Comments concerning texts published in Supplement 11.4

Brief descriptions of the modifications that have been made to new, revised and corrected texts adopted by the European Pharmacopoeia Commission at the March session and published in Supplement 11.4 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

2.7.37. Assay of Phl p 5 allergen

The general chapter describes an assay to detect Phl p 5 in allergen extracts. It has been elaborated based on the following collaborative studies:

- *Vieths S, Barber D, Chapman M et al. Establishment of recombinant major allergens Bet v 1 and Phl p 5a as Ph. Eur. reference standards and validation of ELISA methods for their measurement. Results from feasibility studies. Pharmeur Bio Sci Notes. 2012:118-134;*

- *Zimmer J, Schmidt S, Kaul S et al. Standardisation of allergen products: 4. Validation of a candidate European Pharmacopoeia standard method for quantification of major grass pollen allergen Phl p 5. Allergy. 2022; 77(2):633-642;*

- *Zimmer J, Schmidt S, Costanzo A et al. Validation of an ELISA method for quantification of the major Timothy grass pollen allergen Phl p 5a (BSP090). Pharmeur Bio Sci Notes. 2022.*

5.2.6. Evaluation of safety of veterinary vaccines and immunosera

Safety of the administration of 1 dose (section 1-1): updated to clarify that animals 'that are expected to be the most sensitive' are usually animals of the youngest recommended age, but there may be specific cases, such as *Coccidiosis vaccine (live) for chickens (2326)*, published in the same supplement, for which the most sensitive animals are 14-day-old chickens.

5.4. Residual solvents

Solvents for which no adequate toxicological data was found: methyltetrahydrofuran deleted from Table 4, in line with ICH Q3C(R8) corrected on 16-Aug-2022.

French version only: editorial changes introduced to align more closely with the English version.

5.22. Names of herbal drugs used in traditional Chinese medicine

Table updated to include 1 new monograph.

VACCINES FOR VETERINARY USE

Aujeszky's disease vaccine (inactivated) for pigs (0744)

3-3 Residual live virus. Deletion of this test performed at the final product stage because it is also performed in-process (see 2-4-1). This deletion is supported by the application of GMP conditions during production, the use of validated production processes to demonstrate consistency and the history of safe use of the products approved in Europe. There is no need to retest a product that has been tested in-process since there is no reversion to virulence.

4 Labelling. Deleted as the remaining residual live virus test (2-4-1) is performed using cell cultures and not rabbits.

Avian infectious bronchitis vaccine (inactivated) (0959)

2-4-2 Batch potency test. Reduction of the number of control birds for the routine batch potency test from "5" to "not fewer than 3" when SPF chickens are used (3*Rs*). In this test, the birds before vaccination serve also as the control.

3-3 Residual live virus. Deletion of this test performed at the final product stage because it is also performed in-process (see 2-4-1). This deletion is supported by the application of GMP conditions during production, the use of validated production processes to demonstrate consistency and the history of safe use of the products approved in Europe. There is no need to retest a product that has been tested in-process since there is no reversion to virulence.

Avian infectious bursal disease vaccine (inactivated) (0960)

2-4-2 Batch potency test. Reduction of the number of control birds for the routine batch potency test from "10" to "not fewer than 3" when SPF chickens are used (3*Rs*), since controls are not used during comparison of titres or included in statistical calculations.

3-3 Residual live virus. Deletion of this test performed at the final product stage because it is also performed in-process (see 2-4-1). This deletion is supported by the application of GMP conditions during production, the use of validated production processes to demonstrate consistency and the history of safe use of the products approved in Europe. There is no need to retest a product that has been tested in-process since there is no reversion to virulence.

Avian infectious encephalomyelitis vaccine (live) (0588)

2-3-3 Immunogenicity. Addition of humane end-points (seriously sick birds may be euthanised).

Avian paramyxovirus 3 vaccine (inactivated) for turkeys (1392)

3-3 Residual live virus. Deletion of this test performed at the final product stage because it is also performed in-process (see 2-4-1). This deletion is supported by the application of GMP conditions during production, the use of validated production processes to demonstrate

consistency and the history of safe use of the products approved in Europe. There is no need to retest a product that has been tested in-process since there is no reversion to virulence.

