WHO GOOD PRACTICES FOR PHARMACEUTICAL QUALITY CONTROL LABORATORIES

DRAFT REVISION FOR COMMENTS

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Revisions following the “Consultation on Specifications for Medicines and Quality Control Laboratory Issues” 27-31 July 2009

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## SCHEDULE FOR THE PROPOSED ADOPTION PROCESS OF DOCUMENT QAS/09.296:
### WHO GOOD PRACTICES FOR PHARMACEUTICAL QUALITY CONTROL LABORATORIES

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BACKGROUND


During the inspections carried out when prequalifying laboratories, the inspectors had noticed that some of the texts of these guidelines might benefit from improvement and clarification.

Within the procedure for prequalification of a quality control laboratory, compliance with the following WHO standards was assessed:

- good practices for national pharmaceutical control laboratories (GPCL);
- good manufacturing practices (GMP) as recommended by WHO for such laboratories.


Inspectors found that laboratories traditionally did not consult the GMP guide. To facilitate the implementation of WHO standards in practice and the inspections and audits carried out in accordance with the prequalification procedure for quality control laboratories, it was deemed useful to add the most important parts directly to the GPCL guidelines and to add references to the relevant part of the GMP guide.

In considering the possible improvement of the guidelines, the following activities were carried out.

1. Review of observations made in laboratories during inspections, in particular repeatedly occurring deficiencies in several laboratories.
2. Review of references indicating the clauses from the guides relevant to the observation in question, as provided by inspectors during inspections.
3. Detailed comparison of GPCL with ISO 17025.

Based on these reviews the following areas were identified in which amendment or clarification could help laboratories improve the implementation of WHO standards in practice:

- control of documentation and document changes;
- internal audits;
- corrective and preventive measures;
- cleaning procedure;
- qualification of equipment;
- purchasing services and supplies; and
- subcontracting of tests.

According to the title the WHO guidelines on *Good practices for national pharmaceutical control laboratories* were mainly pertinent to national quality control laboratories, indicating that similar principles would also be applicable to pharmaceutical quality control laboratories. However, the prequalification procedure is open to any laboratory (private, governmental or nongovernmental). In the future, therefore, to avoid confusion, it was considered useful to make the guidelines more generally applicable, to modify the title accordingly and stress the specifics of national quality control laboratories within the guidance text.
Once the GPCL guidelines have been revised, the guidelines for preparing a laboratory information file (WHO Technical Report Series, No. 917, 2004, Annex 5) should also be revised accordingly.

In light of the above, the Expert Committee recommended that the WHO Secretariat initiate the process of revision of these good practices.

On the basis of the above, the following text is proposed to replace the previously published guidance.
WHO GOOD PRACTICES FOR
PHARMACEUTICAL QUALITY CONTROL LABORATORIES

Annex 3

Good practices for pharmaceutical quality control laboratories

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GENERAL CONSIDERATIONS

The WHO Expert Committee on Specifications for Pharmaceutical Products adopted in 1999 the guideline *WHO Good practices for national pharmaceutical control laboratories*, which was published as Annex 3 of the WHO Technical Report Series, No. 902, 2002. As the other guidelines related to the area of laboratory quality assurance have been updated and subsequent inspections for the compliance with the guideline indicated that some sections require improvement and clarification, it was considered necessary to prepare a revised text.

This guideline provides advice on the quality management system within which the analysis of active pharmaceutical ingredients (APIs), excipients and pharmaceutical products should be performed to demonstrate that reliable results are obtained.

Compliance with the recommendations provided by this guideline will help to international harmonization of laboratory practices and will facilitate cooperation among laboratories and mutual recognition of results.

Special attention must be given to ensuring the correct and efficient functioning of the laboratory. Planning and future budgets must ensure that the necessary resources are available, inter alia, for the maintenance of the laboratory, as well as for an adequate infrastructure and energy supply. Means and procedures must be in place (in case of anticipated supply problems) to ensure that the laboratory can continue its activities.

This guideline is applicable to any pharmaceutical quality control laboratory, be it national, commercial or another non-governmental laboratory. However, it does not include guidance for those laboratories involved in the testing of biological products, e.g. vaccines, blood products, etc. Separate guidance for such laboratories is available.

This guideline is consistent with the requirements of the WHO guidelines for good manufacturing practices (1) and with the requirements of the International Standard ISO/IEC 17025:2005 (2) and provides detailed guidance for laboratories performing quality control of medicines.

Pharmaceutical quality control testing is usually a matter of repetitive testing of samples of active pharmaceutical ingredients or of a limited number of pharmaceutical products, whereas national quality control laboratories have to be able to deal with a much wider range of pharmaceutical substances and products and, therefore, have to apply a wider variety of test methods. Specific recommendations for national pharmaceutical quality control laboratories are addressed in the following text. Particular consideration is given to countries with limited resources wishing to establish a governmental pharmaceutical quality control laboratory, having recently done so, or planning to modernize the existing laboratory.

Quality control laboratories may perform some or all quality control activities, e.g. sampling, testing of APIs, excipients and/or pharmaceutical products, stability testing, testing against specifications, investigative testing, etc.

For the quality of a medicine sample to be correctly assessed:

- the submission of a sample of an API, excipient or pharmaceutical product or a suspected counterfeit material to the laboratory, selected in accordance with national requirements, must be accompanied by a statement of the reason why the analysis has been requested;
- the analysis must be correctly planned and meticulously executed;
- the results must be competently evaluated to determine whether the sample complies with the specifications or other relevant criteria.

**National pharmaceutical quality control laboratories**

The government, normally through the national medicines regulatory authority (NMRA), may establish and maintain a pharmaceutical quality control laboratory to carry out the required tests and assays to verify that APIs, excipients and pharmaceutical products meet the prescribed specifications. Throughout the process of marketing authorization and post-marketing surveillance, the laboratory works closely with the NMRA.
A national pharmaceutical quality control laboratory provides effective support for an NMRA acting together with its inspection services. The analytical results obtained should accurately describe the properties of the samples assessed, permitting correct conclusions to be drawn about the quality of the samples of medicines analysed, and also serving as an adequate basis for any subsequent administrative regulations and legal action.

National pharmaceutical quality control laboratories usually encompass essentially two types of activity:

- compliance testing of APIs, pharmaceutical excipients and pharmaceutical products employing “official” methods including pharmacopoeial methods, validated analytical procedures provided by the manufacturer and approved by the relevant government authority for marketing authorization or validated analytical procedures developed by the laboratory; and
- investigative testing of suspicious, illegal, counterfeit substances or products, submitted for examination by medicine inspectors, customs or police

To ensure patient safety, the role of the national pharmaceutical quality control laboratory must be defined in the general pharmaceutical legislation of the country in such a way that the results provided by it can, if necessary, lead to enforcement of the law and legal action.

GLOSSARY

The definitions given below apply to the terms as used in this guideline. They may have different meanings in other contexts.

**acceptance criterion for an analytical result**
Predefined and documented indicators by which a result is considered to pass or fail the limit(s) indicated in the specification.

**accuracy**
The degree of agreement of test results with the true value or the closeness of the results obtained by the procedure to the true value.

*Note:* It is normally established on samples of the material to be examined that have been prepared to quantitative accuracy. Accuracy should be established across the specified range of the analytical procedure. It is generally acceptable to use a “spiked” placebo which contains a known quantity or concentration of a reference substance.

**active pharmaceutical ingredient (API)**
Any substance or mixture of substances intended to be used in the manufacture of a pharmaceutical dosage form and that, when so used, becomes an active ingredient of that pharmaceutical dosage form. Such substances are intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease or to affect the structure and function of the body (1).

**analytical test report**
Analytical test report usually includes a description of the test procedure(s) employed, results of the analysis, discussion and conclusions and/or recommendations for one or more samples submitted for testing (see Part Three, section 18.7–18.11).

**analytical worksheet**
A printed form, an analytical workbook or electronic means (e-records) for recording information about the sample, as well as reagents and solvents used, test procedure applied, calculations made, results and any other relevant information or comments. (see Part Three, section 15).

