

**European pharmacopoeia**  
3rd Edition Supplement 1999

R921.5

52

# EUROPEAN PHARMACOPOEIA

Third Edition

Supplement 1999

*Published in accordance with the  
Convention on the Elaboration of a European Pharmacopoeia  
(European Treaty Series No. 50)*



Y155988

Council of Europe  
Strasbourg



# EUROPEAN PHARMACOPOEIA

Third Edition

Supplement 1998

Published in accordance with the  
Convention on the Elaboration of a European Pharmacopoeia  
(European Treaty Series No. 50)



© Council of Europe, 67075 Strasbourg Cedex 1998

ISBN: 92-871-3630-0

All rights reserved. Apart from any fair dealing for the purposes of research or private study, this publication may not be reproduced, stored or transmitted in any form or by any means without the prior permission in writing of the publisher.

# I. CONTENTS OF THE THIRD EDITION SUPPLEMENT 1999

For the information of the reader, lists are given below of: new monographs and general chapters added to the Pharmacopoeia with the publication of the first (1998) and second (1999) supplements to the Third Edition; monographs and general chapters that have been technically revised since the publication of the Third Edition (volume 1997); monographs and general chapters that have been corrected since the publication of the Third Edition (volume 1997); suppressed monographs.

**International Harmonisation:** monographs revised or elaborated in collaboration with the Pharmacopoeias of the United States and Japan are identified in the present list by "Q". Residual differences between the harmonised texts are the subject of a commentary in *Pharmeuropa*.

## Monographs from Supplement 1998

*The monographs below appeared in Supplement 1998 and were implemented on 1 January 1998.*

- |  |   |
|--|---|
| Aceclofenac (1281)   | Cefalotin sodium (987)  |
| Acesulfame potassium (1282)  | Chenodeoxycholic acid (1189)                                    |
| Air, medical (1238)  | Chlortalidone (546)   |
| Amoxicillin sodium (577)   | Cinnarizine (816)   |
| Amoxicillin trihydrate (260)   | Clemastine fumarate (1190)                                      |
| Arachis oil, hydrogenated (1171)   | Cloxacillin sodium (661)  |
| Aujeszky's disease vaccine (inactivated) for pigs (744)                                      | Clozapine (1191)  |
| Aujeszky's disease vaccine (live) for pigs for parenteral administration, freeze-dried (745) | Crotamiton (1194)   |
| Benperidol (1172)  | Dalteparin sodium (1195)  |
| Benserazide hydrochloride (1173)   | Desmopressin (712)  |
| Benzylpenicillin potassium (113)   | Dexamethasone (388)   |
| Benzylpenicillin procaine (115)  | Dexamethasone sodium phosphate (549)                            |
| Benzylpenicillin sodium (114)  | Dicloxacillin sodium (663)                                      |
| Betamethasone acetate (975)  | Dicycloverine hydrochloride (1197)                              |
| Betamethasone sodium phosphate (810)   | Diethylene glycol monoethyl ether (1198)                        |
| Birch leaf (1174)  | Diprophylline (486)   |
| Bitter-orange-flower oil (1175)  | Dipyridamole (1199)   |
| Bovine parainfluenza virus vaccine (live), freeze-dried (1176)                               | Dopamine hydrochloride (664)                                    |
| Bovine respiratory syncytial virus vaccine (live), freeze-dried (1177)                       | Doxapram hydrochloride (1201)                                   |
| Bromperidol (1178)   | Egg drop syndrome '76 vaccine (inactivated) (1202)              |
| Brompheniramine maleate (977)  | Equine influenza vaccine (inactivated) (249)                    |
| Bufexamac (1179)   | Etamsylate (1204)   |
| Buprenorphine (1180)   | Etofylline (492)  |
| Buprenorphine hydrochloride (1181)   | Eucalyptus oil (390)  |
| Calcitriol (883)*  | Feline viral rhinotracheitis vaccine (inactivated) (1207)       |
| Calcium ascorbate (1182)   | Feline viral rhinotracheitis vaccine (live) freeze-dried (1206) |
| Calcium phosphate (1052)   | Fenbufen (1209)   |
| Camphor, racemic (655)   | Fentanyl (1210)   |
| Carbasalate calcium (1185)   | Fenticonazole nitrate (1211)                                    |
| Carmellose sodium, low-substituted (1186)  | Flucloxacillin sodium (668)                                     |
| Carmustine (1187)  | Fluocortolone pivalate (1212)                                   |
| Cascara (105)  | Fluorescein sodium (1213)                                       |
|  | Framycetin sulphate (180)                                       |
|  | Frangula bark (25)  |
|  | Frangula bark dry extract, standardised (1214)                  |
|  | Galactose (1215)  |
|  | Gallium ( <sup>67</sup> Ga) citrate injection (555)             |
|  | Gonadorelin acetate (827)                                       |
|  | Guar (1218)   |
|  | Haloperidol (616)   |
|  | Hawthorn berries (1220)   |
|  | Hepatitis A vaccine (inactivated, adsorbed) (1107)              |

\* The monograph on Calcitriol entered into force on 1 October 1995 by virtue of Resolution AP-CSP (95) 1.

