BASIC TESTS FOR DRUGS

Pharmaceutical substances, medicinal plant materials and dosage forms

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1. Introduction

This manual has been designed to be used in conjunction with two earlier World Health Organization (WHO) publications, *Basic tests for pharmaceutical substances*[1] and *Basic tests for pharmaceutical dosage forms*.[2] Most of the pharmaceutical substances and dosage forms covered are included in the WHO Model List of Essential Drugs.[3] The present volume describes procedures for testing a further 23 pharmaceutical substances and 58 pharmaceutical dosage forms and also for testing four medicinal plant materials (sections 3–5).

These basic tests represent one of the many elements of quality assurance in the pharmaceutical supply system. They have been devised with the following objectives:

(a) to provide a simple and readily applicable method for verifying the identity of a substance, using a limited range of easily available reagents, when the labelling and physical attributes give rise to doubt;

(b) to provide a practicable means of confirming the identity of a substance when a fully equipped laboratory is not available;

(c) to indicate whether gross degradation has occurred in certain substances that are known to decompose readily under adverse conditions.

Basic tests are not, in any circumstances, intended to replace the requirements of *The International Pharmacopoeia*[4] or other pharmacopoeial monographs. These give an assurance of quality whereas basic tests merely confirm identity.

In 1994, the WHO Expert Committee on Specifications for Pharmaceutical Preparations[5] agreed that the scope of these tests should be extended to include additional information and references to other simple test methodologies.

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[1] *Basic tests for pharmaceutical substances*. Geneva, World Health Organization, 1986.

[2] *Basic tests for pharmaceutical dosage forms*. Geneva, World Health Organization, 1991.

[3] *The use of essential drugs. Seventh report of the WHO Expert Committee*. Geneva, World Health Organization, 1997 (WHO Technical Report Series, No. 867).

[4] *The International Pharmacopoeia*, 3rd ed. Geneva, World Health Organization. Volume 1: *General methods of analysis*, 1979. Volume 2: *Quality specifications*, 1981. Volume 3: *Quality specifications*, 1988. Volume 4: *Tests, methods, and general requirements. Quality specifications for pharmaceutical substances, excipients, and dosage forms*, 1994.

[5] *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Thirty-fourth Report*. Geneva, World Health Organization, 1996 (WHO Technical Report Series, No. 863).

The usefulness of simplified analytical technology and supporting elements, such as thin-layer chromatography (TLC) kits, reference tablets and associated training materials, was fully endorsed by the Committee. They are considered to be valuable tools for primary screening and could play an important part in identifying counterfeit and spurious products. Several collections of simplified tests are therefore reviewed in this manual (see section 2).

Degradation during storage and transportation is of particular importance in tropical countries. Indeed, an expiry date determined for a temperate climate may be inappropriate in a tropical region even when high standards of packaging are met. For this reason, particular importance is accorded to visual inspection of dosage forms, since this frequently provides a first vital indication of degradation. This also applies in cases where there are reasons to suspect quality defects due to poor manufacture, tampering, or counterfeiting. Visual inspection should precede any testing. Inspection procedures are outlined in *Basic tests for pharmaceutical dosage forms.*

Basic tests need not be carried out by fully qualified pharmacists or chemists, but they should be performed by persons with some understanding of analytical chemistry such as that acquired in courses for pharmaceutical assistants.

The facilities needed for carrying out basic tests, the equipment required and methods for the determination of melting characteristics are described in detail in the two earlier manuals of basic tests. Reagents additional to the ones described in those two manuals are listed in section 6.

Several tests are described for most preparations. Not all of these need to be applied to any one sample. If, however, there is any reason to suspect that the product is mislabelled or substandard, all tests described should be performed. By their nature, simplified tests cannot be totally reliable. An adverse result, even in one test, should be taken as a warning of potential unsuitability of a drug. In these circumstances, a final conclusion should not be drawn until a full analytical examination has been carried out in a properly equipped quality control laboratory.

For easy reference, section 7 provides a cumulative index of WHO basic tests.

Comments on the tests described are invited and should be addressed to: Quality Assurance, Division of Drug Management and Policies, World Health Organization, 1211 Geneva 27, Switzerland.

2. Other collections of simple tests

Various collections of simple tests other than the basic tests published by WHO are available for verifying the identity of drugs, and a selection of these are reviewed here.

In addition to their use in identification, many of these tests can be used to estimate the content of active ingredients; however, they employ more sophisticated techniques than are required for the WHO basic tests, including volumetric or spectrophotometric analysis and thin-layer chromatography. Some of these methods also require reference materials and additional equipment and reagents, as well as better training for operators.

As with the basic tests, these simple tests are not intended to replace pharmacopoeial analyses. Before any of these collections of tests are used, their suitability should be evaluated, and users should validate the methods.

Thin-layer chromatography

Primary screening of imported pharmaceutical substances and dosage forms is designed to establish that consignments contain the right drug(s) in the right amount(s). National ports of entry for such consignments may lack access to standard laboratory resources, but it is important that this primary screening can be done quickly, with simple equipment, at low cost, and without the need for highly trained personnel. TLC techniques have been found to be suitable for the purpose. Both the initial capital investment and the operating costs are low, a large number of samples can be handled in a relatively short time, and results are reliable.

A primary screening facility, with the capacity to conduct both TLC and WHO basic tests and examine product labelling, requires a minimum of two trained individuals. Technical, rather than professional, training is generally necessary, and manual dexterity and literacy are minimum requirements. The test area should be protected but control of temperature and humidity is not essential.

The interested reader can find further discussion of analytical screening procedures in *WHO drug information*, 1997, 11(3):128–130 (Layloff TP, The importance of analytical procedures in regulatory control).

Thin-layer chromatography tests developed by the World Health Organization (unpublished)

More than 150 TLC procedures were developed in the early 1980s through collaborative research conducted under the auspices of WHO, including 128 tests for pharmaceutical substances and 29 for formulations. The majority of these procedures were for drugs contained in the WHO Model List of Essential Drugs. These tests were never published since it was felt that further research is required to reduce the number of mobile phase systems employed (currently over 40). The project has not been finalized but further studies to re-evaluate some of these tests are proposed.

Thin-layer chromatography tests developed in the USA (language: English)

Standardized TLC procedures were developed by a team of researchers from the Division of Drug Analysis of the United States Food and Drug Administration (*1*) in the early 1990s. The test methods are based on the use of a portable kit, which features plastic bags for development and staining (detection) and contains other accessories required to perform the tests. Training materials are included to facilitate the practical application of the test kits. All the tests were field-tested in a number of countries.

The application of the tests is described in detail. These methods are suitable for rapid screening of drugs at ports of entry, pharmacies, or distribution centres, or in areas lacking resources for other methods of analysis. If any results indicate that products do not comply with the specification, the tests should be repeated. Suspect samples must be submitted for official analysis by legal reference methods (LRM).

Test procedures are described for 69 products, 38 of which are on the WHO Model List of Essential Drugs. Small plastic plates (5 × 10 cm) coated with silica gel are recommended. Mobile phase systems are prepared from a list of eight solvents. Sample solutions are prepared with one or two of the solvents used for the mobile phase systems. (*Note*: chloroform and other toxic halogen compounds are not recommended for use.) The two detection methods applied are the exposure to iodine vapour and ninhydrin methods.

Analyses are of a semi-quantitative nature. The test sample is prepared from one unit dose of the product under examination, thus avoiding the influence on the tests of operations such as sample weighing and the preparation of sample solutions from composite samples of dosage units. For detection purposes, a spot of the test solution is compared with two reference spots representing the upper and lower limit concentrations: 85% and 115% (120% as the upper limit for certain antibiotics) in accordance with compendial limits for unit dose uniformity. A single analysis is therefore sufficient to confirm (or disprove) the identity of the active ingredient and to estimate the assay value and the unit dose uniformity of the product.

Reference materials are needed for all the tests in this collection. Either primary (Chemical Reference Substances, CRS) or secondary standards may

be used. Secondary standards can be obtained from previously analysed samples or from reputable suppliers of drug substances.

Since analytical or semi-micro-balances are required for the weighing of reference standards, a study is in preparation to develop reference tablets, i.e. standards in the form of accurately weighed units in tablet form.

The advantage of these tests is that identity, assay value and unit dose uniformity can be determined in one operation. Furthermore, testing is focused on a single method and requires a minimum of equipment. The test kits provided contain basic solvents and reagents and are suitable for analysis outside the laboratory.

Simple thin-layer chromatography tests developed in Germany
(languages: English, German)

The German drug industry (through the German Pharma Health Fund) supported work by the Pharmaceutical Institute of the Rheinische Friedrich Wilhelms University of Bonn during the period 1988–1994 to develop a series of TLC tests for the estimation of quality of some widely used pharmaceutical products in tablet and capsule form (*2*). WHO was involved in the initial phase to develop the objectives and the scope of recommendations. The project was expanded to include testing of different brands of dosage forms from the market. The proposed methods use various types of plates and mobile phase systems, the latter employing 10 different solvents, avoiding halogenated ones, but including water. The test collection includes the results of this comparative testing and high-quality colour reproductions of the chromatograms.

Tests are published for 20 substances, most of which are on the WHO Model List of Essential Drugs. Most tests provide some means of detecting certain impurities that arise during the manufacturing process or by degradation. These studies were performed using commercial batches. For three substances there are two tests available, one of which uses a different development system, chosen specifically to detect impurities.

Tests are based on the use of precoated (mostly silica gel, occasionally cellulose) plates on glass (alternatively aluminium foil) supports, in most cases with chamber saturation. In addition to normal size plates (10 × 20 cm) small high-performance thin-layer chromatography (HPTLC) plates (5 × 5 cm) are also used. Small plates are developed in a horizontal position (Desaga–H chamber). It is recommended that the test solutions are placed as a band (3 × 15 mm), rather than a spot, to facilitate reading of the chromatograms. A shortened distance of development (7–8 cm) is recommended using normal plates to speed the test process (e.g. 10–15 minutes instead of 30–45 minutes). The distance for the development on small plates is 4 cm, which is associated with a development time of 4–5 minutes (even less than for normal plates).

The publication gives valuable advice regarding the use of reference materials for impurities. For epi- and anhydro- forms of tetracycline, for example, use

of the parent substance, decomposed in the laboratory by heating with acids, is recommended in preference to use of a CRS.

The advantage of these tests is the efficient conditions used for the identification of active ingredients of some solid oral dosage forms. In most cases these methods also allow the detection of impurities occurring during manufacture and degradation. Reliable results are achieved with shorter development times, often using greatly reduced amounts of solvents (HPTLC technique); this is more economical and offers greater safety to the operator, as well as being less damaging to the environment.

Thin-layer chromatography tests developed in Japan
(languages: English, Japanese)

At the request of the Japanese Ministry of Health and Welfare, the Committee for Countermeasures against Counterfeit and Substandard Drugs has developed TLC test procedures (*3*). Two investigations on counterfeit and substandard drugs were carried out by the Japan International Corporation of Welfare Services in 1993 and 1994. These investigations were also performed in facilities of local drug quality control laboratories in five southeast Asian countries. The development of the test collection is the result of these investigations. The Japanese Pharmacopoeia Society also collaborated on this project during 1993–1994. Using products from the market, proposed test methods for various dosage forms were validated in quality-control laboratories by more than 30 leading Japanese pharmaceutical manufacturers.

Currently, tests are available for 29 drugs, almost all of which are included in the WHO Model List of Essential Drugs (17 are antibiotics). The drugs were selected on the basis of their association with counterfeiting. They are classified into five categories (three for antibiotics, one for analgesics and one for water-soluble vitamins). Procedures are provided for the preparation of sample solutions according to their dosage forms and for the spotting, development, detection and evaluation of chromatograms. Useful indications and notes are given concerning the preparation of TLC plates in the laboratory and the performance of the tests for a total of 45 items. For each category of drugs there are three to five mobile phase systems (18 systems in total) and two to five detection methods. For each category and each development system the retention factor R_f (the ratio of the distance travelled by the analyte to that travelled by the solvent) is given, and for each detection method a brief indication is provided regarding the expected spots, in terms of "strong", "weak", "tailing" or "no spot".

These tests are primarily designed to verify the identity of active ingredients in drugs. A rough estimate of the content of the active ingredients in the test sample can also be obtained from a comparison of the size and the intensity of the spots for test and reference samples. The collection of tests is supported by colour reproductions of chromatograms using different detection methods.

Standard equipment for TLC is needed for these tests. The tests are performed on normal size glass plates (5 × 20 cm or 20 × 20 cm) coated with silica gel either prepared in the laboratory or available commercially. Brief mention is made of the optional use of small plates (2 × 5 cm) of plastic or aluminium foil coated with silica gel. All procedures require reference materials, such as secondary standards or good quality bulk substances.

Usually there is no need to use all the listed mobile systems and detection methods to test any one drug. For verification of the identity of the active ingredient, it is satisfactory to use one appropriate mobile phase and detection method. Reliability is increased by using all the recommended mobile phase systems for each substance. When reference materials are not available it is recommended that judgement of the identity of the sample under examination is based on a comparison of the R_f values obtained, using all the mobile phase systems listed (R_f values are given in the text).

Identification and assay tests developed in France
(languages: English, French)

The National Association of the French Pharmaceutical Industry (*Syndicat National de l'Industrie Pharmaceutique*) prepared, during the period 1987–1991, a collection of test sheets for identification and assay of finished pharmaceutical products (*4*). Test methods are described on laminated cardboard sheets designed to be resistant to reagents and solvents in a laboratory setting. The field of application of these tests is not defined by the authors, but it appears that they are intended for use in the training of personnel in developing countries rather than for routine quality control operations.

Altogether there are 216 sheets, of which 111 are for preparations included in the WHO Model List of Essential Drugs. A typical sheet contains:

- three (occasionally four or five) colour/precipitation reactions for identification
- one assay method, generally based on a volumetric determination (typically, non-aqueous titration); occasionally, the endpoint is determined potentiometrically.

No limits of acceptance/rejection are indicated for the assay values.

A TLC procedure is included in 45 sheets, determination of melting point (usually of a derivative) in nine, and a spectrophotometric measurement in the ultraviolet (UV) or visible part of the spectrum as identity tests in three. In 56 sheets, two alternative assay methods are provided, one non-instrumental and the other based on the measurement of the absorbance with a UV/visible spectrophotometer.

For some 100 sheets, reference materials are required for spectrophotometric or TLC tests. It is understood that commercial substances of good (pharmacopoeial) quality may be used for this purpose.

The resources needed include:

— glassware

— melting-point apparatus

— analytical balance and an assembly for volumetric assays

— materials for TLC (for spotting, development, visualization, etc.)

— UV/visible spectrophotometer

— potentiometer

— reagents

— reference materials.

These tests provide a considerable degree of flexibility, making them suitable for use in verifying identity and estimating the content of the active ingredient of some 200 widely used products, using limited instrumentation.

Quality control methods for developing countries developed in France (language: French)

During the period 1988–1993, the Faculty of Pharmacy in Nantes (France), which is the WHO Collaborating Centre for Stability Studies of Drugs, elaborated a collection of test methods for use in developing countries (*5*). Originally, research was focused on stability testing of dosage forms to permit the measurement of the content of (unchanged) active ingredients. Later, identification procedures were added. The tests are proposed for use by quality control laboratories in developing countries which are not yet fully equipped for pharmacopoeial analyses. All the tests were developed and validated on finished products manufactured in France. They were also used in the course of stability studies on some 200 products also of French origin. In addition, the tests were all verified in the field.

Test methods for 121 formulations, 65 of which are on the WHO Model List of Essential Drugs, are available. In many cases, the same tests can be used for the corresponding drug substances. All the test sheets in this collection contain an assay procedure that measures absorbance in the UV region of the spectrum or have a volumetric titration (usually non-aqueous) and a TLC method for identification purposes. Reference materials are needed for the spectrophotometric and TLC tests.

The collection includes a general text on major analytical methods, lists of equipment and reagents required and a cost estimate for the reagents needed if only one test is performed or for all the tests described.

The simple assay methods offered can be used, *inter alia*, to monitor the stability of a number of widely used finished pharmaceutical products in the distribution system (by measuring the content of the active ingredient).

Sheets for the identification of medicines in pharmacies developed in Belgium (language: French)

During the period 1987–1993, a subcommittee of the Belgian Pharmacopoeia Committee prepared simple unofficial procedures to assist pharmacists to verify the identity of drugs supplied in pharmacies (*6*).

There are 159 test sheets, all of them for pharmaceutical substances, 17 of which are included in the WHO Model List of Essential Drugs. Typically, a sheet contains a description of the substance, information on its solubility, a melting point, and two to three colour reactions. In 36 sheets, one identity test is replaced by a TLC procedure, which refers to the general recommendations given in the Belgian Pharmacopoeia. The reference materials needed in these tests are issued by the Belgian Pharmacopoeia.

A number of the TLC procedures have a built-in "system suitability test". A test is considered invalid if it fails to reveal a secondary spot in a reference solution that contains an added impurity (e.g. another drug substance, chemically related to the test substance). This feature is considered to give these tests a certain advantage over other TLC tests.

