EXCiPACT

Annex to ISO/IEC 17021-1:2015 Additional Requirements for Conformity Assessment Requirements for Certification Bodies and Auditors

Revision 2017

Foreword to ISO/IEC 17021-1:2015 Annex

Certification of a quality management system provides independent demonstration that the management system of the organisation:

a) conforms to specified requirements,
b) is capable of consistently achieving its stated policy and objectives,
c) is effectively implemented,
d) is regularly assessed.

This part of the set of EXCiPACT Standards provides specific requirements for Certification Bodies performing audit and certification in the field of an excipient GMP and GDP quality management system in addition to the requirements stipulated in ISO/IEC 17021-1:2015. Certification activities involve the audit of an organisation's quality management system. Observance of these requirements is intended to ensure that certification bodies operate quality management system certification in respect to a GMP and GDP quality management system in a competent, consistent and impartial manner, thereby facilitating recognition of such bodies and acceptance of their certifications on a national and international basis.

ISO/IEC 17021-1:2015 "Conformity assessment - Requirements for bodies providing audit and certification of management systems - Part 1: Requirements" provides a set of requirements for management systems auditing at a generic level, aimed at providing a reliable determination of conformity to the applicable requirements for certification, conducted by a competent audit team, with adequate resources and following a consistent process, with the results reported in a consistent manner.

The requirements in ISO/IEC 17021-1:2015 are to be applied to the EXCiPACT Certification Scheme. This document sets out additional requirements to ISO/IEC 17021 for certification to EXCiPACT GMP and GDP quality management systems. Headings and sections in this document are those of ISO/IEC 17021-1:2015 and any additional text stipulates requirements to be implemented together with the ISO/IEC 17021-1:2015 clauses in order to perform EXCiPACT GMP and GDP certification assessments.

Where a heading or section of ISO/IEC 17021-1:2015 is omitted then there are no additional requirements to those already stipulated in ISO/IEC 17021-1:2015.

Thus, the requirements in this document will be simple to implement in organisations that are already using ISO/IEC 17021-1:2015 as the basis of their auditing, and for defining auditor competency.

The main text that follows is based on the headings in ISO/IEC 17021-1:2015 and the details are the EXCiPACT requirements:

Text in Bold are ISO/IEC 17021-1:2015 Headings
Standard Text are EXCiPACT requirements.
Italicised text is from ISO/IEC 17021-1:2015

Changes from the 1st Edition 2012

Due to the changes within ISO/IEC 17021-1:2015 in comparison to the 2006 edition it has been necessary to consolidate all the EXCiPACT requirements into this Annex rather than have an additional separate EXCiPACT Annex to ISO 19011:2011; the key requirements for auditing within that standard are now included in ISO/IEC 17021-1:2015.

In addition, changes have been included based on the feedback from Certification Bodies and suppliers of excipients who have been audited to EXCiPACT standards using the first edition.

1 Scope

The standard contains the principles and requirements for the quality management system operated by EXCiPACT registered Certification Bodies. The requirements ensure the impartiality, competence and consistency of EXCiPACT audits and the certification of the quality management systems of excipient suppliers.

This second edition of this Annex includes requirements previously included in the ISO 19011:2002 annex for auditing to EXCiPACT standards. It therefore includes the principles of auditing, managing audit programmes, and the criteria for auditor competency. In the context of EXCiPACT audits, it indicates that auditors shall have the necessary knowledge and understanding of the principles and application of GMP and GDP. These requirements apply to auditors assessing an organisation's quality management system against the requirements in the EXCiPACT GMP and GDP Standards. In addition, those personnel making the certification decision in the Certification Bodies shall also comply with these requirements.

Where reference is made to EXCiPACT GMP or GDP standards, these may be substituted by other GMP or GDP standards which EXCiPACT asbl declares as equivalent.

2 Normative References

For dated references, the latest edition of the referenced document applies; if undated the current edition cited applies.

ISO/IEC 17021-1:2015 Conformity Assessment – Requirements for bodies providing audit and certification management systems – Part 1: Requirements.

ISO 9001 Quality Management Systems – Requirements.

Joint IPEC-PQG Good Manufacturing Practices Guide for Pharmaceutical Excipients 2006.

IPEC Good Distribution Practices Guide for Pharmaceutical Excipients 2006.

3 Terms and Definitions

Auditee	The organisation, including the sites named on the application, being assessed.
Certified Auditee:	Organisation whose quality management system has been certified.
Objective Evidence	Records, statements of fact or other information which can be verified and are relevant to the audit.
Certification Bodies	Independent third party organisation that issues EXCiPACT Certificates based on the requirements in the EXCiPACT standards.
Technical Experts	Person who provides specific knowledge or expertise and independent advice to an audit team.
Technical Area	For the EXCiPACT Certification Scheme the ISO/IEC 17021 term "technical area" is defined by the context of the organisation (see ISO 9001:2015) and the boundaries within which EXCiPACT GMP and GDP are applied. Elsewhere EXCiPACT refers to the Technical Area as "Scope".
Nonconformities **Note:** ISO/IEC 17021-1:2015 defines Major and Minor nonconformities, but EXCiPACT has defined two further classifications related to the impact on product and patient safety (see also Section 9.4.5).	
Life Threatening	A nonconformity or other situation which has produced product that is harmful to the human or veterinary patient or a product

	which if released would be harmful to the human or veterinary patient.
Critical	The excipient poses significant risk to patient safety. Remediation before further excipient is produced would be indicated and/or a recall should be considered.
Major	No additional requirements.
Minor	No additional requirements.

4 Principles

4.1 General

No additional requirements.

4.2 Impartiality

Certification Bodies shall base decisions on objective evidence collected at audit, from which they can judge conformity or nonconformity to the current EXCiPACT GMP and/or GDP requirements. Such decisions shall not be influenced by other interests or other parties.

4.3 Competence

Note: Competency requirements for Certification Body personnel are set out in Section 7.1 and Annex A.

4.4 Responsibility

The auditee is responsible for conformance to ISO 9001 and EXCiPACT GMP or GDP certification requirements. The Certification Body is responsible for the assessment of the auditee against the certification requirements.

Note: EXCiPACT Certificates may be issued in combination with existing ISO 9001 Certificates or other standards recognised by EXCiPACT asbl.

4.5 Openness

No additional requirements.

4.6 Confidentiality

No additional requirements.

4.7 Responsiveness to complaints

No additional requirements.

4.8 Risk-based approach

No additional requirements.

5 General Requirements

5.1 Legal and Contractual matters

5.1.1 Legal responsibility

No additional requirements.

5.1.2 Certification agreement

No additional requirements.

5.1.3 Responsibility for certification decisions

No additional requirements.

5.2 Management of impartiality

5.2.1

No additional requirements.

5.2.2

The Certification Bodies shall make publically available (see Section 8.1.1. f) a statement that indicates it understands the criticality of impartiality in carrying out EXCiPACT certification assessments, that it manages conflicts of interest and ensures the objectivity of its certification activities.

5.2.3

No additional requirements.

5.2.4

No additional requirements.

5.2.5

No additional requirements.

5.2.6

No additional requirements.

5.2.7

No additional requirements.

5.2.8

No additional requirements.

5.2.9

No additional requirements.

5.2.10

To avoid a conflict of interest, personnel, including ex-employees or consultants, who have provided any management system consultancy (including GMP and or GDP) shall not participate in audit or certification activities of the organisation within two years following the end of the consultancy.

5.2.11

No additional requirements.

5.2.12

No additional requirements.

5.2.13

No additional requirements.

5.3 Liability and financing

5.3.1

No additional requirements.

