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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)

Reference number
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Contents

Page

Foreword ..... **v**

Introduction ..... **vi**

1 Scope **1**

2 Normative references **1**

3 Terms and definitions **2**
3.1 Terms related to organization 2
3.2 Terms related to activity 3
3.3 Terms related to system 4
3.4 Terms related to requirement 5
3.5 Terms related to process 6
3.6 Terms related to results 7
3.7 Terms related to data, information and document 8
3.8 Terms related to action 9
3.9 Terms related to characteristic 10
3.10 Terms related to determination 10
3.11 Terms relating to risk management 11

4 Context of the organization **12**
4.1 Understanding the organization and its context 12
4.2 Understanding the needs and expectations of interested parties 12
4.3 Determining the scope of the quality management system 13
4.4 Quality management system and its processes 13

5 Leadership **14**
5.1 Leadership and commitment 14
5.1.1 General 14
5.1.2 Customer focus 15
5.1.3 Customer audits 15
5.2 Policy 15
5.3 Organizational roles, responsibilities and authorities 16

6 Planning **17**
6.1 Actions to address risks and opportunities 17
6.2 Quality objectives and planning to achieve them 18
6.3 Planning of changes 19

7 Support **19**
7.1 Resources 19
7.1.1 General 19
7.1.2 People 19
7.1.3 Infrastructure 20
7.1.4 Environment for the operation of processes 21
7.1.5 Monitoring and measuring resources 23
7.1.6 Organizational knowledge 24
7.2 Competence 24
7.2.1 General 24
7.2.2 GMP-training 24
7.3 Awareness 25
7.4 Communication 25
7.5 Documented information 26
7.5.1 General 26
7.5.2 Creating and updating 26
7.5.3 Control of documented information 27
7.5.4 Administration of IT systems and data 28

8 Operation **29**

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8.1 Operational planning and control 29
8.2 Requirements for products and services 30
8.2.1 Customer communication 30
8.2.2 Determining the requirements for products and services 31
8.2.3 Review of the requirements for products and services 31
8.2.4 Changes to requirements for products and services 32
8.3 Design and development of products and services 32
8.3.1 General 32
8.3.2 Design and development planning 32
8.3.3 Design and development inputs 33
8.3.4 Design and development controls 33
8.3.5 Design and development outputs 34
8.3.6 Design and development changes 34
8.4 Control of externally provided processes, products and services 35
8.4.1 General 35
8.4.2 Type and extent of control 36
8.4.3 Information for external providers 37
8.5 Production and service provision 38
8.5.1 Control of production and service provision 38
8.5.2 Identification and traceability 41
8.5.3 Property belonging to customers or external providers 42
8.5.4 Preservation 42
8.5.5 Post-delivery activities 43
8.5.6 Control of changes 43
8.6 Release of products and services 44
8.7 Control of nonconforming outputs 44

9 Performance evaluation 45
9.1 Monitoring, measurement, analysis and evaluation 45
9.1.1 General 45
9.1.2 Customer satisfaction 45
9.1.3 Analysis and evaluation 46
9.2 Internal audit 48
9.3 Management review 48
9.3.1 General 48
9.3.2 Management review inputs 49
9.3.3 Management review outputs 49

10 Improvement 50
10.1 General 50
10.2 Nonconformity and corrective action 50
10.3 Continual improvement 51

Annex A (informative) **Clarification of new structure, terminology and concepts 52**

Annex B (informative) **Other International Standards on quality management and quality management systems developed by ISO/TC 176 ..... 56**

Annex C (normative) **GMP requirements for printed primary packaging materials 60**

Annex D (informative) **Guidance on verification, qualification and validation requirements for primary packaging materials 64**

Bibliography 75

Alphabetical index of defined terms used in this document 78

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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.

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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.

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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.

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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.

