for clarification.

DOSAGE FORMS

Eye preparations (1163)

The revision emphasises the requirement to test that liquid eye preparations (e.g. solutions, suspensions and emulsions) are practically free from visible particles and reflects current practice with the following additions:

Production: addition of a statement that liquid eye preparations are practically free from visible particles, including a reference to general chapter 5.17.2. *Recommendations on testing of particulate contamination: visible particles.*

Eye drops and Eye lotions: addition of the test for visible particles according to general chapter 2.9.20 to the Tests sections, including a reference to general chapter 5.17.2. *Recommendations on testing of particulate contamination: visible particles.*

Preparations for irrigation (1116)

The proposed revision emphasises the requirement to test that preparations for irrigation are practically free from visible particles and reflects current practice with the following modifications:

Definition: removal of the statement that preparations for irrigation are clear and practically free from particles.

Production: addition of a statement that the preparations for irrigation are clear and practically free from visible particles including a reference to general chapter 5.17.2. *Recommendations on testing of particulate contamination: visible particles.*

Tests: addition of the test on visible particles according to 2.9.20 with the acceptance criterion to be practically free from particles and including a reference to general chapter 5.17.2. *Recommendations on testing of particulate contamination: visible particles.*

HERBAL DRUGS AND HERBAL DRUG PREPARATIONS

Black cohosh (2069)

Identification C: reference to the test for substitution with *Cimicifuga americana* Michx., *C. foetida* L., *C. dahurica* (Turcz.) Maxim. or *C. heracleifolia* Kom. replaced by a reference to the new test for *Actaea podocarpa* DC., *A. cimicifuga* L. or *A. dahurica* (Turcz. ex Fisch. & C.A.Mey.) Franch.; *Cimicifuga americana* Michx. is a synonym of *Actaea podocarpa* DC., *Cimicifuga foetida* L. is a synonym of *Actaea cimicifuga* L., and *Cimicifuga dahurica* (Turcz.) Maxim. is a synonym of *Actaea dahurica* (Turcz. ex Fisch. & C.A.Mey.) Franch.; *Cimicifuga heracleifolia* Kom. is not considered to be found on the market; TLC replaced by HPTLC in accordance with general chapter 2.8.25; description for results B improved.

With the following two changes, the group of experts proposed to restrict this test to assessing the occurrence of substitution only. Although rare, substitution is more likely to occur than adulteration in herbal drugs used in the preparation of herbal medicinal products.

***Actaea podocarpa* DC., *A. cimicifuga* L. or *A. dahurica* (Turcz. ex Fisch. & C.A.Mey.) Franch.:** following the deletion of the test for adulteration (see below), the title of the test no longer indicates a specific purpose (e.g. substitution); new detection C introduced by examining the plates in ultraviolet light at 366 nm following detection B, making it possible to discriminate *Actaea dahurica* (Turcz. ex Fisch. & C.A.Mey.) Franch.; concentration of actein increased two-fold in the reference solutions containing the intensity marker; addition of a new reference solution containing 23-*epi*-26-deoxyactein and actein, used for the system suitability test in detections B and C; addition of a new reference solution containing a low concentration of cimifugin, used in detection A; introduction of the need to condition the plate at a relative humidity of less than 5 per cent using a molecular sieve; new detection C included, and results A and B improved.

Test for adulteration with *Actaea podocarpa* DC., *A. cimicifuga* L. or *A. dahurica* (Turcz. ex Fisch. & C.A.Mey.) Franch.: test deleted since the monograph aims to test herbal drugs used in medicinal products, where adulteration is considered to be very rare.

Assay: reagent used to describe stationary phase modified; grade of water used in mobile phase A amended in accordance with Technical Guide (2022) ; system suitability test acceptance criterion widened by lowering the minimum peak-to-valley ratio requirement from 3 to 1.5.

Meadowsweet (1868)

Identification C: mobile phase replaced to avoid the use of hexane; TLC replaced by high-performance thin-layer chromatography (HPTLC) in accordance with chapter 2.8.25.

Valerian dry aqueous extract (2400)

Identification: test optimised, now able to identify additional zones in the chromatogram; TLC replaced by high-performance thin-layer chromatography (HPTLC) in accordance with general chapter 2.8.25.

Assay: grade of acetonitrile amended in accordance with the Technical Guide (2022).

