The International Pharmaceutical Excipients Council

Quality Agreement Guide and Template(s)

For Pharmaceutical Excipients

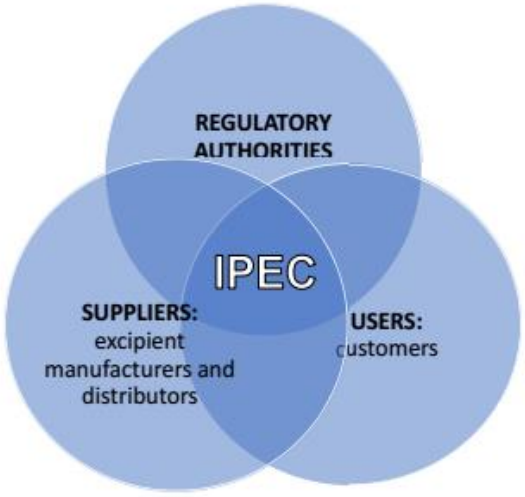
This document represents voluntary guidance for the excipient industry and the contents should not be interpreted as regulatory requirements. Alternatives to the approaches in this Guide may be used to achieve an equivalent level of assurance for excipient quality.

FOREWORD

The International Pharmaceutical Excipients Council (IPEC) is an international industry association formed in 1991 by manufacturers, distributors and end-users of excipients. At the time of writing there are regional pharmaceutical excipient industry associations including the Americas, Europe, Japan, China, and India. 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 considered **suppliers** in this document.
   Note: Within the context of this guide, distributors can be customers as well.
2. Pharmaceutical manufacturers, who are called **users**.
3. Regulatory authorities who regulate medicines.



This document offers best practices and guidance on the content of an excipient **Quality Agreement (QA).** It is important that the reader confirms this document is the latest version of the Guide as found on the appropriate IPEC regional or Federation website at www.ipecamericas.org, www.ipec-europe.org, or www.ipec.org.

NOTE: Refer to the "International Pharmaceutical Excipient Council Glossary: General Glossary of Terms and Acronyms" for definitions. The first use of a term found in the glossary will be **BOLD**.

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1 ACKNOWLEDGEMENTS

This guide was developed by representatives of many of the member companies of the International Pharmaceutical Excipients Council of the Americas (IPEC-Americas®) and the International Pharmaceutical Excipients Council (IPEC) Europe, which are industry associations whose principal members consist of excipient manufacturers, distributors, and their pharmaceutical users. The company representatives who worked on this guide are listed below:

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2 INTRODUCTION

In the current excipient regulatory environment, pharmaceutical manufacturers are under increasing pressure to develop better knowledge of their excipient supply chain. An essential element is understanding the supplier's Good Manufacturing Practice (GMP) quality management system. As part of solidifying supplier relationships, Quality Agreements (QAs) have been introduced because they are considered beneficial in a supply relationship, and define the **GMP** requirements between the supplier and customer. The role of Quality Agreements is explained in the EU GMP Guidelines Chapter 5, section 5.28[1]. Additionally, the FDA has issued a final guidance entitled Contract Manufacturing Arrangements for Drugs: Quality Agreements (November 2016)[2]. Although the FDA guidance is intended for drugs, its general elements are reflected in this Guide.

Quality Agreements enable excipient customers and suppliers to create a partnership between the companies that ensures all quality requirements are defined. QAs are legally binding agreements that are negotiated between customers and suppliers of excipients. Quality Agreements should be reviewed by the quality departments to verify all requirements are addressed and are achievable. Typically, there should also be a legal review. By clearly delineating GMP responsibilities, costly product quality issues resulting from miscommunication can be reduced or eliminated as well as ensuring the customer meets their regulatory expectations and requirements.

IPEC is committed to facilitate communications between excipient customers and suppliers using best practices. Best practice uses the excipient manufacturer's quality system as the basis for the agreement. IPEC QA Templates are designed to provide excipient customers and suppliers with a common starting point to create mutually beneficial and regulatory compliant Quality Agreements. By utilizing the IPEC QA Template structure and level of detail, customers and suppliers will reduce the time and effort needed to complete QAs.

