

# **Supplier Qualification – Industry and Regulator Perspective: Manufacturer's responsibilities, supplier responsibilities and where the regulator fits in**

# Introduction

- What are the manufacturer's responsibilities in approving suppliers?
- Supplier approval on sites were Australian Regulator licenses or grants clearance for a site?
- How do you handle suppliers changing compliance status?



# What are the manufacturer's responsibilities?

- Which suppliers need to be qualified?
- How much is enough?
  - What evidence is required?
  - Do all suppliers require on site suppliers audits?



# Code of GMP requirements

- 2.7. The heads of **Production and Quality Control** generally have some shared, or jointly exercised, responsibilities relating to quality. These may include, subject to any national regulations: ...
  - the approval and monitoring of suppliers of materials;
  - the approval and monitoring of contract manufacturers.....

# Code of GMP requirements

Must be an approved supplier

- 5.25. The purchase of **starting materials** is an important operation which should involve staff who have a particular and thorough knowledge of the suppliers.  
Recommended that it is supplied directly from the manufacturer
- 5.26. Starting materials should **only be purchased from approved suppliers** named in the relevant specification and, where possible, **directly from the producer**. It is recommended that the specifications established by the manufacturer for the starting materials be discussed with the suppliers. It is of **benefit that all aspects of the production and control of the starting material in question, including handling, labelling and packaging requirements, Discussions are recommended as well as complaints and rejection procedures are discussed with the manufacturer and the supplier.**

# Evaluation of potential supplier's ability to meet selection criteria

- How can the potential supplier demonstrate their ability to meet the defined selection criteria?
- Methods of information collections may include but not be limited to:
  - Pre-purchase samples or prototype(s),
  - Questionnaires
  - Auditing of the site
  - Data from other organisations e.g. regulatory database

# Evaluation of potential supplier's ability to meet selection criteria

- Information to be gathered may include but not limited to:
  - Site Master File
  - Location of site of manufacture of the material, alternative sites used and subcontracted sites
  - The GMP status of all manufacturing sites and quality systems used
  - Certificates of Analysis (CoA) and/or certificates of conformance  
Information on test methods and who actually tested the material  
Note: CoA must be on original letter head and not transcribed
  - Information on brokers and/or supply chain

# Evaluation of potential supplier's ability to meet selection criteria

- Information of audits of the manufacturing site and by whom
- Other materials produced on the manufacturing site
- Toxin status: ... pesticides, Bovine Spongiform Encephalopathy (BSE), herbicides ... etc.
- Check that the material is a single source and the origin is identified
- Stability information for transport, how it is transported and packaged
- Other history of the manufacturer

# Evaluation of potential supplier's ability to meet selection criteria

- Confirm the confidence in the information provided
  - If samples are provided, how do you know that they are genuine?
  - Source of CoA's
  - Check for independent background information on the manufacturing site(s)

# GMP Evidence

- In the questionnaires include asking about relevant inspections
  - Evidence of inspection
  - If the site has been inspected by a recognised authority, was the inspection relevant to the product/service supplied?
  - What is the scope of the licences/certificates and is it relevant to the supplied starting material/service?

# Guide from regulator

*Supplier qualification Technical Working Groups (TWG) on  
non-sterile medicines & complementary medicines  
Approval of packaging or starting material supplier*

- When a starting material is supplied from a manufacturer that has a TGA licence or GMP Clearance issued by the TGA, **then no further qualification of the manufacturer is required**
  - Note: This is the case in only very limited circumstances

# Guide from regulator

- Is any action required for a supplier that has a TGA licence or clearance?
  - Yes, the minimum is a questionnaire
  - Must check that the TGA licence/clearance is relevant to the materials/services being used

# Therapeutic Goods Act 1989

- Therapeutic Goods Act 1989; Chapter 1 Preliminary; section 3; Interpretation; (1) In this Act, unless the contrary intention appears:  
**Manufacture**, in relation to therapeutic goods that are not medical devices, means:  
(a) to produce the goods; or  
The Act allows for GMP inspection of component  
(b) to engage in any part of the process of producing the goods or of bringing the goods to their final state, including engaging in the processing, assembling, packaging, labelling, storage, sterilising, testing or releasing for supply of the goods or of any **component or ingredient of the goods as part of that process.**

# Therapeutic Goods Act 1989

- (5B) The listing of a medicine under section 26A is subject to a condition that:
- (a) **each step in the manufacture of the medicine that is carried out in Australia** is carried out by a person who is the **holder of a licence** to carry out that step or who is exempt from the operation of Part 3-3 in relation to that step