Valerian dry hydroalcoholic extract (1898)

Identification: test optimised, now able to identify additional zones in the chromatogram; TLC replaced by high-performance thin-layer chromatography (HPTLC) in accordance with general chapter 2.8.25.

Assay: grades of solvents amended in accordance with the Technical Guide (2022).

Valerian root (0453)

Identification: test C optimised, now able to identify additional zones in the chromatogram; TLC replaced by high-performance thin-layer chromatography (HPTLC) in accordance with general chapter 2.8.25.

Assay for sesquiterpenic acids: grades of solvents amended in accordance with the Technical Guide (2022).

Valerian root, cut (2526)

Identification: test B optimised, now able to identify additional zones in the chromatogram; TLC replaced by high-performance thin-layer chromatography (HPTLC) in accordance with general chapter 2.8.25.

Assay of sesquiterpenic acids: grades of solvents amended in accordance with the Technical Guide (2022).

Valerian tincture (1899)

Identification: test optimised, now able to identify additional zones in the chromatogram; TLC replaced by high-performance thin-layer chromatography (HPTLC) in accordance with general chapter 2.8.25.

Assay: grades of solvents amended in accordance with the Technical Guide (2022).

HOMOEOPATHIC PREPARATIONS

Crocus for homoeopathic preparations (1624)

Characters: section deleted as it was unspecific and based on odour.

Identification D by TLC: method completely overhauled (including change in reagent as naphthol yellow does not become coloured after spraying with *anisaldehyde solution R* and is no longer available in some countries); addition of HPTLC conditions.

Identification E: deleted because identification D by TLC is more appropriate and sufficient.

TESTS/Colouring intensity: deleted because the financial burden related to the use of stigma of *Crocus sativus* L. for this test is not considered justified as the yellow colour is also visible in identification A.

TESTS/Loss on drying: based on data, maximum limit of 10.0 per cent replaced by a maximum limit of 13.0 per cent, which is considered to be safe.

Addition of a section for the **Mother tincture**.

MONOGRAPHS

Alfacalcidol (1286)

Assay: following the comments received during the revision of *Calcitriol (0883)*, the calculation of content has been reviewed for more clarity and harmonised in all the monographs related to vitamin D derivatives.

Aluminium phosphate gel (2166)

Arsenic: in line with the Ph. Eur. Implementation strategy for the ICH Q3D guideline on elemental impurities (please see [Press release](#)), the test has been deleted.

Aluminium phosphate hydrate (1598)

Title: hydration form corrected in the title according to current policy on hydrates (English version only).

Arsenic: in line with the Ph. Eur. Implementation strategy for the ICH Q3D guideline on elemental impurities (please see [Press release](#)), the test has been deleted.

Atorvastatin calcium (2191)

Identification: the current identification test for calcium, based on reaction (b) of calcium (2.3.1), describes a cumbersome sample preparation step involving charring/incinerating the substance to be examined. This has been replaced by an alternative and more user-friendly test, based on a modified reaction (a) of calcium (2.3.1) in which *chloroform R* is replaced by *methylene chloride R*.

Enantiomeric purity: on the basis of data received from users since the publication of the revised text (04/2022:2191) in Ph. Eur. 10.7, the resolution criterion for the system suitability test has been replaced by a minimum 1.5 peak-to-valley ratio.

Related substances: on the basis of data received from users since the publication of the revised text (04/2022:2191) in Ph. Eur. 10.7, the limit for impurity D has been widened to maximum 0.3 per cent, the limits for impurities H and I have been widened to maximum 0.15 per cent, and the CRS strategy has been modified accordingly.

Bromperidol (1178)

Identification: 2nd identification series deleted, since the substance is not used in hospital and community pharmacies.

Related substances: impurities specifications updated to reflect the quality of substances in approved medicinal products on the European market; system suitability CRS now proposed for identification of specified impurities B and E; expression of acceptance criteria proposed in the quantitative style; system suitability criterion amended to avoid the use of external compound; resolution between impurity B and the API now proposed; peak-to-valley ratio between impurities F and E added; description of the stationary phase updated; grade of acetonitrile in mobile phase amended in accordance with Technical Guide (2022).

Assay: colour indicator replaced by potentiometric end-point determination.