5.3.2

No additional requirements.

6 Structural Requirements

6.1 Organisational structure and top management

6.1.1

No additional requirements.

6.1.2

No additional requirements.

6.1.3

The Certification Body shall identify the top management (board, group or persons, or person) having overall authority and responsibility for the following:

k) Oversight of the appeals process.

6.1.4

No additional requirements.

6.2. Operational control

6.2.1

Risks to the competence, consistency and impartiality of the Certification Body arising from organisational arrangements for delivering certification activities shall be evaluated in accordance with Section 5.2.3.

6.2.2

The Certification Body shall justify the method and control of activities undertaken.

6.2.3

Top management shall record and inform EXCiPACT asbl of any instances where the impartiality of its activities has been compromised.

7 Resource Requirements

7.1 Competence of personnel

7.1.1 General considerations

Personnel involved in EXCiPACT certification activities shall meet the competency criteria in Annex A.

The Certification Body shall have processes to ensure that personnel have appropriate knowledge in GMP and / or GDP management in accordance with the requirements of Annex A.

The Certification Body shall ensure all EXCiPACT auditors are registered with EXCiPACT asbl.

7.1.2 Determination of competence criteria

No additional requirements.

7.1.3 Evaluation of processes

The Certification Body shall permit EXCiPACT asbl to witness an EXCiPACT certification audit each year.

Note: EXCiPACT asbl shall share with the Certification Body their conclusions of the auditor evaluation following the witnessed audit.

A new auditor shall be witnessed performing an EXCiPACT audit by another EXCiPACT registered auditor or by a representative of EXCiPACT asbl before they perform audits independently.

Note: See also 7.2.11

At least every three years the Certification Body shall evaluate personnel involved in EXCiPACT certification activities to ensure that they retain the defined knowledge, skills and competencies as defined in Section 7.2. Records of the evaluation shall be retained.

The Certification Body shall require all EXCIPACT auditors to register with EXCIPACT asbl and to renew their registration every three years.

7.1.4 Other considerations

The Certification Body shall have access to the necessary technical expertise for advice on matters relating to excipient regulations, GMP and / or GDP within the geographic areas in which they operate.

7.2 Personnel involved in the certification activities

7.2.1

No additional requirements.

7.2.2

No additional requirements.

7.2.3

No additional requirements.

7.2.4

No additional requirements.

7.2.5

The Certification Body shall demonstrate that all auditors involved in performing EXCiPACT Certification audits meet the EXCiPACT auditor competency requirements and are registered with EXCiPACT asbl.

7.2.6

Auditors shall be knowledgeable of the EXCiPACT Certification Scheme requirements (see also Annex A).

7.2.7

The Certification Body shall identify on-going training needs and provide access to training for personnel involved in EXCiPACT Certification activities in accordance with Section 7.1.2.

7.2.8

Those individuals who are responsible for the decision to grant, maintain, renew, extend, reduce, suspend or withdraw EXCiPACT GMP and/or GDP

certification shall understand the EXCiPACT GMP and/or EXCiPACT GDP standards and certification requirements, shall be independent and free from conflict of interest of the audit process they are to review, and shall have proven knowledge and experience in the pharmaceutical and/or excipient industry.

Note: See also Annex A.

7.2.9

There shall be annual performance evaluation of those involved in the EXCiPACT certification programme plus assessment of audit skills every 3 years.

7.2.10

No additional requirements.

7.2.11

There shall be periodic on-site evaluation of auditor performance at least once in every 3 year period in accordance with EXCiPACT Auditor Competency Requirements (see 7.1.3).

7.3 Use of individual external auditors and external technical experts

External auditors engaged by the Certification Body shall meet all requirements for EXCiPACT auditor competency (see Annex A) and shall be independent of the auditee and verified as free from conflicts of interest.

Note: External auditors may work for more than one Certification Body if these conditions are met on each occasion.

7.4 Personnel records

No additional requirements.

7.5 Outsourcing

7.5.1

The Certification Body shall have documented procedures for qualification and monitoring of outsourced services.

The Certification Body shall not outsource EXCiPACT certification to another organization.

Note: Use of external auditors is not outsourcing, see 7.3.

7.5.2

No additional requirements.

7.5.3

No additional requirements.

7.5.4

No additional requirements.

8 Information Requirements

8.1 Public information

8.1.1

Information describing the EXCiPACT audit and certification process for granting, maintaining, extending, renewing, reducing, suspending, or withdrawing certification shall be publicly accessible.

Note: This EXCiPACT Standard and a list of EXCIPACT Certified organisations is publicly available at www.excipact.org.

8.1.2

If requested, the Certification Body shall provide information about:

d) the authenticity of an EXCiPACT Certificate and or audit report(s)

8.1.3

No additional requirements.

8.2 Certification documents

The Certification Bodies shall permit the auditee to disclose audit reports and any associated documentation (e.g. Corrective Action Plan).

8.2.1

No additional requirements.

8.2.2

No additional requirements.

Note concerning bullet f):

- EXCiPACT GMP applies excipient manufacturers,
- EXCiPACT GDP applies to excipient distributors,
- EXCiPACT GMP and GDP applies to organisations performing both excipient manufacture and excipient distribution activities.

8.3 Reference to certification and use of marks

8.3.1

The Certification Bodies shall comply with the requirements in the legal agreement with EXCiPACT asbl and with the guidance provided by EXCiPACT for the use of EXCiPACT logo and name.

8.3.2

No additional requirements.

8.3.3

No additional requirements.

8.3.4

No additional requirements.

8.3.5

The Certification Bodies shall exercise proper control of ownership and take action to deal with incorrect references to certification status or misleading use of certification documents, marks, or audit reports.

The Certification Bodies shall notify EXCiPACT of any such incidents relating to EXCiPACT certification activities.

8.4 Confidentiality

Proprietary information in the EXCiPACT report may be redacted or made unreadable, if the Certification Bodies agrees the redactions are not material to the Certification status (see also 9.4.8.3).

8.4.1

No additional requirements.

8.4.2

No additional requirements.

8.4.3

The Certification Bodies shall have a written agreement with the certified client that it will respond to requests for authenticating Certificates and Audit reports from third parties without the need for the certified client's consent.

8.4.4

No additional requirements.

8.4.5

No additional requirements.

8.4.6

No additional requirements.

8.4.7

No additional requirements.

8.5 Information exchange between a Certification Body and its clients

8.5.1 Information on the certification activity and requirements

The Certification Body shall provide information and update clients on the following:

g) The requirement to pay EXCiPACT a Certificate Fee before an EXCiPACT Certificate (or renewed certificate) can be issued.

8.5.2 Notice of changes by a Certification Body

Upon receipt of changes from EXCiPACT asbl, an implementation plan shall be developed by the Certification Bodies comprising the following:

- description of the change to the Certification Programme,
- potential impact of the change to auditees and auditees already certified,
- establishment of a future effective date by which all auditees shall comply with the new requirements,
- methods of verifying that the auditees have implemented the changes.

Following implementation, there shall be a review of confirmatory documentation, or on-site verification at the next scheduled site audit that changes have been implemented.

8.5.3 Notice of changes by a certified client

No additional requirements.

9 Process Requirements

9.1 Pre-certification activities

9.1.1 Application

Where the auditee has an ISO 9001 quality management system then the EXCiPACT GMP and or GDP Certification Scope shall not encompass more than the Certification Scope of the ISO 9001 quality management system.

9.1.2 Application review

9.1.2.1

The Certification Bodies shall conduct a review of the application and supplementary information for certification to ensure that:

e) the certification is for Excipient GMP and/or Excipient GDP,
f) any health and safety requirements for the auditors have been identified.

