ACTIVE PHARMACEUTICAL INGREDIENTS COMMITTEE (APIC)

Quality Agreement Guideline & Template

Version 02

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Disclaimer

This document represents voluntary guidance for API manufacturers and their customers, and the contents should not be interpreted as regulatory requirements. Alternative approaches than those described here may be used.

Foreword

The CEFIC* Sector Group APIC (the Active Pharmaceutical Ingredients Committee) was founded in 1992 as a direct consequence of the rapidly increasing European regulatory requirements affecting the manufacture of Active Pharmaceutical Ingredients (APIs).

APIC represents producers of APIs and API intermediates in Europe. Its membership consists of more than 60 companies, located all over Europe, and of several national industry associations. For around 2/3 of its members, selling APIs and intermediates is their major business while ca. 1/3 of the members are primarily marketing final medicinal products.

APIC's focus is on worldwide Quality, Good Manufacturing Practice (GMP) and Regulatory matters relating to APIs and intermediates. Through the years APIC has developed into a high-profile industry association with an excellent, worldwide reputation.

APIC has already developed a series of guidance documents and position papers (see http://apic.cefic.org/). This document offers best industry practice and guidance in the establishment of a Quality Agreement between an API manufacturer and its customer. The guideline highlights the factors to consider when concluding such an agreement between both parties.

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**** CEFIC (the European Chemical Industry Council): The Brussels-based organisation that represents the European Chemical Industry***

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Content

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1. Acknowledgements

This document was drawn up by a group of experts within CEFIC / APIC. We cordially thank them for their hard work and efforts spent as well as for their kind cooperation, intensive discussions and fruitful comments:

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2. Introduction

One of the biggest issues facing the pharmaceutical industry and patients today is quality, integrity and security of the pharmaceutical supply chain, preventing contamination (adulteration) and eliminating counterfeits. Quality Systems, Supplier Quality Management and Supply Chain Integrity have come into focus in the recent past. A suitable **Supplier Qualification Program** has hence to be implemented by each user of purchased APIs (or intermediates). 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. It increases transparency and traceability by improving the supply relationship between all parties involved in the manufacturing and distribution of APIs and intermediates.

Many companies, both users or buyers and manufacturers of APIs and intermediates, have developed their own Quality Agreement templates, often been designed to cover multiple types of products (APIs, intermediates, pharmaceutical excipients, and even packaging components), or to be used for both the purchase of (generic) APIs and contract manufacturing of (exclusive) substances (final APIs or intermediates). The high degree of diversity of agreements to be maintained increases **complexity** on both sides, resulting in extensive discussions between companies, and **significant time and resources spent** during all the review loops. It is a real challenge for all organisations to keep control over all the individual agreements and commitments made between the various parties (as regards, e.g., timelines, document provisions, notifications vs. prior approvals), which can be minimised by the use of standardised templates.

Since APIC is committed to improving the relationship between API/intermediate users or buyers and API/intermediate manufacturers, APIC has developed this Quality Agreement Guideline plus the corresponding template. The APIC Task Force consisted of members from both specialised API/intermediate manufacturers and companies primarily making finished drug products. Hence APIC believes that the result represents best industry practice considering the needs and requirements of both parties that enter into such a Quality Agreement.

2.1 What is a Quality Agreement?

A Quality Agreement under the scope of this guideline is a legally binding agreement that is mutually negotiated and concluded between (the Quality Departments of) API/intermediate manufacturers and their customers. It is intended to define, in a formalised manner, responsibilities relative to quality tasks to assure the manufacture and supply of safe materials (APIs or intermediates) acceptable for pharmaceutical use. A Quality Agreement is based on the quality procedures in place at both the API/intermediate manufacturer and its customer. The Quality Agreement also includes commitments between the parties regarding (a) the provision of information, documents, or samples, and (b) communication and notification rules including contacts. It creates mutual understanding of the quality & regulatory requirements relevant for material supply and both the API/intermediate manufacturer’s and customer’s respective obligations related to quality. By clearly delineating responsibilities, costly product quality issues resulting from miscommunication can be reduced or eliminated.

A Quality Agreement is a major element of an API/intermediate user’s supplier qualification program but, of course, it is not a substitute for the supplier qualification processes, including audits as necessary, and for understanding the supplier processes and capabilities.

A Quality Agreement should not contain any commercial or liability related terms, which should exclusively be dealt with in a Supply Agreement. This very common view is also shared by the

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US FDA, as clearly stated in its new guidance on Quality Agreements (see chapter 4 of this document).

2.2 Relation to Supply Agreements

Supply Agreements (also known as Commercial Agreements) document the legal and business relationship between API/intermediate manufacturers and their customers. Quality Agreements usually complement the Supply Agreements (if present). If and to the extent a Quality Agreement has been agreed upon, it is basically recommended to avoid quality provisions in Supply Agreements, whenever and to the extent possible, and rather to include a simple reference to the specific, complementary Quality Agreement. Items not directly related to Quality and regulatory compliance (e.g., Safety, Health & Environment items) should rather be included in the Supply Agreement. Nonetheless, one may frequently find combined agreements, often called "Technical Agreements", mixing Quality/GMP/Regulatory items with detailed product-specific ("technical") contents and other topics. It is recommended to implement separate agreements because these are easier to maintain.

Quality and Legal review of Supply Agreements should assure quality provisions are aligned/included in the corresponding Quality Agreements. Since Supply and Quality Agreement are often not generated at the same time or reviewed by the same people it is a must to define which document governs in case of conflict (see section III.3 of the Quality Agreement structure given in chapter 5).

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3. Purpose and Scope

3.1 Purpose

This document intends to provide expert guidance to the API/intermediate industry and its customers for the implementation and maintenance of appropriate Quality Agreements.

It is obvious that consistent standards for such agreements will provide the following **benefits** to the industry:

- Lower workload (by reduced drafting time)
- Faster implementation (by reduced review times)
- Less complexity (by reduced diversity)

Following this document will provide the current "state of the art" for Quality Agreements in the pharmaceutical (API/intermediate) supply chain.

The APIC Quality Agreement Guideline and the corresponding template are designed to be a flexible model for preparing Quality Agreements wherever such an agreement is desired. It defines the appropriate items that should be addressed in a Quality Agreement. The template is designed to be global in scope and contents, thus being suitable for the use in all regions.

3.2 Scope

The guideline and template cover agreements between the API/intermediate manufacturer and its customers (whether users or distributors). It does not cover agreements between distributors and their customers and the purchase of chemical/non-GMP raw materials by the API/intermediate manufacturer: the template is not really suitable for these purposes but some parts of the template may be used to compile an agreement for these areas. Furthermore, the template may not always be suitable for Atypical APIs. In such cases, the template may be adjusted or alternative templates may be used, as appropriate (e.g. IPEC template; see reference 1). An APIC guideline and template specifically for out-contracted analytical services can be found under http://apic.cefic.org/publications.html.

The template is suitable for both "generic APIs" and "exclusive substances", including when they are supplied for use in clinical trials.

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, as opposed to APIs that are sold only by the originator company or its exclusive licensees. Such generic APIs are off-patent; they are usually described in pharmacopoeial monographs, and supplied based on standard specifications. "**Exclusive substances**" are APIs or intermediates exclusively made for one customer who typically owns intellectual property rights on the process. This activity is also referred to as "Contract Manufacturing" or "Custom Synthesis". It can be managed under a toll manufacturing supply agreement where main raw material(s) is furnished by Customer to Supplier.

"**Supplier**" is used broadly in this guideline and the corresponding template for a company that provides the "Product", i.e. an API or API intermediate, to its "**Customer**". The terms "Contract Acceptor" (instead of "Supplier") and "Contract Giver" (instead of "Customer") are considered synonymous in practice, and may hence be used alternatively, if preferred by the parties; they are quite common in the custom synthesis area.

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Two separate templates were previously developed by APIC to cover generic APIs and exclusive substances. However, it was acknowledged that a vast majority of the requirements are similar for both categories and that these requirements are ultimately built to ensure the safety and efficacy of a finished drug, irrespective of those categories. Preference was then given to one standard template where some additional requirements usually applicable to exclusive substances are indicated as options.

Besides the IPEC Quality Agreements guideline/template mentioned above, the following documents may be useful in establishing Quality Agreements:

- The "*Rx-360 Best Practices Quality Agreement Guide*" (reference 2), released in January 2016, constitutes a comprehensive guidance document that is intended to assist both customers and suppliers in efficiently managing the initiation, negotiation, implementation, and ongoing maintenance of Quality Agreements. The document covers all kinds of quality-relevant supplies and services purchased by drug product manufacturers (APIs, excipients, packaging materials, contract labs, etc.), and it includes example language for various purposes. It does, however, not provide additional Quality Agreement templates but refers to existing ones, e.g. the APIC template.
- The "*SOCMA Quality Agreement Template*" (published in April 2010; reference 3) does not – from a content perspective – too much differ from the APIC template. In special cases, it has proven to be a suitable alternative, especially for US customers.

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4. Legal Requirements

Quality Agreements have become a common tool in our business and are intensively demanded by the authorities to be implemented. They have increasingly been referred to or described in international guidelines.

Written contracts/agreements defining the responsibilities and communication processes for quality-related activities of the involved parties are mandatory for "**contract manufacture**" (see EU GMP Guide Part I, chapter 7 [see Reference 4], and ICH Q7 Guideline, chapter 16 [see Reference 5]) or "**outsourced activities**" (see ICH Q10 Guideline, chapter 2.7 [see Reference 6]), respectively. In principle, it is the responsibility of the contract giver to request the closure of such a contract/agreement with its contract acceptor(s).

The situation is similar for "**purchased (starting) materials**" (see EU GMP Guide Part I, chapter 5.28 [see reference 4] or ICH Q10, chapter 2.7), in other words the purchase of "generic" APIs.

In line with the above, some countries are requesting such agreements. For instance, the French Code de la Santé Publique (article R5124-47) [see Reference 7] requires a written contract on the respective GMP obligations between the manufacturers of medicines and their raw material manufacturers.