Calcifediol monohydrate (1295)

Assay: following the comments received during the revision of *Calcitriol (0883)*, the calculation of content has been reviewed for more clarity and harmonised in all the monographs related to vitamin D derivatives.

Calcipotriol (2011)

Assay: following the comments received during the revision of *Calcitriol (0883)*, the calculation of content has been reviewed for more clarity and harmonised in all the monographs related to vitamin D derivatives.

Calcipotriol monohydrate (2284)

Assay: following the comments received during the revision of *Calcitriol (0883)*, the calculation of content has been reviewed for more clarity and harmonised in all the monographs related to vitamin D derivatives.

Calcitriol (0883)

Definition: nomenclature updated.

Related substances: reagent used to describe stationary phase modified; grades of solvents amended in accordance with the Technical Guide (2022).

Content: upper limit tightened in line with current policy for assaying substances by LC.

Assay: repeatability criterion deleted because the general criteria described in 2.2.46. *Chromatographic separation techniques* are applicable; calculation of content reviewed for more clarity.

Storage: after new information received, storage conditions updated to allow the use of other inert gases (e.g. argon).

Impurities: nomenclatures and structure of impurity C updated.

Calcium acetate (2128)

Chlorides, nitrates, sulfates: based on feedback from users and considering the concentration of nitrate is very low, the repeatability requirement for system suitability has been relaxed.

Calcium glycerophosphate (0980)

Formulae: a graphic formula has been added and the molecular formula has been updated to indicate that the substance may be hydrated ("xH₂O") and that the "M_r" refers to the anhydrous substance. The CAS number, available for the anhydrous substance only, has been added.

Definition: the chemical name has been updated and the description of the degree of hydration has been added.

Arsenic: in line with the Ph. Eur. implementation strategy for the ICH Q3D guideline on elemental impurities (please see [Press release](#)), the test has been deleted.

Candesartan cilexetil (2573)

Production: since the general requirements for *N*-nitrosamines given in general monograph 2034 apply to all active substances for human use within its scope (whether or not there is an individual monograph in the Ph. Eur.), the Ph. Eur. Commission decided to delete the Production section covering *N*-nitrosamine impurities from individual monographs.

Chitosan hydrochloride (1774)

Identification A (IR): preparation of the KBr discs deleted.

Degree of deacetylation: formula updated to take into account the ratio of polymerised to free floating molecular mass of *N*-acetylglucosamine.

Chloroquine phosphate (0544)

Related substances: the thin-layer chromatography has been replaced by a liquid chromatography. The list of impurities and their specifications have been revised accordingly: five impurities are now listed and impurity A is specified at 0.5 per cent.

Other changes (e.g. Definition, Identification and Tests) are editorial.

Cholecalciferol (0072)

Assay: following the comments received during the revision of *Calcitriol* (0883), the calculation of content has been reviewed for more clarity and harmonised in all the monographs related to vitamin D derivatives.

Ciprofibrate (2013)

Related substances: introduction of a new CRS for system suitability (new composition) to avoid the saturation of the main peak; the resolution criterion has been adapted accordingly.

Coconut oil, refined (1410)

Melting point: replacement of 2.2.14. *Melting point - capillary method* by 2.2.15. *Melting point - open capillary method*. General chapter 2.2.14 is intended for crystalline substances, which are typically crushed and then filled into a capillary that is closed at one end. Coconut oil is a very soft substance, which is very difficult to introduce into this type of capillary. In addition, the specifications described for this test were originally intended to be used with the procedure described in general chapter 2.2.15.

Colchicine (0758)

Definition: the source (i.e. from natural sources) has been introduced.

Related substances: the stationary phase and column temperature have been modified to improve the separation and allow quantitation of impurity H (cornigerine) as a specified impurity with a limit of 0.2 per cent; it has always been present in the batches but was not separated from impurity G and was therefore wrongly identified and limited as impurity G.

Labelling: a section has been introduced.

Dabigatran etexilate mesilate (3095)

Water: limit increased based on available batch data of substances used in medicinal products recently approved in Europe.

Deferasirox (2933)

Related substances: preparation of reference solution (c) modified following establishment of *deferasirox for system suitability A CRS* (obtained by evaporation of a solution containing deferasirox and impurity D).

Deferasirox dispersible tablets (2934)

Related substances: preparation of reference solution (b) modified following establishment of *deferasirox for system suitability A CRS* (obtained by evaporation of a solution containing deferasirox and impurity D).

