Guidance for Industry, Q7A Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients

I. INTRODUCTION (1)
   A. Objective (1.1)
   B. Regulatory Applicability (1.2)
   C. Scope (1.3)

II. QUALITY MANAGEMENT (2)
   A. Principles (2.1)
   B. Responsibilities of the Quality Unit(s) (2.2)
   C. Responsibility for Production Activities (2.3)
   D. Internal Audits (Self Inspection) (2.4)
   E. Product Quality Review (2.5)

III. PERSONNEL (3)
   A. Personnel Qualifications (3.1)
   B. Personnel Hygiene (3.2)
IV. BUILDINGS AND FACILITIES (4)
   A. Design and Construction (4.1)
   B. Utilities (4.2)
   C. Water (4.3)
   D. Containment (4.4)
   E. Lighting (4.5)
   F. Sewage and Refuse (4.6)
   G. Sanitation and Maintenance (4.7)

V. PROCESS EQUIPMENT (5)
   A. Design and Construction (5.1)
   B. Equipment Maintenance and Cleaning (5.2)
   C. Calibration (5.3)
   D. Computerized Systems (5.4)

VI. DOCUMENTATION AND RECORDS (6)
   A. Documentation System and Specifications (6.1)
   B. Equipment Cleaning and Use Record (6.2)
   C. Records of Raw Materials, Intermediates, API Labeling and Packaging Materials (6.3)
   D. Master Production Instructions (Master Production and Control Records) (6.4)
   E. Batch Production Records (Batch Production and Control Records) (6.5)
   F. Laboratory Control Records (6.6)
   G. Batch Production Record Review (6.7)

VII. MATERIALS MANAGEMENT (7)
   A. General Controls (7.1)
   B. Receipt and Quarantine (7.2)
   C. Sampling and Testing of Incoming Production Materials (7.3)
   D. Storage (7.4)
   E. Re-evaluation (7.5)

VIII. PRODUCTION AND IN-PROCESS CONTROLS (8)
   A. Production Operations (8.1)
   B. Time Limits (8.2)
   C. In-process Sampling and Controls (8.3)
   D. Blending Batches of Intermediates or APIs (8.4)
   E. Contamination Control (8.5)

IX. PACKAGING AND IDENTIFICATION LABELING OF APIs AND INTERMEDIATES (9)
   A. General (9.1)
   B. Packaging Materials (9.2)
   C. Label Issuance and Control (9.3)
   D. Packaging and Labeling Operations (9.4)

X. STORAGE AND DISTRIBUTION (10)
   A. Warehousing Procedures (10.1)
   B. Distribution Procedures (10.2)

XI. LABORATORY CONTROLS (11)
   A. General Controls (11.1)
B. Testing of Intermediates and APIs (11.2)
C. Validation of Analytical Procedures - See Section 12. (11.3)
D. Certificates of Analysis (11.4)
E. Stability Monitoring of APIs (11.5)
F. Expiry and Retest Dating (11.6)
G. Reserve/Retention Samples (11.7)

XII. VALIDATION (12)
A. Validation Policy (12.1)
B. Validation Documentation (12.2)
C. Qualification (12.3)
D. Approaches to Process Validation (12.4)
E. Process Validation Program (12.5)
F. Periodic Review of Validated Systems (12.6)
G. Cleaning Validation (12.7)
H. Validation of Analytical Methods (12.8)

XIII. CHANGE CONTROL (13)

XIV. REJECTION AND RE-USE OF MATERIALS (14)
A. Rejection (14.1)
B. Reprocessing (14.2)
C. Reworking (14.3)
D. Recovery of Materials and Solvents (14.4)
E. Returns (14.5)

XV. COMPLAINTS AND RECALLS (15)

XVI. CONTRACT MANUFACTURERS (INCLUDING LABORATORIES) (16)

XVII. AGENTS, BROKERS, TRADERS, DISTRIBUTORS, REPACKERS, AND RELABELLERS (17)
A. Applicability (17.1)
B. Traceability of Distributed APIs and Intermediates (17.2)
C. Quality Management (17.3)
D. Repackaging, Relabeling, and Holding of APIs and Intermediates (17.4)
E. Stability (17.5)
F. Transfer of Information (17.6)
G. Handling of Complaints and Recalls (17.7)
H. Handling of Returns (17.8)

XVIII. SPECIFIC GUIDANCE FOR APIs MANUFACTURED BY CELL CULTURE/FERMENTATION (18)
A. General (18.1)
B. Cell Bank Maintenance and Record Keeping (18.2)
C. Cell Culture/Fermentation (18.3)
D. Harvesting, Isolation and Purification (18.4)
E. Viral Removal/Inactivation steps (18.5)

XIX. APIs FOR USE IN CLINICAL TRIALS (19)
A. General (19.1)
B. Quality (19.2)
C. Equipment and Facilities (19.3)
D. Control of Raw Materials (19.4)
E. Production (19.5)
I. INTRODUCTION (1)

A. Objective (1.1)

This document is intended to provide guidance regarding good manufacturing practice (GMP) for the manufacturing of active pharmaceutical ingredients (APIs) under an appropriate system for managing quality. It is also intended to help ensure that APIs meet the quality and purity characteristics that they purport, or are represented, to possess.

In this guidance, the term manufacturing is defined to include all operations of receipt of materials, production, packaging, repackaging, labeling, relabeling, quality control, release, storage and distribution of APIs and the related controls. In this guidance, the term should identifies recommendations that, when followed, will ensure compliance with CGMPs. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes. For the purposes of this guidance, the terms current good manufacturing practices and good manufacturing practices are equivalent.

The guidance as a whole does not cover safety aspects for the personnel engaged in manufacturing, nor aspects related to protecting the environment. These controls are inherent responsibilities of the manufacturer and are governed by national laws.

This guidance is not intended to define registration and/or filing requirements or modify pharmacopoeial requirements. This guidance does not affect the ability of the responsible regulatory agency to establish specific registration/filing requirements regarding APIs within the context of marketing/manufacturing authorizations or drug applications. All commitments in registration/filing documents should be met.

B. Regulatory Applicability (1.2)

Within the world community, materials may vary as to their legal classification as an API. When a material is classified as an API in the region or country in which it is manufactured or used in a drug product, it should be manufactured according to this guidance.

C. Scope (1.3)

This guidance applies to the manufacture of APIs for use in human drug (medicinal) products. It applies to the manufacture of sterile APIs only up to the point immediately prior to the APIs being rendered sterile. The sterilization and aseptic processing of sterile APIs are not covered by this guidance, but should be performed in accordance with GMP guidances for drug (medicinal) products as defined by local authorities.

This guidance covers APIs that are manufactured by chemical synthesis, extraction, cell culture/fermentation, recovery from natural sources, or any combination of these processes. Specific guidance for APIs manufactured by cell culture/fermentation is described in Section XVIII (18).

This guidance excludes all vaccines, whole cells, whole blood and plasma, blood and plasma derivatives (plasma fractionation), and gene therapy APIs. However, it does include APIs that are produced using blood or plasma as raw materials. Note that cell substrates (mammalian, plant, insect or microbial cells, tissue or animal sources including transgenic animals) and early process steps may be subject to GMP but are not covered by this guidance. In addition, the guidance does not apply to medical gases, bulk-packaged drug (medicinal) products (e.g., tablets or capsules in bulk containers), or radiopharmaceuticals.

Section XIX (19) contains guidance that only applies to the manufacture of APIs used in the production of drug (medicinal) products specifically for clinical trials (investigational medicinal products).