STANDARD OPERATING PROCEDURE	
Department: Quality Assurance	**SOP No.:**
Title: Technical Agreement	**Effective Date:**
Supersedes: Nil	**Review Date:**
Issue Date:	**Page No.:**

1.0 OBJECTIVE:

1.1 To lay down the procedure to Out sourcing in contract manufacturing and other contract activities of formulations of drug product, Technical Agreement plays an important role in ensuring drug quality and compliance to current good manufacturing practices (cGMP).

2.0 SCOPE:

2.1 The scope of this procedure is to describe the process to be followed by Contract Giver and the Contract Acceptor could result in a product or work of unsatisfactory quality.

3.0 RESPONSIBILITY:

3.1 Head QA: To Coordinate and organize audit.

3.2 Plant manager: To Coordinate and organize audit.

4.0 ACCOUNTABILITY:

4.1 Head – Quality Assurance and Head

5.0 PROCEDURE:

5.1 A contract manufacturer has to deal with several different companies each with different degree of expectations. In such a complex environment where multiple and diverse demands are made on contract manufacturer how can the sponsor ensure that these unique demands are met? One of the realities of the contract manufacturing is that sponsor is ultimately responsible for safety, effectiveness and compliance. Hence it is either a requirement or just a fundamentally sound business practice; you need to construct the frame work for the agreement.

5.2 Need for the agreement

5.2.1 A technical agreement clarifies the functional and technical aspects of a business relationship. It will delineate, in significant detail, the responsibilities of quality, regulatory, production and transportation within each company. It will enhance the communication and build the confidence between the two parties and avoid conflicts and jargon.

5.3 As a good business practice to define the quality and compliance responsibilities in a separate document that is devoid of legal jargon. Thus a technical agreement is written document between sponsor and the contract manufacturer that defines in detail quality and compliance expectations and responsibilities of each party. Technical agreement is often referred as Quality Agreement. A sponsor is referred to as contract giver (the party gives contract) and contract manufacture referred as contract acceptor in European Technical Agreement. Technical agreement and commercial agreement are maintained separate documents; it is good idea to develop both as templates. It is important to remember that agreements are still contracts and should be submitted for legal review

5.4 Regulatory aspects:

5.4.1 When any regulatory agency arrives at the contract site one of the first questions asked will involve how the parties assign the responsibilities, communicate and confirm the compliance with cGMP's. Having a separate technical Agreement allows the contractor to quickly present a response to the investigator or auditor. Conversely, a business agreement is not something that would be shared with investigator.

5.5 **Anatomy of Technical Agreement**: A typical technical agreement is composed of the major following sections:

5.5.1 Objective
5.5.2 Scope (parties & product)
5.5.3 General requirements and responsibilities
5.5.4 Technical agreement points in detail4. Contact Details
5.5.5 Glossary of terms
5.5.6 Appendix I - List of products covered under this agreement
5.5.7 Approval
5.5.8 Changes and Revisions

5.6 GMP Requirements.

5.6.1 All applicable cGMP regulations that govern the manufacture of the product should be listed here. Mainly following points are covered:
5.6.2 Manufacture and package bulk or finished products.
5.6.3 Sourcing of starting materials both actives and excipients in accordance with "note for guidance on minimizing the risk of transmitting.
5.6.4 No change to formulation or process, potentially affecting the TSE status of the product shall be made without the prior written consent of the contract giver.
5.6.5 Manufacture product in strict adherence to the approved marketing authorization/licence.
5.6.6 Permit audits of all relevant premises, procedures and documentation by the contract giver and permit inspection by the regulatory authorities.
5.6.7 Not to subcontract any of the work to a third party without prior agreement.
5.6.8 Approve all manufacturing instructions (Production Operation Instruction)
5.6.9 Make no changes to the product specification or manufacturing process
5.6.10 Document any deviation from defined procedures, including approval by production and QC
5.6.11 Make no changes in the sourcing of any actives and excipients unless otherwise authorised in writing
5.6.12 Batch release by an authorised qualified person
5.6.13 Maintain all batch records for a minimum of one year after expiry of the product and supply all such records to the contract giver

5.7 Production and testing of bulk materials

5.7.1 All the functions related to the production and testing are covered under this heading
5.7.2 Master formula and product specification.
5.7.3 Batch identification system for bulk manufacture.
5.7.4 Sampling and test method of active substances and inactive substances.
5.7.5 Analysis, release of active and inactive substances.
5.7.6 Retain reference samples of active substances and excipients.
5.7.7 Procurement of inactive substances
5.7.8 Retain reference sample of inactive substances.
5.7.9 Process validation and cleaning validation.
5.7.10 Manufacturing instructions