Ergocalciferol (0082)

Assay: following the comments received during the revision of *Calcitriol (0883)*, the calculation of content has been reviewed for more clarity and harmonised in all the monographs related to vitamin D derivatives.

Ethylcellulose (0822)

Functionality-related characteristics: a molecular mass distribution test (2.2.30) has been added for ethylcellulose used as matrix former in modified-release solid dosage forms. The variability in molecular mass distribution between grades has an impact on drug release and is not fully covered by the other characteristics listed. Ethylcellulose is commonly used in capsules and transdermal patches. In order to reflect this situation, the expression “matrix former in modified-release oral dosage forms” had been changed to “matrix former in modified-release solid dosage forms”.

The entire non-mandatory Functionality-related characteristics section is marked with white diamonds to indicate its status as a local Ph. Eur. requirement of this PDG harmonised monograph.

Hydroxypropylcellulose (0337)

Functionality-related characteristics: a molecular mass distribution test (2.2.30) has been added for hydroxypropylcellulose used in modified-release solid dosage forms. The variability in molecular mass distribution between grades has an impact on drug release and is not fully covered by the other characteristics listed. The requirement has been broadened from the original prolonged-release tablets because hydroxypropylcellulose may also be used in other modified-release dosage forms.

The entire non-mandatory Functionality-related characteristics section is marked with white diamonds to indicate its status as a local Ph. Eur. requirement in this PDG harmonised monograph.

Irbesartan (2465)

Production: since the general requirements for *N*-nitrosamines given in general monograph 2034 apply to all active substances for human use within its scope (whether or

not there is an individual monograph in the Ph. Eur.), the Ph. Eur. Commission decided to delete the Production section covering *N*-nitrosamine impurities from individual monographs.

Ketoprofen (0922)

Related substances: impurities limits updated to reflect the quality of substances in approved medicinal products on the European market; expression of acceptance criteria in the quantitative style; grade of solvents used in the mobile phase amended in accordance with the Technical Guide (2022).

Impurities: section updated accordingly.

Losartan potassium (2232)

Production: since the general requirements for *N*-nitrosamines given in general monograph 2034 apply to all active substances for human use within its scope (whether or not there is an individual monograph in the Ph. Eur.), the Ph. Eur. Commission decided to delete the Production section covering *N*-nitrosamine impurities from individual monographs.

Mercaptopurine monohydrate (0096)

Identification: chemical identifications and UV absorbance replaced by IR spectrophotometric test.

Methotrexate (0560)

Related substances: reagent used to describe stationary phase modified; grade of acetonitrile in the mobile phase amended in accordance with the Technical Guide (2022); statement deleted on increasing the flow rate if necessary to meet the system suitability criterion of minimum resolution between impurity D and methotrexate as recent analyses have shown this statement to be obsolete and the adjustment of chromatographic conditions is covered by general chapter 2.2.46. *Chromatographic separation techniques*.

Enantiomeric purity: reagent used to describe stationary phase modified; section on Identification of impurities modified to take into account that the leaflet of *methotrexate for system suitability* CRS will include a chromatogram of reference solution (b).

Montelukast sodium (2583)

Enantiomeric purity: editorial change to the reagent name of the stationary phase and calculation method updated to reflect the manufacturer's approach.

Related substances: grade of solvents used in the mobile phase amended in accordance with the Technical Guide; impurity C is eluted as 2 peaks, the acceptance criteria applies to the sum of the 2 peaks.

Nonoxinol 9 (1454)

Hydroxyl value: acid value removed from the formula – the corresponding test had been removed in a previous revision and the actual acid value (< 0.5) has a negligible effect on the expected hydroxyl value (84-94).

Octoxinol 10 (1553)

Hydroxyl value: acid value removed from the formula – the corresponding test had been removed in a previous revision and the actual acid value (< 0.5) has a negligible effect on the expected hydroxyl value (85-101).

Octyldodecanol (1136)

Hydroxyl value: acid value removed from the formula – the corresponding test had been removed in a previous revision and the actual acid value (< 0.5) has a negligible effect on the expected hydroxyl value (175-190).