**batch (or lot)**
A defined quantity of starting material, packaging material or product processed in a single process or series of processes so that it is expected to be homogeneous. It may sometimes be necessary to divide a batch into a number of sub-batches which are later brought together to form a final homogeneous batch. In the case of terminal sterilization the batch size is determined by the capacity of the autoclave. In continuous manufacture the batch must correspond to a defined fraction of the production, characterized by its intended homogeneity. The batch size can be defined either as a fixed quantity or as the amount produced in a fixed time interval (1).
batch number (or lot number)
A distinctive combination of numbers and/or letters which uniquely identifies a batch on the labels, its batch records and corresponding certificates of analysis, etc. (1).

calibration
The set of operations that establish, under specified conditions, the relationship between values indicated by an instrument or system for measuring (especially weighing), recording and controlling, or the values represented by a material measure, and the corresponding known values of a reference standard. Limits for acceptance of the results of measuring should be established (1).

certificate of analysis
The list of test procedures applied to a particular sample with the results obtained and the acceptance criteria applied. It indicates if the sample does or does not comply with the specification (3).

certified reference material
Reference material, characterized by a metrologically valid procedure for one or more specified properties, accompanied by a certificate that provides the value of the specified property, its associated uncertainty and a statement of metrological traceability (4).

compliance testing
Analysis of active pharmaceutical ingredients (APIs), pharmaceutical excipients, packaging material or pharmaceutical products to the requirements of a pharmacopoeial monograph or a specification in an approved marketing authorization.

control sample
A sample used for testing the continued accuracy and precision of the procedure. It should have a matrix similar to that of the samples to be analysed. It has an assigned value with its associated uncertainty.

design qualification
Documented collection of activities that define the functional and operational specifications of the instrument and criteria for selection of the vendor, based on the intended purpose of the instrument.
Note: Selection and purchase of a new instrument should follow a conscious decision process, based on the needs of the technical management. When designing a new laboratory facility the design specification and the requirements for services should be agreed between the management team and the agreed suppliers and documented.

good manufacturing practice(s) (GMP)
That part of quality assurance which ensures that pharmaceutical products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the marketing authorization (1).

installation qualification (IQ)
The performance of tests to ensure that the analytical equipment used in a laboratory is appropriately selected and correctly installed and operates in accordance with established specifications.

manufacturer
A company that carries out operations such as production, packaging, testing, re-packaging, labelling and/or re-labelling of pharmaceuticals (1).

marketing authorization (product licence, registration certificate)
A legal document issued by the competent medicines regulatory authority that authorizes the marketing or free distribution of a pharmaceutical product in the respective country after evaluation for safety, efficacy and quality. In terms of quality it establishes, inter alia, the detailed composition and formulation of the pharmaceutical product and the quality requirements for the product and its ingredients. It also includes details of packaging, labelling, storage conditions, shelf-life and approved conditions of use.
measurement uncertainty
Non-negative parameter characterizing the dispersion of quantity values being attributed to a measurand (analyte), based on the information used (4).

metrological traceability
Property of a measurement result whereby the result can be related to a reference through a documented, unbroken chain of calibrations, each contributing to the measurement uncertainty (4).

operational qualification (OQ)
Documented verification that the analytical equipment performs as intended over all anticipated operating ranges.

out-of-specification result (OOS)
All test results that fall outside the specifications or acceptance criteria established in product dossiers, drug master files, pharmacopoeias or by the manufacturer (5).

pharmaceutical excipient
A substance, other than the active pharmaceutical ingredient (API), which has been appropriately evaluated for safety and is included in a medicines delivery system to:
- aid in the processing of the medicines delivery system during its manufacture;
- protect, support or enhance stability, bioavailability or patient acceptability;
- assist in pharmaceutical product identification; or
- enhance any other attribute of the overall safety and effectiveness of the medicine during its storage or use (6,7).

pharmaceutical product
Any material or product intended for human or veterinary use, presented in its finished dosage form or as a starting material for use in such a dosage form, that is subject to control by pharmaceutical legislation in the exporting state and/or the importing state (1).

performance qualification (PQ)
Documented verification that the analytical equipment operates consistently and gives reproducibility within the defined specifications and parameters for prolonged periods.

primary reference substance (or standard)
A substance that is widely acknowledged to possess the appropriate qualities within a specified context, and whose assigned content is accepted without requiring comparison with another chemical substance (8). Note: Pharmacopoeial chemical reference substances are considered to be primary reference substances. A manufacturer, in the absence of a pharmacopoeial reference substance, should establish a primary reference substance.

qualification of equipment
Action of proving and documenting that any analytical equipment complies with required specification and performs suitably for its intended purpose (see Part Two, section 12).

quality management system
An appropriate infrastructure, encompassing the organizational structure, procedures, processes and resources, and systematic actions necessary to ensure adequate confidence that a product or service will satisfy given requirements for quality (see Part One, section 2).

quality control
All measures taken, including the setting of specifications, sampling, testing and analytical clearance, to ensure that raw materials, intermediates, packaging materials and finished pharmaceutical products conform with established specifications for identity, strength, purity and other characteristics.
quality manual
A handbook that describes the various elements of the quality management system for assuring the quality of the test results generated by a laboratory (see Part One, section 2.1–2.2).

quality unit(s)
An organizational unit, independent of production, which fulfils both quality assurance and quality control responsibilities. This can be in the form of separate quality assurance and quality control or a single individual or group, depending on the size and structure of the organization.

reference material
Material sufficiently homogeneous and stable with respect to one or more specified properties, which have been established to be fit for its intended use in a measurement process (4).

reference substance (or standard)
An authenticated, uniform material that is intended for use in specified chemical and physical tests, in which its properties are compared with those of the product under examination, and which possesses a degree of purity adequate for its intended use (8).

secondary reference substance
A substance whose characteristics are assigned and/or calibrated by comparison with a primary reference substance. The extent of characterization and testing of a secondary reference substance may be less than for a primary reference substance (8).

Note: Often referred to as “in-house” working standard.

signature (signed)
Record of the individual who performed a particular action or review. The record can be initials, full handwritten signature, personal seal or authenticated and secure electronic signature.

specification
A list of detailed requirements (acceptance criteria for the prescribed test procedures) with which the substance or pharmaceutical product have to conform to ensure suitable quality.

standard operating procedure (SOP)
An authorized written procedure giving instructions for performing operations both general and specific.

standard uncertainty
Uncertainty of the result of a measurement expressed as a standard deviation (9).

system suitability test
A test which is performed to ensure that the analytical procedure fulfils the acceptance criteria which had been established during the validation of the procedure. This test is performed before starting the analytical procedure and are to be repeated regularly, as appropriate, throughout the analytical run to ensure that the system's performance is acceptable at the time of the test.

validation of an analytical procedure
The documented process by which an analytical procedure (or method) is demonstrated to be suitable for its intended use.

verification of an analytical procedure
Process by which a pharmacopeial method or validated analytical procedure, that is being performed for the first time utilizing the equipment and reagents available, is demonstrated to be suitable for its intended use.

verification of performance
Test procedure regularly applied to a system (e.g. liquid chromatographic system) to demonstrate consistency of response.
Part One. Management and infrastructure

1. Organization and management

1.1 The laboratory, or the organization of which it is part, must be an entity that is legally authorized to function and can be held legally responsible.

1.2 The laboratory must be organized and operate so as to meet the requirements laid down in this guideline.

1.3 The laboratory should
(a) have managerial and technical personnel with the authority and resources needed to carry out their duties and to identify the occurrence of departures from the quality management system or the procedures for performing tests and/or calibrations, validation and verification, and to initiate actions to prevent or minimize such departures;
(b) have arrangements to ensure that its management and personnel are not subject to commercial, political, financial and other pressures or conflicts of interest that may adversely affect the quality of their work;
(c) have a policy and procedure in place to ensure confidentiality of:
   – information contained in marketing authorizations,
   – transfer of results/reports, and to protect data in archives (paper and electronic);
(d) define, with the aid of organizational charts, the organization and management structure of the laboratory, its place in any parent organization (such as the ministry or the NMRA in the case of a national pharmaceutical quality control laboratory), and the relationships between management, technical operations, support services and the quality management system;
(e) specify the responsibility, authority and interrelationships of all personnel who manage, perform or verify work which affects the quality of the tests and/or calibrations, validations and verifications;
(f) ensure the precise allocation of responsibilities, particularly in the designation of specific units for particular types of medicines;
(g) nominate trained substitutes/deputies for key management and specialized scientific personnel;
(h) provide adequate supervision of staff, including trainees, by persons familiar with the test and/or calibration, validation and verification methods and procedures, as well as their purpose and the assessment of the results;
(i) have management which has overall responsibility for the technical operations and the provision of resources needed to ensure the required quality of laboratory operations;
(j) designate a member of staff as quality manager who, despite other duties he/she may have, will ensure compliance with the quality management system; the nominated quality manager must have direct access to the highest level of management at which decisions are taken on laboratory policies or resources;
(k) ensure adequate information flow between staff at all levels; staff are to be made aware of the relevance and importance of their activities;
(l) ensure the traceability of the sample from receipt, throughout the stages, to the completion of the analytical test report;
(m) maintain an up-to-date collection of all specifications and related documents (paper or electronic) used in the laboratory; and
(n) have appropriate safety procedures (see Part Four).

1.4 The laboratory must maintain a registry with the following functions:
(a) receiving, distributing and supervising the consignment of the samples to the specific units; and
(b) keeping records on all incoming samples and accompanying documents.

1.5 In a large laboratory, communication and coordination must be guaranteed between the staff involved in the testing of the same sample in different units.
2. Quality management system

2.1 The laboratory management should establish, implement and maintain a quality management system appropriate to the scope of its activities, including the type, range and volume of testing and/or calibration, validation and verification activities it undertakes. The laboratory management must ensure that its policies, systems, programmes, procedures and instructions are described to the extent necessary to enable the laboratory to assure the quality of the test results that it generates. The documentation used in this quality management system must be communicated and available to, and understood and implemented by, the appropriate personnel. The elements of this system must be documented in a quality management system, e.g. a quality manual, for the organization as a whole and/or for a laboratory within the organization.

Note: Quality control laboratories of a manufacturer may not have this information in a quality manual.