# Therapeutic Goods Act 1989

- the registration or listing of therapeutic goods (the subject goods) is subject to the conditions that the person in relation to whom the subject goods are registered or listed will:
- ... Chapter 3 Medicines and other therapeutic goods that are not medical devices, Part 3-2 Registration and listing of therapeutic goods, Division 2 Registration and listing
- Section 28(a) **allow an authorised person:**
- **(i) to enter, at any reasonable time, premises at which the person deals with the subject goods; and**

# Therapeutic Goods Act 1989

- (ii) while on those premises, to inspect those premises and any therapeutic goods on those premises and to examine, take measurements of, conduct tests on or take samples of any therapeutic goods on those premises or any thing on those premises that relates to any therapeutic goods; and
- (iii) while on those premises, to make any still or moving image or any recording of those premises or any thing on those premises; and ...

# Therapeutic Goods Act 1989

- (2A) Without limiting subsection (2), **different conditions may be specified** for:
  - (a) the registration of therapeutic goods; and
  - (b) the listing of therapeutic goods; and
  - (c) different classes of therapeutic goods.

# Australian regulator licenses or grants clearance

- In Australia
- Licensed medicine sites are:
  - All steps in the manufacture of Registered (AUST R) and Listed (AUST L) finished products,  
**(including site that do testing only)**
  - Active Pharmaceutical Ingredients (API) manufacture for Registered medicines

# Australian regulator licenses or grants clearance

- In Australia
- Sites that are **not** licensed:
  - API manufacture for Listed products
  - Excipients for Listed and Registered products
  - Packaging manufacturers

# Australian regulator licenses or grants clearance

- Importation from Overseas
- Clearance for medicine sites are required for:
  - All steps in the manufacture of Registered and Listed finished products (**except subcontracted testing only sites**)
  - API manufacture for Registered medicines

# Australian regulator licenses or grants clearance

- Importation from Overseas
- Sites that do **not** require clearance:
  - API manufacture for Listed products
  - Excipients for Listed and Registered products
  - Packaging manufacturers
  - Sites that perform testing only (with some exceptions)

# Can material from multiple sources be used?

- Annex 8: “SAMPLING OF STARTING AND PACKAGING MATERIALS” allows for validation procedure for the purposes of reduced sampling.
- Validation can occur where:
  - starting materials coming from a **single product manufacturer** or plant;
  - starting materials coming directly from a manufacturer or in the manufacturer's sealed container where there is a history of reliability **and regular audits** of the manufacturer's Quality Assurance system are conducted by the purchaser (the manufacturer of the medicinal products or by **an officially accredited body**)

# Can material from multiple sources be used?

- It is improbable that a procedure could be satisfactorily validated for:
  - starting materials supplied by intermediaries such as brokers where the source of manufacture is unknown or not audited;
  - starting materials for use in parenteral products
- i.e. can not reduce sampling for starting materials from an unknown source.
- While the code allow from material from an unknown source, it is unlikely that a manufacturer could gather enough evidence to be able to approve such a supplier.

# Validated suppliers

- Validation must take account of at least the following aspects:
  - nature and **status** of the **manufacturer and of the supplier** and their understanding of the GMP requirements of the Pharmaceutical Industry;

# Validated suppliers

- To establish a status, the purchaser must conduct a series of full sampling and tests to establish a history before approving for reduced sampling
- Should the material fail quality testing at any time or have other GMP issues, the status of the supplier/manufacturer needs to be reduced
- There are no guidelines in the code as to how to re-establish confidence so a risk based approach is required which could include:
  - Revert back to full sampling/testing
  - Gather additional information on cause of failure
  - Ensure corrective actions have been implemented

# Summary

- The Production and Quality managers are responsible for ensuring starting materials are from approved suppliers
- Evidence of quality of the starting materials must be gathered to support the decision
- Validated suppliers can have reduced sampling in some cases
- A failure in GMP testing or other circumstances leads to a downgrading of status which must be re-established before they can be considered as validated (this is a risk based approach)

# Reference

- Technical guidance on the interpretation of manufacturing standards  
Supplier qualification Technical Working Groups (TWG) on non-sterile medicines & complementary medicines  
Version 1.1, June 2013 Ensure they address the learning outcomes
- GUIDE TO GOOD MANUFACTURING PRACTICE FOR MEDICINAL PRODUCTS (PE 009-8, 15 January 2009)

# Thank You for Participating Any Questions?

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