AN OVERVIEW ON “QUALITY AGREEMENT” BETWEEN MANUFACTURER & CUSTOMER

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ABSTRACT
The API is one of the prime components of the drug. Active Pharmaceutical Ingredients (API) of good quality is core to the Manufacturing of effective and safe essential drugs. Only a limited number of large manufacturers of finished pharmaceutical products have their own API manufacturing capabilities, and none of them can make all required APIs in-house. The author confirms the initial assumption that the API market provides a challenge in particular to small manufacturers, who have limited means to verify the quality of the APIs they are buying. APIC’s target is on worldwide Quality, Good Manufacturing Practice (GMP) and Regulatory matters relating to APIs and intermediates. APIC established of a Quality Agreement between an API manufacturer and its customer. API Suppliers it is essential to ensure high quality of the substances. Thus, a major element of such a supplier qualification program is the “Quality Agreement” between the manufacturer of the API/intermediate and the buyer or user of the API/intermediate.

KEYWORDS: API, Quality, APIC, Agreement.

INTRODUCTION
Active Pharmaceutical Ingredients (API)[¹]
The active ingredient in a pharmaceutical drug is called an 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. API also refers to the active or central ingredient in the product which causes the direct effect on the disease diagnosis, prevention, treatment or cure. The quality of active ingredients in a drug has a direct effect on the safety and efficacy of that drug.

**Quality Agreement**[^2]

APIC represents manufacturer of APIs and API intermediates in Europe. It’s located in Europe and it’s having membership with more than 60 countries also having association with many national industries. APIC’s target is on Quality, good manufacturing practice (GMP) and relating to regulatory motive relating to and intermediate. APIC create a Quality Agreement between suppliers of API and its customer.

A Quality Agreement is a document that defines quality parameters for API. It is an embrace written agreement that defines and builds the responsibilities of the quality units of each of the parties involved in the contract manufacturing of drugs. A Quality Agreement is a legally binding agreement that is mutually concert and concluded between API/intermediate manufacturers and their customers. A Quality Agreement is based on the quality procedures in place at the API /intermediate manufacturer and its customer. It creates mutual understanding of the quality & regulatory requirements applicable for material supply and both the API/intermediate manufacturers and customer’s respective responsibility related to quality. It is a major factor of an API/intermediate user’s supplier qualification program.

**Purpose[^3,4]**

The motivation behind the quality assentation is to characterize who is in charge of value exercises and how quality issues will be determined that will permit API suppliers to give safe items that are suitable for the client’s expected application.

APIC/CEFIC direction gives both industry and controllers with a much more prominent trust in the nature of worldwide mass dynamic pharmaceutical fixings fabricate.

This record plans to give master direction to the API/middle of the road business and its clients for the usage and support of suitable Quality Agreements.

There are advantages to the business:

- Lower workload (by diminished drafting time)
- Faster usage (by decreased audit times)
• Less many-sided quality (by decreased differing qualities)

This archive will give the present "cutting edge" for Quality Agreements in the pharmaceutical store. These current layout's are extremely adaptable for setting up the Quality Agreement where such an assention is craved. It gives data about every proper thing that ought to be clarified in Quality Agreement. This format is intended to be over-the-world in extension and substance. Therefore, it is suitable for the utilization in every one of the districts.

Fig 1: Quality Agreement between manufacturer & supplier

Objectives$^{[3,4]}$

Level playing field: To strongly advocate regulatory compliance in all global market and its enforcement through inspection.

Post approval change authorization

To responsibility to manage change into the hands of industry.

Harmonization

To support global harmonization in the fields of quality and regulatory affairs.

Networking/avocacy

To improve our contacts and increase the profile of APIC with all relevant stakeholders.

• Buyer and supplier define obligations.
• Quality agreement complement supply/commercial agreement.
• Buyer and supplier agree on joint definition of quality with regards on excipients supplied.
• Buyer and supplier adopt additional responsibility.

Scope$^{[4,5]}$

This template covers the agreement between the suppliers and its buyers. It does not cover between the distributors and their buyers. Also not covered are the purchases of chemical/non-GMP raw materials by the API/intermediate manufacturer.
There are two templates for “Generic APIs” and for “Exclusive substances”.

**Templates for “Generic API”**
Establish the manufacturer of a generic API and its customer. The term “generic API” is used for all APIs that in principle can be obtained from multiple sources, or are manufactured and supplied to multiple customers. Such generic APIs are off-patent; they are usually described in pharmacopoeial monographs, and supplied based on standard specifications.