2.2 The quality manual should contain as a minimum:

(a) a quality policy statement, including at least the following:
   (i) a statement of the laboratory management’s intentions with respect to the standard of service it will provide;
   (ii) a commitment to establishing, implementing and maintaining an effective quality management system;
   (iii) the laboratory management’s commitment to good professional practice and quality of testing, calibration, validation and verification;
   (iv) the laboratory management’s commitment to compliance with the content of this guideline;
   (v) a requirement that all personnel concerned with testing and calibration activities within the laboratory familiarize themselves with the documentation concerning quality and the implementation of the policies and procedures in their work;
(b) the structure of the laboratory (organizational chart);
(c) the operational and functional activities pertaining to quality, so that the extent and the limits of the responsibilities are clearly defined;
(d) outline of the structure of documentation used in the laboratory quality management system;
(e) the general internal quality assurance procedures;
(f) references to specific quality assurance procedures for each test;
(g) information on the appropriate qualifications, experience and competencies that personnel are required to possess;
(h) information on initial and in-service training of staff;
(i) a policy for internal and external audit and management review;
(j) a policy and procedure to inform staff of corrective and preventive actions introduced as a consequence of discrepancies detected;
(k) a policy for dealing with complaints;
(l) a policy for selecting, establishing and approving analytical procedures;
(m) a policy for handling of out-of-specifications results;
(n) a policy for the employment of appropriate reference substances and reference materials;
(o) a policy for participation in appropriate proficiency testing schemes and collaborative trials and the evaluation of the performance (applicable to national pharmaceutical quality control laboratories, but may be applied by other laboratories);
(p) a policy to select service and suppliers.

2.3 The laboratory must establish, implement and maintain authorized written standard operating procedures (SOPs) including, but not limited to administrative and technical operations, such as:
(a) personnel matters, including qualifications, training, clothing and hygiene;
(b) the change control;
(c) the purchase and receipt of consignments of materials (e.g. samples, reagents);
(d) the procurement, preparation and control of reference substances and reference materials (8);
(e) the internal labelling, quarantine and storage of materials;
(f) the qualification of equipment (10);
(g) the calibration of equipment;
(h) preventive maintenance and verification of instruments and equipment;
(i) sampling, if performed by the laboratory, and visual inspection;
(j) the testing of samples with descriptions of the methods and equipment used;
(k) atypical and out-of-specification results;
(l) validation of analytical procedures;
(m) verification of pharmacopoeial or validated analytical procedures;
(n) cleaning of laboratory facilities including bench tops, equipment, work stations, clean rooms (aseptic suites), glassware;
(o) monitoring of environmental conditions, e.g. temperature and humidity;
(p) monitoring temperature of storage conditions;
(q) disposal of reagents, solvents samples;
(r) safety measures.

2.4 The effectiveness of the quality management system should be reviewed systematically and periodically (internal and, where appropriate, by external audits or inspections) to ensure the continued compliance with the requirements of the system and to apply any necessary corrective and preventive measures. The quality manager is responsible for planning and organizing internal audits addressing all elements of the quality management system. Such reviews must be recorded, together with details of any corrective and preventive action taken.

2.5 Management review of quality issues should be regularly undertaken (at least annually), including:
(a) reports on internal and external audits or inspections and any follow-up required to correct any deficiencies;
(b) the outcome of investigations carried out as a result of complaints received, atypical or aberrant results reported in collaborative trials and/or proficiency tests;
(c) corrective actions applied and preventive actions introduced as a result of these investigations.

3. Control of documentation

3.1 Documentation is an essential part of the quality management system. The laboratory must establish and maintain procedures to control and review all documents (both internally generated and from external sources) that form part of the quality documentation. A master list identifying the current version status and distribution of documents must be established and readily available.

3.2 The procedures must ensure that:
(a) each document, whether a technical or a quality document, has a unique identifier, version number and date of implementation;
(b) appropriate, authorized SOPs are available at the relevant locations, e.g. near instruments;
(c) documents are kept up to date and reviewed as required;
(d) an invalid document is removed and replaced with the authorized, revised document with immediate effect;
(e) a revised document includes references to the previous document;
(f) old, invalid SOPs are retained in the archive to ensure traceability of the evolution of the procedures; any copies are destroyed; and
(g) all the relevant staff is trained for the new and revised SOPs.

3.3 A system of change control must be in place to inform staff of new and revised procedures. The system must ensure that:
(a) revised documents are prepared by the initiator, or a person who performs the same function, reviewed and approved at the same level as the original document and subsequently released by the quality manager (quality unit); and
(b) staff acknowledge by a signature that they are aware of applicable changes and their date of implementation.

4. Records

4.1 The laboratory must establish and maintain procedures for the identification, collection, indexing, retrieval, storage, maintenance and disposal of, and access to, all quality and technical/scientific
records.

4.2 All original observations, including calculations and derived data, calibration, validation and
verification records and final results should be retained on record for an appropriate period of time
in accordance with national regulations and, if applicable, contractual arrangements whichever is the
maximum. The records should include the data recorded in the analytical worksheet by the
technician/analyst on consecutively numbered pages with references to the appendices containing
the relevant recordings, e.g. chromatograms, spectra, etc. The records for each test must contain
sufficient information to permit the tests and/or the results to be recalculated, if necessary. The
records should include the identity of the personnel involved in the sampling, preparation and
testing of the samples. The records of samples to be used in legal proceedings should be kept
according to the legal requirements applicable to them.

4.3 All quality and technical/scientific records (including analytical test reports, certificates of analysis,
analytical worksheets) must be legible, readily retrievable, stored and retained within facilities that
provide a suitable environment that will prevent modification, damage or deterioration and/or loss.
The conditions under which all original records are stored must be such as to ensure their security
and confidentiality and access to them should be restricted to authorized personnel. Electronic
storage and signatures may also be employed but with restricted access and in conformance with
requirements for electronic records (11-14).

4.4 Quality management records must include reports from internal (and external if performed) audits
and management reviews, as well as records of all complaints and their investigations, including
records of possible corrective and preventive actions.

5. Data-processing equipment

5.1 Detailed recommendations are provided in Appendix 5 to Annex 4 of the Fortieth report of the
WHO Expert Committee on Specifications for Pharmaceutical Preparations - Supplementary
guidelines in good manufacturing practice: validation. Validation of computerized systems (11).

5.2 For computers, automated tests or calibration equipment, and the collection, processing, recording,
reporting, storage or retrieval of test and/or calibration data, the laboratory must ensure that:
(a) calculations and data transfers are validated or systematically subject to appropriate
verifications;
(b) computer software developed by the user is documented in sufficient detail and appropriately
validated or verified as being adequate for use;
(c) procedures are established and implemented for protecting the integrity of data. Such
procedures must include, but are not limited to, measures to ensure the integrity and
confidentiality of data entry or collection, and the storage, transmission and processing of data.
In particular, electronic data must be protected from unauthorized access and an audit trail of
any amendments must be maintained;
(d) computers and automated equipment are maintained so as to function properly, and are
provided with the environmental and operating conditions necessary to ensure the integrity of
test and calibration data;
(e) procedures are established and implemented for making, documenting and controlling changes
to information stored in computerized systems;
(f) electronic data must be backed up at appropriate regular intervals according to a documented
procedure. Backed-up data must be retrievable and stored in a manner to prevent data loss.

Note: For further guidance on validation of data-processing equipment refer to documents published by
the International Society for Pharmaceutical Engineering (12), U.S. Food and Drug Administration (13),
European Commission (14) and the Official Medicines Control Laboratories Network of the Council of
Europe (15).

6. Personnel

6.1 The laboratory must have sufficient personnel with the necessary education, training, technical
knowledge and experience for their assigned functions.
6.2 The technical management should ensure the competence of all persons operating specific equipment, instruments or other devices, who are performing tests and/or calibrations, validations or verifications. Their duties also involve the evaluation of results as well as signing analytical test reports and certificates of analysis (see Part Three, sections 18.7–18.11 and 19).

6.3 Staff undergoing training should be appropriately supervised and should be assessed on completion of the training. Personnel performing specific tasks must be appropriately qualified in terms of their education, training, and experience, as required.

6.4 The laboratory personnel must be permanently employed or under contract. The laboratory must ensure that additional technical and key support personnel who are under contract are supervised and sufficiently competent, and that their work is in accordance with the quality management system.

6.5 The laboratory should maintain current job descriptions for all personnel involved in tests and/or calibrations, validations and verifications. The laboratory should also maintain records of all technical personnel, describing their qualifications, training, and experience.

6.6 The laboratory must have the following managerial and technical personnel:

(a) a head of laboratory (supervisor), should have qualifications appropriate to the position, with extensive experience in medicines analysis and laboratory management in a pharmaceutical quality control laboratory in the regulatory sector or in industry. The head of laboratory is responsible for the content of certificates of analysis and analytical testing reports. The person’s function is also to ensure that:

(i) all key members of the laboratory staff have the requisite competence for the required functions and their grades reflect their responsibilities;

(ii) the adequacy of existing staffing, management and training procedures is reviewed periodically;

(iii) the technical management is adequately supervised;

(b) the technical management takes the following delegated tasks to ensure:

(i) procedures for performing calibration, verification and (re-)qualification of instruments, monitoring of environmental and storage conditions are in place and are conducted as required;

(ii) regular in-service training programmes to update and extend the skills of both professionals and technicians are arranged;

(iii) the safe keeping of any materials subject to poison regulation or to the controls applied to narcotic and psychotropic substances (see Part One, sections 7.12) kept in the work place is under the supervision of an authorized person;

(iv) national pharmaceutical quality control laboratories regularly participate in suitable proficiency testing schemes and collaborative trials to assess analytical procedures or reference substances;

(c) analysts, who should normally be graduates in pharmacy, analytical chemistry, microbiology or other relevant subjects with the requisite knowledge, skills and ability to adequately perform the tasks assigned to them by management and to supervise technical staff;

(d) technical staff, who should hold diplomas in their subjects awarded by technical or vocational schools;

(e) a quality manager (see Part One, section 1.3(j)).

