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Primary packaging materials for medicinal products — Particular requirements for the application of ISO 9001:2015, with reference to good manufacturing practice (GMP)

Articles d'emballage primaire pour médicaments — Exigences particulières pour l'application de l'ISO 9001:2015 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 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 ISO/TC 76, *Transfusion, infusion and injection, and blood processing equipment for medical and pharmaceutical use*.

This fourth edition cancels and replaces the third edition (ISO 15378:2015), which has been technically revised. The main technical and editorial changes comprise:

— the integration of the sector-specific requirements on quality management systems for medicinal products into ISO 9001:2015;

— the deletion of the requirements on quality manual;

— the inclusion of all annexes of ISO 9001:2015 into this document;

— adjustments to the terminology of ISO 9000:2015, where relevant;

— the inclusion of an alphabetical index of defined terms used in this document.

Introduction

0.1 General

This document 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 document is an application standard for primary packaging materials, which contains the text of ISO 9001:2015.

The conventions for the layout of this document are the following.

— Those clauses, subclauses or annexes that are quoted directly and unchanged from ISO 9001:2015 and ISO 9000:2015 (under Clause 3) are in boxes.

— Additional GMP related requirements and recommendations as well as terms and definitions relevant to the manufacture of primary packaging materials are outside boxes.

ISO 9001:2015, Quality management systems — Requirements

0.1 General

The adoption of a quality management system is a strategic decision for an organization that can help to improve its overall performance and provide a sound basis for sustainable development initiatives.

The potential benefits to an organization of implementing a quality management system based on this International Standard are:

a) the ability to consistently provide products and services that meet customer and applicable statutory and regulatory requirements;

b) facilitating opportunities to enhance customer satisfaction;

c) addressing risks and opportunities associated with its context and objectives;

d) the ability to demonstrate conformity to specified quality management system requirements.

This International Standard can be used by internal and external parties.

It is not the intent of this International Standard to imply the need for:

— uniformity in the structure of different quality management systems;

— alignment of documentation to the clause structure of this International Standard;

— the use of the specific terminology of this International Standard within the organization.

The quality management system requirements specified in this International Standard are complementary to requirements for products and services.

This International Standard employs the process approach, which incorporates the Plan-Do-Check-Act (PDCA) cycle and risk-based thinking.

The process approach enables an organization to plan its processes and their interactions.

The PDCA cycle enables an organization to ensure that its processes are adequately resourced and managed, and that opportunities for improvement are determined and acted on.

Risk-based thinking enables an organization to determine the factors that could cause its processes and its quality management system to deviate from the planned results, to put in place preventive controls to minimize negative effects and to make maximum use of opportunities as they arise (see Clause A.4).

Consistently meeting requirements and addressing future needs and expectations poses a challenge for organizations in an increasingly dynamic and complex environment. To achieve this objective, the organization might find it necessary to adopt various forms of improvement in addition to correction and continual improvement, such as breakthrough change, innovation and re-organization.

In this International Standard, the following verbal forms are used:

— "shall" indicates a requirement;

— "should" indicates a recommendation;

— "may" indicates a permission;

— "can" indicates a possibility or a capability.

Information marked as "NOTE" is for guidance in understanding or clarifying the associated requirement.

A key objective of this document is to specify GMP for primary packaging materials.

0.2 Quality management principles

ISO 9001:2015, Quality management systems — Requirements

0.2 Quality management principles

This International Standard is based on the quality management principles described in ISO 9000. The descriptions include a statement of each principle, a rationale of why the principle is important for the organization, some examples of benefits associated with the principle and examples of typical actions to improve the organization's performance when applying the principle.

The quality management principles are:

— customer focus;

— leadership;

— engagement of people;

— process approach;

— improvement;

— evidence-based decision making;

— relationship management.

0.3 Process approach

0.3.1 General

ISO 9001:2015, Quality management systems — Requirements

0.3 Process approach

0.3.1 General

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. Specific requirements considered essential to the adoption of a process approach are included in 4.4.

Understanding and managing interrelated processes as a system contributes to the organization's effectiveness and efficiency in achieving its intended results. This approach enables the organization to control the interrelationships and interdependencies among the processes of the system, so that the overall performance of the organization can be enhanced.

The process approach involves the systematic definition and management of processes, and their interactions, so as to achieve the intended results in accordance with the quality policy and strategic direction of the organization. Management of the processes and the system as a whole can be achieved using the PDCA cycle (see 0.3.2) with an overall focus on risk-based thinking (see 0.3.3) aimed at taking advantage of opportunities and preventing undesirable results.