Modifications to the templates may be made to meet any special needs of the customer and the supplier.

In this Guide, the terminology "should" and "it is recommended" does not mean "must." Common sense should be used in the application of this Guide.

2.1 Purpose and Scope

The scope of the quality agreement is all quality management system requirements that must be met by either the supplier or customer so that the listed excipient was manufactured in conformance with regulatory requirements or customer expectations.

The purpose of the QA is to define which party is responsible for delineated quality activities and how quality issues will be resolved**.** The agreements are intended to formalize quality commitments between the parties to ensure there are appropriate quality procedures in place.

[1] http://ec.europa.eu/health/files/eudralex/vol-4/chapter_5.pdf

[2] http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm353925.pdf

The intent of this document is not to "rewrite" GMP requirements. QAs cannot replace the purpose and outcomes of supplier qualification elements, such as an audit.

2.2 Principles Adopted – Key words

This key word section helps to define the relationships between the manufacturer, distributor, supplier, and customer. These definitions are critical to understanding the language in the Guide and for usage of its templates. For this reason, the definitions below are given.

1. Manufacturer – The excipient manufacturer; a party who performs the final processing step.

2. Distributor – A company other than the manufacturer procuring, importing, holding, supplying or exporting excipients. A distributor takes possession and ownership of the excipient(s) including e.g., repackaging[3], warehousing and transportation, but not altering the excipients' physical and/or chemical characteristics e.g., processing/reprocessing.

3. Supplier* – Either a distributor or manufacturer that receives payment for providing the excipient. The supplier is involved in a commercial relationship as the person or company providing the excipient on request.

4. Customer** – The organization receiving the excipient once it has left the control of the excipient supplier.

*For the purpose of this guide, Traders are excluded.
**For the purpose of this guide, Brokers, and Agents are excluded

2.3 Layout

The layout of this guide is as follows:

- Quality Agreement Responsibilities and Review
- Format of the Excipient Quality Agreement Document
- Templates

3 QUALITY AGREEMENT RESPONSIBILITIES AND REVIEW

Effective implementation of any QA is dependent on both excipient supplier and customer ensuring that the obligations of the agreement are consistent with the quality systems at their respective companies. Use of a template facilitates the process for all parties. Any obligations or commitments added during the negotiation phase of an agreement should require additional review of the affected quality systems to assure compliance prior to signature.

QAs should be used to complement commercial supply agreements, or other business agreements. Since Supply and Quality Agreements are often not generated at the same time or reviewed and approved by the same people, business agreements may already contain references to quality responsibilities and activities. It is good practice during the creation of a QA to check other existing agreements for references to quality responsibilities or activities and

[3] For more guidance regarding "repackaging", consult IPEC GDP Guide section 7, Repackaging and Relabeling.

ensure there is no conflict with the proposed QA. Where there is reference to quality requirements in an existing agreement, the QA should reference the other business agreement and define in the QA which document governs in case of conflict. However, to prevent disparity and ensure consistency, it is recommended to avoid quality provisions in Supply Agreements and other commercial or technical agreements and simply reference the QA in the other agreement.

It is the responsibility of both parties to ensure the QA is maintained as a current and accurate document during the effective period. Amendment(s) and/or addendum(s) may be needed to assure the QA remains current with both customer and regulatory requirements and/or responsibilities. Both parties are responsible for reviewing requests for amendments or addendums to assure the quality systems support such changes.

All QAs and amendments or addendums require legally binding signatures. Those parties authorized to sign should be clearly identified.

4 FORMAT OF THE EXCIPIENT QUALITY AGREEMENT DOCUMENT

The IPEC QA Template uses a mixture of text and tables to present the details of the agreement. Sections A – K and N - P of the template are presented in legal-style text format and addresses the terms and conditions as well as the scope of the agreement. Sections L and M (if used) are presented in a table which allows for quick and easy identification of quality responsibilities and can be modified with additions or deletions.

The template addresses the quality activities and responsibilities that should be included in a QA appropriate for excipients; however, it does not list every element of the GMP or Good Distribution Practice (GDP) compliant quality system. It is not necessary to reiterate agreement on every GMP/GDP requirement when there is stated general agreement. However, included in the template are quality responsibilities that should require action by one or both parties.

