**Manufacturer’s Quality Agreement[[1]](#footnote-1)**

by and between

|  |  |
| --- | --- |
| **Supplier Name** |  |
|  |  |
| **Address:** |  |

and

|  |  |
| --- | --- |
| **Client Name:** |  |
|  |  |
| **Address:** |  |

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# Parties to the Agreement

*Supplier’s Name* (“Supplier”) and *Client’s Name* (“Client”) wish to define the individual responsibilities of the Supplier and Client (hereafter “Parties”) as to the quality aspects of manufacturing and release of Product as defined in [**Appendix 1**](#_APPENDIX_1:_) to ensure compliance with the approved Product application and/or Client requirements, and current good manufacturing practices as defined herein.

In order to do so, this Quality Agreement (“Quality Agreement”) takes the form, in part, of a detailed listing of activities associated with manufacture, analysis, storage, and distribution of Product. Unless otherwise indicated, responsibility for each activity is assigned to either Client, Supplier, or is assigned to both Supplier and Client.

In consideration of the Parties’ agreement to perform the activities provided in this Quality Agreement and for other valuable consideration the receipt and sufficiency of which is hereby acknowledged and included in this Quality Agreement, and intending to be legally bound, Supplier and Client agree as provided in this Quality Agreement as follows:

|  |  |  |
| --- | --- | --- |
|  |  |  |
| **Signature** |  | **Signature** |
|  |  |  |
|  |  |  |
| **Name** |  | **Name** |
|  |  |  |
|  |  |  |
| **Title** |  | **Title** |
|  |  |  |
|  |  |  |
| **Date** |  | **Date** |

# Manufacturer’s Quality Agreement Template[[2]](#footnote-2)

## **Effective Date**

The Effective Date of this Quality Agreement shall be the date of last signature (the “Effective Date”) or a specified date of mutual agreement included in this Agreement

## **Scope**

This Quality Agreement outlines the responsibilities of the Parties with respect to the quality assurance of the Product manufactured and/or supplied by Supplier for Client.

## **Other Agreements**

This Quality Agreement is in addition to all other agreements between the parties, if any, (the “Supply Agreement”) regarding the subject matter hereof. If there are any direct conflicts between the terms of this Quality Agreement and the Supply Agreement, the following will prevail:

|  |  |
| --- | --- |
|  | Quality Agreement |
|  |  |
|  | Supply Agreement |

## **Definitions and Abbreviations**

**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.

**Batch Number (or Lot Number)** - A unique combination of numbers, letters, and/or symbols that identifies a batch (or lot) and from which the production and distribution history can be determined.

**Business Day** – Any day Monday through Friday except any official national or regional holidays or shut down of the plant.

**CEP** – A certificate issued by the European Directorate for the Quality of Medicines and Healthcare which demonstrates that the Product complies with the requirements of the European Pharmacopoeia monograph. Also known as “CoS” = Certificate of Suitability.

**Certificate of Analysis** – A document identified as such, provided by the Supplier signed by the person(s) within the Quality Unit who is accountable for the release of product, 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 pharmacopeial monographs, as applicable. This is also known as a Certificate of Compliance. The certification may be issued as a separate document or combined with the Certificate of Analysis.

**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 Health 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.

**Drug Product** – The dosage form in the final immediate packaging indented for marketing.

**Drug Substance** – An Active Pharmaceutical Ingredient (API). See above.

**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.

**HAPI - Highly Active Pharmaceutical Ingredient.**  HAPIs are material classified as 4 by the Safebridge® methodology (John P. Farris, J.P; Ader, A.W.; and Ku, R.H.: *History, Implementation and Evolution of the Pharmaceutical Hazard Categorization and Control Systems*, Chemistry Today, Vol. 24, **March/April 2006**.) or equivalent.

**Health 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), European Directorate for the Quality of Medicines & Healthcare (EDQM), or the World Health Organization (WHO), that is charged with protecting Public Health through the management of medicines, and medical equipment & devices.

**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 authorization 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 authorization, or applicable law.

**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) the Parties. It is intended to define, in a formalized manner, responsibilities relative to quality tasks to assure the 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.

**Reprocess** - Introducing an intermediate, API or Product, including one that does not conform to standards or specifications, back into the process and repeating a crystallization step or other appropriate chemical or physical manipulation steps (e.g. distillation, filtration, chromatography, and milling) that are part of the manufacturing process.

**Rework** - Subjecting an intermediate, API or Product that does not conform to standards or specifications to one or more processing steps that are different from the established manufacturing process to obtain an acceptable quality intermediate or API (*e.g.* recrystallizing with a different solvent).

**Significant Change –** Any change that could impact the identity, strength, safety, potency, stability, purity, or regulatory status of the Product.

**Significant 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 quality, stability, and/or physical characteristics of the Product.

