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Traditional Chinese medicine — General requirements for the manufacturing process of natural products

Médecine traditionnelle chinoise — Exigences générales relatives au procédé de fabrication des produits naturels

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Foreword

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For an explanation on 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 the following URL: www.iso.org/iso/foreword.html.

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

Introduction

Natural products used in traditional Chinese medicine (TCM) are manufactured from materials of natural origin, the quality of which is varied according to geographical, climatic and seasonal conditions. For quality assurance of final products, quality evaluation on starting materials for natural products used in TCM is essential. On the other hand, it is also important to handle these natural materials appropriately and to control manufacturing processes for natural products used in TCM.

The management of manufacturing processes under good manufacturing practice (GMP) is indispensable to ensure quality of medicinal products. International GMP was issued by World Health Organization (WHO) in 1967, and a number of regional and international GMPs have subsequently been established. Recently, Pharmaceutical Inspection Convention (PIC)/Pharmaceutical Inspection Cooperation Scheme (PIC/S) has been widely applied around the world. At present, two-thirds of the member bodies of ISO/TC 249 are affiliated with PIC/S and some other countries are waiting for review of their applications.

These general GMPs were extensively applied to different fields and complimented with special supplements for herbal medicines in some countries and organizations. However, these herbal GMPs are focusing on European herbal medicines, but not covering those in the East Asian regions such as China, Japan and Korea where traditional medicines are used.

The current herbal GMPs of WHO, EU or PIC/S are mainly based on single herbal products, and the products consisting of more than one herbs were stipulated as special cases. However, multi-herbal products are more common than single-herbal products in the East Asian regions. In addition, raw materials in herbal GMPs of WHO, EU or PIC/S are only exclusive for plant origin, while traditional medicines in East Asia also include animal and mineral materials. In order to use correct materials, it is important to identify the starting materials not only by physical/chemical examinations but also by perceptive identification by well-trained experts. However, the requirement for experts on natural materials are not described in these international herbal GMPs. For a better safety and quality control of TCM products, conventional GMPs for the manufacturing of herbal medicines are in need of improving by this proposed standard.

Therefore, based on Chinese, Japanese and Korean herbal GMPs, and with reference to international GMPs, this document specifies general requirements for manufacturing processes that are particularly applied to natural products used in TCM. Implementation of this document with conventional GMPs for general pharmaceutical products would make it possible for manufacturers to ensure the safety and quality of natural products used in TCM, and at the same time prevent people in countries where such products are used from health hazards caused by poor quality products as well as improving their health. It will allow people to enjoy the benefits of natural products used in TCM for treatments of diseases as well as promoting health. This document will also allow non-PIC/S member countries to request quality assurance of the products to manufacturers and manufacturing countries with reference to this document. Finally, this document will make it possible to complement and/or amend WHO, EU and PIC/S herbal GMPs.

Traditional Chinese medicine — General requirements for the manufacturing process of natural products

1 Scope

This document specifies the general requirements for manufacturing processes to ensure the quality of finished products used in traditional Chinese medicine (TCM). This document covers premises, documentation, personnel, training, manufacturing control and quality control. This document applies to the manufacturing of natural products used in and as TCM.

This document does not conflict with general pharmaceutical good manufacturing practices (GMPs).

This document applies to all materials of natural origin: medicinal plants, medicinal animals, medicinal minerals, crude drugs or crude drug preparations.

2 Normative references

There are no normative references in this document.

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 http://www.iso.org/obp

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

NOTE Traditional Chinese medicines include various types of items. The same material can be classified in different categories (e.g. a powdered plant material can be both a crude herbal drug and a crude herbal drug preparation or, in a packed form, a traditional Chinese medicinal product).

3.1
active ingredient
crude drug(s) or the crude drug preparation(s) of a traditional Chinese medicine(s)

[SOURCE: WHO guidelines on good manufacturing practices (GMP) for herbal medicines, modified]

3.2
constituent of known therapeutic activity
substance or group of substances that is chemically defined and known to contribute to the therapeutic activity of a crude drug or of a preparation

[SOURCE: WHO guidelines on good manufacturing practices (GMP) for herbal medicines, modified]

3.3
marker substance
chemically defined constituent of a crude drug utilized for control purposes

Note 1 to entry: Marker substances contribute or not to the clinical efficacy. When they contribute to the clinical efficacy, however, evidence that they are solely responsible for the clinical efficacy can be available or not.