9.1.2.2

No additional requirements.

9.1.2.3

No additional requirements.

9.1.3 Audit programme

9.1.3.1

Certification and recertification audits shall examine all GMP and / or GDP requirements. The Certification Body shall use the first audit in the two-stage audit Certification process to verify the scope of Certification and to determine the audit duration necessary for Certification, recertification and surveillance audits. The two annual surveillance audits between Certifications shall cover at least the entire GMP and or GDP requirements. The Certification Body shall re-evaluate the audit durations if there are significant changes to the auditees scope of Certification and or activities.

9.1.3.2

No additional requirements.

9.1.3.3

No additional requirements.

Note: See also the Guidance on the Frequency of EXCiPACT Surveillance and Recertification Audits on the EXCiPACT website.

9.1.3.4

No additional requirements.

9.1.3.5

No additional requirements.

9.1.4 Determining audit time

9.1.4.1

The audit time shall be determined according to the scope and complexity of the GMP / GDP system and excipients produced in order to assess

conformance to the excipient GMP / GDP requirements at each individual site.

As a minimum, audit durations for an EXCiPACT GMP/GDP stand-alone audit shall be:

- initial Certification: 2 days,
- surveillance Audit:1 day,
- recertification Audit:2 days.

In exceptional cases, less time than the minimum may be determined as appropriate, however in such cases approval for such a deviation shall first be sought from EXCiPACT asbl.

Note: See Annex F for guidance on audit durations.

9.1.4.2

In determining the audit time, the Certification Body shall consider, among other things, the following aspects:

i) the number of excipients in scope,
j) the complexities of the activities at each location,
k) any other activities within the scope of the certification.

Note: The audit time determined should be verified as suitable at the Stage 1 audit (see 9.3.1.2).

Note: See Annex F for guidance on audit durations.

9.1.4.3

The justification for GMP/GDP audit times shall be documented and records retained of each decision for each auditee.

9.1.4.4

No additional requirements.

9.1.5 Multi-site sampling

The Certification Bodies shall audit all sites at initial certification, surveillance and recertification to the GMP / GDP requirements. Multi-site sampling does not apply for EXCiPACT GMP/GDP.

9.1.6 Multiple management systems standards

No additional requirements.

9.2 Planning audits

9.2.1 Determining audit objectives, scope and criteria

9.2.1.1

The Certification Bodies shall request the following documentation for review prior to the site audit:

- documentation describing conformance to the GMP / GDP standards and the required scope of the audit,
- documentation showing the layout and size of the excipient operations conducted at the facility,
- current organisation chart.

9.2.1.2

The Certification Bodies shall not communicate areas for potential improvement against the EXCiPACT GMP or GDP Standards.

9.2.1.3

The audit shall cover the following:

- GMP covering all operations performed to produce the excipient from the point at which full GMP begins through to storage and shipment of the packaged excipient where the applicant is a manufacturer and / or,
- GDP where the applicant is a distributor or a manufacturer distributing excipients.

Where audits are being planned for multiple sites, the requirements of Section 9.1.5 shall be addressed.

9.2.1.4

No additional requirements.

9.2.2 Audit team selection and assignments

9.2.2.1 General

The auditee and the auditors shall be notified of the intended auditors prior to the assessment,

- both the auditors and the auditee have a duty to notify the Certification Bodies if there is any conflict of interest with the assignment,
- if there is any conflict of interest, then other auditors shall be assigned (see also 9.2.3.5).

9.2.2.1.1

Where the audit is conducted to certify conformance with ISO 9001 plus the GMP/GDP Standard, the audit team shall include an ISO 9001

Registered Lead Auditor and at least one team member shall be an EXCiPACT Auditor meeting the competency criteria in Section 7. Where the audit is conducted solely to the GMP/GDP Standard (or another EXCiPACT declared equivalent standard), the audit team does not require an ISO 9001 Registered Lead Auditor.

9.2.2.1.2

The same auditor shall not audit the same client more than three times consecutively. If this requirement cannot be met, EXCiPACT shall be notified to identify a suitable solution.

9.2.2.1.3

No additional requirements.

9.2.2.1.4

No additional requirements.

9.2.2.1.5

No additional requirements.

9.2.2.2 Observers, technical experts and guides

9.2.2.2.1

No additional requirements.

9.2.2.2.2

No additional requirements.

9.2.2.2.3

No additional requirements.

9.2.3 Audit plan

9.2.3.1

No additional requirements.

9.2.3.2

An audit shall not be conducted remotely.

Note: See Section 9.1.4 for guidance on EXCiPACT audit durations.

9.2.3.3

No additional requirements.

9.2.3.4

No additional requirements.

9.2.3.5

No additional requirements.

9.3 Initial Certification

9.3.1 Initial certification audit.

9.3.1.1. General

No additional requirements.

9.3.1.2 Stage 1

9.3.1.2.1

A formal audit plan shall be prepared for Stage 1 audits.

The Stage 1 audit shall be conducted on site. The Stage 1 audit shall be used to justify the Stage 2 audit plan.

9.3.1.2.2

No additional requirements.

9.3.1.2.3

No additional requirements.

9.3.1.2.4

The interval between a stage 1 and stage 2 audit shall not exceed 6 months.

9.3.1.3 Stage 2

The purpose of the stage 2 audit is to evaluate the implementation, including effectiveness, of the client's management system. The stage 2 audit shall take place at the site(s) of the client. It shall include at least the following:

g) information and evidence of conformity to the GMP / GDP standards.

9.3.1.4 Initial Certification Conclusions

No additional requirements.

9.4 Conducting audits

9.4.1 General

The Certification Bodies shall have a documented process for conducting on site GMP / GDP audits.

Virtual audits shall not be conducted for EXCiPACT GMP or GDP purposes.

9.4.2 Conducting the opening meeting

No additional requirements.

9.4.3 Communication during the audit

No additional requirements.

9.4.4 Obtaining and verifying information

No additional requirements.

9.4.5 Identifying and recording audit findings

9.4.5.1

No additional requirements.

9.4.5.2

The Certification Bodies shall not communicate areas for potential improvement against the EXCiPACT GMP or GDP Standards.

Note: Opportunities for potential improvement could be perceived as consultancy.

9.4.5.3

Nonconformities shall be classified as:

- life threatening, or
- critical, or
- major, or
- minor.

9.4.5.4

No additional requirements.

9.4.6 Preparing audit conclusions

No additional requirements.

9.4.7 Conducting the closing meeting

No additional requirements.

9.4.8 Audit report

9.4.8.1

EXCiPACT audit reports shall be prepared in English. The client shall be permitted to share copies of the complete audit report with their customers. Where requested by the client's customers, the Certification

Body shall verify that copies of the audit report are complete and a true record.

Note: A translated copy of the audit report may be prepared in another language if requested by the client.

9.4.8.2

The audit report shall disclose any areas of excipient GMP and/or GDP requirements that were not covered.

Any nonconformities remedied during the audit shall be classified as in Section 9.4.5.3 and noted accordingly in the audit report.

Any nonconformities remedied after the audit and prior to the certification decision shall be classified as in Section 9.4.5.3 and noted accordingly in a suitably revised audit report.

9.4.8.3

The audit report shall include:

- the operational activities examined,
- the excipients and grades covered,
- a list of the client's personnel involved in the audit.

Proprietary information in the EXCiPACT report may be redacted or made unreadable by the certified organisation, if the Certification Bodies agrees the redactions are not material to the Certification status (see also 8.4).

The audit report shall not include opportunities for improvement against the GMP / GDP Standards.

