The IPEC Excipient Information Package (EIP): Template and User Guide

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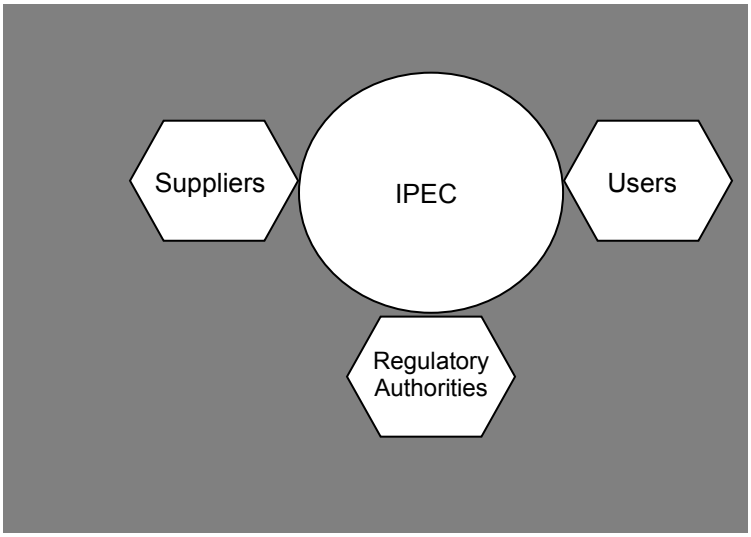
FOREWORD

IPEC is an international industry association formed in 1991 by manufacturers and end-users of excipients. It is an association comprising four regional pharmaceutical excipient industry associations covering North America, Europe, China and Japan (which are known respectively as IPEC-Americas, IPEC Europe, IPEC-China and JPEC). IPEC's objective is to contribute to the development and harmonization of international excipient standards, the introduction of useful new excipients to the marketplace and the development of best practice and guidance concerning excipients.

IPEC has three major stakeholder groups;

1. Excipient manufacturers and distributors, who are called suppliers
2. Pharmaceutical manufacturers, who are called users
3. Regulatory authorities who regulate medicines



This document offers best practice and guidance in the establishment of an excipient information package. The excipient supplier may be a manufacturer or a distributor (or both). The Guide highlights the factors to consider when preparing such a package.

ACKNOWLEDGEMENTS

This guideline is the result of the hard work and substantial resources, of IPEC member companies. IPEC greatly appreciates the many hours the following individuals devoted to develop this guide and the generous support of their employers for providing the necessary time and resources.

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INTRODUCTION

SCOPE AND PURPOSE

In order to use an excipient, users need to obtain a significant amount of data about the excipient manufacturer, distributor, where applicable, and the excipient itself. Many users have resorted to sending questionnaires and surveys to obtain this information using their own individual formats. Often these surveys and questionnaires address essentially the same quality and regulatory concerns. It is also difficult in some cases, due to the phrasing of specific questions, to interpret the intent of the question.

While excipient suppliers want to provide information to the user as quickly as possible, many excipient suppliers receive such a large volume of questionnaires and surveys from their customers that they are unable, due to resource constraints, to individually complete each customer's specific form. Further, because these surveys and questionnaires vary to some degree in the specific questions asked, if a change in the information occurs, it is not feasible for the excipient supplier to determine which completed surveys and questionnaires are affected by the change. Significant time and resources are spent, both by the user and supplier, to send, complete, return, review and track these non-standardized questionnaires and surveys.

This guide was developed in order to address these issues. It defines the Standardized Excipient Information Package that comprises:

- Product Regulatory Datasheet
- Site Quality Overview
- Site And Supply Chain Security Overview

The primary goal of the template is to provide standards for the exchange of data between excipient suppliers and users that will simplify this process. By responding to surveys, questionnaires and other requests for information in this format, excipient suppliers can respond in a timely and efficient manner to all requests as well as ensure that consistent information is provided. Excipient users will be able to anticipate the type and format of the standard data that they receive from excipient suppliers. This will assist both users and suppliers in the management of such information. In the future, electronic transmission of this data for direct download may be possible. Additionally, this standardization will facilitate any necessary change notifications pertaining to previously supplied information further strengthening the excipient suppliers' change notification program.