Coccidiosis vaccine (live) for chickens (2326)

Field studies (new section 2-3-1-2). Added to make clear that the safety tests performed in the laboratory (sections 2-3-1-1, 2-3-1-3 and 2-3-1-4) have to be performed using 14-day-old chickens and the field trials have to be performed using e.g. 1-day-old chickens, if this is the minimum recommended age of vaccination. As a consequence, for this specific case where the most sensitive animals are 14-day-old chickens contrary to chickens at the youngest recommended age, double testing has not to be done.

Immunogenicity (previous section 2-3-4). Clarification of the acceptance and validity limits - 'e.g.' replaced by 'i.e.', since this is a clarification and not an example.

Egg drop syndrome '76 vaccine (inactivated) (1202)

2-4-2 Batch potency test. Reduction of the number of control birds for the routine batch potency test from "5" to "not fewer than 3" when SPF chickens are used (3*Rs*) since controls are not used during comparison of titres or included in statistical calculations.

3-3 Residual live virus. Deletion of this test performed at the final product stage because it is also performed in-process (see 2-4-1). This deletion is supported by the application of GMP conditions during production, the use of validated production processes to demonstrate consistency and the history of safe use of the products approved in Europe. There is no need to retest a product that has been tested in-process since there is no reversion to virulence.

Equine influenza vaccine (inactivated) (0249)

3-3 Residual live virus. This test performed at the final product stage by inoculating 0.2 mL of the vaccine into the allantoic cavity of each of 10 embryonated eggs has been deleted because it was also performed in-process (see 2-4-1). This deletion was supported by the application of GMP conditions during production, the use of validated production processes to demonstrate consistency and the history of safe use of the products approved in Europe. There is no need to retest a product that has been tested in-process since there is no reversion to virulence.

Fowl cholera vaccine (inactivated) (1945)

2-2-2 Immunogenicity. Addition of humane end-points (seriously sick birds may be euthanised).

2-3-1 Batch potency test. Reduction of the number of control birds for the routine batch potency test from "5" to "not fewer than 3" when SPF chickens are used (3*Rs*) since controls are not used during comparison of titres or included in statistical calculations.

Mycoplasma gallisepticum vaccine (inactivated) (1942)

2-3-2 Batch potency test. Reduction of the number of control birds for the routine batch potency test from "not fewer than 5" to "not fewer than 3" when SPF chickens are used (3*Rs)* since controls are not used during comparison of titres or included in statistical calculations. The same approach has been taken for turkeys although SPF turkeys do not exist.

Newcastle disease vaccine (inactivated) (0870)

2-4-2 Batch potency test / 2-4-2-3 Serological assay. Reduction of the number of control birds for the routine batch potency test from “not fewer than 5” to “not fewer than 3” when SPF chickens are used (3*Rs*), since controls are not used during comparison of titres or included in statistical calculations.

3-3 Residual live virus. Deletion of this test performed at the final product stage because it is also performed in-process (see 2-4-1). Any detail of interest described in the former section 3-3 have been moved to section 2-4-1. This deletion is supported by the application of GMP conditions during production, the use of validated production processes to demonstrate consistency and the history of safe use of the products approved in Europe. There is no need to retest a product that has been tested in-process since there is no reversion to virulence.

Porcine influenza vaccine (inactivated) (0963)

3-3 Residual live virus. Deletion of this test performed at the final product stage because it is also performed in-process (see 2-4-1). This deletion is supported by the application of GMP conditions during production, the use of validated production processes to demonstrate consistency and the history of safe use of the products approved in Europe. There is no need to retest a product that has been tested in-process since there is no reversion to virulence.

Rabbit haemorrhagic disease vaccine (inactivated) (2325)

2-2-2 Immunogenicity. Addition of humane end-points (seriously sick rabbits may be euthanised).

