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Traditional Chinese Medicine — General requirements for herbal raw material and materia medica

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Foreword

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The procedures used to develop this document and those intended for its further maintenance are described in the ISO/IEC Directives, Part 1. In particular, the different approval criteria needed for the different types of ISO documents should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2 (see www.iso.org/directives).

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For an explanation of the voluntary nature of standards, the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the World Trade Organization (WTO) principles in the Technical Barriers to Trade (TBT), see www.iso.org/iso/foreword.html.

This document was prepared by Technical Committee ISO/TC 249, *Traditional Chinese medicine.*

Any feedback or questions on this document should be directed to the user's national standards body. A complete listing of these bodies can be found at www.iso.org/members.html.

Introduction

At present, Chinese herbal medicine, as an important component of traditional Chinese medicine, has been widely used in many countries because of its high value to human health and huge market. The annual sale of Chinese herbal medicine has reached more than USD 16 billion and is increasing at a rate of 10 % to 20 % per year with great future potential. Such great opportunities for trade call for international standards specifying the requirements for herbal medicine, in order to ensure their quality and safety, and to avoid misuses due to varietal complexity, harmful foreign matters, and adverse drug reactions (ADR).

There are specific standards for important species, such as ISO 20409:2017 for *Panax notoginseng* root and rhizome. However, it is impractical to develop one-on-one standards for thousands of species of herbal medicine used in TCM in the different traditions and regions. It is wiser to develop one international standard of general requirements for herbal medicine, because herbal medicines have many aspects in common.

The purpose of this document is to:

1) provide a standard for the species not covered in the existing ISO individual standards for single species of herbal medicine;

2) be used as an outline and reference for ISO individual standards for single species of herbal medicine

The principles that were followed in preparing the standard are:

1) cover all general requirements of herbal medicine recorded by national, regional and organizational pharmacopoeia, such as the *Pharmacopoeia of the People's Republic of China*, the *Japanese Pharmacopoeia*, the *Korean Pharmacopoeia*, the *European Pharmacopoeia*;

2) distill the common characters of herbal medicine and formulate general requirements;

3) fully consider and respect the testing method and specific requirements on national or regional pharmacopoeias, legislation and norms.

As national implementation may differ, National Standards Bodies are invited to modify the limit values of 5.3.1, 5.3.2, 5.4.1, 5.4.2, 6.1.1, 6.1.2, 6.1.3, 6.1.4, 6.1.5, 6.1.6, 6.2.1, 6.2.2, 6.2.3, 6.2.4, and 6.2.5 in their national standards. Examples of national and regional values are given in Annex A.1. The limit value should refer to the requirements of the regulatory bodies of the destination country or region. If there is none, the limit value listed in relevant ISO standards, such as ISO 18664, ISO 1573, *et al* or one of the national or regional pharmacopoeias, such the *Pharmacopoeia of the People's Republic of China*, the *European Pharmacopoeia*, *et al* shall be chosen and the given method shall be applied.

Traditional Chinese Medicine –General requirements for herbal raw material and materia medica

1 Scope

This document specifies the general requirements and test methods for herbal raw material and materia medica.

This document is applicable to provide minimum requirements for those herbal materials that are not covered by individual standards. This document is applicable to developing the documents of herbal raw materials, too.

2 Normative references

The following documents are referred to in the text in such a way that some or all of their content constitutes requirements of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 1573, Tea - *Determination of loss in mass at 103 degrees C*

ISO 1575, *Tea - Determination of total ash*

ISO 1577, *Tea - Determination of acid-insoluble ash*

ISO 18664, *Traditional Chinese Medicine -- Determination of heavy metals in herbal medicines used in Traditional Chinese Medicine*

ISO 21371, *Traditional Chinese medicine -- Labelling requirements of products intended for oral or topical use*

ISO/DIS 19609-2, *Traditional Chinese medicine -- Quality and safety of natural materials and manufacturing products made with natural materials -- Part 2: Identity testing*

ISO/DTS 21310, *Traditional Chinese medicine -- Microscopic examination on medicinal herbs*

ISO/FDIS 22217, *Traditional Chinese medicine --Storage requirements for raw materials and decoction pieces*

ISO/FDIS 22258, *Traditional Chinese medicine- Determination of pesticide residues in natural products by GC*

ISO/FDIS 22283, *Traditional Chinese medicine -- Determination of Aflatoxins in natural products by LC-FLD*

ISO/DIS 22467, *Traditional Chinese Medicine- Determination of microorganism in natural products*

ISO/FDIS 22590, *Traditional Chinese medicine- Determination of Sulfur Dioxide in natural products by titration*

ISO/DIS 23190, *Traditional Chinese medicine – Determination of aristolochic acids in natural products by HPLC*

ISO/FDIS 23191, *Traditional Chinese Medicine – Determination of selected Aconitum alkaloids by HPLC*

World Health Organization: *Quality control methods for herbal materials*.