**Specification -** A list of tests, references to analytical procedures, and appropriate acceptance criteria that are numerical limits, ranges, or other criteria for the test described. It establishes the set of criteria to which a material should conform to be considered acceptable for its intended use. Conformance to specification means that the material, when tested according to the listed analytical procedures, will meet the listed acceptance criteria.

**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 Product 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 Product. 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 the Product 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.

## **Amendments to Quality Agreement**

This Quality Agreement may be amended by the written consent of both parties.

The parties agree to amend terms of this Quality Agreement that must be amended in order that the Product continue to meet changing regulatory requirements of applicable regulatory agencies, as may exist from time to time.

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 Client for review and internal approval. The appropriate contact person at Supplier and Client is listed in [**Appendix 2**](#_APPENDIX_2:_) (Contacts and Responsibilities). These amendments may be tracked in [**Appendix 5**](#_APPENDIX_6:_Revisions): Revisions to the Executed Quality Agreement.

## **Term of Quality Agreement**

This Quality Agreement shall commence on the Effective Date and shall remain in effect for as long as Supplier provides Product to Client unless the Quality Agreement is terminated earlier in accordance with the terms of this Quality Agreement, or if a specified termination date is included in this agreement.

Either party may terminate this Quality Agreement upon thirty (30) days written notice to the other party.

## **Use of Third-Parties**

Supplier shall not allow a third-party to manufacture, package, label, inspect, test release or store Product unless Supplier has disclosed in writing to Client the Supplier’s use of a third-party and in what capacity to which the third-party is used ([**Appendix 3**](#_APPENDIX_3:_)). If Supplier employs a third-party to perform any or part of the manufacturing, packaging, labelling, inspection, testing, release, storing and/or handling of Product that is supplied to Client, Supplier shall assure that the third-party has been fully qualified via the Supplier’s third-party qualification process prior to performing such activity(ies). Supplier shall have entered into a written confidentiality agreement with any third-party providing for confidentiality of all Client information under obligations of confidentiality similar to and requiring the same protection or greater protection of confidential information as the obligations of confidentiality between Supplier and Client. Supplier shall, however, retain all obligations under this Agreement whether or not a third-party manufactures, packages, labels, inspects, tests, releases and/or handles Product. If a third-party is used by Supplier to manufacture, package, label, inspect, test, release and/or handle Products, Client may, upon request, review the list of such third-party(ies) during an on-site audit. Client agrees to treat such information as Confidential Information of Supplier and agrees not to contact any such parties regarding this Agreement without Supplier’s prior consent**.**

## **Survival Clause**

All legal and regulatory obligations contained herein that are required of either party or both parties by an applicable regulatory authority shall survive termination of this Quality Agreement.

## **Assignment**

Supplier shall not assign any or all of its rights or obligations under this Quality Agreement without Client’s prior written consent. Client’s consent shall not be required regarding a merger, a consolidation, or a sale of all or substantially all of Supplier’s assets or the subject matter of this Quality Agreement to another party (an “Assignment Transaction”). In the event of an Assignment Transaction, Supplier shall provide written notice to Client to the appropriate contact person indicated in [**Appendix 2**](#_APPENDIX_2:_) **(**Contacts and Responsibilities). Client shall have the right to assign any or all its rights or obligations under this Quality Agreement without the consent of Supplier. In the event of an assignment, the assigning party shall continue to be bound by all pre-existing obligations under this Quality Agreement including all obligations of confidentiality and non-disclosure.

## **Product Specifications**

Product specifications are listed in [**Appendix 4**](#_APPENDIX_4:_).

Changes to the agreed upon specifications must be mutually agreed upon and communicated in writing between the parties to this Quality Agreement, except for compendial changes which can be implemented without mutual agreement. Compendial changes must be implemented by the compendial implementation date.

## **Resolution of Quality Issues**

Quality related disagreements between Supplier and Client that are not resolved in the normal course of business shall be brought to the attention of the appropriate contact person for notices at the Supplier and Client, in writing, as listed in [**Appendix 2**](#_APPENDIX_2:_) (Contacts and Responsibilities). If both parties agree that a resolution of the disagreement is reasonably possible, then both Supplier and Client shall agree to work jointly to develop a strategy for such resolution. Supplier and Client further agree to record such resolution in writing.

## **Debarment**

Supplier warrants and represents that it is not debarred under the Generic Drug Enforcement Act of 1992, 21 U.S.C. 335[a] (the “Generic Drug Enforcement Act”), and that it has not been convicted of a crime for which it could be debarred under the Generic Drug Enforcement Act. Regarding the Product, the Supplier further warrants and represents, in that it shall not use in any capacity the services of any person debarred under the Generic Drug Enforcement Act, or convicted of a crime for which a person can be debarred under the Generic Drug Enforcement Act.