Note: The EXCiPACT Website contains more guidance on the audit report contents.

9.4.9 Cause analysis of nonconformities

The auditee shall be required to submit a corrective action plan for all nonconformities and this shall be included with the audit report for review under 9.5.

9.4.10 Effectiveness of corrections and corrective actions

The auditee shall be required to provide evidence of the progress of any corrective action plans in accordance with the timings defined in the plans.

The Certification Bodies shall ensure an EXCiPACT Registered auditor verifies the adequacy of corrective action plans.

The progress of the corrective action plan shall be verified on site at the next audit(s).

Additional Audits

A further on-site audit is required to verify the effectiveness of any correction and corrective actions for Life Threatening and Critical nonconformities. Major nonconformities can be verified remotely where the client provides objective evidence that they have addressed the issue and by direct observation at the next audit.

9.5 Certification decision

No additional requirements.

9.5.1 General

9.5.1.1

Individuals responsible for the decision to grant, maintain, renew, extend, reduce, suspend or withdraw an EXCiPACT GMP and/or GDP certificate shall understand the EXCiPACT GMP and/or EXCiPACT GDP standards and certification requirements. These individuals shall be independent and free from conflict of interest of the audit process they are to review and shall have proven knowledge and experience in the pharmaceutical and/or excipient industry.

Note: See Annex A.

9.5.1.2

No additional requirements.

9.5.1.3

No additional requirements.

9.1.5.4

No additional requirements.

9.5.2 Actions prior to making a decision

The Certification Body shall have a process to conduct an effective review prior to making a decision for granting certification, expanding or reducing the scope of certification, renewing, suspending or restoring, or withdrawing of certification, including, that

d) the audit report complies with the requirements of 9.4.8,
e) correction and corrective action plans for all Life Threatening, Critical and Major nonconformities have been reviewed, accepted, and verified.

9.5.3 Information for granting initial certification

For Certification, the acceptance criteria are:

1. No items rated as Life Threatening,
2. No items rated as Critical,
3. No items rated as Major.

For continuing Certification, the Surveillance audit shall have:

1. No items rated as Life Threatening or Critical,
2. No items rated as Major unless the deficiency has been remediated or an interim control is in-place i.e. Corrective Action plan accepted by the Certification Bodies and verified,
3. No items rated as Minor from a prior audit that have either not been corrected or for which an acceptable Corrective Action plan has not been developed.

The certification decision shall be made by at least two persons, one of whom should meet the competency requirements for an EXCiPACT GMP/ GDP auditor (see Annex A).

9.5.3.1

No additional requirements.

9.5.3.2

If the Certification Body is not able to verify the implementation of corrections and corrective actions of any Life Threatening or Critical nonconformity within 6 months after the last day of the stage 2, the Certification Body shall conduct another stage 2 prior to recommending certification.

9.5.3.3

When transferring certification, the recertification date on the last certificate cannot be extended without another full certification audit.

9.5.4 Information for granting recertification

No additional requirements.

9.6 Maintaining Certification

No additional requirements.

9.6.1 General

The Certification Body shall maintain certification based on demonstration that the client continues to satisfy the requirements of the management system standard. It may maintain a client's certification based on a positive

conclusion by the audit team leader without further independent review and decision, provided that:

c) for any Life Threatening or Critical nonconformity that may lead to suspension or withdrawal of certification, the Certification Body has a system that requires the audit team leader to report to the Certification Body the need to initiate a review by competent personnel (see 7.2.8), different from those who carried out the audit, to determine whether certification can be maintained.

9.6.2 Surveillance activities

9.6.2.1 General

No additional requirements.

9.6.2.2 Surveillance Audit

Surveillance audits shall be conducted at least annually and cover at least half of the quality system such that the entire excipient quality system will be reviewed by the two surveillance audits that occur in between recertification audits.

9.6.3 Recertification

9.6.3.1 Recertification audit planning

9.6.3.1.1

Recertification shall occur at intervals of not more than three years after initial certification or last recertification. The recertification audit shall be planned and conducted to confirm that the requirements of excipient GMP /GDP continue to be met.

Note: See also the Guidance on the Frequency of EXCiPACT Surveillance and Recertification Audits on the EXCiPACT website.

9.6.3.1.2

No additional requirements.

9.6.3.1.3

No additional requirements.

9.6.3.2 Recertification audit

9.6.3.2.1

No additional requirements.

9.6.3.2.2

For any Life Threatening, Critical or Major nonconformity, the Certification Body shall define time limits for correction and corrective actions. These actions shall be implemented and verified prior to issue of the new certificate.

9.6.3.2.3

A new certificate shall not be issued with a period of validity in excess of 39 months from the date or the recertification audit.

9.6.3.2.4

If the Certification Body has not completed the recertification audit or the Certification Body is unable to verify the implementation of corrections and corrective actions for any Life Threatening or Critical nonconformity (see 9.5.2.1) prior to the expiry date of the certification, then recertification shall not be recommended and the validity of the certification shall not be extended. The client shall be informed and the consequences shall be explained.

9.6.3.2.5

No additional requirements.

9.6.4 Special Audits

9.6.4.1 Expanding Scope

No additional requirements.

9.6.4.2 Short notice audits

No additional requirements.

9.6.5 Suspending, withdrawing or reducing the scope of certification

9.6.5.1

Certifications granted, suspended, or withdrawn must be reported without delay to EXCiPACT, who will make such information publicly available.

9.6.5.2

The Certification Bodies shall suspend certification should a regulatory authority inspection find a Life Threatening or Critical Nonconformity from GMP/GDP requirements.

9.6.5.3

The Certification Body shall have enforceable arrangements with its clients to ensure that in case of suspension the client refrains from further promotion of its certification. The Certification Body shall inform EXCIPACT of the suspended status of the certification (see 9.6.5.1).

9.6.5.4

No additional requirements.

9.6.5.5

No additional requirements.

9.7 Appeals

9.7.1

No additional requirements.

9.7.2

No additional requirements.

9.7.3

No additional requirements.

9.7.4

The appeals handling process shall include at least the following elements and methods:

d) where the appeal concerns EXCiPACT Certification and it cannot be resolved to the satisfaction of the auditee using the standard Certification Bodies appeals procedure, the appellant shall be informed they have the right to request EXCiPACT asbl to review the decision.

9.7.5

No additional requirements.

9.7.6

When a final decision is communicated and the decision is not accepted, the appellant shall be notified that they may request EXCiPACT to review the decision.

9.7.7

No additional requirements.

9.7.8

No additional requirements.

9.8 Complaints

9.8.1

No additional requirements.

9.8.2

No additional requirements.

9.8.3

No additional requirements.

9.8.4

No additional requirements.

9.8.5

No additional requirements.

9.8.6

The complaints-handling process shall include at least the following elements and methods:

d) EXCiPACT shall be notified of all complaints about the EXCiPACT Certification Scheme and their outcomes,

e) where the complaint concerns EXCiPACT Certification and it cannot be resolved to the satisfaction of the complainant using the standard Certification Bodies complaints procedure, the complainant shall be informed that they have the right to request EXCiPACT asbl to review the decision.

9.8.7

No additional requirements.

9.8.8

No additional requirements.

9.8.9

No additional requirements.

9.8.10

No additional requirements.

9.8.11

No additional requirements.

9.9 Client records

9.9.1

No additional requirements.

9.9.2

No additional requirements.

9.9.3

No additional requirements.

9.9.4

Records of EXCiPACT Certification shall be retained for a minimum of 6 years.

Note: The Certification Body is required to verify the authenticity of audit reports and this service may need to be provided for any reports issued in the previous 6 years.