Oleyl alcohol (2073)

Composition of fatty alcohols:

- relative retention times corrected;
- “elaidyl alcohol co-elutes with oleyl alcohol” changed to “elaidyl alcohol may co-elute with oleyl alcohol” because current GC columns are able to separate, at least partially, elaidyl alcohol from oleyl alcohol and this may lead to an incorrect analytical result being obtained for oleic alcohol; ‘α’ added to reagent name ‘*linolenyl alcohol R*’ to highlight that it covers the alpha isomer and not the gamma isomer;
- reagent changed from “*palmityl alcohol R*” to “*cetyl alcohol R*” because both describe the same quality of hexadecan-1-ol and “*palmityl alcohol R*” is used in this monograph only.

Olmesartan medoxomil (2600)

Production: since the general requirements for *N*-nitrosamines given in general monograph 2034 apply to all active substances for human use within its scope (whether or not there is an individual monograph in the Ph. Eur.), the Ph. Eur. Commission decided to delete the Production section covering *N*-nitrosamine impurities from individual monographs.

Oxytetracycline dihydrate (0199)

Related substances: newly introduced impurity G has been found to co-elute with impurity A. Consequently, these two impurities have been specified by their sum, keeping the current limit of 0.7 per cent, which is based on batch data. A new reference solution has been added to allow identification of the peak due to impurity G.

The test has also been revised in order to include impurity F as a specified impurity, present in current batches at levels above the limit for any other impurity; as this impurity was found to degrade into impurities D and E, a limit for the sum of impurities D, E and F has been introduced.

Impurities: impurity G has been introduced.

Oxytetracycline hydrochloride (0198)

Related substances: newly introduced impurity G has been found to co-elute with impurity A. Consequently, these two impurities have been specified by their sum, keeping the current limit of 0.5 per cent, which is based on batch data. A new reference solution has been added to allow identification of the peak due to impurity G.

Impurities: impurity G has been introduced.

Pefloxacin mesilate dihydrate (1460)

Identification: wording modified to delete reference to examination of residue as a disc in IR test.

Related substances: quantitation of impurities optimised, carried out at one detection wavelength and versus a 0.10 per cent diluted test solution; concentration of the test solution increased 5-fold to achieve sufficient sensitivity at the only detection wavelength prescribed; system suitability test acceptance criterion based on the more critical chromatographic pair of impurity G and pefloxacin added; limits expressed in quantitative style and updated based on batch data provided by manufacturers; thiodiethylene glycol is replaced by acetonitrile in solution A, which is used to prepare the mobile phase, because it can be complicated to procure (thiodiethylene glycol is a Schedule 2 substance under the Chemical Weapons Convention).

Sulfated ash: use of platinum crucible introduced due to the presence of fluoride in the API.

Impurities: section updated in accordance with the update of specifications in the test for related substances.

Polysorbate 20 (0426)

Identification A: reference spectrum replaced by reference substance according to current policy.

Characters: modified to state that the substance is hygroscopic.

Polysorbate 40 (1914)

Identification A: reference spectrum replaced by reference substance according to current policy.

Characters: modified to state that the substance is hygroscopic.

Polysorbate 60 (0427)

Identification A: reference spectrum replaced by reference substance according to current policy.

Characters: modified to state that the substance is hygroscopic.

Polysorbate 80 (0428)

Identification A: reference spectrum replaced by reference substance according to current policy.

Characters: modified to state that the substance is hygroscopic.

Propylene glycol (0430)

Compared to the monograph published in the 11th Edition of the Ph. Eur., the following changes have been made:

Definition: chemical nomenclature changed to be in line with the IUPAC nomenclature.

Characters: text separated into two subsections, “appearance” and “solubility”.

Identification: IR comparison with CRS introduced as 1st identification as it is an easy and specific method for identification; tests for relative density, refractive index and boiling point kept as 2nd identification series for pharmacies; non-specific wet chemical identification (formerly identification D) deleted.

Appearance: addition of the criterion for degree of coloration (2.2.2, *Method II*) in order to clarify the “colourless” requirement.

Acidity: procedure and acceptance criteria modified to harmonise them with the other PDG pharmacopoeias.

Oxidising substances: addition of the limit expressed in ppm, calculated as H₂O₂, as the indication of the limit in ppm is useful information for the user.

Ethylene glycol and diethylene glycol: addition of the test as both compounds are potential adulterants of the substance.

