

## **1. Purpose**

The purpose of this International Procedure is to describe the requirements for the quality management of contractors; to describe the role of contract giver sites in this context and to provide a model for the development of Quality Assurance Agreements with Contractors

## **2. Scope**

This procedure is applicable to the management of contractors to contract giver Operations that supply APIs, API intermediates and starting materials, bulk formulated products, finished packs, QC testing, distribution and commercial stability studies.

Taking into account the exceptions listed in Section 5.7, the procedure is applicable to in-licensed products that continue to be manufactured by the licensor and are supplied to contract giver for marketing/distribution.

Out-licensed products and the tactical supply of materials/products required for Research and Development, including clinical trials are outside the scope of this procedure unless the same contractor is expected to supply materials/products for commercial use.

## **3. Definitions**

### **3.1 Contract Acceptor (Contractor)**

A person or entity agreeing to provide the sponsor with a service or material/product according to sponsor's specified requirements and intellectual property.

Note: Sponsor will retain ownership of any method or process used to manufacture the material made at a contractor.

### **3.2 Contract Giver**

The Sponsor or a person who approves the acquisition of a service or material/product on behalf of Sponsor.

### **3.3 Receiving Site**

A Manufacturing Site receiving a specified material/product from a contractor.

### **3.4 Lead Site**

In this Procedure the Lead Site is the site nominated in the Vendor and Contractor Database to be accountable for conducting specified material/product related QA activities.

Out Sourcing and Procurement group will undertake some parts (material/product release excepted) of the role of the Lead Site during the selection and establishment of new contractors for API and API intermediates and starting materials. These responsibilities shall

specifically required to meet regional/local GMP and/or import regulations.

### **3.11 De-certification**

Is the act of reverting back to full or partially increased laboratory testing of a specific material/product on its receipt from the supplier or contractor.

### **3.12 Certified Material/Product – (Includes starting materials, intermediates, APIs, excipients, formulated products and finished products)**

A certified material/product is a material/product supplied to Sponsor that is released by Sponsor or released by the supplier or contractor directly into Sponsor's distribution chain, without repeat laboratory testing by Sponsor or an independent laboratory approved by Sponsor.

A certified material/product may undergo additional laboratory testing by Sponsor or an independent laboratory approved by Sponsor, if the contractor does not perform all tests required to release the material/product.

### **3.13 De-Certified Material/Product**

A de-certified material/product is a material/product that has had its 'certified' status revoked.

## **4 Responsibilities**

**4.1** Supply Chain group is responsible for maintaining an up to date list of contractors to Sponsor Operations.

**4.3** The Quality Management group is responsible for assigning a Quality Assurance Agreement Co-ordination Site for each contractor that supplies APIs, intermediates, starting materials, formulated and or packed products to the Lead Site. This assignment will be based on technical know-how and geographical proximity.

**4.4** Dossier Management Group is responsible for providing relevant Chemistry, Manufacturing and Controls (CMC) documentation relating to internationally sourced or internationally marketed materials/products to the contractor via the Lead Site, to enable the contractor to create regulatory compliant Master Batch Records and laboratory test methods.

**4.5** Dossier Management Group is also responsible for distributing an electronic copy of the 'contractor version' of the Quality and Compliance Manual to all Lead Sites and Quality Assurance Coordination Sites.

## **Sponsor Legal Affairs**

**4.12** Sponsor Legal Affairs is responsible for reviewing any Quality Assurance Agreement that involves more than one Sponsor Legal entity and/or is not based on the standard template agreed with Sponsor legal Affairs.

## **Lead Site**

Note: When there is no Quality Assurance Agreement Co-ordination Site assigned, e.g. when the contractor makes only materials/products for one Lead Site, the Lead Site shall fulfill all responsibilities assigned to the Quality Assurance Agreement Coordination Site and the Lead Site in this Procedure.

**4.13** Each Lead Site is responsible for ensuring that appropriate links are maintained between the contractor and Sponsor QA and Regulatory processes including but not exclusively:

- Manufacturing Change Management Process (MCM)
- Dossier Management Group (DMG), to maintain the currency and accuracy of the Chemistry, Manufacture and Controls (CMC) Dossier for internationally sourced or internationally marketed products.
- Labeling Changes
- The commercial stability program, including timely Out of Specification (OOS) reporting and periodic data reporting.
- Product Defect, Customer Complaints and Product Recall procedures.
- Annual Product Review

**4.14** Each Lead Site (together with its local regulatory group) is responsible for maintaining the currency and accuracy of the Chemistry, Manufacture and Controls (CMC) Dossier for locally marketed products made at a contractor.