## **Choice of Law: Jurisdiction/Miscellaneous**

This Quality Agreement shall be construed and the relationship between the parties determined in accordance with the laws in the State of      , United States of America, without regard to the conflicts of law principals thereof. Any and all disputes between the parties arising out of or related to this Quality Agreement shall be heard in the state and federal courts located in the State of      , and the parties hereby consent and submit to the jurisdiction of such courts.

All appendices to this Quality Agreement are attached hereto and incorporated herein by reference. In this Quality Agreement, unless the contrary intention appears: (a) the words "including" and "include" mean "including, but not limited to";(b) the singular includes the plural and vice versa; (c) a reference to a person or entity (including Supplier or Client) includes a reference to the person's executors, administrators, successors, substitutes and assigns; and (d) headings are for reference only and do not form part of this contract.

## **Manufacturing and Testing Locations**

Product will be manufactured and tested at the following location:

Company Name:

Address:

Product will be stored at the following location (if different than above):

Company Name:

Address:

For activities sub-contracted, see [**APPENDIX 3**](#_APPENDIX_3:_): List of Qualified Subcontractors

## **Severability**

If any clause or provision of this Agreement is found by a court of competent jurisdiction to be illegal, invalid, or unenforceable under present or future laws effective during the term of this Agreement, then and in that event, it is the intention of the parties hereto that the remainder of this Agreement shall not be affected thereby, and it is also the intention of the parties to this Agreement that in lieu of each clause or provision that is illegal, invalid or unenforceable, there be added as a part of this Agreement a clause or provision as similar in terms to such illegal, invalid or unenforceable clause or provision as may be possible and be legal, valid and enforceable. The caption of each paragraph hereof is added as a matter of convenience only and shall be considered to be of no effect in the construction of any provision of this Agreement.