In the United States, Quality Agreements are simply assumed but not necessarily a (legal) requirement. The Food and Drug Administration (FDA) issued its final guidance for industry on Quality Agreements in the pharmaceutical industry only recently ("*Contract Manufacturing Arrangements for Drugs - Quality Agreements* –", November 2016). see Reference 8]. This guideline covers "manufacturing activities of the parties involved in contract drug manufacturing subject to CGMP", and it makes reference to ICH Q7, chapter 16.11.

Specifically, this guidance addresses the relationship between "*owners*" and "*contract facilities*". For purposes of its guidance for industry, the FDA defines owners as "*manufacturers of APIs, drug substances, in-process materials, finished drug products, including biological products, and combination products*" and contract facilities as "*parties that perform one or more manufacturing operations on behalf of an owner or owners*".

While the FDA guidance document is focused on contract manufacturing, there is no such guideline for requirements of agreements for *purchased APIs*. In its guide the FDA only encourages "*entities that engage in manufacturing related solely to drug distribution to follow the recommendations in this guidance document, as appropriate*".

Furthermore, the FDA states that "*Quality Agreements should not cover general business terms and conditions such as confidentiality, pricing or cost issues, delivery terms, or limits on liability or damages*". The agency recommends that "*Quality Agreements be separate documents, or at least severable, from commercial contracts such as master services agreements or supply agreements*".

The Japanese "Ministerial Ordinance on Standards for Quality Assurance for Drugs, Quasi-drugs, Cosmetics and Regenerative medical products" [see Reference 9] and the "Ministerial Ordinance on Standards for Manufacturing Control and Quality Control of Drugs and Quasi-Drugs" [see Reference 10] require that the Marketing Authorisation Holders of drugs should conclude a contract with their manufacturers (mentioned in the MA dossier) "*to ensure that the manufacturing control and quality control are conducted properly and efficiently by the manufacturers*". Typically, for these GQP (Good Quality Practice) Agreements a specific template is used that significantly differs from the APIC template.

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5. Format and Structure of a Quality Agreement

5.1 General Aspects

The appendix to this APIC guideline constitutes a ready-to-use Quality Agreement (see typical structure of such an agreement in 5.2). The introduction and general provisions sections address the scope and terms and conditions of the agreement. The "Quality Responsibilities" section – in some cases also called "division (or: delimitation) of responsibilities" – includes the main quality and regulatory points and corresponding responsibilities that should typically be found in a Quality Agreement.

The template does, however, not mention every item of the pharmaceutical quality system since quality requirements that are sufficiently covered by reference to the applicable quality/GMP standard (as stated in section 1 of the template) do not need to be reiterated in the agreement.

The quality responsibilities may be assigned to one or both parties, as appropriate. In order to allow a convenient and quick overview a tabular format has been chosen for that section.

The format of the template is intended to be flexible with the template offering all the single elements needed for most Quality Agreements.

There are different possibilities how both parties may benefit from the use of a standardised template:

- The template may **completely replace** an own agreement
- The template may be **used as a basis** for a (slightly) modified, customized draft agreement
- **Certain sections** of the template may be used when drafting an own agreement
- The template's wording may be **used to resolve dispute** if mutually understood as good industry practice.

Hence the template constitutes the ideal common starting point for any further negotiations on a Quality Agreement (see chapter 6 of this guideline).

Where necessary or requested by either party, country-specific or product-specific requirements may be added to the standard text.

The template is available in English only as the English language is the most used language in global business and communication, hence constitutes the best common basis between parties of different native tongues.

Timelines mentioned in a Quality Agreement may be given in a descriptive way (most common terms: immediately, promptly, without undue delay, in a timely manner, within a reasonable period of time) or by a precise figure. Widely accepted definitions of the descriptive terms can be found in the glossary of this document. Time differences between the regions involved should be considered.

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5.2 Standard Structure

The following sections should normally be included in a Quality Agreements:

I. Introduction/Purpose/Scope

- I.1 Parties to the agreement
- I.2 Products covered by the agreement
- I.3 Site(s) involved
- I.4 Definitions and abbreviations (optional)

II. General Provisions

- II.1 Effective date
- II.2 Term of agreement
- II.3 Assignment
- II.4 Related agreements
- II.5 Amendments
- II.6 Confidentiality (optional)
- II.7 Resolution of quality disputes (optional)
- II.8 Choice of law (optional)
- II.9 Survival clause (optional)

III. Quality Responsibilities

IV. Signatories

V. Contacts

VI. List of Appendices

VII. History / Change Log

5.3 How to create your "working template"?

Simply take the APIC template (Appendix) and

- Remove all explanatory "notes", unless deemed helpful for clarification purposes,
- Keep or remove the articles "for exclusive PRODUCT", as applicable in your specific case,
- Keep or remove the "optional" text and/or select the appropriate "alternative" text, as needed.

For further details, also see the "Use instructions for sections I to III" after the table of contents in the template; these instructions should be removed as well, by the way.

You have to do this exercise only once, prior to the first use of the APIC template. Thereafter, your individual core template is ready for instant use and has to be filled with the variable information only (e.g. CUSTOMER address, your sites(s) address(es), PRODUCT concerned, contact data). Finally, you may add any required appendices (e.g. PRODUCT specifications, approved sub-contractors), assigned as e.g. Appendix A, Appendix B etc.

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6. Negotiation and Maintenance

6.1 Negotiation, Review and Approvals

Prior to starting negotiations, the expectations of both parties should be clarified, e.g. scope of the agreement (products, services, sites to be covered), use of a standard template vs. use of an individual document. Furthermore, it is recommended to mutually agree upon a timeline for review at the very beginning.

Basically, negotiation will become significantly easier and faster if standardized templates – ideally pre-reviewed by Legal – are used. The "time argument" will also be most convincing for a number of suppliers or customers to accept the use of a standard template ("*if we can agree upon the ABC template we may be ready for signature within two weeks*"). Different options how to use a standard template have been given in chapter 5.1 already.

Modifying the template should, however, be done with care and only as necessary to avoid lengthy negotiations. It is suggested that the (generic) API manufacturer prepares a Quality Agreement based on the APIC template to begin the negotiation process with its customer when a Quality Agreement is requested. In Contract Manufacturing (i.e. for exclusive PRODUCT) the process will typically run the other way round.

Individuals negotiating should have full knowledge of the rationale behind the text. It is best practice to provide justification for any changes to major terms, to explain why a certain paragraph is written as it is, or to have a reasoned justification ready for any non-negotiable elements to explain why the clause cannot be changed. If major changes are made to the standard template, especially the general provisions, Legal experts may need to be consulted. It would significantly facilitate the discussion if any such alterations are clearly indicated by the drafting party to the other party (e.g., by coloured text) as this will help to achieve speedier closure of agreements.

The negotiation and review of a Quality Agreement should always be a collaborative 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. Other departments (e.g., Purchasing, Marketing) may be involved, as appropriate. It is recommended that in the negotiation phase a sole functional unit, preferably the Quality Unit, acts as the voice of the entire company.

The Quality representatives at API/intermediate manufacturer and customer must assure that the quality provisions can be met, i.e., that the obligations of the agreement are consistent with the quality systems established at the respective sites [*Note: this is very important in case multiple sites or affiliates at either party are affected by the agreement*], and both parties must understand the impact of the agreement provisions on patient safety and product quality.

In order to allow review of any modified wording or any requirements added during the negotiation phase and to ensure transparency and traceability the "track changes mode", i.e. redline rather than clean versions should be used. A "cleaned" version would be created only directly before signature, after all parties are satisfied with the draft agreement.

Clarity of language in the Quality Agreement is essential. Quality Agreements have no room for ambiguity. It is generally recommended that the wording of Quality Agreements is kept "simple" or "non-legal" (at least all sections except the "general provisions") since it is primarily written for Quality people, and these people have to understand and follow the provisions.

A Legal review of the final draft agreement is recommended, irrespective if the Quality Agreement is a stand-alone document or if the Supply Agreement is negotiated at the same time. Not having the Quality Agreement undergo a qualified review by Legal department may expose

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the company to potential liability. It is, however, not the Legal representatives' task to interpret GMPs and change the language unless potential liability exists. It is their job to look at the document from the point of view of someone who is providing a level of protection to the company.

The following wording recommendations 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 template:

- 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 extended statute of limitations.
- Instead use "neutral" expressions like "SUPPLIER shall", "SUPPLIER undertakes", or "SUPPLIER shall make reasonable endeavours" (but not "best" endeavours).

When a supply agreement exists, or is being generated at the same time as the Quality Agreement, the reviewers should assure that any quality provisions captured in the supply agreement are also reflected and/or not contradicted in the Quality Agreement. Preferably, no quality provisions should be captured in a Supply Agreement (see also chapters 2 and 4).

Since all Quality Agreements require legally binding signatures, it is the responsibility of each party to assure the signatures in the Quality Agreement reflect the legally binding signatures representing each party. Depending on the signing rules in each company two or even more signatures might be required. At least one signature should come from an authorised Quality Unit representative.

Once the parties have finished their discussion on the content, they should agree upon the signature/approval process (e.g. who signs first?) and the form of the final approved contract (e.g. use of wet ink vs. electronic signatures, paper copies vs. pdf files, number of –where required– hardcopies for each party, all signatures on one page vs. compilation of pages with one or more signatures). All these options are basically acceptable from a Legal view, so the parties' company-internal rules or preferences will determine the outcome. Some companies are used to initial each page of the Quality Agreement, which is, however, not required from a Legal perspective.

6.2 Maintaining Agreements

Any Quality Agreement should be readily available to all persons or units with obligations stipulated in the agreement. It is recommended to have a system in place for tracking commitments originating from the various Quality Agreements.

Once approved all Quality Agreements must be kept current by both parties during the entire effective period. An amendment/addendum process should allow for simple updating, i.e. updating without requiring the entire document to go back through review and approval steps, e.g., for contact or specification updates. Any amendment/addendum should be maintained with the original agreement.

