

## REVISED TEXTS PUBLISHED IN THE 4<sup>th</sup> EDITION OF THE EUROPEAN PHARMACOPOEIA

A summary of the technical modifications to the revised texts (adopted in the March, June and November 2000 Sessions) is indicated below.

### GENERAL TEXTS

#### 1. General notices

General revision.

#### 2.2.24. Infrared absorption spectrophotometry

Preparation of the sample: addition of the section "for recording by attenuated total reflectance".

#### 2.2.25. Absorption spectrophotometry, ultraviolet and absorption

Revision of the section Limit of stray light.

#### 2.2.46. Chromatographic separation techniques

Harmonisation of terminology with IUPAC.  
Deletion of the first two lines in Table 2.2.46-1.

#### 2.4.8. Heavy metals

Revision of method F.

#### 2.4.14. Sulphated ash

Revision to harmonise with the Japanese and United States Pharmacopoeias.

Deletion of the use of ammonium carbonate during the ashing procedure.

Replacement of dilute sulphuric acid with concentrated sulphuric acid.

#### 2.9.17. Extractable volume

Harmonisation with the United States Pharmacopoeia and Japanese Pharmacopoeia.

#### 2.9.19. Particulate contamination: sub-visible particles

Harmonisation with the United States Pharmacopoeia and Japanese Pharmacopoeia with the exception of the requirements for preparations supplied in containers with a nominal volume of 100 ml.

#### 3.2.9. Rubber closures for containers for aqueous parenteral preparations for powders and for freeze-dried powders

Revision of chapter 3.2.9 and deletion of the chapter 3.1.12 (see explanations in Pharmeuropa 12.3).

#### 4.2.1. Primary standards for volumetric solutions

#### 4.2.2. Volumetric solutions

Elimination of the use of arsenious trioxide and osmium tetroxide.

Introduction of a method of standardisation of 0.1 M sodium hydroxide when used in the titration of halogen salts of organic bases.

Deletion of 0.02 M mercuric nitrate, which is no longer used.

Addition of a statement concerning the use of primary standards from commercial sources.

Deletion of the statement that solutions below 0.1 M are freshly prepared.

#### 5.2.8. Minimising the risk of animal spongiform encephalopathy agents via medicinal products

Revision to take account of the latest version of the EMEA Note for Guidance.

### MONOGRAPHS

#### Air, medicinal (1238)

Modification of the title of the monograph.

#### Amitriptyline hydrochloride (0464)

Related substances: modification of the drying and detection conditions.

#### Ammonium chloride (0007)

Identification B: indication of the volume of solution suitable for the test.

#### Amoxicillin sodium (0577)

Bacterial endotoxins: deletion of the reference to method C.

#### Apomorphine hydrochloride (0136)

Related substances: replacement of TLC by HPLC.  
Assay: replacement of mercuric acetate.

#### Aprotinin (0580)

#### Aprotinin concentrated solution (0579)

Replacement of the pyrogen test with the bacterial endotoxin test.

#### Arachis oil, refined (0263)

Definition: possibility to add a suitable antioxidant.

Composition of fatty acids: use of a specific reference solution, modification of some limits and deletion of the ratio linoleic acid: behenic acid.

Deletion of the tests for Semi-drying oils and Sesame oils.

#### Aspartic acid (0797)

Modification of the test for chlorides.

**Aujeszký's disease vaccine (live) for pigs for parenteral administration, freeze-dried (0745)**

Safety test E : this test is not necessary for gE-negative strains.

**Bearberry leaf (1054)**

Definition and Assay: replacement of the assay of hydroquinone derivatives by spectrophotometry with an assay of arbutin by liquid chromatography, consequently the content in the definition has been decreased from 8 per cent to 7 per cent.

**Benzoyl peroxide, hydrous (0704)**

Revision of the test for related substances.

**Benzyl alcohol (0256)**

Harmonisation with the Japanese Pharmacopoeia and United States Pharmacopoeia.

Content: modification of the lower limit to 98.0 per cent.

Characters: relative density moved from Tests to Characters.

Identification: replacement of the chemical identification by infrared spectrophotometry.

Appearance of solution: addition of the requirement for a colourless solution.