10 Management System Requirements for Certification Bodies

10.1 Options

No additional requirements.

10.2 Option A: General management system requirements

10.2.1 General

The Certification Body shall appoint a member of management who, irrespective of other duties, shall have the responsibility and authority that includes:

a) ensuring the processes and procedures needed for the management system are established, implemented and maintained,

b) reporting to top management on the performance of the management system and any need for improvement.

10.2.2 Management system manual

No additional requirements.

10.2.3 Control of documents

No additional requirements.

10.2.4 Control of records

No additional requirements.

10.2.5 Management review

10.2.5.1

No additional requirements.

10.2.5.2

No additional requirements.

10.2.5.3

No additional requirements.

10.2.6 Internal audits

10.2.6.1

No additional requirements.

10.2.6.2

No additional requirements.

10.2.6.3

No additional requirements.

10.2.6.4

No additional requirements.

10.2.7 Corrective actions

No additional requirements.

10.3 Option B: Management system requirements in accordance with ISO 9001

10.3.1 General

No additional requirements.

10.3.2 Scope

No additional requirements.

10.3.3 Customer focus

No additional requirements.

10.3.4 Management review

No additional requirements.

Annex A (normative) Required knowledge and skills

A.1 General

Table A.1 – Table of knowledge and skills

Additional EXCiPACT Requirements (all other entries as ISO/IEC 17021-1:2015)

Knowledge and skills	Conducting the application review to determine audit team competence required, to select the audit team members, and to determine the audit time	Reviewing audit reports and making certification decisions	Auditing and leading the audit team
Qualifications requirements for EXCiPACT			See A.1.1
Knowledge of business management practices	See A.2.1	See A.2.1	

A.1.1 Qualification Requirements for EXCiPACT Auditors

EXCiPACT Auditors shall meet the knowledge and competency criteria in this Annex.

EXCiPACT Auditors shall also hold at least one of the following:

- be registered as a quality management systems Auditor by an accredited Certification Bodies,
- be registered with a recognised auditor registration organisation, (e.g. International Register of Certificated Auditors (IRCA), American Society for Quality (ASQ)),

have demonstrated their ability to perform management system audits such as ISO 9001, ISO 14001, audits or pharmaceutical or excipient or API GMP/GDP audits and completed at least 5 audits in the last two years.

EXCiPACT Auditors shall have:

a) A tertiary scientific qualification,

Note: Examples of such qualifications are Higher National Diploma (UK), Associates Degree (US.).

b) A minimum of five years quality related work experience, such as:
   - a Technical, Managerial, or Professional role within:
     - ✓ an excipient or API supplier,
     - ✓ a pharmaceutical company.
   - a role with responsibilities that include conformance to GMP requirements,
   - performing quality system or GMP audits of chemical operations to a recognised standard, e.g. ISO 9001.

c) A registration with the EXCiPACT auditor registration scheme (see www.excipact.org) which includes:
   i. attendance at an EXCiPACT approved auditor training course which includes a minimum of 7 contact hours applicable to GMP and GDP for excipients,
   ii. a satisfactory examination result after attending an EXCiPACT approved auditor training course,
   iii. successful completion of one audit witnessed by an EXCiPACT approved observer, demonstrating acceptable:
     - ✓ audit skills,
     - ✓ knowledge of excipient GMP conformance requirements,
     - ✓ preparation of audit reports,
     - ✓ appropriate rating of findings.

Note: A successful witnessed audit is where the auditor has demonstrated their skills in planning, conducting and documenting an audit.

A.2 Competency requirements for management system auditors

A.2.1 Knowledge of business management practices

No additional requirements.

A.2.2 Knowledge of audit principles, practices and techniques

Auditors shall demonstrate the ability to apply a breadth of knowledge and skills which will enable them to be effective in respect of ensuring that GMP and GDP audits are conducted in a consistent manner.

- reaching agreement with the excipient supplier to audit findings and conclusions,
- effectively reviewing the resulting correction and corrective actions arising from EXCiPACT Certification audits.

A.2.3 Knowledge of specific management system standards/ normative references

Auditors shall have current knowledge of:

- management system definitions,
- industry guidance,
- relevant legislation,
- the application of excipient GMPs to different excipient production processes,
- regulatory requirements for the excipient in the intended markets, for example:
  a. basic microbiology and chemistry,
  b. appropriate Pharmacopoeias,
  c. cleaning principles as applied to manufacturing processes,
  d. IPEC-PQG Excipient GMPs,
  e. regulations in the intended market (e.g. TSE, Residual Solvents),
  f. risk assessment techniques (ICH Q9, HACCP, etc.).
- information systems and technology used in GMP and GDP operations (demonstration of the proper use and control of computer systems),
- good distribution practices, including:
  a. the different operations of distributors,
  b. operations involving repackaging and relabelling of excipients,
  c. office-only operations,
  d. an understanding of distribution related safety and quality systems:
     1. responsible Care and/or Responsible Distribution Programmes,
     2. distributors assessment systems (e.g. for Europe Safety Quality Assessment Systems; European Single Assessment for Chemical Distributors (SQAS ESAD II)).

A.2.4 Knowledge of certification Body's processes

Auditors shall have knowledge of the processes required for EXCiPACT auditing and certification.

A.2.5 Knowledge of client's business sector

Auditors shall have knowledge and understanding of:

- business processes affecting the excipient and pharmaceutical industries,
- terminology used by the excipient and pharmaceutical industries,
- methods used to distribute excipients.

A.2.6 Knowledge of client's products, processes and organisation

Auditors shall have knowledge and understanding of:

- the science and technology of excipient manufacture and distributor operations,
- the critical activities that assure excipient quality,
- the relevance of the functionality of the excipient to the finished dosage form,
- the relevance of the route of administration of the finished dosage form in terms of the GMP and GDP to be applied to the excipient,
- the differing operations to produce the excipient ranging from mineral extraction and purification to chemical or biochemical synthesis.

A.2.7 Language skills appropriate to all levels within the client organisation

No additional requirements.

A.2.8 Note-taking and report-writing skills

No additional requirements.

A.2.9 Presentation Skills

No additional requirements.

A.2.10 Interviewing skills

No additional requirements.

A.2.11 Audit-management skills

No additional requirements.

A.3 Competence requirements for personnel reviewing audit reports and making certification decisions

A.3.1 Knowledge of audit principles, practices and techniques

Personnel reviewing audit reports shall demonstrate the ability to apply a breadth of knowledge and skills which will enable them to be effective in respect of ensuring that GMP and GDP audits are conducted in a consistent manner.

- reaching agreement with the excipient supplier to audit findings and conclusions,
- effectively reviewing the resulting correction and corrective actions arising from EXCiPACT Certification audits.

A.3.2 Knowledge of specific management system standards/ normative references

Personnel reviewing audit reports shall have current knowledge of:

- management system definitions,
- industry guidance,
- relevant legislation,
- the application of excipient GMPs to different excipient production processes.
- regulatory requirements for the excipient in the intended markets, for example:
  a. basic microbiology and chemistry,
  b. appropriate Pharmacopoeias,
  c. cleaning principles as applied to manufacturing processes,
  d. IPEC-PQG Excipient GMPs,
  e. regulations in the intended market (e.g. TSE, Residual Solvents),
  f. risk assessment techniques (ICH Q9, HACCP, etc.).
- information systems and technology used in GMP and GDP operations (demonstration of the proper use and control of computer systems),
- good distribution practices, including:
  a. the different operations of distributors,
  b. operations involving repackaging and relabelling of excipients
  c. office-only operations,
  d. an understanding of distribution related safety and quality systems:
     1. responsible care and/or responsible distribution programmes,
     2. distributors assessment systems (e.g. for Europe Safety Quality Assessment Systems; European Single Assessment for Chemical Distributors (SQAS ESAD II)).