Hexetidine (1221)  
Histidine (911)  
Hop strobile (1222)  
Human coagulation factor VII, freeze-dried (1224)  
Human coagulation factor VIII, freeze-dried (275)  
Human coagulation factor IX, freeze-dried (1223)  
Human hepatitis B immunoglobulin for intravenous use (1016)

Human prothrombin complex, freeze-dried (554)  
Hydrochlorothiazide (394)  
Hydroxyethyl salicylate (1225)  
◇ Hypromellose phthalate (347)

Indium (<sup>111</sup>In) chloride solution (1227)  
Java tea (1229)

Ketoconazole (921)

Labetalol hydrochloride (923)  
Lactulose (1230)  
Liquorice root (277)  
Lomustine (928)  
Lovage root (1233)

Maltitol (1235)  
Maltitol liquid (1236)  
Mefloquine hydrochloride (1241)  
Mepivacaine hydrochloride (1242)  
Metformin hydrochloride (931)  
Mitoxantrone hydrochloride (1243)  
Morphine hydrochloride (97)

Neomycin sulphate (197)  
Nitrendipine (1246)  
Nitrogen (1247)  
Nitrous oxide (416)  
Nystatin (517)

Olive oil (518)  
Omega-3-acid ethyl esters (1250)  
Oxybuprocaine hydrochloride (1251)  
Oxygen (417)  
Oxytocin (780)  
Oxytocin concentrated solution (779)

Penicillamine (566)  
Phenytoin (1253)  
Pimozide (1254)  
Pivampicillin (852)  
◇ Potato starch (355)  
Prazosin hydrochloride (856)  
Prednisolone acetate (734)  
Prednisolone sodium phosphate (735)  
Protamine hydrochloride (686)  
Protamine sulphate (569)  
Proxyphylline (526)  
Pyridostigmine bromide (1255)

Rabies vaccine (inactivated) for veterinary use (451)  
Riboflavine sodium phosphate (786)  
Rifamycin sodium (432)

Salbutamol (529)  
Salbutamol sulphate (687)  
Salicylic acid (366)  
Selegiline hydrochloride (1260)  
Senna leaf (206)  
Senna leaf dry extract, standardised (1261)

Senna pods, Alexandrian (207)  
Senna pods, Tinnevely (208)  
Sodium laurilsulfate (98)  
Sodium nitroprusside (565)  
Soya-bean oil, hydrogenated (1265)  
Stannous chloride dihydrate (1266)  
◇ Sucrose (204)  
Sulfasalazine (863)\*  
Sulindac (864)  
Sulphur for external use (953)

Tenoxicam (1156)  
Terconazole (1270)  
Tinzaparin sodium (1271)  
RRR- $\alpha$ -Tocopherol (1256)  
RRR- $\alpha$ -Tocopheryl acetate (1257)  
DL- $\alpha$ -Tocopheryl hydrogen succinate (1258)  
RRR- $\alpha$ -Tocopheryl hydrogen succinate (1259)  
Triamcinolone acetate (533)  
Triamcinolone hexacetate (867)  
Tryptophan (1272)

Ursodeoxycholic acid (1275)

Vaccines for human use (153)  
Valerian root (453)

◇ Wheat starch (359)

Xylose (1278)

Zinc acexamate (1279)  
Zopiclone (1060)

## General Monographs on Dosage Forms

Chewing gums, medicated (1239)  
Intraruminal devices (1228)  
Tablets (478)

## General Chapters from Supplement 1998

- 2.1.6. Gas detector tubes
- 2.2.41. Circular dichroism
- 2.4.23. Sterols in fatty oils
- 2.5.7. Unsaponifiable matter
- 2.5.29. Sulphur dioxide
- 2.5.30. Oxidising substances
- 2.5.31. Ribose in polysaccharide vaccines
- 2.6.1. Sterility test
- 2.6.7. Mycoplasmas
- 2.6.16. Test for extraneous agents in viral vaccines for human use
- 2.7.11. Assay of human coagulation factor IX
- 2.7.12. Assay of heparin in coagulation factor concentrates

\* The monograph on sulfasalazine entered into force on 1 January 1997 by virtue of resolution AP-CSP(96) 4.



- 2.9.4. Dissolution test for transdermal patches
- 2.9.22. Softening time determination of lipophilic suppositories
- 3.1.4. Polyethylene without additives for containers for parenteral and ophthalmic preparations
- 3.1.5. Polyethylene with additives for containers for parenteral and ophthalmic preparations
- 3.1.6. Polypropylene for containers and closures for parenteral and ophthalmic preparations
- 5.1.4. Microbiological quality of pharmaceutical preparations

## New Monographs

*The monographs below appear for the first time in Supplement 1999 and will be implemented on 1 January 1999.*