Since organisations, responsibilities, scope of the agreement, regulatory environment or other aspects may change over the time, both parties should review the existing Quality Agreement in regular intervals. Basically, there are different options to define the review frequency for an established Quality Agreement: periodic review (e.g., during the compilation of the annual PQRs or every 2 or 3 years) or a frequency based on risk. A combination of both options might be the best solution, e.g. a 3-years review period in the absence of serious quality incidents or significant risks.

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7. References

1. The IPEC Quality Agreement Guide and Template 2009 (Link: www.ipec-europe.org/index.php?option=com_docman&task=doc_download&gid=280&&Itemid=46)
2. Rx-360 Best Practices Quality Agreement Guide, December 2015 (Link: http://www.a3p.org/index.php/infos-reglementaires/1782-rx-360-best-practices-quality-agreement-guide.html)
3. SOCMA Quality Agreement Template, April 2010 (Link: http://images.alfresco.advanstar.com/alfresco_images/pharma/2014/08/21/64ae0741-06af-4bda-8d0d-8c28c1ed22dd/article-682864.pdf)
4. EU GMP Guide Part I, Basic Requirements for Medicinal Products
5. ICH Q7 Guideline “Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients”, November 2000
6. ICH Q10 Guideline “Pharmaceutical Quality System”, June 2008
7. Code de la Santé Publique Française, article R5124-47, July 2016 (Link: https://www.legifrance.gouv.fr/telecharger_pdf.do?cidTexte=LEGITEXT000006072665)
8. FDA Guidance for Industry: Contract Manufacturing Arrangements for Drugs - Quality Agreements -, Draft Guidance, May 2013 (Link: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM353925.pdf)
9. MHLW Ministerial Ordinance No. 136, September 2004
10. Ministerial Ordinance on Standards for Manufacturing Control and Quality Control of Drugs and Quasi-Drugs” (MHLW Ordinance No.179, 2004/revised July 2014)
11. EC “Guidelines of 19 March 2015 on principles of Good Distribution Practice of active substances for medicinal products for human use” (2015/C 95/01)
12. Annex 5 WHO good distribution practices, WHO Technical Report Series, No. 957, 2010 (Link: http://www.who.int/medicines/areas/quality_safety/quality_assurance/GoodDistributionPracticesTRS957Annex5.pdf)

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8. Glossary

Active Pharmaceutical Ingredient (API) - Any substance or mixture of substances, intended to be used in the manufacture of a drug (or: medicinal) product and that, when used in the production of a drug, becomes an active ingredient of the drug product. Such substances are intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment or prevention of disease or to affect the structure or any function of the body of man or animals.

Adverse trend – A trend in the values of any measure of the quality of product or process which is outside the normal process capability or which indicates a reasonable probability that the product will fail to comply with specification before the end of its assigned shelf-life or retest period.

Agreement – Arrangement undertaken by and legally binding on parties.

Atypical API – A substance, which primary use is not in a medicinal product, and the producer may therefore not be aiming to meet the specific requirements of pharmaceutical customers that represent an insignificant volume of business. Such substances are addressed in the "questions and answers document" of the European Medicines Agency on good manufacturing practice (section "EU GMP guide part II: Basic requirements for active substances used as starting materials: GMP compliance for active substances", point 6).

(Governmental or **Regulatory) Authority** – Any court, tribunal, arbitrator, agency, legislative body, commission, official or other instrumentality of (a) any government of any country, (b) a federal, state, province, or other political subdivision thereof, or (c) any supranational body including without limitation the European Medicines Agency (EMA).

Business day – Any day of the week, other than Saturday, Sunday, or day on which the party required to take action is regularly closed for business, i.e., Monday to Friday (European working hours) except any official national or regional bank holidays or shut down of the plant.

CEP – A certificate issued by the European Directorate for the Quality of Medicines which demonstrates that the Product complies with the requirements of the European Pharmacopoeia monograph and / or Transmissible Spongiform Encephalopathy (TSE) requirements. Also known as “CoS” = Certificate of Suitability.

Certificate of Analysis – A document identified as such, provided by the supplier signed by its Responsible Person, or produced by a computer system which provides a degree of control equivalent to that given by a signature, which sets forth the analytical test results, obtained from testing of a representative sample, against the specifications for the batch to be delivered.

Certificate of Conformance – A document identified as such, provided by the supplier and signed by a nominated representative of its Quality Unit, or produced by a computer system which provides a degree of control equivalent to that given by a signature, which certifies that each batch of Product was produced and tested in compliance with the agreed specifications, GMP, and the relevant pharmacopoeial monographs, as applicable. Also known as Certificate of Compliance.

Contract – Business agreement for supply of goods or performance of work at a specified price.

Contract Manufacture – Performance of some aspect of manufacture, under a contract, on behalf of the original manufacturer.

Critical deviation – A departure from an approved instruction, a standard operation, or a predefined critical parameter, or an unanticipated event that could have an adverse impact, respectively, on the final SUBSTANCE quality and/or stability and/or physical characteristics.

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Customer – The company or organisation receiving the product (API or intermediate) once it has left the control of the supplier; includes users and distributors.

Data Integrity – The extent to which all data is complete, consistent and accurate throughout the data lifecycle. Data should be attributable, legible, contemporaneously recorded, original or a true copy, and accurate (ALCOA).

Distributor – Any party in the distribution/supply chain starting from the point at which an API or intermediate is transferred outside the control of the original manufacturer's material management system including parties involved in trade and distribution, such as (re)processors, (re)packagers, transport and warehousing companies, forwarding agents, brokers, traders, and suppliers other than the original manufacturer.

DMF – Drug Master File. The supplier's dossier for providing confidential information to a regulatory authority about facilities, processes, or articles relating to product (usually an API) used in the manufacturing, processing, packaging, and storing of one or more drug (or: medicinal) products.

GDP – Good Distribution Practice. GDP deals with the distribution of products, including requirements for purchase, receiving, storage and export. GDP regulates the movement of products from the premises of the manufacturer to the end user, or to an intermediate point by means of various transport methods.

GMP – Good Manufacturing Practice. Requirements for the Quality System under which drug (or: medicinal) products and their (active) ingredients are manufactured. Current Good Manufacturing Practice (CGMP) is the applicable term in the United States. For the purposes of this guideline, the terms GMP and CGMP are equivalent.

Immediately – Generally no more than twenty-four (24) business hours. This period may be exceeded due to events or circumstances beyond the reasonable control of the responsible party.

Laws – All laws, statutes, rules, regulations (including, without limitation, GMPs, NDA regulations, and other relevant provisions enforced by any applicable governmental authority), ordinances and other pronouncements having the binding effect of law of any governmental authority.

Manufacturing License – With respect to a country, any regulatory authorisation required to manufacture one or more products or classes of product as granted by the relevant governmental authority.

Non-conformance –Departure of a quality characteristic from its intended level or state such as to cause an associated material or activity not to comply with its specification, GMP, marketing authorisation or applicable law.

OOE – Out-of-expectation. A value obtained that still meets the set requirements but is significantly different from the previous values or former trend

Original Manufacturer – Person or company manufacturing a material to the stage at which it is designated as a pharmaceutical starting material.

Product Quality Review – The PQR is an assessment to verify the operational consistency of a process based on results trending and non-conformances.

Promptly – Generally no more than three (3) business days. This period may be exceeded due to events or circumstances beyond the reasonable control of the responsible party.

Quality Agreement – A legally binding agreement that is mutually negotiated and concluded between (the Quality Departments of) API/intermediate manufacturers and their customers. It is intended to define, in a formalised manner, responsibilities relative to quality tasks to assure the

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manufacture, supply and use of safe materials acceptable for pharmaceutical use. It may also include commitments between the parties regarding (a) the provision of information, documents, or samples, and (b) communication and notification rules including contacts.

Quality Incident – An incident relating to an issue or defect which is not necessarily detected by the specification parameters but which potentially could result in a non-conformance. A "critical" quality incident is relating to a defect or fault that makes a product unsuitable for use and which could potentially result in a recall, retrieval or withdrawal.

Record – Document stating results obtained and/or providing evidence of activities performed. The medium may be paper, magnetic, electronic or optical, photography etc. or a combination thereof.

Responsible Person – The person(s) within the Quality Unit at the supplier who is accountable for the release of batches of product.

Sample – A part or parts of the product taken to show the quality of the whole.

Site – A location where the API or intermediate is manufactured. This may be any operational area within the supplier's facility referred to in the section "Parties to the agreement" of the Quality Agreement (see chapter 5.2, I.1 of this guideline), or at a remote facility that may be the facility of an affiliate of the supplier or a sub-contractor.

Sub-Contractor – A third party contractor, engaged and qualified by the supplier or original contract acceptor to perform any part of the supplier's or original contract acceptor's GMP obligations under the License, Supply or Quality Agreements.

Supplier – Person or company providing APIs or intermediates on request. For the purpose of this guideline, a supplier is the (original) manufacturer or another legal entity of the same company that supplies the material. In general, suppliers may also be traders or distributors.

Supply chain – For the purpose of this guideline, supply chain is defined as all steps in the entire chain of distribution starting from the point at which an API or intermediate is transferred outside the control of the original manufacturer's material management system downstream to the final user(s).

Timely manner – As soon as can be expected considering the typical operations and processes at manufacturers, the defined responsibilities and the agreed communication pathways. A "reasonable period of time" is considered as practically synonymous. The exact period of time depends on the respective subject.

User – A party who utilises an API in the manufacture of a drug product or an intermediate in the manufacture of an API.

WHO – World Health Organization

Without undue delay – Generally no more than five (5) business days. This period may be exceeded due to events or circumstances beyond the reasonable control of the responsible party.

Note: For all other GMP-relevant terms it is referred to the glossary of the ICH Q7 Guideline.

9. Appendix

- APIC Quality Agreement Template for APIs (25 pages)

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Quality Agreement Template for APIs

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Contents

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Use instructions for sections I to III:

Text highlighted in yellow indicates **alternative or optional wordings**.

Notes in orange boxes are **for information/explanation purposes only**, and they would not appear in the actual Quality Agreement.