5.7.11 Production of bulk material
5.7.12 In-process controls
5.7.13 Bulk material sampling plan.
5.7.14 Test method validation.
5.7.15 Analysis and release of bulk materials for sampling.
5.7.16 Release of bulk materials for packaging.
5.7.17 Certificate of analysis for bulk material.
5.7.18 Retention of reference samples.
5.7.19 Finished product specification
5.7.20 Batch identification system for finished product
5.7.21 Artwork and labeling text (blister, carton, leaflet, label, etc)
5.7.22 Labeling review and approval
5.7.23 Specifications and test method for packaging materials
5.7.24 Procurement of packaging materials
5.7.25 Inspection of packaging materials
5.7.26 Release of packaging materials
5.7.27 Retain samples of printed packaging materials as per policy
5.7.28 Validation of packaging process
5.7.29 Bill of materials (BOM) for packaging
5.7.30 Packaging instructions (POI for packaging)
5.7.31 Packaging operations (including documentation)
5.7.32 In-process control instructions
5.7.33 In-Process controls during packaging (including documentation)
5.7.34 Finished product sampling plan.
5.7.35 Sampling and release of finished product
5.7.36 Retain reference samples of finished product.
5.7.37 Reconciliation of packaging materials
5.8 Testing and release of finished product
5.8.1 The following points are covered under this heading.
5.8.2 Test method for finished product
5.8.3 Analysis of finished products (including documentation)
5.8.4 Release of finished product by Q.A.
5.8.5 Certificate of analysis for finished product
5.8.6 Stability testing and protocol.
5.8.7 Place the first 3 batches in market packs on stability at 25°/65% RH, 30ºC/65% RH and 40°/75% RH Place 1 batch of product on stability per annum at 25°/65% RH
5.8.8 Test frequencies as per ICH guidelines or as per the agreed stability protocol.
5.8.9 Results concurrent with marketing authorization.
5.8.10 Complaints, Collection and logging, Investigation and issue of reports, Follow up on corrective action.
5.8.11 Adverse event reporting

5.8.12 Annual product review
5.8.13 Product recall, Decision to initiate recall, Management recall, Management of returned product, Responsibility to authorities
5.8.14 Check that sub-contractor has an appropriate manufacturing license. Maintain safety/hazard and handling data on product and raw materials.
5.8.15 Liaison with health & safety authorities and environmental protection authorities, Pollution prevention.
5.9 Storage and transportation of bulk material, finished product and waste disposal
5.9.1 Storage of bulk material up to packaging or delivery ex-plant Storage of finished product
5.9.2 Storage under special conditions, e.g. refrigeration (specify conditions)
5.9.3 Transportation of bulk material to contract giver or designated third party
5.9.4 Transportation of finished product to contract giver or designated distributor
5.9.5 Transport under special condition (Specify)
5.9.6 Insurance for transportation
5.9.7 Customs formalities
5.9.8 Disposal of waste
5.9.9 Disposal of special waste, e.g. toxic waste, solvents, etc. (specify nature of waste and - Special disposal methods required)
5.10 Batch Documentation
5.10.1 Provide copy of the complete batch documentation for each batch to the contract Giver and the following documentation to the Contact Giver for all batches as specified below:
5.10.2 Manufacturing batch record
5.10.3 Packaging batch record
5.10.4 Certificate of compliance
5.10.5 Bill of Materials (BOM) for bulk manufacture
5.10.6 Analytical results for raw materials
5.10.7 Manufacturing instructions
5.10.8 In-process control record for manufacture
5.10.9 Certificate of analysis for active material
5.10.10 Bill of Materials (BOM) for packaging, Packaging Instructions, In-process control record for packaging, Reconciliation of packaging materials
5.10.11 Certificate of analysis for finished product. In summary technical agreement can be powerful tool for maintaining product quality and productive contact giver and contract acceptor partnership. To ensure effectiveness, the agreement needs to written in a clear and focused. manner and must set the stage for managing the quality relationship between contract giver and contract acceptor.

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6.0 ABBREVIATIONS:

6.1 QA - Quality assurance
6.2 SOP - Standard Operating Procedure

7.0 CROSS REFERENCES:

7.1 NA

8.0 REFERENCES:

8.1 In House

9.0 ATTACHMENTS:

9.1 NIL

10.0 CIRCULATION LIST:

10.1 Quality Assurance
10.2 Production
10.3 Engineering
10.4 Quality Control
10.5 Warehouse
10.6 Personnel & Administration
10.7 Purchase
10.8 Account

11.0 REVISION HISTORY:

SOP NUMBER	REASION FOR CHANGE	VERSION NUMBER	SUPERSEDES	CHANGE CONTROL No.
	New SOP		NIL	NA