References

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2. Pachaly P et al. *Simple thin-layer chromatographic identification of active ingredients in essential drugs*. Bonn, Pharmaceutical Institute of the Rheinische Friedrich Wilhelms University, 1994.

3. *Technology transfer promotion project for pharmaceutical field.* Tokyo, Committee on Countermeasures against Counterfeit and Substandard Drugs, 1993–1995.

4. Fabiani P, Pesez M. *Fiches d'identification et de dosage des médicaments.* [*Drugs identification and assay sheets.*] Paris, Syndicat de l'Industrie Pharmaceutique, 1987–1991.

5. Vincent-Ballereau F et al. *Contrôle de qualité des médicaments essentiels dans les pays en développement, méthodes standardisées.* [*Quality control of essential drugs in developing countries.*] Nantes, Groupe d'Etudes Epidémiologiques et Prophylactiques et Centre Collaborateur de l'OMS pour l'Etude de la Stabilité des Médicaments, Faculté de Pharmacie, 1993.

6. *Fiches de vérifications d'identité des médicaments en officine.* [*Sheets for the verification of the identity of medicines in pharmacies.*] Brussels, Secrétariat de la Commission Belge de la Pharmacopée, 1987–1993.

3. Test procedures for pharmaceutical substances

AMIKACIN SULFATE

Identity tests

Description. A white to yellowish white, crystalline powder; almost odourless.

Colour and other reactions

1. Dissolve 10 mg in 1 ml of water, add 1 ml of sodium hydroxide (~80 g/l) TS and mix, then add 2 ml of cobalt(II) nitrate (10 g/l) TS; a violet colour is produced.
2. Dissolve 0.05 g in 3 ml of water and add slowly 4 ml of anthrone TS; a bluish violet colour is produced.
3. Dissolve 20 mg in 1 ml of water and add 1 ml of barium chloride (50 g/l) TS; a white precipitate is produced which is practically insoluble in hydrochloric acid (~250 g/l) TS.

BACITRACIN ZINC

Composition. Bacitracin zinc is a zinc complex of bacitracins, polypeptides produced by the growth of an organism of the licheniformis group of *Bacillus subtilis*. The main components are the bacitracins A, B1 and B2.

Identity tests

Description. A white or pale brownish yellow powder; odourless or with a faint, characteristic odour; hygroscopic.

Colour and other reactions

1. Shake 5 mg with 1 ml of water, add 1 ml of triketohydrindene/butanol TS and 0.5 ml of pyridine R and heat to 100 °C for 5 minutes; a violet colour is produced.
2. Transfer about 0.5 g to a silica crucible and ignite. Dissolve the residue in 5 ml of sulfuric acid (~5 g/l) TS and filter. Divide the filtrate into 2 equal volumes.

(*a*) To 1 volume add 1 ml of potassium ferrocyanide (45 g/l) TS; a white precipitate is produced which is insoluble in hydrochloric acid (~250 g/l) TS.

(*b*) To 1 volume add 1 drop of copper(II) sulfate (1 g/l) TS and 1 ml of ammonium mercurithiocyanate TS; a violet precipitate is produced.

Degradation tests

Discoloration of the test substance and non-compliance with the following test usually indicate gross degradation:

Dissolve 0.10 g in 100 ml of water; a clear, colourless or slightly yellowish solution is produced.

CAPTOPRIL

Identity tests

Description. A white or almost white, crystalline powder; odour, characteristic but faint.

Colour and other reactions

1. Dissolve 10 mg in 2 ml of hydrochloric acid (0.1 mol/l) VS and add about 1 ml of iodine TS; the colour of the iodine disappears immediately and a white, turbid solution is produced.
2. Dissolve 10 mg in 2 ml of water and add 0.5 ml of lead acetate (80 g/l) TS; a white precipitate is produced.
3. Dissolve 10 mg in 5 ml of ethanol (~750 g/l) TS, add 0.5 ml of tetramethylammonium hydroxide/ethanol TS and shake. Then add 0.5 ml of triphenyltetrazolium chloride/ethanol TS and shake again; a red colour is produced.

CHLORAMPHENICOL SODIUM SUCCINATE

Identity tests

Description. A white or almost white powder; hygroscopic.

Colour and other reactions

Dissolve about 1.4 g in 5 ml of water and use as the test solution for the following tests:

1. To 1 drop of the test solution add 5 ml of ethanol (~750 g/l) TS, 0.2 g of zinc R powder and 1 ml of sulfuric acid (~100 g/l) TS and allow to stand for 10 minutes. Filter; to the filtrate add 0.5 ml of sodium nitrite (10 g/l)

TS and allow to stand for 2 minutes. Then add about 1 g of urea R and a solution containing 10 mg of 2-naphthol R in 2 ml of sodium hydroxide (~80 g/l) TS; a red colour is produced.

2. Repeat test 1 omitting the zinc R powder; no red colour is produced.
3. Carefully heat 1 drop of the test solution with 10 mg of resorcinol R and 3 drops of sulfuric acid (~1760 g/l) TS, cool and add 2 ml of water. Cool again and pour the solution into a mixture of 100 ml of water and about 1 ml of sodium hydroxide (~400 g/l) TS; a yellow-green fluorescence appears which disappears on the addition of 1 ml of hydrochloric acid (~250 g/l) TS.
4. Introduce the test solution into a non-luminous flame using a magnesia stick or a nichrome or platinum wire sealed to a glass rod; the flame acquires an intense yellow colour.

Degradation tests

Discoloration of the test substance and non-compliance with the following test usually indicate gross degradation:

Dissolve 0.2 g in 10 ml of water; a clear solution is produced.

CISPLATIN

Identity tests

Description. White to yellowish crystals or a yellow powder.

***Note.* This substance is very toxic and should be handled with care.**

Colour and other reactions

1. Dissolve 5 mg in 5 ml of hydrochloric acid (~420 g/l) TS and heat to boiling. To half of the solution (keep the unused portion for test 2) add a few crystals of potassium iodide R; a brownish yellow colour is produced which changes to reddish brown on standing.
2. To the remaining solution from test 1 add a few crystals of tin(II) chloride R; a reddish orange colour is produced which changes to reddish brown on standing.
3. Transfer 0.05 g to a glass dish and add 2 ml of sodium hydroxide (~80 g/l) TS. Evaporate to dryness and dissolve the residue in a mixture of 0.5 ml of nitric acid (~1000 g/l) TS and 1.5 ml of hydrochloric acid (~420 g/l) TS. Again evaporate to dryness; an orange-coloured residue is produced. Dissolve the residue in 0.5 ml of water and add 0.5 ml of ammonium chloride (100 g/l) TS; a yellow, crystalline precipitate is produced.

COAL TAR

Composition. Coal tar is a by-product usually obtained during the destructive distillation of coal. It is a complex and undefined mixture of a great number of chemical compounds. The product is available in various compositions.

Identity tests

Description. Brown-black or black, viscous liquid; odour, characteristic and strong, resembling naphthalene. On exposure to air the liquid solidifies.

Heating behaviour. When ignited, the liquid burns in air with a luminous sooty flame and almost no residue remains.

Colour and other reactions

1. Shake 1 drop vigorously with 5 ml of ethanol (~750 g/l) TS and filter; the filtrate is yellow with a bluish green fluorescence.
2. Shake about 1 g vigorously with 9 ml of water for 10 minutes and filter; the filtrate gives a neutral or only slightly acid reaction when tested with litmus paper R (unlike wood tar) and an odour of naphthalene is discernible (keep the filtrate for test 3).
3. To 5 ml of the filtrate from test 2 add a few drops of bromine TS; a yellow turbidity develops (phenols).

Degradation test

If the substance does not pass the following test, this usually indicates that gross degradation has occurred:

Dissolve 0.10 g in 10 ml of nitrobenzene R; a clear or almost clear solution is produced.

DOXORUBICIN HYDROCHLORIDE

Identity tests

Description. A red-orange, crystalline powder; hygroscopic.

Note. **This substance is very toxic and should be handled with care.**

Colour and other reactions

1. Place a small quantity of the test substance on a white test plate and add 1 drop of formaldehyde/sulfuric acid TS; the orange-red colour of the substance changes to violet.

2. Dissolve about 2 mg in 2 ml of methanol R and add 2 ml of water and 1 drop of sodium hydroxide (~80 g/l) TS; the orange-red colour of the solution changes to blue-violet.
3. Dissolve 0.05 g in 1 ml of water, add 5 drops of ammonia (~100 g/l) TS and filter. Acidify the filtrate with nitric acid (~130 g/l) TS and add 1 ml of silver nitrate (40 g/l) TS; a white, curdy precipitate is produced which is soluble in ammonia (~100 g/l) TS but practically insoluble in nitric acid (~1000 g/l) TS.

FLUPHENAZINE DECANOATE

Identity tests

Description. A pale yellow, viscous liquid or a yellow, crystalline solid with an oily appearance; odour, faint and ester-like.

Colour and other reactions

1. Dissolve 5 mg in 2 ml of sulfuric acid (~1760 g/l) TS and allow to stand for 5 minutes; a reddish brown colour is produced.
2. Dissolve 5 mg in about 2 ml of formaldehyde/sulfuric acid TS; an orange colour is produced. Heat in a water-bath for 2 minutes; the colour changes to dark brown.
3. Dissolve 5 mg in 2 ml of water and add 3 drops of potassium dichromate (100 g/l) TS; a yellow precipitate is produced.
4. Dissolve 5 mg in about 1 ml of sucrose/hydrochloric acid TS and allow to stand for 5 minutes; a red colour is produced.

Degradation tests

Discoloration and a change in the physical state of the test substance usually indicate gross degradation.

GALLAMINE TRIETHIODIDE

Identity tests

Description. A white or almost white powder; odourless; hygroscopic.

Colour and other reactions

1. Dissolve 0.05 g in 5 ml of water and add 1 ml of potassio-mercuric iodide TS; a yellow precipitate is produced.
2. Dissolve 0.05 g in 5 ml of water and add 1 ml of sulfuric acid (~100 g/l) TS and 1 ml of potassium nitrite (100 g/l) TS; a brownish coloration is produced.

3. Dissolve 0.05 g in 5 ml of water and add 1 drop of nitric acid (~1000 g/l) TS and 1 ml of silver nitrate (40 g/l) TS; a yellow precipitate is produced which is insoluble in ammonia (~100 g/l) TS and nitric acid (~1000 g/l) TS.

HYDROCORTISONE SODIUM SUCCINATE

Identity tests

Description. A white or almost white, crystalline powder or amorphous solid; odourless; hygroscopic.

Colour and other reactions

1. Dissolve about 2 mg in 1 ml of alkaline potassio-mercuric iodide TS; a dark precipitate is produced.

2. Dissolve a small quantity in about 2 ml of sulfuric acid (~1760 g/l) TS; a yellow solution with a greenish fluorescence is produced. Very cautiously pour the solution into 10 ml of water; the colour of the solution changes to brownish yellow but the fluorescence remains.

3. Dissolve a small quantity in about 1 ml of phosphoric acid (~1440 g/l) TS and heat cautiously; a yellow solution is produced with a pale greenish fluorescence.

4. Dissolve about 2 mg in 1 ml of water and introduce the solution into a non-luminous flame using a magnesia stick or a nichrome or platinum wire sealed to a glass rod; the flame acquires an intense yellow colour.

5. Heat carefully 10 mg with 1 drop of water, 10 mg of resorcinol R and 3 drops of sulfuric acid (~1760 g/l) TS, cool and add 2 ml of water. Cool again and pour the solution into a mixture of 100 ml of water and 1 ml of sodium hydroxide (~400 g/l) TS; a yellowish green fluorescence appears.

Degradation tests

Discoloration of the substance and non-compliance with the following test usually indicate gross degradation:

Dissolve 0.20 g in 1.0 ml of water; a clear and colourless solution is produced.

KETAMINE HYDROCHLORIDE

Identity tests

Description. A white, crystalline powder; odour, characteristic.

Melting behaviour. About 260 °C.

Colour and other reactions

1. Dissolve about 0.2 g in 4 ml of water and chill the solution in ice. Add potassium carbonate (100 g/l) TS, drop by drop, until the solution is slightly alkaline when tested with pH-indicator paper R and allow to stand to crystallize. Filter and dry the crystals in a vacuum over phosphorus pentoxide R; melting temperature, about 92 °C.
2. Dissolve 10 mg in 4 ml of water and add 0.5 ml of nitric acid (~130 g/l) TS and 0.5 ml of silver nitrate (40 g/l) TS; a white, curdy precipitate is produced. Separate the precipitate, wash it with water and add an excess of ammonia (~100 g/l) TS; the precipitate dissolves.
3. Dissolve 10 mg in 4 ml of sulfuric acid (~5 g/l) TS and add 1 drop of potassium iodobismuthate/acetic acid TS; a reddish brown precipitate is produced.

LEVAMISOLE

Identity tests

Description. A white, crystalline powder.

Melting point. About 59 °C.

Colour reaction

Dissolve 0.05 g in 20 ml of water. Add 1 ml of sodium hydroxide (~80 g/l) TS, boil for 10 minutes and cool. Add a few drops of sodium nitroprusside (45 g/l) TS; a red colour is produced which fades with time.

LEVAMISOLE HYDROCHLORIDE

Identity tests

Description. A white to pale cream-coloured, crystalline powder; odourless or almost odourless.

Melting point. About 228 °C.

Colour and other reactions

1. Dissolve 0.25 g in 20 ml of water and add 1.5 ml of sodium hydroxide (~80 g/l) TS. Extract with 20 ml of dichloromethane R, discard the aqueous layer and wash the dichloromethane layer with 10 ml of water. Discard the aqueous layer, shake the dichloromethane layer with about 1 g of anhydrous sodium sulfate R and filter. Evaporate the filtrate at room temperature and dry in a vacuum at a temperature not exceeding 40 °C; the residue melts at about 59 °C.
2. Dissolve 0.10 g in 40 ml of water. To 20 ml of this solution (keep the unused portion for test 3) add 1 ml of sodium hydroxide (~80 g/l) TS, boil for 10 minutes and cool. Add a few drops of sodium nitroprusside (45 g/l) TS; a red colour is produced which fades with time.
3. To 20 ml of the solution prepared for test 2 add 1 ml of nitric acid (~130 g/l) TS and a few drops of silver nitrate (40 g/l) TS; a white precipitate is produced. Separate the precipitate, wash with water and add an excess of ammonia (~100 g/l) TS; the precipitate dissolves.

MAGNESIUM SULFATE

Identity tests

Description. Brilliant, colourless crystals or a white, crystalline powder; odourless; effloresces in warm and dry air.

Colour and other reactions

1. Dissolve 10 mg in 2 ml of water and add 1 ml of ammonia (~100 g/l) TS; a white precipitate is produced. Add 1 ml of ammonium chloride (100 g/l) TS; the precipitate dissolves. Add 1 ml of disodium hydrogen phosphate (100 g/l) TS; a white precipitate is produced.
2. Dissolve 10 mg in 2 ml of water and add 3 drops of titan yellow TS and 2 ml of sodium hydroxide (~80 g/l) TS; a distinct pink colour is produced.
3. Dissolve 0.05 g in 5 ml of water. Add 1 ml of hydrochloric acid (~70 g/l) TS and 1 ml of barium chloride (50 g/l) TS; a white precipitate is produced.

MEDROXYPROGESTERONE ACETATE

Identity tests

Description. A white or almost white, crystalline powder; odourless or almost odourless.

Melting point. About 204 °C.

Colour and other reactions

1. Dissolve 5 mg in 5 ml of sulfuric acid (~1760 g/l) TS. Incline the tube and carefully add, without mixing, 5 ml of ethanol (~750 g/l) TS; a blue-violet colour is produced at the interface of the two liquids.

2. Heat 0.05 g with 2 ml of potassium hydroxide/ethanol TS in a water-bath for 5 minutes. Cool and add 1 ml of water and about 1 ml of sulfuric acid (~1760 g/l) TS. Boil gently for 1 minute; ethyl acetate, perceptible by its odour (proceed with caution), is produced.

3. Dissolve 5 mg in 0.5 ml of methanol R in a small test-tube, add about 3 mg of sodium nitroprusside R, 0.05 g of sodium carbonate R and 0.5 g of ammonium acetate R and shake. Allow to stand for 10–30 minutes; a violet-red colour is produced (distinction from progesterone).

4. Dissolve a few crystals in about 1 ml of sulfuric acid (~1760 g/l) TS. Incline the tube and carefully add, without mixing, 1 ml of water; a green colour is produced at the interface of the two liquids. Allow to stand; the colour changes to bluish violet (distinction from hydroxyprogesterone caproate).

METHIONINE

Identity tests

Description. White crystals or a white, crystalline powder; odour, characteristic.

Colour and other reactions

1. Dissolve about 0.1 g in 5 ml of hydrochloric acid (0.1 mol/l) VS, add 0.2 ml of triketohydrindene/ethanol TS and heat; a violet colour is produced.