## **Quality Responsibilities Table**

| **§** | | **Responsibilities** | | **Not Applicable** | | | **Client** | **Supplier** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | **1.0 Compliance Requirements** | |  | | |  |  |
| **1.01** | | Implement procedures and/or documented training to meet obligations under this Agreement. | |  | | |  |  |
| **1.02** | | Follow applicable current Good Manufacturing Practices (cGMPs), including International Conference on Harmonization (ICH) Q7 Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients (API)), ICH Q9 Quality Risk Management, ICH Q10 Pharmaceutical Quality System and locally imposed requirements. | |  | | |  |  |
| **1.03** | | Manufacture, package, ship, store and test the Product and materials in an environment meeting the applicable GMP regulations, which is designed, constructed and maintained in a manner that a) permits the operation therein to be performed under clean, sanitary and orderly conditions; b) permits the effective cleaning of pertinent surfaces; and c) prevents the contamination of the Product and the addition of extraneous material to the Product. | |  | | |  |  |
| **1.04** | | Manufacture the Product in adherence to applicable regulatory submissions, such as a Drug Master File (DMF), Active Substance Master File (ASMF), or Certificate of Suitability (CEP), if applicable. | |  | | |  |  |
| **1.05** | | Operate in compliance with applicable environmental, occupational health and safety laws and regulations. | |  | | |  |  |
| **1.06** | | Maintain a quality unit that is independent of production that fulfils both quality assurance and quality control responsibilities. | |  | | |  |  |
| **1.07** | | Involve the quality unit in all quality related matters and have them review and approve all quality critical related documents. | |  | | |  |  |
| **1.08** | | As it relates to this Quality Agreement, notify the other party of name change, corporate reorganization, consolidation, merger or acquisition or sale of the party’s company. | |  | | |  |  |
| **1.09** | | Maintain internal GMP audit program. | |  | | |  |  |
|  | |  | |  | | |  |  |
|  | | **2.0 Right to Audit** | |  | | |  |  |
| **2.01** | | Client has the right to audit Supplier’s facilities and systems and review documents as they relate to the manufacture of Product. Such audits and document review shall be conducted by Client at a time, date and duration mutually agreeable to the Supplier and Client and subject to Client signature of a separate confidentiality agreement with the Supplier entity owning the production site. Audits are to be conducted within the normal business hours of operation of the auditee. | |  | | |  |  |
| **2.02** | | 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. | |  | | |  |  |
| **2.03** | | Client retains the right to conduct reasonable "for cause" audits. Specific goals/scope of the audit, proposed dates and names of the auditors will be agreed upon mutually by the Client and the Supplier. | |  | | |  |  |
| **2.04** | | Issue Supplier a confidential written audit report summarizing audit observations. | |  | | |  |  |
| **2.05** | | Issue responses to all observations documented in the issued audit report in writing to Client Quality Assurance within 30 days of receipt of the report. | |  | | |  |  |
|  | |  | |  | | |  |  |
|  | | **3.0 Regulatory Inspections and Exchanges** | |  | | |  |  |
| **3.01** | | Notify Client within five (5) Business Days of the receipt of a Health Authority inspection report, deficiency letter or written regulatory compliance observation, which contains any significant adverse findings that relate specifically to the Product or the facilities used to produce, test or warehouse the Product sold to Client. A significant adverse finding is herein defined as the following: conditions, practices, or processes that adversely affect or may potentially adversely affect Product or service quality and/or the rights, safety or well-being of subjects/patients and/or the quality and integrity of data, documentation, or other materials or information addressed in the inspection. | |  | | |  |  |
| **3.02** | | Upon written request of Client, provide copies of the inspection report, deficiency letter or written regulatory compliance observation that specifically relate to the Product or the facilities used to produce, test or warehouse the Product sold to Client. This shall be redacted to exclude Supplier or other Client's proprietary information. Alternatively, a summary of the applicable regulatory observations or deficiency questions should be provided. | |  | | |  |  |
|  | |  | |  | | |  |  |
|  | | **4.0 Regulatory Filings and Regulatory Status** | |  | | |  |  |
| **4.01** | | Responsible for submission, maintenance, approvals and updates/amendments to regulatory filings for Product (including API DMFs/ASMFs). Client will be notified as per Health Authority requirements. | |  | | |  |  |
| **4.02** | | Responsible for providing to the Health Authorities all requested documentation/data required for regulatory filings. | |  | | |  |  |
| **4.03** | | Client or Supplier shall notify the other regarding regulatory actions taken by the prevailing Health Authority concerning submissions, amendments, or updates to the Products’ dossier. | |  | | |  |  |
| **4.04** | | Responsible for submission and maintenance of Product registration, current site registration, and label registrations as required by Health Authorities. | |  | | |  |  |
| **4.05** | | Client shall provide Supplier with the following information regarding the use of the Product:   * Clinical phase of development of the drug product or drug substance that the Product is used in and any change regarding this status * Intended use of the drug product or drug substance in which that Product is used. This includes dosage form, administration route and maximum daily dose. * Health Authorities with which the drug product or drug substance is filed and if Product is included in the filing. | |  | | |  |  |
| **4.06** | | Notify Supplier if Supplier will be named in any Health Authority filings prior to such filings being made. | |  | | |  |  |
| **4.07** | | Coordinate the activities necessary to ensure readiness prior to Regulatory Agency Pre-Approval Inspection (PAI). | |  | | |  |  |
| **4.08** | | Provide Letter of Access/Authorization or an executed CEP for Client to permit reference to Supplier’s regulatory submissions in the registration of the Client’s drug product. | |  | | |  |  |