FORMAT OF THE EXCIPIENT INFORMATION PACKAGE DOCUMENTS

The Excipient Information Package (EIP) is set up much like a Material Safety Data Sheet (MSDS) with designated sections to include specified data. Each section covers specific topics. The minimum topics that should be covered in each section are defined, however, additional related information can also be provided at the discretion of the excipient supplier. If particular topics are not applicable to a particular excipient or site, it should be so indicated in the document. Where information is considered confidential, the document should reflect how the excipient user can obtain this information. For example, the document may state that the information may only be obtained under a confidentiality agreement.

The presentation and format of the information is at the discretion of the supplier. Short, bulleted formats are encouraged. Specific phrasing is not prescribed but suggested phrasing is provided in some sections and can be used if desired. Job titles should be used rather than names.

These documents should be version controlled by the excipient supplier. Suppliers should have a process in association with their management of change policy for updating EIP documents in a timely manner including updates to company and product information and EIP template revisions. The current version of the EIP template can be found on the regional IPEC websites.

The documents do not require signatures, however they must be an official company document.

APPLICATION AND USAGE

The EIP documents are intended for individuals experienced and competent in the area of evaluating excipient suppliers and should not be viewed as a replacement for audits. While the documents are intended to form a complete package of information, each document within the EIP was designed to also be functional as a stand-alone document and therefore, some basic information may be common among the documents.

In order to provide additional guidance on specific topics, IPEC-Americas maintains a Regulatory Reference Guide. The Regulatory Reference Guide lists links to the specific regulatory references applicable in different regions to various sections in the EIP documents. These references can provide preparers of EIP documents detailed guidance on the information that needs to be addressed in various sections. IPEC-Americas's Regulatory Reference Guide is accessible through the IPEC-Americas website at the following address: www.ipecamericas.org.

SECTION BY SECTION EVALUATION OF THE EXCIPIENT INFORMATION DOCUMENTS

I. Product Regulatory Datasheet

The Product Regulatory Datasheet is designed as a means to assist in communicating to the user important physical, manufacturing and regulatory information specific to the excipient. This information is intended to facilitate the use of the excipient in drug products. Not every point is necessarily applicable to each excipient.

The following sections are expected to be included in the document unless otherwise specified.

Section 1 – General Product Information

This section provides identification information for the product .

Topics for this section:

- Product name/code
- Scope of document
- Other general product information (optional)

Section 2 – Manufacturing, Packaging, Release Site and Supplier Information

This section provides general information about where the product is manufactured and other supply chain information. It includes cross references to the Site Quality Overview and Site and Supply Chain Security Overview, where applicable.

Topics for this section:

- Sites of manufacturing, processing, packaging, product release and other related sites such as warehousing, terminals, contract labs, etc.
- Exclusive distribution channels (if applicable)
- GMP or GDP compliance statement, as applicable
- Multi purpose / dedicated equipment

Section 3 – Physico-chemical Information

This section provides general information about the chemistry and physical characteristics of the product and its manufacture.

Topics for this section:

- CAS number
- Origin information (synthetic, animal, vegetable, mineral, product of biotechnology, product of fermentation, etc.)
- Synonyms (including INCI name if applicable) (Optional)
- Morphological form (Optional)
- Brief description of manufacture (blend, reaction, continuous / batch process etc.)
- Mixed excipient ingredient statement
- Country of origin for ingredients used in mixed excipients (optional)

Section 4 - Regulatory Information

This section includes information related to the regulatory status of the excipient as well as addressing pertinent product specific topics of general regulatory concern.

Topics for this section:

- See Annex I for the type of information which may be included in this section

Section 5 - Miscellaneous Product Information

This section should be used by the supplier to provide any additional information that may be pertinent to the product but is not covered elsewhere in this document or in the other EIP documents.

Topics for this section could include:

- Explanation of the lot/batch numbering system
- Batch definition statement
- Statement as to Expiration date and/or recommended re-evaluation interval (see IPEC Stability guide)
- Specific storage and shipping conditions which are required to assure excipient quality
- Common uses (Optional)
- Nutritional information (Optional)
- Packaging e.g. specification, size, types, new/recycled, bulk tankers, type of tamper evidence devices and labelling information (Optional)

Section 6 – Revisions

This section provides information related to version control for the document. The document should have a date and a version number. This section should also describe the changes made since the last revision.