2. Dissolve 10 mg in 1 ml of water and add 1–2 drops of hydrochloric acid (~250 g/l) TS, 0.5 ml of copper(II) sulfate (1 g/l) TS and 1–2 ml of sodium hydroxide (~150 g/l) TS; a blue-violet colour is produced.

3. Dissolve about 0.1 g in 5 ml of potassium hydroxide (~110 g/l) TS and add about 0.3 ml of sodium nitroprusside (45 g/l) TS with shaking. Heat the solution in a water-bath at a temperature of 35–40°C for 10 minutes. Cool in ice for 2 minutes, add about 2 ml of hydrochloric acid (~250 g/l) TS and shake well; a red colour is produced.

METHYLROSANILINIUM CHLORIDE

Identity tests

Description. A dark green powder or greenish, glistening pieces with a metallic lustre; odourless or almost odourless.

Colour and other reactions

1. Add a few crystals to about 1 ml of sulfuric acid (~1760 g/l) TS and shake; an orange or brown-red coloured solution is produced. Cautiously dilute with water; the colour changes to brown, then to green and finally to blue.
2. Dissolve 20 mg in 10 ml of water and add 5 drops of hydrochloric acid (~420 g/l) TS. To 5 ml of this solution (keep the unused portion for test 3) add, drop by drop, tannic acid (100 g/l) TS; a blue precipitate is produced.
3. To the remaining solution from test 2 add 0.5 g of zinc R powder and warm the mixture; the solution discolours rapidly. On a filter-paper, place 1 drop of this solution adjacent to 1 drop of ammonia (~100 g/l) TS; a blue colour is produced at the zone of contact.

PENTAMIDINE ISETIONATE

Identity tests

Description. A white or almost white, crystalline powder; odourless; hygroscopic.

Melting point. About 190 °C.

Colour and other reactions

1. To about 1 g add 10 ml of water and heat to 80 °C to dissolve. Add 15 ml of sodium hydroxide (~80 g/l) TS, cool in ice and filter. To 2 ml of the filtrate (keep the unused portion for tests 2 and 3) add about 0.2 ml of nitric acid (~1000 g/l) TS and about 0.2 ml of ceric ammonium nitrate TS; a red-orange colour is produced.
2. Neutralize 5 ml of the remaining filtrate from test 1 with hydrochloric acid (~70 g/l) TS, testing with pH-indicator paper R, then add 3 ml of the same acid and a few drops of barium chloride (50 g/l) TS; no precipitate is produced.
3. Transfer a further 10 ml of the remaining filtrate from test 1 to a crucible, add 2.5 ml of hydrogen peroxide (~60 g/l) TS, mix and evaporate to dryness over a water-bath. Dissolve the residue in 1 ml of water, add about 1 ml of glacial acetic acid R, evaporate again and ignite until free

from carbon. After cooling, add 5 ml of water and filter. If necessary, neutralize the filtrate with hydrochloric acid (~70 g/l) TS, testing with pH-indicator paper R, add 3 ml of the same acid, heat to boiling for 30 seconds, cool and add a few drops of barium chloride (50 g/l) TS; a white precipitate is produced which is practically insoluble in hydrochloric acid (~250 g/l) TS.

PENTAMIDINE MESILATE

Identity tests

Description. A white or light pink, granular powder; almost odourless.

Melting behaviour. About 265 °C.

Colour and other reactions

1. To about 1 g add 10 ml of water and heat to 80 °C to dissolve. Add 15 ml of sodium hydroxide (~80 g/l) TS, cool in ice and filter. To 2 ml of the filtrate (keep the unused portion for tests 2 and 3) add about 0.2 ml of nitric acid (~1000 g/l) TS and about 0.2 ml of ceric ammonium nitrate TS; a yellow colour is produced.
2. Neutralize 5 ml of the remaining filtrate from test 1 with hydrochloric acid (~70 g/l) TS, testing with pH-indicator paper R, and add 3 ml of the same acid and a few drops of barium chloride (50 g/l) TS; no precipitate is produced.
3. Transfer a further 10 ml of the remaining filtrate from test 1 to a crucible, add 2.5 ml of hydrogen peroxide (~60 g/l) TS, mix and evaporate to dryness over a water-bath. Dissolve the residue in 1 ml of water, add about 1 ml of glacial acetic acid R, evaporate again and ignite until free from carbon. After cooling, add 5 ml of water and filter. If necessary, neutralize the filtrate with hydrochloric acid (~70 g/l) TS, testing with pH-indicator paper R, add 3 ml of the same acid, heat to boiling for 30 seconds, cool and add a few drops of barium chloride (~50 g/l) TS; a white precipitate is produced which is practically insoluble in hydrochloric acid (~250 g/l) TS.

PREDNISOLONE SODIUM PHOSPHATE

Identity tests

Description. A white or almost white powder; odourless; hygroscopic.

Colour and other reactions

1. Dissolve about 2 mg in about 2 ml of sulfuric acid (~1760 g/l) TS and allow to stand for 5 minutes; a wine-red solution is produced. Dilute the

solution very cautiously with 10 ml of water; the colour fades and a greyish brown, flocculent precipitate is produced.

2. Dissolve 5 mg in about 1 ml of phosphoric acid (~1440 g/l) TS and heat cautiously; the solution changes from colourless to yellow, then to orange and later to reddish brown.

3. Dissolve 10 mg in 1 ml of methanol R, add 1 ml of potassio-cupric tartrate TS and heat in a water-bath; an orange precipitate is gradually produced.

4. Carefully heat 0.04 g with about 2 ml of sulfuric acid (~1760 g/l) TS until white fumes are evolved. Add, drop by drop, nitric acid (~1000 g/l) TS until oxidation is complete. Allow to cool, add 10 ml of water and heat again until white fumes are evolved. Cool, add 10 ml of water and neutralize with ammonia (~100 g/l) TS, using pH-indicator paper R. Introduce an aliquot of this solution into a non-luminous flame using a magnesia stick or a nichrome or platinum wire sealed to a glass rod; the flame acquires an intense yellow colour. To the remaining solution add 5 ml of ammonium molybdate (95 g/l) TS, acidify with nitric acid (~130 g/l) TS and heat; a bright yellow precipitate is produced.

PYRIMETHAMINE

Identity tests

Description. A white, crystalline powder; odourless.

Melting point. About 240 °C.

Colour and other reactions

1. Dissolve 0.05 g in 5 ml of sulfuric acid (~100 g/l) TS and add about 0.2 ml of freshly prepared potassio-mercuric iodide TS; a creamy white precipitate is produced.

2. To 1 ml of methyl orange/ethanol TS add 5 ml of water and 2 ml of ethyl acetate R and shake; the ethyl acetate layer remains colourless. Add a solution of 5 mg of the test substance dissolved in 5 ml of sulfuric acid (~5 g/l) TS, shake and allow to separate (about 30 minutes); a yellow colour is produced in the ethyl acetate layer.

3. Ignite about 0.1 g with 0.5 g of anhydrous sodium carbonate R, extract the residue with water and filter. Neutralize the filtrate with nitric acid (~130 g/l) TS and add 0.5 ml of silver nitrate (~40 g/l) TS; a white precipitate is produced. Add ammonia (~100 g/l) TS; the precipitate dissolves.

TAMOXIFEN CITRATE

Identity tests

Description. A white or almost white, crystalline powder.

Melting behaviour. About 142 °C with decomposition.

Colour and other reactions

1. Shake 10 mg with 5 ml of dehydrated ethanol R. Add 3 ml of water, 0.5 ml of ammonia (~100 g/l) TS and 2 ml of phosphomolybdic acid/ethanol TS; within a few minutes the colour of the solution changes to light blue.
2. To 10 mg add 4 ml of pyridine R and about 2 ml of acetic anhydride R and shake; a yellow colour is immediately produced. Heat in a water-bath for 2 minutes; a light pink to red colour is produced.

VINBLASTINE SULFATE

Identity tests

Description. A white to slightly yellow, amorphous or crystalline powder; hygroscopic.

Note. **This substance is very toxic and should be handled with care.**

Colour and other reactions

1. To about 0.5 mg add 2 drops of a 10 mg/ml solution of ceric ammonium sulfate R in phosphoric acid (~1440 g/l) TS; a purplish red colour is produced which darkens with time.
2. To about 1 mg add 0.2 ml of a freshly prepared 10 mg/ml solution of vanillin R in hydrochloric acid (~420 g/l) TS; after about 1 minute a pink colour is produced (distinction from vincristine sulfate).
3. Mix about 0.5 mg with 5 mg of 4-dimethylaminobenzaldehyde R, about 0.2 ml of glacial acetic acid R and about 0.2 ml of sulfuric acid (~1760 g/l) TS; a reddish brown colour is produced which changes to pink after addition of about 1 ml of glacial acetic acid R.
4. Dissolve 10 mg in 2 ml of water. Add 1 ml of hydrochloric acid (~70 g/l) TS and 1 ml of barium chloride (50 g/l) TS; a white precipitate is produced which is practically insoluble in hydrochloric acid (~250 g/l) TS.

4. Test procedures for medicinal plant materials

IPECACUANHA ROOT

Composition. Ipecacuanha root is the dried rhizome and roots of the shrub *Cephaëlis ipecacuanha* (Brotero) A. Richard (family Rubiaceae) or of *C. acuminata* Karsten, or of a mixture of both species. The principal alkaloids are emetine and cephaëline.

Identity tests

Description. Odour, slight; taste, bitter, nauseous and acrid.

Macroscopic characteristics

C. ipecacuanha. Dark brick-red to very dark brown. A somewhat tortuous root, seldom more than 15 cm in length or 6 mm in diameter; the root is closely annulated externally, with rounded ridges that completely encircle it; the fracture is short in the bark and splintery in the wood; a transversely cut surface shows a wide greyish bark and a small uniformly dense wood. The rhizomes are short lengths attached to the roots; they are cylindrical, up to 2 mm in diameter, finely wrinkled longitudinally, and with pith occupying approximately one-sixth of the whole diameter.

C. acuminata. In general, resembles the root of *C. ipecacuanha*, but differs in the following particulars: often up to 9 mm in diameter; external surface greyish brown or reddish brown with transverse ridges at intervals of about 1–3 mm; the ridges are about 0.5–1 mm wide, extending about half-way round the circumference and fading at the extremities into the general surface level.

Colour and other reactions

1. Coarsely powder the root, mix 0.05 g with about 2 ml of hydrochloric acid (~420 g/l) TS and 1 drop of hydrogen peroxide (~330 g/l) TS and warm the mixture; an orange colour is produced (rubremetine).

2. Coarsely powder the root, mix about 0.2 g with 2 drops of ammonia (~260 g/l) TS and 2 ml of dichloromethane R, shake and filter. Evaporate to dryness about 1 ml of the filtrate (keep the unused portion for test 3), dissolve the residue in about 0.2 ml of water and add 3 drops of potassium iodobismuthate/acetic acid TS; an orange precipitate is produced.

3. To the remaining filtrate from test 2 add 0.5 ml of ethanol (~750 g/l) TS and transfer to a small test-tube, 100 × 10 mm. Dip vertically into the tube a strip of filter-paper, 100 × 6 mm, and allow the solution to ascend 70 mm. Dry the paper strip in air and expose it to iodine vapours for 30 seconds. Observe under ultraviolet light at 365 nm; a blue fluorescence appears.

Degradation test

Discoloration of the test material usually indicates gross degradation.

PODOPHYLLUM RESIN

Composition. Podophyllum resin is a mixture of resins obtained from the rhizomes and roots of the herbaceous plant *Podophyllum hexandrum* Royle (*P. emodi* Wall.) or *P. peltatum* L. after percolation with ethanol and precipitation from water or very dilute acids.

Identity tests

Description. Light brown to greenish yellow or brownish grey masses or an amorphous powder. Darkens when exposed to light or stored at temperatures above 25 °C.

Note. **This material is very toxic and should be handled with care.**

Colour and other reactions

1. Finely powder the resin, dissolve about 0.2 g in 10 ml of potassium hydroxide (~55 g/l) TS; a clear, yellow solution is formed which darkens on standing. Acidify with hydrochloric acid (~70 g/l) TS; the resin precipitates.

2. Finely powder the resin, add 0.4 g to 2 ml of ethanol (~750 g/l) TS, then add 0.5 ml of potassium hydroxide (~55 g/l) TS, shake gently and allow to stand; the resin of *P. hexandrum* produces a stiff jelly whereas that of *P. peltatum* does not gelatinize.

3. Dissolve 10 mg in 2 ml of ethanol (~750 g/l) TS and add 1 drop of ferric chloride (25 g/l) TS; a deep, dark green colour is produced and the solution appears black in reflected light.

4. Dissolve 10 mg in 1 ml of ethanol (~750 g/l) TS, add 4 ml of water and about 1 ml of sulfuric acid (~1760 g/l) TS and cool; the resin of *P. hexandrum* forms an orange to brownish red solution whereas that of *P. peltatum* forms a yellowish green solution.

SENNA FRUIT

Composition. Alexandrian or Khartoum senna fruit is the dried ripe fruit of *Cassia senna* L. (*C. acutifolia* Delile) and Tinnevelly senna fruit is the dried ripe fruit of *C. angustifolia* Vahl.

Identity tests

Description. Odour, slight; taste, first mucilaginous and sweet, then slightly bitter.

Macroscopic characteristics

Leaflike, flat and thin pods, yellowish green to yellowish brown with a dark brown central area, oblong or reniform.

Alexandrian senna fruit. Pale to greyish green; length, about 40–50 mm; width, 20–25 mm; stylar point at one end; containing 6–7 obovate green to pale brown seeds, with prominent longitudinal ridges on the testa.

Tinnevelly senna fruit. Brown to greyish black; length, about 35–60 mm; width, 14–18 mm; stylar point at one end; containing up to 10 obovate green to pale brown seeds, with indefinite transverse ridges on the testa.

Colour and other reactions

Before carrying out any tests, crush the fruit to a fine powder.

1. Mix about 0.2 g of the powdered fruit with 5 ml of hydrochloric acid (~250 g/l) TS and warm for 2 minutes. Cool and filter, shake the filtrate with 5 ml of toluene R and evaporate 1 ml of the yellowish coloured toluene extract to dryness. Dissolve the residue in 0.5 ml of ammonia (~100 g/l) TS and warm the solution; a pink to red-violet colour is produced.
2. Sprinkle 10 mg of the powdered fruit on the surface of about 1 ml of sulfuric acid (~1760 g/l) TS without stirring; within 5 minutes a greenish to brownish colour appears (other colours such as red indicate the presence of other species, e.g. *C. auriculata* L., *C. goratensis* Fres.).

Degradation test

Discoloration of the test material usually indicates gross degradation.

SENNA LEAF

Composition. Senna leaf consists of the dried leaflets of *Cassia senna* L., known as Alexandrian or Khartoum senna (*C. acutifolia* Delile), and Tinnevelly senna (*C. angustifolia* Vahl), or a mixture of both species.

Identity tests

Description. Odour, slight; taste, first mucilaginous and sweet, then slightly bitter.

Macroscopic characteristics

Alexandrian senna leaf. Pale greyish green, thin, fragile leaflets; lanceolate, mucronate; length, 20–40 mm; width, 5–15 mm, the maximum width being at a point slightly below the centre; lamina, slightly undulant; both surfaces covered with fine, short trichomes; pinnate venation, slightly prominent midrib with lateral veins leaving the midrib at an angle of about 60° and anastomosing to form a ridge parallel to the margin.

Tinnevelly senna leaf. Yellowish green leaflets; elongated and lanceolate; length, 25–50 mm; width at the centre, 7–20 mm; lamina, flat; both surfaces are smooth, with a very small number of trichomes, and marked with impressed transverse or oblique lines.

Colour and other reactions

Before carrying out any tests, powder the leaves to a particle size that allows them to pass through a sieve no. 45 (nominal aperture size, 0.045 mm).

1. To 0.5 g of powdered leaves add 10 ml of ethanol (~375 g/l) TS, warm in a water-bath for 5 minutes and filter while hot. To the filtrate add about 1 ml of hydrochloric acid (~420 g/l) TS, heat in a water-bath for 10 minutes and cool. Mix with 5 ml of ethyl acetate R, shake and allow to stand. Separate the ethyl acetate layer, add 2 ml of sodium hydrogen carbonate (40 g/l) TS and shake; a reddish yellow colour is produced in the aqueous layer. Remove the ethyl acetate layer, add 1 drop of hydrogen peroxide (~330 g/l) TS and heat in a water-bath; the colour of the solution changes to red.

2. Heat 0.10 g of powdered leaves with 10 ml of water in a water-bath for 30 minutes and filter. To the filtrate add 1 drop of hydrochloric acid (~420 g/l) TS, shake with 2 quantities, each of 5 ml, of dichloromethane R and discard the dichloromethane layer. Adjust the pH of the aqueous layer to 7–8, adding sodium carbonate (50 g/l) TS and testing with pH-indicator paper R. Add 10 ml of a solution composed of 4 ml of ferric chloride (25 g/l) TS and 6 ml of water, mix and heat in a water-bath for 20 minutes. Add about 1 ml of hydrochloric acid (~420 g/l) TS and continue to heat for a further 20 minutes, shaking the flask frequently. Filter, extract the filtrate with 10 ml of dichloromethane R, evaporate the dichloromethane extract to dryness over a water-bath and dissolve the residue in 2 ml of potassium hydroxide (~55 g/l) TS; a red-orange colour is produced.