3-3 Residual live virus. Deletion of this test performed at the final product stage because it is also performed in-process (see 2-4-1). This deletion is supported by the application of GMP conditions during production, the use of validated production processes to demonstrate consistency and the history of safe use of the products approved in Europe. There is no need to retest a product that has been tested in-process since there is no reversion to virulence.

Salmonella Enteritidis vaccine (inactivated) for chickens (1947)

2-3-1 Batch potency test. Reduction of the number of control birds for the routine batch potency test from “not fewer than 5” to “not fewer than 3” when SPF chickens are used (3*Rs*) since controls are not used during comparison of titres or included in statistical calculations.

Salmonella Typhimurium vaccine (inactivated) for chickens (2361)

2-3-1 Batch potency test. Reduction of the number of control birds for the routine batch potency test from “not fewer than 5” to “not fewer than 3” when SPF chickens are used (3*Rs*) since controls are not used during comparison of the titres or included in statistical calculations.

RADIOPHARMACEUTICAL PREPARATIONS AND STARTING MATERIALS FOR RADIOPHARMACEUTICAL PREPARATIONS

PSMA-1007 (^{18}F) injection (3116)

PSMA-1007 and related substances. For the preparation of reference solution (c) it had been stated so far to use the trifluoroacetic acid salt of defluorotrimethylaminium-PSMA-1007 (*defluorotrimethylaminium-PSMA-1007 trifluoroacetate R*). This reagent is not available and has been replaced by the acetate salt of defluoromethylaminium-PSMA-1007 (*defluorotrimethylaminium-PSMA-1007 acetate R*) which is indeed available.

Technetium (^{99m}Tc) tin pyrophosphate injection (0129)

Definition: the substance is now defined as a complex derived from sodium [^{99m}Tc] pertechnetate and sodium pyrophosphate in the presence of a stannous salt. Information related to the quality of sodium pertechnetate (^{99m}Tc) has been transferred to the newly created Production section.

Production: section created stipulating that *Stannous chloride dihydrate (1266)*, *Sodium pyrophosphate decahydrate for radiopharmaceutical preparations (2552)* and one of the three following sodium pertechnetate (^{99m}Tc) injections are used to prepare Technetium (^{99m}Tc) tin pyrophosphate injection: *Sodium pertechnetate (^{99m}Tc) injection (fission) (0124)*, *Sodium pertechnetate (^{99m}Tc) injection (non-fission) (0283)*, *Sodium pertechnetate (^{99m}Tc) injection (accelerator-produced) (2891)*.

Radiochemical purity, impurity A: editorial modification.

Radiochemical purity, impurity B: replacement of TLC test by paper chromatography test, as suitable TLC plates are no longer commercially available.

HERBAL DRUGS AND HERBAL DRUGS PREPARATION

Green tea (2668)

Title: Latin title revised according to editorial conventions.

Identification C:

- fast blue B salt as derivatisation reagent replaced by anisaldehyde due to toxicity;

- HPTLC in accordance with 2.8.25 introduced.

Ribwort plantain (1884)

Identification C and test for Digitalis lanata Ehrh. leaves: test optimised, now allowing reliable identification of adulteration; TLC replaced by high-performance thin-layer chromatography (HPTLC) in accordance with chapter *2.8.25*.

Shepherd's purse (2947)

Identification: detection section of the HPTLC procedure in test C updated to accurately reflect the corresponding method validated.

Assay: relative retentions of isorhoifolin and hesperidin updated and system suitability test requirement widened, based on results obtained with the use of new liquid chromatography columns; addition of a statement on the possible inversion of the elution order of isorhoifolin and hesperidin.

MONOGRAPHS

Alfadex (1487)

Specific optical rotation: revised to an identification test only.

Related substances: method revised from a limit test to a quantitative test. Column particle size revised as columns with a 10 µm particle size are not available.

Impurities: Gammadex added as a synonym for Impurity B.

Amphotericin B (1292)

Related substances: the preparation of reference solution (c) has been corrected to prescribe dilution with the solvent mixture instead of reference solution (a). In addition, the reagent used to describe the stationary phase has been modified.

Betadex (1070)

Specific optical rotation: revised to an identification test only.

Related substances: column particle size revised as columns with a 10 µm particle size are not available.