Text in green boxes represents specific conditions for "**exclusive PRODUCT**" only, i.e. APIs or intermediates exclusively made for one customer under a toll manufacturing contract as to EU GMP Guide Part I, chapter 7 or ICH Q7, chapter 16 ("Contract Manufacturing", also known as "Custom Synthesis"). These articles should be removed if not applicable.

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I. Introduction / Purpose / Scope

I.1 Parties to the agreement

Note: Although the APIC template is intended for Quality Agreements between API/intermediate "manufacturers" (but not "traders" or "distributors") and their customers, the more general term "SUPPLIER" is used in the template instead of "MANUFACTURER". The reason is that even if you buy an API or intermediate from the original manufacturer you may be invoiced by another legal entity or the Supply Agreement is concluded with another legal entity of the same company, especially if the manufacturing site is part of a bigger company (also see next note).

This Quality Agreement is by and between < full supplier name > located at < full supplier address >, hereafter referred to as SUPPLIER and < full customer name > located at < full customer address >, hereafter referred to as CUSTOMER.

Whereas, SUPPLIER manufactures and supplies Active Pharmaceutical Ingredients (APIs) suitable for pharmaceutical use (alternatively: API intermediates suitable for production of APIs) to CUSTOMER.

CUSTOMER and SUPPLIER may each be referred to herein individually as a "Party" and collectively as the "Parties."

Note: In case the Party that supplies the API(s) or intermediate(s) is a different legal entity within the same company, or the manufacturing sites involved in the manufacture of the API(s) or intermediate(s) are different legal entities of the same company, the following additional paragraph would be appropriate:

SUPPLIER sells and markets products produced by itself or its affiliates, inter alia <full affiliate(s) name> located at <full affiliate(s) address>, which affiliates have the ability and desire to, as sub-contractors, manufacture and SUPPLIER has the desire to supply the products. SUPPLIER is responsible for the trade and sample packaging of the released products. Each reference to SUPPLIER shall in the following hence be interpreted as a reference to SUPPLIER and/or the manufacturing entity, as applicable.

Note: If necessary, the following definition of "Affiliate" may be added to the preceding paragraph or listed in the Definitions section (I.4).

For the purposes of this Quality Agreement, the term "Affiliate" shall mean any company controlling, controlled by or under common control with the respective Party. The term "control" shall mean the possession, directly or indirectly, of more than 50 % of the respective shares or the power to direct the management or policies of such company or Party.

The mentioned Parties wish to further define the individual responsibilities in relation to the quality aspects of manufacturing, control and acceptability of the products manufactured and supplied to CUSTOMER by SUPPLIER to ensure compliance with the applicable Good Manufacturing Practices (GMPs), the marketing authorizations of CUSTOMER related to finished drug products including SUPPLIER's APIs, applicable regulatory requirements and any further requirements laid down in this agreement.

In order to achieve this purpose, this Quality Agreement includes a detailed list of the activities associated with the manufacture, inspection, GMP compliance and acceptability of the products

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as defined in article I.2 below. Unless otherwise indicated, responsibility for each activity is assigned to either CUSTOMER or SUPPLIER, or to both Parties.

I.2 Products covered by the agreement

This Quality Agreement pertains to the following product(s), hereafter referred to as PRODUCT: <list here or refer to Appendix X>.

I.3 Site(s) involved

Note: The SUPPLIER sites involved in the manufacture of PRODUCT, as from introduction of the starting material(s), can be specified here, if needed, or may be referred to in an appendix. If the sites involved are not listed in this agreement, it should be indicated where the agreed sites are specified. The sites can also be sites of affiliates of the SUPPLIER (see also I.1). CUSTOMER sites receiving the PRODUCT may be listed as well.

I.4 Definitions and abbreviations (optional)

Capitalised terms used but not otherwise defined in this Quality Agreement will have the meanings ascribed thereto in the Supply Agreement, as applicable. Unless this Quality Agreement will expressly provide to the contrary, the following terms used herein, whether used in the singular or plural, will have the respective meanings set forth below:

<List definitions/abbreviations>

Note: Definitions of timelines from the glossary may be included here in order to get clarity on terms like 'immediately' or 'promptly'.

II. General Provisions

Note: The general provisions mentioned hereunder are required for a stand-alone Quality Agreement, however, in case the Quality Agreement is part of or appendix to a Supply Agreement they would usually be included in the Supply Agreement and do not need to be repeated in the Quality Agreement.

II.1 Effective date

This Quality Agreement shall become effective and binding upon the date of the final signature.

Note: In case the effective date is not determined by the final signature, the effective date should be given elsewhere in the Quality Agreement.

II.2 Term of agreement

This Quality Agreement shall remain in effect until 2 years after the last delivery of PRODUCT by SUPPLIER to CUSTOMER unless the Parties specifically agree in writing an extension of

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the Quality Agreement. Either Party may terminate this Quality Agreement by giving 6 months' written notice to the other Party.

Note: The definition of the period of validity "until 2 years after the last delivery of PRODUCT by SUPPLIER to CUSTOMER" *is very common, hence recommended by APIC. This could be different by each company's preference.*

II.3 Assignment

Neither Party shall have the right to assign any or all of its rights or obligations under this Quality Agreement without the other Party's prior written consent, which consent shall not unreasonably be withheld. The foregoing notwithstanding, prior written consent shall not be required (i) in case of an assignment of rights or obligations to an Affiliate of the assignor (optional extension: provided that the assignor procures that any such Affiliate assigns such rights back to the assignor immediately before ceasing to be an Affiliate of the assignor), or (ii) 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.

II.4 Related agreements

If a supply agreement is in place between SUPPLIER and CUSTOMER, and there are any inconsistencies between the supply agreement and the Quality Agreement, the supply agreement will take precedence over the Quality Agreement in all non-quality related matters unless otherwise stated in the supply agreement. The Quality Agreement will take precedence in all quality related matters.

II.5 Amendments

Amendments to this Quality Agreement shall be in writing and signed by appropriate representatives of both Parties.

The Parties agree to amend terms of this Quality Agreement that need to be amended in order to ensure that the PRODUCT continues to meet regulatory requirements of applicable jurisdictions and CUSTOMER requirements.

If an amendment to this Quality Agreement is proposed, the proposing Party will circulate the proposed amendment to the appropriate contact person at SUPPLIER and CUSTOMER for review and approval. The appropriate contacts are listed in section V.

Note: Appendices may be amended in the same manner as the agreement without the need for revision, review or approval of the agreement in its entirety.

II.6 Confidentiality (optional)

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Note: It is recommended to refer to separate documents pertaining to confidentiality, e.g. confidentiality agreement (also referred to as a confidential disclosure agreement) but may be defined here according to SUPPLIER's policy.

II.7 Resolution of quality disputes (optional)

Quality-related disagreements between SUPPLIER and CUSTOMER that are not resolved in the normal course of business shall be brought to the attention of the appropriate contact person at SUPPLIER and CUSTOMER, in writing, as listed in section V. Both parties shall use all reasonable efforts to agree to a reasonable resolution to the disagreement, and agree to work jointly to develop a strategy for such resolution. SUPPLIER and CUSTOMER further agree to record such resolution in writing.

In the event that resolution of a quality related disagreement cannot be reached, the dispute resolution procedures in the commercial agreement shall be followed. In the absence of a commercial agreement or a dispute resolution procedure and in the case of a PRODUCT non-compliance with this Quality Agreement, CUSTOMER reserves the right to terminate the Services on providing one month's written notice.

II.8 Choice of Law (optional)

Note: A choice of law should always be specified in a supply agreement. If a reference shall also be included in the Quality Agreement the following wording is recommended:

"The Parties agree that this Quality Agreement shall be governed by and construed in accordance with the law applicable to the supply agreement between the Parties or their Affiliates pertaining to the PRODUCT."

Typically, the law of the country where the SUPPLIER is located is chosen. For instance, in Europe (except Denmark and the UK), the new EU Regulation No. 593/2008 - "Rome I" - will apply as of December 17, 2009, and as most of the jurisdictions it declares that the law of the country where the party required to effect the characteristic performance of the contract has its habitual place of residence shall govern the contract.

II.9 Survival Clause (optional)

All regulatory obligations required of CUSTOMER and SUPPLIER by an applicable regulatory authority or effective regulations shall survive termination of this Quality Agreement.

In detail, < list particular provisions > shall survive < give number > years from expiration or termination of this Quality Agreement.

Note: This clause relates to provisions that by their sense or context are intended to be continued beyond termination of the Quality Agreement, for instance the right to audit, maintenance of lot traceability, responses to complaints or authority requests, ongoing stability studies, or document/record/sample retention. This clause is more common in the custom synthesis business.