The template format is intended to be flexible, offering the elements needed for most excipient QAs. To avoid lengthy negotiations, modification of the template should be done with care and only as necessary. It is suggested that excipient suppliers prepare in advance a QA based on the IPEC QA Template and have it reviewed by supplier's counsel. To facilitate execution of the QA, the supplier's agreement, based upon the IPEC Template, should be used as the starting point for negotiating the QA with customers.

As with any binding agreement, it is advisable to have the final QA reviewed by legal counsel before execution with customers. If commercial agreements do not exist, or if there are local regulations, legal counsel may want to include topics such as warranty or limitation of liability, confidentiality, compliance, termination, and extension. For these topics, the IPEC Quality Agreement Guide and Templates does not suggest wording but recommends text based on the business relationship between supplier and customer. These topics are usually best addressed in commercial agreements linked to the QA, rather than in the QA itself.

5 TEMPLATES

There may be as many as three potential parties involved in the supply and use of excipients: the excipient manufacturer, the distributor, and the pharmaceutical manufacturer (customer). Nonetheless, the QA guide is limited to two-party agreements. In the sections below you will find three example templates based on the individual relationships between the two parties that are executing the agreements.

The two relationships that require a quality agreement are as follows:

1) Direct relationship between the manufacturer and customer.
2) Direct relationship between the distributor and customer.

Note: The Manufacturer's Template can be used to define the Quality Agreement between the excipient manufacturer and a pharmaceutical manufacturer OR between the excipient manufacturer and a distributor.

Where the relationship is with the distributor but the customer wants the manufacturer involved, three templates are available:

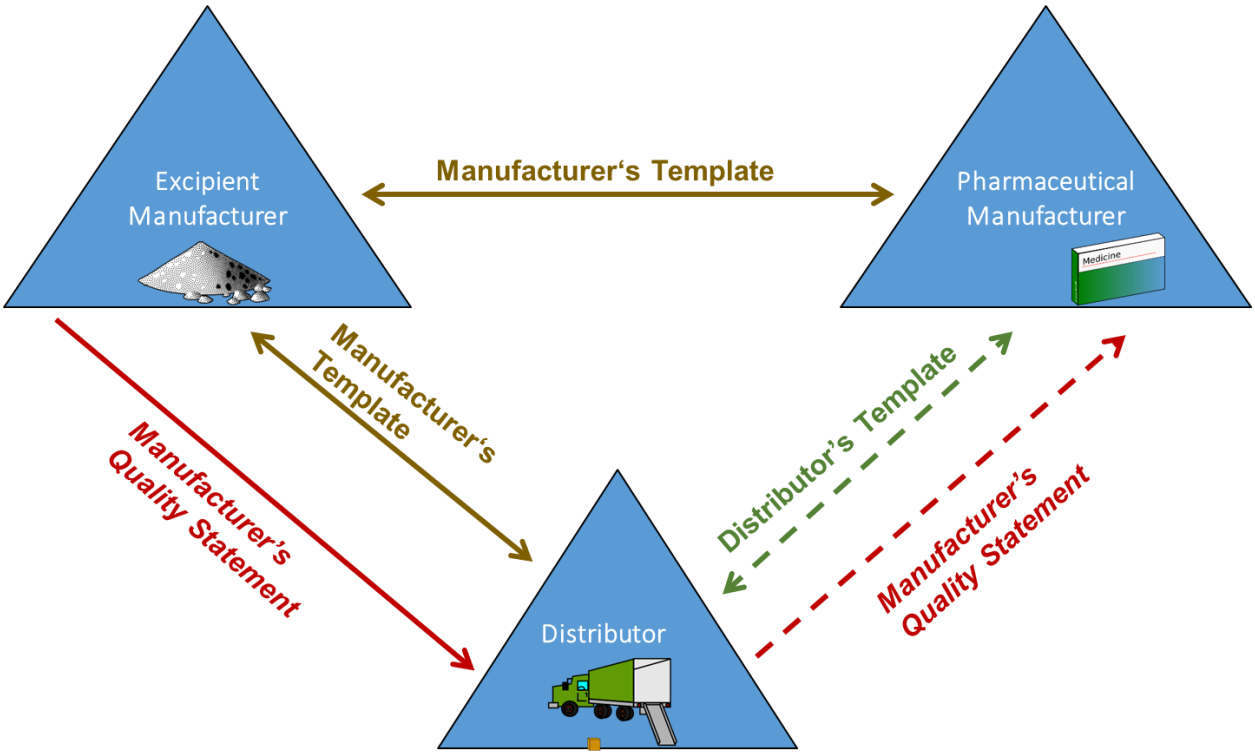
1) Manufacturer's Template
2) Distributor's Template
3) Manufacturer's Quality Statement.