Impurities: Gammadex added as a synonym for Impurity B.

Betamethasone acetate (0975)

Second identification: in test C, in line with experimental results, the description of the resulting colour after addition of sulfuric acid has been modified to allow discrimination of the substance from betamethasone valerate.

Betamethasone valerate (0811)

Identification: second identification added since the substance is used in pharmacies.

Related substances: grade of solvents amended in accordance with the Technical Guide (2022). In the preparation of reference solutions (b) and (c), volume/mass expressed using fewer significant figures due to the qualitative use of these solutions.

Calcium folinate hydrate (0978)

Related substances: addition of the correction factors for impurities B, C, D and I, which become specified (at 0.2%); new CRS for system suitability described and reference solution (c) preparation changed accordingly.

Calcium levofolinate hydrate (1606)

Related substances: addition of the correction factors for impurities B, C and D which become specified (at 0.2%); new CRS for system suitability described and reference solution (c) preparation changed accordingly.

Carbasalate calcium (1185)

Identification: test E modified in order to avoid the use of chloroform.

Carmellose calcium (0886)

Identification D: test revised in-line with the PDG sign-off text.

Chlorides and sulfates: solution volumes adjusted to be in-line with the PDG sign-off text.

Labelling: statement added as a consequence of revision to sulfates test.

Cholesterol (0993)

Definition: supplemented to take into account the other sterols included in the content of total sterols; addition of a statement allowing the use of an antioxidant.

Content: upper limit for total sterols tightened based on the capability of the method.

Identification: aligned with the monograph *Cholesterol for parenteral use (2397)*: deletion of melting point, TLC and colour reaction; introduction of IR and reference to the assay by GC.

Acidity: test deleted, it requires the use of ether and is not included in the monograph *Cholesterol for parenteral use (2397)*.

Assay: reference to the main peak omitted as the symmetry factor suitability test applies by default to the peak used for quantitation.

Impurities: section updated and renamed “Other sterols” as the compounds listed there are taken into account in the assay for the calculation of the total sterols content.

Dapsone (0077)

Identification: identification by infrared absorption spectrophotometry introduced to replace current section.

Daunorubicin hydrochloride (0662)

Impurities: the trivial names of impurities B and E have been corrected.

Dextromethorphan hydrobromide monohydrate (0020)

Title: addition of the degree of hydration.

Identification: changes to include the test for enantiomeric purity as an alternative to the test for specific optical rotation.

Enantiomeric purity: owing to serious incidents due to abnormally high concentration of levomethorphan in dextromethorphan, a test for enantiomeric purity by LC has been added. It is more specific than the current test for optical rotation; the latter will be kept for identification only.

Disodium edetate (0232)

Identification: test D modified to reduce the requirement from 'reactions of sodium' to only one reaction of sodium (test a); in the second identification series, previous test B omitted and test C replaced by a more specific colour reaction.

Doxazosin mesilate (2125)

Characters: solubility in heptane added.

Related substances: description of the stationary phase updated.

Assay: symmetry factor requirement widened to maximum 3.0.

Ethylcellulose (0822)

Assay: editorial change to highlight the apparatus required to perform the Zeisel reaction so that the *Ethylcellulose (0822)*, *Hydroxyethylcellulose (0336)*, *Hydroxypropylcellulose (0337)*, *Hydroxypropylcellulose, low-substituted (2083*), *Hypromellose (0348)* and *Methylcellulose (0345)* monographs are aligned. Time periods in the gradient table have been aligned with the Global text.

The changes have no impact on the PDG harmonisation status.

Fenbendazole for veterinary use (1208)

Characters: solubility in heptane included.

Related substances: new UHPLC procedure introduced that improves the selectivity of the test, and covers one new unspecified impurity (impurity C); limits updated based on batch data provided by manufacturers.

Impurities: section updated in accordance with new procedure for the test for related substances.

Fenticonazole nitrate (1211)

Related substances: change to the quantitative determination of impurities; based on recent batch data, impurity E is the only remaining specified impurity, impurities A, B, C and D become unspecified and the limit for total impurities is lowered to 0.3 per cent.