| **4.09** | | Supplier, under the provisions of an executed and in-force non-disclosure agreement, will provide Client current & reasonable information required for the Client’s regulatory dossier for finished drug products made using Supplier’s Product. Examples of such information include access to the CEP (including the appropriate stability data for the respective Product, if no retest date is defined in the CEP), or applicants’ part to the DMF/ASMF, or equivalent. | |  | | |  |  |
|  | |  | |  | | |  |  |
|  | | **5.0 Complaints** | |  | | |  |  |
| **5.01** | | Have written procedures in place to document, investigate, and respond to all quality related complaints and any necessary follow-up. | |  | | |  |  |
| **5.02** | | Inspect Product upon receipt and Promptly notify Supplier in writing of any defect or shortage. If requested by Supplier, provide sample of Product suspected of defect. | |  | | |  |  |
| **5.03** | | Respond to Client complaints in writing within thirty (30) calendar days. If Supplier investigation is not concluded in this timeframe then Supplier shall provide an interim report. | |  | | |  |  |
| **5.04** | | Supplier will inform the Client if any confirmed complaint received from another client could also have a serious impact on lots supplied to Client, that is, the complaint constitutes a potential risk to patients’ health or safety. | |  | | |  |  |
| **5.05** | | Assist in investigations as reasonably requested by Client for complaints associated with Product. | |  | | |  |  |
| **5.06** | | Retain complaint investigation Records and evaluate trends and severity. Implement corrective and preventive actions as necessary. | |  | | |  |  |
|  | |  | |  | | |  |  |
|  | | **6.0 Certificates, Statements, and Declarations** | | |  | | |  |  |
| **6.01** | | GMP certificate(s):  Upon written request, documentation of cGMP compliance shall be provided to the Client in the form of a cGMP Certificate or a Certificate of Pharmaceutical Product (CPP) covering the Product. Alternatively and under an executed and in-force non-disclosure agreement, a redacted Health Authority Inspection Report or a third party audit report may be provided. | | |  | | |  |  |
| **6.02** | | Declarations/Certification:  Upon written request, Supplier shall provide to Client each of the following checked statements for Product. An updated statement may be requested after changes to the manufacture of Product, if applicable.  Allergens (REGULATION (EU) No 1169/2011 Annex II)  BSE/TSE (EMEA/410/01)  Dioxin  Elemental Impurities (ICH Q3D)  Gluten  GMO  Melamine (Guidance for Industry: Pharmaceutical Components at Risk for Melamine Contamination (August 2009)”)  Latex  Residual Solvents (ICH Q3C)  Synthetic Origin  Other \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ | | |  | | |  |  |
|  | |  | | |  | | |  |  |
|  | |  | | |  | | |  |  |
|  | | **7.0 Validation/Qualification** | | |  | | |  |  |
| **7.01** | | Determine according to Product lifecycle and guidance documents when process validation is required. | | |  | | |  |  |
| **7.02** | | Have a written master validation/qualification plan for the facilities, equipment/instruments, utilities, manufacturing process, cleaning procedures, analytical procedures, in process control tests, and computerized systems as appropriate. | | |  | | |  |  |
| **7.03** | | Responsible for developing, preparing and maintaining validation documentation approved by the quality unit, including protocols, reports and associated documentation. | | |  | | |  |  |
| **7.04** | | Qualify as necessary all critical systems and equipment used for the manufacture and control of Product (Installation Qualification (IQ), Operational Qualification (OQ), and/or Performance Qualification (PQ)). This would include amendments to these associated documents when changes are made to the equipment or its operating parameters. | | |  | | |  |  |
| **7.05** | | Allow Client viewing of the validation documentation for the Product during an onsite audit. | | |  | | |  |  |
| **7.06** | | Validation documents should be archived for as long as Product is supplied or for 7 years after the version becomes obsolete. | | |  | | |  |  |
|  | |  | | |  | | |  |  |
|  | | **8.0 Documentation and Records** | | |  | | |  |  |
| **8.01** | | Have a controlled system to initiate, review, revise, approve, obsolete and archive all Good Manufacturing Practices documentation. At a minimum, all production, control, and distribution Records should be retained for at least one (1) year after the expiry date of the batch. For Product with a retest date, Records should be retained for at least three (3) years after the batch is completely distributed. | | |  | | |  |  |
| **8.02** | | Have written procedures for the review and approval of all batch documentation. | | |  | | |  |  |
| **8.03** | | Maintain a document control system for specifications and test methods, including: raw materials, Product labeling, packaging materials and other materials that would likely affect Product quality. | | |  | | |  |  |
| **8.04** | | Provide a complete Certificate of Analysis for the Product, containing "at minimum" the following information:   * Supplier Product number/code * Supplier lot/batch number * Name of Product * Name of the test * Specification limit * Expiration or retest date, if applicable * Test result (as a numerical value, unless designated Pass/Fail in the specification limit, statistical values can be used if data supports their use except for assays and impurity tests), including retest results if required * Quality Assurance approval and date. * Manufacturing Site (name and address)   Manufacturing Date | | |  | | |  |  |
| **8.05** | | Provide certification that the Product was manufactured in a cGMP compliant facility, and was tested in accordance with and meets specifications. This may be provided on the Certificate of Analysis itself, or a separate Certificate of Conformance. | | |  | | |  |  |
| **8.06** | | Where applicable, electronic signatures used on the Certificate of Analysis or other controlled documents should be authenticated and secure. | | |  | | |  |  |
|  | |  | | |  | | |  |  |
|  | | **9.0 Annual Product Reviews** | | |  | | |  |  |
| **9.01** | | Have procedures to conduct and document annual product reviews, if applicable. | | |  | | |  |  |
| **9.02** | | Allow Client viewing of the Annual Product Review (APR) for the Product during an on-site audit. | | |  | | |  |  |
|  | |  | | |  | | |  |  |
|  | | **10.0 Change Control** | | |  | | |  |  |