Note 2 to entry: Marker substances are generally employed when constituents of known therapeutic activity are not known or are not clearly identified, and are used to identify the crude drug or preparation or calculate their quantity in the finished product.

[SOURCE: WHO guidelines on good manufacturing practices (GMP) for herbal medicines, modified]

3.4
medicinal animal
animal (wild or bred) used for medicinal purposes

3.5
medicinal mineral
mineral used for medicinal purposes

3.6
medicinal plant
plant (wild or cultivated) used for medicinal purposes

Note 1 to entry: Medicinal plants include crude drugs which could be derived from lichen, algae, fungi or higher plants, such as leaves, flowers, fruit, fruiting bodies, seeds, stems, wood, bark, roots, rhizomes or other parts, which are entire, fragmented or powdered.

[SOURCE: WHO guidelines on good manufacturing practices (GMP) for herbal medicines, modified]

3.7
bulk product
product that has completed all processing stages up to, but not including, final packaging

[SOURCE: WHO good manufacturing practices for pharmaceutical products: main principles, modified]

3.8
crude drug
medicinal part obtained from plants or animals, cell inclusions and secretions separated from the origins, their extracts, and minerals

Note 1 to entry: Herbal materials include, in addition to medicinal parts, fresh juices, gums, fixed oils, essential oils, resins and dry powders of herbs.

Note 2 to entry: In some countries, these materials are processed by various local procedures, such as steaming, roasting or stir-baking with honey, alcoholic beverages or other materials.

3.9
crude drug preparation
basis for finished traditional medicinal products that may include comminuted or cut crude drugs, or extracts, tinctures and fatty oils of crude drugs

Note 1 to entry: Crude drug preparations are produced by extraction, fractionation, purification, concentration, or other physical or biological processes. They also include preparations made by steeping or heating crude drugs in alcoholic beverages and/or honey, or in other materials.

3.10
extract
preparation of liquid (liquid extracts and tinctures), semi-solid (soft extracts and oleoresins) or solid (dry extracts) consistency, obtained from medicinal plants, animals and minerals

3.11
finished product
finished dosage form that has undergone all stages of manufacture, including packaging in its final container and labelling

Note 1 to entry: Natural products in this document includes finished products made from one or more crude drugs.

[SOURCE: WHO good manufacturing practices for pharmaceutical products: main principles, modified]

3.12
finished traditional Chinese medicinal product
product consisting of crude drug preparations made from one or more crude drugs

Note 1 to entry: If more than one crude drug is used, the term “mixture crude drugs product” can also be used.

Note 2 to entry: Finished traditional Chinese medicinal products and mixture crude drugs products contain excipients in addition to the active ingredients. However, finished traditional Chinese medicinal products or mixture crude drugs products to which chemically defined active substances have been added, including synthetic compounds and/or isolated constituents from crude drugs, are not considered to be crude drug products.

3.13
material of natural origin
medicinal plant, animal or mineral

3.14
pharmaceutical product
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

Note 1 to entry: It is subject to control by pharmaceutical legislation in the exporting state and/or the importing state.

[SOURCE: WHO good manufacturing practices for pharmaceutical products: main principles, modified]

3.15
starting material
substance of a defined quality used in the production of a pharmaceutical product, but excluding packaging materials

[SOURCE: WHO good manufacturing practices for pharmaceutical products: main principles, modified]

3.16
manufacture
operations of purchase of materials and products, production, quality control, release and storage of pharmaceutical products, and the related controls

[SOURCE: WHO good manufacturing practices for pharmaceutical products: main principles, modified]

3.17
manufacturer
company that carries out operations such as production, packaging, repackaging, labelling and relabelling of pharmaceuticals

[SOURCE: WHO good manufacturing practices for pharmaceutical products: main principles, modified]

3.18
blending
process of combining materials or different batches to produce a homogeneous intermediate or finished product

[SOURCE: WHO guidelines on good manufacturing practices (GMP) for herbal medicines, modified]

3.19
packaging
operations, including filling and labelling, that a bulk product has to undergo in order to become a finished product

Note 1 to entry: Filling of a sterile product under aseptic conditions or a product intended to be terminally sterilized would not normally be regarded as part of packaging.