Note: When there is a distributor involved, there is no business relationship between the pharmaceutical manufacturer (customer) and the excipient manufacturer.

The three templates are designed to be flexible models for establishing QAs since they define the relevant topics to be addressed.

Figure 1 shows the potential scenarios for QA relationships between suppliers and customers and their related templates in this Guide.

Figure 1



A particular challenge is ensuring both final customers' and manufacturers' needs are addressed when the customer buys from a distributor. Business arrangements that are very different can be established; therefore, this Guide cannot provide one solution that fits all arrangements.

Only a very small number of excipient manufacturers provide QAs to customers who purchase through a distributor for various reasons but mainly since there is no legal or commercial relationship between the manufacturer and the customer. This Guide does not provide a QA template suitable for execution between all three parties, excipient manufacturer, distributor and pharmaceutical manufacturer (customer).

However, since issuance of the IPEC QA Guide in 2009, it was recognized an excipient customer would need to ensure the excipient was manufactured in accordance with appropriate GMPs. In this revision of the IPEC QA Guide, a new Manufacturer's Quality Statement template is provided to address this matter.

In the QA between the excipient manufacturer and the distributor, a Manufacturer's Quality Statement based on certain provisions of the QA Guide and Templates responsibility tables may be provided to establish the excipient was manufactured in accordance with stated Good Manufacturing Practice. The Manufacturer's Quality Statement is a subset of the manufacturer's quality responsibilities QA template that is a tool to provide specific information for which the manufacturer is solely responsible.

Figure 1 contains a visual representation of this relationship.

The Manufacturers Quality Statement is provided to the distributor so that it may be included in the QA between the distributor and the customer, perhaps. The manufacturer issues the statement and signs it as the owner of the document. The distributor also signs the statement as acknowledgement of receipt of the statement. It can then be included as an attachment to the QA between the distributor and customer. When updating the QA between the manufacturer and the distributor, the Manufacturer's Quality Statement should also be reviewed.

It should be unnecessary for the distributor to provide the QA from the manufacturer (which ensures confidentiality remains in place) when using the Manufacturer's Quality Statement.

This section concludes the Guide itself. The following pages and embedded documents include the Templates.

Note: Example wording is given in each of the QA Template sections. Anything additional which is not meant as an example is denoted with "Note" and is italicized.

IPEC QA Template

Note: It is recommended to apply version control according to company standards.
(The use of company letterhead may be considered.)

Note: This template commonly applies to Manufacturer and Distributor. However, a choice must be made in section L to use either the Manufacturer or the Distributor Template as appropriate.

A. Scope

This Quality Agreement (QA) including its Responsibility Table defines the scope and responsibilities of the parties for the GMP / GDP requirements as they relate to the excipients listed.

B. Parties to the Agreement

This Quality Agreement is by and between <Supplier Name> with office at <address>, hereafter referred to as <Supplier> and <Customer Name> with office at <address>, hereafter referred to as <Customer>. Whereas, <Supplier> supplies excipients, referenced in section C, suitable for pharmaceutical use to <Customer>.

Note: Supplier / Customer name can be expanded to include further descriptive information about the company such as "Company X, a manufacturer of pharmaceutical excipients duly organized and existing under the laws of <list appropriate jurisdiction>". Consideration should be made to include the Supplier's and Customer's affiliates covered by this Agreement.