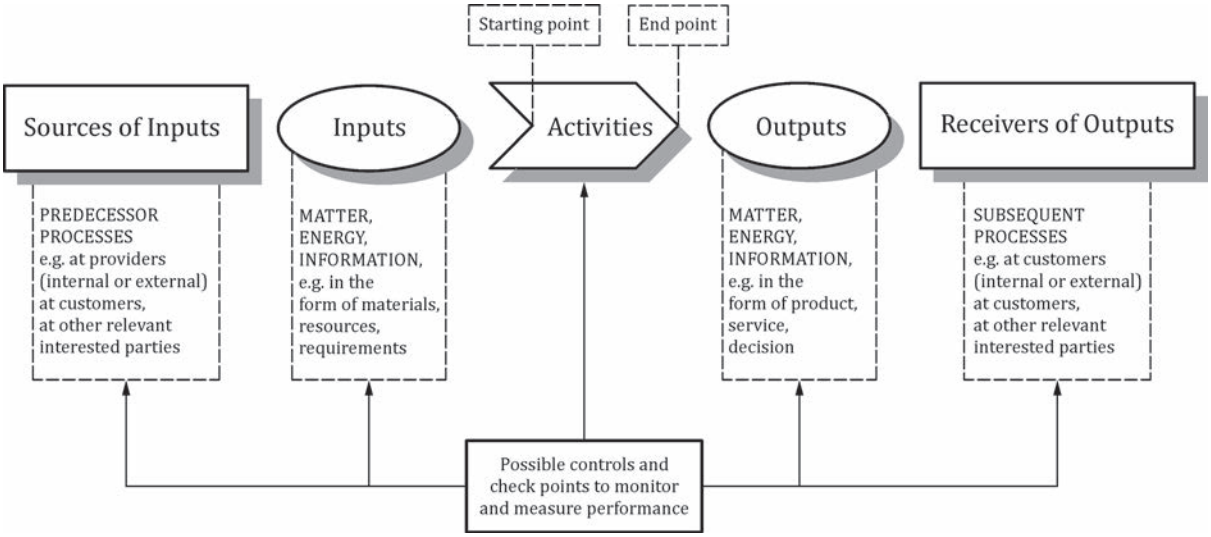


Figure 1 — Schematic representation of the elements of a single process

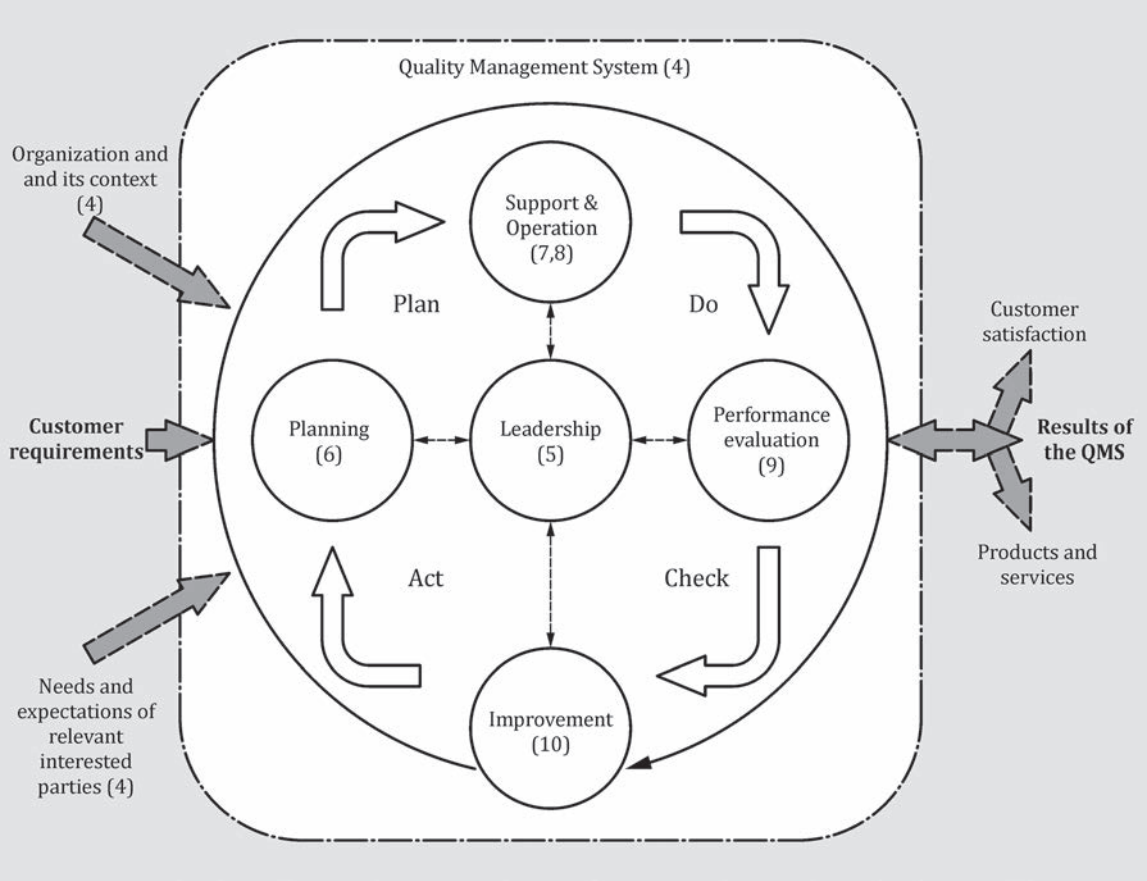
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0.3.2 Plan-Do-Check-Act cycle