Section 7 - Contact Information

This section explains how the user should contact the supplier to get additional information, if needed, regarding the topics provided in this document.

II. Site Quality Overview

The Site Quality Overview is a tool to assist in evaluating the manufacturing practices and quality systems of suppliers, as well as a reference to inform users of the systems in place to assure appropriate GMP requirements. The “Joint IPEC-PQG Good Manufacturing Practice Guide for Pharmaceutical Excipients 2006" was used as the basis to construct this document and should serve as the primary source for evaluating responses provided by the supplier. Users of this document should be familiar with the introduction, definitions, and general guidance that are contained within the IPEC-PQG GMP Guide, and should refer to the guide if further details are needed.

The Site Quality Overview is intended to communicate a summary of the Quality Systems and GMP used to manufacture the excipient(s). It may not necessarily include all of the details included in the Quality Manual, or covered in an audit, nor are all of the points necessarily appropriate to every site.

The following sections are expected to be included in the document unless otherwise specified.

Section 1 - Site Overview

The purpose of this section is to describe the supplier's organization and production capabilities.

Topics for this section:

- Scope
  - Site Name(s)
  - Address(es)
  - Excipients covered by this document (optional)
- Corporate ownership (if different from site identified in Scope)
- Customer audit policy (optional)
- Site Details
  - General Site Information (e.g. size, history, number of employees, shift operations, site plan, union workforce (optional), etc)
  - Site activities conducted (e.g. blending, packaging, testing, R&D)
  - Primary applications of products produced at this site (pharmaceutical, food, cosmetic, etc)
  - Facility production of antibiotics, steroids, or hormone products
  - Organizational chart (including responsibility for product release)
  - Use scope and control of sub-contractors, if applicable

Section 2 - Compliance Evidence

This section should be used to describe any specific compliance information pertinent to the facility being described.

Suggested examples of compliance information:

- ISO registration information e.g. 9001, 14001, OHSAS 18001, etc. (number, registrar, copies of certificates)
- GMP Inspections by Competent Authorities (Regulatory Agencies) including outcome
- General GMP statements
- Other certifications or external audit programs: IPEA, AIB, GMA-SAFE, BRC, etc.

Section 3 – IPEC-PQG GMP Compliance Details:

This section should be used to address how the supplier complies with each applicable element of the IPEC-PQG GMP Guide. Non-applicable elements should be noted as such. For more detail on the specific items that may be covered under each topic, please refer to the IPEC-PQG GMP Guide. Parenthetical references in the document template refer to sections in the IPEC-PQG GMP Guide. Additional reference information can be found in the IPEC-PQG GMP Audit Guideline for Pharmaceutical Excipients.

Section 4 - Miscellaneous Site Information

This section should be used by the supplier to provide any additional information that may be pertinent to the site but is not covered elsewhere in this document or in the other EIP documents. This section is optional and should be used as needed.

Suggested topics for this section:

- Risk management plans such as HACCP
- Statistical Process Control / Process Analytical Technology (PAT)

Section 5 – Revisions

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Section 6 - Contact Information

This section explains how the user should contact the supplier to get additional information, if needed, regarding the topics provided in this document.

III. Site And Supply Chain Security Overview

The Site And Supply Chain Security Overview is designed to provide users with information concerning the supplier's plans to ensure the protection of the product and the continuity of supply. It is intended to provide a high level overview of these plans while preserving confidential information.

The following sections are expected to be included in the document unless otherwise specified.

Section 1 - Scope

The purpose of this section is to identify the manufacturing site and distribution site(s) (where applicable) covered by this document.

Topics for this section:

- Scope
- Site Name(s)
- Address(es)
- Excipients covered by this document (optional)
- Corporate ownership (if different from site identified in Scope)

Section 2 - Supply Chain Security

The purpose of this section is to describe how the supplier assures the integrity of the excipient during storage and distribution and also complies with appropriate regulations. Any arrangements to comply with appropriate regulations concerning the transportation of the excipient should also be covered. More details on these issues can be found in the IPEC Good Distribution Practices Guide 2006.