3 Terms and definitions

For the purposes of this document, the following terms and definitions apply.

ISO and IEC maintain terminological databases for use in standardization at the following addresses:

— ISO Online browsing platform: available at https://www.iso.org/obp

— IEC Electropedia: available at http://www.electropedia.org/

3.1
Chinese Materia Medica (CMM)
medicinal parts of medicinal plants, animals and minerals after preliminary processing, which are used in TCM as decoction pieces and raw materials to make decoction pieces

Note 1 to entry: The different nomenclatures of the Chinese Materia Medica in use are described as follows:

— Latin name: Latin pharmaceutical name of the Chinese Materia Medica. In the Latin name, the genus name or genus name plus species name is followed by the applicable medicinal parts. Items are listed in alphabetical order of the Latin name for easy and convenient search.

— Chinese name: Han (Chinese) character name of the Chinese Materia Medica. Han characters include both the simplified character and the traditional character, which is given in parentheses.

— Pinyin name: Pinyin name (Chinese phonetic) of the Chinese Materia Medica. The “four tones” have been added in Pinyin to facilitate practice by users. Pinyin syllabication (in parentheses) is provided to facilitate correct pronunciation.

— Scientific name: Latin scientific name of the source of the Chinese Materia Medica.

— English name: Commonly used English name of the Chinese Materia Medica.

[SOURCE: ISO 18662-1, 3.1]

3.2
Foreign matters
non-medicinal parts or components which may be carried or mixed in herbal raw material and materia medica, such as material consisting of any or all of the following:

— parts of the herbal material or materials other than those named with the limits specified for the herbal material concerned;

— any organism, part or product of an organism, other than that named in the specification and description of the herbal material concerned;

— mineral admixtures such as soil, stones, sand, and dust; and glass, metal and plastics or any other extraneous materials. These may be loose or adhering to these herbal materials.

4 General principle

For the single herbs with existing ISO standards, the confirmative assessment shall refer to their existing ISO standard.

For the single herbs without existing ISO standards, the confirmative assessment shall refer to this standard.

For the single herbs with existing ISO standards, but some requirements were not specified in these ISO standards, the confirmative assessment should refer to this standard as well.

5 Recommended requirements for all CMM

5.1 General

The presence of moldy plant material, obvious deterioration of physical appearance, external contaminants and living insects which are visible to the naked eye shall not be permitted.

The presence of moldy smell or taste shall not be permitted.

5.2 Identification

The identify shall be authenticated based on

— macroscopic features of the whole or/and fragmented material, or

— microscopic features of the powdered material, or

— a TLC or HPLC fingerprint to verify the presence of characteristic compounds, and, where applicable, to exclude characteristic compounds of known adulterations

5.3 Quality requirements

5.3.1 Moisture and loss of drying

The contents of water or loss of drying shall be determined.

5.3.2 Foreign matters

The percentage and nature of foreign matters shall be determined.

5.4 Safety requirements

5.4.1 Heavy metals and arsenic

The contents of lead, cadmium, mercury, and arsenic shall be determined.

5.4.2 Pesticide residues

The contents of pesticide residues listed in ISO/FDIS 22258 shall be determined.

6 Requirements for specific CMM

6.1 Quality requirements

6.1.1 Total ash and acid-insoluble ash

To limit the content of inorganic impurities (such as clay and sand) in herbal material, the content of total ash and acid insoluble ash can be determined.

6.1.2 Assay

For some specific materials that contain chemical substance(s) that serve as marker compounds, an assay can be applied.

6.1.3 Extractives

For some specific materials, the content of water-soluble extractive, ethanol-soluble extractive, or ether-soluble extractives can be determined.

6.1.4 Essential oil

For some specific materials containing volatile oils, the content of essential oil can be determined.

6.1.5 Rancidity

For some specific materials containing volatile oils or fatty oils which are liable to become rancid, rancidity can be determined.

6.1.6 Degree of colouration

For some specific materials containing volatile oils or fatty oils which are liable to get oil extravasation, degree of colouration can be determined.