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.

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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.

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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.

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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)

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*

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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).

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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.

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3.2.7
performance qualification
PQ
verification (3.7.13) that the proposed specification for the facility, equipment or system is suitable for the intended use

[SOURCE: ISO/TS 11139:2006, 2.30]

3.2.8
qualification
process to demonstrate the ability to fulfil specified requirements

Note 1 to entry: The term "qualified" can be used to designate the corresponding status.

Note 2 to entry: Qualification comprises design qualification (DQ), *installation qualification (IQ)* (3.2.4), *operational qualification (OQ)* (3.2.5) and could include *performance qualification (PQ)* (3.2.7) as well as re-qualification.

Note 3 to entry: Qualification can be applied to facilities, equipment and utilities.

3.2.9
quality control
part of quality management focused on fulfilling quality requirements

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

[SOURCE: ISO 9000:2015, 3.3.7, modified by adding Note 1 to entry]

3.3 Terms related to system

3.3.1
airlock
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.

3.3.2
calibration
process of checking or adjusting (by comparison with a reference standard) the accuracy of a measuring instrument

Note 1 to entry: 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.

3.3.3
cleanroom
room within which the number concentration of airborne particles is controlled and classified, and which is designed, constructed and operated in a manner to control the introduction, generation and retention of particles inside the room

Note 1 to entry: The class of airborne particle concentration is specified.

Note 2 to entry: Levels of other cleanliness attributes such as chemical, viable or nanoscale concentrations in the air, and also surface cleanliness in terms of particle, nanoscale, chemical and viable concentrations might also be specified and controlled.

Note 3 to entry: Other relevant physical parameters might also be controlled as required, e.g. temperature, humidity, pressure, vibration and electrostatic.

[SOURCE: ISO 14644-1:2015, 3.1.1]

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3.3.4
clean zone
defined space within which the number concentration of airborne particles is controlled and classified, and which is constructed and operated in a manner to control the introduction, generation, and retention of contaminants inside the space

Note 1 to entry: This class of airborne particle concentration is specified.

Note 2 to entry: Levels of other cleanliness attributes such as chemical, viable or nanoscale concentrations in the air, and also surface cleanliness in terms of particle, nanoscale, chemical and viable concentrations might also be specified and controlled.

Note 3 to entry: A clean zone(s) can be a defined space within a cleanroom or might be achieved by a separative device. Such a device can be located inside or outside a cleanroom.