| **10.01** | | Have established written procedures for control of changes impacting the Product including manufacturing components or process, computer hardware/software, Product specifications, test methods, vendors, and subcontractors, if applicable. | | |  | | |  |  |
| **10.02** | | Notify Client of intent to make Significant Changes that could impact the identity, strength, safety, potency, stability, purity, or regulatory status prior to implementation of the change. | | |  | | |  |  |
| **10.03** | | Issue to Client a written evaluation of the Significant Change including change justification so that Client can determine the impact of use of Product in Client’s finished product. | | |  | | |  |  |
| **10.04** | | Have Significant Changes reviewed and approved by the Supplier’s quality unit. | | |  | | |  |  |
| **10.05** | | Jointly establish a strategy to secure Health Authority approvals for Significant Changes, as necessary, including if, how and when to notify the Health Authority, and when the change may be implemented for Product distributed to Client. | | |  | | |  |  |
|  | |  | | |  | | |  |  |
|  | | **11.0 Deviations** | | |  | | |  |  |
| **11.01** | | Have procedures for the identification, investigation, and reporting of deviations and Out-of-Specification (OOS) results that occur during the manufacture and testing of the Product. Ensure that any OOS and deviations are closed prior to release of the Product. | | |  | | |  |  |
| **11.02** | | Document and explain all deviations. Investigate OOS results and Critical Deviations. Extend the investigation to other lots that may have been associated with the failure as appropriate. Include preventive actions and track these to completion. | | |  | | |  |  |
| **11.03** | | Evaluate deviations to determine impact on validation/qualification studies. | | |  | | |  |  |
|  | |  | | |  | | |  |  |
|  | | **12.0 Reprocess & Rework** | | |  | | |  |  |
| **12.01** | | Have procedures for reprocessing, if applicable. Reprocessing steps should not be routinely run. | | |  | | |  |  |
| **12.02** | | Will not blend Out of Specification batches with other batches for the purpose of meeting specifications. | | |  | | |  |  |
| **12.03** | | Have procedures for reworking, if needed. Any rework procedure must be validated and be a part of the DMF. Reworking steps should not be routinely run. | | |  | | |  |  |
| **12.04** | | Notify Client prior to shipping a reworked performed outside of a previously filed rework processes. Any rework procedure must be validated and become part of the DMF. Rework validations may be executed concurrently. These rework procedures should not be routinely run. | | |  | | |  |  |
| **12.05** | | Will not introduce recovered materials and/or solvents into the process unless approved procedures and specifications are in place. | | |  | | |  |  |
|  | |  | | |  | | |  |  |
|  | | **13.0 Production and In Process Controls, Packaging and Labelling** | | |  | | |  |  |
| **13.01** | | Procure, test as required, and release raw materials and packaging and labeling materials used in manufacture of Product. | | |  | | |  |  |
| **13.02** | | Establish and document specifications for raw materials, Product labelling and packaging materials and other materials that would likely affect product quality. | | |  | | |  |  |
| **13.03** | | Maintain external risk-based GMP audit program for suppliers of raw materials and components, or other suitable qualification program. | | |  | | |  |  |
| **13.04** | | Prepare/develop master batch production Records in accordance with applicable cGMP requirements or guidelines, as applicable for lifecycle of product. | | |  | | |  |  |
| **13.05** | | Inspect, weigh and measure raw materials used for Product manufacturing and verify critical weighing by a second individual or validated automated system. | | |  | | |  |  |
| **13.06** | | Manufacture Product in a manner that prevents contamination by other materials including carryovers. | | |  | | |  |  |
| **13.07** | | Maintain suitable traceability measures to primary packaging materials. | | |  | | |  |  |
| **13.08** | | Provide product label to include: name and address of the manufacturer, identifying code, batch number, quantity of contents, storage and special transport conditions if applicable, the retest or expiry date and any special requirements. Revise label per change control as necessary. | | |  | | |  |  |
| **13.09** | | Review and approval of batch production Records by quality unit prior to batch release. | | |  | | |  |  |
| **13.10** | | Release Product by quality unit. | | |  | | |  |  |
|  | | **14.0 Storage, Distribution, and Good Distribution Practices** | | |  | | |  |  |
| **14.01** | | Maintain storage facilities appropriate for conditions specified on the Product label. Maintain Records of any critical storage conditions. | | |  | | |  |  |
| **14.02** | | Have systems for controlling quarantined, rejected or recalled materials. | | |  | | |  |  |
| **14.03** | | Provide SDS (Safety Data Sheet) or equivalent, with each shipment or at least on an annual basis. | | |  | | |  |  |
| **14.04** | | Notify Client in a Timely Manner if Supplier finds a quality issue post Supplier release/shipment. | | |  | | |  |  |
| ***Provisions 14.05 – 14.13 are written for a case where the Supplier is responsible for the transportation from the manufacturing site to the Client’s receiving site****.* | | | | | | | | | |
| **14.05** | | Supplier shall make commercially reasonable efforts to exclude, during shipping of Product, the possibility of deterioration, contamination, or mix-ups with any other material. | | |  | | |  |  |
| **14.06** | | Supplier will qualify hauliers and shipping agents used to transport the Product. | | |  | | |  |  |
| **14.07** | | Where storage or transportation is contracted out, Supplier 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. | | |  | | |  |  |
| **14.08** | | Supplier shall comply with any applicable legal requirements in relation to the transportation of Product. | | |  | | |  |  |
| **14.09** | | Supplier will keep Supply Chain traceability records available and retained. | | |  | | |  |  |
| **14.10** | | Upon reasonable request, Supplier will provide information to Client on the Supply Chain for Product between Supplier’s manufacturing site(s) and Client’s receiving site(s), including any transportation services or interim storage locations. | | |  | | |  |  |
| **14.11** | | 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 | | |  | | |  |  |
| **14.12** | | Supplier will inform Client on changes to the identified Supply Chain according to the established change control procedures. | | |  | | |  |  |
