Comments concerning new and revised texts published in the 11th Edition (11.0)

A brief description of the technical modifications that have been made to new and revised texts adopted by the European Pharmacopoeia Commission at the November 2021 session and published in the 11th Edition (11.0) is provided below. 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

1. General notices

1.1.2.1 Scope: paragraph on medicinal products deleted (see 1.5.3.1 Titles).

1.1.2.1 Scope, Shelf life and retest period: statement rephrased to state that for some substances (e.g. substances known to be labile, biotechnological/biological substances and certain antibiotics) a shelf life is established rather than a re-test period.

1.2.7 Reagents and solvents: terms 'alcohol' and 'ethanol' without qualification: sentence deleted.

1.5.3.1 Titles: paragraph on medicinal products containing active substance salts added.

1.7 ABBREVIATIONS AND SYMBOLS: definitions of R_F and R_{st} deleted (included in revised chapter *2.2.46*).

2.1.3. Ultraviolet ray lamps for analytical purposes

Mercury lamps are seldom used nowadays so alternatives have been added to reflect current lab practices.

2.2.46. Chromatographic separation techniques

This text corresponds to the sign-off text signed by the Pharmacopoeial Discussion Group (Ph. Eur., JP, USP). The coordinating pharmacopoeia is the Ph. Eur.

The items that are local requirements, i.e. only included in the Ph. Eur., have been placed between white diamonds (◊◊).

The text has undergone a general revision, but compared to the last publication the principal changes are the following:

- symmetry factor: 0.8-1.8 instead of 0.8-1.5;

- statement that retention times and relative retentions are not requirements but given for information in the monographs;

- system repeatability in assay: applicable to both active substances and excipients;

- adjustments of the stationary phase, column dimensions, mobile phase, flow rate, injection volume (isocratic and gradient liquid chromatography); under conditions much stricter than in the current text, a UHPLC column may be used instead of an HPLC one;

- adjustments of the column dimensions, injection volume and split ratio, injection port and transfer-line temperatures (gas chromatography);

- adjustments for supercritical fluid chromatography deleted as technique not used in the Ph. Eur.

2.7.36. Assay of Bet v 1 allergen

The general chapter describes an assay to detect monomeric Bet v 1 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 2012:118-34;

- Kaul S, Zimmer J, Dehus O et al. Validation of ELISA methods for quantification of the major birch allergen Bet v 1 (BSP090) Pharmeur Bio Sci Notes 2017:69-87.

It should be noted that Bet v 1 molecules in birch pollen extract are able to oligomerise; whether these oligomers are detected by the procedure has not been evaluated.

2.9.2. Disintegration test for solid rectal and vaginal dosage forms

Title: changed to reflect the applicability of this general chapter.

Apparatus: addition of detailed description of the disintegration apparatus, indicating the cylinder dimensions.

Test procedure for vaginal tablets: clearly separated from those of the rectal and other vaginal dosage forms.

2.9.3. Dissolution test for solid dosage forms

The following changes were made:

- the term “conventional-release” was replaced by “immediate-release” throughout the text to align it with the current terminology used in European regulations and guidelines as well as with the wording used by the other PDG members, JP and USP; the Glossary (1502) already defines these two terms as equivalent, therefore the change could be considered as solely editorial;

- in the various Acceptance Tables in the Interpretation section, the term "unit(s)" was replaced by "value(s)" and "unit" was replaced by "dosage unit" to reflect better the PDG sign-off text and to improve consistency and clarity;

- other minor editorial changes for consistency reasons.

5.17.1. Recommendations on dissolution testing

This minor revision was triggered by the revision of the general chapter *Dissolution test of solid dosage forms (2.9.3)* in which the term "conventional-release" was replaced by "immediate-release". The purpose of the revision of *2.9.3* was to align the text with the current terminology used in European regulations and guidelines as well as with the wording used by the other PDG members, JP and USP. These two terms are considered equivalent.