3. Sprinkle 10 mg of the powdered leaves on the surface of about 1 ml of sulfuric acid (~1760 g/l) TS without stirring; within 5 minutes a greenish

to brownish colour appears (other colours such as red indicate the presence of other species, e.g. *C. auriculata* L., *C. goratensis* Fres.).

Degradation test

Discoloration of the test material usually indicates gross degradation.

5. Test procedures for pharmaceutical dosage forms

ALLOPURINOL TABLETS

Description. Each tablet usually contains 100 mg of allopurinol.

Preparation of the sample

1. Weigh 1 tablet and calculate the amount equivalent to 0.30 g of allopurinol.
2. Grind the tablets, weigh out the above-calculated equivalent amount as powdered material, triturate it with 10 ml of sodium hydroxide (0.1 mol/l) VS and filter. Acidify the filtrate with acetic acid (~60 g/l) TS, filter, wash the precipitate with 3 ml of dehydrated ethanol R and allow to dry in air for 5 minutes. Then dry at 105 °C for 3 hours and use the dried material as the test substance, dividing it into 6 equal parts.

Identity tests

Colour and other reactions

1. Dissolve 1 part of the test substance in 5 ml of sodium hydroxide (~80 g/l) TS, add 1 ml of alkaline potassio-mercuric iodide TS, heat to boiling and allow to stand; a yellow, flocculent precipitate is produced.
2. Dissolve 4 parts of the test substance in a mixture of 2 ml of sodium hydroxide (~80 g/l) TS and 2 ml of water. Add 3 ml of citric acid (90 g/l) TS and shake vigorously; a white precipitate is produced.
3. Dissolve 1 part of the test substance in 25 ml of water by warming, cool and filter. To 5 ml of the filtrate (keep the unused portion for test 4) add 1 ml of ammonia (~100 g/l) TS and 1 ml of silver nitrate (40 g/l) TS; a white precipitate is produced.
4. To 5 ml of the filtrate from test 3 add 0.5 ml of copper(II) sulfate (160 g/l) TS; a blue precipitate is produced.

AMIKACIN SULFATE INJECTION

Description. The injection is a sterile solution usually containing 250 mg of amikacin sulfate in 1.0 ml of a suitable vehicle.

Preparation of the sample

1. Pool the contents of the ampoules equivalent to 1.0 g of amikacin sulfate and use directly as test solution 1, dividing it into 2 equal volumes.
2. Dilute 1 volume of test solution 1 to 25 ml with water and use it as test solution 2.

Identity tests

Colour and other reactions

1. To 3 ml of test solution 2 add 1 ml of sodium hydroxide (~80 g/l) TS, mix and add 2 ml of cobalt(II) nitrate (10 g/l) TS; a violet colour is produced.
2. To 1 volume of test solution 1 add slowly 2 ml of anthrone TS; a bluish violet colour is produced.
3. To 2 ml of test solution 2 add a few drops of barium chloride (50 g/l) TS; a white precipitate is produced which is practically insoluble in hydrochloric acid (~250 g/l) TS.

Degradation tests

Discoloration and a change in the physical state of test solution 1 usually indicate gross degradation.

AZATHIOPRINE SODIUM POWDER FOR INJECTION

Description. Each vial contains a sterile powder of azathioprine sodium usually equivalent to 50–100 mg of azathioprine.

Preparation of the sample

1. Weigh the contents of 1 vial and calculate the amount equivalent to 0.05 g of azathioprine.
2. Empty the vials, weigh out the above-calculated equivalent amount and use directly as the test substance, dividing it into 3 equal parts.
3. Dissolve 1 part of the test substance in 100 ml of water and use it as the test solution.

Identity tests

Colour and other reactions

1. To 5 ml of the test solution add 1 ml of hydrochloric acid (~70 g/l) TS and 10 mg of zinc R powder and allow to stand for 5 minutes; the colour of the solution changes to yellow. Filter, cool in ice and add 3–4 drops of sodium nitrite (10 g/l) TS and 5–6 drops of hydrochloric acid (~70 g/l) TS. Shake and allow to stand for 2 minutes. Then add about 0.25 g of

urea R, shake and again allow to stand for 2 minutes. Add 0.5 ml of *N*-(1-naphthyl)ethylenediamine/ethanol TS; a red-violet solution is produced.

2. Transfer 2 parts of the test substance to a test-tube, add 0.05 g of potassium nitrate R and about 0.1 g of potassium hydroxide R and heat carefully until fused. Cool, dissolve the residue in 20 ml of water and filter. To 5 ml of the filtrate add 1.5 ml of hydrochloric acid (~70 g/l) TS and 5–6 drops of barium chloride (50 g/l) TS; a white turbidity appears.
3. To about 1 ml of the test solution add 0.5 ml of phosphotungstic acid (10 g/l) TS and 0.5 ml of hydrochloric acid (~70 g/l) TS; a white precipitate is produced.

BARIUM SULFATE POWDER FOR SUSPENSION

Description. A white or creamy white powder; bulky or granular.

Preparation of the sample. Use the powder directly as the test substance.

Identity tests

Colour and other reactions

1. Suspend 20 mg of the test substance in about 1 ml of hydrochloric acid (~420 g/l) TS and introduce it into a non-luminous flame using a magnesia stick or a nichrome or platinum wire sealed to a glass rod; a pale green colour appears in the flame.
2. To 0.30 g of the test substance add 10 ml of water and about 1 g of anhydrous sodium carbonate R, boil for 5 minutes and filter. Acidify the filtrate with hydrochloric acid (~420 g/l) TS and add 1 ml of barium chloride (50 g/l) TS; a white precipitate is produced.
3. To about 1 g of the test substance add 1 ml of acetic acid (~300 g/l) TS and 25 ml of water and boil. While shaking, cool and filter; if the filtrate is turbid, repeat the filtration until a clear solution is obtained and then add 1 ml of sulfuric acid (~100 g/l) TS; no opalescence is produced within 30 minutes (absence of soluble barium salts).

BECLOMETASONE DIPROPIONATE INHALATION (AEROSOL)

Description. The inhalation, supplied in a pressurized canister, contains a fine suspension of beclometasone dipropionate in a suitable propellant, usually equivalent to 50 µg per spray dose.

Preparation of the sample

1. Place 25 ml of ethanol (~750 g/l) TS in a small beaker and expel under the surface of the solvent 60 spray doses equivalent to about 3 mg of beclometasone dipropionate. Use this solution as the test solution.
2. Evaporate 10 ml of the test solution and use the residue as test substance 1.
3. Evaporate 15 ml of the test solution and use the residue as test substance 2.

Identity tests

Colour and other reactions

1. Dissolve test substance 1 in about 2 ml of sulfuric acid (~1760 g/l) TS and allow to stand for 5 minutes; a dark reddish brown solution is produced. Very cautiously pour the solution into 10 ml of water; a very light bluish grey precipitate is produced.
2. Dissolve test substance 2 in 2.0 ml of ethanol (~750 g/l) TS and add 1.0 ml of tetramethylammonium hydroxide/ethanol TS and 1.0 ml of triphenyltetrazolium chloride/ethanol TS, shaking thoroughly after each addition. Allow to stand in the dark for 20 minutes; a red colour is produced.

BENZATHINE BENZYLPENICILLIN POWDER FOR INJECTION

Description. Each vial contains a sterile powder of benzathine benzylpenicillin, usually equivalent to 1.44 g (2.4 million IU) of benzylpenicillin.

Preparation of the sample. Empty the vials and use directly as the test substance.

Identity tests

Colour and other reactions

1. To 5 mg of the test substance add 3 ml of water, 0.1 g of hydroxylamine hydrochloride R and 1 ml of sodium hydroxide (~80 g/l) TS, mix and allow to stand for 5 minutes. Then add 2 ml of hydrochloric acid (~70 g/l) TS and 0.5 ml of ferric chloride (25 g/l) TS; a violet-brown colour is produced.
2. To 2 mg of the test substance add carefully 1 drop of water and 2 ml of sulfuric acid (~1760 g/l) TS and mix; the solution is almost colourless. Heat in a water-bath for 1 minute; the solution remains almost colourless or changes to slightly yellow.
3. To 2 mg of the test substance add 1 drop of water and 2 ml of sulfuric acid (~1760 g/l) TS. After cooling, add 2 drops of formaldehyde TS; the

solution remains almost colourless. Heat in a water-bath for 1 minute; a reddish brown colour is produced.

4. Dissolve 10 mg of the test substance in 1 ml of sodium hydroxide (~80 g/l) TS and add 3 ml of water and 1 ml of potassium permanganate (10 g/l) TS; a green colour is produced. Heat the solution; an odour of benzaldehyde is perceptible.

CALCIUM GLUCONATE INJECTION

Description. The injection is a sterile solution usually containing 100 mg of calcium gluconate in 1.0 ml of a suitable vehicle.

Preparation of the sample. Dilute the contents of 1 ampoule to obtain a concentration of 10 mg of calcium gluconate in 1 ml of water and use as the test solution.

Identity tests

Colour and other reactions

1. Evaporate 1 ml of the test solution to dryness over a water-bath, add 5 mg of 2-naphthol R dissolved in about 1 ml of sulfuric acid (~1760 g/l) TS and heat in a water-bath for 1 minute; a dark blue-green colour is produced.

2. To 2 ml of silver nitrate (40 g/l) TS add ammonia (~100 g/l) TS, drop by drop, until the initially formed brown precipitate just dissolves. Add 1 ml of the test solution and heat to boiling for 1–2 minutes; a silver mirror is produced.

3. To 2 ml of the test solution add 5 drops of ammonium oxalate (25 g/l) TS; a white precipitate is produced. To a portion of the precipitate add a few drops of hydrochloric acid (~70 g/l) TS; the precipitate dissolves. To the remaining precipitate add a few drops of acetic acid (~300 g/l) TS; the precipitate is practically insoluble.

Degradation test

Discoloration of the test solution usually indicates gross degradation.

CETRIMIDE CREAM

Description. The cream usually contains 5 mg of cetrimide in 1.0 g of a suitable cream base.

Preparation of the sample

1. Withdraw and weigh an amount equivalent to 10 mg of cetrimide and use directly as the test substance.
2. Withdraw and weigh an amount equivalent to 20 mg of cetrimide, transfer to a test-tube, add 10 ml of sodium chloride (100 g/l) TS and shake thoroughly. While warming in a water-bath, keep shaking to effect separation of the emulsion, remove the test-tube from the bath, cool, filter the aqueous phase and use the filtrate as the test solution.

Identity tests

Colour and other reactions

1. Transfer the test substance to a stoppered test-tube and shake with 10 ml of water; a large amount of foam is produced (keep the solution for test 2).
2. To 5 ml of the solution from test 1 add 5 ml of nitric acid (~130 g/l) TS, shake, filter and add 5 ml of silver nitrate (40 g/l) TS; a faint opalescence is produced. Allow to stand in the dark for 30 minutes; a faint yellow-grey precipitate is produced.
3. To 5 ml of water add 1 ml of sulfamic acid (100 g/l) TS, 1 drop of methyl orange/ethanol TS and 2 ml of dichloromethane R and shake; the dichloromethane layer remains colourless. Add 3 ml of the test solution (keep the unused portion for test 4) to the tube, shake and allow the layers to separate; a yellow colour is produced in the dichloromethane layer.
4. Place the remaining test solution from test 3 over a water-bath, reduce the volume to about 2 ml and add 2 ml of potassium ferricyanide (50 g/l) TS; a yellow precipitate is produced.

CHLORPROMAZINE HYDROCHLORIDE INJECTION

Description. The injection is a sterile solution usually containing 25 mg of chlorpromazine hydrochloride in 1.0 ml of a suitable vehicle.

Preparation of the sample. Pool the contents of the ampoules equivalent to 0.05 g of chlorpromazine hydrochloride, evaporate to dryness over a water-bath and use the residue as the test substance.

Identity tests

Colour and other reactions

1. Dissolve 10 mg of the test substance in 1.5 ml of water and add 1 ml of tosylchloramide sodium (40 g/l) TS; a cloudy, blue-violet solution is produced. Shake; a dark resinous deposit separates on the walls of the

test-tube. Add 4 ml of ethyl acetate R and shake; a red-violet colour is produced in the ethyl acetate layer.

2. Dissolve about 10 mg of the test substance in 3 ml of water and add 1 ml of ethyl acetate R, 2 drops of hydrochloric acid (~70 g/l) TS and 2 drops of chloramine B (50 g/l) TS; a red colour is produced in the aqueous layer and the ethyl acetate layer remains colourless (distinction from promethazine).

3. Dissolve the remaining test substance in 5 ml of water, add 5 drops of ammonia (~100 g/l) TS, warm until oily drops separate and filter. To the filtrate add 1 ml of nitric acid (~130 g/l) TS and a few drops of silver nitrate (40 g/l) TS; a white precipitate is produced. Separate the precipitate, wash it with water and add an excess of ammonia (~100 g/l) TS; the precipitate dissolves.

CIMETIDINE INJECTION

Description. The injection is a sterile solution usually containing 200 mg of cimetidine in 1.0 ml of a suitable vehicle.

Preparation of the sample. Pool the contents of the ampoules equivalent to 0.4 g and use directly as the test solution, dividing it into 2 equal volumes.

Identity tests

Colour and other reactions

1. Place 1 volume of the test solution in a test-tube and evaporate to dryness over a water-bath. Ignite the residue; the vapours produced darken moistened lead nitrate paper R.

2. Dilute 1 volume of the test solution with 10 ml of water. To 1 ml (keep the unused portion for test 3) add 1 drop of ammonia (~100 g/l) TS and 1 drop of copper(II) sulfate (160 g/l) TS and heat in a water-bath; a greyish green precipitate is produced which is soluble in an excess of ammonia (~100 g/l) TS.

3. To 1 ml of the diluted solution from test 2 add a few drops of potassium iodobismuthate/acetic acid TS; an orange precipitate is produced.

CLOXACILLIN SODIUM POWDER FOR INJECTION

Description. Each vial contains a sterile powder of cloxacillin sodium, usually equivalent to 500 mg of cloxacillin.

Preparation of the sample

1. Weigh the contents of 1 vial and calculate the amount equivalent to 30 mg of cloxacillin sodium.
2. Empty the vial, weigh out the above-calculated equivalent amount and use directly as the test substance, dividing it into 6 equal parts.

Identity tests

Colour and other reactions

1. Dissolve 1 part of the test substance in 3 ml of water and filter. To the filtrate add 0.10 g of hydroxylamine hydrochloride R and 1 ml of sodium hydroxide (~80 g/l) TS and allow to stand for 5 minutes. Then add 1.3 ml of hydrochloric acid (~70 g/l) TS and 0.5 ml of ferric chloride (25 g/l) TS; a dark violet-red colour is produced.
2. Dissolve 2 parts of the test substance in 2 ml of water and add 2 ml of a solution composed of 2 ml of potassio-cupric tartrate TS and 6 ml of water; a light blue solution is immediately produced.
3. Dissolve 1 part of the test substance in 1 ml of water, shake and filter. To the filtrate add 1 drop of ferric chloride (25 g/l) TS; a greenish yellow precipitate is produced.
4. To 10 mg of paraformaldehyde R dissolved in about 1 ml of sulfuric acid (~1760 g/l) TS add a small quantity of the test substance; a light yellow colour is produced. Heat the mixture in a water-bath for 2 minutes and cool; the colour of the solution changes to brownish.
5. Dissolve 1 part of the test substance in 5 ml of water and filter. Acidify with about 0.5 ml of glacial acetic acid R and filter using a coarse-porosity filter-paper. To 2 ml of the filtrate add 1 ml of magnesium uranyl acetate TS and scratch the inside of the tube with a glass rod to induce crystallization; a yellow, crystalline precipitate is produced.

DEXTRAN 70 INJECTION

Description. The injection is a sterile solution usually containing 6 g of dextran 70 in 100 ml of a suitable vehicle (normally dextrose or sodium chloride solution).

Preparation of the sample. Pool a volume equivalent to 0.12 g of dextran 70 and use directly as the test solution, dividing it into 4 equal volumes.

Identity tests

Colour and other reactions

For dextran 70 in dextrose solution:

To 1 volume of the test solution add 5 ml of potassio-cupric tartrate TS and boil; a brick-red precipitate is formed. Filter and to the filtrate add about 1.5 ml of hydrochloric acid (~420 g/l) TS. Boil for 5 minutes, cool and neutralize by adding sodium carbonate R until the effervescence ceases. Add 2 ml of potassio-cupric tartrate TS and boil again; a brick-red precipitate is again produced.

