INTERNATIONAL STANDARD

ISO 15378

Second edition
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Primary packaging materials for medicinal products — Particular requirements for the application of ISO 9001:2008, with reference to Good Manufacturing Practice (GMP)

Articles de conditionnement primaire pour médicaments — Exigences particulières pour l'application de l'ISO 9001:2008 prenant en considération les Bonnes Pratiques de Fabrication (BPF)

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Foreword

ISO (the International Organization for Standardization) is a worldwide federation of national standards bodies (ISO member bodies). The work of preparing International Standards is normally carried out through ISO technical committees. Each member body interested in a subject for which a technical committee has been established has the right to be represented on that committee. International organizations, governmental and non-governmental, in liaison with ISO, also take part in the work. ISO collaborates closely with the International Electrotechnical Commission (IEC) on all matters of electrotechnical standardization.

International Standards are drafted in accordance with the rules given in the ISO/IEC Directives, Part 2.

The main task of technical committees is to prepare International Standards. Draft International Standards adopted by the technical committees are circulated to the member bodies for voting. Publication as an International Standard requires approval by at least 75 % of the member bodies casting a vote.

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights.

ISO 15378 was prepared by Technical Committee ISO/TC 76, *Transfusion, infusion and injection, and blood processing equipment for medical and pharmaceutical use.*

This second edition cancels and replaces the first edition (ISO 15378:2006), which has undergone a minor revision to adapt this International Standard to ISO 9001:2008 and update references.

Introduction

0.1 General

This International Standard identifies Good Manufacturing Practice (GMP) principles and specifies requirements for a quality management system applicable to primary packaging materials for medicinal products. The realization of GMP principles in production and control of primary packaging materials within organizations is of great importance for the safety of a patient using the medicinal product, because of their direct product contact. The application of GMP for pharmaceutical packaging materials helps ensure that these materials meet the needs and requirements of the pharmaceutical industry.

This International Standard is an application standard for primary packaging materials, which contains the normative text of ISO 9001:2008.

The conventions for the layout of this International Standard are the following.

— *Those clauses or subclauses that are quoted directly and unchanged from ISO 9001:2008 are in boxed text.*

— *Texts in italics contain additional relevant GMP information regarding primary packaging materials.*

GMP terms and definitions are included in Clause 3. If listed, the source is referred to in brackets.

ISO 9001:2008, Quality management systems — Requirements

0.1 General

The adoption of a quality management system should be a strategic decision of an organization. The design and implementation of an organization's quality management system is influenced by

a) its organizational environment, changes in that environment, and the risks associated with that environment,

b) its varying needs,

c) its particular objectives,

d) the products it provides,

e) the processes it employs,

f) its size and organizational structure.

It is not the intent of this International Standard to imply uniformity in the structure of quality management systems or uniformity of documentation.

The quality management system requirements specified in this International Standard are complementary to requirements for products. Information marked "NOTE" is for guidance in understanding or clarifying the associated requirement.

This International Standard can be used by internal and external parties, including certification bodies, to assess the organization's ability to meet customer, statutory and regulatory requirements applicable to the product, and the organization's own requirements.

The quality management principles stated in ISO 9000 and ISO 9004 have been taken into consideration during the development of this International Standard.

A key objective of this International Standard is to define harmonized primary packaging material requirements. It includes some particular requirements for primary packaging materials, which are derived from Good Manufacturing Practices for the production, control, etc. of medicinal products.

0.2 Process approach

ISO 9001:2008, Quality management systems — Requirements

0.2 Process approach

This International Standard promotes the adoption of a process approach when developing, implementing and improving the effectiveness of a quality management system, to enhance customer satisfaction by meeting customer requirements.

For an organization to function effectively, it has to determine and manage numerous linked activities. An activity or set of activities using resources, and managed in order to enable the transformation of inputs into outputs, can be considered a process. Often the output from one process directly forms the input to the next.

The application of a system of processes within an organization, together with the identification and interactions of these processes, and their management to produce the desired outcome, can be referred to as the “process approach”.

An advantage of the process approach is the ongoing control that it provides over the linkage between the individual processes within the system of processes, as well as over their combination and interaction.

When used within a quality management system, such an approach emphasizes the importance of

a) understanding and meeting requirements,

b) the need to consider processes in terms of added value,

c) obtaining results of process performance and effectiveness, and

d) continual improvement of processes based on objective measurement.

The model of a process-based quality management system shown in Figure 1 illustrates the process linkages presented in Clauses 4 to 8. This illustration shows that customers play a significant role in defining requirements as inputs. Monitoring of customer satisfaction requires the evaluation of information relating to customer perception as to whether the organization has met the customer requirements. The model shown in Figure 1 covers all the requirements of this International Standard, but does not show processes at a detailed level.

NOTE In addition, the methodology known as “Plan-Do-Check-Act” (PDCA) can be applied to all processes. PDCA can be briefly described as follows.

Plan: establish the objectives and processes necessary to deliver results in accordance with customer requirements and the organization's policies.

Do: implement the processes.

Check: monitor and measure processes and product against policies, objectives and requirements for the product and report the results.

Act: take actions to continually improve process performance.

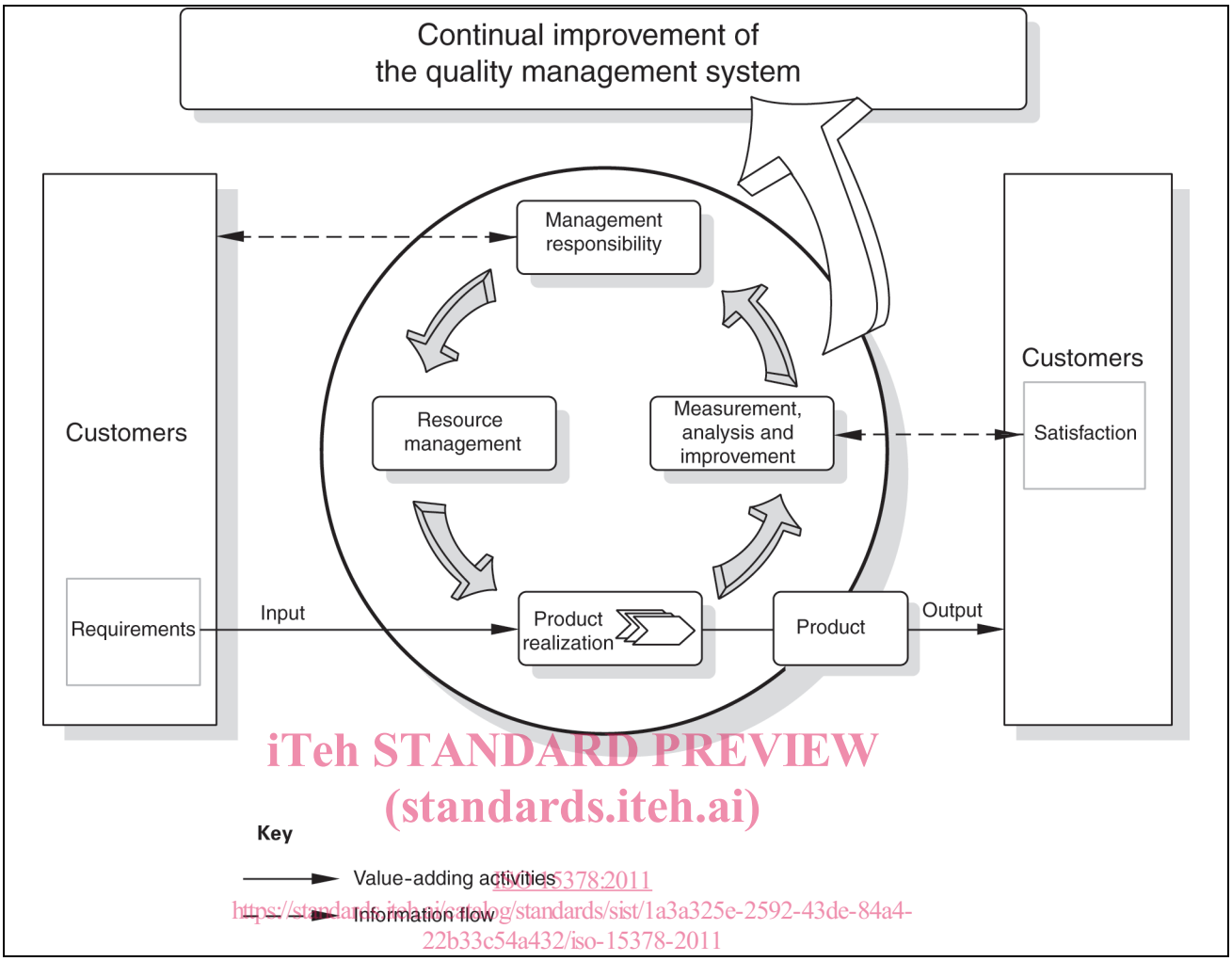

Figure 1 — Model of a process-based quality management system

0.3 Relationship with ISO 9004

ISO 9001:2008, Quality management systems — Requirements

0.3 Relationship with ISO 9004

ISO 9001 and ISO 9004 are quality management system standards which have been designed to complement each other, but can also be used independently.

ISO 9001 specifies requirements for a quality management system that can be used for internal application by organizations, or for certification, or for contractual purposes. It focuses on the effectiveness of the quality management system in meeting customer requirements.

At the time of publication of this International Standard, ISO 9004 is under revision. The revised edition of ISO 9004 will provide guidance to management for achieving sustained success for any organization in a complex, demanding, and ever changing, environment. ISO 9004 provides a wider focus on quality management than ISO 9001; it addresses the needs and expectations of all interested parties and their satisfaction, by the systematic and continual improvement of the organization's performance. However, it is not intended for certification, regulatory or contractual use.

0.4 Compatibility with other management systems

This International Standard incorporates the requirements of ISO 9001:2008 and, additionally, particular requirements for primary packaging materials, which are derived and adapted, as appropriate, from Good Manufacturing Practices for the production and control of medicinal products.

ISO 9001:2008, Quality management systems — Requirements

0.4 Compatibility with other management systems

During the development of this International Standard, due consideration was given to the provisions of ISO 14001:2004 to enhance the compatibility of the two standards for the benefit of the user community. Annex A shows the correspondence between ISO 9001:2008 and ISO 14001:2004.

This International Standard does not include requirements specific to other management systems, such as those particular to environmental management, occupational health and safety management, financial management or risk management. However, this International Standard enables an organization to align or integrate its own quality management system with related management system requirements. It is possible for an organization to adapt its existing management system(s) in order to establish a quality management system that complies with the requirements of this International Standard.

Primary packaging materials for medicinal products — Particular requirements for the application of ISO 9001:2008, with reference to Good Manufacturing Practice (GMP)

1 Scope

1.1 General

This International Standard specifies requirements for a quality management system where an organization needs to demonstrate its ability to provide primary packaging materials for medicinal products, which consistently meet customer requirements, including regulatory requirements and International Standards applicable to primary packaging materials.

In this International Standard the term "if appropriate" is used several times. When a requirement is qualified by this phrase, it is deemed to be "appropriate" unless the organization can document a justification otherwise.

ISO 9001:2008, Quality management systems — Requirements

1.1 General

This International Standard specifies requirements for a quality management system where an organization

a) needs to demonstrate its ability to consistently provide product that meets customer and applicable statutory and regulatory requirements, and

b) aims to enhance customer satisfaction through the effective application of the system, including processes for continual improvement of the system and the assurance of conformity to customer and applicable statutory and regulatory requirements.

NOTE 1 In this International Standard, the term "product" only applies to

a) product intended for, or required by, a customer,

b) any intended output resulting from the product realization processes.

NOTE 2 Statutory and regulatory requirements can be expressed as legal requirements.

1.2 Application

This International Standard is an application standard for the design, manufacture and supply of primary packaging materials for medicinal products. It is also applicable for certification purposes.

ISO 9001:2008, Quality management systems — Requirements

1.2 Application

All requirements of this International Standard are generic and are intended to be applicable to all organizations, regardless of type, size and product provided.

Where any requirement(s) of this International Standard cannot be applied due to the nature of an organization and its product, this can be considered for exclusion.

Where exclusions are made, claims of conformity to this International Standard are not acceptable unless these exclusions are limited to requirements within Clause 7, and such exclusions do not affect the organization's ability, or responsibility, to provide product that meets customer and applicable statutory and regulatory requirements.

2 Normative references

The following referenced documents are indispensable for the application 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 9001:2008, Quality management systems — Requirements

2 Normative references

The following referenced documents are indispensable for the application 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 9000:2005, *Quality management systems — Fundamentals and vocabulary*

ISO 14644-1:— [1], *Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration*

ISO 14644-2, Cleanrooms and associated controlled environments — Part 2: Specifications for monitoring and periodic testing to prove continued compliance with ISO 14644-1

ISO 14644-3, *Cleanrooms and associated controlled environments — Part 3: Test methods*

ISO 14644-5, Cleanrooms and associated controlled environments — Part 5: Operations

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 9000 apply.

1) To be published. (Revision of ISO 14644-1:1999)

ISO 9001:2008, Quality management systems — Requirements

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 9000 apply.

Throughout the text of this International Standard, wherever the term “product” occurs, it can also mean “service”.

Additional terms and definitions used in this International Standard are specific to Good Manufacturing Practices applicable to the manufacture of primary packaging materials for medicinal products.

3.1
air-lock
enclosed space to control air-flow

NOTE The space typically has at least two interlocked doors between two or more rooms, used either by people or for goods, to control for different conditions, e.g. cleanliness, air-flow upon entering.

3.2
approved
confirmed conformity status

NOTE Conformity can be confirmed for any stage of the process (starting materials, process aids, packaging material or finished product).

3.3
assembly

*fitting together of **primary packaging materials** (3.35.1) and/or components*

NOTE Examples may include pipette assemblies for filling, prepared components of injection systems or positioning of needle shields on prefillable syringes.

3.4
automated inspection
conformity evaluation performed by inspection equipment without manual intervention

NOTE The inspection equipment can include optoelectronics (cameras), laser systems, ultrasonics and their associated data processing functions or others.

3.5
batch
lot
*defined quantity of **primary packaging material** (3.35.1) manufactured in one process or series of processes intended to have uniform characteristics with consistent, homogeneous quality*

NOTE 1 To meet production requirements or customer needs, a batch can be divided up into a number of sub-batches that are later combined to form a single, consistent batch.

NOTE 2 In the case of continuous production, the batch is a fraction of the production defined either as a fixed quantity or as the amount produced in a fixed time interval.

3.6
batch document
batch record
*documents and records that provide a history of the **batch** (3.5), including information relating to its production and control, and which facilitate its **traceability** (3.63)*

3.7
batch number
lot number
*unique identifier to identify a **batch** or **lot** (3.5)*

NOTE A batch number can be a combination of numbers, letters and/or symbols which identifies a batch (or lot) and from which the production and distribution history can be determined.

3.8
batch release
*decision to release the **batch** (3.5) for sale or supply, following a formal review of the **batch document** (3.6) performed by the **quality unit** (3.41) or a person authorized by the quality unit(s)*

3.9
calibration
process of checking or adjusting (by comparison with a reference standard) the accuracy of a measuring instrument

NOTE Calibration can also be described as the set of operations which establish, under specified conditions, the relationship between values indicated by a measuring instrument or values represented by a material measure, and the corresponding known values of a reference standard.

3.10
change control
documented control of changes

NOTE Changes can include, for example, changes in raw materials, specifications, facilities, equipment, production processes and test methods.

3.11
cleanroom

room in which the concentration of airborne particles is controlled, and which is constructed and used in a manner to minimize the introduction, generation, and retention of particles inside the room, and in which other relevant parameters, e.g. temperature, humidity, and pressure, are controlled as necessary

[ISO 14644-1:—, 3.1.1]

3.12
clean zone
dedicated space in which the concentration of airborne particles is controlled, and which is constructed and used in a manner to minimize the introduction, generation, and retention of particles inside the zone, and in which other relevant parameters, e.g. temperature, humidity, and pressure, are controlled as necessary

[ISO 14644-1:—, 3.1.2]

NOTE This zone may be open or enclosed and may or may not be located within a cleanroom.

3.13
contamination
*introduction of any unwanted material into the **primary packaging material** (3.35.1)*

NOTE 1 A finished product can be contaminated by physical (particulate), chemical or biological (bio- and endotoxin burden) action.

NOTE 2 Contamination can occur during production, packaging, storage and/or distribution from contaminated air systems, personnel, sampling equipment, materials, premises or containers.

3.14
controlled area
controlled environment
area or environment constructed and operated to control the possible introduction of potential contaminants

NOTE 1 The area is typically constructed and operated to control the introduction of potential contamination and the consequences of accidental release of living organisms.

NOTE 2 An appropriate pressure differential allows for the efficient removal of airborne contaminants, potential contamination and the consequences of accidental release.

3.15
cross-contamination
mix-up
contamination *(3.13) of a material or of a product with another material or product*

NOTE 1 Cross-contamination may also be referred to as admixture.

NOTE 2 See Reference [24].

3.16
customer complaint
information provided by a customer about deficiencies and/or nonconformities

NOTE 1 The information may be verbally communicated or written.

NOTE 2 The subject of a complaint can include primary packaging material quality, quantity or supply.

3.17
date of manufacture
date on which one of the first stages in the process of manufacture of the primary packaging material, or the packaging, or the final release, occurs, and which may be subject to customer agreement

3.18
deviation
departure from an approved ***standard operating procedure (SOP)*** *(3.58) or established standard*

3.19
documented procedure
procedure that is established, documented, authorized, implemented and maintained

3.20
double-check
documented ***verification*** *(3.65) of an activity, result or record by a second person or system*

NOTE A second in-process control check signature, production and quality records for a batch signed by a second person or electronic checks can be part of this verification process. Typically, double-checks are signed by a second person.

3.21
expiration date
expected suitable use limit

NOTE 1 See also definition ***shelf-life*** *(3.56).*

NOTE 2 This is typically the period during which a primary packaging material is expected to remain suitable for use if stored under defined conditions and after which it should not be used.