**Templates for “Exclusive substances”**
Establish the manufacturer of APIs or intermediates exclusively made for one customer under a manufacturing contract. Also includes substances still under development or for use in clinical trials.

The template for exclusive substances is more comprehensive than Generic API. For “generic” APIs there will generally be a lower service level provided by the API manufacturers, compared to the higher service level in the custom synthesis business. So, there are two templates for the Quality Agreement.

**Format of Quality Agreement**[^6]
The layouts’ configuration is planned to be adaptable with the formats offering all the single components required for the consistence area of most Quality Agreements.

There are diverse conceivable outcomes how both sides may profit by the utilization of an institutionalized layout: The format might totally supplant an own understanding.

The layout may be utilized as a premise for a (marginally) altered, redid draft assention certain areas of the format may be utilized when drafting an own understanding.

The layouts wording may be utilized to determine question if commonly comprehended as great industry hone.

Quality Agreement may be given in an expressive manner. Where essential or asked for by gathering, nation particular or item – particular necessities may be added to the standard content. Change of the formats ought to, on the other hand, be finished with consideration and just as important to maintain a strategic distance from long arrangement.

[^6]: Reference to a specific page or source is included.
Approval and issuance\cite{7}

![Diagram of approval process]

**Fig 2: Approval process**

After completion and final review of the quality agreement, the responsible GMP operational department initiating the service with the CMO or vendor quality assurance department representatives and the CMO/vendor quality and management personnel approve the agreement by signature and date. The quality agreement may be a standalone document or incorporated into the business agreement.

**Standard structure**\cite{8}

1. **Introduction/Purpose/Scope**
   - Parties to the agreement
   - Products covered by the agreement
   - Site(s) involved
   - Definitions and abbreviations (optional)
2. Compliance Section

   - Term of agreement
   - Assignment
   - Related agreements
   - Confidentiality (optional)
   - Choice of Law (optional)
   - Survival Clause (optional; for exclusive substances)

4. Signatories

5. Quality Contacts

6. List of Appendices

Quality Agreement Review [8]

Review of a Quality Agreement should always be a conjoin effort of different departments of the parties involved: Quality representatives negotiate and review the quality sections, and Legal representatives negotiate and review the legal provisions. The Quality representatives at API /intermediate manufacturer and customer must assure that the quality provisions can be met.

Viable usage of any quality understanding is subject to both API supplier and clients. Utilization of a layout permits a Supplier to direct this audit once, preceding starting any quality concurrences with clients.

It is indigent upon both sides to guarantee the quality understanding is kept up as a present, precise report amid the whole successful period. Keeping in mind the end goal to permit audit of any adjusted wording or any necessities included amid the arrangement stage and to guarantee straightforwardness and traceability the "track changes mode" ought to be utilized. "Cleaned" adaptation would be made just specifically before signature, after all gatherings are fulfilled by the draft understanding. Clarity of dialect in the Quality Agreement is vital. Quality Agreements have no space for uncertainty.

Quality Agreements is kept "straightforward" or "non-lawful". A Legal audit of the last draft assent is an "absolute necessity", independent if the Quality Agreement is a stand-alone archive or if the Supply Agreement is arranged in the meantime.
The following wording’s aim to avoid future dispute and unexpected liability With respect to requirements and commitments in Quality Agreements, and they have been considered in the APIC templates:

- Do not use expressions such as “SUPPLIER guarantees”, “SUPPLIER represents and warrants”, or “SUPPLIER ensures”, in Quality Agreements. “Guarantee, in particular, triggers extended rights of the purchaser, liability without any fault, and leads to extend destitute of limitations.
- Instead use “neutral” expressions like “SUPPLIER shall”, “SUPPLIER undertakes”, or “SUPPLIER shall make reasonable endeavors” (but not “best” endeavors).

Quality Agreements require legally binding signatures; it is the responsibility of each party to assure the signatures in the Quality Agreement. At least one signature should come from an authorized Quality representative.

CONCLUSION

Quality is a much more complicated term than it appears. Quality is exceeding customer expectations. Customers judge quality through their perceptions.

Quality is an experience of the customer. Product quality perception comes from design specifications and manufacture standards achieved. Service quality perception comes from service process design and the customer contact impressions."Quality in a product or service is not what the supplier puts in. It is what the customer gets out and is willing to pay for."

The manufacturer can’t leave anything to assumption so, the Agreement between manufacture and customers are necessary for the better Quality of API. Quality Agreement is the document containing complete information on Active Pharmaceutical Ingredients (API). Quality is the new frontier. Supplier quality issue should be front and center for review and enhancement in all compliance and quality plans to avoid serious regulatory enforcement actions and business disputes.

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REFERENCE


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