2013 Certificate of Analysis Guide for Pharmaceutical Excipients

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AGENDA

- Purpose of Certificate Of Analysis Guide (COA)
- Design and Required Elements of a COA
  - Requirements
  - Examples
- Establishing Dates of COA
- Reporting of Data
- Use of Electronically Generated COA
- Distributor Information
The **Certificate Of Analysis (COA)** is a critical element of the overall supply chain controls needed to provide the user with assurance of excipient conformance to specification and its suitability for use in pharmaceuticals.
The COA is a legal document that certifies the quality of the excipient and demonstrates that the batch conforms to the defined specifications, has been manufactured under excipient GMP, and is suitable for use in pharmaceuticals.

A COA for excipients should be prepared and issued by the company responsible for the material.

When analysis is performed by a distributor, the distributor should issue a COA to the user for any analysis performed by or on behalf of the distributor.
Purpose of Certificate Of Analysis Guide (COA)

- This guide is meant to serve as a guide for the preparation and appropriate use of a **Certificate of Analysis (COA)** for pharmaceutical excipients.

- The goal is to standardize the content and suggest a format for COAs for excipients, and to clearly define the roles and responsibilities for the excipient **manufacturer** and **distributor**.
The excipient supplier (manufacturer or distributor) **may organize the elements** on the COA **at their discretion**; however, some information are required and other are optional.
Design and Required Elements of a COA

- **Identifying Information**
  - Title “Certificate of Analysis”
  - Identity and address of original manufacturing site
  - Responsible organization that issues the COA,
  - Name and Compendial Designation, as applicable
  - Grade
  - Trade Name
  - Batch Number
Design and Required Elements of a COA

- **Body**
  - Date of Manufacture
  - Unique identifier to the excipient specification
  - Expiration or Retest Date (as applicable) or Stability Statement
  - Specification
  - Analysis
Design and Required Elements of a COA
Body Example

Certificate of Analysis
[sample tests, limits and statements are for demonstration purposes]

Supplier Company Name
Supplier Company Address

Manufacturing Location
Name of Manufacturer (if different from Supplier)
Manufacturing Site Address

Product: Trade Name and Descriptor or Common Name

Grade: Grade Designation
Customer Code: xxxxxx (if applicable)

Batch Number: xxxxxx
Date of Manufacture: dd/mmm/yyyy

Recommended Retest Date: <time from date of manufacture>

Compendial Name and listing USP-NF, Ph.Eur., JP, or JPE
(List multiple names and designations if nomenclature is different in each compendium)
Design and Required Elements of a COA

- **Specification**
  - Test Name
  - Reference to the Test Method
  - Acceptance Criteria

- **Analysis**
  - Test Results
  - Alternate test results, as appropriate
  - Date Retested (if appropriate)
## Design and Required Elements of a COA

### Specification and testing Example

#### TEST RESULTS (sample tests & limits for demonstration purposes)

<table>
<thead>
<tr>
<th>Test</th>
<th>Test Method</th>
<th>Specification</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance</td>
<td>Visual Examination</td>
<td>White Granular Powder</td>
<td>Complies</td>
</tr>
<tr>
<td>Foreign Matter</td>
<td>Visual Examination</td>
<td>Free from visible contamination</td>
<td>Complies</td>
</tr>
<tr>
<td>Identification-JPE</td>
<td>Tests A-C</td>
<td>Pass</td>
<td>Complies</td>
</tr>
<tr>
<td>Clarity and Color</td>
<td>JPE</td>
<td>Clear and colorless</td>
<td>Complies</td>
</tr>
<tr>
<td>pH (x% solution)</td>
<td>USP</td>
<td>5.0 – 7.0</td>
<td>#.#</td>
</tr>
<tr>
<td>Residue on Ignition</td>
<td>JPE</td>
<td>NMT 1.0% (450 –550°C)</td>
<td>#.# %</td>
</tr>
<tr>
<td>Viscosity (x% solution)</td>
<td>Ph.Eur.</td>
<td>4.0 – 7.0 mPa-s (@20°C)</td>
<td>#.# mPa-s</td>
</tr>
<tr>
<td>Water Insoluble Sub.</td>
<td>USP</td>
<td>NMT 0.1%</td>
<td>#.# %</td>
</tr>
<tr>
<td>Loss on Drying (110°C)</td>
<td>USP</td>
<td>NMT 5.0%</td>
<td>#.# %</td>
</tr>
<tr>
<td>Loss on Drying (105°C)</td>
<td>JPE</td>
<td>NMT 6.0%</td>
<td>#.# %</td>
</tr>
<tr>
<td>Particle Size</td>
<td>Supplier Method #</td>
<td>99.5% &lt;150 Microns</td>
<td>######</td>
</tr>
</tbody>
</table>

#### ADDITIONAL INFORMATION (sample tests & limits for demonstration purposes)

<table>
<thead>
<tr>
<th>Heavy Metals</th>
<th>JPE</th>
<th>NMT 10 ppm (as Pb)</th>
<th>NMT 10 ppm*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arsenic</td>
<td>JPE</td>
<td>NMT 2 ppm</td>
<td>NMT 2 ppm*</td>
</tr>
</tbody>
</table>

* This test is performed in-process on each batch and the material has been shown not to change in the finished excipient sample.