Benzaldehyde and other related substances: modification of the method and limits.

Halogenated compounds and halides: deletion of the test.

**Betamethasone valerate (0811)**

Related substances: modification of the solvent used for preparation of the test solution and reference solutions.

**Bifonazole (1395)**

Revision of the solubility in ethanol.

**Budesonide (1075)**

Modification of the impurities section.

**Bupivacaine hydrochloride (0541)**

Identification A (infrared absorption spectrophotometry): modification of the sample preparation.

Related substances: replacement of TLC by GC.

**Buprenorphine (1180)**

Addition of impurities D and E to the transparency list.

**Calcium stearate (0882)**

Tests for cadmium, nickel and lead: replacement of the air-acetylene flame with a graphite furnace as atomic generator.

**Captopril (1079)**

Identification: deletion of the second identification series.

Specific optical rotation: replacement of water with ethanol and modification of limits.

**Carbamazepine (0543)**

Modification of the impurities section.

**Carbimazole (0884)**

Thiamazole and other related substances test: replacement of the current TLC method by an HPLC method.

**Carbon dioxide (0375)**

Revision of the test for nitrogen monoxide and nitrogen dioxide.

**Catgut, sterile (0317)**

Production: addition of the statement "Production complies with relevant regulations on the use of animal tissues in medical devices, notably concerning the risk of transmission of animal spongiform encephalopathy agents".

**Cefaclor (0986)**

Modification of the impurities section.

**Cefamandole nafate (1402)**

Assay: revision of system suitability criteria.

**Cefoperazone sodium (1404)**

Impurities: addition of an impurity derived from another synthetic pathway.

**Ceftriaxone sodium (0991)**

Identification: deletion of the second identification series.

Introduction of tests for *N,N*-dimethylaniline and for 2-ethylhexanoic acid.

Storage: deletion of the storage temperature.

**Cefuroxime sodium (0992)**

Identification: deletion of the second identification series.

Introduction of tests for *N,N*-dimethylaniline and for 2-ethylhexanoic acid.

Storage: deletion of the storage temperature.

**Chlorhexidine dihydrochloride (0659)**

Revision of the test for Chloroaniline.

**Ciclopirox olamine (1302)**

Revision of the tests for related substances and for loss on drying.

**Ciprofloxacin hydrochloride (0888)**

Modification of the impurities section.

**Cocaine hydrochloride (0073)**

Cinnamoylcocaines and reducing substances: deletion of the test.

Addition of a related substances test by liquid chromatography.

Assay: modification of the method to replace mercuric acetate.

### **Colistimethate sodium (0319)**

pH: revision to harmonise the limits with those of the United States Pharmacopeia and Japanese Pharmacopoeia.

### **Copovidone (0891)**

Harmonisation with the related monographs Povidone (0685) and Crospovidone (0892): aldehyde test replaced with the test described in the Povidone monograph and introduction of a test for 2-pyrrolidone (impurity A).

### **Cortisone acetate (0321)**

Related substances: addition of the statement "Prepare the solutions immediately before use".

### **Couch grass rhizome (1306)**

Revision of the test for *Cynodon dactylon*, imperata cylindrical.

### **Crospovidone (0892)**

Water soluble substances test: the limit has been lowered to 1 per cent.

Vinylpyrrolidone test: modification and harmonisation with the monograph on Povidone.

### **Crotamiton (1194)**

Content: upper limit increased to 102.0 per cent following revision of the general method Chromatographic separation techniques (2.2.46).

### **Daunorubicin hydrochloride (0662)**

Revision of the HPLC method used for the related substances test and the assay.

Replacement of the test for acetone and butanol with a test for butanol using the general method for residual solvents.

Replacement of the test for pyrogens with a test for bacterial endotoxins.

### **Dequalinium chloride (1413)**

Revision of IR identification test B.

### **Dextrans for injection (1506, 0999, 1000, 1001)**

Introduction of a Production section.

### **Dextropropoxyphene hydrochloride (0713)**

Addition of an Impurities section.

### **Diclofenac potassium (1508)**

Heavy metals: revision to specify that a quartz crucible must be used.