- Alcuronium chloride (1285)
- Alfacalcidol (1286)
- Alfuzosin hydrochloride (1287)
- Allantoin (1288)
- Amikacin (1289)
- Amikacin sulphate (1290)
- Aminogluthethimide (1291)
- Amphotericin B (1292)
- Bambuterol hydrochloride (1293)
- Belladonna leaf dry extract, standardised (1294)
- Calcifediol (1295)
- Calcium levulinate dihydrate (1296)
- Calendula flower (1297)
- Canine adenovirus vaccine (inactivated) (1298)
- Carbomers (1299)
- Cefuroxime axetil (1300)
- Centaury (1301)
- Ciclopirox olamine (1302)
- Clebopride malate (1303)
- Coriander (1304)
- Cottonseed oil, hydrogenated (1305)
- Couch grass rhizome (1306)
- Decyl oleate (1307)
- Deptropine citrate (1308)
- Dihydralazine sulphate (hydrated) (1310)
- Dinoprost trometamol (1312)
- Dinoprostone (1311)
- Dirithromycin (1313)
- Dosulepin hydrochloride (1314)
- Duck viral hepatitis vaccine (live) (1315)
- Erythropoietin concentrated solution (1316)
- Ethanol (96 per cent) (1317)
- Ethanol, anhydrous (1318)
- Ethyl oleate (1319)
- Eucalyptus leaf (1320)
- Feline leukaemia vaccine (inactivated) (1321)
- Fenofibrate (1322)
- Fenugreek (1323)
- Flecainide acetate (1324)
- Fludeoxyglucose (<sup>18</sup>F) injection (1325)
- Flumazenil (1326)
- Flumethasone pivalate (1327)
- Fosfomycin calcium (1328)
- Fosfomycin sodium (1329)
- Glucose liquid (1330)
- Glycerol trinitrate solution (1331)
- Isoprenaline hydrochloride (1332)
- Ispaghula husk (1334)
- Ispaghula seed (1333)
- Itraconazole (1335)
- Ivermectin (1336)
- Lactitol monohydrate (1337)
- Lavender oil (1338)
- Levocarnitine (1339)
- Macroglol stearyl ether (1340)
- Magnesium chloride 4.5-hydrate (1341)
- Maize oil, refined (1342)
- Malathion (1343)
- Metamizole sodium (1346)
- Metixene hydrochloride (1347)
- Metoclopramide (1348)
- Myrrh (1349)
- Nabumetone (1350)
- Netilmicin sulphate (1351)
- Omega-3-acid triglycerides (1352)
- Oxolinic acid (1353)
- Oxybutynin hydrochloride (1354)
- Pentaerythrityl tetranitrate, diluted (1355)
- Pertussis vaccine (acellular component, adsorbed) (1356)
- Pheniramine maleate (1357)
- Picotamide monohydrate (1358)
- Piperacillin (1169)
- Piperacillin sodium (1168)
- Pivmecillinam hydrochloride (1359)
- Porcine actinobacillosis vaccine (inactivated) (1360)
- Porcine progressive atrophic rhinitis vaccine (inactivated) (1361)
- Prilocaine (1362)
- Prilocaine hydrochloride (1363)
- Primrose root (1364)
- Promazine hydrochloride (1365)
- Propacetamol hydrochloride (1366)
- Pseudoephedrine hydrochloride (1367)
- Ramipril (1368)
- Rapeseed oil, refined (1369)
- Sage leaf (1370)
- Sunflower oil, refined (1371)
- Technetium (99mTc) mertiatide injection (1372)
- Testosterone (1373)
- Thyme oil (1374)
- Tick-borne encephalitis vaccine (inactivated) (1375)
- Triamcinolone (1376)
- Triflusal (1377)
- Valproic acid (1378)
- Wheat-germ oil, refined (1379)
- Wormwood (1380)
- Xylitol (1381)
- Yarrow (1382)

## New General Chapters

- 2.4.26. *N,N*-Dimethylaniline
- 2.5.32. Coulometric titration, micro-method
- 2.6.21. Nucleic acid amplification techniques
- 2.9.23. Pycnometric density of solids
- 2.9.24. Resistance to rupture of suppositories and pessaries
- 3.1.10. Materials based on non-plasticised poly(vinyl chloride) for containers for non-injectable, aqueous solutions
- 3.1.11. Materials based on non-plasticised poly(vinyl chloride) for containers for dry dosage forms for oral administration
- 5.4.  $\diamond$  Residual solvents
- 5.5. Alcoholimetric tables

## Revised monographs

*The monographs below have been technically revised since the publication of Supplement 1998 and will be implemented on 1 January 1999.*