A.3.3 Knowledge of certification Body's processes

Personnel reviewing audit reports shall have knowledge of the processes required for EXCiPACT auditing and certification.

A.3.4 Knowledge of client's business sector

Personnel reviewing audit reports shall have knowledge and understanding of:

- business processes affecting the excipient and pharmaceutical industries,
- terminology used by the excipient and pharmaceutical industries,
- methods used to distribute excipients.

A.4 Competence requirements for personnel conducting the application review to determine the audit team competence required, to select the audit team members, and to determine the audit time

A.4.1 Knowledge of specific management system standards/normative references

Personnel conducting the application review etc. shall have current knowledge of:

- management system definitions,
- industry guidance,
- relevant legislation,
- the application of excipient GMPs to different excipient production processes,
- regulatory requirements for the excipient in the intended markets, for example:
  a. basic microbiology and chemistry,
  b. appropriate Pharmacopoeias,
  c. cleaning principles as applied to manufacturing processes,
  d. IPEC-PQG Excipient GMPs,
  e. regulations in the intended market (e.g. TSE, Residual Solvents),
  f. risk assessment techniques (ICH Q9, HACCP, etc.).
- information systems and technology used in GMP and GDP operations (demonstration of the proper use and control of computer systems),
- good distribution practices, including:
  a. the different operations of distributors,
  b. operations involving repackaging and relabelling of excipients,
  c. office-only operations,
  d. an understanding of distribution related safety and quality systems:
     1. responsible Care and/or Responsible Distribution Programmes,
     2. distributors assessment systems (e.g. for Europe Safety Quality Assessment Systems; European Single Assessment for Chemical Distributors (SQAS ESAD II)).

A.4.2 Knowledge of certification Body's processes

Personnel conducting the application review etc. shall have knowledge of the processes required for EXCiPACT auditing and certification.

A.4.3 Knowledge of client's business sector

Personnel conducting the application review etc. shall have knowledge and understanding of:

- business processes affecting the excipient and pharmaceutical industries,
- terminology used by the excipient and pharmaceutical industries,
- methods used to distribute excipients.

A.4.4 Knowledge of client's products, processes and organisation

Personnel conducting the application review etc. shall have knowledge and understanding of:

- the science and technology of excipient manufacture and distributor operations,
- the critical activities that assure excipient quality,
- the relevance of the functionality of the excipient to the finished dosage form,
- the relevance of the route of administration of the finished dosage form in terms of the GMP and GDP to be applied to the excipient,
- the differing operations to produce the excipient ranging from mineral extraction and purification to chemical or biochemical synthesis.

Annex B (informative) Possible evaluation methods

B1 General

No additional Guidance

B2 Review of Records

- an annual review of audit reports issued by the auditor,
- analysis of new records of further education, training, employment and excipient GMP / GDP audit experience since the last review.

B3 Feedback

- surveys, questionnaires, complaints, etc. from applicants and others,
- audit Team Leader (if there was one) feedback on team participants (and vice versa).

B4 Interviews

No additional Guidance

B5 Observations

- any observation of audit skills, (e.g. report from an EXCiPACT asbl witness or a certification Body witness).

B6 Examinations

No additional Guidance

Annex C (informative) Examples of a process flow for determining and maintaining competence

No additional requirements.

Annex D (informative) Desired personal behaviour

Examples of personal behaviours that are important for personnel involved in certification activities for any type of management system are described as follows:

n) sound judgement,
o) integrity,
p) proven ability to put people at ease and understand the auditee's perspective,
q) proven ability to assure conduct of the audit to the audit schedule and within the scope.

Ethical Conduct includes:

- not accepting any inducements that may affect decision-making,
- not disclosing any confidential information to a third party without written authorisation,
- not practicing when barred.

Fair Presentation includes:

- truthful audit reports,
- accurate report content,
- report of obstacles and unresolved opinions.

Due Professional Care:

- the auditor should only undertake assignments for which they are qualified, e.g. Audit a quality management system for conformance to levels of GMP or GDP for which the auditor has been trained and qualified in accordance with EXCiPACT Auditor Competency and Qualification Requirements.

Independence includes:

- demonstrate lack of bias and conflict of interest,
- financial independence,
- organisational independence,
- evidence-based rather than subjective.

Annex E (informative) Audit and certification process

No additional guidance

Annex F (informative) Determination of Audit Duration

This annex provides guidance on Clause 9.1.4 Determining Audit Time.

The mandated durations are given on the basis of an independent EXCiPACT audit. Where a combined ISO 9001 and EXCiPACT audit is conducted additional time should be added to allow for assessment of the ISO 9001 requirements.

Where an audit is conducted against the requirements of the NSF/IPEC/ANSI 363-2016 US National standard, then the audit time would be expected to be similar to a combined ISO 9001 and EXCiPACT GMP/GDP Standard audit.

For scope extension, the minimum additional duration should be recalculated after considering the complexity of the added activity.

Deviations in audit durations

The minimum audit durations in 9.1.4.1 identify a starting point which should be adjusted for any special attributes of the organisation and or system to be audited.

The following factors, and any other as identified as relevant to the organisation and its activities, should be considered and used to increase the allocated audit time (non-exhaustive):

- complexity of logistics (e.g. involving more than one location),
- staff speaking more than one language, where translators are required or auditors are unable to audit independently,
- complexity and quantity of manufacturing processes, technologies,
- quantity of product groups/families of different types,
- size and dispersion of the site,
- older sites, difficult material flow,
- time consuming access procedures to high risk areas,
- number of non-conformances recorded in any previous evaluation,
- difficulties experienced during previous evaluations,
- any outsourcing within the scope of certification.

The above points for deviations in the audit duration are indicative and do not cover all situations and all attributes of the specific organisation's system, processes and products or services that should be considered when determining audit time.

Bibliography

No additional bibliography

Appendix 1 Definitions

Terms used in this document, which have a specific technical meaning, are defined here.

1. **Acceptance criteria**: Numerical limits, ranges, or other suitable measures of acceptance for test results [Q7]
2. **Active pharmaceutical ingredient (API)**: Any substance or mixture of substances, intended to be used in the manufacture of a drug product and that, when used in the production of a drug, becomes an active ingredient of the drug product. Such substances are intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment or prevention of disease or to affect the structure or any function of the body of man or animals. [IPEC]
3. **Adequate**: Sufficient, although not necessarily the most or the best.
4. **Appropriate**: A quality of being sufficient to meet the requirements.
5. **Audit team leader**: A qualified individual who organises, coordinates, and is qualified to conduct audits to the GMP or GDP Annexes as applicable.
6. **Batch (lot)**: A specific quantity of material produced in process or a series of processes so that it can be expected to be homogenous. In the case of a continuous process, a batch may correspond to a defined fraction of the production. The batch size can be defined by a fixed quantity or by the amount produced in a fixed time interval. [IPEC] ANSI NSF reworded to: batch: A specific quantity of material produced in a process or a series of processes so that it may be expected to be uniform in character and quality, within specified limits. In the case of a continuous process, a batch may correspond to a defined fraction of the production. The batch size may be defined by a fixed quantity or by the amount produced in a fixed time interval.
7. **Batch number (Lot Number)**: A unique combination of numbers, letters and/or symbols that identifies a batch (or lot) and from which the production and distribution history can be determined. [Q7]
8. **Batch process**: A process that produces the excipient from a discrete supply of raw materials that is present before the completion of the reaction. [Q7]