Note: The more routine analyses performed, the greater the proportion of technicians required. Non-routine work, and particularly the investigative testing, requires a higher proportion of fully qualified specialists. In general the ratio of technicians to analysts in a routine testing environment has been shown to be 3:1 in a chemical or physicochemical unit, and 5:2 in a biological or microbiological laboratory.

7. Premises

7.1 The laboratory facilities are to be of a suitable size, construction and location. These facilities are to be designed to suit the functions and operations to be conducted. Rest and refreshment rooms should be separate from laboratory areas. Changing areas and toilets should be easily accessible and
appropriate for the number of users.

7.2 The laboratory facilities must have adequate safety equipment located appropriately and measures must be in place to ensure good housekeeping. Each laboratory is equipped with adequate work benches, work stations, fume hoods, etc. and instrumentation/equipment.

7.3 The environmental conditions, including lighting, energy sources, temperature, humidity, air pressure, etc., are to be appropriate to the functions and operations to be performed. The laboratory shall ensure that the environmental conditions are monitored, controlled and documented and do not invalidate the results or adversely affect the quality of the measurements.

7.4 Special precautions must be taken and, if necessary, there should be separate and dedicated unit/equipment (e.g. isolator, laminar flow work bench) to handle, weigh and manipulate highly toxic substances, including genotoxic substances. Procedures must be in place to avoid exposure and contamination.

7.5 Archive facilities should be provided to ensure the secure storage and retrieval of all documents. The design and condition of the archives should be such as to protect the contents from deterioration. Access to the archives must be restricted to designated personnel.

7.6 Procedures must be in place for the safe removal of types of waste including toxic waste (chemical and biological), reagents, samples, solvents and air filters.

7.7 Microbiological testing, if performed, should be contained in an appropriately designed and constructed laboratory unit. For further guidance see the draft working document WHO guideline on Good Practices for pharmaceutical microbiology laboratories QAS/09.297.

7.8 If in vivo biological testing (e.g. rabbit pyrogen test) is included in the scope of the laboratory then the animal houses must be isolated from the other laboratory areas with separate entrance and air-conditioning system. The relevant guidance and regulations are to be applied (16).

**Laboratory storage facilities**

7.9 The storage facilities should be well organized for the correct storage of samples, reagents and equipment.

7.10 Separate storage facilities must be maintained for the secure storage of samples, retained samples (see Part Three, section 20), reagents and laboratory accessories (see Part Two, sections 10.13–10.14), reference substances and reference materials (see Part Two, section 11). Storage facilities must be equipped to store material, if necessary, under refrigeration (2°C to 8°C) and frozen (-20°C) and securely locked. Access must be restricted to designated personnel.

7.11 Appropriate safety procedures should be drawn up and rigorously implemented wherever toxic or flammable reagents are stored or used. The laboratory must provide separate rooms or areas for storing flammable substances, fuming and concentrated acids and bases, volatile amines and other reagents, such as hydrochloric acid, nitric acid, ammonia and bromine. Self-igniting materials, such as metallic sodium and potassium, must also be stored separately. Small stocks of acids, bases and solvents may be kept in the laboratory store but the main stocks of these items should be retained preferably in a store separate from the laboratory building.

7.12 Reagents subject to poison regulations or to the controls applied to narcotic and psychotropic substances must be clearly marked as required by national legislation. They must be kept separately from other reagents in locked cabinets. A designated responsible member of staff must maintain a register of these substances. The head of each unit must accept personal responsibility for the safe keeping of any of these reagents kept in the workplace.

7.13 Gases also should be stored in a dedicated store, if possible isolated from the main building. Wherever possible gas bottles are to be avoided in the laboratory and distribution is preferred from the external gas store. If gas bottles are present in the laboratory, then they should be safely secured.

*Note: Consideration should be given to the installation of gas generators.*
8. Equipment, instruments and other devices

8.1 Equipment, instruments and other devices must be designed, constructed, adapted, located, calibrated, qualified, verified and maintained as required by the operations to be carried out in the local environment. The user should purchase the equipment from an agent capable of providing full technical support and maintenance when necessary.

8.2 The laboratory must have the required test equipment, instruments and other devices for the correct performance of the tests and/or calibrations, validations and verifications (including the preparation of samples and the processing and analysis of test and/or calibration data).

8.3 Equipment, instruments and other devices, including those used for sampling, must meet the laboratory’s requirements and comply with the relevant standard specifications, as well as being verified, qualified and/or calibrated regularly (see Part Two, section 12).

9. Contracts

Purchasing services and supplies

9.1 The laboratory should have a procedure for the selection and purchasing of services and supplies it uses that affect the quality of testing.

9.2 The laboratory should evaluate suppliers of critical consumables, supplies and services, which affect quality of testing, maintain records of these evaluations and list approved suppliers, that have been demonstrated to be of a suitable quality with respect to the requirements of the laboratory.

Subcontracting of testing

9.3 When a laboratory subcontracts work, which may include specific testing, it is to be done with approved organizations for the type of activity required. The laboratory is responsible for periodic assessing the competence of a contracted organization.

9.4 When a laboratory performs testing for a customer and subcontracts part of the testing, it should advise the customer of the arrangement in writing and, if appropriate, gain his/her approval.

9.5 There must be a written contract which clearly establishes the duties and responsibilities of each party, defines the contracted work and any technical arrangements made in connection with it. The contract should permit the laboratory to audit the facilities and competencies of the contracted organization and ensure the access of the laboratory to records and retained samples.

9.6 The contracted organization should not pass to a third party any work entrusted to it under contract without the laboratory's prior evaluation and approval of the arrangements.

9.7 The laboratory must maintain a register of all subcontractors that it uses and a record of the evidence of the assessment of the competence of subcontractors.

9.8 The laboratory takes the responsibility for all results reported, including those furnished by the subcontracting organization.

Part Two. Materials, equipment, instruments and other devices

10. Reagents

10.1 All reagents and chemicals, including solvents and materials used in tests and assays, must be of appropriate quality.

10.2 Reagents should be purchased from reputable, approved suppliers and should be accompanied by the certificate of analysis, and the material safety data sheet, if required.

10.3 In the preparation of reagents solutions in the laboratory:
   (a) responsibility for this task must be clearly specified in the job description of the person
assigned to carry it out; and
(b) prescribed procedures must be used which are in accordance with published pharmacopoeial or other standards, where available. Records should be kept of the preparation and standardization of volumetric solutions.

10.4 The labels of all reagents must clearly specify:
(a) content;
(b) manufacturer;
(c) date received and date of opening of the container;
(d) concentration, if applicable;
(e) storage conditions; and
(f) expiry date or re-test date, as justified.

10.5 The labels of reagent solutions prepared in the laboratory must clearly specify:
(a) name;
(b) date of preparation and initials of technician/analyst; and
(c) expiry date or re-test date, as justified.

10.6 The labels for volumetric solutions prepared in the laboratory must clearly specify:
(a) name;
(b) molarity (or concentration);
(c) date of preparation and initials of technician/analyst;
(d) date of standardization and initials of technician/analyst; and
(e) standardization factor.

10.7 In the transportation and subdivision of reagents:
(a) whenever possible, they must be transported in the original containers; and
(b) when subdivision is necessary, clean containers must be used and appropriately labelled.

Visual inspection

10.8 All reagent containers must be visually inspected to ensure that the seals are intact, both when they are delivered to the store and when they are distributed to the units.

10.9 Reagents appearing to have been tampered with should be rejected; however, this requirement may exceptionally be waived if the identity and purity of the reagent concerned can be confirmed by testing.

Water

10.10 Water should be considered as a reagent. The appropriate grade for a specific test should be used as described in the pharmacopoeias or in an approved test, when available.

10.11 Precautions must be taken to avoid contamination during its supply, storage and distribution.

10.12 The quality of the water must be verified regularly to ensure that various grades of water meet the appropriate specifications.

Storage

10.13 Stocks of reagents must be maintained in a store under the appropriate storage conditions (ambient temperature, under refrigeration or frozen). The store must contain a supply of clean bottles, vials, spoons, funnels and labels, as required, for dispensing reagents from larger to smaller containers. Special equipment may be needed for the transfer of larger volumes of corrosive liquids.

10.14 The person responsible for the store is responsible for looking after the storage facilities and their inventory, and for noting the expiry date of chemicals and reagents. Training may be needed in handling chemicals with the necessary care and safety.

11. Reference substances and reference materials

11.1 Reference substances (primary reference substances or secondary reference substances (8)) are used
for the testing of a sample.

Note: Pharmacopoeia reference substances should be employed when available and appropriate for the analysis. When a pharmacopoeia reference substance has not been established then the manufacturer must use his own reference substance.

11.2 Reference materials may be necessary for the calibration and/or qualification of equipment, instruments or other devices.

Registration and labelling

11.3 An identification number should be assigned to all reference substances, except for pharmacopoeial reference substances.

11.4 A new identification number must be assigned to each new batch.

11.5 This number must be marked on each vial of the reference substance.

11.6 The identification number should be quoted on the analytical worksheet every time the reference substance is used (see Part Three, section 15.5). In case of pharmacopoeial reference standards the batch number and/or the batch validity statement should be attached to the worksheet.