Note 4 to entry: Other relevant physical parameters might also be controlled as required, e.g. temperature, humidity, pressure, vibration and electrostatic.

[SOURCE: ISO 14644-1:2015, 3.1.2]

3.3.5
controlled area
controlled environment
area or environment constructed and operated to control the possible introduction of potential contaminants

3.3.6
working area
defined area where *origination* (3.2.6), *production* (3.5.7), packaging, test or inspection operations are carried out and where such activity will usually be subject to a *line clearance* (3.5.4)

Note 1 to entry: These areas are physically defined by the use of barriers, floor marking or similar means of definition, and can contain equipment, e.g. production machinery, test equipment, computers, work benches, proofing equipment.

3.4 Terms related to requirement

3.4.1
expiration date
expected suitable use limit

Note 1 to entry: See also definition *shelf-life* (3.4.2).

Note 2 to entry: This is typically the period during which a *primary packaging material* (3.6.4) is expected to remain suitable for use if stored under defined conditions and after which it should not be used.

3.4.2
shelf-life
period during which a *primary packaging material* (3.6.4) is expected to comply with the requirements (specifications)

Note 1 to entry: See also *expiration date* (3.4.1)

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3.5 Terms related to process

3.5.1
batch
lot
defined quantity of *primary packaging material* (3.6.4) manufactured in one process or series of processes intended to have uniform characteristics with consistent, homogeneous quality

Note 1 to entry: 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 to entry: 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.

3.5.2
contamination
introduction of any unwanted material into the *primary packaging material* (3.6.4)

Note 1 to entry: A *finished product* (3.6.1) can be contaminated by physical (particulate), chemical or biological (bioburden and endotoxin) action.

Note 2 to entry: Contamination can occur for e.g. during *production* (3.5.7), packaging, storage and/or distribution from contaminated air systems, personnel, sampling equipment, materials, premises or containers.

3.5.3
cross-contamination
contamination (3.5.2) of a material or of a product with another material or product

Note 1 to entry: Cross-contamination can also be referred to as mix-up or admixture.

Note 2 to entry: See Reference [50].

3.5.4
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* (3.5.3). Typically, it is required that a production facility (line) and its associated *working area* (3.3.6) 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.

3.5.5
manufacturing
all operations including purchasing and receipt of materials to *production* (3.5.7), packaging, labelling, *quality control* (3.2.9), release, storage, distribution of products and the related controls

3.5.6
process aids
material used to facilitate process realization

Note 1 to entry: The material is not included in the product specification and can be removed at or before the final processing stage.

EXAMPLE Mould release agents, compressed air, rolling lubricants.

3.5.7
production
processes resulting in *primary packaging material* (3.6.4)

Note 1 to entry: The processes form the full production cycle, from receipt of *starting materials* (3.5.13) through processing and packaging, to completion as a *finished product* (3.6.1).

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3.5.8
quarantine
status of materials or products isolated pending a decision on their subsequent approval or rejection

Note 1 to entry: Quarantined material is typically isolated by physical or other effective means.

3.5.9
realization
result of applying all processes required to achieve the desired output from design to product delivery

3.5.10
reconditioning
processing or reprocessing *primary packaging material* (3.6.4) to meet specification requirements

3.5.11
reprocessing
repeating part of a production process

Note 1 to entry: Continuation of part of a process after an in-process control test has shown that the part is incomplete, is considered to be part of the normal process, and is not considered reprocessing.

3.5.12
retained samples
materials or *finished products* (3.6.1) stored for future reference

Note 1 to entry: These samples are generally taken in a sufficient amount and stored under recommended conditions for reference during a defined period of time.

3.5.13
starting material
raw material, components and substances used to produce *primary packaging materials* (3.6.4)

3.5.14
surface treatment
process to improve *primary packaging material* (3.6.4) surface

EXAMPLE Siliconization or other treatment of internal glass surfaces, coating of internal or external surfaces of glass containers or rubber parts.