6.2 Safety requirements

6.2.1 Sulfur dioxide residues

For some specific materials where the contamination with sulfur dioxide is a known safety issue, sulfur dioxide can be determined.

6.2.2 Aflatoxins

For some specific materials where the contamination with aflatoxins is known as safety issue, aflatoxin B_1 and total aflatoxins can be determined according to ISO/FDIS 22283.

6.2.3 Aristolochic acids

For some specific materials originated from the *Aristolochia* genus, aristolochic acids can be determined according to ISO/DIS 23190.

6.2.4 Aconitum alkaloids

For some specific materials originated from the Aconitum genus, aconitum alkaloids shall be determined according to ISO/FDIS 23191.

6.2.5 Microbial contamination

For some specific materials where the contamination with microorganism is a known safety issue, microbial contamination shall be determined.

7 Methods

7.1 Identification

7.1.1 Macroscopic identification

Macroscopic identification includes shape, size, color, texture, odour and taste of herbal material. Perform macroscopic identification according to ISO/DIS 19609-2.

7.1.2 Microscopic identification

The testing method specified ISO/DTS 21310 applies.

7.1.3 TLC identification and HPLC identification

The testing method specified in monographs of existing national or regional pharmacopoeias applies, such as Chinese Pharmacopeia, Japanese Pharmacopeia, Korea Pharmacopeia and European Pharmacopeia.

7.2 Quality tests

7.2.1 Moisture and loss of drying

The testing method of water content specified in World Health Organization: *Quality Control Methods for Herbal Materials* applies.

The testing method of loss of drying specified in ISO 1573 applies.

7.2.2 Foreign matters

Weigh a quantity of the substance to be examined and spread it out in a thin layer. Examine for foreign matter by inspection with the unaided eye or by use of a lens (5×-10×). To separate the foreign matter, a suitable sieve can be used if necessary. Weigh separately each kind of foreign matter and calculate its percentage content.

NOTE1 When the foreign matters closely resemble the official drug and difficult to distinguish them, it may be necessary to use either microscopical, chemical or physical method to identify the foreign matters.

NOTE 2 Cut the big crude drugs and examine for the occurrence of insects, moulds and deterioration.

NOTE 3 Unless otherwise specified, the quantity of substance to be examined for the determination of foreign matter is accordant with requirement of sampling of crude drugs.

7.2.3 Total ash and acid-insoluble ash

The testing methods specified in ISO 1575 and ISO 1577 applies, respectively.

7.2.4 Assay

For chemical characterization, an assay may be suitable if methods and technologies are available for example in monographs of existing national or regional pharmacopoeias. When the method of a certain pharmacopoeia is chosen, the limit value of that pharmacopoeia monograph shall apply.

7.2.5 Extractives

Extractives include water-soluble extractives, ethanol-soluble extractives, and ether-soluble extractives. The testing methods specified in World Health Organization: *Quality Control Methods for Herbal Materials* applies.

7.2.6 Essential oil

Weigh the quantity of the test sample for analysis in a 1-L hard glass-stoppered flask, and add from 5 to 10 times as much water as the drug. Set up an apparatus for essential oil determination (Fig. 1), inserting the left lower mouth of it (1) to the flask and inserting a reflux condenser in the upper mouth of it (2), and heat the content of the flask in an oil bath between 130℃ and 150℃ to boiling. The graduated tube of the apparatus is to be previously filled with water to the standard line (3), and 2.0 mL of xylene is added to the graduated tube. Unless otherwise specified, continue boiling for 5 hours, allow to stand for some time, and open the stopper of the apparatus. Draw off the water slowly until the surface of the oil layer corresponds to the preparation line (4), and allow it to stand for more than 1 hour at ordinary temperature. Then lower the surface of the oil layer to the zero line, and read the volume (mL) of the oil at ordinary temperature. Subtract the volume (mL) of xylene from the volume of the total oil.