C. Specify Excipients covered by this Agreement

This Agreement pertains to the following excipient(s), hereafter referred to as <Excipients>: <list or see attachment>.

Excipient list:

Supplier Product Number	Supplier Product Name	Customer Product Number	Customer Product Name
123456	Name1	111111	Name5
567890	Name2	222222	Name6
987654	Name3	333333	Name7
321098	Name4	444444	Name8

Note: The table may be extended with other types of information. E.g., product types, production location, brand names.

D. Definitions and References - Quality Criteria / Systems

Supplier will conduct all its activities concerning the Excipients in accordance with the following quality criteria and / or system(s):

Note: The Parties may remove what is not applicable. If there is anything else that applies, it may be added to the list of quality criteria after mutual agreement.

Current versions:

- The Joint IPEC – PQG Good Manufacturing Practices Guide for Pharmaceutical Excipients (for excipient manufacturers)
- The IPEC Good Distribution Practices Guide for Pharmaceutical Excipients (for excipient distributors)
- NSF/IPEC/ANSI 363 Good Manufacturing Practices (GMP) for Pharmaceutical Excipients
- EXCiPACT™ Certification Standards for Pharmaceutical Excipient Suppliers: GMPs and GDPs
- USP General Chapter 1078 Good Manufacturing Practices for Bulk Pharmaceutical Excipients
- Pharmacopoeias, as applicable for compendial Excipients (e.g. Ph.Eur., USP)
- ISO 9001 Quality Management Systems
- ISO 14001 Environmental management systems
- Other regional certifications, as applicable

For specific processes as detailed in the Responsibility Table the following guides are included:

Note: The references mentioned below are essential elements within the Responsibility Table. Therefore, they should not be removed without adjustment of the Responsibility Table.

- The IPEC Significant Change Guide for Pharmaceutical Excipients
- Certificate of Analysis Guide for Pharmaceutical Excipients

Note: The parties may mutually decide if the glossary definitions will be used as reference.

- The IPEC General Glossary of Terms and Acronyms

E. Site(s) involved

Note: Sites supplying Excipients should be mutually agreed upon. The Supplier sites involved can be specified here if needed (may refer to an attachment). If the sites involved are not listed in this Agreement, it should be indicated where the agreed sites are specified.

F. Use of Third Parties

Note: If Third Party information is considered confidential, specify how this information can be disclosed to the customer, for example under confidentiality agreement.

Action: Select one of the two paragraphs underneath and remove the one that's not applicable.

If the Supplier is the Excipient manufacturer:

If <Supplier> uses third parties to manufacture, package, label, test, release, store or handle Excipients, such use is set forth <list here or specify attachment>. Significant Changes in the use of third parties as set forth in this Agreement will not be made without prior written notification to <Customer>. (*Note: Would be as detailed in Responsibility Table section 5.0, Change Control.)* <Supplier> shall, however, retain all obligations under this Agreement whether or not a third-party manufacturer, packages, labels, inspects, tests, releases, stores or handles Excipients.

If the Supplier is a distributor:

If <Supplier> uses third parties to store or handle Excipients, such use is set forth <list here or specify attachment>. Significant Changes in the use of third parties as set forth in this Agreement will not be made without prior written notification to <Customer>. (*Note: Would be as detailed in Responsibility Table section 5.0, Change Control.)* <Supplier> shall, however, retain all obligations under this Agreement whether or not a third party stores or handles Excipients.

Responsibilities regarding manufacture, packaging, labelling, testing and release of the Excipients are confirmed by the Excipient manufacturer in the Manufacturer's Quality Statement (see attachment).

Note: If Third Party information is considered confidential, specify how this information can be disclosed to the customer, for example under confidentiality agreement.

G. Assignment

Neither party shall have the right to assign any or all of its rights or obligations under this Agreement without the other party's prior written consent, which shall not unreasonably be withheld. The foregoing notwithstanding, prior written consent shall not be required in connection with a merger, consolidation, or a sale of all or substantially all of party's assets to a third party, except if such merger, consolidation or sale is with a competitor of the other party.

Note: The legal language in this example may be excluded based on review. Companies may choose to remove this section.