3.6 Terms related to results

3.6.1
finished product
primary packaging material (3.6.4) which has completed all stages of *production* (3.5.7)

3.6.2
intermediate product
primary packaging material (3.6.4) 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* (3.6.1).

3.6.3
medicinal product
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 [50].

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Note 3 to entry: *Medicinal products* (3.6.3) can also be referred to as pharmaceutical or drug products, including clinical trial products.

3.6.4
primary packaging material
material used in pharmaceutical packaging which will contain, seal or be used for dose application of a medicinal product and which will have direct contact with the *medicinal product* (3.6.3)

3.6.5
secondary packaging materials
non-contact packaging materials

EXAMPLE Printed or unprinted cartons, labels, leaflets or inserts (or outserts), over-wraps, and transit containers such as folding boxes.

3.7 Terms related to data, information and document

3.7.1
approved
confirmed conformity status

Note 1 to entry: Conformity can be confirmed for any stage of the process [*starting materials* (3.5.13), *process aids* (3.5.6), packaging material or *finished product* (3.6.1)].

3.7.2
batch document
batch record
documents and records that provide a history of the *batch* (3.5.1), including information relating to its *production* (3.5.7) and control, and which facilitate its traceability

3.7.3
batch number
lot number
unique identifier to identify a *batch* (3.5.1) or *lot* (3.5.1)

Note 1 to entry: A batch number can be a combination of numbers, letters and/or symbols which identifies a *batch* (3.5.1) [(or *lot* (3.5.1)] and from which the *production* (3.5.7) and distribution history can be determined.

3.7.4
date of manufacture
date on which one of the first stages in the process of manufacture of the *primary packaging material* (3.6.4), or the packaging, or the final release, occurs, and which can be subject to customer agreement

3.7.5
deviation
departure from an *approved* (3.7.1) *standard operating procedure (SOP)* (3.7.10) or established standard

3.7.6
documented procedure
procedure that is established, documented, authorized, implemented and maintained

Note 1 to entry: The documentation can be in any form or type of medium.

Note 2 to entry: See *SOP* (3.7.10).

3.7.7
double-check
documented *verification* (3.7.13) of an activity, result or record by a second person or system

Note 1 to entry: A second in-process control check signature, *production* (3.5.7) and quality records for a *batch* (3.5.1) signed by a second person or electronic checks can be part of this verification process. Typically, double-checks are signed by a second person.

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3.7.8
out of specification
OOS
test results that do not comply with the specification

3.7.9
rejected
status of *starting materials* (3.5.13), *process aids* (3.5.6), *intermediate products* (3.6.2) or *finished products* (3.6.1) whose test results do not comply with one or more of the requirements of the specification, and which have been deemed, usually by the *quality unit(s)* (3.1.2), as not suitable for use

3.7.10
standard operating procedure
SOP
authorized, *documented procedure* (3.7.6), or set of procedures, work instructions and test instructions

3.7.11
user requirement specification
URS
approved (3.7.1) document that states the product specifications of the material produced on this equipment as well as functional, operational and/or technical aspects of the equipment or process required to produce the desired product

3.7.12
validation
confirmation, through the provision of objective evidence, that the requirements for a specific intended use or application have been fulfilled

Note 1 to entry: The objective evidence needed for a validation is the result of a test or other form of determination such as performing alternative calculations or reviewing documents.

Note 2 to entry: The word "validated" is used to designate the corresponding status.

Note 3 to entry: The use conditions for validation can be real or simulated.

Note 4 to entry: Validation can be applied to processes, products and software.

[SOURCE: ISO 9000:2015, 3.8.13, modified by adding Note 4 to entry]

3.7.13
verification
confirmation, through the provision of objective evidence, that specified requirements have been fulfilled

Note 1 to entry: The objective evidence needed for a verification can be the result of an inspection or of other forms of determination such as performing alternative calculations or reviewing documents.

Note 2 to entry: The activities carried out for verification are sometimes called a qualification process.

Note 3 to entry: The word "verified" is used to designate the corresponding status.

