USP Standards for Quality Vaccines

The United States Pharmacopeia–National Formulary (USP-NF) contains general chapters that provide requirements and best practices for manufacturers, regulators and laboratories that are developing, manufacturing, testing and releasing drug substances and products.

Learn more about some of the key standards that apply to quality vaccine development below.

Accessing *USP–NF Online*

To access details about the standards below and other relevant information, you must be signed in to USP–NF Online. *If you are a scientist, developer or manufacturer working on COVID-19 vaccines or treatments, and would like to request free access, complete this online request.*

General Vaccine Development and Manufacturing

Standard name	Brief description
<1> Injections and Implanted Drug Products—Product Quality Tests	This chapter is divided into three main sections: (1) universal product quality tests that are applicable to parenteral dosage forms; (2) specific product quality tests, which are tests that should be considered in addition to universal tests; and (3) product quality tests for specific dosage forms, which list applicable tests (universal and specific) for the specific dosage form. Although some pharmacopeial definitions for sterile preparations for parenteral use may not apply to some biologics because of their special nature and licensing requirements, some biological finished drug products, such as vaccines, must meet the requirements of General Chapter <1>. **Intended to convey requirements enforceable by regulatory agencies.**
<71> Sterility Tests	This chapter demonstrates process control and is a general indicator of the microbiological quality of a product. It is important to note that pharmacopeial procedures are not by themselves designed to ensure that a product or batch is sterile or has been sterilized. This is accomplished primarily by validation of the sterilization process or of the aseptic processing procedures. **Intended to convey requirements enforceable by regulatory agencies.**
<85> Bacterial Endotoxins Test	This is a test used to detect or quantify bacterial endotoxins that may be present in a substance. Endotoxins are bacterial structural components that are released when such a cell is lysed, or broken down. These components are toxic to humans and animals, causing a pyrogenic response, which includes a rise in body temperature and other harmful effects. **Intended to convey requirements enforceable by regulatory agencies.**
<151> Pyrogen Test	A pyrogen is any chemical substance that will cause a fever if present at high enough levels within the body. The pyrogen test, or the rabbit pyrogen test, is an in vivo test for the presence of pyrogens and is designed to limit the amount of pyrogens with an injectable pharmaceutical. **Intended to convey requirements enforceable by regulatory agencies.**
<1044> Cryopreservation of Cells	This chapter presents best practices for cryopreservation, maintenance and use of a wide range of cells, cell therapy products and cell banks derived from a variety of sources, including human, animal and microbial cultures. Cryopreserved cells provide a ready source of viable cells that can be used, either directly or indirectly, for the purposes of diagnostic tests, therapy, manufacture of drug substances and vaccines, and bioassays used to evaluate the potency of therapeutic drugs and vaccines. **Not intended to convey requirements enforceable by regulatory agencies.**
<1048> Quality of Biotechnological Products: Analysis of the Expression Construct in Cells Used for Production of r-DNA Derived Protein Products	This chapter presents guidance regarding the characterization of the expression construct used for the production of recombinant DNA (r-DNA) protein products. The chapter describes the types of information that are considered valuable in assessing the structure of the expression construct used to produce r-DNA-derived proteins. **Not intended to convey requirements enforceable by regulatory agencies.**
<1049> Quality of Biotechnological Products—Stability Testing of Biotechnological/Biological Products	The purpose of this chapter is to offer guidance regarding the type of stability studies that should be provided in support of development of and marketing applications for biologic products. It is understood that, during the review and evaluation process of a biological product, continuing updates of initial stability data may occur. **Not intended to convey requirements enforceable by regulatory agencies.**

