Changes in the EXCiPACT 2017 Edition Requirements from the 2012 Edition

Blue text indicates changes to both GMP and GDP requirements
Orange text indicates specific changes to the GDP requirements
Items in italics are the 2012 clause numbers

EXCiPACT 2017 Edition

Reason for Update

Alignment with ISO 9001:2015

- EXCiPACT certification can be achieved by utilizing an organisation's existing ISO 9001 Certification
- Therefore the clauses in the GDP and GMP Annexes needed to be aligned with ISO 9001:2015 clause structure
- Mostly this involved moving existing clauses to their new locations – the correlation matrix is as follows
- ISO 9001:2015_Correlation_Matrices from ISO

EXCiPACT 2017 Edition

Reasons for Update

- **Update to the Auditor Competency and Certification Body Requirements**
  - **ISO 19011 has been integrated into a revised ISO 17021 and that has been updated again to form ISO 17021-1:2015**
  - **The EXCiPACT Annexes for auditor competency and certification body requirements have been integrated and then the clauses aligned with the new clause structure in ISO 17021-1:2015**
  - **Some clarifications of the requirements in both sections have been made following use and feedback from all EXCiPACT stakeholders**
- **For all Annexes there has been no dilution of requirements.**

Changes in the GMP / GDP requirements

4. Context of the Organisation

4.1 Understanding the Organisation and its context (*4, 5.6)*

- The organisation shall define the intended use(s) of the excipients. These definitions shall be recorded.
- External and internal issues shall include outsourced activities (see Section 8.4) that can affect excipient quality and for which the organisation has control and responsibility.

4.2 Understanding the needs and expectations of interested parties (*4, 5.6*)

- Note: The regulatory authorities governing pharmaceutical products should be included as interested parties, even in cases where they have no direct jurisdiction over the excipient supplier.

Changes in the GMP / GDP requirements

5. Leadership

5.3: Roles, responsibilities and authorities (*5.5.1, 5.5.2, 5.4.2)*

- **Top management shall designate a member of the site's management who, irrespective of other responsibilities, shall have responsibility and authority that includes:**

  a) ensuring that processes needed for the quality management system are established, implemented and maintained.

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

  c) ensuring the promotion of awareness of customer requirements throughout the organisation,

  d) ensuring the promotion and awareness of regulatory requirements throughout the organisation.

Changes in the GMP / GDP requirements

5.3: Roles, responsibilities and authorities (*5.5.1, 5.5.2, 5.4.2)*

Top management shall assign the authority and responsibility for:

- **f) a Quality Unit independent from production which shall be responsible at a minimum for:**
  - **…**
  - **releasing the finished excipient,**
  - **ensuring corrections, corrective actions and actions to address risks and opportunities are implemented,**
  - **GDP: approving suppliers of quality critical materials and services**
  - **reviewing and approving significant changes (see 6.3), including those to quality critical equipment, processes, specifications, procedures, and test methods**

Changes in the GMP / GDP requirements

6.3 Planning of changes (*4.3)*

- **There shall be a documented procedure defining the responsibilities and requirements for the evaluation and approval of changes that may impact the quality of the excipient, including the impact on any regulatory submissions made by the organisation. Evaluation and approval of changes shall occur prior to implementation.**
  The procedure shall describe the means by which a change is determined as significant.

Changes in the GMP / GDP requirements

6.3 Planning of changes (*4.3)*

- Changes determined to be significant shall be approved by the Quality Unit and customers notified. Customer communication shall occur in advance whenever possible. Where applicable, significant changes shall also be communicated to regulatory authorities (see 8.2.1 *(7.2.3)*). Records of the change control process shall be retained.
- Note 3: If changes have been discovered as being implemented without prior approval then they should be investigated as nonconformity and the potential consequences assessed (see 10.2.1).

Changes in the GMP / GDP requirements

7.1 Support

- **7.1.3: Infrastructure *(6.3)***
  - **The organisation shall conduct a risk assessment based on the organisation's intended use of the infrastructure to identify areas where the excipient is at risk of contamination from deficiencies in buildings and/ or facilities. The risk assessment shall consider the following at a minimum to identify where the excipient is at risk from contamination:**
    - a) location of the operations (e.g. internal, external),
    - b) state of repair of the building and facility,
    - c) suitable size, construction and location,
    - d) ability to maintain a suitably clean building and facility environment,
    - e) operations that can affect excipient quality,
    - f) presence of airborne contaminants, especially highly sensitizing or toxic substances,
    - **g) presence of environmental contaminants, including microorganisms.**