GENERAL MONOGRAPHS

Vaccines for veterinary use (0062)

Final bulk and final batch (section 2-3-3): specific requirements for non-liquid vaccines for non-parenteral use have been added to cover new pharmaceutical forms such as oral vaccines in tablets, effervescent tablets, freeze-dried spheres, presented in novel packaging presentations such as blister packs or plastic sealed cups. However, since these final stages of packaging are difficult or impossible to perform under aseptic conditions as currently required, the requirements have been revised to introduce "suitable conditions" and "suitable containers". These changes must be justified and agreed by the competent authority and are also in line with the new Regulation (EU) 2019/6 coming into force on 28 January 2022.

It has also been clarified that batches of live bacterial antigen cannot be tested for sterility since they contain a living micro-organism. Nevertheless, this is the only exception. Any other type of antigen and all substances must be sterile at this stage. The blending must be performed under aseptic conditions.

Bacteria and fungi (section 3-8): specific requirements for non-liquid vaccines for non-parenteral use have been added. The sterility requirements may be replaced by absence of relevant pathogenic micro-organisms and an appropriately low number of contaminating micro-organism based on batch data and process validation, provided that the product remains stable throughout its shelf life.

DOSAGE FORMS

Glossary (1502)

This minor revision was triggered by the revision of the general chapter *Dissolution test of solid dosage forms (2.9.3)* in which the term "conventional-release" was replaced by "immediate-release". The purpose of the revision of *2.9.3* was to align the text with the current

terminology used in European regulations and guidelines as well as with the wording used by the other PDG members, JP and USP. These two terms are considered equivalent.

RADIOPHARMACEUTICAL PREPARATIONS AND STARTING MATERIALS FOR RADIOPHARMACEUTICAL PREPARATIONS

Tetra-*O*-acetyl-mannose triflate for radiopharmaceutical preparations (2294)

Related substances/Assay. The column used in the LC procedure for the related substances test and for the Assay is no longer available in the required quality. A new and much faster LC procedure is proposed using a different column.

HERBAL DRUGS AND HERBAL DRUG PREPARATIONS

Codonopsis root (2714)

Identification C (HPTLC): preparation of the test solution revised to better reflect what had been done during the development of the analytical procedure.

Platycodon root (2660)

Identification C (HPTLC): preparation of the test solution revised to better reflect what had been done during the development of the analytical procedure.

HOMOEOPATHIC PREPARATIONS

Ferrum metallicum for homoeopathic preparations (2026)

Assay: optimisation of the titration method following users comments on the poor solubility of the substance in hot copper sulfate solution. In the assay proposed, the use of toxic copper sulfate is avoided, no filtration step of the dissolved substance is necessary, the end point of titration with ferroin solution is more easily visible (change of colour from red-orange to blue) and cerium sulfate is more stable than potassium permanganate which had to be freshly prepared.

Hyoscyamus for homoeopathic preparations (2091)

Mother tincture

Definition: revised to determine the total alkaloid content as the sum of hyoscyamine and hyoscine.

Production: updated to include all the production methods.

TLC identification of the mother tincture: the TLC method has been harmonised with the TLC method of the monographs for other tropane alkaloids and the HPTLC conditions have been added.

Tests: the test for atropine has been deleted because it is not necessary for fresh plant material, for which atropine is not contained in significant amounts and will not arise if the mother tincture is stored correctly.

Assay: the titration is replaced by the HPLC assay that is also included in the other tropane alkaloid monographs based on the assay developed for *Belladonna for homoeopathic preparations (2489*), with some amendments, e.g.:

- *the amount of the mother tincture in the test solution has been adjusted to the expected content;*

- *a cartridge filled with cation-exchange material with a greater surface (30-33 µm instead of 60 µm) is now used for the mother tinctures;*

- *the reference solutions now have the same concentrations and injection volumes;*

- *two further gradient steps have been added to ensure constant and reproducible conditions for all tropane alkaloid monographs.*

The monograph has also been updated according to the current Guide for the elaboration of monographs on homoeopathic preparations (https://www.edqm.eu/en/technical-guides).

MONOGRAPHS

Acitretin (1385)

Second Identification section included as the substance is used in pharmacies.