9. **Batch record**: Documents that provide a history of the manufacture of a batch of excipient. [IPEC PQG GMP]
10. **Broker / brokering**: Brokers resell excipients without conducting physical handling of the product such as warehousing, transport, repackaging etc. [IPEC GDP]
11. **Bulk excipient**: Excipient in any transportation or storage equipment (tanks, silos, ISO-Containers, tank/silo trucks etc.) to be filled/ repackaged into others (tanks, silos, drums, bags, containers etc.).
12. **Certificate of analysis (CoA)**: A document listing the test methods, specification and results of testing a representative sample from the batch to be delivered. [IPEC]
13. **Change**: anything that alters an excipient's physical, chemical and/or microbiological characteristics from the norm, or that is likely to alter the excipient performance in the dosage form.
14. **Change control**: A process used for management review of proposed changes that may impact the quality or regulatory conformance of the excipient. [IPEC]
15. **Competency**: The demonstrated personal attributes and demonstrated ability to apply knowledge and skills. [ISO 19011:2002].
16. **Component**: Any material present in the excipient that arises as a consequence of the raw materials and/or manufacturing process. [IPEC]
17. **Computer system**: A group of hardware components and associated software designed and assembled to perform a specific function or group of functions. [IPEC]
18. **Contaminant**: An undesired material of a chemical or microbiological nature or foreign matter introduced from a raw material, intermediate, or excipient during production, sampling, packaging, storage or transport. [IPEC]
19. **Contamination**: The undesired introduction of impurities of a chemical or microbiological nature or foreign matter into or onto a raw material, intermediate or excipient during production, sampling, packaging or repackaging, storage or transport. [IPEC]
20. **Continual improvement**: Recurring activity to increase the ability to fulfil requirements. [IPEC]

21. **Continuous process**: A process that continually produces material from a continuing supply of raw material. [IPEC]
22. **Contract**: Business agreement for supply of goods or performance of work at a specified price. [WHO GTDP]
23. **Corrective action**: Action to eliminate the cause of a detected non-conformity or other undesirable situation. NOTE – Corrective action is taken to prevent recurrence whereas preventive action is taken to prevent occurrence. [IPEC]
24. **Critical**: A process step, process condition, test requirement or other relevant parameter or item that must be controlled within predetermined criteria to ensure that the excipient meets its specification. [IPEC]
25. **Cross-contamination**: Contamination of a material or product with another material or product. [Q7]
26. **Customer**: The organisation receiving the excipient once it has left the control of the excipient manufacturer; includes brokers, agents and users. [IPEC]
27. **Deviation**: Departure from an approved instruction or established standard. [Q7]
28. **Distributor(s)**: For the purpose of this Annex "distributors" includes those parties involved in trade and distribution, (re)processors, (re) packagers, (re) labellers, transport and warehousing companies, forwarding agents, brokers, traders, and suppliers other than the original manufacturer.
29. **Distribution**: The division and movement of excipients from the premises of the manufacturer via distributor(s) to the excipient user.
30. **Documented procedure**: A written procedure meeting the requirements of 4.2.3.
31. **Drug product**: Dosage form intended for use by a patient.
32. **Effectiveness**: An expression of the degree to which activities have produced the effects planned. [IPEC]
33. **Excipient**: Substances other than the API which have been appropriately evaluated for safety and are intentionally included in a drug delivery system. [IPEC]

34. **Expiry (expiration) date**: The date designating the time during which the excipient is expected to remain within specifications and after which it should not be used. [IPEC].
35. **Functionality**: A desirable property of an excipient that aids and/or improves the manufacture, quality, or performance of the drug product. [IPEC]
36. **Good distribution practices (GDP)**: Requirements for the quality system under which drug products and their ingredients are handled and distributed.
37. **Good manufacturing practices (GMP)**: Requirements for the quality system under which drug products and their ingredients are manufactured. Current Good Manufacturing Practice (cGMP) is the applicable term in the United States. For the purposes of this guide, the terms GMP and cGMP are equivalent. [IPEC]
38. **ICH**: International Conference on Harmonisation. [IPEC]
39. **IPEC**: International Pharmaceutical Excipients Council. [IPEC]
40. **IPEC PQG**: International Pharmaceutical Excipients Council and the Pharmaceutical Quality Group. [IPEC]
41. **Impurity**: An undesirable component of an excipient that is present as a consequence of the raw materials, excipient manufacturing process, or excipient degradation. Impurities are expected to be controlled at a specified level.
42. **In-process control/testing**: Checks performed in production to monitor and, if appropriate, to adjust the process and or to ensure that the intermediate or excipient conforms to its specification. [IPEC PQG GMP]
43. **Intermediate**: Material that must undergo further manufacturing steps before it becomes an excipient. [IPEC PQG GMP]
44. **Label**: The display of written, printed or graphic matter on the Immediate container of the excipient (inactive ingredient) product. [IPEC]
45. **Labelling**: The action involving the selection of the correct label, with the required information, followed by line-clearance and application of the label. [WHO GTDP]
46. **Justified**: A documented explanation.

47. **Lot**: see Batch [IPEC]
48. **Manufacture / manufacturing process**: All operations of receipt of materials, production, packaging, repackaging, labelling, relabelling, quality control, release, storage, and distribution of excipients and related controls. [IPEC PQG GMP].
49. **Material**: A general term used to denote raw materials (starting materials, reagents, and solvents), process aids, intermediates, excipients and packaging and labelling materials. [Q7]
50. **Nonconformity / non-conformance**: A non-fulfilment of requirements.
51. **Nonconforming material**: Material that does not meet the manufacturer's specifications or has not been manufactured according to applicable GMPs [IPEC GDP].
52. **Organisation**: As in ISO 9001:2008, "organisation" is used in this Annex to indicate the entity to which the requirements apply.
53. **Original manufacturer**: Person or company manufacturing a material to the stage at which it is designated as a pharmaceutical starting material. [WHO GTDP]
54. **Packaging material**: A material intended to protect an intermediate or excipient during storage and transport. [IPEC]
55. **Pharmaceutical starting materia**l: A pharmaceutical starting material is an active pharmaceutical ingredient (API) or an excipient intended or designated for use in the production of a pharmaceutical product. [WHO GTDP]
56. **Preventive action**: Action to eliminate the cause of a potential nonconformity or other undesirable potential situation. NOTE – [IPEC] Preventive action is taken to prevent occurrence whereas corrective action is taken to prevent recurrence. [IPEC]
57. **Primary reference standard**: A substance that has been shown by an extensive set of analytical tests to be authentic material that is of high purity and to which all like standards are traced and qualified or certified. This standard is preferably obtained from an officially recognised source. If no official recognised source is available, the reference standard selected shall be appropriately characterised.
58. **Procedure**: Written, authorised instruction for performing specified operations. (see documented procedure) [IPEC GTDP]

59. **Process**: The combination of operating steps including synthesis, isolation, purification, packaging, etc. that produces the finished excipient. [IPEC]

60. **Production**: Operations involved in the preparation of an excipient from receipt of materials through processing and packaging of the excipient. [IPEC]

61. **Quality**: The suitability of an excipient for its intended use as indicated by relevant physical, chemical, and microbiological properties and as assured by compliance with these standards

62. **Quality assurance**: The sum total of the organised arrangements made with the object of ensuring that all excipients are of the quality required for their intended use and that quality systems are maintained. [IPEC PQG GMP]

63. **Quality control (QC)**: Checking or testing that specifications are met. [IPEC]

64. **Quality critical**: Describes a material, process step or process condition, test requirement or any other relevant parameter that directly influences the quality attributes of the excipient and which must be controlled within predetermined criteria. [IPEC]

65. **Quality management system (QMS)**: A management system that directs and controls how the organisation implements quality policies and achieves quality objectives.

