2000

USP 24

NF 19

THE UNITED STATES PHARMACOPEIA

THE NATIONAL FORMULARY

By authority of the United States Pharmacopeial Convention, Inc., meeting at Washington, D.C., March 9–12, 1995. Prepared by the Committee of Revision and published by the Board of Trustees

Official from January 1, 2000

UNITED STATES PHARMACOPEIAL CONVENTION, INC.
12601 Twinbrook Parkway, Rockville, MD 20852

NOTICE AND WARNING

Concerning U.S. Patent or Trademark Rights

The inclusion in the Pharmacopeia or in the National Formulary of a monograph on any drug in respect to which patent or trademark rights may exist shall not be deemed, and is not intended as, a grant of, or authority to exercise, any right or privilege protected by such patent or trademark. All such rights and privileges are vested in the patent or trademark owner, and no other person may exercise the same without express permission, authority, or license secured from such patent or trademark owner.

Concerning Use of USP or NF Text

Attention is called to the fact that USP and NF text is fully copyrighted. Authors and others wishing to use portions of the text should request permission to do so from the Secretary of the USPC Board of Trustees.

ISSN 0195-7996
ISBN 1-889788-03-1

Printed by National Publishing, Philadelphia, PA

Commingling: the blending of trace carryover material from one grade of an excipient with another, usually due to a continuous process.

Contaminant: an impurity not intended to be present in an excipient, which may be introduced by poor cleaning, processing, or lack of appropriate environmental and personnel controls during the manufacturing process.

Continuous Process: a manufacturing process that continually produces an excipient from a continuous supply of raw materials.

Critical Process: a manufacturing process step that may cause variation in quality attributes.

Cross-contamination: contamination during production of a raw material, intermediate, or of a finished excipient with another raw material, intermediate, or product.

DMF: detailed information submitted to the United States Food and Drug Administration concerning a specific facility, process, or product intended for incorporation by reference into a new drug application, supplemental new drug application, abbreviated new drug application, or investigational new drug application.

Excipient: any substances, other than the active drug or product, that have been appropriately evaluated for safety and are included in a drug delivery system to either aid the processing of the drug delivery system during its manufacture, protect, support or enhance stability, bioavailability, or patient acceptability, assist in product identification, or enhance any other attribute of the overall safety and effectiveness of the drug delivery system during storage or use.

Expiration Date: the date beyond which the product may no longer conform to relevant specifications.

Finished Dosage Form (Drug product): a finished pharmaceutical product, prepared for consumer applications, containing excipients and the active drug substance.

Finished Product: any pharmaceutical product that has undergone all stages of production, including packaging and labeling.

Finished Process Materials: any material that has undergone all stages of production and is released from quality control.

Homogeneous Material: throughout the batch, material of uniform consistency and composition.

Impurity: a substance contained in a product other than the desired substance.

In-Process Testing: monitoring checks performed during production to ensure that the product conforms to its specifications.

In-Process Material: any material that must undergo further manufacture before it becomes a bulk product.

Intermediate Product: any material that must undergo further manufacturing steps before it becomes a bulk product.

Lot: See Batch.

Manufacturer: the company that performs the final production steps and release of the product.

Manufacturing Process: all steps necessary to produce a finished product from raw materials.

Master Formula (Master Formula Record): documentation describing the manufacture of the excipient from raw material to completion of the lot or batch.

Material Review Board: a committee or group selected to evaluate the disposition of potentially nonconforming material.

Model Product: a product that simulates a group of like products.

Mother Liquor: a concentrated solution from which the product is obtained by evaporation, freezing, or crystallization.

Re-evaluation Date: that date beyond which the bulk pharmaceutical excipient should not be used without prior adequate re-examination.

Representative Sample: a sample drawn according to an appropriate sampling plan, which may involve regular or random selection.

Reprocessing: introducing back into the process previously processed material that did not conform to standards or specifications and repeating steps that are already part of the normal manufacturing process.

Nonconforming Material: any material that does not meet manufacturer's specifications or applicable good manufacturing practices.

Packaging: the act of filling and labeling a container with a product.

Packaging Material: the containers, closures, and labels employed in the packaging of a product.

Processing Instructions: the manufacturing procedures set forth in the master formula.

Production: all operations involved in the preparation of an excipient pharmaceutical product, from receipt of raw materials through the completion of a finished product.

Purification: the process of removing impurities from a substance.

Quality: the totality of features and characteristics of a product that bear on its ability to satisfy stated or implied needs.

Quality Assurance: all those planned and systematic actions necessary to provide confidence that a product or a service will satisfy given requirements for quality.

Quality Control: all activities such as measuring, examining, testing, or gauging one or more characteristics of a product (including raw materials) and comparing the findings with specified requirements to determine conformity.

Quality Control Instruments: measurement instruments used to monitor the manufacturing process, in-process controls, and the finished excipient products for final quality control approval.

Quarantine: the status of any material isolated physically or by other effective means while awaiting a decision on its use.

Raw Material: any substance used in the production of a product excluding packaging materials.

Reserve (Retained) Sample: a representative sample of the final excipient batch of sufficient quality and quantity necessary to perform quality control analyses twice.

Returned Products: finished products sent back to the manufacturer.

Reworking: introducing previously processed material that did not conform to standards or specifications to processing steps that are different from the normal process.

Significant Processing Step: processing steps that are required to produce an excipient that meets the established physical and chemical criteria.

Shelf life: the length of time during which the excipient exhibits stability.

Specifications: the quality parameters that serve as a basis for quality evaluation and to which the products or materials must conform.

Stability: the continued conformance of the excipient to its specifications.

Standard Operating Procedures (SOPs): a written authorized procedure that gives instructions for performing operations.

Validation: documentation that states that any procedure, process, equipment, material, or activity consistently leads to the expected results.

Vendor: an organization contracted to supply a material or perform a service.

Appendix 2. General Auditing Considerations

Evaluation

Prevention of Contamination—In evaluating the adequacy of measures taken to prevent contamination of materials in the process, it is appropriate to consider the following factors:

- Type of system (e.g., open or closed. Closed systems in chemical plants are often not closed when they are being charged or when the final product is being emptied. Also, the same reaction vessels are sometimes used for different reactions)
- Form of the material (e.g., wet or dry)
- Stage of processing and use of the equipment and/or area (e.g., multi-purpose or dedicated)
- Continuous versus (discrete) batch production

Other factors that should be considered in evaluating an excipient plant are the degree of exposure of the material to adverse environ-