Toluene: no justification for the 100 ppm limit, test deleted in accordance with the Ph. Eur. policy on residual solvents.

Fingolimod hydrochloride (2988)

Related substances - Assay: the resolution criterion was not always met at a column temperature of 40 °C but was fulfilled at a lower temperature: a temperature of 25 °C is therefore included; in the assay, the symmetry factor of the peak due to fingolimod did not comply with the requirements of general chapter *2.2.46*: a less-strict requirement is now described.

Water: sample size increased to improve repeatability in case of low water content.

Gammadex (2769)

Specific optical rotation: revised to an identification test only.

Assay: default symmetry factor requirement (0.8-1.8) of revised general chapter *2.2.46* (Ph. Eur. 11th Edition) applied and previous requirement deleted from monograph.

Human normal immunoglobulin for intramuscular administration (0338)

Protein composition. The test procedure has been updated to take into account current practices:

- removal of the cellulose acetate gel electrophoresis procedure, which is phasing out;

- addition of a reference to capillary zone electrophoresis procedure as an alternative procedure, in order to address the increasing use of this state-of-the art technology in the field.

Human normal immunoglobulin for intravenous administration (0918)

Protein composition. The test procedure has been updated to take into account current practices:

- removal of the cellulose acetate gel electrophoresis procedure, which is phasing out;

- addition of a reference to capillary zone electrophoresis procedure as an alternative procedure, in order to address the increasing use of this state-of-the art technology in the field.

Human normal immunoglobulin for subcutaneous administration (2788)

Protein composition. The test procedure has been updated to take into account current practices:

- removal of the cellulose acetate gel electrophoresis procedure, which is phasing out;

- addition of a reference to capillary zone electrophoresis procedure as an alternative procedure, in order to address the increasing use of this state-of-the art technology in the field.

Hydroxyethylcellulose (0336)

Assay: editorial change to highlight the apparatus required to perform the Zeisel reaction so that the *Ethylcellulose (0822)*, *Hydroxyethylcellulose (0336)*, *Hydroxypropylcellulose (0337)*, *Hydroxypropylcellulose, low-substituted (2083)*, *Hypromellose (0348)* and *Methylcellulose (0345)* monographs are aligned.

Time periods in the gradient table have been aligned with the Global text.

Nitrates: editorial changes made to comply with Ph. Eur. Style Guide.

Editorial and style changes also made to the entire text.

The changes have no impact on the PDG harmonisation status.

Hydroxypropylcellulose (0337)

Assay: editorial change to highlight the apparatus required to perform the Zeisel reaction so that the *Ethylcellulose (0822)*, *Hydroxyethylcellulose (0336)*, *Hydroxypropylcellulose (0337)*, *Hydroxypropylcellulose, low-substituted (2083)*, *Hypromellose (0348)* and *Methylcellulose (0345)* monographs are aligned.

Further editorial and style changes also made to the entire text.

The changes have no impact on the PDG harmonisation status.

Hydroxypropylcellulose, low-substituted (2083)

Assay: This minor revision corresponds to Correction 3 (based on PDG working procedure) within the Pharmacopoeial harmonisation process. The coordinating pharmacopoeia is the Ph. Eur.

Vials with a 5 mL volume that are sufficiently strong and capable of making a tight seal with the corresponding cap are critical for accurately and safely performing the Zeisel reaction.

5 mL pressure-tight vials continue to be prescribed in the monograph, however, the very specific reaction vial and heater dimensions have been removed.

Details of suitable vials, caps and heater blocks have been provided in the Knowledge database.

Time periods in the gradient table have been aligned with the Global text.

An editorial change to the presentation of the calculation has been made so that the *Ethylcellulose (0822)*, *Hydroxyethylcellulose (0336)*, *Hydroxypropylcellulose (0337)*, *Hydroxypropylcellulose, low-substituted (2083)*, *Hypromellose (0348)* and *Methylcellulose (0345)* monographs are aligned.

Hypromellose (0348)

Assay: This minor revision corresponds to Correction 3 (based on PDG working procedure) within the Pharmacopoeial harmonisation process. The coordinating pharmacopoeia is the Ph. Eur.