66. **Quality risk management**: A systematic process for the assessment, control, communication, and review of risks to the quality of the excipient across its lifecycle.

67. **Quality system**: See Quality Management System.

68. **Quality unit**: An organisational unit independent of production which fulfils both Quality Assurance and Quality Control responsibilities. This can be in the form of separate QA and QC units or a single individual or group, depending upon the size and structure of the organisation. [IPEC].

69. **Quarantine**: The status of materials isolated physically or by other effective means pending a decision on their subsequent approval or rejection. [IPEC].

70. **Raw material**: A general term used to denote starting materials, reagents and solvents intended for use in the production of intermediates or excipients. [IPEC].

71. **Recall (USA: retrieval**): A process for withdrawing or removing a pharmaceutical material from the distribution chain because of defects in the materials or complaints of a serious nature. The recall might be initiated by the manufacturer/importer/ distributor or a responsible agency. [WHO GTDP].

    Note: In the USA, the term recall has specific regulatory implications that do not directly apply to excipients. Therefore, the term retrieval is typically used in the USA. In this document "recall" has the same meaning as retrieval.

72. **Record**: Document stating results achieved and/or providing evidence of activities performed. The medium may be paper, magnetic, electronic or optical, photographic etc. or a combination thereof. [IPEC].

73. **Relabelling**: The process of putting a new label on the material (see also labelling). [WHO GTDP].

74. **Repackaging**: The action of changing the packaging of the material. [WHO GTDP].

75. **Representative sample**: A quantity of the excipient taken according to a prescribed rationale so as to accurately portray the material being sampled (e.g. a batch).

76. **Reprocessing**: Repetition of an activity that is a normal part of the manufacturing process and that has been documented previously. [IPEC].

77. **Requirements**: The explicit or implicit needs or expectations of the governing standards. [IPEC]

78. **Resources**: suggested definition: Source of supply, support or aid, especially one that can be readily drawn upon when needed.

79. **Retained sample**: Representative sample of a batch/delivery that is sufficient quantity to perform at least two full quality control analyses and will be kept for a defined period of time. [IPEC].

80. **Retest date**: The date when a material should be re-examined to ensure that it is still suitable for use. [IPEC].

81. **Retest/re-evaluation interval**: The duration, normally expressed in months or years, from the date of manufacture, throughout which the excipient should continue to conform to the specification and after which should be tested to confirm it continues to meet the specification. [IPEC].

82. **Reworking**: Subjecting previously processed material that did not conform to standards or specifications to processing steps that differ from the normal process. [IPEC].

83. **Risk assessment**: A systematic process of organising information to support a risk decision to be made within a risk management process. It consists of the identification of hazards and the analysis and evaluation of risks associated with exposure to those hazards. [IPEC]

84. **Sampling**: Operations designed to obtain a representative portion of a pharmaceutical starting material based on an appropriate statistical procedure, for a defined purpose, e.g. acceptance of consignments, batch release, etc.

85. **Secondary reference standard**: A substance of established quality and purity, as shown by comparison to a primary reference standard, used as a reference standard for routine laboratory analysis. [IPEC].

86. **Significant change**: Any change that has the potential to alter an excipient's physical, chemical, or microbiological property from the norm, or that is likely to alter the excipient's performance in the dosage form.

87. **Solvent**: An inorganic or organic liquid used as a vehicle for the presentation of solutions or suspensions in the manufacture of an excipient. [IPEC].

88. **Specification**: A list of tests, references to analytical procedures and appropriate acceptance criteria that are numerical limits, ranges or other criteria for the tests described for a material, that a material is required to meet. [IPEC].

89. **Stability**: Continued conformance of the excipient to its specifications. [IPEC].

90. **State of control**: A condition in which the set of controls consistently provides assurance of continued process performance and product quality. [IPEC].

91. **Subcontractor**: Third party for outsourced work or services which contribute in whole or in part to the manufacture of excipients.

92. **Supplier**: Person or company providing pharmaceutical starting materials on request. Suppliers may be distributors, manufacturers, traders, etc.

93. **Supply chain**: For the purpose of standards, supply chain is defined as all steps in the entire chain of distribution starting from the point at which an excipient is transferred outside the control of the original manufacturer's material management system downstream to the final user of the excipient.

94. **Top management**: Person or group of people who direct and control an organisation at the highest level. The highest level can either be at the site or corporate level and will depend on the way that the quality management system is organised. [IPEC]

95. **Traceability**: Ability to determine the history, application or location that is under consideration, for example, origin on materials and parts, processing history or distribution of the product after delivery. [IPEC].

96. **Validation**: A documented programme that provides a high degree of assurance that a specific product, method, procedure (i.e. cleaning) or system will consistently produce a result that meets predetermined acceptance criteria. [IPEC].

97. **Verification**: The application of methods, procedures, tests and other evaluations, in addition to monitoring, to determine compliance with the GMP principles. [IPEC]

Appendix 2 References

The following documents were used in the creation of these standards and provide detailed technical information:

- European Commission, EudraLex The Rules Governing Medicinal Products in the European Union Volume 4 Good Manufacturing Practice Medicinal Products for Human and Veterinary Use Part II: Basic Requirements for Active Substances used as Starting Materials[7]
- ICH Harmonised Tripartite Guideline, *Q6A: Specifications: Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances,* November 1999[8]
- ICH Harmonised Tripartite Guideline, *Q8: Pharmaceutical Development,* August 2009[9]
- ICH Harmonised Tripartite Guideline, *Q9: Quality Risk Management*, November 2005[10]
- ICH Harmonised Tripartite Guideline, *Q10 Pharmaceutical Quality System*, June 2008[11]
- ISO 9001:2015, *Quality management systems – Requirements*, October 2008[12]
- International Pharmaceutical Excipients Council, *IPEC Certificate of Analysis Guide for Pharmaceutical Excipients*, 2013[13]
- International Pharmaceutical Excipients Council, and The Pharmaceutical Quality Group Joint *IPEC – PQG Good Manufacturing Practices Guide for Pharmaceutical Excipients*, 2017[14]
- International Pharmaceutical Excipients Council, *IPEC Good Distribution Practices Guide for Pharmaceutical Excipients*, 2017[15]
- International Pharmaceutical Excipients Council, *IPEC-Federation Significant Change Guide for Bulk Pharmaceutical Excipients*, 2014[16]

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[7] https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-4/2014-08_gmp_part1.pdf
[8] http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Quality/Q6A/Step4/Q6Astep4.pdf
[9] http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Quality/Q8_R1/Step4/Q8_R2_Guideline.pdf
[10] http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Quality/Q9/Step4/Q9_Guideline.pdf
[11] http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Quality/Q10/Step4/Q10_Guideline.pdf
[12] https://www.iso.org/iso-9001-quality-management.html
[13] http://ipec-europe.org/page.asp?pid=59
[14] http://www.ipec.org/sites/default/files/files/20170323%20IPEC-PQG%20GMP%20Guide_Final.pdf
[15] http://www.ipec.org/sites/default/files/files/20170515_GDP%20Guide%202017_FINAL.pdf
[16] http://ipec-europe.org/page.asp?pid=59

- International Pharmaceutical Excipients Council. *The IPEC Excipient Stability Program Guide, 2010* [17]

[17] http://ipec-europe.org/page.asp?pid=59