| **14.13** | | If a delivered Product needs to be returned, Supplier and Client will agree on responsibilities and conditions prior to the return shipment. | | |  | | |  |  |
|  | |  | | |  | | |  |  |
|  | | **15.0 Laboratory Controls** | | |  | | |  |  |
| **15.01** | | Have written procedures for sampling, sample management, testing, approval, disposition, recording, storage, retention and disposal of laboratory data. | | |  | | |  |  |
| **15.02** | | Retain samples as required by regulatory agencies. Supplier will store Product retention samples, sufficient to perform at least two (2) full specification analyses, 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. | | |  | | |  |  |
| **15.03** | | Have written procedures and appropriately document the preparation, use and management of reagents, solutions, and standards. | | |  | | |  |  |
| **15.04** | | Use adequately qualified or certified reference standards. All reference standards should be stored in accordance with the suppliers recommended storage conditions and used within their given expiry or retest date. | | |  | | |  |  |
| **15.05** | | Have appropriate specifications and test procedures for the Product which are consistent with the applicable approved filing and/or compendial monograph. | | |  | | |  |  |
| **15.06** | | Test Product in accordance with approved validated or qualified methods and specifications using calibrated equipment. | | |  | | |  |  |
| **15.07** | | Have a program for qualification, calibration, and preventive maintenance of all analytical equipment. | | |  | | |  |  |
| **15.08** | | Responsible for analytical method development, qualification and or validation as appropriate. Likewise Compendial analytical methods must be verified prior to their use for release of commercial Product lots. | | |  | | |  |  |
| **15.09** | | Responsible for transferring any developed methods to Supplier. | | |  | | |  |  |
| **15.10** | | Provide to Client any in-house methods, including validation reports, used for testing according to the agreed specifications (where there are no compendial methods) under an executed and in-force non-disclosure agreement. | | |  | | |  |  |
| **15.11** | | If commercially available reference standards are not available, reference standards for the Product will be made available under agreed-upon terms. | | |  | | |  |  |
|  | |  | | |  | | |  |  |
|  | | **16.0 Stability** | | |  | | |  |  |
| **16.01** | | Maintain a documented, ongoing stability program to monitor the stability of the Product using stability indicating procedures. | | |  | | |  |  |
| **16.02** | | Data analysis and trending reporting will be performed. | | |  | | |  |  |
| **16.03** | | Confirmed OOS notification to Client will be provided in a Timely Manner. | | |  | | |  |  |
| **16.04** | | Inform Client if there are any adversetrends in the stability studies that could impact on current retest date/period. | | |  | | |  |  |
| **16.05** | | Use data to confirm appropriateness of storage conditions and retest or expiry date. | | |  | | |  |  |
| **16.06** | | Store stability samples in commercial size and/or simulated market containers under ICH storage conditions. | | |  | | |  |  |
| **16.07** | | Place the first three commercial production batches and at least one batch per year (if a batch is produced in the year) on stability or as required by applicable regulatory agencies. Supplier is also responsible for performing appropriate stability studies on the Product arising from significant process changes. | | |  | | |  |  |
|  | |  | | |  | | |  |  |
|  | | **17.0 Recalls** | | |  | | |  |  |
| **17.01** | | In the event that either the Client or Supplier determines that an event or circumstance has occurred relating to the manufacture or stability of the Product which may result in the need for a recall, stock recovery or market withdrawal of Client's finished drug product, Supplier and Client shall consult with each other in a Timely Manner. The final decision to recall any of the Client's drug products shall be made by Client. | | |  | | |  |  |
| **17.02** | | Notification of the recall or similar action to the authorities, Distributors and customers of the finished drug product shall be made by Client | | |  | | |  |  |
| **17.03** | | Supplier will have procedures in place to facilitate the recall of an API as necessary. Supplier will provide assistance to the Client for the recall of drug product incorporating the Supplier’s API. These procedures must also incorporate provisions for storage or disposal of the returned Product or drug product. | | |  | | |  |  |
| **17.04** | | Mock recalls shall be conducted to ensure all appropriate management systems are robust. | | |  | | |  |  |
|  | |  | |  | |  | | |  |
|  | | **18.0 Data Integrity** | |  | | |  | |  |
| **18.01** | | Establish procedures 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. This extends also to sub-contractors. | |  | | |  | |  |
| **18.02** | | Will notify Client of any breach to the integrity of the data affecting the quality or the safety of any Product batches already shipped to Client, as soon as possible, but not to exceed three (3) Business Days after becoming aware of the event. | |  | | |  | |  |
|  | |  | |  | | |  | |  |
|  | | **19.0 Sub-Contracting** | |  | | |  | |  |
| **19.01** | | Establish GMP systems for evaluation, qualification, approval and maintenance/monitoring of all sub-contracted services with a GMP impact on Product manufactured. | |  | | |  | |  |
| **19.02** | | Notify Client in the event that the Supplier changes the Sub-Contractor used for any GMP-relevant service, if it has regulatory impact. | |  | | |  | |  |
| **19.03** | | Responsible for the quality of the materials or services provided by sub-contractors. | |  | | |  | |  |
|  | |  | |  | | |  | |  |
|  | |  | |  | | |  | |  |
|  | | **20.0 Containment** | |  | | |  | |  |
| **20.01** | | Not produce and handle 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 and utilities. | |  | | |  | |  |
| **20.02** | | 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, effective cleaning procedures should be in place, based upon a toxicological evaluation for the establishment of threshold values in relation to the products manufactured. | |  | | |  | |  |
| **20.03** | | Inform Client prior to introduction of a Highly Active Pharmaceutical Ingredient (HAPI) in the same facilities where the Product is manufactured, if no HAPIs were produced before. | |  | | |  | |  |