Adrenaline (2303)

Content: reference to the anhydrous instead of the dried substance, due to the replacement of loss on drying by a test for water.

Specific optical rotation: reference to the anhydrous instead of the dried substance, due to the replacement of loss on drying by a test for water.

Loss on drying: test replaced by micro determination of water with a specification of maximum 0.4 per cent.

Argon (2407)

Identification B: modification of the gas chromatographic procedure including an improved system suitability test.

Calcium chloride hexahydrate (0707)

Barium: in line with the Ph. Eur. implementation strategy for the ICH Q3D guideline on elemental impurities, the test is deleted.

Identification B: it is considered sufficient to use only reaction (b).

Carprofen for veterinary use (2201)

Related substances: in preparation of reference solution (a), volume expressed using fewer significant figures due to the qualitative use of this solution; grade of methanol amended in accordance with Technical Guide (2015); Identification of peaks section added; relative retention of impurity C introduced.

Heavy metals: further to the CVMP decision published on 23 January 2020 (EMA/CVMP/QWP/631010/2017-Rev.2) to require a risk assessment to control elemental impurities in all veterinary medicinal products by January 2023, the test has been deleted from monographs "for veterinary use".

Cefoxitin sodium (0990)

Related substances: following the identification of impurity J as cefoxitin lactone, identical to impurity D, the latter has been deleted and the limit for impurity J has been adjusted based on batch data.

It has been shown that impurities E and F elute as two peaks, though it was not possible to assign a peak to each impurity as these were diastereomers.

It has also been found that the newly added impurity K, a degradation product of impurity J, co-elutes with the second of the two peaks due to impurities E/F. As a consequence, the three impurities E, F and K are listed as specified impurities and a limit for their sum has been introduced.

Bacterial endotoxins: the test has been deleted in accordance with the Ph. Eur. policy adopted in February 2015 (see Pharmeuropa online, Technical information).

Impurities: following the identification of impurity J as cefoxitin lactone, impurity D has been deleted. The structures of impurities H, I and J have been introduced. The new impurity K, whose structure is unknown, has been introduced.

Cellulose acetate phthalate (0314)

Storage: black diamonds have been added to indicate that this is a non-harmonised attribute.

Cholecalciferol (0072)

Related substances. In order to overcome a stability issue, reference solution (b) is now prepared using *cholecalciferol impurity A CRS* (produced by vial evaporation) together with the current *cholecalciferol CRS*.

Cholecalciferol concentrate (oily form) (0575)

Related substances. In order to overcome a stability issue, reference solution (b) is now prepared using *cholecalciferol impurity A CRS* (produced by vial evaporation) together with the current *cholecalciferol CRS*.

Cholecalciferol concentrate (powder form) (0574)

Related substances: In order to overcome a stability issue, reference solution (b) is now prepared using *cholecalciferol impurity A CRS* (produced by vial evaporation) together with the current *cholecalciferol CRS*.

Cholesterol for parenteral use (2397)

Content: limits widened to 98.0 to 102.0 per cent in line with the recommendations of the Technical Guide for GC assays.

Assay: symmetry factor applies to the peaks used for quantification.

Ciclopirox olamine (1302)

Loss on drying: use of normal vacuum is appropriate.

Ciprofibrate (2013)

Related substances: impurity limits updated to reflect the current quality of the substances in approved medicinal products on the European market; the limit for unspecified impurities introduced in line with requirements of the general monograph *Substances for pharmaceutical use (2034)*.

Ciprofloxacin hydrochloride (0888)

Identification: test B modified in order to avoid the use of potassium dichromate (REACH).

Codergocrine mesilate (2060)

Definition: limits are expressed as dihydroergocristine and applying correction factors.

Related substances, Composition: the fact that there is about 30 % of dihydroergocristine contained in the substance has been taken into account in the preparation of reference solution (a) and in the dilution of reference solution (b).

Colchicine (0758)

Second identification: thin-layer chromatography test added; previous tests A, C and D deleted.