H. Term of Agreement

This Agreement shall become effective and binding upon the date of the final signature for an initial period of <YEARS> and will continue automatically, for as long as the supply of Excipients to Customer lasts, for <X> years afterwards.

Unless any party gives notice of termination at least six months prior to the end of the then current term.

Note: Automatic renewal may be a case-by-case decision of the parties.

I. Confidentiality

Subject to and consistent with any other confidentiality agreements between the Parties relating to the exchange of specific information, all information, in any form, disclosed by one party to the other party under this Agreement will be maintained strictly confidential for a period of <X> years after termination of this Agreement, and will be used solely for the purpose of performing obligations under this Agreement.

Note: Confidentiality provisions may be contained within a separate agreement (example: supply agreement or non-disclosure agreement).

Companies may choose to modify, remove, or note this section as "not applicable".

J. Other Agreements

In the event of any conflicts or inconsistences between the <Applicable Agreements> (e.g., supply agreement) and this Quality Agreement, this Quality Agreement shall prevail solely with respect to any of the quality and compliance provisions set forth herein.

Note: When a supply agreement or other similar agreement exists, or is being generated at the same time as the quality agreement, reviewers should assure that any quality provisions captured in the supply agreement should not conflict with the quality agreement; if so, a provision should identify and clarify which agreement supersedes in the event of a conflict.

Companies may choose to modify, remove, or note this section as "not applicable".

K. Choice of Law and Place of Jurisdiction

This Quality Agreement shall be governed by and interpreted in accordance with the laws of <Country>. The court of <City/State>, <Country> shall have sole and exclusive jurisdiction.

Note: This example language merely gives some guidance on potential wording, and should be reviewed with the parties' legal departments. A choice of law and a place of jurisdiction should be agreed to between the parties and designated here and should be in line with other agreements as applicable.

L. QA Responsibility Table

The responsibilities of each party are given in the Attachment as noted in Section P.

Note: It is recommended to apply version control according to company standards. (The use of company letterhead may be considered.)

Manufacturer

Distributor

Action: Select the Manufacturer's Template or Distributor's Template as appropriate.

M. Manufacturer's Quality Statement

The responsibility of the manufacturer's quality commitments and responsibilities as it relates to the Manufacturer's Quality Statement is given in the Attachment as noted in Section P. The excipient manufacturer allows <Distributor name> to share the Manufacturer's Quality Statement with the excipient customer or regulator.

Quality Statement

Action: Companies may choose to modify, remove, or note this section as "not applicable".

N. Contacts

Supplier		Customer	
Contact #1	<Name><function>	**Contact #1**	<Name><function>
	<Email>		<Email>
	<Location>		<Location>
	<Phone number>		<Phone number>
Contact #2	<Name><function>	**Contact #2**	<Name><function>
	<Email>		<Email>
	<Location>		<Location>
	<Phone number>		<Phone number>

Note: List the contact persons from each party that will be responsible for communications related to this Agreement. Some contacts may be within the Quality organization, and others may not be (for example, Procurement). Therefore, listing all contacts that are relevant to the agreement is prudent. This information can be provided in an Attachment.

Note: It is recommended to apply version control according to company standards. (The use of company letterhead may be considered.)

O. Approval Signatures

Note: Companies may choose to modify this section according to company standards.

Supplier	**Customer**
Signature, Date	Signature, Date
Name (print):	Name (print):
Function:	Function:

P. List of Attachments

Note: A list of attachments that are commonly attached to the QA, and which are referenced in this template are shown here. Templates are provided for the first three in the list.

It is good practice to number the Attachments.

It is dependent upon both parties to assure the QA and its Attachments are maintained as current, accurate documents during the entire effective period.

- Responsibility Table: Manufacturer's Template or Distributor's Template (MANDATORY). *Note: remove Template that's not used*
- Manufacturer's Quality Statement
- List of Excipients covered by this Quality Agreement (if not already listed in Section C)
- List of Site(s) involved (if not already listed in Section E)
- List of Third Parties (if not already listed in Section F)
- List of contact persons from each party (if not already listed in Section N)
- Attached copies (e.g. Specifications, Example Certificate of Analysis, etc.)