**4.15** Each Lead Site is responsible for supporting the Quality Assurance Agreement Co-ordination Site in carrying out the responsibilities described in 4.8 – 4.11.

**4.16** Each Receiving Site is responsible for ‘certifying’ the materials/products it receives from a contractor site based on advice from the Quality Assurance Agreement Co-ordination Site (on quality and compliance history and current status) and Lead Site (on product quality aspects, including quality history of the contractor).

## **All Groups**

**4.17** Procurement, QA management and Dossier Management Group or the Operations Site assigned as a Receiving Site, Lead Site, or Quality Assurance Agreement Co-ordination Site to a contractor site is responsible for providing sufficient resources to support the Quality Assurance Agreement.

**4.19** All groups are responsible for entering and maintaining the data in the Vendor

- Product Defect, Customer Complaints and Product Recall procedures.
- Annual Product Reviews.
- Sponsor's Legal Affairs shall review any new Quality Assurance Agreement:
- Quality Assurance Agreements shall be reviewed also by the Toll Manufacturing Manager in Supply and Manufacturing to eliminate conflicts with respect to tolling arrangements.

## **5.2 Establishment Phase**

### **5.2.1 Technology Transfer and Validation**

A project team, including technical and QA representatives of the Lead Site, and representatives of the contractor shall be constituted to manage the transfer of technology to the contractors. Dossier Management group shall be assigned to the team to ensure that the CMC aspects of the transfer are adequately covered.

### **5.2.2 Pre-Approval Inspection (PAI)**

The Project Team referred to in Section 5.2.1 shall carry out co-ordination of PAI preparations at contractors. In the case of contractors chosen for new products, the supply chain shall be accountable for the PAI readiness of contractors on a timescale consistent with overall business plans.

Compliance Management Group, in collaboration with the Lead Site, sponsor's QA and the Quality Assurance Agreement Co-ordination Site, shall ensure that an appropriate team is identified to audit any contractor that has not previously supplied the sponsor product to the market and is intended to be used for the supply of product to the market.

Based on the outcome of the audits and other interactions with the contractor, the Quality Assurance Agreement Co-ordination Site and Lead Site shall advise compliance team on the contractor's state of PAI readiness. Compliance shall advise the state of readiness of all contractors included in a submission.

## **5.3 Maintenance Phase**

At the beginning of the Maintenance Phase the Quality Assurance Agreement Co-ordination Site, Lead Site and Receiving Sites shall update the information in the Vendor Assurance and Contractor Database (see Section 5.5), including the status for the quality systems and compliance level of the contractor and the certification status for each material/product supplied by the contractor.

### **5.3.1 Contractor Status (Quality and Compliance Systems)**

Contractor Status shall be assessed/assigned by the Quality Assurance Agreement Co-ordination Site. This status may be:

- Acceptable (approved) - no or minor issues only
- Major issues and concerns with the contractor that are being addressed.

sponsor and the contractor shall retain the originals of other records that each party creates/approves for an appropriate period. (Responsibility for records co-signed by both the contractor and sponsor shall be agreed between the signatories and documented)

Records and samples retention shall be included in the scope of audits of the contractor.

## 5.5 Vendor Assurance and Contractor Database

QA management shall provide and administer a database to retain summary information on vendors and contractors providing materials/products to sponsor or conducting manufacturing, packing, laboratory testing or distribution activities on behalf of sponsor.

The database shall be fully populated and kept current by the appropriate Quality Assurance Agreement Co-ordination, Lead and Receiving Sites with copies of relevant original records held within each site according to the responsibilities of the sponsor site with respect to the contractor and the materials/products/services supplied by the contractor.