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III. Quality Responsibilities

[C = CUSTOMER; S = SUPPLIER]

	Responsibilities	C	S
1	**Applicable GMP Standard / Regulatory Compliance**		
1.01	Manufacturing PRODUCT in compliance with the applicable Current Good Manufacturing Practices (CGMPs). For the purposes of this agreement, CGMP shall mean the principles (i) described in the ICH Q7 Guide (incl. the Q&As published 2015) as well as the ICH Q9 and Q10 Guidelines, (ii) promulgated by any governmental or regulatory authority having jurisdiction over the manufacture of the PRODUCT, in the form of laws or guidance documents, where the guidance documents are to be implemented within the pharmaceutical industry for such PRODUCT.		**X**
1.02	Adhering to approved registration documentation (Marketing Authorization, NDA, IND, DMF, CEP, etc., as applicable)	**X**	**X**
1.03	Maintaining valid manufacturing license(s), as applicable		**X**
1.04	Maintaining site master file complying with the applicable authority requirements (e.g. EU GMP Guide Part III)		**X**
1.05	Establishing synthesis scheme (including definition of API starting materials)		**X**
1.06	Providing test procedures, stability reports, statements, and other quality or regulatory documents as mutually agreed between the parties (see also 8.02, 10.04 and 12)		**X**
2	**Change Control**		
2.01	SUPPLIER shall have a documented and effective change control system in place. SUPPLIER shall inform CUSTOMER of any significant changes to the manufacture of PRODUCT, which may have an impact on the quality of supplied PRODUCT, and/or on any regulatory applications related to PRODUCT. SUPPLIER shall notify CUSTOMER within a reasonable time, prior to implementation, to allow CUSTOMER to assess the potential impact of the change upon the PRODUCT supplied or its use by CUSTOMER.		**X**
2.02	The implementation of changes requiring authorities' pre-approval or changes with a demonstrable effect on the PRODUCT quality shall not occur until the CUSTOMER has given written approval.		**X**
2.02	***Alternative text for exclusive PRODUCT:*** Approval of PRODUCT specific changes related with the process, specifications, product specific analytical methods, primary packaging, storage conditions and stability protocols, unless minor typographic errors. Unless there are justified scientific reasons to reject the change request, CUSTOMER will not unreasonably withhold its approval of the request.	**X**	
2.03	SUPPLIER shall only supply CUSTOMER with PRODUCT described in any applicable, current DMF and/or CUSTOMER's existing regulatory filings until PRODUCT manufactured following such change is permitted under the regulatory filings therefore or if approved in writing by CUSTOMER to receive PRODUCT prior to regulatory approval (e.g. for trial production). SUPPLIER shall inform CUSTOMER about the start of PRODUCT supplies with the new quality after the change (batch number, date).		**X**
2.04	CUSTOMER has the final responsibility for ensuring regulatory compliance for the finished product brought to the market.	**X**	

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	Responsibilities	C	S
2.05	CUSTOMER shall provide SUPPLIER with information about its regulatory filings if they differ from those supplied by SUPPLIER to CUSTOMER.	**X**	
	Note 2.1: 2.05 would not apply for exclusive PRODUCT		
2.06	For those changes required to comply with applicable laws and regulatory authority requirements concerning PRODUCT, SUPPLIER shall notify CUSTOMER of such requirements after SUPPLIER becomes aware of the need for such changes, and vice versa.	**X**	**X**
2.07	Minor changes which are not expected to have impact on PRODUCT quality or the regulatory filings of CUSTOMER shall be processed by SUPPLIER's change control system.		**X**
2.08	CUSTOMER undertakes to submit within a reasonable period of time all necessary change notifications to all competent authorities in full compliance with the applicable regulations, respectively, and to inform SUPPLIER of the receipt of the necessary acknowledgement of the validity of the notification and, depending on the type of change, the acceptance or approval of the change by the competent authorities.	**X**	
3	**Regulatory Documents**		
	Note 3.1: It is assumed that the SUPPLIER is the owner of the registration documents mentioned in the section for generic APIs.		
3.01	SUPPLIER is responsible for maintaining the appropriate registration documents for the PRODUCT (i.e. dossier for CEP, DMF or equivalent) in countries where these documents have been submitted already.		**X**
3.02	Upon mutual agreement with CUSTOMER, SUPPLIER will prepare and submit registration documents in countries where SUPPLIER has not yet registered the product.		**X**
3.03	SUPPLIER is responsible for all regulatory contacts with the relevant regulatory authority with jurisdiction over the PRODUCT.		**X**
3.04	SUPPLIER will provide current information to CUSTOMER Affiliates reasonably requested for submission of any regulatory dossier by CUSTOMER Affiliates for finished drug products made from PRODUCT. Such information will include either access to CEP (including the appropriate stability data for the respective PRODUCT, if no retest date is defined in the CEP), or applicants' part to DMF, or equivalent.		**X**
3.05	CUSTOMER Affiliates are responsible for submitting the regulatory dossier for Marketing Authorization Application associated with any finished drug product made from the respective PRODUCT. Such regulatory dossier, as it pertains to SUPPLIER, will refer to SUPPLIER's CEP, DMF or equivalent, where applicable.	**X**	
3.06	Optional: Appendix **X** will include the list of SUPPLIER's supportive registration documents that are available at the signature of this Quality Agreement.		**X**
	Alternative text for exclusive PRODUCT:		
3.01	CUSTOMER shall be responsible for preparation of registration documents related to PRODUCT and finished drug products made from the PRODUCT and submission of such registration documents to any regulatory authority, including maintaining such submissions (hereafter altogether called 'Regulatory Submissions').	**X**	
3.02	Upon request by, and in mutual consultation with CUSTOMER, SUPPLIER shall be responsible for preparation of documentation on manufacture of PRODUCT as required for the Regulatory Submissions of CUSTOMER, limited to SUPPLIER's activities under this agreement.		**X**

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	Responsibilities	C	S
3.03	CUSTOMER shall provide portions of Regulatory Submissions, related to PRODUCT and SUPPLIER's activities performed under this agreement, to SUPPLIER for review and written consent, prior to submission to any regulatory authority.	**X**	
3.04	SUPPLIER shall review and comment to CUSTOMER on such portions of Regulatory Submissions, within ___ business days from receipt.		**X**
3.05	CUSTOMER shall, upon submission to any regulatory authority, provide SUPPLIER with current copies of portions of Regulatory Submissions, including amendments and supplements thereto, related to the PRODUCT and SUPPLIER's activities performed under this agreement.	**X**	
3.06	SUPPLIER will provide, in mutually agreed timelines, all other information related to the PRODUCT that CUSTOMER may reasonably request for its Regulatory Submissions, including any data for annual reports (e.g. annual stability reports for the PRODUCT).		**X**
3.07	When a change is known to require, or has the potential to require a Regulatory Submission, CUSTOMER will develop a joint strategy to obtain the appropriate regulatory approvals prior to implementation of the change. For change control see section 2.	**X**	
4	**Audits**		
4.01	SUPPLIER shall allow –upon signature of a special (personal) confidentiality agreement– CUSTOMER or its representatives (may also be a 3rd party auditor) to carry out on-site audits by appointment. SUPPLIER shall permit all reasonable access to the manufacturing, packaging, warehousing and laboratory areas related to the manufacture of PRODUCT, including pertinent documentation. Any such audit shall take place during normal business hours and must not interfere with SUPPLIER's manufacturing operations. Alternatively, existing 3rd party audit reports may be used, if agreed by all parties.		**X**
	Note 4.1: In order to manage expectations, the parties may want to add the following paragraph:		
4.02	Optional: CUSTOMER shall notify SUPPLIER of its audit request at least **X** months in advance of the desired audit date.	**X**	
4.03	The results of the audit and the observation(s) shall be sent to SUPPLIER by means of a written report.	**X**	
4.04	SUPPLIER shall send to the customer a formal response to the audit observations including any relevant CAPAs and timelines for implementation..		**X**
	Note 4.2: target timelines for both report and response may be added; a 4-weeks period is quite common, respectively.		
4.05	The audit frequency shall depend upon the results of the previous audit(s) and the quality performance of SUPPLIER. In the absence of critical quality incidents the frequency shall be not more than once every three (3) years.		
	Note 4.3: the 3 years period can be considered as industry standard; it originates from the period of validity of EU GMP certificates (EMA Compilation of Community Procedures on Inspections and Exchange of Information – Union Format for a GMP Certificate) and the QP declaration template (EMA/334808/2014), Part C. Higher audit frequencies are quite common in case of exclusive substances, e.g. once every year or once every two (2) years, or in case of specific risks, e.g. single-source APIs for medicinal products of vital importance for public health.		
4.06	Upon request by regulatory authorities or as required by applicable law, CUSTOMER may disclose all or part of its audit report to regulatory authorities without prior approval by SUPPLIER.	**X**	

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	Responsibilities	C	S
4.07	In case of significant quality incidents or critical GMP deficiencies SUPPLIER will allow CUSTOMER to conduct "for-cause" audits at SUPPLIER's facilities until the issue is resolved to both parties' mutual reasonable satisfaction.		**X**
5	**Authority Inspections**		
5.01	SUPPLIER shall promptly notify CUSTOMER of any regulatory or GMP violations (e.g. FDA Warning Letter or suspension/withdrawal of one or more CEPs) identified during authority GMP inspections and impacting the quality of PRODUCT intended to be shipped to CUSTOMER and/or potentially affecting the ability of SUPPLIER to produce or ship the PRODUCT.		**X**
	For exclusive PRODUCT (5.02 to 5.06):		
5.02	Promptly give prior notification to CUSTOMER of any regulatory inspection.		**X**
5.03	Promptly inform CUSTOMER on the results of the inspection, and share all corresponding post-inspection documents, including but not limited to proposed corrective actions, and any other communication with the authority. SUPPLIER shall consult with CUSTOMER prior to submitting its response to the authority.		**X**
5.04	CUSTOMER shall review and/or approve the draft response prepared by SUPPLIER in a timely manner, considering any timelines set by the regulatory authority.	**X**	
5.05	Allow CUSTOMER representatives to be present on site during the inspection.		**X**
5.06	Confidentiality regarding other customers' exclusive products or, if necessary, other SUPPLER products must be ensured during correspondence with CUSTOMER or on-site presence of CUSTOMER representatives.	**X**	**X**
6	**Data Integrity**		
6.01	SUPPLIER agrees to have procedures in place to ensure quality-relevant data is attributable, legible, contemporaneously recorded, original or a true copy, and accurate (ALCOA); that it can be traced to its source and that it is readily available during regulatory inspections.		**X**
6.02	SUPPLIER further agrees to notify CUSTOMER of any breach to the integrity of the data affecting the quality or the safety of any PRODUCT batches already shipped to CUSTOMER, as soon as possible, but not to exceed two (2) business days after becoming aware of the event.		**X**
7	**Specifications**		
7.01	Setting standard specifications for PRODUCT and intermediates		**X**
7.02	Mutually agree upon specification for PRODUCT, which may include customer-specific items	**X**	**X**
7.03	Optional (if not managed in a separate document): Specifications for PRODUCT are detailed in Appendix **X**.		
7.04	***For exclusive PRODUCT:*** Specifications for PRODUCT, intermediates, key raw materials and packaging components, as applicable, are provided by CUSTOMER as detailed in Appendix **X**.	**X**	
8	**Laboratory Controls**		
8.01	Sampling and testing of intermediates and final PRODUCT		X
8.02	SUPPLIER shall provide to CUSTOMER any in-house methods, including validation reports, used for testing according to the agreed specifications (where there are no compendial methods).		**X**