# APPENDIX 1: Definition of Product

“Product” shall mean the following:

# APPENDIX 2: Contacts and Responsibilities

|  |  |  |
| --- | --- | --- |
| **Contact Person for Notices**  *(including Notices of Amendment, Assignment, Termination, Resolution of Quality Issues)* | | |
|  | | |
|  | **Supplier** | **Client** |
|  |  |  |
| **Name:** |  |  |
|  |  |  |
| **Title:** |  |  |
|  |  |  |
| **Phone/Fax:** |  |  |
|  |  |  |
| **Address *(mail/delivery):*** |  |  |
|  |  |  |
| **E-mail Address:** |  |  |
|  |  |  |
| **With a Copy to:** |  |  |
|  |  |  |
| **Name:** |  |  |
|  |  |  |
| **Title:** |  |  |
|  |  |  |
| **Phone/Fax:** |  |  |
|  |  |  |
| **Address *(mail/delivery):*** |  |  |
|  |  |  |
| **E-mail Address:** |  |  |

# APPENDIX 3: Qualified Subcontractors

# APPENDIX 4: Product Specifications

# APPENDIX 5: Revisions to the Executed Quality Agreement.

Manufacturer’s Quality Agreement Template

Quality Responsibilities Table

| **§** | **Responsibilities** | **Not**  **Applicable** | **Client** | **Supplier** |
| --- | --- | --- | --- | --- |
|  |  |  |  |  |
|  |  |  |  |  |

# APPENDIX 6: Table of Changes to BPTF Template

Manufacturer’s Quality Agreement Template

Quality Responsibilities Table

| **§** | **Responsibilities** | **Not**  **Applicable** | **Client** | **Supplier** |
| --- | --- | --- | --- | --- |
|  |  |  |  |  |
|  |  |  |  |  |

1. **NOTE TO USERS**

   This Quality Agreement template was developed by the Bulk Pharmaceutical Task Force (BPTF), an affiliate organization of the Society of Chemical Manufacturers and Affiliates (SOCMA), as a guide for drafting a Quality Agreement relating to the manufacture and release of substances regulated by the Food and Drug Administration. The template is based on the collective experience of industry members, but is not intended to be exhaustive or inclusive of all pertinent requirements. The information herein is offered in good faith, but is provided WITHOUT ANY WARRANTIES, EXPRESS OR IMPLIED, INCLUDING, WITHOUT LIMITATION, WARRANTIES OF MERCHANTABILITY AND FITNESS FOR A PARTICULAR PURPOSE. Users are cautioned that the information upon which this template is based is subject to change. The responsibility allocations in the template are largely defined by the fact that only one party is in a position to exercise the responsibility identified. To the extent that the responsibility is shown as shared or can be assigned to the other party, the template allocation represents the experience of the BPTF members as to common practice. Parties utilizing the template are free to allocate responsibility and notification timing in any manner that assures all regulatory obligations are met.

   SOCMA and BPTF do not endorse the products or processes of any manufacturer, and this template is not intended to provide specific advice, legal or otherwise. Following this template does not guarantee compliance with applicable laws, rules, and regulations. Users should consult with their legal and technical advisors and other sources. SOCMA, BPTF, and their members and agents do not assume any responsibility for a user’s compliance with applicable laws, rules, and regulations, and disclaim any liabilities arising out of or relating to the use of this template or reliance on any information contained herein.

   This “Note To Users” may be optionally removed from executed agreements. [↑](#footnote-ref-1)
2. Amendments to the Manufacturer’s Quality Agreement Template from that issued by SOCMA’s Bulk Pharmaceutical Task Force may be optionally tracked in [**Appendix 6**](#_APPENDIX_6:_Table)**.**  [↑](#footnote-ref-2)