For dextran 70 in sodium chloride solution:

1. To 1 volume of the test solution add 5 ml of potassio-cupric tartrate TS and boil; the solution remains greenish and no precipitate is formed. Dilute a further 0.5 ml of the test solution to 5 ml with water and add about 0.5 ml of hydrochloric acid (~420 g/l) TS. Boil for 5 minutes, cool and neutralize by adding sodium carbonate R until the effervescence ceases. Add 2 ml of potassio-cupric tartrate TS and boil again; a brick-red precipitate is produced.
2. Introduce the test solution into a non-luminous flame using a magnesia stick or a nichrome or platinum wire sealed to a glass rod; the flame acquires an intense yellow colour.
3. Acidify 1 volume of the test solution with a small volume of nitric acid (~130 g/l) TS and add 2 ml of silver nitrate (40 g/l) TS; a white, curdy precipitate is produced. Separate the precipitate, wash it with water and add a few drops of ammonia (~100 g/l) TS; the precipitate dissolves.

DIPHENHYDRAMINE HYDROCHLORIDE TABLETS

Description. Each tablet usually contains 25–50 mg of diphenhydramine hydrochloride.

Preparation of the sample

1. Weigh 1 tablet and calculate the amount equivalent to 0.20 g of diphenhydramine hydrochloride.
2. Grind the tablets, weigh out the above-calculated equivalent amount as powdered material and use directly as the test substance, dividing it into 4 equal parts.

Identity tests

Colour and other reactions

1. Place a small quantity of the test substance on a white test plate and add 1 drop of a mixture of about 0.5 ml of nitric acid (~1000 g/l) TS and about 0.5 ml of sulfuric acid (~1760 g/l) TS; a momentary violet colour is produced which changes to red and finally to yellow.
2. To 2 parts of the test substance add 5 ml of water, shake and filter. To the filtrate add 3 ml of hydrochloric acid (~250 g/l) TS and boil for 3 minutes.

Cool the test-tube in ice and scratch the inside of the tube with a glass rod to induce crystallization. Separate the crystals and dry over silica gel, desiccant, R; melting point, about 64 °C. If the melting point is lower than 64 °C, recrystallize from 1–2 ml of water.

3. To 1 part of the test substance add 5 ml of water, shake and filter. To the filtrate add 0.5 ml of silver nitrate (40 g/l) TS; a white, curdy precipitate is produced. Separate the precipitate, wash it with water and add an excess of ammonia (~100 g/l) TS; the precipitate dissolves.

DOXORUBICIN HYDROCHLORIDE POWDER FOR INJECTION

Description. Each vial contains a sterile powder usually equivalent to 10–50 mg of doxorubicin hydrochloride.

Preparation of the sample

1. Weigh the contents of 1 vial and calculate the amount equivalent to 0.07 g of doxorubicin hydrochloride.
2. Empty the vials, weigh out the above-calculated equivalent amount and use directly as the test substance.

Identity tests

Colour and other reactions

1. Place a small quantity of the test substance on a white test plate and add 1 drop of formaldehyde/sulfuric acid TS; the orange-red colour of the substance changes to violet.
2. Dissolve about 2 mg of the test substance in 2 ml of methanol R and add 2 ml of water and 1 drop of sodium hydroxide (~80 g/l) TS; the orange-red colour of the solution changes to blue-violet.
3. Dissolve 0.05 g of the test substance in 1 ml of water, add 5 drops of ammonia (~100 g/l) TS and filter. Acidify the filtrate with nitric acid (~130 g/l) TS and add 1 ml of silver nitrate (40 g/l) TS; a white, curdy precipitate is produced which is soluble in ammonia (~100 g/l) TS but practically insoluble in nitric acid (~1000 g/l) TS.

DOXYCYCLINE HYCLATE INJECTION

Description. The injection is a sterile solution usually containing 20 mg of doxycycline hyclate[1] in 1.0 ml of a suitable vehicle.

[1] Referred to as doxycycline hydrochloride in *Basic tests for pharmaceutical substances*, 1986.

Preparation of the sample. Pool the contents of the ampoules equivalent to 0.16 g of doxycycline hyclate and use directly as the test solution, dividing it into 4 equal volumes.

Identity tests

Colour and other reactions

1. To 1 volume of the test solution add about 2 ml of sulfuric acid (~1760 g/l) TS; an intense yellow colour is produced.
2. Place 2 ml of zinc chloride (500 g/l) TS in a porcelain dish and warm on a hotplate or over a small flame until a skin forms on the surface of the solution. Then add 2 drops of the test solution and continue to warm for 1 minute; a yellow-orange colour is produced.
3. To 1 volume of the test solution add 1 drop of ferric chloride (25 g/l) TS; a dark red-brown colour is produced.
4. To 1 volume of test solution add 0.5 ml of nitric acid (~130 g/l) TS and 0.5 ml of silver nitrate (40 g/l) TS; a white, curdy precipitate is produced. Separate the precipitate, wash it with water and add an excess of ammonia (~100 g/l) TS; the precipitate dissolves.

Degradation test

Discoloration of the test solution usually indicates gross degradation.

DOXYCYCLINE HYCLATE TABLETS

Description. Each tablet usually contains 100 mg of doxycycline hyclate.[1]

Preparation of the sample

1. Weigh 1 tablet and calculate the amounts equivalent to 0.10 g and 25 mg of doxycycline hyclate.
2. Grind the tablets, weigh out the above-calculated equivalent amounts as powdered material and use directly, 0.10 g as test substance 1 and 25 mg as test substance 2.
3. Shake test substance 1 with 10 ml of water and filter. Use the filtrate as the test solution.

Identity tests

Colour and other reactions

1. To test substance 2 add about 2 ml of sulfuric acid (~1760 g/l) TS; an intense yellow colour is produced.

[1] Referred to as doxycycline hydrochloride in *Basic tests for pharmaceutical substances*, 1986.

2. Place 2 ml of zinc chloride (500 g/l) TS in a porcelain dish and warm on a hotplate or over a small flame until a skin forms on the surface of the solution. Then add 2 drops of the test solution and continue to warm for 1 minute; a yellow-orange colour is produced.
3. To 2 ml of the test solution add 1 drop of ferric chloride (25 g/l) TS; a dark red-brown colour is produced.
4. To 1 ml of the test solution add 0.5 ml of nitric acid (~130 g/l) TS and 0.5 ml of silver nitrate (40 g/l) TS; a white, curdy precipitate is produced. Separate the precipitate, wash it with water and add an excess of ammonia (~100 g/l) TS; the precipitate dissolves.

EPINEPHRINE HYDROGEN TARTRATE INJECTION

Description. The injection is a sterile solution of epinephrine hydrogen tartrate, usually containing the equivalent of 1.0 mg of epinephrine in 1.0 ml of a suitable vehicle.

Preparation of the sample. Pool the contents of the ampoules equivalent to 10 mg of epinephrine hydrogen tartrate; if necessary, reduce the volume by evaporation to 10 ml or dilute to 10 ml with water. Use directly as the test solution.

Identity tests

Colour and other reactions

1. To 5 ml of the test solution add 1–2 drops of ferric chloride (25 g/l) TS; a green solution is produced. Add 1 drop of ammonia (~260 g/l) TS; the colour changes to dark red.
2. To 2 ml of the test solution add 1 ml of sulfuric acid (~5 g/l) TS and 3 ml of ammonium molybdate (95 g/l) TS and mix; an orange colour is produced. Then add slowly, while mixing, 2 ml of sodium hydroxide (~80 g/l) TS; a yellow-green solution is produced.
3. To 2 ml of the test solution add 2 ml of potassium bromide (100 g/l) TS, 2 ml of resorcinol (20 g/l) TS and 3 ml of sulfuric acid (~1760 g/l) TS. Heat in a water-bath for 5–10 minutes; a dark blue colour is produced which changes to red when the solution is cooled and poured into water.

FERROUS FUMARATE TABLETS

Description. Each tablet contains ferrous fumarate, usually equivalent to 60 mg of iron.

Preparation of the sample

1. Weigh 1 tablet and calculate the amounts equivalent to 0.5 g and 0.05 g of ferrous fumarate.

2. Grind the tablets, weigh out the above-calculated equivalent amounts as powdered material and use directly, 0.5 g as test substance 1 and 0.05 g as test substance 2.

Identity tests

Colour and other reactions

1. To test substance 1 add 20 ml of sulfuric acid (~100 g/l) TS and heat in a water-bath for 15 minutes. Filter while hot and cool the filtrate in ice; a white precipitate is produced (keep the filtrate for test 2). Wash the precipitate with acidified water and dry at 105 °C. Dissolve the precipitate in 5 ml of sodium carbonate (50 g/l) TS and add 0.5 ml of potassium permanganate (10 g/l) TS; the colour of the permanganate fades and a brownish solution is produced.

2. To 2 ml of the filtrate obtained in test 1 add 2 ml of potassium ferricyanide (50 g/l) TS; an intense dark blue precipitate is produced which is insoluble in hydrochloric acid (~70 g/l) TS.

3. Mix test substance 2 with 0.10 g of resorcinol R, add 5–10 drops of sulfuric acid (~1760 g/l) TS and heat gently; a deep red, semi-solid mass is produced. Cool, add 25 ml of water, swirl to dissolve and filter. To 1 ml of the filtrate add 10 ml of water and mix; an orange-yellow solution is produced which exhibits a green fluorescence. Make the solution alkaline by adding a few drops of sodium hydroxide (~80 g/l) TS; a red solution is produced which exhibits a green fluorescence.

FLUCYTOSINE TABLETS

Description. Each tablet usually contains 500 mg of flucytosine.

Preparation of the sample

1. Weigh 1 tablet and calculate the amount equivalent to 0.30 g of flucytosine.

2. Grind the tablets, weigh out the above-calculated equivalent amount as powdered material, shake with 30 ml of water, filter and use the filtrate as the test solution, dividing it into 6 equal volumes.

3. Evaporate 2 volumes of the test solution to dryness over a water-bath and use the residue as the test substance.

Identity tests

Melting behaviour. The test substance melts at about 295 °C with decomposition.

Colour and other reactions

1. To 1 volume of the test solution add 5 ml of water, 1.5 ml of hydrochloric acid (~250 g/l) TS and 0.5 ml of sodium nitrite (10 g/l) TS and shake for 2 minutes. Add 0.5 ml of 2-naphthol TS; a yellowish brown precipitate is produced.
2. To 1 volume of the test solution add 5 ml of water and 2 ml of silver nitrate (40 g/l) TS, shake and allow to stand for 2–3 minutes; a white precipitate is produced.
3. To 0.5 volume of the test solution add 2 ml of bromine TS; the colour of bromine is discharged. Add 4 ml of freshly prepared barium hydroxide (40 g/l) TS; a purple precipitate is produced.
4. Mix 3 drops of potassium dichromate (100 g/l) TS with about 0.5 ml of sulfuric acid (~1760 g/l) TS and heat in a water-bath for 5 minutes; the solution wets the sides of the tube. Add 10 mg of the test substance, shake well and heat again for 5 minutes in a water-bath; the colour changes to green and the solution no longer wets the sides of the tube.

GENTAMICIN SULFATE INJECTION

Description. The injection is a sterile solution usually containing 10–40 mg of gentamicin sulfate in 1.0 ml of a suitable vehicle.

Preparation of the sample. Pool the contents of the ampoules equivalent to 0.20 g of gentamicin sulfate; if necessary, reduce the volume by evaporation to about 5 ml or dilute to 5 ml with water. Use directly as the test solution.

Identity tests

Colour and other reactions

1. To 1 ml of the test solution add a solution of 5 mg of 1-naphthol R dissolved in 1 drop of ethanol (~750 g/l) TS, 4 drops of water and about 0.5 ml of sulfuric acid (~1760 g/l) TS; a yellow colour is produced.
2. To 1 ml of the test solution add a solution of 20 mg of triketohydrindene hydrate R dissolved in 2 ml of water and 0.10 g of sodium acetate R. Mix and heat in a water-bath for 5 minutes; a dark violet colour is produced.
3. Dilute 1 ml of the test solution with 1 ml of water and add 5 drops of alkaline potassio-mercuric iodide TS; a yellowish white, turbid solution is produced.

4. Dilute 1 ml of the test solution with 2 ml of water and add 5 drops of hydrochloric acid (~70 g/l) TS and 5 drops of barium chloride (50 g/l) TS; a white precipitate is produced.

HYDRALAZINE HYDROCHLORIDE TABLETS

Description. Each tablet usually contains 25–50 mg of hydralazine hydrochloride.

Preparation of the sample

1. Weigh 1 tablet and calculate the amounts equivalent to 5 mg and 0.05 g of hydralazine hydrochloride.
2. Grind the tablets, weigh out the above-calculated equivalent amounts as powdered material and use directly, 5 mg as test substance 1 and 0.05 g as test substance 2.
3. Shake test substance 2 with 5 ml of water, filter and use the filtrate as the test solution.

Identity tests

Colour and other reactions

1. Shake test substance 1 with 2 ml of water, add 3 drops of freshly prepared ferrous sulfate (15 g/l) TS and heat to boiling for 3 minutes; a brown-red colour is produced. Add 5–10 drops of iodine TS; the colour changes to dark violet.
2. To about 1 ml of the test solution add 0.5 ml of nitric acid (~130 g/l) TS and 5 ml of silver nitrate (40 g/l) TS; a white, curdy precipitate is produced. Separate the precipitate, wash it with water and add an excess of ammonia (~100 g/l) TS; the precipitate dissolves.
3. To 4 ml of the test solution add a mixture of 100 ml of water and 8 ml of hydrochloric acid (~70 g/l) TS, then add 20 ml of sodium nitrite (10 g/l) TS and allow to stand for 10 minutes; a white to ivory-coloured precipitate is produced.

HYDROCORTISONE OINTMENT

Description. The ointment usually contains 10–25 mg of hydrocortisone in 1.0 g of a suitable ointment base.

Preparation of the sample. Withdraw and weigh an amount equivalent to 20 mg of hydrocortisone, add 10 ml of ethanol (~750 g/l) TS and heat in a water-bath for 5 minutes with frequent shaking. Cool to solidify the

ointment base, filter and use the filtrate as the test solution, dividing it into 4 equal volumes.

Identity tests

Colour and other reactions

1. Evaporate 1 volume of the test solution to dryness over a water-bath. Add about 2 ml of sulfuric acid (~1760 g/l) TS and allow to stand for 5 minutes; a yellow solution is produced with a greenish fluorescence. Very cautiously pour the solution into 10 ml of water; the colour of the solution changes to brownish yellow, but the fluorescence remains (certain excipients may interfere with the reaction and the colour of the solution may fade to nearly colourless).
2. Evaporate 1 volume of the test solution to dryness over a water-bath. Add about 1 ml of phosphoric acid (~1440 g/l) TS and heat cautiously; the solution, initially colourless, changes to yellow and shows a slightly greenish fluorescence.
3. Evaporate 2 volumes of the test solution to about 2 ml over a water-bath and add an equal volume of potassio-cupric tartrate TS; an orange-red precipitate is produced.

HYDROCORTISONE ACETATE CREAM

Description. The cream usually contains 10 mg of hydrocortisone acetate in 1.0 g of a suitable cream base.

Preparation of the sample. Withdraw and weigh an amount equivalent to 0.10 g of hydrocortisone acetate, add 30 ml of methanol R, boil and cool in ice for 30 minutes. Filter, evaporate the filtrate to dryness and use the residue as the test substance.

Identity tests

Colour and other reactions

1. Dissolve about 2 mg of the test substance in about 2 ml of sulfuric acid (~1760 g/l) TS and allow to stand for 5 minutes; a yellow solution with a greenish fluorescence is produced. Very cautiously pour the solution into 10 ml of water; the colour of the solution changes to brownish yellow, but the fluorescence remains (certain excipients may interfere with the reaction and the colour of the solution may fade to nearly colourless within a very short period of time).
2. Dissolve about 2 mg of the test substance in about 1 ml of phosphoric acid (~1440 g/l) TS. Heat cautiously; the colourless solution changes to yellow and shows a slightly greenish fluorescence.

3. Dissolve 20 mg of the test substance in 2 ml of methanol R. Add 1 ml of tetramethylammonium hydroxide/ethanol TS and 1 ml of triphenyltetrazolium chloride/ethanol TS, mixing thoroughly after each addition, and allow to stand in the dark for 20 minutes; a red colour is produced.
4. Place 15 mg of the test substance in a test-tube and add 3 drops of phosphoric acid (~1440 g/l) TS. Close the tube with a stopper through which passes a smaller test-tube filled with water to act as a condenser. Allow a drop of lanthanum nitrate (30 g/l) TS to hang on the outside of this smaller tube. Heat the apparatus in a water-bath for 5 minutes. Transfer the drop of lanthanum nitrate to a white test plate, mix it with 1 drop of iodine (0.05 mol/l) VS and add, at the edge of the two liquids, 1 drop of ammonia (~100 g/l) TS; after 1–2 minutes a blue colour is produced at the interface of the two liquids which persists for a short time.

HYDROCORTISONE SODIUM SUCCINATE POWDER FOR INJECTION

Description. Each vial contains a sterile powder usually equivalent to 100 mg of hydrocortisone sodium succinate.

Preparation of the sample

1. Weigh the contents of 1 vial and calculate the amount equivalent to 0.10 g of hydrocortisone sodium succinate.
2. Empty the vial, weigh out the above-calculated equivalent amount and use directly as the test substance.