11.7 The register for all reference substances and reference materials should be maintained and contain the following information:

(a) the identification number of the substance/material;
(b) a precise description of the substance/material;
(c) the source;
(d) the date of receipt;
(e) the batch designation or other identification code;
(f) the intended use of the substance/material (e.g. as an infrared reference substance, as an impurity reference substance for thin-layer chromatography, etc.);
(g) the location of storage in the laboratory, and any special storage conditions;
(h) any further necessary information (e.g. the results of visual inspections);
(i) expiry date or re-test date;
(j) certificate (batch validity statement) of a pharmacopoeial reference substance and a certified reference material which indicates its use, the assigned content, if applicable, and its status (validity). Secondary reference substances prepared and supplied by the manufacturer should be accompanied by the certificate of analysis.

11.8 A person should be nominated to be responsible for reference substances and reference materials.

11.9 If a national pharmaceutical quality control laboratory is required to establish reference substances for use by other institutions, a separate reference substances unit should be established.

11.10 In addition a file must be kept in which all information on the properties of each reference substance is entered including the safety data sheets.

11.11 For reference substances prepared in the laboratory the file must include the results of all tests and verifications used to establish the reference substances and expiry date or re-test date; these must be signed by the responsible analyst.

Re-testing (monitoring)

11.12 All reference substances prepared in the laboratory or supplied externally, except for pharmacopoeial reference substances, should be re-tested at regular intervals to ensure that deterioration has not occurred and that the storage conditions are appropriate for the substance or material concerned.

11.13 The results of these tests must be recorded and signed by the responsible analyst.

11.14 In case the result of re-testing of a reference substance is non-compliant, a retrospective check of tests performed using this reference substance since its previous examination must be carried out. For evaluation of retrospective check outcomes and consideration of possible corrective actions, risk
analysis should be applied.

11.15 Further details on the handling and storage of reference substances are given in the general guidelines for the establishment, maintenance and distribution of chemical reference substances (8).

12. Calibration, verification of performance and qualification of equipment, instruments and other devices

12.1 Each item of equipment, instrument or other device used for testing, verification and/or calibration must, when practicable, be uniquely identified.

12.2 All equipment, instruments and other devices requiring calibration must be labelled, coded or otherwise identified to indicate the status of calibration and the date when re-calibration is due.

12.3 Laboratory equipment should undergo design qualification, installation qualification, operation qualification and performance qualification (see definitions of these terms in the Glossary) (10).

12.4 As applicable, the performance of equipment should be verified at an appropriate frequency according to a plan pre-established by the laboratory.

12.5 Measuring equipment must be regularly calibrated according to a plan pre-established by the laboratory (10).

12.6 Specific procedures must be established for each type of measuring equipment, taking into account the type of equipment, the extent of use and supplier's recommendations. For example:
   (a) pH meters are verified with standard certified buffer solutions before use;
   (b) Balances are to be checked daily using internal calibration and regularly using suitable test weights, and re-qualification should be performed annually using certified reference weights.

12.7 Only authorized personnel should operate equipment, instruments and devices. Up-to-date instructions on the use, maintenance, verification, qualification and calibration of equipment, instruments and devices (including any relevant manuals provided by the manufacturer) should be readily available for use by the appropriate laboratory personnel together with a schedule of the dates on which it is due for verification and/or calibration.

12.8 Records must be kept of each item of equipment, instrument or other device used to perform testing, verification and/or calibration. The records must include at least the following:
   (a) the identity of the equipment, instrument or other device;
   (b) the manufacturer’s name, model, serial number or other unique identification;
   (c) the qualification, verification and/or calibration required;
   (d) the current location, where appropriate;
   (e) the equipment manufacturer’s instructions, if available, or an indication of their location;
   (f) the dates, results and copies of reports, verifications and certificates of all calibrations, adjustments, acceptance criteria and the due date of the next qualification, verification and/or calibration;
   (g) the maintenance carried out to date and the maintenance plan;
   (h) a history of any damage, malfunction, modification or repair.
   It is also recommended that records should be kept and additional observations made of the time for which the equipment, instruments or devices were used.

12.9 Procedures should include instructions for the safe handling, transport and storage of measuring equipment. On re-installation, re-qualification of the equipment is required to ensure that it functions properly on installation.

12.10 Maintenance procedures should be established, e.g. regular servicing must be performed by a team of maintenance specialists, whether internal or external, followed by verification of performance.

12.11 Equipment, instruments and other devices, either subjected to overloading or mishandling, giving suspect results, shown to be defective or outside specified limits, must be taken out of service and clearly labelled or marked. Wherever possible they must not be used until they have been repaired and re-qualified.
12.12 When the equipment, instruments and other devices are outside the direct control of the laboratory for a certain period of time or have undergone a major repair, the laboratory must re-qualify the equipment to ensure its suitability for use.

**Note:** For further guidance on calibration, verification of performance and qualification of equipment refer to:

(a) Procedures for verifying and calibrating refractometers, thermometers used in determinations of melting temperatures and potentiometers for pH determinations and methods for verifying the reliability of scales for ultraviolet and infrared spectrophotometers and spectrofluorometers in *The International Pharmacopoeia* (17);

(b) Specific guidelines for qualification of equipment elaborated by the European Network of Official Medicines Control Laboratories (OMCL) (18); and

(c) General chapter of the U.S. Pharmacopoeia on Analytical Instrument Qualification (19).

13. **Traceability**

13.1 The result of an analysis should be traceable, when appropriate, ultimately to a primary reference substance.

13.2 All calibrations or qualification of instruments should be traceable to Certified Reference Materials and so to SI units (metrological traceability).

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**Part Three. Working procedures**

14. **Incoming samples**

14.1 Samples received by a laboratory may be for compliance testing or for investigative testing. Samples for compliance testing include routine samples for control, samples suspected of not complying with the specifications or samples submitted in connection with a marketing authorization process. Close collaboration with those providing the samples is important. In particular it is important that the sample is large enough to enable, if required, a number of replicate tests to be carried out (see Part Three, section 14.5) and for part of the sample to be retained (see Part Three, section 19).

14.2 Samples for investigative testing may also be submitted by various sources including customs, police and medicines inspectors. These samples comprise of suspicious, illegal or counterfeit substances or products where, usually, the primary objective is to identify the substance or the ingredient in the product and, if sufficient substance or product is available, to estimate the purity or content respectively. Well-documented screening procedures must be in place as well as confirmatory analytical procedures to positively identify the substance or the ingredient(s). If an estimation of the content of an identified ingredient is required then an appropriate quantitative analytical procedure should be applied. The value obtained should be reported with an indication of the uncertainty of measurement, if required (see Part Three, section 18.10).

14.3 It is common for a sample to be taken and divided into three approximately equal portions for submission to the laboratory:

(a) one for immediate testing;
(b) the second for confirmation of testing if required; and
(c) the third for retention, in case of dispute.

14.4 If the laboratory is responsible for sampling of substances, materials or products for subsequent testing then it must have a sampling plan and an internal procedure for sampling, available to all analysts and technicians within the laboratory. Samples should be representative of the batches of material from which they are taken and sampling should be carried out so as to avoid contamination and other adverse effects on quality or mix-up of, or by, the material being sampled. All the relevant data related to sampling must be recorded.

**Note:** Guidelines for sampling of pharmaceutical products and related materials were adopted by the WHO Expert Committee on Specifications for Pharmaceutical Preparations at its thirty-ninth
Test request

14.5 A standard test request form should be filled out and accompany each sample submitted to the laboratory. In case of a pharmaceutical manufacturer's laboratory the requirements may be given in the master production instructions.

14.6 The test request form must provide or leave space for the following information:
(a) the name of the institution or inspector that supplied the sample;
(b) the source of the material;
(c) a full description of the medicine, including its composition, International Nonproprietary Name (INN) (if available), brand name(s);
(d) dosage form and concentration or strength, the manufacturer, the batch number (if available) and the marketing authorization number;
(e) the size of the sample;
(f) the reason for requesting the analysis;
(g) the date on which the sample was collected;
(h) the size of the consignment from which it was taken, when appropriate;
(i) the expiry date (for pharmaceutical products) or re-test date (for APIs and pharmaceutical excipients);
(j) the specification to be used for testing;
(k) a record of any further comments (e.g. discrepancies found, associated hazard, etc.);
(l) the required storage conditions.

14.7 The laboratory must review the test request to ensure that:
(a) the requirements are adequately defined and the laboratory has the capability and resources to meet them;
(b) the appropriate tests and/or methods are selected and capable of meeting customer's requirements.
Any issue must be resolved with the originator of the request for analysis before testing starts and record of review must be kept.

Registration and labelling

14.8 All newly delivered samples and accompanying documents (e.g. the test request) must be assigned a registration number. Separate registration numbers must be assigned to requests referring to two or more medicines, different dosage forms, or different batches of the same medicine or different sources of the same batch. If applicable a unique registration number must also be assigned to any incoming retained sample (see Part Three, section 20).

14.9 A label bearing the registration number must be affixed to each container of the sample. Care must be taken to avoid obliterating any other markings or inscriptions.

14.10 A register must be kept, which may be a record book, a card file or data-processing equipment, where the following information is recorded:
(a) the registration number of the sample;
(b) the date of receipt;
(c) the specific unit to which the sample was forwarded.