Cyclophosphamide monohydrate (0711)

Title: the degree of hydration has been added.

Related substances: the test has been updated, the current TLC has been replaced by a liquid chromatography supplemented by 2 TLCs to cover impurities which are not detected by LC.

Cytarabine (0760)

Loss on drying: description of normal vacuum which has been shown to be appropriate.

Daunorubicin hydrochloride (0662)

Definition: the wording has been adjusted to clearly indicate fermentation as the only means by which the substance is obtained.

Related substances, Assay: an improved method giving better separation has been introduced; impurity limits have been adapted based on batch data.

Assay: the content calculation has been clarified to take into account the assigned content of *daunorubicin hydrochloride CRS*.

Impurities: impurity G has been added to the list and the section now distinguishes between specified and other detectable impurities.

Dequalinium chloride (1413)

Definition: it is clarified that the substance contains a variable quantity of water.

Content: the limits updated to reflect the repeatability of the procedure and recent batch data.

Related substances: specifications updated to reflect the current quality of substances in approved medicinal products on the market; an explicit criterion for unspecified impurities introduced in accordance with the general monograph *2034 Substances for pharmaceutical use*.

Loss on drying: test replaced by semi-micro determination of water for a more accurate determination of the water content.

Impurities: transparency list updated.

Difloxacin hydrochloride trihydrate for veterinary use (2239)

Related substances: grade of water in Solution A amended in accordance with Technical Guide (2015); in preparation of reference solution (c), volume expressed using fewer significant figures due to the qualitative use of this solution.

Heavy metals: further to the CVMP decision published on 23 January 2020 (EMA/CVMP/QWP/631010/2017-Rev.2) to require a risk assessment to control elemental impurities in all veterinary medicinal products by January 2023, the test has been deleted from monographs “for veterinary use”.

Dihydroergotamine mesilate (0551)

Loss on drying: use of normal vacuum is appropriate.

Dihydrostreptomycin sulfate for veterinary use (0485)

Heavy metals: further to the CVMP decision published on 23 January 2020 (EMA/CVMP/QWP/631010/2017-Rev.2) to require a risk assessment to control elemental impurities in all veterinary medicinal products by January 2023, the test has been deleted from monographs “for veterinary use”.

Enrofloxacin for veterinary use (2229)

Heavy metals: further to the CVMP decision published on 23 January 2020 (EMA/CVMP/QWP/631010/2017-Rev.2) to require a risk assessment to control elemental impurities in all veterinary medicinal products by January 2023, the test has been deleted from monographs "for veterinary use".

Sulfated ash: use of a platinum crucible indicated since the substance contains fluorine.

Erythromycin (0179)

Assay: the symmetry factor requirement for the peak due to erythromycin A has been adjusted from 2.0 to 2.5 based on batch data.

Erythromycin estolate (0552)

Related substances: the grades of solvents have been amended in accordance with Technical Guide (2015).

Assay: the symmetry factor requirement for the peak due to erythromycin A has been adjusted from 2.0 to 2.5 based on batch data.

Erythromycin ethylsuccinate (0274)

Assay: the symmetry factor requirement for the peak due to erythromycin A has been adjusted from 2.0 to 2.5 based on batch data.

Erythromycin lactobionate (1098)

Related substances: the grades of solvents have been amended in accordance with Technical Guide (2015).

Assay: the symmetry factor requirement for the peak due to erythromycin A has been adjusted from 2.0 to 2.5 based on batch data.

Erythromycin stearate (0490)

Related substances: the grades of solvents have been amended in accordance with Technical Guide (2015).

Assay: the symmetry factor requirement for the peak due to erythromycin A has been adjusted from 2.0 to 2.5 based on batch data.

Etodolac (1422)

Related substances, reference solution (c), the API has been omitted from the reference standard for peak identification.

Febantel for veterinary use (2176)

Heavy metals: further to the CVMP decision published on 23 January 2020 (EMA/CVMP/QWP/631010/2017-Rev.2) to require a risk assessment to control elemental impurities in all veterinary medicinal products by January 2023, the test has been deleted from monographs "for veterinary use".