+ This test is performed quarterly based on process validation.
Design and Required Elements of a COA

- **Certification and Compliance Statements** (may be provided in other documents, e.g. Excipient Information Package)
  - Standard of GMP applied (e.g., IPEC-PQG Excipient, ICH Q7)
  - Additional compliance statements and applicable references to standards
  - Potential to meet additional Compendial Standards
  - Content listing and grade of ingredients (if a mixture)
  - Customer specified information
Certification and Compliance Statements

**GMP compliance:** This batch of *<Trade Name>* has been manufactured using excipient Good Manufacturing Practices.

**Compendial Standards:** This batch of *<Trade Name>* complies with all of the current requirements listed in the United States Pharmacopeia (USP), the European Pharmacopeia (Ph.Eur.) and the Japanese Pharmaceutical Excipients (JPE).

**Other Certification Statements:** Any other type of certification, e.g., Residual Solvents, Genetically Modified Organism (GMO) derived, or customer specific information should be listed here. These may vary depending on regional regulatory requirements, specific GMP issues and customer desired information based on their use of the excipient.
Design and Required Elements of a COA

- **Authorization**
  - Identity of authorized individual for approval or electronic signature statement
  - Date of approval or suitable alternative
  - Page Number (i.e., 1 of X pages)

Identity of Authorized Individual for Approval: XXXXXXXXXX

Title

Date of approval: dd/mmm/yyyy

This COA was released from a controlled electronic document management system.
Establishing Dates on a COA

- In reporting dates on COAs for excipients, it is important that a **clear and unambiguous** format be used to prevent possible misinterpretation.

- Inappropriate as can be read as 1\textsuperscript{st} October 2013 or 10\textsuperscript{th} January 2013
Establishing Dates on a COA

- The **Date of Manufacture** should be clearly defined by the original manufacturer and **consistently applied** and procedures.

- It is important to note that while **re-packaging** operations are to conform to GMP requirements, repackaging alone is not considered as a **processing step** that can be used in determining the Date of Manufacture.

**Date of Manufacture: dd/mmm/yyyy**
Establishing Dates on a COA

- Appropriate **Expiration and/or Recommended Retest Dates** for excipients should be **established from** the results of a **documented stability-testing program**.

- The **Expiration date** of an excipient cannot be extended.

- The **Retest Date** for an excipient is the **date** indicated by the supplier after which the **excipient should be re-evaluated** to ensure continued compliance with appropriate specifications.

- It is **acceptable to report both** an Expiration Date and a Recommended Retest Date on the COA if applicable.
Many excipients are listed in pharmacopeias and other standard reference works compliance.

All the parameters should be checked at an appropriate frequency.

The USP-NF and Ph.Eur. allow the use of alternate methods of testing provided the alternate methods have been shown to be as effective or better than the monograph ones.

For excipients that are not included in any pharmacopeia, specifications should be set by the supplier to ensure that the quality of the material is maintained on a continuing basis.
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For excipients that are not included in any pharmacopeia, specifications should be set by the supplier to ensure that the quality of the material is maintained on a continuing basis.
Measurements reported on a COA can be derived from:

- Testing a representative sample from the finished excipient batch,
- In-process testing of a representative sample where the attribute remains unaffected by further routine processing,
- Continuous monitoring of an attribute in combination with statistical process controls.

Where 2 or 3 apply, the technique for how the test result was obtained should be described.
Skip testing based on a satisfactory product quality history alone, is not acceptable from a cGMP standpoint because such an approach does not adequately verify that each lot meets all specifications.

In all cases there should be justification behind strategy chosen.
The **supplier** of an excipient should **develop and maintain documentation which outlines the process control systems and validation data** which justify the use of alternatives to finished excipient testing.

This documentation should also include procedures for handling the impact of **significant changes** on the testing...
Use of Electronically Generated COA

- **Certificates of Analysis issued from computer systems without a handwritten signature are common place and are acceptable provided the appropriate controls are in-place**
  - **Access to the computer system** for COA management, entering and editing of data **should be limited to authorized personnel**.
  - **Authentication** by username and password
  - **Change of each individual password** at an **appropriate frequency** should be required.
Use of Electronically Generated COA

- Confirmation of the **integrity and accuracy of the information** stored in the system and transferred to the printed record **should be completed** during **implementation** and then **periodically checked** thereafter.

- **Data entered** into a computer system from which information is extracted for a COA **and changes made thereafter** should be accompanied by time- and date-stamped **audit trails**.
Distributor Information

- **Distributors provide excipients and associated services such as:**
  - Provide excipient in the manufacturers unopened original package (pass through)
  - Repackage from bulk quantities
  - Purchase of excipients for re-packaging under a different label.

- **The nature of the associated services may impact the COA provided as discussed in therefore it is expected that the distributor will have the appropriate level of good manufacturing (see IPEC Guidelines)**
Key Takeaways

- It is all about Supply Chain Control and ensuring Strength, Identity, Safety, Purity, Quality of Medicinal Products and safety of our Patients.

- Behind an Excipients Manufacturers, a Distributor there is a Pharmaceutical Company and at the end there is Patients that needs us.
Key Takeaways

- As a Little reminder, they are not just our patients, they might be our family or friends
References

- IPEC Europe

- Guide for certificate Of Analysis for Pharmaceutical Excipients

- IPEC Europe Guidelines