8.3.2 Quality Management

The system for managing quality should encompass the organizational structure, procedures, processes, and resources, as well as the activities to ensure confidence that the API will meet its intended specifications for quality and purity. All quality-related activities should be defined and documented. There should be a quality unit(s) that is independent of production and that fulfills both the QA and QC responsibilities. The quality unit can be in the form of separate QA and QC units or a single individual or group, depending on the size and structure of the organization. The persons authorized to release intermediates and APIs should be specified. All quality-related activities should be recorded at the time at which they are performed. Any deviation from the established procedures should be documented and explained. Critical deviations should be investigated, and the investigation and its conclusions should be documented.

No materials should be released or used before the satisfactory completion of evaluation by the quality unit(s), unless there are appropriate systems in place to allow for such use or the use of raw materials or intermediates pending completion of evaluation.

Procedures should exist for notifying responsible management in a timely manner of regulatory inspections, serious GMP deficiencies, product defects, and related actions (e.g., quality-related complaints, recalls, and regulatory actions).

Equipment used in the manufacture of intermediates and APIs should be of appropriate design and adequate size and suitably located for its intended use, cleaning, sanitation (where appropriate), and maintenance. Equipment should be constructed so that surfaces that contact the raw materials, intermediates, or APIs do not alter the quality of the intermediates and APIs beyond the official or other established specifications. Production equipment should be used only within its qualified operating range. Major equipment (e.g., reactors and storage containers) and permanently installed processing lines used during the production of an intermediate or an API should be appropriately identified.

Any substance associated with the operation of the equipment, such as lubricants, heating fluids, and coolants, should not contact the intermediates or APIs so as to alter the quality of APIs or intermediates beyond the official or other established specifications. Any deviations from this practice should be evaluated to ensure that there are no detrimental effects on the material's fitness for use. Wherever possible, food-grade lubricants and oils should be used.

Closed or contained equipment should be used whenever appropriate. Where open equipment is used, or equipment is opened, appropriate precautions should be taken to minimize the risk of contamination. A set of current drawings should be maintained for equipment and critical installations (e.g., instrumentation and utility systems).

For each batch of intermediate and API, appropriate laboratory tests should be conducted to determine conformance to specifications. An impurity profile describing the identified and unidentified impurities present in a typical batch produced by a specific controlled production process should normally be established for each API. The impurity profile should include the identity or some qualitative analytical designation (e.g., retention time), the range of each impurity observed, and the classification of each identified impurity (e.g., inorganic, organic, and solvent). The impurity profile is normally dependent on the production process and the origin of the API. Impurity profiles are normally not necessary for APIs from herbal or animal tissue origin. Biotechnology considerations are covered in ICH guidance Q6B. The impurity profile should be compared at appropriate intervals against the impurity profile