[SOURCE: WHO good manufacturing practices for pharmaceutical products: main principles, modified]

3.20
production
operations involved in the preparation of a pharmaceutical product, from receipt of materials, through processing, packaging and repackaging, labelling and relabelling, to completion of the finished product

[SOURCE: WHO good manufacturing practices for pharmaceutical products: main principles, modified]

3.21
qualification
action of proving that any premises, systems and items of equipment work correctly and actually lead to the expected results

Note 1 to entry: The meaning of the word "validation" is sometimes extended to incorporate the concept of qualification.

[SOURCE: WHO good manufacturing practices for pharmaceutical products: main principles, modified]

3.22
quality assurance
concept covering all matters that individually or collectively influence the quality of a product

Note 1 to entry: It is the totality of the arrangements made with the object of ensuring that pharmaceutical products are of the quality required for their intended use. Quality assurance therefore incorporates GMP and other factors, including those outside the scope of this guide such as product design and development.

Note 2 to entry: Information on manufacturing control and quality control are provided in Annex A and B, respectively.

[SOURCE: WHO good manufacturing practices for pharmaceutical products: main principles, modified]

3.23
quarantine
physical or other effective means of isolation implemented while a decision is awaited on the release, rejection or reprocessing of starting or packaging materials, intermediates or bulk or finished products

[SOURCE: WHO good manufacturing practices for pharmaceutical products: main principles, modified]

3.24
specification
list of detailed requirements with which the products or materials used or obtained during manufacture have to conform

Note 1 to entry: They serve as a basis for quality evaluation.

[SOURCE: WHO good manufacturing practices for pharmaceutical products: main principles, modified]

3.25
validation
action of proving, in accordance with the principles of GMP, that any procedure, process, equipment, material, activity or system actually leads to the expected results

Note 1 to entry: See also *qualification* (3.21).

[SOURCE: WHO good manufacturing practices for pharmaceutical products: main principles, modified]

3.26
packaging material
material, including printed material, employed in the packaging of a pharmaceutical, but excluding any outer packaging used for transportation or shipment

Note 1 to entry: Packaging materials are referred to as primary or secondary according to whether or not they are intended to be in direct contact with the product.

[SOURCE: WHO good manufacturing practices for pharmaceutical products: main principles, modified]

3.27
contamination
undesired introduction of impurities of a chemical or microbiological nature, or of foreign matter, into or on to a starting material or intermediate during production, sampling, packaging or repackaging, storage or transport

[SOURCE: WHO good manufacturing practices for pharmaceutical products: main principles, modified]

3.28
cross-contamination
contamination of a starting material, intermediate product or finished product with another starting material or product during production

[SOURCE: WHO good manufacturing practices for pharmaceutical products: main principles, modified]

3.29
clean area
area with defined environmental control of particulate and microbial contamination, constructed and used in such a way as to reduce the introduction, generation, and retention of contaminants within the area

[SOURCE: WHO good manufacturing practices for pharmaceutical products: main principles, modified]

3.30
batch
lot

defined quantity of starting material, packaging material, or product that are processed in a single process or series of processes so that it is expected to be homogeneous

Note 1 to entry: It is sometimes necessary to divide a batch into a number of sub-batches, which are later brought together to form a final homogeneous batch.

Note 2 to entry: In the case of terminal sterilization, the batch size is determined by the capacity of the autoclave. In continuous manufacture, the batch corresponds to a defined fraction of the production, characterized by its intended homogeneity.

Note 3 to entry: The batch size can be defined either as a fixed quantity or as the amount produced in a fixed time interval.

[SOURCE: WHO good manufacturing practices for pharmaceutical products: main principles, modified]

3.31
consignment
delivery
quantity of a pharmaceutical(s), made by one manufacturer and supplied at one time in response to a particular request or order

Note 1 to entry: A consignment comprises one or more packages or containers and includes material belonging to more than one batch.

[SOURCE: WHO good manufacturing practices for pharmaceutical products: main principles, modified]