Water: inclusion of the term “at least” to allow larger sample amounts if needed to accommodate the linearity range of the instrument available. Further editorial change to delete the type of the water content determination method as it is already specified by referring to the respective general chapter.

Riboflavin sodium phosphate hydrate (0786)

Definition, structure, nomenclature and composition: updated to include riboflavin, previously listed as impurity D, in the minor components of riboflavin sodium phosphate.

Related substances: impurity D and corresponding reference solution (a) containing *riboflavin CRS* no longer needed; limit for the total up-dated accordingly.

Impurities: impurity D no longer needed in the list of impurities.

Rifampicin (0052)

Characters: a statement on polymorphism has been introduced.

Identification: test B has been revised to introduce a recrystallisation procedure as the substance shows polymorphism.

Loss on drying: the vacuum pressure has been adjusted to reflect the equipment performances.

Sodium selenite (2740)

pH: in light of current batch data and taking into consideration the theoretical pH of 11.04, the upper limit has been changed to 11.3; the lower limit has been kept as 9.8.

Solutions for organ preservation (1264)

The proposed revision emphasises the requirement to test that solutions for organ preservation are practically free from visible particles and reflects current practice with the following modifications:

Definition: removal of the statement that solutions for organ preservation are clear and practically free from particles. This statement has been moved into the Production section.

Production: addition of a statement that the solutions for organ preservation are clear and practically free from particles including a reference to general chapter 5.17.2.

Recommendations on testing of particulate contamination: visible particles.

Tests: addition of the test on visible particles according to 2.9.20 with the acceptance criterion to be practically free from particles and including a reference to general chapter 5.17.2. *Recommendations on testing of particulate contamination: visible particles.*

Sugar spheres (1570)

Identification A: modified in order to avoid the use of ethylene chloride (REACH). Separation criterion removed in line with the current Technical Guide (8th Edition, II.6.7. Thin-layer chromatography, §2).

Sulbactam sodium (2209)

Related substances: the text now states that the solutions are to be prepared immediately before use, as this improves their stability; the stationary phase description has also been updated.

Assay: an individual requirement has been introduced for the symmetry factor as this parameter was outside the range 0.8-1.8 prescribed in general chapter 2.2.46.

Tacalcitol monohydrate (2272)

Assay: following the comments received during the revision of *Calcitriol (0883)*, the calculation of content has been reviewed for more clarity and harmonised in all the monographs related to vitamin D derivatives.

Tetracosactide (0644)

Identification: A reference to the assay and clarification regarding the reference solution to be used have been introduced in Identification A; for Identification B, Method 4 of general chapter 2.2.56 has been included as a second possibility for the analysis, in addition to Method 1.

Related peptides: The test has been replaced by one that has superior selectivity; a separate CRS has been introduced for the identification of impurities A, C, D, E, F, G, H, I and J (*tetracosactide for peak identification CRS*); the limits have been revised to reflect the quality of the substance available on the European market: the limit for impurity A has been lowered from 3 per cent to 2.0 per cent; impurity B (unknown structure) has been removed as it is no longer present in the substances used in products on the European market; four additional limits for specified impurities or their sum have been introduced; the limit for total impurities has been lowered from 9 per cent to 5.0 per cent; the limit for unspecified impurities has been lowered from 2.5 per cent to 0.5 per cent and a reporting threshold of 0.1 per cent has been introduced in accordance with general monograph 2034.

Assay: The assay has been revised to refer to the newly introduced test for related peptides.

Impurities: The transparency section has been revised to remove impurity B and to add eight additional specified impurities, one of which is of unknown structure.

Valsartan (2423)

Production: since the general requirements for *N*-nitrosamines given in general monograph 2034 apply to all active substances for human use within its scope (whether or

not there is an individual monograph in the Ph. Eur.), the Ph. Eur. Commission decided to delete the Production section covering *N*-nitrosamine impurities from individual monographs.

Wool alcohols (0593)

Loss on drying: addition of a specific drying time of 1 h. Drying to constant mass is not suitable for wool alcohols as a slow but continuous further loss of mass occurs upon prolonged drying beyond 1 h, believed to be due to partial evaporation of some intrinsic components of the substance.

Assay: addition of a run time with a duration of 30 min. Some wool alcohol components have a longer retention time than cholesterol and they need to be eluted from the column before the run ends.