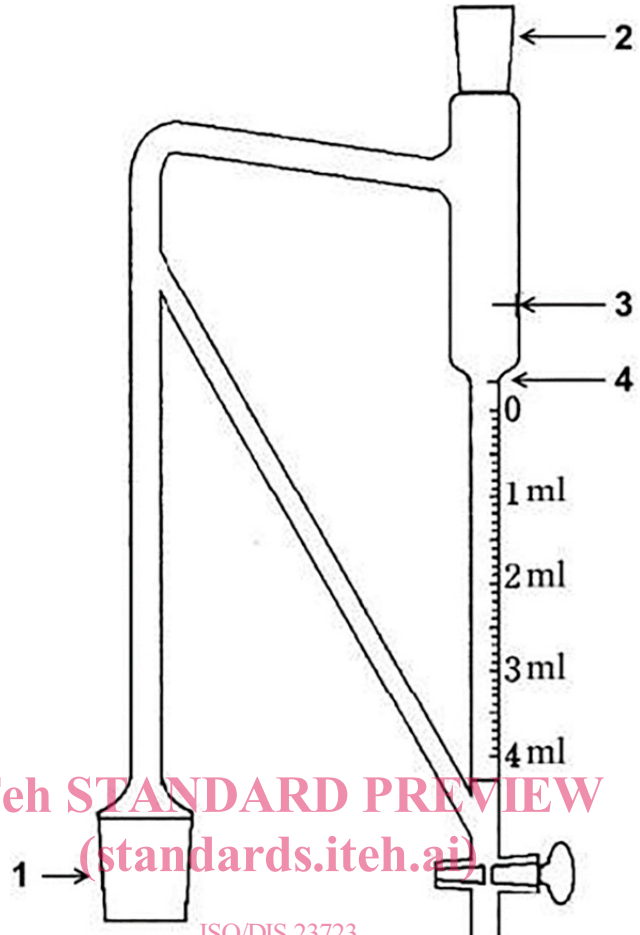

Fig. 1. An apparatus for essential oil determination

Keys

1 left lower mouth

2 upper mouth

3 standard line

4 preparation line

7.2.7 Rancidity

The testing method specified in World Health Organization: *Quality Control Methods for Herbal Materials* applies.

7.2.8 Degree of colouration

Rancidity includes acid value, peroxide value, and carbonyl value. The testing method specified in World Health Organization: *Quality Control Methods for Herbal Materials* applies.

7.3 Safety test

7.3.1 Heavy metal and arsenic

The testing method specified in ISO 18664 applies.

7.3.2 Pesticide residues

The testing method specified in ISO/FDIS 22258 applies.

7.3.3 Sulfur dioxide residues

The testing method specified in ISO/FDIS 22590 applies.

7.3.4 Aflatoxins

The testing method specified in ISO/FDIS 22283 applies.

7.3.5 Aristolochic acids

The testing method specified in ISO/DIS 23190 applies.

7.3.6 Aconitum alkaloids

The testing method specified in ISO/FDIS 23191 applies.

7.3.7 Microbial contamination

The testing method specified in ISO/DIS 22467 applies.

8 Sampling

Sampling shall be carried out in accordance with the method described in the World Health Organization: *Quality Control Methods for Herbal Materials*. Sampling shall be conducted in terms of the following steps:

a) from a batch of five containers or packaging units, take a sample from each one;

b) from a batch of 6–50 units, take a sample from five;

c) from a batch of over 50 units, sample 10%, rounding up the number of units to the nearest multiple of 10. For example, a batch of 51 units would be sampled as for 60 — i.e. take samples from six packages;

d) from each container or package selected, take three original samples from the top, middle and bottom of the container or package;

e) the three original samples shall then be combined into a pooled sample which shall be mixed carefully;

f) the average sample is obtained by quartering:

- from the pooled sample, adequately mixed into an even and square-shaped heap;
- divide it diagonally into four equal parts;
- take two diagonally opposite parts and mix carefully.
- repeat the process as necessary until the required quantity, to within ± 10%, is obtained;

g) using the same quartering procedure, divide the average sample into four final samples, taking care that each portion is representative of the bulk material;

h) the final samples are used for the tests, measurements and analyses.

9 Test report

For each test method, the test report shall specify the following:

a) all information necessary for the complete identification of the sample;

b) the sampling method used;

c) the test method used, with reference to this international standard;

d) the test result(s) obtained;

e) all operating details not specified in this international standard, or regarded as optional, together with details of any incidents which may have influenced the test result(s);

f) any unusual features (anomalies) observed during the test;

g) the date of the test.

10 Packaging

The packaging and transportation shall not transmit any odour or flavour to the product and shall not contain substances which may damage the product or constitute a health risk. The packaging shall be strong enough to withstand normal handling and transportation.

11 Labelling

See the label content specified in ISO 21371. The following items shall be marked or labeled on the packages:

a) all quality features indicated in 4, determined in accordance with methods specified in 5;

b) gross weight and net weight of the package;

c) country of origin and province / state of the products;

d) date of production and expiry date of the products;

e) storage method;

any items required by regulatory bodies of destination country.

12 Storage and transportation

The requirements given in ISO/FDIS 22217 shall be applied.