Identity tests

Colour and other reactions

1. Dissolve about 2 mg of the test substance in 1 ml of alkaline potassiomercuric iodide TS; a dark precipitate is produced.
2. Dissolve a small quantity of the test substance in about 2 ml of sulfuric acid (~1760 g/l) TS and allow to stand for 5 minutes; a yellow solution with a greenish fluorescence is produced. Very cautiously pour the solution into 10 ml of water; the colour of the solution changes to brownish yellow, but the fluorescence remains (certain excipients may interfere with the reaction and the colour may fade to nearly colourless within a very short period of time).
3. Dissolve a small quantity of the test substance in about 1 ml of phosphoric acid (~1440 g/l) TS and heat cautiously; a yellow solution with a pale greenish fluorescence is produced.

4. Dissolve about 2 mg of the test substance in 1 ml of water and introduce the solution into a non-luminous flame using a magnesia stick or a nichrome or platinum wire sealed to a glass rod; the flame acquires an intense yellow colour.
5. Heat carefully 10 mg of the test substance with 1 drop of water, 10 mg of resorcinol R and 3 drops of sulfuric acid (~1760 g/l) TS, cool and add 2 ml of water. Cool again and pour the solution into a mixture of 100 ml of water and 1 ml of sodium hydroxide (~400 g/l) TS; a yellowish green fluorescence appears.

INDOMETACIN TABLETS

Description. Each tablet usually contains 25 mg of indometacin.

Preparation of the sample

1. Weigh 1 tablet and calculate the amount equivalent to 0.05 g of indometacin.
2. Grind the tablets, weigh out the above-calculated equivalent amount as powdered material and use directly as the test substance, dividing it into 2 equal parts.

Identity tests

Colour and other reactions

1. To 1 part of the test substance add 1 ml of water and 1 drop of sodium hydroxide (~80 g/l) TS, shake and filter. To the filtrate add 1 ml of sodium nitrite (10 g/l) TS, allow to stand for 5 minutes and cautiously add 0.5 ml of hydrochloric acid (~250 g/l) TS; a green colour is produced.
2. Mix 1 part of the test substance with 2 ml of water and 2 ml of sodium hydroxide (~80 g/l) TS; a strong yellow colour is produced which fades rapidly.

IRON DEXTRAN INJECTION

Description. The injection is a sterile solution of iron dextran, usually containing the equivalent of 50 mg of iron in 1.0 ml of a suitable vehicle.

Preparation of the sample. Pool the contents of the ampoules equivalent to 0.15 g of iron; if necessary, reduce the volume to about 3 ml or dilute with water to 3 ml. Use directly as the test solution.

Identity tests

Colour and other reactions

1. Place 1 ml of the test solution on a watch-glass and add 2 drops of ammonia (~260 g/l) TS; no precipitate is observed. Add about 2 ml of hydrochloric acid (~420 g/l) TS, mix and add about 2 ml of ammonia (~260 g/l) TS; a reddish brown precipitate is produced.
2. Acidify 1 ml of the test solution with hydrochloric acid (~70 g/l) TS and add 1 ml of ammonium thiocyanate (75 g/l) TS; a blood-red colour is produced. Extract with 5 ml of amyl alcohol R and add a few drops of mercuric chloride (65 g/l) TS or phosphoric acid (~1440 g/l) TS; the colour is discharged.
3. Dilute about 0.2 ml of the test solution with 20 ml of water. To 10 ml of this solution add 4 drops of hydrochloric acid (~420 g/l) TS and boil for 30 seconds. Cool rapidly and add 4 ml of ammonia (~260 g/l) TS and 10 ml of hydrogen sulfide TS. Boil to remove the excess hydrogen sulfide, cool and filter. Boil 5 ml of the filtrate with 5 ml of potassio-cupric tartrate TS; the colour of the solution remains greenish and no precipitate is produced. Boil a further 5 ml of the filtrate with about 0.5 ml of hydrochloric acid (~420 g/l) TS for 5 minutes, cool, add 2.5 ml of sodium hydroxide (~80 g/l) TS and 5 ml of potassio-cupric tartrate TS and boil again; a reddish precipitate is produced.

KETAMINE HYDROCHLORIDE INJECTION

Description. The injection is a sterile solution of ketamine hydrochloride, usually containing the equivalent of 50 mg of ketamine in 1.0 ml of a suitable vehicle.

Preparation of the sample. Pool the contents of the ampoules equivalent to 0.15 g of ketamine hydrochloride and use directly as the test solution, dividing it into 3 equal volumes.

Identity tests

Colour and other reactions

1. To one-third of 1 volume of the test solution add a few drops of sodium hydroxide (~80 g/l) TS; a white turbidity is produced. Add a few drops of methanol R; the turbidity disappears.
2. To one-third of 1 volume of the test solution add 0.5 ml of trinitrophenol/ethanol TS; a yellow precipitate is produced.
3. Acidify one-third of 1 volume of the test solution with a small volume of nitric acid (~130 g/l) TS and add 2 ml of silver nitrate (40 g/l) TS; a white, curdy precipitate is produced. Separate the precipitate, wash it

with water and add an excess of ammonia (~100 g/l) TS; the precipitate dissolves.

4. Evaporate 2 volumes of the test solution to dryness. Recrystallize the residue from ethanol (~750 g/l) TS and dry at 105 °C for 2 hours; melting point, about 261 °C.

LEVOTHYROXINE SODIUM TABLETS

Description. Each tablet usually contains 50–100 µg of levothyroxine sodium.

Preparation of the sample

1. Weigh 1 tablet and calculate the amount equivalent to 5 mg of levothyroxine sodium.
2. Grind the tablets, weigh out the above-calculated equivalent amount as powdered material and use directly as test substance 1, dividing it into 2 equal parts.
3. Divide 1 part of test substance 1 into 5 equal parts and use as test substance 2.
4. Shake 2 parts of test substance 2 with 3 ml of dehydrated ethanol R for 5 minutes, then allow to stand for 5 minutes. Place a strip of filter-paper into the suspension and allow the liquid to ascend about 4 cm. Take out the strip, cut away the lower dipped portion as well as the part that has not been wetted by the solution, dry the remaining part of the strip in air at room temperature and use as the test paper.

Identity tests

Colour and other reactions

1. To 1 part of test substance 2 add 1.5 ml of ethanol (~750 g/l) TS, 1.5 ml of water and 0.5 ml of sodium hydroxide (~80 g/l) TS, shake well and filter. To the filtrate add about 0.5 ml of hydrochloric acid (~250 g/l) TS and 0.2 ml of sodium nitrite (100 g/l) TS; a yellow colour is produced. Allow to stand for 5 minutes and add 1 drop of ammonia (~260 g/l) TS; the colour of the solution changes to orange-red.
2. Place 1 part of test substance 2 in a silica crucible and ignite. To the residue add 2 ml of water, shake and filter. To the filtrate add 0.5 ml of magnesium uranyl acetate TS and allow to stand for a few minutes; a yellow precipitate is produced.
3. Heat test substance 1 with about 0.2 g of sodium carbonate R. To the fused mass add 3 ml of water, shake and filter. Acidify the filtrate with a few drops of hydrochloric acid (~250 g/l) TS and add 2–3 drops of starch TS; a blue-violet colour is produced.

4. Place 1 drop of triketohydrindene/ethanol TS on the test paper and place in an oven at 105 °C for 5 minutes; a violet spot or ring is produced.

LIDOCAINE HYDROCHLORIDE JELLY

Description. The jelly usually contains 20–40 mg of lidocaine hydrochloride in 1.0 g of a suitable water-soluble, viscous base.

Preparation of the sample

1. Add 10–15 ml of water to a separator, add a quantity of the jelly equivalent to 0.15 g of lidocaine hydrochloride and mix. Add 2.0 ml of ammonia (~100 g/l) TS and extract with 2 portions of 30 ml of dichloromethane R. Evaporate the combined dichloromethane extracts to dryness with the aid of a current of warm air and use the residue as test substance 1.

2. Withdraw and weigh an amount equivalent to 0.20 g of lidocaine hydrochloride and use directly as test substance 2, dividing it into 3 equal parts.

Identity tests

Colour and other reactions

1. To test substance 1 add 1 ml of ethanol (~750 g/l) TS and 0.5 ml of cobalt(II) chloride (30 g/l) TS and shake for 2 minutes; a bluish green precipitate is produced.

2. To 1 part of test substance 2 add 2 ml of water and 3 drops of iodine TS and mix; a brown precipitate is produced.

3. Shake 2 parts of test substance 2 with 5 ml of water and add 1 ml of nitric acid (~130 g/l) TS and 1 ml of silver nitrate (40 g/l) TS; a white precipitate is produced. Separate the precipitate, wash it with water and add an excess of ammonia (~100 g/l) TS; the precipitate dissolves.

MAGNESIUM HYDROXIDE ORAL SUSPENSION

Description. The suspension usually contains the equivalent of 55 mg of magnesium oxide in 1.0 ml of a suitable vehicle.

Preparation of the sample. Take a portion of the suspension equivalent to 0.20 g of magnesium hydroxide and use directly as the test solution, dividing it into 2 equal volumes.

Identity tests

Colour and other reactions

1. To 1 volume of the test solution add 5 ml of hydrochloric acid (~70 g/l) TS and filter. To the filtrate add 5 ml of ammonium chloride (100 g/l) TS, 3 ml of disodium hydrogen phosphate (100 g/l) TS and 5 ml of ammonia (~100 g/l) TS; a white precipitate is produced which is soluble in acetic acid (~300 g/l) TS.
2. To 1 volume of the test solution add 5 ml of hydrochloric acid (~70 g/l) TS and 5 ml of sodium hydroxide (~80 g/l) TS; a white, gelatinous precipitate is produced which is insoluble in an excess of sodium hydroxide (~80 g/l) TS. Add a few drops of iodine TS; the colour of the precipitate changes to dark brown.

MAGNESIUM SULFATE POWDER

Description. Brilliant, colourless crystals or a white, crystalline powder; odourless.

Preparation of the sample. Use the powder directly as the test substance.

Identity tests

Colour and other reactions

1. Dissolve 10 mg of the test substance in 2 ml of water and add 1 ml of ammonia (~100 g/l) TS; a white precipitate is produced. Add 1 ml of ammonium chloride (100 g/l) TS; the precipitate dissolves. Add 1 ml of disodium hydrogen phosphate (100 g/l) TS; a white precipitate is produced.
2. Dissolve 10 mg of the test substance in 2 ml of water and add 3 drops of titan yellow TS and 2 ml of sodium hydroxide (~80 g/l) TS; a distinct pink colour is produced.
3. Dissolve 0.05 g of the test substance in 5 ml of water and add 1 ml of hydrochloric acid (~70 g/l) TS and 1 ml of barium chloride (50 g/l) TS; a white precipitate is produced.

METHYLROSANILINIUM CHLORIDE SOLUTION

Description. The solution usually contains 10 mg of methylrosanilinium chloride (gentian violet) in 1.0 ml of a suitable vehicle.

Preparation of the sample. Take a volume of the solution equivalent to 25 mg of methylrosanilinium chloride and use directly as the test solution.

Identity tests

Colour and other reactions

1. Add 2 drops of the test solution to about 1 ml of sulfuric acid (~1760 g/l) TS and shake; an orange or brown-red colour is produced. Cautiously dilute with water; the colour changes to brown, then to green and finally to blue.
2. Dilute the remaining test solution to 10 ml with water and add 5 drops of hydrochloric acid (~420 g/l) TS. To 5 ml of this solution (keep the unused portion for test 3) add, drop by drop, 0.6 ml of tannic acid (100 g/l) TS; a deep blue precipitate is produced.
3. To the remaining solution from test 2 add about 1 ml of hydrochloric acid (~420 g/l) TS and 0.5 g of zinc R powder; a gas is evolved and the solution fades rapidly. Filter and, on a filter-paper, place 1 drop of the filtrate adjacent to 1 drop of ammonia (~100 g/l) TS; a blue colour is produced at the zone of contact.

METOCLOPRAMIDE HYDROCHLORIDE INJECTION

Description. The injection is a sterile solution usually containing 5 mg of metoclopramide hydrochloride in 1.0 ml of a suitable vehicle.

Preparation of the sample. Pool the contents of the ampoules equivalent to 0.06 g of metoclopramide hydrochloride and use directly as the test solution, dividing it into 6 equal volumes.

Identity tests

Colour and other reactions

1. To 2 volumes of the test solution add 1 ml of hydrochloric acid (~70 g/l) TS and 2 ml of sodium nitrite (10 g/l) TS; a yellow colour is produced.
2. To 2 volumes of the test solution add 1 drop of sulfuric acid (~1760 g/l) TS, 1 drop of potassium bromide (100 g/l) TS and 2 drops of potassium bromate (15 g/l) TS; a green colour is produced.
3. Mix 2 drops of potassium bromide (100 g/l) TS with 4 drops of potassium bromate (15 g/l) TS and dilute to about 1 ml with water. Add 2 drops of sulfuric acid (~1760 g/l) TS and 1 volume of the test solution; a yellowish precipitate is produced.
4. To 1 volume of the test solution add 1 ml of nitric acid (~130 g/l) TS and 1 ml of silver nitrate (40 g/l) TS; a white, curdy precipitate is produced. Separate the precipitate, wash it with water and add an excess of ammonia (~100 g/l) TS; the precipitate dissolves.

METOCLOPRAMIDE HYDROCHLORIDE TABLETS

Description. Each tablet usually contains 10 mg of metoclopramide hydrochloride.

Preparation of the sample

1. Weigh 1 tablet and calculate the amount equivalent to 0.35 g of metoclopramide hydrochloride.
2. Grind the tablets and weigh out the above-calculated equivalent amount as powdered material, shake it with 10 ml of water and filter. Use the filtrate as the test solution, dividing it into 3 equal volumes.

Identity tests

Colour and other reactions

1. To 1 volume of the test solution add 1 ml of hydrochloric acid (~70 g/l) TS and 2 ml of sodium nitrite (10 g/l) TS; a yellow colour is produced.
2. Mix 2 drops of potassium bromide (100 g/l) TS with 4 drops of potassium bromate (15 g/l) TS and dilute to 1 ml with water. Add 2 drops of sulfuric acid (~1760 g/l) TS and 1 volume of the test solution; a yellowish precipitate is produced.
3. To 1 volume of the test solution add 1 ml of nitric acid (~130 g/l) TS and 1 ml of silver nitrate (40 g/l) TS; a white, curdy precipitate is produced. Separate the precipitate, wash it with water and add an excess of ammonia (~100 g/l) TS; the precipitate dissolves.

METRONIDAZOLE SUPPOSITORIES

Description. Each suppository usually contains 500 mg–1 g of metronidazole.

Preparation of the sample. Dissolve a quantity of the suppository equivalent to 0.5 g of metronidazole in 20 ml of hot water. Allow to stand overnight to crystallize. Filter to separate the crystals, dry them at 105 °C for about 3 hours and use as the test substance.

Identity tests

Description of the test substance. A white or pale yellow, crystalline powder.

Melting point of the test substance. About 161 °C.

Colour and other reactions

1. To 20 mg of the test substance add 0.05 g of 4-dimethylaminobenzaldehyde R dissolved in 2 ml of hydrochloric acid (~70 g/l) TS; the solution is almost colourless or has a yellow tint. Add 0.05 g of zinc R powder; a deep red colour is produced.
2. Boil 20 mg of the test substance with 5 ml of sodium hydroxide (~80 g/l) TS; the solution shows the following colours in turn: pink, pink-violet, red-violet, red, red-brown, yellow-brown and yellow.

MICONAZOLE NITRATE CREAM

Description. The cream usually contains 20 mg of miconazole nitrate in 1.0 g of a suitable cream base.

Preparation of the sample

1. Withdraw and weigh an amount equivalent to 0.10 g of miconazole nitrate and use directly as the test substance, dividing it into 2 equal parts.
2. Dissolve 1 part of the test substance in sufficient methanol R to produce 50 ml, filter, and use as the test solution.

Identity tests

Colour and other reactions

1. To 1 part of the test substance add 2 ml of sodium hydroxide (~80 g/l) TS and 20 g of zinc R powder. Boil gently; ammonia is produced which shows an alkaline range on moistened pH-indicator paper R.
2. Place 5 ml of the test solution in a porcelain crucible, add 0.1 g of anhydrous sodium carbonate R, evaporate to dryness over a water-bath and ignite. Cool, dissolve the residue in 3 ml of nitric acid (~130 g/l) TS and add a few drops of silver nitrate (40 g/l) TS; a white precipitate is produced. Separate the precipitate, wash with water and add an excess of ammonia (~100 g/l) TS; the precipitate dissolves.
3. Cool 3 ml of the test solution in ice and add 0.4 ml of potassium chloride (100 g/l) TS, 0.1 ml of diphenylamine/sulfuric acid TS and 10 ml of sulfuric acid (~1760 g/l) TS; an intense blue colour is produced.

NICLOSAMIDE TABLETS

Description. Each tablet usually contains 500 mg of niclosamide.