### **Diclofenac sodium (1002)**

Title: change in the English title (previously "Sodium diclofenac") in order to harmonise with the monograph Diclofenac potassium.

Heavy metals: revision to specify that a quartz crucible must be used.

### **Dihydroergocristine mesilate (1416)**

Revision of the test for related substances.

### **Dihydroergotamine mesilate (0551)**

Replacement of the method used for the assay.

### **Dihydroergotamine tartrate (0600)**

Replacement of the method used for the assay.

### **Dihydrostreptomycin sulphate for veterinary use (0485)**

Revision of title only: addition of "for veterinary use".

### **Docosate sodium (1418)**

Revision to replace the assay method and the definition.

### **Doxapram hydrochloride (1201)**

Revision of identification B and the related substances test.

### **Doxepin hydrochloride (1096)**

Related substances: modification of the drying conditions.

### **Doxorubicin hydrochloride (0714)**

Deletion of the second identification series (parenteral use only).

Replacement of the TLC method used in the related substances test and the HPLC method used in the assay with the HPLC method used in the related substances test for Daunorubicin hydrochloride.

Replacement of the test for acetone and ethanol with a test for ethanol using the general method for residual solvents.

Addition of a transparency statement.

### **Erythropoietin concentrated solution (1316)**

Identification B: replacement of isoelectric focusing by capillary zone electrophoresis.

### **Ethanol (96 per cent) (1317)**

### **Ethanol, anhydrous (1318)**

Volatile impurities test: revision of the method.

### **Ethinylestradiol (0140)**

Related substances test: revision of the limits.

### **Ethylene glycol monopalmitostearate (1421)**

Identification B: cross-reference to the test for composition of fatty acids.

Introduction of a test for composition of fatty acids.

**Etofenamate (1513)**

Revision of the related substances test.

**Fenbendazole for veterinary use (1208)**

Revision of title only: addition of "for veterinary use".

**Fenoterol hydrobromide (0901)**

Identification: use of a reference spectrum instead of the CRS.

Diastereoisomers : addition of a warning statement concerning the preparation of the solutions.

**Fentanyl citrate (1103)**

Modification of the impurities section.

**Fibrin sealant kit (0903)**

Water content: replacement of the limit of maximum 3.0 per cent with a reference to the limits approved by the competent authority.

**Fluocinolone acetonide (0494)**

Revision of Characters, Identification and the tests for specific optical rotation and for related substances.

**Fluoxetine hydrochloride (1104)**

Content: upper limit increased to 102.0 per cent following revision of the general method Chromatographic separation techniques (2.2.46).

**Framycetin sulphate (0180)**

Introduction of a test for related substances.

Deletion of the tests for alcohol content, neamine and neomycin C (neamine and neomycin C are now controlled by the related substances test).

Replacement of the test for pyrogens with a bacterial endotoxins test.

Revision of the impurities section.

**Furosemide (0391)**

Modification of the impurities section.

**Glucose, liquid, spray-dried (1525)**

Loss on drying: increase in the quantity of the substance to be examined due to the formation of a superficial crust on small samples.

**Glutamic acid (0750)**

Modification of the test for chlorides.

**Glycerol (0496)****Glycerol (85 per cent) (0497)**

Related substances: use of the peak corresponding to glycerol in the chromatogram obtained with reference solution (c) to estimate the impurities other than impurity A.

**Gonadotrophin, chorionic (0498)**

Water: replacement of GC method by coulometric titration.

Replacement of the pyrogen test with the bacterial endotoxin test.

**Gonadotrophin (equineserum for veterinary use) (0719)**

Replacement of the pyrogen test with the bacterial endotoxin test.

**Haemophilus type b conjugate vaccine (1219)**

General revision following updating of the corresponding WHO requirements.

**Human albumin solution (0255)**

Temperature of the virus inactivation step: the tolerance has been widened to  $\pm 1.0$  °C instead of  $\pm 0.5$ °C.

The wavelength for atomic spectrophotometric measurement of potassium has been corrected to the value in current tables (766.5 nm).

Limit for aluminium:  $\leq 200$  µg/l.

Labelling: deletion of the requirement for the statement on storage conditions and expiry date.