Note 4 to entry: In this document the term verification is used to ensure manufacturing systems are properly installed and operating correctly; alternatively this could be done by *IQ* (3.2.4) and *OQ* (3.2.5).

[SOURCE: ISO 9000:2015, 3.8.12, modified by adding Note 4 to entry]

3.8 Terms related to action

3.8.1
batch release
decision to release the *batch* (3.5.1) for sale or supply, following a formal review of the *batch document* (3.7.2) performed by the *quality unit* (3.1.2) or a person authorized by the *quality unit(s)* (3.1.2)

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3.8.2
rejection
process whereby *starting materials* (3.5.13), *process aids* (3.5.6), *intermediate products* (3.6.2) or *finished products* (3.6.1) which have been deemed, usually by the *quality unit(s)* (3.1.2), as not suitable for use

3.8.3
return
process for sending back *primary packaging material (s)* (3.6.4) to the *organization* (3.1.1)

3.8.4
rework
action on a nonconforming product, or service to make it conform to the requirements

Note 1 to entry: Rework can affect or change parts of the nonconforming product or service.

Note 2 to entry: to entry:Sorting can be considered to be rework.

[SOURCE: ISO 9000:2015, 3.12.8, modified by adding Note 2 to entry]

3.9 Terms related to characteristic

3.9.1
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.

3.9.2
sterile
free from viable microorganisms

[SOURCE: ISO/TS 11139:2006, 2.43]

3.10 Terms related to determination

3.10.1
automated inspection
conformity evaluation performed by inspection equipment without manual intervention

Note 1 to entry: The inspection equipment can include optoelectronics (cameras), laser systems, ultrasonics and their associated data processing functions or others.

3.10.2
final inspection
tests carried out on the *finished product* (3.6.1) to determine compliance with the specification

3.10.3
in-process control
actions taken during the production process to test product conformity to its specification

Note 1 to entry: Monitoring processes and adjusting the means of *production* (3.5.7) can be necessary to meet product requirements.

Note 2 to entry: The control of the environment or equipment can also be regarded as a part of in-process control.

3.10.4
reconciliation
comparison between the amount of *finished product* (3.6.1) theoretically and actually produced or used, making allowance for normal variation

Note 1 to entry: The comparison considers waste, samples or other losses inherent in the process.

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3.11 Terms relating to risk management

3.11.1
quality critical
parameter affecting *primary packaging material* (3.6.4) quality

Note 1 to entry: A material, process step or process condition, test requirement or any other relevant parameter can be considered to be quality critical if nonconformity to its requirements could have significant detrimental consequences.

3.11.2
risk analysis
process to comprehend the nature of risk and to determine the level of risk

Note 1 to entry: Risk analysis provides the basis for *risk evaluation* (3.11.4) and decisions about risk treatment.

Note 2 to entry: Risk analysis includes risk estimation.

[SOURCE: ISO Guide 73:2009, 3.6.1]

3.11.3
risk assessment
overall process of *risk identification* (3.11.5), *risk analysis* (3.11.2) and *risk evaluation* (3.11.4)

[SOURCE: ISO Guide 73:2009, 3.4.1]

3.11.4
risk evaluation
process of comparing the results of *risk analysis* (3.11.2) with risk criteria to determine whether the risk and/or its magnitude is acceptable or tolerable

Note 1 to entry: Risk evaluation assists in the decision about risk treatment.

[SOURCE: ISO Guide 73:2009, 3.7.1]

3.11.5
risk identification
process of finding, recognizing and describing risks

Note 1 to entry: Risk identification involves the identification of risk sources, events, their causes and their potential consequences.

Note 2 to entry: Risk identification can involve historical data, theoretical analysis, informed and expert opinions, and stakeholder's needs.

[SOURCE: ISO Guide 73:2009, 3.5.1]

3.11.6
risk management
coordinated activities to direct and control an organization with regard to risk

[SOURCE: ISO Guide 73:2009, 2.1]

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