Related substances: relative retentions of impurities A, B and C added.

Fenbendazole for veterinary use (1208)

Related substances: grade of water in mobile phase amended in accordance with Technical Guide (2015).

Heavy metals: further to the CVMP decision published on 23 January 2020 (EMA/CVMP/QWP/631010/2017-Rev.2) to require a risk assessment to control elemental impurities in all veterinary medicinal products by January 2023, the test has been deleted from monographs "for veterinary use".

Fish oil, rich in omega-3 acids (1912)

Definition: oil obtained from fish of the genera Thunnus and Sarda within the family of Scombridae is no longer excluded as source for fish oil rich in omega-3 acids, type I.

Acid value: *light petroleum R3* replaced by *ether R*.

Follitropin (2285)

Oxidised follitropin: calculation of total oxidised follitropin was modified to include an additional peak identified as an oxidised form of the follitropin α-subunit which was also included in the *follitropin CRS* leaflet; a paragraph on identification of peaks was added.

Follitropin concentrated solution (2286)

Oxidised follitropin: calculation of total oxidised follitropin was modified to include an additional peak identified as an oxidised form of the follitropin α-subunit which was also included in the *follitropin CRS* leaflet; a paragraph on identification of peaks was added.

Hydroxyethyl salicylate (1225)

Identifications D and E deleted.

Test for related substances added.

Isradipine (2110)

Related substances: the limit for unspecified impurities introduced in line with requirements of the general monograph *Substances for pharmaceutical use (2034)*.

Levocarnitine (1339)

Test for related substances improved.

Levomepromazine maleate (0925)

Identification: test A deleted from second identification testing; description of sample preparation in test B deleted; retardation factors added in test D.

Related substances: TLC method replaced by a new LC method, three additional impurities covered.

Impurities: section updated.

Lufenuron for veterinary use (2177)

Heavy metals: further to the CVMP decision published on 23 January 2020 (EMA/CVMP/QWP/631010/2017-Rev.2) to require a risk assessment to control elemental impurities in all veterinary medicinal products by January 2023, the test has been deleted from monographs "for veterinary use".

Magnesium chloride 4.5-hydrate (1341)

Arsenic: in line with the Ph. Eur. implementation strategy for the ICH Q3D guideline on elemental impurities, the test is deleted.

Mannitol (0559)

Bacterial endotoxins: black diamonds have been deleted to indicate that this test is a harmonised attribute not stipulated by all pharmacopoeias.

Functionality-related characteristics: white diamonds have been added to clarify that this section, which is non-mandatory, is only present in the Ph. Eur. text and not subject to pharmacopoeial harmonisation.

Marbofloxacin for veterinary use (2233)

Related substances: expression of acceptance criteria in the quantitative style; specification 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 specification for unspecified impurities; specifications for known impurities updated; additional system suitability test criterion based on minimum signal-to-noise ratio added; CRS strategy modified.

Heavy metals: further to the CVMP decision published on 23 January 2020 (EMA/CVMP/QWP/631010/2017-Rev.2) to require a risk assessment to control elemental impurities in all veterinary medicinal products by January 2023, the test has been deleted from monographs "for veterinary use".

Mesna (1674)

LOD: normal vacuum is appropriate.

Related substances: update of the grade of the solvents used in the preparation of the mobile phase.

Methylene chloride (0932)

Introduction of a reference spectrum instead of a CRS due to toxicity of the substance.

Morantel hydrogen tartrate for veterinary use (1546)

Heavy metals: further to the CVMP decision published on 23 January 2020 (EMA/CVMP/QWP/631010/2017-Rev.2) to require a risk assessment to control elemental impurities in all veterinary medicinal products by January 2023, the test has been deleted from monographs "for veterinary use".

Related substances: grade of solvents used in the mobile phase amended in accordance with Technical Guide; retention time and relative retentions updated; example of chromatogram added for information.

Moxidectin for veterinary use (1656)

Related substances: grades of solvents amended in accordance with Technical Guide (2015).