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	Responsibilities	C	S
8.03	Compendial analytical methods must be verified and all others must be validated prior to their use for release of commercial PRODUCT batches.		**X**
8.04	SUPPLIER shall use adequately qualified or certified reference standards		**X**
8.05	All reference standards should be stored in accordance with the suppliers recommended storage conditions and used within their given expiry or retest date.		**X**
8.06	Optional: SUPPLIER shall provide to CUSTOMER reasonable quantities of any non-compendial, commercially not available reference standards necessary to perform the tests included in the PRODUCT specification.		**X**
	Notes *9.1: a definition of "reasonable" might be given here.* *9.2: in case of exclusive PRODUCT the CUSTOMER may be responsible for provision of reference standards; in this case 8.06 needs to be adjusted accordingly.*		
8.07	SUPPLIER will store PRODUCT retention samples, sufficient to perform at least two (2) full specification analyses (see Note 7.2), in containers that are equivalent to or more protective than the commercial packaging. Samples are to be retained for at least one (1) year after the expiry or retest date of the batch assigned by SUPPLIER or for three (3) years after distribution, whichever is the longer.		**X**
	Note 9.3: "specification analysis" means "analysis according to the agreed specification" that may be identical with "compendial analysis" (if specification is equivalent to current pharmacopoeial monograph), or different in case there is no pharmacopoeial monograph, or if the agreed specification exceeds the monograph.		
8.08	***For exclusive PRODUCT:*** Optional: SUPPLIER shall inform CUSTOMER prior to destruction of reserve samples of PRODUCT and transfer such samples to CUSTOMER, if requested by CUSTOMER.		**X**
9	**Product Release**		
9.01	Release of PRODUCT batches for delivery to CUSTOMER.		**X**
	Note 24.1: For exclusive PRODUCT, SUPPLIER may, alternatively, provide a pre-shipment sample to CUSTOMER. CUSTOMER will test that sample, and if OK, will give its approval for shipment to SUPPLIER. To be added here, as applicable.		
9.02	Optional: SUPPLIER will not ship any PRODUCT to CUSTOMER until the PRODUCT is released, unless prior written approval has been received from CUSTOMER to perform such a shipment under quarantine.	**X**	**X**
9.03	***For exclusive PRODUCT*:** Optional: CUSTOMER delegates, in its sole discretion, the final release authority for PRODUCT to SUPPLIER. CUSTOMER reserves the right to withdraw the delegated final release authority from SUPPLIER at any time.	**X**	
10	**Stability**		
10.01	SUPPLIER has assigned retest dates (or expiry dates, where applicable), storage and shipping conditions, based upon stability studies.		**X**
10.02	SUPPLIER is responsible for performing on-going stability studies for the PRODUCT. At least one batch per year should be tested to ICH requirements (a batch representing routine production; long-term storage conditions only).		**X**
	Note 10.1: in case the PRODUCT is not manufactured in a certain year the above requirement is not applicable.		

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	Responsibilities	C	S
10.03	SUPPLIER is responsible for performing appropriate stability studies on the PRODUCT arising from process changes.		**X**
	Note 10.2: responsibility for performing stability studies arises from what is defined in the Supply Agreement. In case Stability Studies are performed by CUSTOMER, items 10.02 and 10.03 above need to be re-written accordingly.		
10.04	SUPPLIER will provide stability data to CUSTOMER upon reasonable request (e.g., if required according to the applied registration procedure).		**X**
	Note 10.3: results of the on-going stability program are not routinely provided to customers.		
10.05	SUPPLIER will inform CUSTOMER if there are any adverse trends in the stability studies that could impact on current retest date/period.		**X**
10.06	***For exclusive PRODUCT:*** Optional: CUSTOMER is responsible for approving stability protocols, methods and specification.	**X**	
11	**Certificate of Analysis / Conformance (optional)**		
11.01	A Certificate of Analysis and a Certificate of Conformance (optional) are required for each batch of PRODUCT shipped to CUSTOMER.		**X**
11.02	The Certificates of Analysis and Conformance (optional) shall be dated and signed by a responsible person of the SUPPLIER's Quality Unit, or it may be produced by a computer system, which provides a degree of control equivalent to that given by a signature.		**X**
11.03	The Certificate of Analysis states that the batch is suitable for release, and it must include – as a minimum – ❑ SUPPLIER name and address, incl. telephone number ❑ Name and address of original manufacturer, if SUPPLIER is not the original manufacturer ❑ PRODUCT name and grade (if applicable), ❑ SUPPLIER batch/lot number, ❑ Reference to the agreed specification, ❑ Test parameters and corresponding specification requirements, ❑ Test results (numerical, where applicable) for each chemical, physical or microbiological test performed, ❑ Date of release and expiration or retest date of the PRODUCT		**X**
	Note 11.1: the date of manufacture is considered as optional		
11.04	Optional: The Certificate of Conformance states that the subject lot was produced in accordance to the applicable DMF, CEP or pharmacopoeial monograph(s), and in compliance with all applicable GMP requirements. Certificate of Analysis and Certificate of Conformance may be issued as separate documents or combined to a single document, as appropriate.		**X**
	Note 11.2: the Certificate of Analysis may be attached as an appendix; in any case it should match the PRODUCT specification		

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	Responsibilities	C	S
12	**Certificates, Statements and Declarations**		
	Note 12.1: the items listed below constitute the most frequently requested ones. Other statements, which are applicable to APIs and either required by regulations or related to requirements to which the customer must comply as well, may be added as appropriate (also see "CEFIC/APIC Position on statements requested by API customers")		
12.00	SUPPLIER shall provide the following certificates and statements at the approval of this Quality Agreement and any time these certificates are renewed:		**X**
12.01	GMP certificate(s): Where not publicly accessible, SUPPLIER shall provide CUSTOMER with copies of the current GMP certificates or GMP licenses, pertaining to the manufacture of PRODUCT, issued by European or other local/national health authorities.		**X**
12.02	BSE/TSE*: SUPPLIER shall provide to CUSTOMER a BSE/TSE certificate for PRODUCT in accordance with the EMEA Note for Guidance EMEA/410/01 (current revision). The certificate shall indicate if PRODUCT is of human or animal origin, and if materials of human or animal origin are used during the manufacturing process of PRODUCT. An updated BSE/TSE certificate must be issued after any change to the manufacturing process, which involves new raw materials, or for raw materials that have been sourced from a different supplier.		**X**
12.03	Residual solvents*: SUPPLIER shall provide to CUSTOMER a residual solvents statement for PRODUCT in accordance with the ICH Q3C guideline. An updated statement must be issued after changes to the manufacture of PRODUCT, if applicable.		**X**
12.04	Elemental impurities*: SUPPLIER shall provide to CUSTOMER a statement on metal residues for PRODUCT in accordance with the ICH Q3D Guidelines on elemental impurities and other applicable regulations. An updated statement must be issued after changes to the manufacture of PRODUCT, if applicable.		**X**
	*) If the CEP contains the required information on BSE/TSE, residual solvents or metal catalyst/reagent residues, then the CEP itself may be used instead of separate supplier declarations.		
	Note 12.2: if the manufacturing site is located in a country outside the EU and not included on the "EU list of equivalent countries" (see: http://ec.europa.eu/health/human-use/quality/index_en.htm), the following section must be included in the quality agreement.		
12.05	Importation into the EU: SUPPLIER shall ensure that a valid 'written confirmation' according to EU Directive 2011/62/EU, related to PRODUCT and signed by the competent local authority is available. SUPPLIER shall ensure that a copy of this 'written confirmation' will accompany every shipment of PRODUCT into the EU. SUPPLIER shall have a system in place to renew the 'written confirmation' with the competent local authority before expiry. SUPPLIER shall inform CUSTOMER immediately in case the "written confirmation' is withdrawn by competent local authority or the renewal is not completed before expiration.		**X**

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	Responsibilities	C	S
13	**Product Quality Review and Quality Metrics**		
13.01	SUPPLIER shall allow CUSTOMER to review the annual Product Quality Review (PQR) for the PRODUCT during an on-site audit. In case the PQR contains any proprietary customer-specific information, the entire file may not be available for review or may be redacted, as appropriate.		**X**
13.02	***For exclusive PRODUCT:*** The PQR for the PRODUCT should address, besides the requirements of ICH Q7, any additional requirements mutually agreed between the parties.		**X**
	Note 13.1: a reference to an appendix specifying such additional requirements might be included, if applicable. Since the PQR as to ICH Q7 is usually applicable to commercial products, the parties should define how to handle in case of development products.		
13.03	***For exclusive PRODUCT:*** SUPPLIER will provide CUSTOMER with copies of the relevant information of its PQR of the previous annual period.		**X**
14	**Retention of Records/Documentation**		
14.01	SUPPLIER will store the original master batch records, the executed batch records, and all other original documentation that is related to the manufacture of substance and that is required to be maintained under GMP, protected from destruction and unauthorised access, for at least one (1) year after the expiry or retest date of the batch assigned by SUPPLIER or for three (3) years after distribution, whichever is the longer.		**X**
14.02	SUPPLIER will make the original records related to the manufacture of PRODUCT available for CUSTOMER during an on-site audit.		**X**
14.03	Validation documents should be archived for as long as PRODUCT is supplied or for 7 years after the version became obsolete.		**X**
	Note 14.2: a period of 7 years is recommended by the APIC "How to do" Document on the ICH Q7 guideline. A 10 years period is also often used		
14.04	***For exclusive PRODUCT:*** Upon CUSTOMER request, SUPPLIER will promptly make copies of the original batch production and control records available for CUSTOMER.		**X**
14.05	***For exclusive PRODUCT:*** SUPPLIER will offer CUSTOMER the option to take over the manufacturing and validation documents before destruction after **X** years		**X**
15	**Materials**		
15.01	Setting specifications for materials (incl. API starting materials, raw materials, process aids, and packaging materials, as applicable).		**X**
15.02	Purchasing materials according to specifications		**X**
15.03	Sampling and inspecting or testing of incoming materials, as appropriate. Materials supplied by qualified vendors can be subject to reduced testing but a minimum ID testing (or visual examination of containers, labels and documentation in case of hazardous or highly toxic raw materials) needs to be performed for each delivery and each lot.		**X**
15.04	Qualifying and monitoring material suppliers (with the exception of materials supplied by CUSTOMER).		**X**
15.05	SUPPLIER shall ensure that its material suppliers ship their goods on compliant pallets; i.e. in case wooden pallets are used, these should be marked as Heat Treated (HT). Any material that is received on a wooden pallet that does not meet these requirements shall be transferred to a compliant pallet.		**X**