Vials with a 5 mL volume that are sufficiently strong and capable of making a tight seal with the corresponding cap are critical for accurately and safely performing the Zeisel reaction. 5 mL pressure-tight vials continue to be prescribed in the monograph, however, the very specific reaction vial and heater dimensions have been removed.

Details of suitable vials, caps and heater blocks have been provided in the Knowledge database.

An editorial change to the presentation of the calculation has been made so that the *Ethylcellulose (0822)*, *Hydroxyethylcellulose (0336)*, *Hydroxypropylcellulose (0337)*, *Hydroxypropylcellulose, low-substituted (2083)*, *Hypromellose (0348)* and *Methylcellulose (0345)* monographs are aligned.

Editorial and style changes also made to the entire text.

Indometacin (0092)

Second identification: previously described tests B (UV), D and E (two colour reactions) deleted and replaced by a newly established TLC method.

Isopropyl palmitate (0839)

Definition: upper content limit added in accordance with the Technical Guide for the Elaboration of Monographs 7th Edition (2015) and to reflect the current quality of substances in approved medicinal products on the European market.

Chemical name modified to reflect current IUPAC rules and give a common name.

Assay: clarification added that the assigned content of the CRS needs to be taken into account for the calculation.

Ketoconazole (0921)

Second identification: previously described tests A (melting point), C (TLC) and D (reaction of chlorides) deleted and replaced by a mixed melting point.

Methylcellulose (0345)

Assay: This minor revision corresponds to Correction 3 (based on PDG working procedure) within the Pharmacopoeial harmonisation process. The coordinating pharmacopoeia is the Ph. Eur.

Vials with a 5 mL volume that are sufficiently strong and capable of making a tight seal with the corresponding cap are critical for accurately and safely performing the Zeisel reaction. 5 mL pressure-tight vials continue to be prescribed in the monograph, however, the very specific reaction vial and heater dimensions have been removed.

Details of suitable vials, caps and heater blocks have been provided in the Knowledge database.

An editorial change to the presentation of the calculation has been made so that the *Ethylcellulose (0822)*, *Hydroxyethylcellulose (0336)*, *Hydroxypropylcellulose (0337)*, *Hydroxypropylcellulose, low-substituted (2083)*, *Hypromellose (0348)* and *Methylcellulose (0345)* monographs are aligned.

Editorial and style changes also made to the entire text.

Methylprednisolone acetate (0933)

Second identification series added (TLC and colour reaction) as the substance is used in pharmacies.

Nicardipine hydrochloride (2776)

Second identification series added as the substance is used in pharmacies.

Niflumic acid (2115)

Related substances: Lichrospher C8 column deleted from footnote since no longer available; co-elution of impurities B and E observed when using Lichrospher RP-8 column; elution order of impurities B and E inverted when using Nucleosil C8 column; consequently, relative retentions adapted and corresponding chromatogram included.

Paraffin, white soft (1799)

Consistency test: indication of the penetrating object to be used and the procedure to be followed in order to be in line with the harmonised text.

Paraffin, yellow soft (1554)

Consistency test: indication of the penetrating object to be used and the procedure to be followed in order to be in line with the harmonised text.

Povidone (0685)

Viscosity, expressed as K-value: removal of the specific requirement for a size no. 1 viscometer as the important point is to maintain the required minimum flow time for an acceptable precision of the measurement.

Identification A, Viscosity, expressed as K-value, Formic acid, Impurity A, Impurity B, Assay: several editorial changes have been made.

Formic acid: reagent used to describe stationary phase modified.

Pramipexole dihydrochloride monohydrate (2416)

Test for enantiomeric purity: reference solution (a) slightly adapted to facilitate the dissolution of pramipexole impurity D.

Prednisolone (0353)

Second identification: colour reaction added to increase the specificity (i.e. discrimination from methylprednisolone).

Impurities: name of impurity G corrected.

Sildenafil citrate (2270)

Identification: second identification series added since the substance is used in pharmacies.