- Acetone (872)
- Alginic acid (591)
- Amidotrizoic acid dihydrate (873)
- Ascorbic acid (253)
- Bacampicillin hydrochloride (808)
- Beeswax, white (69)
- Beeswax, yellow (70)
- Benzalkonium chloride (372)
- Benzalkonium chloride solution (371)
- Biotin (1073)
- Butyl parahydroxybenzoate (881)
- Calcium folinate (978)
- Canine distemper vaccine (live), freeze-dried (448)
- Carbenicillin sodium (812)
- Cefixime (1188)
- Cetostearyl alcohol (Type A) emulsifying (801)
- Cetostearyl alcohol (Type B) emulsifying (802)
- Cetylpyridinium chloride (379)
- Chlorocresol (384)
- Chlorpropamide (1087)
- Chlorprothixene hydrochloride (815)
- Cholesterol (993)
- Copovidone (891)
- Cyclizine hydrochloride (1092)
- Cyproterone acetate (1094)
- Daunorubicin hydrochloride (662)
- Dexchlorpheniramine maleate (1196)
- Digitoxin (78)
- Dimeticone (138)
- Disodium phosphate dodecahydrate (118)
- Enoxaparin sodium (1097)
- Ethyl parahydroxybenzoate (900)
- Etilefrine hydrochloride (1205)
- Etoposide (823)
- Eugenol (1100)
- Feline infectious enteritis (feline panleucopenia) vaccine (inactivated) (794)
- Feline infectious enteritis (feline panleucopenia) vaccine (live) (251)
- Fenbendazole (1208)
- Fennel, bitter (824)
- Fennel, sweet (825)
- Gallamine triethiodide (181)
- Halothane (393)
- Homoeopathic preparations (1038)
- Hydrocortisone (335)
- Imipenem (1226)
- Insulin (276)
- Insulin human (838)
- Insulin injection, biphasic isophane (832)
- Insulin injection, isophane (833)
- Insulin preparations, injectable (854)
- Insulin zinc injectable suspension (837)
- Insulin zinc injectable suspension (amorphous) (835)
- Insulin zinc injectable suspension (crystalline) (836)
- Iobenguane ( $^{123}\text{I}$ ) injection (1113)
- Iobenguane ( $^{131}\text{I}$ ) injection for diagnostic use (1111)
- Iobenguane ( $^{131}\text{I}$ ) injection for therapeutic use (1112)
- Iohexol (1114)
- Iopamidol (1115)
- Iopanoic acid (700)
- Iotalamic acid (751)
- Isopropyl alcohol (970)
- Lorazepam (1121)
- Magnesium chloride hexahydrate (402)
- Measles vaccine (live) (213)
- Measles, mumps and rubella vaccine (live) (1057)
- Medroxyprogesterone acetate (673)
- Mefenamic acid (1240)
- Methacrylic acid - ethyl acrylate copolymer (1:1) (1128)
- Methacrylic acid - ethyl acrylate copolymer (1:1) dispersion 30 per cent (1129)
- Methacrylic acid - methyl methacrylate copolymer (1:1) (1127)
- Methacrylic acid - methyl methacrylate copolymer (1:2) (1130)
- $\diamond$  Methyl parahydroxybenzoate (409)
- Methylprednisolone (561)
- Methylprednisolone hydrogen succinate (1131)
- Metrifonate (1133)
- Minocycline hydrochloride (1030)
- Mumps vaccine (live) (538)
- Nadroparin calcium (1134)
- Norfloxacin (1248)
- Nortryptiline hydrochloride (941)
- Pentamidine diisetonate (1137)
- Phenoxymethylpenicillin (148)
- Phenoxymethylpenicillin potassium (149)
- Phytomenadione (1036)
- Pilocarpine hydrochloride (633)
- Pilocarpine nitrate (104)
- Poliomyelitis vaccine (inactivated) (214)
- Prednisolone (353)
- Propranolol hydrochloride (568)

Propyl gallate (1039)  
Propyl parahydroxybenzoate (431)

Quinidine sulphate (17)  
Quinine hydrochloride (18)  
Quinine sulphate (19)

Roxithromycin (1146)  
Rubella vaccine (live) (162)

Sodium alginate (625)  
Sodium amidotrizoate (1150)  
Sodium cetostearyl sulphate (847)  
Sodium valproate (678)  
Somatropin (951)  
Somatropin bulk solution (950)  
Somatropin for injection (952)  
Starch, pregelatinised (1267)\*

Talc (438)  
Terbutaline sulphate (690)  
 $\alpha$ -Tocopherol (692)  
 $\alpha$ -Tocopheryl acetate (439)  
Tuberculin, old for human use (152)  
Tuberculin, purified protein derivative for human use (151)  
Tylosin for veterinary use (1273)  
Tylosin tartrate for veterinary use (1274)

Verapamil hydrochloride (573)

Xanthan gum (1277)

Yellow fever vaccine (live) (537)

Zolpidem tartrate (1280)

## General Monographs on Dosage Forms

Preparations for inhalation (671)  
Rectal preparations (1145)

## Revised General Chapters

- 2.2.27. Thin-layer chromatography
- 2.3.2. Identification of fatty oils by thin-layer chromatography
- 2.4.8. Heavy metals
- 2.4.22. Foreign oils in fatty oils by gas chromatography
- 2.4.24. Identification and control of residual solvents
- 2.5.5. Peroxide value
- 2.6.2. Mycobacteria
- 2.6.12. Microbiological examination of non-sterile products - total viable count
- 2.6.13. Microbiological examination of non-sterile products - test for specified organisms
- 2.6.14. Bacterial endotoxins
- 2.7.2. Microbiological assay of antibiotics