Changes in the GMP / GDP requirements

7.1 Support

- **7.1.3: Infrastructure *(6.3)***
  - **Water, where used in contact with excipients shall conform to written specifications and be monitored to confirm it is of a suitable quality for its intended use.**
    - **Note: The intended use will determine which chemical and microbiological specifications should be monitored.**
    - **Where water of multiple qualities is available, provision shall be made to avoid mix-up.**

Changes in the GMP / GDP requirements

7.1.4 Environment for the operating of processes *(6.4)*

- **The work environment shall be managed and controlled to minimize risks of excipient contamination. A documented risk assessment shall be carried out to determine the necessary controls. The risk assessment shall take into account any customer requirements and the intended use of the excipient.**
- **The documented risk assessment shall consider the following controls, as applicable:**
  - **a) air handling systems**
  - **b) special environments,**
  - **c) cleanliness and sanitary conditions,**
  - **d) waste segregation and disposal**
  - **e) pest control,**
  - **f) personnel hygiene**
  - **g) other risk assessments required by this Annex**

Changes in the GMP / GDP requirements

7.3 Awareness (*6.2.2)*

- ***The organisation shall ensure that persons doing work under the organisation's control are aware of:***
  - **e) the point from which processes have to be performed under the GMP requirements defined by this Annex,**
  - **f) the consequences of contamination**

Changes in the GMP / GDP requirements

7.5.3 Control of Documented information (*4.2.3, 4.2.4*)

- **7.5.3.1 Documented information required by the quality management system and by this International Standard shall be controlled to ensure:**
  - **c) designated personnel approve documents for adequacy prior to issue,**
  - **d) they are periodically reviewed, updated as necessary and re-approved,**
  - **e) obsolete documented information is prevented from unintended use,**
  - **f) suitable identification is applied if they are retained for any purpose.**

  [these clauses have been omitted from ISO 9001:2015]

Changes in the GMP / GDP requirements

8.2.1 Customer satisfaction (*7.2.3*)

- **The organisation shall establish a system for releasing EXCiPACT audit reports to customers including any action plans agreed with the Certification Body.**

Changes in the GMP / GDP requirements

8.4 Externally provided processes, products, services (*4.1, 7.4.1*)

- 8.4.1: GDP
  - Where testing or other operations that could affect excipient quality are outsourced the organisation shall define:
    - g) the responsibility for quality and the control measures within the quality management system,
    - h) the applicable GDP principles in accordance with this Annex which are to be applied to those operations.

Changes in the GMP / GDP requirements

8.4 Externally provided processes, products, services (*7.4.1, 7.4.3*)

- **8.4.2: Type and extent of control**
  - **The organisation shall:**
    - **e) define the responsibility for quality and the control measures within the quality management system,**
    - **f) communicate the applicable GMP principles in accordance with this Annex which are to be applied to those operations.**
  - **GDP: Where manufacturing, testing or other operations that could affect excipient quality are outsourced the organisation shall demonstrate that the applicable GDP principles in accordance with this Annex are applied to those operations.**

Changes in the GMP / GDP requirements

8.5.4 Preservation (*7.5.5*)

- The selection of excipient packaging systems shall be justified and documented by the organisation. An excipient packaging system shall include the following features:
  - a) written packaging specifications, including any special storage conditions required to preserve the packaging,
  - b) containers that do not interact with or contaminate the excipient,
  - c) tamper evident seals, unless written justification demonstrates these are not feasible to apply;
  - d) where containers are to be re-used for the excipient, verified cleaning procedures including means of removing previous labels shall be applied. Records of cleaning shall be retained.

Changes in the GMP / GDP requirements

8.6 Release of Products and Services (*8.2.4*)

- **GDP: The original manufacturers name and address shall be communicated to the customer.**

Changes in the GMP / GDP requirements

8.7 Control of nonconforming outputs (*8.3*)

- **8.7.1: There shall be a documented procedure defining how to manage excipient recall.**
  The regulatory authorities that require notification of a recall shall be identified.
  All recall processes shall be documented, notified to the original manufacturer, regulatory authorities as identified, and records retained. Recalled materials shall be identified and quarantined.

Changes in the GMP / GDP requirements

9.3.2 Management review input (*5.6.2, 5.6.3*)

- The management review shall be planned and carried out taking into consideration:

  g) new, revised or proposed regulatory requirements.

  h) the suitability of the quality policy (see 5.3)

9.3.3 Management review output (5.6.3)

- The outputs of the management review shall include decisions and actions related to:

  d) improvements necessary as a result of the review of regulatory requirements

  e) any need to update the quality policy

  Note: Necessary changes identified in the management reviews should be assessed and implemented via the change control procedure (6.3).