Simvastatin (1563)

Loss on drying: milder vacuum conditions introduced since no significant differences in results appear to occur when carrying out the test at a pressure not exceeding 2.5 kPa (i.e. *in vacuo*) or at a pressure not exceeding 0.1 kPa (under high vacuum). Moreover, the conditions of ‘high vacuum’ are reported to be difficult to achieve with available instruments and has not been covered in general chapter *2.2.32. Loss on drying* since Supplement 9.8.

Sodium lauroylsarcosinate (2542)

Title: as the wording “for external use” is not defined in the Ph. Eur. or in Standard Terms and does not appear in any definition of pharmaceutical dosage forms, it is proposed to delete it from the title of the monograph.

Sulfobutylbetadex sodium (2804)

Reducing sugars: clarification of test method.

Impurities A, C and D: method revised to use a column that is widely available. The method has been updated to a quantitative test and instructions to prepare a calibration curve have been included because the evaporative light-scattering detector provides a logarithmic response.

Assay (Sulfobutylbetadex sodium): default symmetry factor requirement (0.8-1.8) of revised general chapter *2.2.46* (Ph. Eur. 11th Edition) applied and previous requirement deleted from monograph.

Suxibuzone for veterinary use (1574)

Title: restricted to veterinary use only.

Characters: solubility in cyclohexane replaced by solubility in a less toxic solvent, i.e. heptane.

Related substances: column dimensions changed in accordance with the type of column validated and used by known manufacturers; expression of acceptance criteria in the quantitative style; limit for unspecified impurities and reporting threshold aligned with the general monograph *Substances for pharmaceutical use (2034)*; concentration of reference solution (a) set at the same level as limit for unspecified impurities; system suitability test modified; limits updated in accordance with batch data.

Assay: need to neutralise anhydrous ethanol avoided; volume of anhydrous ethanol increased to ensure electrode is fully covered by the test solution.

Impurities: section updated.

Temazepam (0954)

Content: limits adjusted to the new LC assay.

Impurity A: test deleted, as the impurity is now controlled by the test for related substances.

Related substances: introduction of a more robust analytical procedure to control additional impurities; limits updated to reflect the quality of substances in approved medicinal products on the European market.

Assay: the titration has been replaced by a cross-reference to the LC method for related substances.

Tiamulin for veterinary use (1660)

Related substances: the grades of solvents have been amended in accordance with the Technical Guide.

Impurities: the structure of impurity D has been revised based on recent structural elucidation data.

Tiamulin hydrogen fumarate for veterinary use (1659)

Related substances: the grades of solvents have been amended in accordance with the Technical Guide.

Impurities: the structure of impurity D has been revised based on recent structural elucidation data.

Trolamine (1577)

Sulfated ash: the sentence “Do not carry out the initial heating on a water-bath” was deleted because it referred to a step that is no longer included in general chapter *2.4.14*.

Vanillin (0747)

Second identification: previously described reaction C (TLC) deleted to avoid the use of dinitrophenylhydrazine (explosive). The remaining tests are considered sufficiently specific for the purpose of the second identification.

Identification test B: preparation of the sample as disks deleted.

Editorial and style changes have also been made to the entire text.

Water for injections (0169)

Water for injections in bulk. Nitrates: deleted. Scientific evidence demonstrates that if a sample meets the conductivity requirements described, it will also comply with the test for nitrates.

Water for injections in bulk and Sterilised water for injections. Bacterial endotoxins: the possibility of performing the control of bacterial endotoxins using recombinant factor C (rFC) test has been introduced.

Water, purified (0008)

Purified water in bulk - Tests.

Nitrates: addition of a sentence stating that if the sample complies with the conductivity requirements prescribed for *Water for injections (0169)* in bulk, it is not necessary to perform the test for nitrates.

Bacterial endotoxins: the possibility of performing the control of bacterial endotoxins using recombinant factor C (rFC) test has been introduced.

Zopiclone (1060)

Related substances: test updated; impurities now determined quantitatively.

2-Propanol: test revised to avoid the use of ethylene chloride proscribed under the REACH regulation; analytical procedure described in the monograph.