The application of the process approach in a quality management system enables:

a) understanding and consistency in meeting requirements;

b) the consideration of processes in terms of added value;

c) the achievement of effective process performance;

d) improvement of processes based on evaluation of data and information.

Figure 1 gives a schematic representation of any process and shows the interaction of its elements. The monitoring and measuring check points, which are necessary for control, are specific to each process and will vary depending on the related risks.

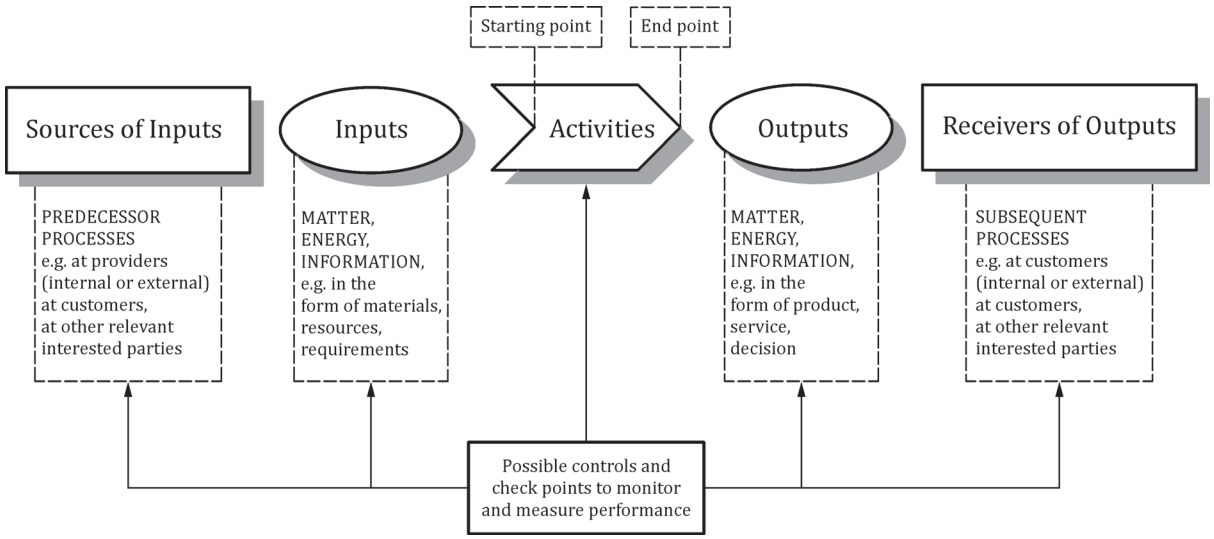


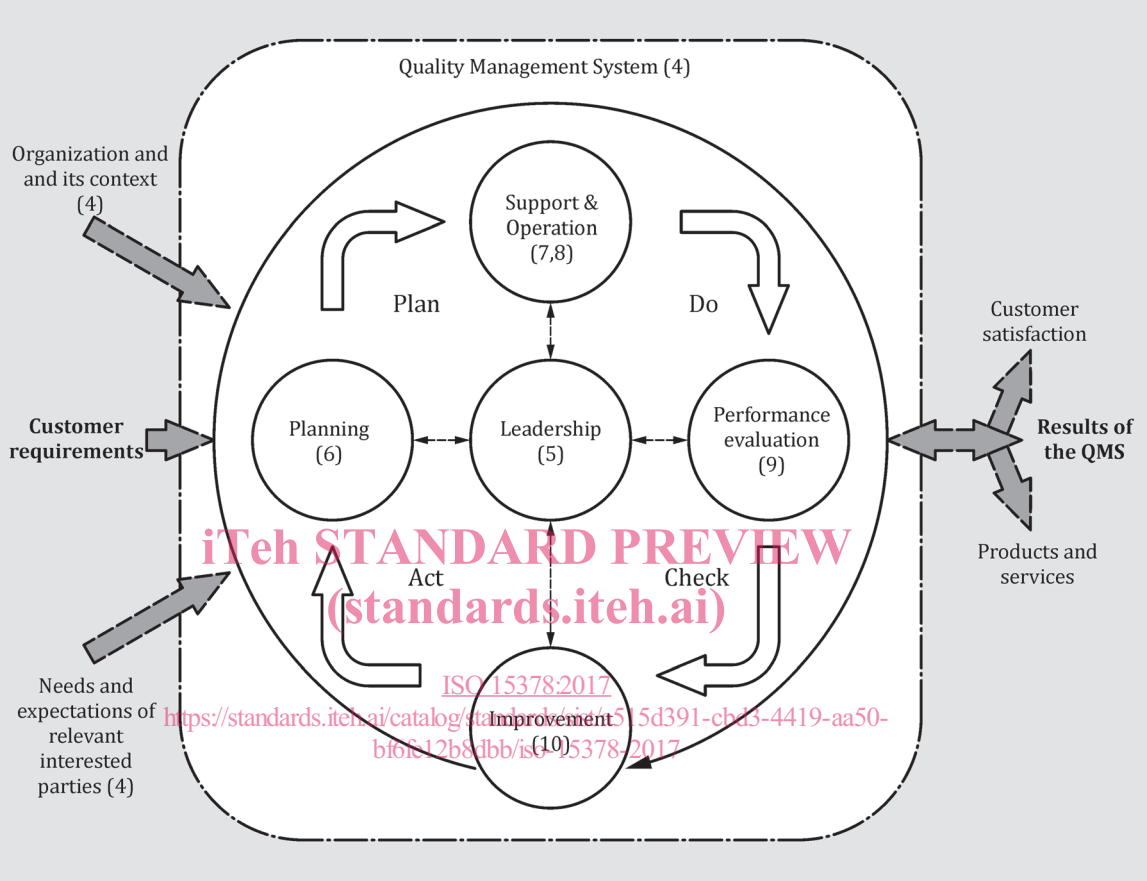
Figure 1 — Schematic representation of the elements of a single process

