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Annex 4
Considerations for requesting analysis of drug samples[1]

Many WHO Member States do not have adequate drug quality control facilities of their own. For drugs imported into such countries, manufacturers' batch certificates issued in accordance with the WHO Certification Scheme (*1*) will normally provide sufficient information on the quality and origin of a product. This assumes that an official inspection of the manufacturing site has been performed and that the manufacturer complies with good manufacturing practices (*2*). For domestically manufactured pharmaceuticals, manufacturers' batch certificates may be relied upon to indicate the quality of a product. This implies that the results of an inspection by the competent national authority have shown that the manufacturer is capable of reliably producing a product of the required quality.

However, in certain situations a need may arise for national authorities to test drug samples when testing facilities are not available. For this purpose, laboratories in other countries or contract laboratories in the same or in another country may be contacted (for a model certificate of analysis, see Annex 10). General considerations before approaching them are set out below.

Important note: **Any laboratory contacted has the right to decline a request for analysis without furnishing any explanation or remark.**

Reason for analysis

Full-scale pharmacopoeial testing is expensive. The national authority may prefer to limit analysis to those products which:

— show physical signs of instability or deterioration (*3*);
— are of unidentifiable origin;
— emanate from a supplier suspected of dealing in substandard products;
— have given rise to disputed analytical results;
— are suspected of causing adverse reactions;

[1] These considerations are applicable to national drug regulatory authorities, but may also apply to the independent analysis of pharmaceuticals in trade.

— will be used as evidence in litigation;
— are provided through drug donations.

Where the information on the quality of a product is important and needs to be communicated rapidly (such as the presence of products of deterioration or a new impurity profile), selected purity tests may be performed instead of full-scale pharmacopoeial testing. These tests should include a potency test, and any tests additional to those in the pharmacopoeial monograph that might be required. Since the selected tests may not always be capable of detecting all the impurities of unknown source, a combination of analytical methods, such as several different chromatographic methods or differential scanning calorimetry together with gas or liquid chromatography, could be used. The suitability of the pharmacopoeial monograph from the point of view of the detection of impurities should be evaluated, especially if the drug is from a new source, which may cause it to have a different impurity profile. If necessary, the advice of an experienced laboratory should be sought.

Communication before samples are submitted

Before a sample of a product is sent to a laboratory in another country or a contract laboratory and its analysis is requested, the laboratory concerned must be asked whether it is willing to carry out the analysis. The request should be accompanied, as a minimum, by the following information, which should be given in writing:

— the reason(s) for the request;
— the name and address of the manufacturer and/or distributor;
— the marketing authorization and its number or reference;
— the pharmaceutical dosage form;
— the composition of the product (using International Nonproprietary Names (INNs), where possible);
— the concentration or strength;
— the date of manufacture;
— details of the storage conditions and the expiry date;
— any background information about the route of synthesis of the ingredients, if available;
— a reference to pharmacopoeial or other specifications, including details of the analytical methods that should be used;
— the purpose of the analyses;
— the number of separate samples to be analysed and their batch (lot) number(s);
— the proposed mode of payment for the analysis;
— the preferred language and format of the report containing the results (see below).

It is recommended that a contract between the requesting party and the laboratory that will perform the tests should be drawn up to settle issues such as liability, and the mode of payment for the expenses involved. The responsibilities of the two parties should be defined. The laboratory that has been contacted should indicate, at the earliest possible opportunity, its decision whether or not to undertake the analyses.

If the laboratory agrees to undertake the analysis, the following should be communicated to the requesting party:

— the nature and size of the sample required;
— any additional non-pharmacopoeial tests which may be required;
— the cost and the mode of payment;
— a tentative estimate of the time that the analysis will take;
— the method to be used to transmit the results.

Submission of samples

Upon agreement with a laboratory, the sample should be dispatched by the national drug regulatory authority or the requesting party. The sample must be suitably packaged and labelled (*4*). It should be divided into two portions, each of which must be properly packed and sealed. The laboratory should analyse one sealed portion only, and retain the other for presenting during litigation or investigation. In the case of products that are subject to legal controls on exportation, appropriate arrangements must be made by the national drug regulatory authority to ensure due compliance with customs requirements.

Analytical results

All analyses undertaken by a laboratory should be in accordance with the specified pharmacopoeial or other specifications mentioned in the request for analysis, or as subsequently agreed (see Annex 3). If requested, results of the analyses can be transmitted by facsimile or other means (e.g. electronic mail), and confirmed with a detailed signed report. The report should be in the working language of the laboratory, or as agreed between the parties (see Annex 3).

References

1. Guidelines for implementation of the WHO Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce. In: *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Thirty-fourth report*. Geneva, World Health Organization, 1996, Annex 10 (WHO Technical Report Series, No. 863).

2. Good manufacturing practices for pharmaceutical products. In: *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Thirty-second*

report. Geneva, World Health Organization, 1992, Annex 2 (WHO Technical Report Series, No. 823).

3. *The international pharmacopoeia*, 3rd ed. *Vol. 4. Tests, methods, and general requirements. Quality specifications for pharmaceutical substances, excipients, and dosage forms*. Geneva, World Health Organization, 1994.
4. Sampling procedure for industrially manufactured pharmaceuticals. In: *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Thirty-first report*. Geneva, World Health Organization, 1990, Annex 2 (WHO Technical Report Series, No. 790).