Heavy metals: further to the CVMP decision published on 23 January 2020 (EMA/CVMP/QWP/631010/2017-Rev.2) to require a risk assessment to control elemental impurities in all veterinary medicinal products by January 2023, the test has been deleted from monographs "for veterinary use".

Nitrogen (1247)

Assay: detection temperature of 130 °C was not suitable for certain instrumental setups and was replaced by a constant temperature within the range of 50 °C to 200 °C. The instruction to adjust the injected volumes and operating conditions so that the height of the peak due to nitrogen in the chromatogram obtained with reference gas (a) was at least 35 per cent of the full scale of the recorder was replaced by the instruction to inject 1 mL of the gas. With modern instrumentation recorder adjustment is no longer relevant.

Paraffin, white soft (1799)

This text corresponds to the sign-off text signed by the Pharmacopoeial Discussion Group (Ph. Eur., JP, USP). The coordinating pharmacopoeia is the USP. Non-harmonised attributes have been placed between black diamonds (♦ ♦), while local requirements only present in the Ph. Eur. text have been placed between white diamonds (◊ ◊).

Compared to the chapter published in the 10th Edition of the Ph. Eur., the following principal changes are included:

Definition: the statement concerning unsuitability for oral use has been introduced as a local attribute since this reflects regulatory requirements in Europe. Slight changes have been introduced to harmonise the wording.

Characters: slight clarifications introduced to harmonise the wording. Section is flagged as non-harmonised.

Identification: 2nd identification is flagged as a local attribute. IR preparation is simplified.

Drop point: procedure slightly modified to improve the melting of the substance.

Appearance: the description of the test modified to align the three Pharmacopoeias.

Consistency: test moved to the FRC section as it is considered appropriate to assess the functionality of white soft paraffin used as a basis in semi-solid preparations; the lower limit is flagged as non-harmonised.

UV absorbance limit for polycyclic aromatic hydrocarbons: limit decreased based on proposal for international harmonisation (specification to cover limits by FDA 21CFR172.880). Path length adjusted to reflect standard cells with 1 cm.

Paraffin, yellow soft (1554)

This text corresponds to the sign-off text signed by the Pharmacopoeial Discussion Group (Ph. Eur., JP, USP). The coordinating pharmacopoeia is the USP. Non-harmonised attributes are placed between black diamonds (♦ ♦), while local requirements only present in the Ph. Eur. text are placed between white diamonds (◊ ◊).

Compared to the chapter published in the 10th Edition of the Ph. Eur., the following principal changes are included:

Definition: the statement concerning unsuitability for oral use has been introduced as a local attribute since this reflects regulatory requirements in Europe. Slight changes introduced to harmonise the wording.

Characters: slight clarifications introduced to harmonise the wording. Section is flagged as non-harmonised.

Identification: 2nd identification is flagged as a local attribute. IR preparation simplified.

Drop point: limits and procedure slightly modified to improve the melting of the substance.

Appearance: the description of the test modified to align the three Pharmacopoeias.

Consistency: test moved to the FRC section as it is considered appropriate to assess the functionality of yellow soft paraffin used as a basis in semi-solid preparations.

UV absorbance limit for polycyclic aromatic hydrocarbons: limit decreased based on proposal for international harmonisation (specification to cover limits by FDA 21CFR172.880). Path length adjusted to reflect standard cells with 1 cm.

Pimobendan for veterinary use (2179)

Heavy metals: further to the CVMP decision published on 23 January 2020 (EMA/CVMP/QWP/631010/2017-Rev.2) to require a risk assessment to control elemental impurities in all veterinary medicinal products by January 2023, the test has been deleted from monographs “for veterinary use”.

Potassium iodide (0186)

Iodates and Thiosulfates: a colour produced in the reaction is corrected, based on laboratory results.

Selamectin for veterinary use (2268)

Related substances, Assay: grades of solvents amended in accordance with Technical Guide (2015).

Heavy metals: further to the CVMP decision published on 23 January 2020 (EMA/CVMP/QWP/631010/2017-Rev.2) to require a risk assessment to control elemental impurities in all veterinary medicinal products by January 2023, the test has been deleted from monographs “for veterinary use”.

Sodium hyaluronate (1472)

Intrinsic viscosity: description of conditions for validity of the test clarified.

Protein: test description clarified to include both test solutions in the analysis.

Sodium iodide (0196)

Iodates and Thiosulfates: a colour produced in the reaction is corrected, based on laboratory results.

Spiramycin (0293)

Composition and related substances: the general requirement given in the general chapter *2.2.46* for the symmetry factor being too strict, specific requirements have been introduced in the monograph based on batch data; the grades of solvents have been amended in accordance with Technical Guide (2015).

Stearic acid (1474)

This text corresponds to the sign-off text signed by the Pharmacopoeial Discussion Group (Ph. Eur., JP, USP). The coordinating pharmacopoeia is the JP. Non-harmonised attributes have been placed between black diamonds (♦ ♦), while local requirements only present in the Ph. Eur. text have been placed between white diamonds (◊ ◊).

Compared to the monograph published in the 10th Edition of the Ph. Eur., the following changes are proposed.

Freezing point: an alternative apparatus complying with JP <2.42> has been added.

Nickel: in line with the Ph. Eur. implementation strategy for the ICH Q3D guideline on elemental impurities, deletion of the test has already been published in Pharmeuropa and would be deleted in Supplement 10.4 (implementation date April 1st, 2021).

Functionality-related characteristics: white diamonds have been added showing that this section is only present in the Ph. Eur. text.

Sucrose (0204)

Functionality-related characteristics: addition of section (considered as non-harmonised); for sucrose used as filler/diluent in solid dosage forms, cross-reference to Particle-size distribution and Bulk and tapped density.

Sulfadimethoxine sodium for veterinary use (2745)

Heavy metals: further to the CVMP decision published on 23 January 2020 (EMA/CVMP/QWP/631010/2017-Rev.2) to require a risk assessment to control elemental impurities in all veterinary medicinal products by January 2023, the test has been deleted from monographs “for veterinary use”.

Sulfamethoxypyridazine for veterinary use (0638)

Heavy metals: further to the CVMP decision published on 23 January 2020 (EMA/CVMP/QWP/631010/2017-Rev.2) to require a risk assessment to control elemental impurities in all veterinary medicinal products by January 2023, the test has been deleted from monographs “for veterinary use”.

Thioridazine hydrochloride (0586)

Identification: test B modified in order to avoid the use of potassium dichromate (REACH).

Related substances: the limit for unspecified impurities aligned with the requirements of the general monograph *Substances for pharmaceutical use (2034)*.

Tinidazole (1051)

Second identification: tests B (UV) and D (TLC) deleted; the remaining tests are considered sufficiently specific for the purpose of the second identification.

Related substances: grade of water amended in accordance with Technical Guide (2015); identification of impurities section included.

Tretinoin (0693)

Second identification: TLC and colour reaction tests combined in a newly established TLC method.

Related substances: stationary phase description and retention time updated in line with the columns that are suitable.

Vedaprofen for veterinary use (2248)

Related substances: in preparation of the test solution, mass expressed using more significant figures due to the quantitative use of this solution; in preparation of reference solution (b), volume expressed using fewer significant figures due to the qualitative use of this solution; reagent used to describe stationary phase modified; grade of water in mobile phase amended in accordance with Technical Guide (2015).

Heavy metals: further to the CVMP decision published on 23 January 2020 (EMA/CVMP/QWP/631010/2017-Rev.2) to require a risk assessment to control elemental impurities in all veterinary medicinal products by January 2023, the test has been deleted from monographs “for veterinary use”.

Xylazine hydrochloride for veterinary use (1481)

Heavy metals: further to the CVMP decision published on 23 January 2020 (EMA/CVMP/QWP/631010/2017-Rev.2) to require a risk assessment to control elemental impurities in all veterinary medicinal products by January 2023, the test has been deleted from monographs “for veterinary use.