Visual inspection of the submitted sample

14.11 The sample received must be visually inspected by laboratory staff to ensure that the labelling is in conformity with the information contained in the test request. The findings must be recorded, dated and signed. If discrepancies are found, or if the sample is obviously damaged, the fact must be recorded without delay on the test request form. Any queries must be immediately referred back to the provider of the sample.

Storage

14.12 The sample prior to testing, the retained sample (see Part Three, section 20) and any portions of the
sample remaining after performance of all the required tests must be stored safely, taking into account the storage conditions (20,21) specified for the sample.

**Forwarding to testing**

14.13 The specific unit to which the sample is sent for testing is determined by the person responsible.
14.14 The examination of a sample must not be started before the relevant test request has been received.
14.15 The sample must be properly stored until all relevant documentation has been received.
14.16 A request for analysis may be accepted verbally only in case of emergencies. All details must immediately be placed on record pending the receipt of written confirmation.
14.17 Copies or duplicates of all documentation must accompany each numbered sample when sent to the specific unit.
14.18 Testing must be performed as described under Part Three, section 17.

**15. Analytical worksheet**

15.1 The analytical worksheet is an internal document for recording information by the analyst about the sample, the test procedure, calculations and the results of testing. It is to be complemented by the raw data obtained in the analysis.

**Purpose**

15.2 The analytical worksheet contains documentary evidence either:
   (a) to confirm that the sample being examined is in accordance with the requirements; or
   (b) to support an out-of-specification result (see Part Three, sections 18.1–18.3).

**Use**

15.3 A separate analytical worksheet should usually be used for each numbered sample or group of samples.
15.4 Analytical worksheets from different units relating to the same sample should be assembled together.

**Content**

15.5 The analytical worksheet must provide for the following information:
   (a) the registration number of the sample (see Part Three, section 14.9);
   (b) page numbering, including the total number of pages (including annexes);
   (c) the date of the test request;
   (d) the date on which the analysis was started and completed;
   (e) the name and signature of the analyst;
   (f) a description of the sample received;
   (g) references to the specifications and a full description of test methods to which the sample was tested, including the limits;
   (h) the identity of the test equipment used (see Part Two, section 12.1);
   (i) the identification number of any reference substance used (see Part Two, section 11.5);
   (j) if applicable, the results of the system suitability test;
   (k) the identification of reagents and solvents employed;
   (l) the results obtained;
   (m) the interpretation of the results and the final conclusions (whether or not the sample was found to comply with the specifications), signed by each of the analysts involved and approved and signed by the supervisor;
   (n) any further comments, for example, for internal information (see Part Three, section 17.1) or detailed notes on the specifications selected and the methods of assessment used (see Part Three, section 15.9) or any deviation from the prescribed procedure, which must be approved
and reported, or whether and when portions of the sample were forwarded to other units for special tests, and the date when the results were received.

15.6 All values obtained from each test, including blank results, must immediately be entered on the analytical worksheet and all graphical data, whether obtained from recording instruments or plotted by hand, must be attached or be traceable to an electronic record file or document where the data is available.

15.7 The completed analytical worksheet must be signed by the responsible analyst(s) and approved and signed by the supervisor.

15.8 When a mistake is made in analytical worksheets or when data or text need to be amended, the old information should be deleted by means of a single line (not erased or made illegible) and the new information added alongside. All such alterations should be signed by the person making the correction and the date of the change inserted. The reason for the change should also be given on the worksheet (suitable procedures should be in place for electronic worksheets).

Selection of the specifications to be used

15.9 The specification necessary to assess the sample may be that given in the test request or master production instructions. If no precise instruction is given, the specification in the officially recognized national pharmacopoeia may be used or, failing this, the manufacturer’s officially approved or other nationally recognized specification. If no suitable method is available:
(a) the specification contained in the marketing authorization/product licence may be requested from the marketing authorization holder or manufacturer and verified by the laboratory; or
(b) the requirements are set by the laboratory itself on the basis of published information and any procedure employed is to be validated by the testing laboratory (see Part Three, section 16).

15.10 For official specifications, the current version of the relevant pharmacopoeia must be available.

Filing

15.11 The analytical worksheet must kept safely, together with any attachments, including calculations and recordings of instrumental analyses.

16. Validation of analytical procedures

16.1 The laboratory should have the documented evidence that any analytical procedure used for testing is suitable under actual conditions for the intended use. This evidence is obtained through validation (22). Validation also serves to establish acceptance criteria for system suitability test.

16.2 Validation should be performed according to a validation protocol, which includes analytical performance characteristics to be verified for various types of analytical procedures (see Table 1). The results should be documented in the validation report.

Table 1. Characteristics to consider during validation of analytical procedures

<table>
<thead>
<tr>
<th>Type of analytical Procedure</th>
<th>Identification</th>
<th>Testing for impurities</th>
<th>Assay</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Quantitative tests</td>
<td>Limit tests</td>
<td>(measurement only)</td>
</tr>
<tr>
<td>Accuracy</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Precision</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Repeatability</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Intermediate precision*</td>
<td>-</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Specificity</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Detection limit</td>
<td>-</td>
<td>b</td>
<td>+</td>
</tr>
<tr>
<td>Quantitation limit</td>
<td>-</td>
<td></td>
<td>-</td>
</tr>
<tr>
<td>Linearity</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Range</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

- Characteristic is normally not evaluated.
+ Characteristic should normally be evaluated.
16.3 A pharmacopoeial method or externally validated analytical method, that is being performed for the first time utilizing the equipment and reagents available, should be verified under actual conditions of use in order to demonstrate that it is suitable for the substance or product to be tested. The extent of verification should be justified on the basis of risk management principles.

Note: Verification consists of assessing selected characteristics, which are important for the particular procedure, use and sample to be tested.

As an example only, specificity is a key parameter in verifying that a pharmacopoeial procedure is suitable for assay and related substances test of a substance or pharmaceutical product. System suitability resolution requirement for a chromatographic method may be acceptable, but in case that a substance or pharmaceutical product may contain impurities not addressed by the pharmacopoeial procedure, or a pharmaceutical product contains excipients potentially interfering with the procedure, more thorough assessment of specificity may be required. Other characteristics such as the limit of detection or quantitation and precision for related substances may be useful to demonstrate suitability of the pharmacopoeial procedure under actual conditions of use.

Verification is not required for basic pharmacopoeial methods such as (but not limited to) pH, loss on drying, wet chemical methods.

16.4 System suitability testing is an integral part of many analytical procedures. The tests are based on the concept that the equipment, electronics, analytical operations and samples to be analysed constitute an integral system that can be evaluated as such. System suitability test parameters that need to be established for a particular procedure depend on the type of procedure being evaluated, for instance a resolution test for an high performance liquid chromatography (HPLC) procedure.

16.5 A major change in the analytical procedure, or in the composition of the product tested, or in the synthesis of the medicine substance, will require revalidation of the analytical procedure.

Note: Further guidance on validation of analytical procedures:
(a) Guideline elaborated by the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) (23);
(b) Guideline elaborated by the European Network of Official Medicines Control Laboratories (OMCL) (24);
(c) General chapters of the U.S. Pharmacopeia on Validation of compendial procedures and on Verification of compendial procedures (25).

17. Testing
17.1 The sample must be tested in accordance with the work plan of the laboratory after completion of the preliminary procedures. If this is not feasible, the reasons must be noted, e.g. in the analytical worksheet (see Part Three, section 15), and the sample must be stored in a special place which is kept locked (see Part Three, section 14.12).

17.2 Specific tests required may need to be carried out by another unit or by a specialized external laboratory (see Part One, section 9). The responsible person should prepare the request and arrange for the transfer of the required number of units (bottles, vials, tablets) from the sample. Each of these units must bear the correct registration number. When the analytical test report contains results performed by subcontractors these results must be indicated.

17.3 Detailed guidance on official pharmacopoeial requirements is usually given in the general notices and specific monographs of the pharmacopoeia concerned. Test procedures should be described in detail and should provide sufficient information to allow properly trained analysts to perform the analysis in a reliable manner. Where system suitability criteria are defined in the method they should be fulfilled. Any deviation from the test procedure must be approved and documented.

18. Evaluation of test results
18.1 Test results must be reviewed and, where appropriate, evaluated statistically after completion of all
the tests to determine whether they are mutually consistent and if they meet the specifications used. The evaluation should take into consideration the results of all the tests (all test data). Whenever doubtful (atypical) results are obtained they should be investigated. The complete testing procedure needs to be checked according to the internal quality management system (see also Part One, section 2).

18.2 When a doubtful result (suspected out-of-specification result) has been identified a review of the different procedures applied during the testing process is to be undertaken by the supervisor with the analyst/technician before re-testing is permitted. The following should be addressed:
(a) confirm with the analyst/technician that the appropriate procedure(s) was applied and followed correctly;
(b) examine the raw data to identify possible discrepancies;
(c) check all calculations;
(d) check that equipment employed was qualified, calibrated and that system suitability tests were performed and were acceptable;
(e) ensure that the appropriate reagents, solvents and reference substances were employed.

18.3 The identification of an error which caused an aberrant result will invalidate the result and a re-test of the sample will be necessary. Doubtful results can be rejected only if they are clearly due to an identified error. Sometimes the outcome of the investigation is inconclusive – no obvious cause has been identified – in which case a confirmatory determination is to be performed by another analyst who should be, at least, as experienced and competent in the analytical procedure as the original analyst. A similar value would indicate an out-of-specification result. However, further confirmation using another validated method, if available, may be advised.