**Human antithrombin III concentrate (0878)**

Title: deletion of "freeze-dried" and "cryodesiccatus".

Water content: replacement of the limit of maximum 3.0 per cent with a reference to the limits approved by the competent authority.

Assay: reference to 2.7.17.

**Human coagulation factor VII (1224)**

Title: deletion of "freeze-dried" and "cryodesiccatus".

Water content: replacement of the limit of maximum 3.0 per cent with a reference to the limits approved by the competent authority.

Test for activated coagulation factors: reference to 2.6.22.

Addition of tests for factor II, factor IX and factor X with reference to 2.7.18, 2.7.11, 2.7.19 and introduction of limits for maximum content.

Assay: upper limit for potency estimate and confidence interval ( $p = 0.95$ ) increased to 125 %.

Labelling: deletion of the requirement for the statement on storage conditions and expiry date and addition of a requirement for a statement on the maximum content of factors II, IX and X per container.

**Human coagulation factor VIII (0275)**

Title: deletion of "freeze-dried" and "cryodesiccatus".

Water content: replacement of the limit of maximum 3.0 per cent with a reference to the limits approved by the competent authority.

Labelling: deletion of the requirement for the statement on storage conditions and expiry date.

### Human coagulation factor IX (1223)

Title: deletion of “freeze-dried” and “cryodesiccatus”.

Test for activated coagulation factors: reference to 2.6.22.

Water content: replacement of the limit of maximum 3.0 per cent with a reference to the limits approved by the competent authority.

Labelling: deletion of the requirement for the statement on storage conditions and expiry date.

### Human fibrinogen (0024)

Title: deletion of “freeze-dried” and “cryodesiccatum”.

Water content: replacement of the limit of maximum 3.0 per cent with a reference to the limits approved by the competent authority.

### Human normal immunoglobulin (0338)

Water content: replacement of the limit of maximum 3.0 per cent with a reference to the limits approved by the competent authority.

Labelling: deletion of the requirement for the statement on storage conditions and expiry date.

### Human normal immunoglobulin for intravenous administration (0918)

Water content: replacement of the limit of maximum 3.0 per cent with a reference to the limits approved by the competent authority.

Labelling: deletion of the requirement for the statement on storage conditions and expiry date.

### Human plasma for fractionation (0853)

Freezing conditions revised:

— plasma obtained from plasmapheresis is frozen at  $-30\text{ }^{\circ}\text{C}$  within 24 h of collection;

— for the manufacture of non-labile proteins, plasma obtained from whole blood is frozen at  $-20\text{ }^{\circ}\text{C}$  within 72 h of collection.

### Human prothrombin complex (0554)

Title: deletion of “freeze-dried” and “cryodesiccatum”.

Test for activated coagulation factors: reference to 2.6.22.

Water content: replacement of the limit of maximum 3.0 per cent with a reference to the limits approved by the competent authority.

Assay: reference to 2.7.18 for factor II and reference to 2.7.19 for factor X ( $p = 0.95, 90-111\%$ ).

Labelling: deletion of the requirement for the statement on storage conditions and expiry date.

### Hydroxyethyl salicylate (1225)

Characters: revision.

Assay: correction to use 0.0167 M potassium bromate instead of 0.02 M.

### Insulin (0276)

Deletion of the monograph on Insulin (0276) following the elaboration of separate monographs on Insulin, bovine (1637) and Insulin, porcine (1638).

Specifications for assay content and related proteins have been aligned with those of the monograph on Insulin, human (0838).

### Iohexol (1114)

Modification of the impurities section.

### Isoleucine (0770)

Specific optical rotation: limits modified to  $+40.0$  to  $+43.0$ .

### Ispaghula seed (1333)

Revision of the test for swelling index.

### Ivermectin (1336)

Definition: revision to correct the requirement for the content of the  $\text{H}_2\text{B}_{1a}$  compound.

Ethanol and formamide: modification of the GC in order to improve the separation.

### Java tea (1229)

Addition of an assay of sinensetin by liquid chromatography.

### Ketamine hydrochloride (1020)

Introduction of a test for optical rotation following the marketing of (*S*)-ketamine hydrochloride.