- 2.9.18. Preparations for inhalation: aerodynamic assessment of fine particles
- 2.9.20. Particulate contamination: visible particles

## Monographs corrected in 1998

*The monographs below were included in the Corrigenda in Supplement 1998, and appear in their entirety in the present Supplement.*

Acetazolamide (454)  
Alfentanil hydrochloride (1062)  
Anise oil (804)

Buserelin (1077)

Calcium gluconate for injection (979)  
Cellulose acetate phthalate (314)  
Cetirizine dihydrochloride (1084)  
Chlorcyclizine hydrochloride (1086)  
Chlortetracycline hydrochloride (173)  
Cyanocobalamin (547)

Dithranol (1007)

Ethinylestradiol (140)

Fentanyl citrate (1103)  
Formaldehyde solution (35 per cent) (826)

Haemodialysis solutions, concentrated,  
water for diluting (1167)  
Haemofiltration, solutions for (861)

Ipecacuanha root (94)  
Ipratropium bromide (919)  
Isosorbide mononitrate, diluted (1118)

Lidocaine hydrochloride (227)  
Lisinopril dihydrate (1120)

Macrogol 7 glycerol cocoate (1122)

Neostigmine bromide (46)

Pancreas powder (350)  
Paracetamol (49)  
Polymixin B sulphate (203)  
Polysorbate 80 (428)  
Potassium clavulanate (1140)  
Protirelin (1144)

Sodium chloride (193)  
Sodium lactate solution (1151)  
Sutures, sterile non-absorbable (324)

## General Monographs on Dosage Forms

Eye preparations (1163)

## General Chapters corrected in 1998

- 2.2.7. Optical rotation
- 2.5.26. Nitrogen monoxide and nitrogen dioxide in medicinal gases

\* The monograph on pregelatinised starch entered into force on 1 January 1998 by virtue of resolution AP-CSP (97) 2.



- 2.9.14. Specific surface area by air permeability
- 3.2. Containers
- 5.1.3. Efficacy of antimicrobial preservation

## Monographs corrected in 1999

*The monographs below have been corrected since the publication of Supplement 1998. They will be implemented on the date of publication of the present Supplement.*

Aciclovir (968)  
 ◇ Alteplase for injection (1170)  
 Ampicillin sodium (578)

Betadex (1070)

Calcium dobesilate monohydrate (1183)  
 Caprylocaproyl macrogolglycerides (1184)  
 Carbon dioxide (375)  
 Cefaclor (986)  
 Cefotaxime sodium (989)  
 Cod-liver oil (type A) (1192)  
 Cod-liver oil (type B) (1193)  
 Corticotropin (759)

Dobutamine hydrochloride (1200)  
 Doxycycline hyclate (272)

Elder flower (1217)  
 Ergocalciferol (82)  
 Estriol (1203)  
 ◇ Ethylcellulose (822)

Fluoxetine hydrochloride (1104)

Garlic powder (1216)  
 Guar galactomannan (908)

Haemophilus type b conjugate vaccine (1219)  
 Human plasma for fractionation (853)  
 ◇ Hydroxyethylcellulose (336)

Lactulose liquid (924)  
 Lauroyl macrogolglycerides (1231)  
 Linoleoyl macrogolglycerides (1232)

Macrogol stearate (1234)  
 Maprotiline hydrochloride (1237)  
 Morphine sulphate (1244)

Nimodipine (1245)

Oleoyl macrogolglycerides (1249)  
 Omeprazole (942)

Parnaparin sodium (1252)  
 Promethazine hydrochloride (524)

Rabies vaccine for human use prepared in cell cultures (216)

Sesame oil, refined (433)  
 Sodium methyl parahydroxybenzoate (1262)  
 Sodium propyl parahydroxybenzoate (1263)  
 Solution for organ preservation (1264)  
 Stearoyl macrogolglycerides (1268)  
 Sufentanil citrate (1269)

Technetium (<sup>99m</sup>Tc) medronate injection (641)  
 Thyme (865)  
 Ticarcillin sodium (956)

Vindesine sulphate (1276)

## General Chapters corrected in Supplement 1999

- 2.4.24. Residual ethylene oxide and dioxan
- 2.7.4. Assay of blood coagulation factor VIII
- 2.7.10. Assay of human coagulation factor VIII

## Suppression of Monographs

*The following monographs will be deleted on 1 January 1999.*

- Ethisterone (142)
- Sterile reconstituted collagen strands (323)

# II. CORRIGENDA

## CONTENTS

The page number for the reagents in the table of contents should read '187' instead of '1875'.

## GENERAL NOTICES

### 1.5. ABBREVIATIONS AND SYMBOLS

#### Page 6. COLLECTIONS OF MICRO-ORGANISMS.

Replace:

C.I.P. Collection de l'Institut Pasteur (strains of bacteria)

I.P. Institut Pasteur (strains of other micro-organisms)  
Service de la Collection Nationale de Culture de  
Micro-organismes (C.N.C.M.)  
25 Rue du Docteur-Roux  
F-75015 Paris, France

by:

C.I.P. Collection de Bactéries de l'Institut Pasteur  
B.P. 52, 25 Rue du Docteur Roux  
75724 Paris Cedex 15, France

I.P. Collection Nationale de Culture de Microorganismes  
(C.N.C.M.),  
Institut Pasteur,  
25 Rue du Docteur Roux  
75724 Paris Cedex 15, France

## GENERAL CHAPTERS

### 2.2.29. LIQUID CHROMATOGRAPHY

Page 33. Replace:

'The **number of theoretical plates** ( $n$ ) may be calculated from data obtained under isothermal conditions from the formula:'

by:

'The **number of theoretical plates** ( $n$ ) may be calculated from data obtained under isocratic conditions from the formula:'

### 5.3. STATISTICAL ANALYSIS OF RESULTS OF BIOLOGICAL ASSAYS AND TESTS

Page 315. In the following table insert the figure 34.2 for the sum of squares due to non-parallelism;

Table 3.2.8.1.-VI. – Analysis of variance without data or preparation Z

Source of variation	Degree of freedom	Sum squares	Mean square	F-ratio	Prob-ability
Preparations	1	390.6	390.6		
Regression	1	66 830.6	66 830.6	90.5	<0.01
Non-parallelism	1	34.2	34.2	0.05	<0.05
Treatments	3	67 255.5			
Residual error	36	26 587.3	738.5		
Total	39	93 842.8			

Page 332. Section 4.3. EXAMPLE - Top of the right-hand column replace:

'In (confidence limits) were calculated:

$$\ln 40.8 + x_s - x_u + C(M' - x_s + x_u) \pm 0.051786 = 3.7316 \pm 0.2276$$

Confidence limits were 33.2 to 52.4 units per millilitre.'

by:

'In (confidence limits) were calculated:

$$\ln 40 + x_s - x_u + C(M' - x_s + x_u) \pm 0.051786 = 3.7120 \pm 0.2276$$

Confidence limits were 32.6 to 51.4 units per millilitre.'

## MONOGRAPHS

### ALPRAZOLAM (1065)

Page 365. TESTS - Related substances. Replace the following:

'– a stainless steel column 0.25 m long and 4.6 mm in internal diameter packed with *phenylsilyl silica gel for chromatography R* (5  $\mu$ m),'

by:

'– a stainless steel column 0.25 m long and 4.6 mm in internal diameter packed with *phenylsilyl silica gel for chromatography R1* (5  $\mu$ m),'

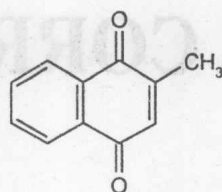
### BETAMETHASONE DIPROPIONATE (809)

Page 475. TESTS - Related substances. Replace:

'In the chromatogram obtained with the test solution: the area of any peak apart from the principal peak is not greater than 0.75 times the area of the principal peak in the chromatogram obtained with reference solution (b) (2.0 per cent) and not more than one such peak has an area greater than half the area of the principal peak in the chromatogram obtained with reference solution (b) (1.0 per cent);'

by:

'In the chromatogram obtained with the test solution: the area of any peak apart from the principal peak is not greater than 0.75 times the area of the principal peak in the chromatogram obtained with reference solution (b) (1.5 per cent) and not more than one such peak has an area greater than half the area of the principal peak in the chromatogram obtained with reference solution (b) (1 per cent);'



## CELLULOSE, MICROCRYSTALLINE (316) AND CELLULOSE, POWDERED (315)

Page 576. Table 315.-1.— Intrinsic Viscosity Table.

In the bottom right-hand corner of the table, replace the value 3.417 by 2.417 which corresponds to the co-ordinate for 5.9 and  $\eta_{rel}$  0.09.

Page 577. Insert new values for  $\eta_{rel}$  after the line commencing 9.9 as follows:

$\eta_{rel}$  0.0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9

## HYALURONIDASE (912)

Page 972. ASSAY. Replace the following:

'Plot  $(\ln h)^{-1}$  as a function of the reaction time  $(t_1 + t_2/2)$  in seconds. A linear relationship is obtained.'

by:

'Plot  $(\ln \eta)^{-1}$  as a function of the reaction time  $(t_1 + t_2/2)$  in seconds. A linear relationship is obtained.'

## LYSINE HYDROCHLORIDE (930)

Page 1115. **Ninhydrin-positive substances.** Replace the following:

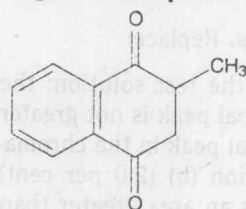
'The test is not valid unless the chromatogram obtained with test solution (c) shows two clearly separated spots.'

by:

'The test is not valid unless the chromatogram obtained with reference solution (c) shows two clearly separated spots.'

## MENADIONE (507)

Page 1154. Replace the chemical formula:



by:

## OXYTETRACYCLINE (199)

Page 1273. **Related substances.** Replace the following: 'the area of any peak corresponding to 4-epioxytetracycline or tetracycline is not greater than the area of the corresponding peak in the chromatograms obtained with reference solution (e) (0.5 per cent)'.

by:

'the area of any peak corresponding to 4-epioxytetracycline or tetracycline is not greater than the area of the corresponding peak in the chromatograms obtained with reference solution (e) (0.5 per cent and 2.0 per cent respectively)'.

## PROPYLENE GLYCOL MONOSTEARATE (1143)

Page 1400. Identification B - Replace the following:

'The retention time and size of the two principal peaks in the chromatogram obtained..'

by:

'The retention times of the two principal peaks in the chromatogram obtained..'

## RADIOPHARMACEUTICAL PREPARATIONS (125)

Page 1424. **DEFINITION.** In the right-hand column replace:

'1 microcurie (mCi) = ....  $3.7 \times 10^4$  becquerels'

by:

'1 microcurie ( $\mu$ Ci) = ....  $3.7 \times 10^4$  becquerels'

## TETRACOSACTIDE (644)

Page 1621. **Amino acids.** Glycine has been omitted from the table of amino acids which should now read as follows:

Lysine	Threonine	Glycine	Isoleucine
Histidine	Serine	Alanine	Leucine
Arginine	Glutamic acid	Valine	Tyrosine
Aspartic acid	Proline	Methionine	Phenylalanine

## VACCINES FOR VETERINARY USE (62)

Page 1702. **TESTS - Mycoplasmas.** Following the republication of the test for mycoplasmas in Supplement 1998 the test may be amended by deleting the sentence:

'Depending on the origin of any cells used for production of the vaccine, the composition of the culture media and the target species, carry out either the test for avian mycoplasmas, or the test for non-avian mycoplasmas and ureaplasmas, or both.'



# CONTENTS

I.	Contents of the Third Edition Supplement 1999	i
II.	Corrigenda	vii
<b>General Chapters</b>		
<b>2.</b>	<b>Methods of Analysis</b>	<b>3</b>
2.1.	<i>Apparatus</i>	3
2.1.6.	Gas detector tubes	3
2.2.	<i>Physical and Physico-chemical methods</i>	5
2.2.7.	Optical rotation	5
2.2.27.	Thin-layer chromatography	5
2.2.41.	Circular dichroism	7
2.3.	<i>Identification</i>	9
2.3.2.	Identification of fatty oils by thin-layer chromatography	9
2.4.	<i>Limit Tests</i>	11
2.4.8.	Heavy metals	11
2.4.22.	Foreign oils in fatty oils by gas chromatography	11
2.4.23.	Sterols in fatty oil	12
2.4.24.	Identification and control of residual solvents	14
2.4.25.	Residual ethylene oxide and dioxan	19
2.4.26.	<i>N,N</i> -Dimethylaniline	20
2.5.	<i>Assays</i>	21
2.5.5.	Peroxide value	21
2.5.7.	Unsaponifiable matter	21
2.5.26.	Nitrogen monoxide and nitrogen dioxide in medicinal gases	22
2.5.29.	Sulphur dioxide	22
2.5.30.	Oxidising substances	23
2.5.31.	Ribose in polysaccharide vaccines	23
2.5.32.	Micro-method - coulometric titration	23
2.6.	<i>Biological Tests</i>	25
2.6.1.	Sterility	25
2.6.2.	Mycobacteria	29
2.6.7.	Mycoplasmas	29
2.6.12.	Microbiological examination of non-sterile products - total viable count	33
2.6.13.	Microbiological examination of non-sterile products - test for specified organisms	36
2.6.14.	Bacterial endotoxins	41
2.6.16.	Tests for extraneous agents in viral vaccines for human use	50
2.6.21.	Nucleic acid amplification techniques	51

2.7. <i>Biological Assays</i>	55
2.7.2. Microbiological assay of antibiotics	55
2.7.4. Assay of blood coagulation factor VIII	61
2.7.10. Assay of human coagulation factor VII	63
2.7.11. Assay of human coagulation factor IX	64
2.7.12. Assay of heparin in coagulation factor concentrates	64
2.9. <i>Pharmaceutical Technical Procedures</i>	67
2.9.4. Dissolution test for transdermal patches	67
2.9.14. Specific surface area by air permeability	67
2.9.18. Preparations for inhalation: aerodynamic assessment of fine particles	68
2.9.20. Particulate contamination: visible particles	75
2.9.22. Softening time determination of lipophilic suppositories	75
2.9.23. Pycnometric density of solids	76
2.9.24. Resistance to rupture of suppositories and pessaries	76
3.1. <i>Materials used for the Manufacture of Containers</i>	79
3.1.4. Polyethylene without additives for containers for parenteral and ophthalmic preparations	79
3.1.5. Polyethylene with additives for containers for parenteral and ophthalmic preparations	80
3.1.6. Polypropylene for containers and closures for parenteral and ophthalmic preparations	83
3.1.10. Materials based on non-plasticised poly(vinylchloride) for containers for non-injectable, aqueous solutions	87
3.1.11. Materials based on non-plasticised poly(vinylchloride) for containers for dry dosage forms for oral administration	89
3.2. <i>Containers</i>	92
4. <i>Reagents</i>	93
4.1. <i>Reagents, Standard solutions, Buffer solutions</i>	93
4.1.1. Reagents	93
4.1.2. Standard solutions for limit tests	186
4.1.3. Buffer solutions	190
4.2. <i>Volumetric Analysis</i>	195
4.2.1. Primary standards for volumetric solutions	195
4.2.2. Volumetric solutions	195
5. <i>General Texts</i>	201
5.1.3. Efficacy of antimicrobial preservation	201
5.1.4. Microbiological quality of pharmaceutical preparations	202
5.4. <i>Residual solvents</i>	205
5.5. <i>Alcoholimetric tables</i>	215
Monographs	229
Monographs on dosage forms	979
Index	995