Preparation of the sample

1. Weigh 1 tablet and calculate the amount equivalent to 0.25 g of niclosamide.
2. Grind the tablets, weigh out the above-calculated equivalent amount as powdered material, shake it with 20 ml of acetone R and filter. Evaporate the filtrate to dryness over a water-bath and use the residue as the test substance.

Identity tests

Melting point of the test substance. About 228 °C.

Colour and other reactions

1. To 0.05 g of the test substance add 5 ml of hydrochloric acid (~70 g/l) TS and about 0.1 g of zinc R powder, heat over a water-bath for 10 minutes, cool and filter. To the filtrate add 1 ml of sodium nitrite (10 g/l) TS, shake and cool in ice for 2–3 minutes. Add 1 g of urea R, swirl until dissolved and allow to stand for 10 minutes. Add 2 ml of 2-naphthol TS and 2 ml of sodium hydroxide (~400 g/l) TS; a dark red colour is produced.
2. Place about 0.1 g of the test substance in a mortar and mix quickly with about 0.1 g of ground sodium hydroxide R. Transfer to a porcelain crucible and heat until melted. Cool, dissolve the melt in 4 ml of nitric acid (~130 g/l) TS, filter and to 1 ml of the filtrate add 5 drops of silver nitrate (40 g/l) TS; a white, curdy precipitate is produced. Separate the precipitate, wash with water and add about 0.4 ml of ammonia (~260 g/l) TS; the precipitate dissolves but precipitates again on the addition of about 0.75 ml of nitric acid (~1000 g/l) TS.
3. Shake 20 mg of the test substance with 5 ml of ethanol (~750 g/l) TS; a yellow solution is produced. Add 1 drop of sodium hydroxide (~80 g/l) TS; the yellow colour becomes more intense. Then add 2 drops of hydrochloric acid (~70 g/l) TS; the yellow colour fades and a colourless solution is produced.

NYSTATIN OINTMENT

Description. The ointment usually contains 100 000 IU of nystatin in 1.0 g of a suitable ointment base.

Preparation of the sample. Withdraw and weigh an amount equivalent to 22 000 IU of nystatin, add 25 ml of dimethylformamide R and shake well. Filter, evaporate the filtrate to dryness and use the residue as the test substance.

Identity tests

Colour and other reactions

1. To 5 mg of the test substance add about 2 ml of sulfuric acid (~1760 g/l) TS; a dark violet colour is produced.
2. To 5 mg of the test substance add 1 ml of ethanol (~750 g/l) TS and about 1 ml of hydrochloric acid (~250 g/l) TS, shake and filter. To the filtrate add a few crystals of resorcinol R and heat in a water-bath for 2 minutes; a pink colour is produced.
3. To 5 mg of the test substance add 2 ml of ethanol (~750 g/l) TS, shake and filter. To the filtrate add about 1 ml of hydrochloric acid (~250 g/l) TS and 2 drops of a solution composed of 1 ml of ferric chloride (25 g/l) TS and 10 ml of water; a dark green colour is produced.

NYSTATIN PESSARIES

Description. Each pessary usually contains 100 000 IU of nystatin.

Preparation of the sample

1. Weigh 1 pessary and calculate the amount equivalent to 22 000 IU of nystatin.
2. Grind the pessaries, weigh out the above-calculated equivalent amount as powdered material, shake it vigorously with 25 ml of dimethylformamide R, filter, evaporate the filtrate to dryness and use the residue as the test substance.

Identity tests

Colour and other reactions

1. To 5 mg of the test substance add about 2 ml of sulfuric acid (~1760 g/l) TS; a dark violet colour is produced.
2. To 5 mg of the test substance add 1 ml of ethanol (~750 g/l) TS and about 1 ml of hydrochloric acid (~250 g/l) TS, shake and filter. To the filtrate add a few crystals of resorcinol R and heat in a water-bath for 2 minutes; a pink colour is produced.
3. To 5 mg of the test substance add 2 ml of ethanol (~750 g/l) TS, shake and filter. To the filtrate add about 1 ml of hydrochloric acid (~250 g/l) TS and 2 drops of a solution composed of 1 ml of ferric chloride (25 g/l) TS and 10 ml of water; a dark green colour is produced.

ORAL REHYDRATION SALTS (COMPOSITION A)

Description. Each packet contains a white, crystalline powder composed of:

glucose, anhydrous	20.0 g
sodium chloride	3.5 g
sodium hydrogen carbonate	2.5 g
potassium chloride	1.5 g

Preparation of the sample

1. Weigh the contents of 1 packet; it should weigh between 26.0 g and 29.0 g.
2. Use the contents of 1 packet directly as the test substance.
3. Dissolve the contents of 1 packet in 250 ml of water and use as the test solution.

Identity tests

Melting behaviour. Gently heat a small quantity of the test substance; the melt changes first to yellow and then to brown and an odour of burning sugar is perceptible. Then ignite; the melt swells, ignites and chars.

Colour and other reactions

1. The test solution is slightly alkaline when tested with pH-indicator paper R.
2. Add a few drops of the test solution to 5 ml of hot potassio-cupric tartrate TS; a copious red precipitate is produced (glucose).
3. Acidify 5 ml of the test solution with acetic acid (~300 g/l) TS, add 2 ml of magnesium uranyl acetate TS and scratch the sides of the beaker with a glass rod; a light yellow, crystalline precipitate is slowly produced (sodium).

   Alternative test:
   Introduce the test solution into a non-luminous flame using a magnesia stick or a nichrome or platinum wire sealed to a glass rod; the flame acquires an intense yellow colour (sodium).
4. To 5 ml of the test solution add 0.5 ml of nitric acid (~130 g/l) TS and 0.5 ml of silver nitrate (40 g/l) TS; a white, curdy precipitate is produced. Separate the precipitate, wash with water and add an excess of ammonia (~100 g/l) TS; the precipitate dissolves (chlorides).
5. To 5 ml of the test solution add 2 drops of phenolphthalein/ethanol TS; a pink colour is produced. Heat to boiling; a gas is evolved and the colour of the solution changes to red-violet (hydrogen carbonate).
6. To 5 ml of the test solution add 1 ml of acetic acid (~60 g/l) TS and 4 drops of sodium cobaltinitrite (100 g/l) TS; a yellow-orange precipitate is produced (potassium).

ORAL REHYDRATION SALTS (COMPOSITION B)

Description. Each packet contains a white, crystalline powder composed of:

glucose, anhydrous	20.0 g
sodium chloride	3.5 g
sodium citrate dihydrate	2.9 g
potassium chloride	1.5 g

Preparation of the sample

1. Weigh the contents of 1 packet; it should weigh between 26.5 g and 29.5 g.
2. Use the contents of 1 packet directly as the test substance.
3. Dissolve the contents of 1 packet in 250 ml of water and use as the test solution.

Identity tests

Melting behaviour. Gently heat a small quantity of the test substance; the melt changes first to yellow and then to brown and an odour of burning sugar is perceptible. Then ignite; the melt swells, ignites and chars.

Colour and other reactions

1. The test solution is slightly alkaline when tested with pH-indicator paper R.
2. Add a few drops of the test solution to 5 ml of hot potassio-cupric tartrate TS; a copious red precipitate is produced (glucose).
3. Acidify 5 ml of the test solution with acetic acid (~300 g/l) TS, add 2 ml of magnesium uranyl acetate TS and scratch the sides of the beaker with a glass rod; a light yellow, crystalline precipitate is slowly produced (sodium).

   Alternative test:
   Introduce the test solution into a non-luminous flame using a magnesia stick or a nichrome or platinum wire sealed to a glass rod; the flame acquires an intense yellow colour (sodium).
4. To 5 ml of the test solution add 0.5 ml of nitric acid (~130 g/l) TS and 0.5 ml of silver nitrate (40 g/l) TS; a white, curdy precipitate is produced. Separate the precipitate, wash with water and add an excess of ammonia (~100 g/l) TS; the precipitate dissolves (chlorides).
5. To 5 ml of the test solution add 3 ml of calcium chloride (55 g/l) TS; no precipitate is produced. Boil the solution; a white solid is produced which is soluble in acetic acid (~300 g/l) TS (citrates).
6. To 5 ml of the test solution add 1 ml of acetic acid (~60 g/l) TS and 4 drops of sodium cobaltinitrite (100 g/l) TS; a yellow-orange precipitate is produced (potassium).

PARACETAMOL SUPPOSITORIES

Description. Each suppository usually contains 100 mg of paracetamol.

Preparation of the sample

1. Weigh 1 suppository and calculate the amount equivalent to 0.5 g of paracetamol.

2. Dissolve a quantity of the suppositories equivalent to 0.5 g of paracetamol in 25 ml of light petroleum R by warming carefully over a water-bath. Collect the residue by decanting, wash with 3 portions of 25 ml of light petroleum R and use as the test substance.

Identity tests

Description of the test substance. A white, crystalline powder.

Melting point of the test substance. About 170 °C.

Eutectic temperature of the test substance. With benzanilide R, about 137 °C; with phenacetin R, about 114 °C.

Colour and other reactions

1. Dissolve 0.10 g of the test substance in 10 ml of water and add 1 drop of ferric chloride (~25 g/l) TS; an intense violet-blue colour is produced.

2. To 0.10 g of the test substance add 1 ml of hydrochloric acid (~70 g/l) TS and boil for 1 minute. Add 10 ml of water and cool; no precipitate is produced. Add 1 drop of potassium dichromate (100 g/l) TS and shake; a violet colour slowly develops and does not change to red (distinction from phenacetin).

PHENYTOIN TABLETS

Description. Each tablet usually contains 50 mg of phenytoin.

Preparation of the sample

1. Weigh 1 tablet and calculate the amount equivalent to 0.08 g of phenytoin.

2. Grind the tablets, weigh out the above-calculated equivalent amount as powdered material and use directly as the test substance, dividing it into 2 equal parts.

Identity tests

Colour and other reactions

1. To 1 part of the test substance add 4 ml of ethanol (~750 g/l) TS, shake and filter. To the filtrate add 4 drops of cobalt(II) chloride (30 g/l) TS and 1 drop of ammonia (~260 g/l) TS; a blue-violet colour is produced.
2. To half of 1 part of the test substance placed on a white test plate add 2 drops of ammonia (~100 g/l) TS and 1 small drop of copper(II) sulfate (160 g/l) TS and mix thoroughly with a glass rod; a pink precipitate is produced.

PHENYTOIN SODIUM CAPSULES

Description. Each capsule usually contains 25–100 mg of phenytoin sodium.

Preparation of the sample

1. Weigh the contents of 1 capsule and calculate the amount equivalent to 0.08 g of phenytoin sodium.
2. Empty the capsules, weigh out the above-calculated equivalent amount and use directly as the test substance, dividing it into 4 equal parts.

Identity tests

Colour and other reactions

1. To 2 parts of the test substance add 4 ml of dichloromethane R and 4 drops of cobalt(II) chloride (30 g/l) TS and shake; a voluminous precipitate is produced in a blue-violet coloured solution (distinction from phenytoin).
2. Place half of 1 part of the test substance on a white test plate, add 2 drops of ammonia (~100 g/l) TS and 1 small drop of copper(II) sulfate (160 g/l) TS and mix thoroughly with a glass rod; a pink precipitate is produced.

PHYTOMENADIONE INJECTION

Description. The injection is a sterile solution usually containing 10 mg of phytomenadione in 1.0 ml of a suitable vehicle.

Preparation of the sample. Pool the contents of the ampoules equivalent to 20 mg of phytomenadione; if necessary, reduce the volume by evaporation to about 2 ml or dilute to about 2 ml with water. Use directly as the test solution.

Identity tests

Colour and other reactions

1. Dilute about 1 ml of the test solution with 10 ml of ethanol (~750 g/l) TS and add 3 ml of potassium hydroxide/ethanol TS; a green colour is produced. Allow to stand for 1–2 minutes; the colour changes to blue. Again allow to stand for about 15 minutes; the colour changes to red-brown.
2. To about 1 ml of sulfuric acid (~1760 g/l) TS add 3 drops of the test solution; a brown-orange colour is produced. Heat the solution; the colour changes to dark brown.
3. To 3 drops of the test solution add 5 ml of ethanol (~750 g/l) TS and 2–5 drops of potassium permanganate (10 g/l) TS and shake; the colour of the permanganate is immediately discharged.

PIPERAZINE CITRATE SYRUP

Description. The syrup contains piperazine citrate, usually equivalent to 500 mg of piperazine hydrate in 5 ml of a suitable vehicle.

Preparation of the sample. Use the well homogenized contents of one container or the equivalent of 0.5 g of piperazine hydrate and use directly as the test solution, dividing it into 3 equal volumes.

Identity tests

Colour and other reactions

1. To 2 volumes of the test solution add 5 ml of hydrochloric acid (~70 g/l) TS and then add while stirring 1 ml of sodium nitrite (500 g/l) TS. Cool in ice for 15 minutes, stirring if necessary to induce crystallization. Filter, wash the crystals with 10 ml of ice-water and dry at 105 °C; melting point, about 158 °C.
2. To 1 volume of the test solution add 3 ml of calcium chloride (55 g/l) TS; no precipitate is produced. Boil the solution; a white solid is produced which is soluble in acetic acid (~300 g/l) TS.

POTASSIUM CHLORIDE SOLUTION

Description. The solution usually contains 112 mg of potassium chloride in 1.0 ml of a suitable vehicle.

Preparation of the sample

1. Pool the contents of the containers equivalent to 0.30 g of potassium chloride and use directly as test solution 1.

2. Dilute 1.0 ml of test solution 1 with sufficient water to produce 10 ml and use as test solution 2.

Identity tests

Colour and other reactions

1. Introduce test solution 1, together with hydrochloric acid (~250 g/l) TS, into a non-luminous flame using a magnesia stick or a nichrome or a platinum wire sealed to a glass rod; the flame acquires a violet colour which, when viewed through a suitable blue glass, appears reddish violet.
2. To 1.0 ml of test solution 2 add 3 ml of water and 5 drops of silver nitrate (40 g/l) TS; a white, curdy precipitate is produced. Separate the precipitate, wash with water and add a few drops of ammonia (~100 g/l) TS; the precipitate dissolves.
3. Heat 2–3 drops of test solution 1 with a few drops of sodium hydroxide (~80 g/l) TS; no odour of ammonia is perceptible.

PROCAINE BENZYLPENICILLIN POWDER FOR INJECTION

Description. Each vial contains a sterile powder usually equivalent to 1–3 g of procaine benzylpenicillin.

Preparation of the sample

1. Weigh the contents of 1 vial and calculate the amount equivalent to 30 mg of procaine benzylpenicillin.
2. Empty the vial, weigh out the above-calculated equivalent amount and use directly as the test substance, dividing it into 6 equal parts.

Identity tests

Colour and other reactions

1. Dissolve 1 part of the test substance in 3 ml of water, add 0.1 g of hydroxylamine hydrochloride R and 1 ml of sodium hydroxide (~80 g/l) TS and allow to stand for 5 minutes. Add 1.3 ml of hydrochloric acid (~70 g/l) TS and 10 drops of ferric chloride (25 g/l) TS; a violet-red colour is produced.
2. Dissolve 1 part of the test substance in 2 ml of water and add 2–3 drops of ferric chloride (25 g/l) TS; a cream-coloured, flocculent precipitate is produced.
3. To half of 1 part of the test substance add a solution of 10 mg of paraformaldehyde R in about 1 ml of sulfuric acid (~1760 g/l) TS; an almost colourless solution is produced. Heat the solution in a water-bath for 2 minutes; a brownish violet colour is produced.

4. Dissolve 1 part of the test substance in 2 ml of water and add 5 drops of iodine TS; a brown precipitate is produced.
5. Dissolve 1 part of the test substance in 2 ml of water and add 5 drops of potassio-mercuric iodide TS; a white precipitate is produced.
6. Dissolve 1 part of the test substance in 1 ml of water and add 5 drops of hydrochloric acid (~70 g/l) TS, 10 drops of sodium nitrite (10 g/l) TS and 1 ml of sodium hydroxide (~80 g/l) TS. Then add 5 mg of 2-naphthol R; a red colour is produced.

PYRIDOXINE HYDROCHLORIDE INJECTION

Description. The injection is a sterile solution usually containing 25 mg of pyridoxine hydrochloride in 1.0 ml of a suitable vehicle.

Preparation of the sample. Pool the contents of the ampoules equivalent to 0.05 g of pyridoxine hydrochloride and use directly as the test solution, dividing it into 4 equal volumes.

Identity tests

Colour and other reactions

1. Dilute 1 volume of the test solution to 2 ml with water and add 2 ml of ferric chloride (25 g/l) TS; a red-brown colour is produced. Add 4 ml of hydrochloric acid (~70 g/l) TS; the colour of the solution changes to yellow.
2. To 0.5 ml of sulfanilic acid TS add 3 drops of sodium nitrite (10 g/l) TS, 1 ml of sodium hydroxide (~80 g/l) TS and 1 volume of the test solution and allow to stand for 2 minutes; a golden yellow colour is produced. Add 2 ml of acetic acid (~300 g/l) TS; the colour remains almost the same or changes to orange.
3. Dilute 1 volume of the test solution to 2 ml with water and add 0.5 ml of nitric acid (~130 g/l) TS and 1 ml of silver nitrate (40 g/l) TS; a white precipitate is produced. Separate the precipitate, wash with water and add an excess of ammonia (~100 g/l) TS; the precipitate dissolves almost completely (some excipients may interfere with the reaction).
4. To 1 volume of the test solution add 1 ml of water, 1 drop of copper(II) sulfate (160 g/l) TS and 1 ml of sodium hydroxide (~80 g/l) TS; the colour of the solution changes to deep blue.

Degradation tests

Discoloration and a change in the physical state of the test solution usually indicate gross degradation.

PYRIMETHAMINE TABLETS

Description. Each tablet usually contains 25 mg of pyrimethamine.

Preparation of the sample

1. Weigh 1 tablet and calculate the amount equivalent to 0.25 g of pyrimethamine.
2. Grind the tablets, weigh out the above-calculated equivalent amount as powdered material, shake it with 50 ml of ethanol (~750 g/l) TS heated to 60 °C, filter and evaporate to dryness. Dry the residue to constant weight at 105 °C and use as the test substance.

Identity tests

Melting behaviour. The test substance melts at about 239 °C.

Colour and other reactions

1. Dissolve 0.05 g of the test substance in 5 ml of sulfuric acid (~100 g/l) TS and add 0.2 ml of freshly prepared potassio-mercuric iodide TS; a creamy white precipitate is produced.
2. To 1 ml of methyl orange/ethanol TS add 5 ml of water and 2 ml of ethyl acetate R and shake; the ethyl acetate layer remains colourless. Add a solution of 5 mg of the test substance dissolved in 5 ml of sulfuric acid (~5 g/l) TS, shake and allow to separate (about 30 minutes); a yellow colour is produced in the ethyl acetate layer.
3. Ignite about 0.1 g of the test substance with 0.5 g of anhydrous sodium carbonate R, cool, add 5 ml of hot water and heat in a water-bath for 5 minutes. Filter, neutralize the filtrate with nitric acid (~130 g/l) TS and add 5 drops of silver nitrate (40 g/l) TS; a white, curdy precipitate is produced. Add an excess of ammonia (~100 g/l) TS; the precipitate dissolves.

RESERPINE INJECTION

Description. The injection is a sterile solution usually containing 1 mg of reserpine in 1.0 ml of a suitable vehicle.

Preparation of the sample. Pool the contents of the ampoules equivalent to 2.0 mg of reserpine and use directly as the test solution, dividing it into 4 equal volumes.

Identity tests

Colour and other reactions

1. To 1 volume of the test solution add 1 ml of dichloromethane R, shake and allow to stand. Separate the dichloromethane layer and evaporate

it to dryness over a water-bath. Mix the residue with 5 mg of 4-dimethylaminobenzaldehyde R and 4 drops of glacial acetic acid R. Then add 4 drops of sulfuric acid (~1760 g/l) TS; a green colour is produced. Add about 1 ml of glacial acetic acid R; the colour changes to red.

2. To 2 volumes of the test solution add 1 drop of sulfuric acid (~100 g/l) TS and a few drops of sodium nitrite (10 g/l) TS; a yellowish green solution is produced which exhibits a greenish fluorescence.
3. To 1 volume of the test solution add a few drops of ammonium vanadate (5 g/l) TS; a green colour is produced.

SODIUM CHLORIDE INJECTION

Description. The injection is a sterile solution usually containing 9 mg of sodium chloride in 1.0 ml of a suitable vehicle.

Preparation of the sample. Pool the contents of the containers equivalent to about 30 mg of sodium chloride; if necessary, reduce the volume by evaporation to about 3 ml or dilute to about 3 ml with water. Use directly as the test solution.

Identity tests

Colour and other reactions

1. Introduce a few drops of the test solution into a non-luminous flame using a magnesia stick or a nichrome or platinum wire sealed to a glass rod; the flame acquires an intense yellow colour.
2. To 2 ml of the test solution add 3 drops of nitric acid (~130 g/l) TS and 3 drops of silver nitrate (40 g/l) TS and shake; a white, curdy precipitate is produced. Separate the precipitate, wash with water and add an excess of ammonia (~100 g/l) TS; the precipitate dissolves.

SODIUM CROMOGLICATE CAPSULES FOR INHALATION

Description. Each capsule usually contains 20 mg of sodium cromoglicate mixed with lactose in a 1 : 1 ratio.

Preparation of the sample

1. Weigh the contents of 1 capsule and calculate the amount equivalent to 0.06 g of sodium cromoglicate.
2. Empty the capsules, weigh out the above-calculated equivalent amount and use directly as the test substance, dividing it into 3 equal parts.

Identity tests

Colour and other reactions

1. To 1 part of the test substance add 2 ml of water and 2 ml of sodium hydroxide (~200 g/l) TS. Boil for 1 minute; a yellow solution is produced. Allow to stand for 30 minutes and add 0.5 ml of diazobenzenesulfonic acid TS2; a deep red colour is produced.
2. To 1 part of the test substance add 2 ml of potassio-cupric tartrate TS and heat; a red precipitate is produced.
3. Moisten 1 part of the test substance with 2 drops of hydrochloric acid (~70 g/l) TS and introduce the mixture into a non-luminous flame using a magnesia stick or a nichrome or platinum wire sealed to a glass rod; the flame acquires an intense yellow colour.

SODIUM HYDROGEN CARBONATE INJECTION

Description. The injection is a sterile solution usually containing 14 mg of sodium hydrogen carbonate in 1.0 ml of a suitable vehicle.

Preparation of the sample. Pool the contents of the ampoules equivalent to 0.30 g of sodium hydrogen carbonate and use directly as the test solution, dividing it into 3 equal volumes.

Identity tests

Colour and other reactions

1. Introduce a few drops of the test solution into a non-luminous flame using a magnesia stick or a nichrome or platinum wire sealed to a glass rod; the flame acquires an intense yellow colour.
2. Dilute 1 volume of the test solution with 3 ml of water and add 2 drops of phenolphthalein/ethanol TS; a pink colour is produced. Heat to boiling; a colourless and odourless gas evolves and the colour of the solution changes to red-violet.
3. Dilute 1 volume of the test solution with 3 ml of water and add a few drops of magnesium sulfate (50 g/l) TS; no precipitate is produced. Boil the mixture; a white precipitate is produced.

SODIUM LACTATE INJECTION

Description. The injection is a sterile solution usually containing 500 mg of monosodium lactate in 1.0 ml of a suitable vehicle.

Preparation of the sample. Dilute a volume of the solution equivalent to 0.5 g of sodium lactate to 5 ml with water and use directly as the test solution.

Identity tests

Colour and other reactions

1. To 0.5 ml of the test solution add 2 ml of sulfuric acid (~100 g/l) TS and 3 ml of potassium permanganate (10 g/l) TS; the colour of the permanganate is discharged and an odour of acetaldehyde is perceptible.
2. To 1 ml of the test solution add 4 ml of water and mix. Add 1 ml of acetic acid (~300 g/l) TS and 1 ml of ammonium oxalate (25 g/l) TS; no precipitate is produced (distinction from calcium lactate).
3. To a few drops of the test solution add a small volume of hydrochloric acid (~250 g/l) TS and introduce the mixture into a non-luminous flame using a magnesia stick or a nichrome or platinum wire sealed to a glass rod; the flame acquires an intense yellow colour.

   Alternative test:
   To 5 drops of the test solution add 1 ml of water, acidify with acetic acid (~300 g/l) TS and add 2 ml of magnesium uranyl acetate TS; a light yellow, crystalline precipitate is produced.
4. To 2 ml of the test solution add, along the wall of the test-tube, 5 ml of a reagent composed of 0.10 g of catechol R dissolved in 10 ml of sulfuric acid (~1760 g/l) TS; a deep red colour is produced at the junction of the two liquids.

SULFASALAZINE TABLETS

Description. Each tablet usually contains 500 mg of sulfasalazine.[1]

Preparation of the sample

1. Weigh 1 tablet and calculate the amounts equivalent to 10 mg and 0.05 g of sulfasalazine.
2. Grind the tablets, weigh out the above-calculated equivalent amounts as powdered material and use directly, 10 mg as test substance 1 and 0.05 g as test substance 2.

Identity tests

Colour and other reactions

1. To test substance 1 add 5 ml of water, shake and filter. To the filtrate add 1 ml of sodium hydroxide (~80 g/l) TS; an orange-red to deep red colour is produced.

[1] Referred to as salazosulfapyridine in *Basic tests for pharmaceutical substances*, 1986.

2. To test substance 2 add 2 drops of ethanol (~750 g/l) TS and 4 ml of hydrochloric acid (~70 g/l) TS and mix. Then add 0.2 g of zinc R powder, heat in a water-bath for 5 minutes and filter.
   (*a*) To 1 ml of the filtrate add 4 ml of water and 2 drops of ferric chloride (25 g/l) TS; a red colour is produced.
   (*b*) To 1 ml of the filtrate add 1 ml of sodium nitrite (10 g/l) TS and allow to stand in ice for 1 minute. Add 2 ml of sodium hydroxide (~80 g/l) TS and 2 drops of 2-naphthol TS; an intense red colour is produced.

VERAPAMIL HYDROCHLORIDE INJECTION

Description. The injection is a sterile solution usually containing 2.5 mg of verapamil hydrochloride in 1.0 ml of a suitable vehicle.

Preparation of the sample. Pool the contents of the ampoules equivalent to 15 mg of verapamil hydrochloride and use directly as the test solution, dividing it into 3 equal volumes.

Identity tests

Colour and other reactions

1. To 1 volume of the test solution add about 0.2 ml of mercuric chloride (65 g/l) TS; a white precipitate is produced.
2. To 1 volume of the test solution add 0.5 ml of sulfuric acid (~100 g/l) TS and 4 drops of potassium permanganate (10 g/l) TS; a violet precipitate is produced which immediately dissolves to produce a very pale yellow solution.
3. Acidify 1 volume of the test solution with nitric acid (~130 g/l) TS and add 2 ml of silver nitrate (40 g/l) TS; a white, curdy precipitate is produced. Separate the precipitate, wash with water and add an excess of ammonia (~100 g/l) TS; the precipitate dissolves.

Degradation tests

Discoloration and a change in the physical state of the test solution usually indicate gross degradation.

WARFARIN SODIUM TABLETS

Description. Each tablet usually contains 1–5 mg of warfarin sodium.

Preparation of the sample

1. Weigh 1 tablet and calculate the amount equivalent to 0.10 g of warfarin sodium.

2. Grind the tablets, weigh out the above-calculated equivalent amount as powdered material.
3. Extract the powdered material with two quantities, each of 15 ml, of water. Filter and to the filtrate add 2 drops of hydrochloric acid (~70 g/l) TS. Filter, wash the precipitate with water and dry at 110 °C for 3 hours; melting point, about 162 °C. Use the crystals as the test substance.

Identity tests

Colour and other reactions

1. Dissolve 20 mg in 1 ml of water and add 5 drops of sodium hydroxide (~80 g/l) TS and 5 drops of iodine TS; a yellow precipitate is produced and a characteristic odour of iodoform is perceptible.
2. Moisten 10 mg with 1 drop of hydrochloric acid (~70 g/l) TS and introduce the mixture into a non-luminous flame using a magnesia stick or a nichrome or platinum wire sealed to a glass rod; the flame acquires an intense yellow colour.

6. Reagents

Most of the reagents, test solutions and volumetric solutions needed to perform the test procedures outlined in sections 4–6 of this manual are described in *Basic tests for pharmaceutical substances* and/or *Basic tests for pharmaceutical dosage forms* and only additional reagents are given below. Reagents are denoted by the abbreviation R, test solutions by the abbreviation TS, and volumetric solutions by the abbreviation VS. The concentration of the reagent solutions is expressed in g/l, that is, grams of anhydrous substance per litre of water or solvent, as indicated. Where no solvent is indicated, demineralized water should be used. The procedures for the preparation of test solutions that require special attention are given in detail.

Ammonium acetate R.

Ammonium mercurithiocyanate TS.
Procedure. Dissolve 30 g of ammonium thiocyanate R and 27 g of mercuric chloride R in sufficient water to produce 1000 ml.

Ammonium vanadate R.

Ammonium vanadate (5 g/l) TS.

Amyl alcohol R.

Anthrone R.

Anthrone TS.
Procedure. Dissolve 35 mg of anthrone R in 100 ml of sulfuric acid (~1760 g/l) TS.

Catechol R.

Ceric ammonium nitrate R.

Ceric ammonium nitrate TS.
Procedure. Dissolve 6.25 g of ceric ammonium nitrate R in 10 ml of nitric acid (15 g/l) TS.
Shelf life. Use the solution within 3 days.

Chloramine B R.

Chloramine B (50 g/l) TS.
Note. Chloramine B (50 g/l) TS must be freshly prepared.

Cobalt(II) nitrate (10 g/l) TS.

Copper(II) sulfate (1 g/l) TS.

Diazobenzenesulfonic acid TS2.
Procedure. To 0.2 g of sulfanilic acid R add 20 ml of hydrochloric acid (0.1 mol/l) VS, boil to dissolve, cool to 4 °C in ice, add drop by drop while stirring 0.9 ml of sodium nitrite (100 g/l) TS and allow to stand in ice for 10 minutes. Then add 0.5 ml of sulfamic acid (100 g/l) TS.
Note. Diazobenzenesulfonic acid TS2 must be freshly prepared.

Ethanol (~375 g/l) TS.

Iodine (0.05 mol/l) VS.
Procedure. Dissolve 1.27 g of iodine R and 1.80 g of potassium iodide R in sufficient water to produce 100 ml.

Lanthanum nitrate R.

Lanthanum nitrate (30 g/l) TS.
Procedure. Dissolve 4.3 g of lanthanum nitrate R in 1 ml of nitric acid (~130 g/l) TS and sufficient water to produce 100 ml.

***N*-(1-Naphthyl)ethylenediamine hydrochloride R.**

***N*-(1-Naphthyl)ethylenediamine/ethanol TS.**
Procedure. Dissolve 0.10 g of *N*-(1-naphthyl)ethylenediamine hydrochloride R in a mixture of equal volumes of ethanol (~750 g/l) TS and water.

Nitric acid (15 g/l) TS.

Nitrobenzene R.

Phosphomolybdic acid R.

Phosphomolybdic acid/ethanol TS.
Procedure. Dissolve 5 g of phosphomolybdic acid R in sufficient dehydrated ethanol R to produce 100 ml.

Phosphotungstic acid R.

Phosphotungstic acid (10 g/l) TS.

Potassium carbonate (100 g/l) TS.

Potassium chloride R.

Potassium chloride (100 g/l) TS.

Potassium hydroxide (~110 g/l) TS.

Potassium hydroxide (~55 g/l) TS.

Potassium nitrite R.

Potassium nitrite (100 g/l) TS.

2-Propanol R.

Resorcinol (20 g/l) TS.

Sodium chloride (100 g/l) TS.

Sodium nitrite (500 g/l) TS.

Sodium nitrite (100 g/l) TS.

Sodium nitroprusside R.

Sodium nitroprusside (45 g/l) TS.
Note. Sodium nitroprusside (45 g/l) TS must be freshly prepared.

Sucrose R.

Sucrose/hydrochloric acid TS.
Procedure. Dissolve about 0.1 g of sucrose R in 10 ml of hydrochloric acid (~420 g/l) TS.

Tetramethylammonium hydroxide (~100 g/l) TS.

Tetramethylammonium hydroxide/ethanol TS.
Procedure. Dilute 10 ml of tetramethylammonium hydroxide (~100 g/l) TS with sufficient ethanol (~750 g/l) TS to produce 100 ml.

Tin(II) chloride R.

Titan yellow R.

Titan yellow TS.
Procedure. Dissolve 0.05 g of titan yellow R in sufficient water to produce 100 ml.

Tosylchloramide sodium R.

Tosylchloramide sodium (40 g/l) TS.

Triketohydrindene/butanol TS.
Procedure. Dissolve 0.2 g of triketohydrindene hydrate R in sufficient 1-butanol R to produce 100 ml.

Triphenyltetrazolium chloride R.

Triphenyltetrazolium chloride/ethanol TS.
Procedure. Dissolve 0.5 g of triphenyltetrazolium chloride R in sufficient dehydrated ethanol R to produce 100 ml.

7. Cumulative index of basic tests

This section provides a cumulative index of the pharmaceutical substances, pharmaceutical dosage forms and medicinal plant materials for which WHO has published basic tests in the two previous publications, *Basic tests for pharmaceutical substances* (1) and *Basic tests for pharmaceutical dosage forms* (2), and in this manual, *Basic tests for drugs: pharmaceutical substances, medicinal plant materials and dosage forms* (3). The list indicates the page numbers and, in parentheses, the volume in which each test procedure can be found.

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[1] Previously referred to as doxycycline hydrochloride.

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[1] Previously referred to as salazosulfapyridine.

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