0.3.2 Plan-Do-Check-Act cycle

ISO 9001:2015, Quality management systems — Requirements

0.3.2 Plan-Do-Check-Act cycle

The PDCA cycle can be applied to all processes and to the quality management system as a whole. Figure 2 illustrates how Clauses 4 to 10 can be grouped in relation to the PDCA cycle.



NOTE Numbers in brackets refer to the clauses in this International Standard.

Figure 2 — Representation of the structure of this International Standard in the PDCA cycle

The PDCA cycle can be briefly described as follows:

— **Plan**: establish the objectives of the system and its processes, and the resources needed to deliver results in accordance with customers' requirements and the organization's policies, and identify and address risks and opportunities;

— **Do**: implement what was planned;

— **Check**: monitor and (where applicable) measure processes and the resulting products and services against policies, objectives, requirements and planned activities, and report the results;

— **Act**: take actions to improve performance, as necessary.

0.3.3 Risk-based thinking

ISO 9001:2015, Quality management systems — Requirements

0.3.3 Risk-based thinking

Risk-based thinking (see Clause A.4) is essential for achieving an effective quality management system. The concept of risk-based thinking has been implicit in previous editions of this International Standard including, for example, carrying out preventive action to eliminate potential nonconformities, analysing any nonconformities that do occur, and taking action to prevent recurrence that is appropriate for the effects of the nonconformity.

To conform to the requirements of this International Standard, an organization needs to plan and implement actions to address risks and opportunities. Addressing both risks and opportunities establishes a basis for increasing the effectiveness of the quality management system, achieving improved results and preventing negative effects.

Opportunities can arise as a result of a situation favourable to achieving an intended result, for example, a set of circumstances that allow the organization to attract customers, develop new products and services, reduce waste or improve productivity. Actions to address opportunities can also include consideration of associated risks. Risk is the effect of uncertainty and any such uncertainty can have positive or negative effects. A positive deviation arising from a risk can provide an opportunity, but not all positive effects of risk result in opportunities.

Because of the nature of primary packaging materials the risk-based approach is applied throughout all processes of the organization.

0.4 Relationship with other management system standards

This document incorporates the requirements of ISO 9001:2015 and, additionally, particular requirements for primary packaging materials, which are derived and adapted, as appropriate, from GMP for the production and control of medicinal products.

ISO 9001:2015, Quality management systems — Requirements

0.4 Relationship with other management system standards

This International Standard applies the framework developed by ISO to improve alignment among its International Standards for management systems (see Clause A.1).

This International Standard enables an organization to use the process approach, coupled with the PDCA cycle and risk-based thinking, to align or integrate its quality management system with the requirements of other management system standards.

This International Standard relates to ISO 9000 and ISO 9004 as follows:

— ISO 9000 *Quality management systems — Fundamentals and vocabulary* provides essential background for the proper understanding and implementation of this International Standard;

— ISO 9004 *Managing for the sustained success of an organization — A quality management approach* provides guidance for organizations that choose to progress beyond the requirements of this International Standard.