18.4 An SOP must be in place for the conduct of an investigation of an out-of-specification test result. The SOP gives clear guidance on a number of re-tests allowed (based on sound statistical principles). All investigations and their conclusions must be recorded. In the event of an error any corrective action taken and any preventive action introduced must be recorded and implemented.

18.5 All individual results (all test data) with acceptance criteria should be reported.

18.6 All conclusions must be entered on the analytical worksheet (see Part Three, section 15) by the analyst and signed by the supervisor.

Note: Further guidance on evaluation and reporting test results:
(a) Guideline elaborated by the U.S. Food and Drug Administration (5);
(b) Guideline elaborated by the European Network of Official Medicines Control Laboratories (OMCL) (26).

Analytical test report

18.7 The analytical test report is a compilation of the results and states the conclusions of the examination of a sample. It must be:
(a) issued by the laboratory;
(b) based on the analytical worksheet (see Part Three, section 15).

18.8 Any amendments to the original analytical test report will require the issue of a new corrected document.

18.9 Pharmacopoeial content limits are set, taking into account the uncertainty of measurement, and the production capability and acceptance criteria for an analytical result should be predefined. Under presently applied rules neither the pharmacopoeias nor the NMRAs require the value found to be expressed with its associated expanded uncertainty for compliance testing. However, when reporting results of investigative testing, although the primary objective is to identify a substance in the sample, a determination of its concentration may be also requested in which case the estimated uncertainty should also be given.

18.10 Measurement uncertainty can be estimated in a number of ways, e.g.
(a) by preparing an uncertainty budget for each uncertainty component identified in an analytical procedure (bottom-up approach);
(b) from validation data and control charts (27);
(c) from the data obtained from proficiency tests or collaborative trials (top-down approach).

*Note:* Further guidance can be found in various guidelines (9,28,29).

**Content of the analytical test report**

18.11 The analytical test report should provide the following information:

(a) the laboratory registration number of the sample;
(b) the laboratory test report number;
(c) the name and address of the laboratory testing the sample;
(d) the name and address of the originator of the request for analysis;
(e) the name and description and batch number of the sample, where appropriate;
(f) an introduction giving the background and the purpose of the investigation;
(g) a reference to the specifications used for testing the sample or a detailed description of the procedures employed (sample for investigative testing), including the limits;
(h) the results of all the tests performed or the numerical results with the standard deviation of all the tests performed (if applicable);
(i) a discussion of the results obtained;
(j) a conclusion whether or not the sample(s) was found to be within the limits of the specifications used, or for a sample for investigative testing the substance(s) or ingredient(s) identified;
(k) the date on which the test(s) was completed;
(l) the signature of the head of the laboratory or authorized person;
(m) the name and address of the original manufacturer and, if applicable, those of the re-packer and/or trader;
(n) whether or not the sample(s) complies with the requirements;
(o) the date on which the sample was received;
(p) the expiry date or re-test date, if applicable;
(q) a statement indicating that the analytical test report, or any portion thereof, cannot be reproduced without the authorization of the laboratory.

19. **Certificate of analysis**

19.1 A certificate of analysis is prepared for each batch of a substance or product and contains the following information:

(a) the registration number of the sample;
(b) date of receipt;
(c) the name and address of the laboratory testing the sample;
(d) the name and address of the originator of the request for analysis;
(e) the name and description and batch number of the sample, where appropriate;
(f) the name and address of the original manufacturer and, if applicable, those of the re-packer and/or trader;
(g) the reference to the specification used for testing the sample;
(h) the results of all tests performed (mean and standard deviation) with the prescribed limits;
(i) a conclusion whether or not the sample was found to be within the limits of the specification;
(j) expiry date or re-test date, if applicable;
(k) date on which the test(s) was completed;
(l) the signature of the head of laboratory or other authorized person.

*Note:* Guideline on Model certificate of analysis was adopted by the WHO Expert Committee on Specifications for Pharmaceutical Preparations at its thirty-sixth meeting (3).

20. **Retained samples**

20.1 Samples should be retained as required by the legislation or by the originator of the request for analysis. There should be sufficient retained sample to allow at least two re-analyses. Retained sample should be kept in its final pack.
Part Four. Safety

21. General rules

21.1 General and specific safety instructions reflecting identified risk, must be made available to each staff member and supplemented regularly as appropriate (e.g. with written material, poster displays, audiovisual material and occasional seminars).

21.2 General rules for safe working in accordance with national regulations and SOPs normally include the following requirements:

(a) safety data sheets must be available to staff before testing is carried out;
(b) smoking, eating and drinking in the laboratory must be prohibited;
(c) staff must be familiar with the use of fire-fighting equipment, including fire extinguishers, fire blankets and gas masks;
(d) staff must wear laboratory coats or other protective clothing, including eye protection;
(e) special care must be taken, as appropriate, in handling, for example, highly potent, infectious or volatile substances;
(f) highly toxic and/or genotoxic samples should be handled in a specially designed facility to avoid the risk of contamination;
(g) all containers of chemicals must be fully labelled and include prominent warnings (e.g. “Poison”, “Flammable”, “Radiation”, etc.) whenever appropriate;
(h) adequate insulation and spark-proofing must be provided for electrical wiring and equipment, including refrigerators;
(i) safety rules in handling cylinders of compressed gases must be observed and staff must be familiar with the relevant colour identification codes;
(j) staff must be aware of the need to avoid working alone in the laboratory;
(k) first-aid materials must be provided and staff instructed in first-aid techniques, emergency care and the use of antidotes.

21.3 Protective clothing must be available, including eye protection, masks and gloves. Water showers should be installed. Rubber suction bulbs must be used on manual pipettes and siphons. Staff must be instructed in the safe handling of glassware, corrosive reagents and solvents and particularly in the use of safety containers or baskets to avoid spillage from containers. Warnings, precautions and instructions must be given for work with violent, uncontrollable or dangerous reactions when handling specific reagents (e.g. mixing water and acids, or acetone–chloroform and ammonia), flammable products, oxidizing or radioactive agents and especially biologicals such as infectious agents. Peroxide-free solvents should be used. Staff must be aware of methods for the safe disposal of unwanted corrosive or dangerous products by neutralization or deactivation and of the need for safe and complete disposal of mercury and its salts.

21.4 Poisonous or hazardous products must be singled out and labelled appropriately, but it must not be taken for granted that all other chemicals and biologicals are safe. Unnecessary contact with reagents, especially solvents and their vapours, must be avoided. The use of known carcinogens and mutagens as reagents must be limited or totally excluded if required by local regulations. Replacement of toxic solvents and reagents by less toxic materials or reduction of their use must always be the aim, particularly when new techniques are developed.

References


2. International Organization for Standardization. General requirements for the competence of testing and


9. International Organization for Standardization:

   - Guidance for the Use of repeatability, reproducibility and trueness estimates in measurement uncertainty estimation. 2004, ISO Guide 21748,


12. International Society for Pharmaceutical Engineering (ISPE) - Good Automated Manufacturing Practice (GAMP) Good Practice Guides:

   - Validation of Laboratory Computerized Systems, April 2005,


- PA/PH/OMCL (08) 87 2R - Annex 1: Validation of computerised calculation systems: example of validation of in-house software (http://www.edqm.eu/site/NEW_Annex_1_Validation_of_computerised_calculationpdf-en-8391-2.html),
- PA/PH/OMCL (08) 88 R - Annex 2: Validation of Databases (DB), Laboratory Information Management Systems (LIMS) and Electronic Laboratory Notebooks (ELN) (http://www.edqm.eu/site/NEW_Annex_2_Validation_of_Databases_DB_Laboratory_pdf-en-8392-2.html),


18. Official Medicines Control Laboratories Network of the Council of Europe, Quality Assurance Documents:


28. Official Medicines Control Laboratories Network of the Council of Europe, Quality Assurance Documents:

29. EURACHEM / CITAC Guides:
   - Quantifying uncertainty in analytical measurement, 2nd edition, 2000,
   - Use of uncertainty information in compliance assessment, 2007 (http://www.measurementuncertainty.org/).
Appendix

Equipment for a first-stage and medium-size pharmaceutical quality control laboratory

A list of equipment considered by the Committee to be adequate either for a first-stage or medium-size pharmaceutical quality control laboratory is given below. In the case of a medium-size laboratory specific sections are devoted to a microbiology unit and pharmacognosy / phytochemistry unit. In the case that a first stage laboratory is testing herbal medicines additional equipment recommended is specified in the table.

National medicines regulatory authorities or laboratories wishing to perform pharmaceutical analyses may consider the following list in the establishment or upgrading of their testing facilities. For budgetary reasons it is necessary, besides the cost of equipment, to take into consideration the cost of reference materials, reagents, solvents, glassware, other laboratory commodities and personnel charges. Experience has shown that for sustainability, a laboratory should allow a margin of 10–15% per year of the purchasing expenditure on equipment to cover the cost of maintenance.