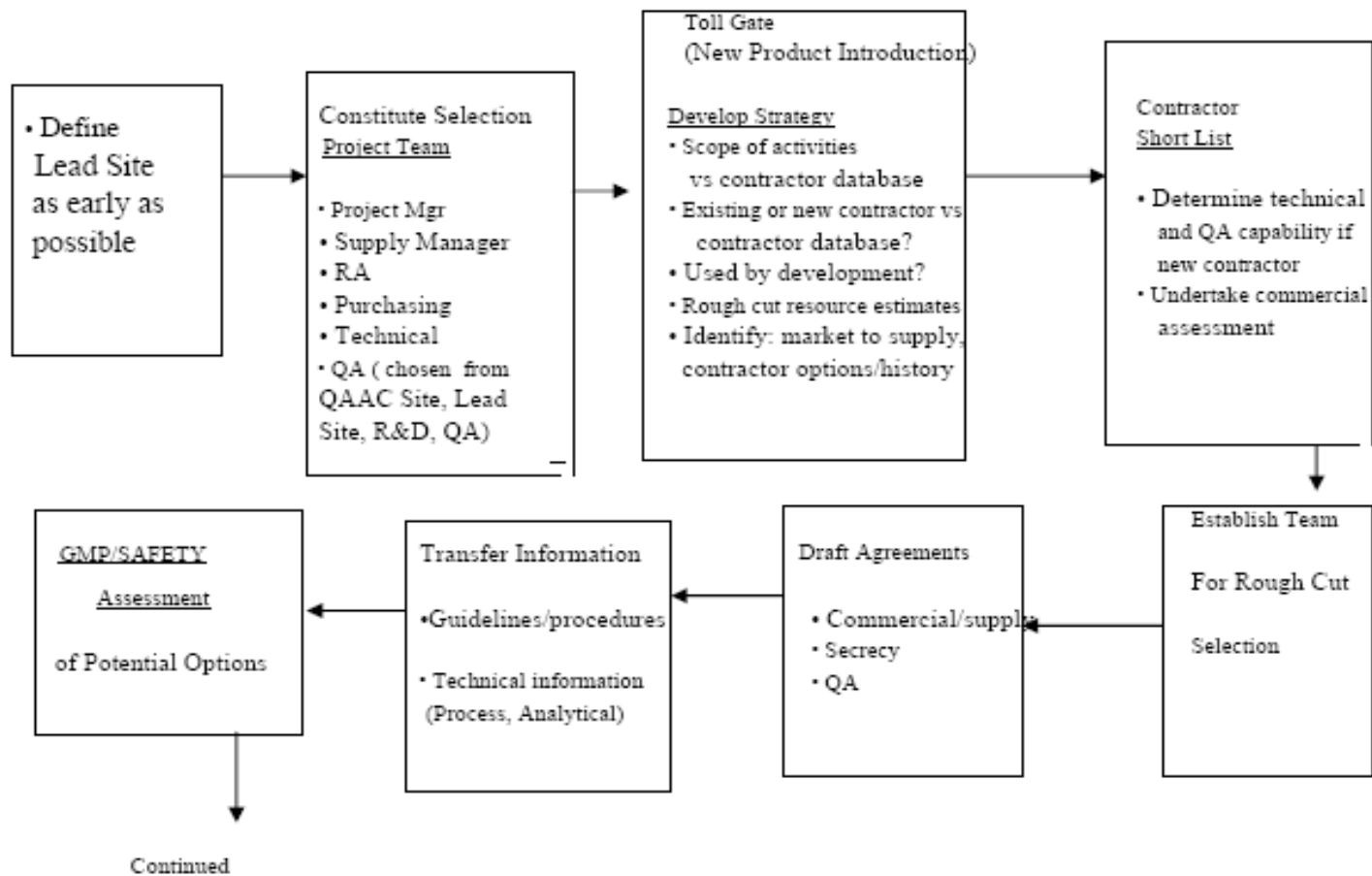
The following information/records are required:

- Contractor Name\*
  - Contractor Site Location Name\*
  - Contractor Site Country\*
  - Contractor Site Plant/Facility/Unit Name\*
  - Material Name\*
  - Material Type\*
  - Material Manufacturing Stage\*
  - Lead Site\*
  - Receiving Site\*
  - Contractor Site Address Note: include name of Contractor's QA Contact(s) and e-mail address(es) in comments field.
  - Contractor Site Phone Number
  - Contractor Site Fax Number
  - Quality Assurance Agreement Document
  - GMP Certification Document
  - QAAC Site (if assigned)
  - Primary sponsor QA Contact(s) for Contractor
  - Annual Contractor Review Document
  - Audit Frequency
  - Date of last audit.
  - Manufacturing Stage Quality and Compliance Systems Status(es)
  - TSE Document
  - TSE Status
  - Solvents Document
  - AHPIS Document
  - Product Certification Status
  - Receiving Site Contact
- \* Denotes the minimum information required to create a new product record in the Database.

Further details are included in the Database User Guide.

## QUALITY MANAGEMENT OF CONTRACTORS

### SELECTION PHASE



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