Annex B provides details of other International Standards on quality management and quality management systems that have been developed by ISO/TC 176.

This International Standard does not include requirements specific to other management systems, such as those for environmental management, occupational health and safety management, or financial management.

Sector-specific quality management system standards based on the requirements of this International Standard have been developed for a number of sectors. Some of these standards specify additional quality management system requirements, while others are limited to providing guidance to the application of this International Standard within the particular sector.

A matrix showing the correlation between the clauses of this edition of this International Standard and the previous edition (ISO 9001:2008) can be found on the ISO/TC 176/SC 2 open access website at: www.iso.org/tc176/sc02/public.

Primary packaging materials for medicinal products — Particular requirements for the application of ISO 9001:2015, with reference to good manufacturing practice (GMP)

1 Scope

ISO 9001:2015, Quality management systems — Requirements

1 Scope

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

a) needs to demonstrate its ability to consistently provide products and services that meet customer and applicable statutory and regulatory requirements, and

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

All the requirements of this International Standard are generic and are intended to be applicable to any organization, regardless of its type or size, or the products and services it provides.

NOTE 1 In this International Standard, the terms "product" or "service" only apply to products and services intended for, or required by, a customer.

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

In addition to ISO 9001, this document specifies Good Manufacturing Practice (GMP) requirements applicable to primary packaging materials 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.

In this document 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.

This document is an application standard for the design, manufacture and supply of primary packaging materials for medicinal products.

2 Normative references

ISO 9001:2015, Quality management systems — 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 9000:2015, *Quality management systems — Fundamentals and vocabulary*

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 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

ISO 9001:2015, Quality management systems — Requirements
3 Terms and definitions
For the purposes of this document, the terms and definitions given in ISO 9000:2015 apply.

For the purposes of this document, the terms and definitions given in ISO 9000:2015 and the following 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 1 This document only duplicates terms and definitions of ISO 9000:2015 when they have been amended in order to address the specific needs of this document.

NOTE 2 The structure of terms and definitions in this document corresponds to that used in ISO 9000:2015, as far as applicable. An additional heading “Terms related to risk management” has been added in this document.

NOTE 3 An index of defined terms is found at the end of this document.

3.1 Terms related to organization

3.1.1
organization
person or group of people that has its own functions with responsibilities, authorities and relationships to achieve its objectives

Note 1 to entry: The concept of organization includes, but is not limited to sole-trader, company, corporation, firm, enterprise, authority, partnership, association, charity or institution, or part or combination thereof, whether incorporated or not, public or private.

Note 2 to entry: In this document the organization is the company manufacturing the *primary packaging material* (3.6.4).

[SOURCE: ISO 9000:2015, 3.2.1, modified by deleting Note 2 to entry and adding a new Note 2 to entry]

3.1.2
quality unit
organizational unit which fulfils both quality assurance (QA) and quality control (QC) 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* (3.1.1).

3.2 Terms related to activity

3.2.1
assembly
fitting together of *primary packaging materials* (3.6.4) 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.

3.2.2
change control
documented control of changes with an appropriate *risk management* (3.11.6)

Note 1 to entry: Changes can include, for example, changes in raw materials, specifications, facilities, equipment, production processes and test methods.

3.2.3
Good Manufacturing Practice
GMP
quality control and quality assurance applied in *manufacturing* (3.5.5)

Note 1 to entry: For the definitions of *quality control* (3.2.9) and quality assurance, see ISO 9000:2015, (3.3.6 and 3.3.7).

Note 2 to entry: Requirements for Good Manufacturing Practice in the pharmaceutical industry are specified in a quality assurance standard, see Reference [50].

Note 3 to entry: Good Manufacturing Practice (GMP) for *primary packaging materials* (3.6.4) requires, in addition to suitable provision of personnel, premises and equipment, a quality management system that includes controls for incoming *starting materials* (3.5.13), manufacture, corresponding documentation, factory hygiene, final inspection, 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* (3.1.1) take account of current GMP within their continual improvement programmes.

3.2.4
installational qualification
IQ
process of obtaining and documenting evidence that equipment has been provided and installed in accordance with its specification

[SOURCE: ISO/TS 11139:2006, 2.22]

3.2.5
operational qualification
OQ
process of obtaining and documenting evidence that installed equipment operates within predetermined limits when used in accordance with its operational procedures

[SOURCE: ISO/TS 11139:2006, 2.27]

3.2.6
origination
artwork
all preparative activities prior to print

Note 1 to entry: These include concept, design, graphics, reprographics, film, plate making, silk screens and digital files and masters.