<table>
<thead>
<tr>
<th>First-stage laboratory</th>
<th>Equipment and major instruments</th>
<th>Quantity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Top-loading balance</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Analytical balance (5 digits)</td>
<td>1 or 2</td>
</tr>
<tr>
<td></td>
<td>Melting-point apparatus</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>pH meter (with assorted electrodes)</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Microscope</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Polarimeter</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>High-performance liquid chromatograph (HPLC) with ultraviolet detector</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Ultraviolet/visible spectrophotometer</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Infrared spectrophotometer with pellet press</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Karl Fischer titrator (semi-micro determination of water)</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Agate mortar with pestle</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Equipment for thin-layer chromatography (TLC)</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>TLC spotter</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Developing chambers</td>
<td>6 + 1*</td>
</tr>
<tr>
<td></td>
<td>Atomizers</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Ultraviolet viewing lamp</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Disintegration test equipment (1 basket for 6 tablets)</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Dissolution apparatus</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Soxhlet extraction apparatus (60 ml)</td>
<td>3 + 1*</td>
</tr>
<tr>
<td></td>
<td>Micrometer callipers</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Pycnometers</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Burettes/pipettes (10ml&amp;25ml / 1,2,5,10,20,25,50ml)</td>
<td>3 of each</td>
</tr>
<tr>
<td></td>
<td>Desiccator</td>
<td>1 + 1*</td>
</tr>
<tr>
<td></td>
<td>Centrifuge (table-top model, 4-place swing rotor)</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Water-bath (20 litres)</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Hot plates with magnetic stirrers</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Vacuum pump (rotary, oil)</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Drying oven (60 litres)</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Vacuum oven (17 litres)</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Muffle furnace</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Refrigerator (explosion-proof)</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Water distilling apparatus (8 litres/hour)</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Water deionizer (10 litres/hour)</td>
<td>1</td>
</tr>
<tr>
<td>Equipment and major instruments</td>
<td>Quantity</td>
<td></td>
</tr>
<tr>
<td>---------------------------------------------------------------------</td>
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<td></td>
</tr>
<tr>
<td>Top-loading balance</td>
<td>1 or 2</td>
<td></td>
</tr>
<tr>
<td>Analytical balance (5 digits)</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Analytical microbalance</td>
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<td></td>
</tr>
<tr>
<td>Microscope</td>
<td>1 or 2</td>
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</tr>
<tr>
<td>Equipment for TLC</td>
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<td></td>
</tr>
<tr>
<td>TLC multispotter</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Developing chambers</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Atomizers</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Ultraviolet viewing lamp</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Potentiometric titrimeter</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Micro-Kjeldahl equipment (including fume flasks)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Soxhlet extraction apparatus (60 ml)</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Pycnometers</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Burettes / pipettes (10ml &amp; 25ml/1,2,5,10,20,25,50ml)</td>
<td>6 of each</td>
<td></td>
</tr>
<tr>
<td>Micrometer callipers</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Heating mantles for flasks (assorted sizes: 50, 200 and 2000ml)</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Sieves (assorted sizes)</td>
<td>1 set</td>
<td></td>
</tr>
<tr>
<td>Centrifuge (floor model)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Shaker (wrist-action)</td>
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</tr>
<tr>
<td>Vortex mixers</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Water-bath (electrical, 20 litres)</td>
<td>2 or 3</td>
<td></td>
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<tr>
<td>Hot plates with magnetic stirrers</td>
<td>3 or 4</td>
<td></td>
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<tr>
<td>Vacuum pump (rotary, oil)</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Vacuum rotary evaporator</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Drying oven (60 litres)</td>
<td>2 or 3</td>
<td></td>
</tr>
<tr>
<td>Muffle furnace (23 litres)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Vacuum oven (17 litres)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Desiccators</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Refrigerator (explosion-proof)</td>
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<td></td>
</tr>
<tr>
<td>Freezer</td>
<td>1</td>
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<tr>
<td>Ultrasonic cleaners (5 litres)</td>
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<tr>
<td>Laboratory glassware washing machine</td>
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<tr>
<td>Water distilling apparatus (8 litres/hour)</td>
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</tr>
<tr>
<td>Water deionising equipment (10 litres/hour)</td>
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<td></td>
</tr>
<tr>
<td>Fume hoods</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

* Needed in the case that also herbal medicines are tested.
<table>
<thead>
<tr>
<th>Equipment</th>
<th>Quantity</th>
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<tbody>
<tr>
<td>Melting-point apparatus</td>
<td>1</td>
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<td>Polarimeter</td>
<td>1</td>
</tr>
<tr>
<td>pH meters (with assorted electrodes)</td>
<td>2</td>
</tr>
<tr>
<td>High-performance liquid chromatograph (HPLC) with variable wavelength ultraviolet/visible detector</td>
<td>3 or 4</td>
</tr>
<tr>
<td>Ultraviolet/visible spectrophotometer, double-beam</td>
<td>1</td>
</tr>
<tr>
<td>Infrared spectrophotometer with pellet press</td>
<td>1</td>
</tr>
<tr>
<td>Agate mortar with pestle</td>
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</tr>
<tr>
<td>Gas chromatograph (flame ionization, direct &amp; static head space injection)</td>
<td>1</td>
</tr>
<tr>
<td>Refractometer</td>
<td>1</td>
</tr>
<tr>
<td>Karl Fischer titrators (1 semi-micro and 1 coulometric for micro-determination of water)</td>
<td>2</td>
</tr>
<tr>
<td>Oxygen flask combustion apparatus</td>
<td>1</td>
</tr>
<tr>
<td>Disintegration test equipment (1 basket for 6 tablets)</td>
<td>1</td>
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<tr>
<td>Dissolution test equipment (for 6 tablets/capsules)</td>
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<tr>
<td><strong>Optional items</strong></td>
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<td>Atomic absorption spectrophotometer</td>
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<td>Spectrofluorometer</td>
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<td>High-performance liquid chromatograph (HPLC) detectors:</td>
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<td>- fluorescence</td>
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<tr>
<td>- diode-array</td>
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<tr>
<td>- refractive index</td>
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<td>- evaporative light scattering (ELSD)</td>
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<td>- charged aerosol (CAD)</td>
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<td>- mass spectrometric (MS)</td>
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<td>Gas chromatograph detectors:</td>
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<td>- conductivity</td>
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<tr>
<td>- nitrogen/phosphorous (NPD)</td>
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<tr>
<td>- mass spectrometric (MS)</td>
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<tr>
<td>TLC scanner</td>
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<td>Crushing strength tester</td>
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<tr>
<td>Friability tester</td>
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<td>Viscometer</td>
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<td>Ice machine</td>
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<tr>
<td>Ice machine</td>
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<td>Solvent-recovery apparatus</td>
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<td><strong>Equipment for microbiology unit</strong></td>
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<tr>
<td>pH meter</td>
<td>1</td>
</tr>
<tr>
<td>Ultraviolet/visible spectrophotometer, single-beam</td>
<td>1</td>
</tr>
<tr>
<td>Microscopes (for bacteriology)</td>
<td>2</td>
</tr>
<tr>
<td>Membrane filter assembly for sterility tests</td>
<td>1</td>
</tr>
<tr>
<td>Colony counter with magnifier</td>
<td>1</td>
</tr>
<tr>
<td>Laminar air flow unit</td>
<td>1</td>
</tr>
<tr>
<td>Hot-air sterilizer</td>
<td>1</td>
</tr>
<tr>
<td>Incubators, 60 litres</td>
<td>2 or 3</td>
</tr>
<tr>
<td>Anaerobic jar</td>
<td>1</td>
</tr>
<tr>
<td>Zone reader</td>
<td>1</td>
</tr>
<tr>
<td>Centrifuge</td>
<td>1</td>
</tr>
<tr>
<td>Water-bath (thermostatically controlled)</td>
<td>2</td>
</tr>
<tr>
<td>Autoclaves (100 litres, top-loading)</td>
<td>2</td>
</tr>
<tr>
<td>Refrigerators (340 litres)</td>
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</tr>
<tr>
<td>Deep freezer</td>
<td>1</td>
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<tr>
<td>Laboratory glassware washing machine</td>
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</tr>
<tr>
<td>Equipment for pharmacognosy / phytochemistry unit</td>
<td></td>
</tr>
<tr>
<td>-------------------------------------------------</td>
<td>-------</td>
</tr>
<tr>
<td>Grinder / Mill (for preparation of sample of herbal materials)</td>
<td>1</td>
</tr>
<tr>
<td>Top loading balance</td>
<td>1</td>
</tr>
<tr>
<td>Sieves</td>
<td>1 set</td>
</tr>
<tr>
<td>Microscope (i)</td>
<td>1</td>
</tr>
<tr>
<td>Soxhlet extraction apparatus</td>
<td>2 or 3</td>
</tr>
<tr>
<td>Water-bath</td>
<td>1</td>
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<tr>
<td>Heating mantles for flasks</td>
<td>1 or 2</td>
</tr>
<tr>
<td>Hot plates with magnetic stirrers</td>
<td>2</td>
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<tr>
<td>Equipment for TLC</td>
<td>1 or 2</td>
</tr>
<tr>
<td>Developing chambers</td>
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<tr>
<td>Desiccators</td>
<td>2</td>
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<tr>
<td>Rotary vacuum apparatus</td>
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</tr>
<tr>
<td>Distillation equipment</td>
<td>1</td>
</tr>
<tr>
<td>Conical Percolators</td>
<td>2 or 3</td>
</tr>
<tr>
<td>Apparatus for determination of water content by Azeotropic method (i)</td>
<td>1</td>
</tr>
<tr>
<td>Apparatus for determination of volatile oils (i)</td>
<td>1</td>
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<tr>
<td>Apparatus for determination of arsenic limit test (ii)</td>
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</table>

References:
