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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 d'emballage 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.

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).

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. Details of any patent rights identified during the development of the document will be in the Introduction and/or on the ISO list of patent declarations received (see www.iso.org/patents).

Any trade name used in this document is information given for the convenience of users and does not constitute an endorsement.

For an explanation on the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the WTO principles in the Technical Barriers to Trade (TBT) see the following URL: Foreword - Supplementary information

The committee responsible for this document is ISO/TC 76, *Transfusion, infusion and injection, and blood processing equipment for medical and pharmaceutical use*.

This third edition cancels and replaces the second edition (ISO 15378:2011), which has been technically revised to

— include requirements on risk management and replace the former guidance on risk management by references to relevant standards and guidelines,

— extensively revise the guidance on verification, qualification and validation requirements for primary packaging materials, and

— amend the requirements on infrastructure, work environment, maintenance and cleaning activities, customer communication, control of production and service provision and batch release.

Introduction

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

— *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.

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.

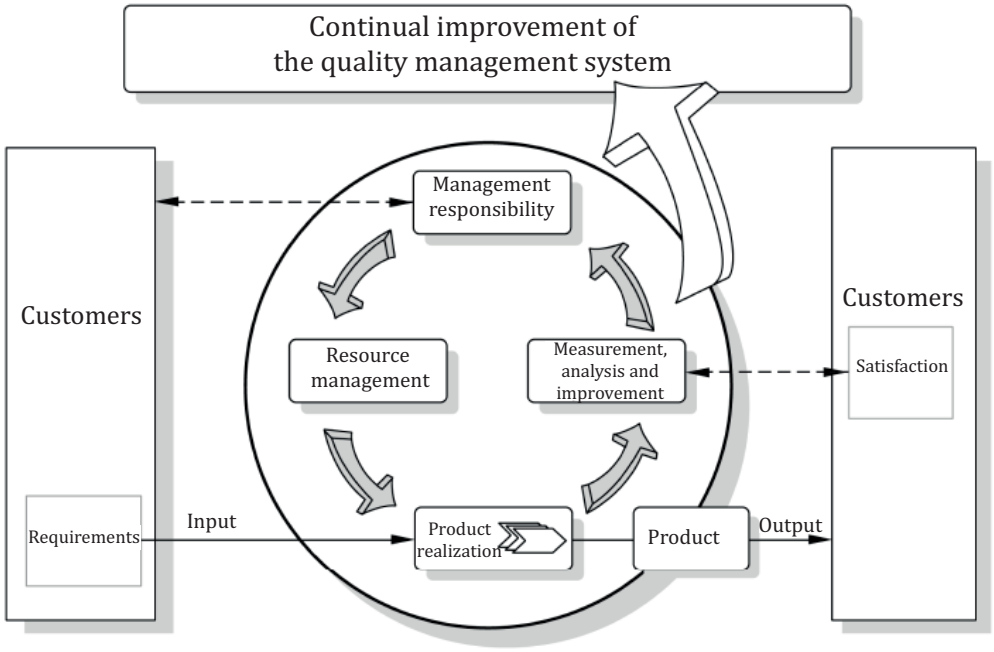
NOTE In addition, the methodology known as "Plan-Do-Check-Act" (PDCA) can be applied to all processes. PDCA can be briefly described as follows.

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



Key

value-adding activities

information flow

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

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.

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.

NOTE ISO 9001:2008, Annex A is not included in 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 documents, in whole or in part, are normatively referenced in this document and are indispensable for its application. 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 14698-1, *Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods*

ISO 14698-2, *Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data*

3 Terms and definitions

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

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.[1)]

1) The systematic used for the grouping of the terms and definitions in this International Standard is based on that used in ISO 9000.

3.1 *Terms relating to quality*

3.1.1
customer complaint
information provided by a customer about deficiencies and/or nonconformities

Note 1 to entry: *The information can be verbally communicated or written.*

Note 2 to entry: *The subject of a complaint can include* ***primary packaging material*** *(3.4.18.1) quality, quantity or supply.*

3.2 *Terms relating to management*

3.2.1
Good Manufacturing Practice
GMP
quality control *(3.2.2) and quality assurance applied in* ***manufacturing*** *(3.4.15)*

Note 1 to entry: to entry: *For the definitions of* ***quality control*** *(3.2.2) and quality assurance, see* ISO 9000:2005, 3.2.10 and 3.2.11.

Note 2 to entry: *Requirements for* ***Good Manufacturing Practice*** *in the pharmaceutical industry are specified in a quality assurance standard. See Reference [32].*

Note 3 to entry: ***Good Manufacturing Practice (GMP)*** *for* ***primary packaging material*** *(3.4.18.1) requires, in addition to suitable provision of personnel, premises and equipment, a quality management system that includes controls for incoming* ***starting materials*** *(3.4.28), manufacture, corresponding documentation, factory hygiene,* ***final inspection*** *(3.8.5), records of distribution, processing of complaints and self-inspection.*

Note 4 to entry: ***GMP*** *and current* ***Good Manufacturing Practice*** *(cGMP) are equivalent.* ***GMP*** *guidelines are continually updated to the ever-changing requirements of the state-of-the-art. This has resulted in the term cGMP sometimes being used. The pharmaceutical industry expects that* ***organizations*** *(3.3.1) take account of current* ***GMP*** *within their continual improvement programmes.*

3.2.2
quality control
part of quality management focused on fulfilling quality requirements

Note 1 to entry: ***Quality control*** *includes checking or testing that* ***specifications*** *(3.7.3) are met.*

[SOURCE: ISO 9000:2005, 3.2.10*]*

3.3 *Terms relating to organization*

3.3.1
organization
group of people and facilities with an arrangement of responsibilities, authorities and relationships

Note 1 to entry: *In this International Standard, the* ***organization*** *is the company* ***manufacturing*** *(3.4.15) the* ***primary packaging material*** *(3.4.18.1).*

[SOURCE: ISO 9000:2005, 3.3.1 *modified by adding note 1 to entry]*

3.3.2
outsourcing
provision of all or part of a process by another ***organization*** *(3.3.1)*

Note 1 to entry: ***Outsourcing*** *is often referred to as subcontracting.*

3.3.3
quality unit
organizational unit which fulfils both quality assurance (QA) and ***quality control*** *(QC) (3.2.2) responsibilities*

Note 1 to entry: *The* ***quality unit(s)*** *can consist of separate QA and QC units or of a single individual (or group), depending upon the size and structure of the* ***organization*** *(3.3.1).*

3.4 *Terms relating to processes and product*

3.4.1
air-lock
enclosed space to control air-flow

Note 1 to entry: *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.*

3.4.2
assembly
fitting together of ***primary packaging materials*** *(3.4.18.1) and/or components*

Note 1 to entry: *Examples can include pipette assemblies for filling, prepared components of injection systems or positioning of needle shields on prefillable syringes.*

3.4.3
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

[SOURCE: ISO 14644-1:1999, 2.1.1]

3.4.4
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

Note 1 to entry: *This zone may be open or enclosed and may or may not be located within a* ***cleanroom*** *(3.4.3).*

[SOURCE: ISO 14644-1:1999, 2.1.2*]*

3.4.5
contamination
introduction of any unwanted material into the ***primary packaging material*** *(3.4.18.1)*

Note 1 to entry: *A* ***finished product*** *(3.4.11) can be contaminated by physical (particulate), chemical or biological (bio- and endotoxin burden) action.*

Note 2 to entry: ***Contamination*** *can occur e.g. during* ***production*** *(3.4.20), for packaging, storage and/or distribution from contaminated air systems, personnel, sampling equipment, materials, premises or containers.*

3.4.6
controlled area
controlled environment
area or environment constructed and operated to control the possible introduction of potential contaminants

3.4.7
cross-contamination
mix-up
contamination *(3.4.5) of a material or of a product with another material or product*

Note 1 to entry: ***Cross-contamination*** *can also be referred to as admixture.*

Note 2 to entry: *See Reference [31].*

3.4.8
date of manufacture
date on which one of the first stages in the process of manufacture of the ***primary packaging material*** *(3.4.18.1), or the packaging, or the final release, occurs, and which can be subject to customer agreement*

3.4.9
documented procedure
procedure that is established, documented, authorized, implemented and maintained

3.4.10
expiration date
expected suitable use limit

Note 1 to entry: *See also definition* ***shelf-life*** *(3.4.26).*

Note 2 to entry: *This is typically the period during which a* ***primary packaging material*** *(3.4.18.1) is expected to remain suitable for use if stored under defined conditions and after which it should not be used.*

3.4.11
finished product
primary packaging material *(3.4.18.1) which has completed all stages of* ***production*** *(3.4.20)*

3.4.12
homogeneity
uniformity of characteristics and their values throughout a defined quantity of material

Note 1 to entry: ***Homogeneity*** *can include uniformity of materials or certain characteristics of materials of special significance.*

3.4.13
intermediate product
primary packaging material *(3.4.18.1) which has completed some but not all production stages*

Note 1 to entry: *An* ***intermediate product*** *needs further processing before it becomes a* ***finished product*** *(3.4.11).*

3.4.14
line clearance
removal (line purge) of everything associated with the prior production run

Note 1 to entry: *Typically,* ***line clearance*** *is done prior to a production run to prevent any error and* ***cross-contamination*** *(3.4.7). Typically, it is required that a production facility (line) and its associated* ***working area*** *(3.4.31) are completely clear of all materials, waste, products, samples, documents, etc. used in the previous production run before the introduction of materials, product samples, documents, etc. needed for the commencement of the next production run.*

3.4.15
manufacturing
all operations including purchasing and receipt of materials to ***production*** *(3.4.20), packaging, labelling,* ***quality control*** *(3.2.2), release, storage, distribution of products and the related controls*

3.4.16
medicinal product
any substance or combination of substances presented for treating or preventing disease in human beings or animals

Note 1 to entry: *Any substance or combination of substances that can be administrated to human beings or animals with a view to making a medical diagnosis or to restoring, correcting or modifying physiological functions in human beings or in animals is likewise considered a* ***medicinal product****.*

Note 2 to entry: *See Reference [31].*