### Lactic acid (0458)

General revision following the elaboration of a separate monograph on (*S*)-lactic acid (1771).

### Levamisole hydrochloride (0726)

Identification: deletion of the second identification series.

Related substances test: replacement of TLC with HPLC.

Addition of an impurities section.

### Levonorgestrel (0926)

Modification of the impurities section.

### Liothyronine sodium (0728)

Content: upper limit increased to 102.0 per cent following revision of the general method Chromatographic separation techniques (2.2.46).

### Macrogolglycerol hydroxystearate (1083)

Title: change in the English title (previously “Castor oil, polyoxyl hydrogenated”) in order to reflect the

chemical structure of the product instead of the production method used.

Identification C: spraying reagent and preparation of the test solution and reference solution.

Residual ethylene oxide and dioxan: reference to the general method (2.4.25).

Heavy metals: method A or B according to the solubility of the substance.

#### **Macroglycerol ricinoleate (1082)**

Title: change in the English title (previously “Castor oil, polyoxyl”) in order to reflect the chemical structure of the product instead of the production method used.

Characters: indication that the substance may be semi-solid.

Identification C: spraying reagent and preparation of the test solution and reference solution.

Residual ethylene oxide and dioxan: reference to the general method (2.4.25).

Heavy metals: standard solution.

#### **Macrogol stearate (1234)**

Definition: 2 types of macrogol stearate are defined according to the type of stearic acid used for production.

Identification B: cross-reference to the test for composition of fatty acids.

Acidity or alkalinity: replacement of the test with a test for alkalinity.

Melting point: modification of the upper limit for 100 ethylene oxide unit products.

Introduction of a test for composition of fatty acids.

#### **Macrogols (1444)**

Characters: information presented as a table.

#### **Magnesium carbonate, heavy (0043)**

#### **Magnesium carbonate, light (0042)**

Test for apparent volume moved from Characters to Identification.

#### **Magnesium hydroxide (0039)**

Identification: reference to the test for loss on ignition.

#### **Magnesium oxide, heavy (0041)**

#### **Magnesium oxide, light (0040)**

Test for apparent volume moved from Characters to Identification.

Identification: reference to the test for loss on ignition.

#### **Magnesium stearate (0229)**

Tests for cadmium, nickel and lead: replacement of the air-acetylene flame with a graphite furnace as atomic generator.

#### **Magnesium sulphate heptahydrate (0044)**

Modification of the title of the monograph.

#### **Maize starch (0344)**

Identification B: deletion of the reappearance of colour on cooling.

#### **Maltodextrin (1542)**

Identification B: the concentration of the solution has been increased to take into account maltodextrins with a low dextrose equivalent.

Loss on drying: increase in the quantity of the substance to be examined due to the formation of a superficial crust on small samples.

#### **Mannitol (0559)**

Bacterial endotoxins: harmonisation of the definition of the 2 categories of mannitol solution with the United States Pharmacopeia.

#### **Metronidazole (0675)**

Related substances test: replacement of the TLC method with an HPLC method.

#### **Miconazole (0935)**

Modification of the impurities section.

#### **Miconazole nitrate (0513)**

Modification of the impurities section.

#### **Minocycline hydrochloride (1030)**

Modification of the impurities section.

#### **Morantel hydrogentartrate for veterinary use (1546)**

Revision of title: addition of “for veterinary use”.

Related substances: deletion of the TLC and of impurity F from the transparency of the monograph.

#### **Mupirocin (1450)**

IR identification: revision to take the polymorphism of the substance into account.

#### **Neomycin sulphate (0197)**

Introduction of an HPLC test for related substances.

Deletion of the TLC test for neamine and neomycin C (neamine and neomycin C are now controlled by the related substances test).

Revision of the impurities section.

#### **Netilmicin sulphate (1351)**

Related substances test: replacement of the TLC method with an HPLC method.

Revision of the impurities section.

#### **Nitrous oxide (0416)**

Revision of the test for nitrogen monoxide and nitrogen dioxide.

### Octyldodecanol (1136)

Assay: use of an internal standard, a temperature gradient and a chemical reference substance for the quantification.

### Oleic acid (0799)

Definition: modification of content limits.