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	Responsibilities	C	S
	For exclusive PRODUCT (5.06 to 5.11):		
15.06	Setting specifications for materials supplied by CUSTOMER or purchased by SUPPLIER according to CUSTOMER instructions. A list with those materials should be provided (can be as an annex)	**X**	
15.07	The materials purchased by SUPPLIER must meet the specifications filed by CUSTOMER.		**X**
15.08	Optional: CUSTOMER shall supply SUPPLIER with enough amount of intermediate to manufacture the quantities of batches ordered. CUSTOMER ensures that any intermediate supplied to SUPPLIER shall comply with the defined specifications. A Certificate of Analysis shall be submitted by CUSTOMER to SUPPLIER and shall accompany each shipment. The specification in force for the intermediate is attached as Appendix X.	**X**	
15.09	Optional: CUSTOMER shall be responsible for the maintenance and storage of appropriate retain samples of any material supplied to SUPPLIER.	**X**	
15.09	***Alternative text:*** Optional: SUPPLIER shall be responsible for the maintenance and storage of appropriate retain samples of any material supplied by CUSTOMER.		**X**
15.10	Optional: If SUPPLIER believes that any shipment of intermediate does not meet specification he will notify it to CUSTOMER in writing, including a detailed explanation of the non-conformity.		**X**
15.11	Optional: CUSTOMER shall investigate such alleged non-conformity and, if agrees, such intermediate is non-conformance and CUSTOMER will replace the material or the SUBSTANCE(s) will be manufactured at the sole risk of CUSTOMER. If CUSTOMER disagrees it will notify it to SUPPLIER in writing. Manufacturing of the PRODUCT will be at the sole risk of CUSTOMER. SUPPLIER shall not be responsible of intermediate's defects or not meeting specifications.	**X**	
	Note 15.1: for exclusive PRODUCT, if necessary and agreed by the parties, responsibilities with respect to purchasing, manufacturing, and testing of materials and intermediates before the API SMs may be added here.		
16	**Manufacturing (incl. Qualification / Validation)**		
16.01	Qualifying of equipment, utilities and facilities		**X**
16.02	Validating the manufacturing process, cleaning procedures, analytical methods, and computerised systems		**X**
16.03	SUPPLIER shall allow CUSTOMER to review qualification and validation documentation for the PRODUCT during an on-site audit.		**X**
16.04	Analytical methods validation should be concluded prior to the release of the Process Validation batches.		**X**
	Note 16.1: qualification and validation activities according ICH Q7, chapter 12; not necessary to give more details in the agreement.		
16.05	SUPPLIER shall have appropriate control procedures in place to ensure that only authorised personnel has access to SUPPLIER's manufacturing facilities.		**X**
	For exclusive PRODUCT (16.06 to 16.10):		
16.06	On request, CUSTOMER will get copies or summaries of the validation reports.		**X**

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	Responsibilities	C	S
16.07	Prepare the Master Batch Record for the PRODUCT, based on CUSTOMER's instructions, as applicable, and manufacture PRODUCT accordingly.		X
16.08	Review and approve the Master Batch Record prior to manufacture of commercial PRODUCT batches.	X	X
16.09	Optional: Validation of analytical methods (product specific) and process validation: Approval of protocols and reports may be shared by CUSTOMER and SUPPLIER	X	X
	Note 16.2: regarding clause 16.08 and in case optional clause 16.09 is used, the respective responsibilities of both parties should be clearly defined.		
16.10	Optional: Share with SUPPLIER information on toxicity of PRODUCT and raw materials, process aids and intermediates, if available	X	
	Note 16.3: for exclusive PRODUCT, more stringent acceptance criteria for cleaning may be agreed between both parties if requested by CUSTOMER. Such special agreements should be included here.		
17	**Reprocessing / Reworking**		
17.01	Reprocessing of a PRODUCT batch is permissible if the reprocessing complies with the current regulatory dossier; the reason for the reprocessing has to be investigated and documented, respectively.		X
17.02	For any lots undergoing a reprocessing, SUPPLIER should consider the need to put the respective batch(es) on stability.		X
17.03	SUPPLIER has demonstrated that the reprocessed batch is of at least equivalent quality as a normal batch.		X
	Note 17.1: If ICH Q7 as well as the registered procedures are followed there is actually no justified reason to refuse the delivery of reprocessed batches of PRODUCT.		
17.04	***For exclusive PRODUCT:*** Any reprocessed batches and the reasons for the reprocessing shall be reported to CUSTOMER.		X
17.05	***For exclusive PRODUCT:*** Optional: In case reprocessing is deemed necessary, SUPPLIER shall obtain prior agreement from CUSTOMER.		X
17.06	Reworking must be performed, if at all, according to the PRODUCT registration documents, if it is part of the dossier, or according to ICH Q7, chapter 14.3. CUSTOMER should be informed of such batches/lots.		X
	Note 17.2: on agreement reworking might be prohibited; if permitted, additional stability tests and/or analytical testing of reworked batches may be required		
18	**Highly Active Pharmaceutical Ingredients (HAPIs)**		
18.01	SUPPLIER shall not conduct production and handling of highly sensitizing materials (such as penicillins or cephalosporins) in the equipment being used for the PRODUCT. Production of such materials in the same building being used for the PRODUCT is permitted only if performed in a closed and dedicated system.		X
18.02	In case material of an infectious nature or high pharmacological activity or toxicity (e.g., certain steroids or cytotoxic anti-cancer agents) is manufactured by the SUPPLIER in the same facilities as used for PRODUCT, validated inactivation and/or cleaning procedures should be in place, based upon a toxicological evaluation for the establishment of threshold values in relation to the products manufactured.		X
18.03	SUPPLIER shall inform CUSTOMER prior to introduction of an HAPI in the same facilities where the PRODUCT is manufactured, if no HAPIs were produced before.		X

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	Responsibilities	C	S
18.04	***For exclusive PRODUCT:*** Optional: In case SUPPLIER intends to conduct production of any such product in the same equipment used for the PRODUCT, it shall provide CUSTOMER with the necessary information to allow CUSTOMER a proper risk assessment. CUSTOMER will then approve or reject SUPPLIER's request on a scientific basis.		**X**
19	**Sub-contracting**		
19.01	SUPPLIER will use its established GMP systems for evaluation, qualification, approval and maintenance/monitoring of all sub-contracted services with a GMP impact on PRODUCT manufactured.		**X**
19.02	SUPPLIER shall notify CUSTOMER of any change to existing or introduction of new sub-contractor used for any GMP-relevant service if the regulatory filings of the PRODUCT are concerned.		**X**
19.03	SUPPLIER shall remain fully responsible for the quality of the materials or services provided by sub-contractors and for all commitments as agreed upon with this Quality Agreement.		**X**
19.04	SUPPLIER will allow CUSTOMER access to audit reports of its subcontractors during an audit (see Appendix **X** for listing of qualified subcontractors).		**X**
19.05	***For exclusive PRODUCT:*** SUPPLIER may not subcontract any of its obligations under this Quality Agreement unless CUSTOMER provides prior written approval to SUPPLIER for such subcontracting. Before CUSTOMER grants any such written approval, CUSTOMER may require that SUPPLIER enters into a written agreement with the third-party ("Third Party Agreement"). This Third-Party Agreement shall define the respective quality responsibilities of SUPPLIER and the third-party and shall provide for confidentiality and non-disclosure of all CUSTOMER confidential information requiring at least the same degree of protection for CUSTOMER's confidential information as the obligations of confidentiality and non-disclosure that exists between SUPPLIER and CUSTOMER.		**X**
19.06	***For exclusive PRODUCT:*** SUPPLIER shall ensure that CUSTOMER will be permitted the right of access to subcontractors, as if it were a SUPPLIER site, to carry out audits and other assessments and be accompanied by the SUPPLIER's representatives (see Appendix X for listing of qualified subcontractors). Contact of the subcontractor shall always go through the SUPPLIER, and a SUPPLIER representative is present during any CUSTOMER audit at SUPPLIER's subcontractor. Subcontractors cannot be changed without CUSTOMER's prior written approval.		**X**
	Note 19.1: although "distribution" is part of "manufacture" as to the definition given in the ICH Q7 guideline it is understood that the use of contractors for transportation (haulers) is not in the scope of this section		
20	**Packaging**		
20.01	In addition to the requirements in ICH Q7 the following shall apply to the packaging of PRODUCT: The specifications for packaging materials including tamper evident seals must be in accordance with the regulatory documentation related to PRODUCT.		**X**
20.01	***Alternative text for exclusive PRODUCT:*** SUPPLIER shall use packaging materials including tamper evident seals, which are in accordance with the specifications provided by the CUSTOMER		**X**
20.02	SUPPLIER shall apply suitable traceability measures to primary packaging materials such that the packaging material manufacturer's batch can be traced from the batch of PRODUCT supplied.		**X**