# GENERAL CHAPTERS





## 2. METHODS OF ANALYSIS

### 2.1. APPARATUS

#### 2.1.6. GAS DETECTOR TUBES

Gas detector tubes are cylindrical, sealed tubes consisting of an inert transparent material and constructed to allow the passage of gas. They contain reagents adsorbed onto inert substrates that are suitable for the visualisation of the substance to be detected and, if necessary, they also contain preliminary layers and/or adsorbent filters to eliminate substances that interfere with the substance to be detected. The layer of indicator contains either a single reagent for the detection of a given impurity or several reagents for the detection of several substances (monolayer tube or multilayer tube).

The test is carried out by passing the required volume of the gas to be examined through the indicator tube. The length of the coloured layer or the intensity of a colour change on a graduated scale gives an indication of the impurities present.

The calibration of the detector tubes is verified according to the instructions of the manufacturer.

*Operating conditions.* Examine according to the instructions of the manufacturer or proceed as follows:

The gas supply is connected to a suitable pressure regulator and needle valve. Connect the flexible tubing fitted with a Y piece to the valve and adjust the flow of gas to be examined to purge the tubing to an appropriate flow (see Figure 2.1.6.-1). Prepare the indicator tube and fit to the metering pump following the manufacturer's instructions. Connect the open end of the indicator tube to the short leg of the tubing and operate the pump by the appropriate number of strokes to pass a suitable volume of gas to be examined through the tube. Read the value corresponding to the length of the coloured layer or the intensity of the colour on the graduated scale. If a negative result is achieved, indicator tubes can be verified with a

calibration gas containing the appropriate impurity. For the verification of the oil tube, use another tube from the same batch.

**Carbon dioxide detector tube.** Sealed glass tube containing adsorbent filters and suitable supports for hydrazine and crystal violet indicators. The minimum value indicated is 100 ppm with a relative standard deviation of at most  $\pm 15$  per cent.

**Sulphur dioxide detector tube.** Sealed glass tube containing adsorbent filters and suitable supports for the iodine and starch indicator. The minimum value indicated is 0.5 ppm with a relative standard deviation of at most  $\pm 15$  per cent.

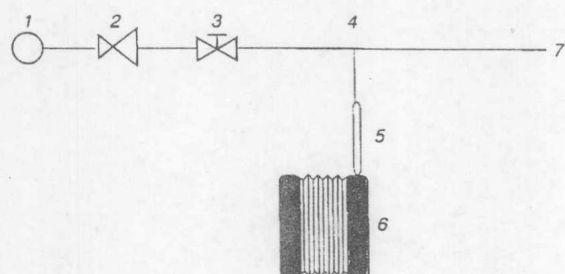
**Oil detector tube.** Sealed glass tube containing adsorbent filters and a suitable support for the sulphuric acid indicator. The minimum value indicated is 0.1 mg/m<sup>3</sup> with a relative standard deviation of at most  $\pm 30$  per cent.

**Nitrogen monoxide and nitrogen dioxide detector tube.** Sealed glass tube containing adsorbent filters and suitable supports for an oxidising layer Cr(VI) salt and the diphenylbenzidine indicator. The minimum value indicated is 0.5 ppm with a relative standard deviation of at most  $\pm 15$  per cent.

**Carbon monoxide detector tube.** Sealed glass tube containing adsorbent filters and suitable supports for di-iodine pentoxide, selenium dioxide and fuming sulphuric acid indicators. The minimum value indicated is 5 ppm or less, with a relative standard deviation of at most  $\pm 15$  per cent.

**Hydrogen sulphide detector tube.** Sealed glass tube containing adsorbent filters and suitable supports for an appropriate lead salt indicator. The minimum value indicated is 1 ppm or less, with a relative standard deviation of at most  $\pm 10$  per cent.

**Water vapour detector tube.** Sealed glass tube containing adsorbent filters and suitable supports for the magnesium perchlorate indicator. The minimum value indicated is 60 ppm or less, with a relative standard deviation of at most  $\pm 20$  per cent.



1. gas supply
2. pressure regulator
3. needle valve
4. "Y" piece
5. indicator tube
6. indicator tube pump
7. end open to atmosphere

Figure 2.1.6.-1. — Apparatus for gas detector tubes