Identification: cross-reference to the test for composition of fatty acids and deletion of reference to the assay.

Tests: modification of limits for acid value and iodine value, introduction of a test for composition of fatty acids.

Assay: deleted.

Labelling: mention the origin of the substance.

### Oxprenolol hydrochloride (0628)

Related substances: replacement of chloroform with methylene chloride. Addition of a system suitability test.

### Oxytetracycline (0199)

Water content: modification of the limits.

### Parenteral preparations (0520)

Revision of the tests for bacterial endotoxins and pyrogens: preparations with a nominal value of less than 15 ml are exempt, but the emphasis is still placed on the test for bacterial endotoxins.

### Pentamidine diisetonate (1137)

Identification: deletion of the second series since the replacement of ammonium and cerium nitrate with cerium sulphate in identification test D is not possible.

### Pethidine hydrochloride (0420)

Related substances: replacement of the TLC test with an HPLC method allowing impurity B (MPTP) to be controlled at a very low limit.

### Piperacillin sodium (1168)

Modification of the impurities section.

### Piroxicam (0944)

Related substances: use of piroxicam spiked with impurity B in the resolution test.

### Pneumococcal polysaccharide vaccine (0966)

Table 0966.-1, row 16, column 1: replacement of "17F" by "17A or 17F".

### Poliomyelitis vaccine (inactivated) (0214)

Substrate for virus propagation: concerning the risk of contamination with simian virus 40 (SV40), it is stated that the blood sample used in testing for SV40 antibodies must be taken as close as possible to the time of removal of the kidneys.

*In vivo* test: reference to the general chapter (2.7.20).

### Poliomyelitis vaccine (oral) (0215)

General revision to take account of recent changes to the WHO requirements and of requests from the CPMP concerning tests for simian virus 40 and retroviruses.

### Poloxamers (1464)

Definition: deletion of Poloxamers 182, 184 and 331 since they are not available for CRS purposes.

Test for residual ethylene oxide, propylene oxide and dioxan: the use of poloxamer 124 of CRS quality for the reference preparation is not necessary.

### Potato starch (0355)

Identification C: deletion of the reappearance of colour on cooling.

### Povidone (0685)

Test for 1-vinylpyrrolidin-2-one (impurity A): modification of column, mobile phase and detection wavelength.

Test for 2-pyrrolidone (impurity B) added.

Test for aldehydes: replacement of acetaldehyde reagent with acetaldehyde ammonia trimer reagent.

### Products of fermentation (1468)

Revision of the introduction.

Down-stream processing: revision of the section.

### Propylene glycol monopalmitostearate (1469)

Identification B: cross-reference to the test for composition of fatty acids.

Saponification value: change in the upper limit.

Introduction of a test for composition of fatty acids.

### Protamine hydrochloride (0686)

### Protamine sulphate (0569)

Replacement of the pyrogen test with the bacterial endotoxin test.

### Recombinant DNA technology, products of (0784)

Revision of the introduction.

### Rice starch (0349)

Identification B: deletion of the reappearance of colour on cooling.

### Rosemary leaf (1560)

Revision of identification tests A, B and C.

Assay: addition of the assay of total hydroxycinnamic derivatives.

### Roxithromycin (1146)

Content: upper limit increased to 102.0 per cent following revision of the general method Chromatographic separation techniques (2.2.46).

**Saccharin (0947)**

*o*- and *p*- toluenesulphonamide: modification of the flow rate.

**Saccharin sodium (0787)**

*o*- and *p*- toluenesulphonamide: modification of the flow rate.

**Salbutamol (0529)****Salbutamol sulphate (0687)**

Introduction of a test for salbutamone (impurity J).  
Related substances: replacement of the TLC method with an HPLC method (the TLC is maintained in identification test C).

Addition of an impurities section.

**Semi-solid preparations for cutaneous application (0132)**

Revision of the definitions.

Production: addition of statements concerning homogeneity and the particle size of solids.

**Simeticone (1470)**

Assay: deletion of the reference to the general chapter on thermogravimetry.

**Sodium chloride (0193)**

Characters: indication that the substance can also exist as pearls.

**Sodium lactate solution (1151)**

General revision following the elaboration of a separate monograph on sodium (*S*)-lactate solution (2033).