Topics for this section:

- Controls to assure the integrity and security of the product in transit from manufacturer to end user. The following are suggested areas that may be discussed where applicable:
  - Evaluation of carriers

  - Tamper evident seals or packaging
  - Environmental control (if appropriate)
  - Qualification of distributors
  - Qualification of forwarders/brokers
  - Qualification of intermediate storage locations
  - Repacking/relabeling activities
- Registrations with the FDA under the BioTerrorismAct, if applicable
- C-TPAT or AEO participation, if applicable
- Wood pallet certification statement, if applicable
- Approved distributors and how material pedigree/traceability is assured (where applicable) (Optional)

Section 3 - Security Information

The purpose of this section is to describe the elements of the supplier's overall security program.

Topics for this section:

- Scope of security plan including:
  - Roles and Responsibilities, including title of person responsible for implementing security
  - Policies & Procedures
  - Training
  - Data and computer system protection
  - Site access control (e.g. security fencing, visitor registration, employee badges, employee training, vehicular access, camera monitoring)
- Personnel security
  - Pre-employment background checks
  - Background checks on temporary and contract personnel
  - Training
  - Termination of employees or contractors and preventing subsequent access to the site and computer systems

Section 4 - Safety & Environmental Information

The purpose of this section is to describe the supplier's personnel safety and environmental programs.

Topics for this section:

- Description of documented health and safety program
- Registrations to ISO 14001, OHSAS 18001 and/or Responsible Care etc.

Section 5 – Business Continuity Plan

This purpose of this section is to communicate to the user the availability of a business continuity plan that addresses continuation of supply in case of disaster, pandemic or other disruptions. Optionally, additional details regarding the elements of the plan may be included.

Section 6 - Miscellaneous Site Information

This section should be used by the supplier to provide any additional information e.g. corporate responsibility programs that may be pertinent to the site but is not covered elsewhere in this document or in the other EIP documents. This section is optional and should be used as needed.

Section 7 – Revisions

This section provides information related to version control for the document. The document should have a date and a version number. This section should also describe the changes made since the last revision.

Section 8 - Contact Information

This section explains how the user should contact the supplier to get additional information, if needed, regarding the topics provided in this document

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EIP Guide Revision History

Changes Since Last Revision:

Product Regulatory Datasheet
Section 4: Moved Section 4 topics to Annex 1
Section 4: Added the following topics to Annex 1 – Nanotechnology
Section 5: Changed – Expiration date and/or recommended re-evaluation interval from Optional to Expected
Section 5: Changed – Storage and shipping conditions from Optional to Expected
Site and Supply Chain Security Overview
Section 2: Added – Wood pallet certification statement
Section 4: Removed – Description of emergency response plan
Section 5: Added Section 5 – Business Continuity Plan; Renumbered remaining sections.
Section 6 (formerly Section 5): Relocated Business Continuity Plan to new Section 5

Annex 1

Product Regulatory Datasheet
Section 4, Regulatory Information

Compendial compliance (for example, *USP-NF*, FCC, PhEur or BP, JP, JPE, JSFA) and other regulatory status (For example, 21 CFR, GRAS, other status as a food additive)
Precedence of Use (For Non-compendial Excipients), if applicable.
Drug Master File (DMF) or EDQM Certificate of Suitability (CEP) information
BSE / TSE Information (both related to the product and the potential for cross-contamination). EDQM Certificate of Suitability information, if applicable
Allergens / Hypersensitivities Information (both related to the product and the potential for cross-contamination) – Reference the Regulation or specific allergens evaluated.
GMO Information
Residual Solvents Information
Metal catalyst and metal reagent residues
Kosher / Halal status
Irradiation treatment, if applicable
Use of nanotechnology, if applicable
Bioburden/pyrogens (Optional)
Proposition 65 (Optional)
Aflatoxin (Optional)
Preservatives (Optional)
Latex (Optional)
Silicones (Optional)
Organic Certification (Optional)
Potential for economic adulteration (Optional)