General Vaccine Development and Manufacturing

Standard name	Brief description
<1050> Viral Safety Evaluation of Biotechnology Products Derived From Cell Lines of Human or Animal Origin	This chapter focuses on testing and evaluation of the viral safety of biotechnology products derived from characterized cell lines of human or animal origin (i.e., mammalian, avian, insect), and outlines data that should be submitted in the marketing application/registration package. The purpose of this chapter is to describe a general framework for virus testing, experiments for the assessment of viral clearance, and a recommended approach for the design of viral tests and viral clearance studies. **Not intended to convey requirements enforceable by regulatory agencies.**
<1074> Excipient Biological Safety Evaluation Guidelines	This informational chapter presents a scientifically based approach for the safety assessment of new pharmaceutical excipients (i.e., those excipients that have not been previously used or permitted for use in a pharmaceutical preparation). The guidelines presented herein provide a protocol for developing an adequate database on which to establish conditions for the safe use of a new excipient intended for use in products administered by various routes of administration. **Not intended to convey requirements enforceable by regulatory agencies.**
<1116> Microbiological Control and Monitoring of Aseptic Processing Environments	This general information chapter provides information and recommendations for environments where the risk of microbial contamination is controlled through aseptic processing. Products manufactured in such environments include pharmaceutical sterile products, bulk sterile drug substances, sterile intermediates, excipients and, in certain cases, medical devices. The guidance provided in this chapter and the monitoring parameters given for microbiological evaluation should be applied only to clean rooms, restricted-access barrier systems and isolators used for aseptic processing. **Not intended to convey requirements enforceable by regulatory agencies.**
<1132> Residual Host Cell Protein Measurement in Biopharmaceuticals	Many medicinal products are produced through recombinant technology via a host cell (e.g., bacteria; yeast; mammalian, insect or plant cell lines). During the manufacture of such products, some amount of non-product, host cell-derived material will inevitably be introduced into the process stream. This process results in a mixture of the desired product and host cell-derived impurities, (process impurities), including host cell proteins (HCPs). This chapter focuses on HCP immunoassays for recombinant therapeutic products. It does not address products such as vaccines or gene-, cell- or tissue-based therapies, although the general principles discussed may apply to the measurement of HCPs in these products as well. **Not intended to convey requirements enforceable by regulatory agencies.**
<1229.4> Sterilizing Filtration of Liquids	Sterilization processes are divided broadly into two categories: destruction of microorganisms or their physical removal from the material to be sterilized. Multiple factors contribute to the effectiveness of any sterilizing filtration process. These factors, as well as the type and number of microorganisms, the properties of the liquid, the filter design and membrane polymer, and the filtration process parameters, are discussed in this document. **Not intended to convey requirements enforceable by regulatory agencies.**
<1234> Vaccines for Human Use—Polysaccharide and Glycoconjugate Vaccines	This chapter describes best practices for production, conjugation and characterization of polysaccharide and glycoconjugate vaccines. It describes key quality attributes at each step of the process and suggests best methods to assess these attributes. The scope of this chapter includes vaccines consisting of one or more purified polysaccharides (such as pneumococcal, meningococcal and Typhoid Vi vaccines) and components involved in their production, and vaccines consisting of one or more glycoconjugate immunogens in which a polysaccharide has been covalently attached to a suitable carrier protein. **Not intended to convey requirements enforceable by regulatory agencies.**
<1235> Vaccines for Human Use—General Considerations	This chapter provides background information on vaccine manufacturing and tests, including information relative to U.S. requirements and references to requirements in other countries. There are multiple forms of vaccines, like bacterial vaccines, viral vaccines and DNA-based vaccines (under development), as well as a high number of other vaccine components, like adjuvants; the chapter focuses on commonalities throughout the manufacturing process, from raw material qualification to final release tests. **Not intended to convey requirements enforceable by regulatory agencies.**
<1238> Vaccines for Human Use—Bacterial Vaccines	Bacterial vaccines can be derived from whole cells, either killed or attenuated in their ability to cause disease, or from some component(s) of the intact cell that are important for virulence or damaging to the host and can lead to a protective immunologic response. Another subset of bacterial vaccines, derived from toxins, is the toxoids (inactivated toxins). Bacterial vaccine products can be mixtures of components from different species, from different strains or different serotypes of the same species, or from different components from cells of the same species. This informational chapter provides an overview of these bacterial vaccines and quality attributes associated with their development and manufacturing. **Not intended to convey requirements enforceable by regulatory agencies.**

Assays for Vaccine Validation

Standard name	Brief description
<111> Design and Analysis of Biological Assays	Biological assays (also called bioassays) are an integral part of the quality assessment required for the manufacturing and marketing of many biological and some non-biological drug products. Bioassays commonly used for drug potency estimation can be distinguished from chemical tests by their reliance on a biological substrate (e.g., animals, living cells, functional complexes of target receptors). This chapter presents a concise account of certain essential biometrical procedures for bioassays in chapters or monographs of the USP–NF, namely outlier identification, confidence intervals for relative potency measurements and combination of independent assays. **Intended to convey requirements enforceable by regulatory agencies.**
<1032> Design and Development of Biological Assays	This chapter describes the methodology for the development of bioassay procedures that have sound experimental design, that provide data that can be analyzed using well-founded statistical principles and that are fit for their specific use. **Not intended to convey requirements enforceable by regulatory agencies.**
<1033> Biological Assay Validation	As new biological drug products and new technologies emerge, the scope of bioassay approaches is likely to expand. This chapter emphasizes validation approaches that provide flexibility to adopt new bioassay methods, new biological drug products or both in conjunction for the assessment of drug potency. **Not intended to convey requirements enforceable by regulatory agencies.**
<1034> Analysis of Biological Assays	This chapter provides guidance for the analysis of results both of bioassays described in the USP and of non-USP bioassays that seek to conform to the quality parameters of bioassay analysis recommended by the USP. Topics addressed include statistical concepts and methods of analysis for the calculation of potency and confidence intervals for a variety of relative potency bioassays, including those referenced in the USP. The chapter is intended for use primarily by those who do not have extensive training or experience in statistics and by statisticians who are not experienced in the analysis of bioassays. **Not intended to convey requirements enforceable by regulatory agencies.**
<1103> Immunological Test Methods-ELISA	Enzyme-linked immunosorbent assays (ELISA) are one of the most widely used immunological test methods (ITMs) for characterization, release and stability testing of biotechnology products to help ensure the identity of biological drug substances and drug products and the potency of vaccines. This chapter provides analysts with general information about principles, procedures, experimental configurations, assay development and validation for solid-phase ITMs like ELISA, and covers reference standards and controls used for immunoassays. **Not intended to convey requirements enforceable by regulatory agencies.**