**Sodium stearyl fumarate (1567)**

Revision of the test for related substances.

**Somatostatin (0949)**

Replacement of the pyrogen test with the bacterial endotoxin test.

Acetic acid: replacement of the current method with the new HPLC general method "Acetic acid in synthetic peptides" (2.5.34).

Liquid chromatography: revision following the collaborative study for the establishment of somatostatin CRS Batch 2.

**Sorbitan laurate (1040)**

Identification C: replacement of acid value by the test for composition of fatty acids.

**Sorbitan oleate (1041)**

Identification C: replacement of acid value by the test for composition of fatty acids.

**Sorbitan palmitate (1042)**

Identification C: replacement of acid value by the test for composition of fatty acids.

**Sorbitan stearate (1043)**

Identification C: replacement of acid value by the test for composition of fatty acids.

**Sorbitan trioleate (1044)**

Identification C: replacement of acid value by the test for composition of fatty acids.

**Spiramycin (0293)**

Modification of the impurities section.

**Star anise (1153)**

Test for *Illicium anisatum*: replacement of the TLC with a macroscopic and microscopic botanical identification of *I. anisatum*; the TLC is maintained in Identification test C.

**Sulfamethoxypyridazine for veterinary use (0638)**

Revision of title only: addition of "for veterinary use".

**Sulindac (0864)**

Related substances: test modified to take into account the batch-to-batch variability of the *E*-isomer content in sulindac CRS.

**Suxibuzone (1574)**

Related substances: modification of the limit for impurity A.

**Talc (0438)**

Solution S2: deletion of the use of caesium chloride.

**Terbutaline sulphate (0690)**

Related substances: run time of the liquid chromatography increased to control an additional impurity which has been added to the transparency statement.

**Tormentil (1478)**

Revision of identification test A.

Identification test C: descriptions of the chromatograms have been modified.

**Tranexamic acid (0875)**

Related substances: modification of the quantity of tranexamic acid impurity C CRS used to prepare reference solution (b).

**Triamcinolone (1376)**

Revision of the related substances test to control an additional impurity (pretriamcinolone (impurity C)); limits reduced, column and mobile phase modified.

Assay: change in the preparation of the solution to improve the accuracy.

**Trimethoprim (0060)**

Revision of the characters.

Introduction of a test for aniline.

**Tuberculin purified protein derivative, bovine (0536)**

Potency: deletion of the use of tuberculin purified protein derivative, bovine BRP in order to refer only to the International Unit (as for avian tuberculin).

**Urofollitropin (0958)**

Water: replacement of GC method with coulometric titration.

Replacement of the pyrogen test with the bacterial endotoxin test.

**Wheat starch (0359)**

Identification C: deletion of the reappearance of colour on cooling.

**Xylazine hydrochloride for veterinary use (1481)**

Revision of title only: addition of "for veterinary use".

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*COMMUNIQUÉ*

**ADVANCING SCIENCE AND ELIMINATION OF THE USE OF  
LABORATORY ANIMALS FOR DEVELOPMENT AND CONTROL  
OF VACCINES AND HORMONES:**

**REALISTIC GOAL OR MISSION IMPOSSIBLE?**

**12-14 November 2001**

**Jaarbeurs Congress Centre, Utrecht, The Netherlands**

*Symposium organized by the  
International Association for Biologicals (IABS)*

**Programme Chairman**

**Coenraad Hendriksen (RIVM, NL)**

**Dorothea Sesardic (NIBSD, UK)**

**Klaus Cussler (PEI, D)**

A number of physico-chemical, immuno-chemical, biochemical and cell biological methods have been proposed for the replacement, reduction and refinement of animal tests in the development and control of vaccines and hormones. However, the validation, standardization, implementation and ultimately regulatory acceptance of these procedures are still at a very early stage. The purpose of this meeting is to bring together research scientists, manufacturers and regulators to promote the rational development and acceptance of alternative methods.

The scope of the Conference falls broadly into four main session categories:

- **Replacement, reduction and refinement alternatives,**
- **Emerging technologies in production and control,**
- **Test validation and regulatory acceptance,**
- **Test implementation.**