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	Responsibilities	C	S
20.03	Optional: SUPPLIER shall package the PRODUCT using the components, closures and tamper evident seals as specified in Appendix **X**.		**X**
	Note 21.1: the list in Appendix X may include both primary packaging materials and secondary ones, e.g. pallets, wrapping etc. There may be the need to define and explain any coding on the seals		
	< List other security measures here, as applicable. >		
	Note 21.2: the following paragraph is only applicable in very specific cases		
20.04	Optional: When primary packaging material is returned from CUSTOMER to SUPPLIER for reuse, SUPPLIER will validate the cleaning procedure(s) used to clean the packaging material.		**X**
21	**Labelling**		
21.01	Labelling operations, including label printing and label reconciliation, should be done in a manner that prevents mislabelling and mix-ups.		**X**
21.02	Applicable regulatory requirements should be considered in order to permit shipments without delays or other issues (e.g. at customs).		**X**
	Notes: *21.1: the shipping label may include additional information (e.g., CUSTOMER material code); details may be defined in the Supply Agreement;* *21.2: labelling should be described in sufficient detail if done on behalf of the CUSTOMER;* *21.3: an example of the label may be provided in an appendix to the Quality Agreement.*		
21.03	Optional: SUPPLIER shall indicate the retest date on the PRODUCT label.		**X**
21.04	***For exclusive PRODUCT:*** Optional: SUPPLIER shall use the following batch/lot number format <xxyyzz> where <xx> means <…> and <yy> …..		**X**
22	**Storage and distribution (incl. Supply Chain Traceability)**		
	Notes: *22.1: Storage: special storage requirements for the PRODUCT should be clear.* *22.2: Distribution: either in the Supply Agreement or in the Quality Agreement the responsibilities for the whole supply chain should be defined; reference to GDP (EC Guidelines on principles of Good Distribution Practice of active substances for medicinal products for human use, WHO) is recommended. The following text is written for a case where the SUPPLIER is responsible for the transportation from the manufacturing site to the CUSTOMER's receiving site (and needs to be changed, if responsibilities are different).*		
22.01	SUPPLIER shall make commercially reasonable efforts to exclude, during packaging, storage, and shipping of PRODUCT, the possibility of deterioration, contamination, or mix-ups with any other material.		**X**

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	Responsibilities	C	S
22.02	SUPPLIER shall comply with the following requirements in relation to distribution of the PRODUCT: ❑ Distribution - until agreed transition point - in accordance with the conditions specified by the manufacturer and in a manner that does not adversely affect their quality (ref. EU GDP 6.14.) ❑ Ability to recall the PRODUCT from distribution network ❑ Quarantine PRODUCT with questionable quality ❑ Utilise tamper evident seals on all packaging ❑ All outbound shipments on wooden pallets must be on pallets that are marked as Heat Treated (HT)		**X**
22.03	SUPPLIER will qualify hauliers and shipping agents used to transport the PRODUCT.		**X**
22.04	Where storage or transportation is contracted out, SUPPLIER or CUSTOMER (as to respective responsibilities), should ensure that the external service provider knows and follows the appropriate storage and transport conditions. There must be a written contract, which clearly establishes the duties of each party, and the contract acceptor should not subcontract any of the work entrusted to him under the contract without the contract giver's written approval.	**X**	**X**
22.05	SUPPLIER will provide an up-to-date MSDS to CUSTOMER with each shipment or at least on an annual basis.		**X**
22.05	***Alternative text for exclusive PRODUCT:*** CUSTOMER will provide an up-to-date MSDS to SUPPLIER before the first production and after each change to the MSDS.	**X**	
22.06	SUPPLIER shall comply with any applicable legal requirements in relation to the transportation of PRODUCT.		**X**
22.07	SUPPLIER will keep supply chain traceability records available and retained.		**X**
22.08	Upon reasonable request, SUPPLIER will provide information to CUSTOMER on the supply chain for PRODUCT between SUPPLIER's manufacturing site(s) and CUSTOMER's receiving site(s), including any transportation services or interim storage locations.		**X**
	Note 22.3: For complex supply chains involving distributors or agents the use of a separate "Supply Chain Traceability document" or an Appendix to this agreement may be preferable.		
22.09	Providing documentation to ensure supply chain traceability for each delivery of PRODUCT. This includes: ❑ reference to purchase order and date of supply ❑ name of PRODUCT, manufacturer's batch number and quantity supplied ❑ name and address of SUPPLIER, or of the shipping agent and/or the consignee ❑ bills of lading, transportation and distribution records ❑ a certificate of analysis for each batch in the delivery		**X**
22.10	SUPPLIER will inform CUSTOMER on changes to the identified supply chain according to the established change control procedures.		**X**
22.11	If a delivered PRODUCT needs to be returned, SUPPLIER and CUSTOMER will agree on responsibilities and conditions prior to the return shipment.	**X**	**X**
23	**Deviations / OOS (incl. stability)**		
23.01	SUPPLIER shall document all deviations and investigate OOS results and critical deviations.		**X**
23.02	In case of serious quality incidents observed only after shipment of batches of PRODUCT to CUSTOMER, SUPPLIER shall promptly and appropriately notify CUSTOMER thereof.		**X**

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	Responsibilities	C	S
	Note 23.1: information on OOS results in stability is only necessary if there is an impact on the retest period or the storage condition or the packaging material (such information would be given through a change control procedure anyway; see also section 3).		
	For exclusive PRODUCT (23.03 to 23.07):		
23.03	Promptly inform of any deviation that might affect the quality of a batch of material and provide supporting documentation of the investigation. Optional: Batch disposition must not be performed until approval of the deviation has been received from CUSTOMER.		**X**
23.04	Any advice by CUSTOMER on the handling of the deviation or the affected material (e.g., on root cause analysis or corrective actions) shall be given promptly so that further production is not unreasonably hindered.	**X**	
23.05	Provide copies of investigation reports regarding quality incidents (critical deviations, OOS results, or similar), as applicable.		**X**
23.06	CUSTOMER may participate in any full-scale investigation concerning OOS results.	**X**	
23.07	Optional: For all confirmed OOS stability test results that indicate that PRODUCT has failed to remain within specifications, SUPPLIER will notify CUSTOMER promptly and provide the stability data.		**X**
24	**Complaints**		
24.01	CUSTOMER shall inspect the goods upon delivery and promptly notify any defect or shortage to SUPPLIER	**X**	
24.02	All complaints related to the PRODUCT, regardless of source (e.g., consumers, doctors, pharmacists, sales representatives) will be communicated to SUPPLIER in writing.	**X**	
24.03	SUPPLIER will respond to complaints by the CUSTOMER in a timely manner and according to formally agreed procedures.		**X**
	Note 24.1: it is good practice to give an initial response (at least an acknowledgement of receipt) within max. 7 days from receipt of the complaint		
24.04	SUPPLIER will inform CUSTOMER in a timely manner and in writing on the conclusions driven by the investigation performed and the corrective/preventive actions defined.		**X**
24.05	In case the investigation could not be finalized within 30 calendar days, SUPPLIER will provide an interim report to CUSTOMER.		**X**
	Note 24.2: target timelines for both initial and concluding responses may be added; for the concluding response a period of 30 calendar days (in practice equivalent to "20 business days") is quite common.		
24.06	CUSTOMER will make relevant information and samples of the affected PRODUCT batch(es)/lot(s) available in a timely manner to assist in the investigation of SUPPLIER (as appropriate).	**X**	
24.07	SUPPLIER will inform CUSTOMER if any received complaint could also have a serious impact on batches supplied to CUSTOMER (i.e., the complaint constitutes a potential risk to patients' health or safety).		**X**
25	**Recall**		
25.01	Immediately after SUPPLIER has become aware of it, SUPPLIER will inform CUSTOMER of any serious quality issue that may result in a recall of supplied PRODUCT or finished drug product made thereof.		**X**

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	Responsibilities	C	S
25.02	SUPPLIER and CUSTOMER consult and decide on roles and responsibilities regarding co-ordination of the investigation and decisions as well as notification of any regulatory authorities.	**X**	**X**
25.03	Make available relevant information relating to recall or field alert activities within two (2) business days of the request to assist in investigations relating to product recalls.	**X**[1)]	**X**[2)]
25.04	CUSTOMER is responsible for the final decision and the coordination of any recalls or field alert activities related to finished drug product, with prior notice to SUPPLIER, whereas SUPPLIER shall not be prohibited hereunder from taking any action that is deemed necessary based on science and risk or that is required to be taken by applicable law.	**X**[1)]	**X**[2)]
25.05	Notifying regulatory authorities, external customers, consumers or other relevant organizations or parties	**X**[1)]	**X**[2)]
25.06	Storing or disposing affected/returned product	**X**[1)]	**X**[2)]
25.07	CUSTOMER shall notify SUPPLIER of any drug product recalls relating to the PRODUCT.	**X**	
25.08	***For exclusive PRODUCT:*** SUPPLIER will not initiate any notifications to health authorities concerning a (potential) non-conformance without the prior agreement of CUSTOMER.		**X**
	[1)] Responsibility regarding drug product made from PRODUCT [2)] Responsibility regarding PRODUCT; ***for exclusive PRODUCT*** this would also be the responsibility of CUSTOMER		

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IV. Signatories

Agreement of the Parties to perform the activities and fulfil the responsibilities detailed in this Quality Agreement is indicated by the representatives' approval below:

< CUSTOMER name >	**< SUPPLIER name >**
Name	Name
Title / Quality Function	Title / Quality Function
Date and Signature	Date and Signature

< CUSTOMER name >	**< SUPPLIER name >**
Name	Name
Title / Function	Title / Function
Date and Signature	Date and Signature

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V. Contacts

Note: List the relevant contact persons (name, position, phone number, e-mail) from each party that will be responsible for communications related to this Quality Agreement. This information can alternatively be provided in an appendix.

< CUSTOMER name >	**< SUPPLIER name >**
Name	Name
Title / Quality Function	Title / Quality Function
Phone	Phone
E-mail	E-mail
Name	Name
Title / Function	Title / Function
Phone	Phone
E-mail	E-mail
Name	Name
Title / Function	Title / Function
Phone	Phone
E-mail	E-mail

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VI. List of Appendices

Examples of documents typically attached to a Quality Agreement (list not exhaustive): definition of PRODUCT, PRODUCT specification(s), example CoA(s), list of sub-contractors, example label, information on storage/transport conditions, statements and description of the packaging.

VII. History / Change Log

Version Number	Prepared By	Approval / Signature date	Reason for Change

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