Methods for Nucleic Acid-Based Vaccines

Standard name	Brief description
<1125> Nucleic Acid-Based Techniques—General	Nucleic acid-based assays are used in a variety of settings, the most common of which include the detection of infectious agents (e.g., viruses, bacteria) and residual cellular materials (e.g., host cell DNA), as well as disease profiling. More recently, such assays have also been used for forensic purposes and for the detection of trace contamination in biological materials. The latter includes pharmaceutical development applications, such as viral clearance and adventitious agent testing in vaccine seed lots and tissue culture cell banks. This chapter introduces a series of general information chapters that provide techniques that support procedures for the detection and analysis of nucleic acids. The assays using these techniques may be presented in a USP general chapter or in another specification. **Not intended to convey requirements enforceable by regulatory agencies.**
<1126> Nucleic Acid-Based Techniques—Extraction, Detection, and Sequencing	This chapter discusses general steps in the extraction and purification of nucleic acids from a variety of sample types, focusing on (1) collection, handling and storage of samples; (2) disruption of samples; (3) subsequent extraction and purification of nucleic acids; and (4) storage of purified nucleic acids. **Not intended to convey requirements enforceable by regulatory agencies.**
<1127> Nucleic Acid-Based Techniques—Amplification	Polymerase chain reaction (PCR) is a method widely used to rapidly make many copies of a specific DNA sequence, allowing scientists to take a very small sample of DNA and amplify it to a large enough amount to study in detail. This chapter describes the main assay, or test, components necessary for a PCR procedure and includes a discussion of the general optimization of PCR assays. **Not intended to convey requirements enforceable by regulatory agencies.**
<1130> Nucleic Acid-Based Techniques—Approaches for Detecting Trace Nucleic Acids (Residual DNA Testing)	This chapter covers the analytical procedures used to quantify residual DNA in biopharmaceuticals. Removing residual DNA from a product is an indicator of the quality and consistency of the development process. **Not intended to convey requirements enforceable by regulatory agencies.**

Standards That Relate to Packaging and Distribution of Medicines

Standard name	Brief description
<2027> Package Integrity Evaluation—Sterile Products	This chapter provides guidance on the integrity assurance of nonporous packages intended for sterile pharmaceutical products. Background instruction is provided on the topics of leaks, leakage rate and package sealing/closure mechanisms. Explanation is given as to how packages that conform to specified leakage limits help to ensure the contained product meets and maintains sterility and relevant physicochemical specifications. **Not intended to convey requirements enforceable by regulatory agencies.**
<1031> The Biocompatibility of Materials Used in Drug Containers, Medical Devices, and Implants	This chapter provides guidance on the identification and performance of procedures for evaluating the biocompatibility of drug containers, elastomeric closures, medical devices and implants. Biocompatibility refers to the tendency of these products to remain biologically inert throughout the duration of their contact with the drug product or the body. The biocompatibility testing procedures referenced in this chapter are designed to detect the nonspecific, biologically reactive, physical or chemical characteristics of medical products or the materials used in their construction. **Not intended to convey requirements enforceable by regulatory agencies.**
<1079> Good Storage and Distribution Practices for Drug Products	This general information chapter describes good storage and distribution practices to ensure that drug products (medicines) reach the end user (practitioners and patient/consumers) with quality intact. **Not intended to convey requirements enforceable by regulatory agencies.**
<1178> Good Packaging Practices	This chapter is intended to provide guidance to those engaged in repackaging of oral solid drug products. The chapter also provides information relevant to any person who removes drugs from their original container-closure system (new primary package) and repackages them into a different container-closure system for sale and/or for distribution. **Not intended to convey requirements enforceable by regulatory agencies.**
<1663> Assessment of Extractables Associated With Pharmaceutical Packaging/Delivery Systems	This general information chapter presents a framework for the design, justification and execution of an extractables assessment for pharmaceutical packaging and delivery systems. The chapter establishes critical dimensions of an extractables assessment and discusses practical and technical aspects of each dimension. The principles and best demonstrated practices outlined in this general chapter represent a consensus interpretation of sound science and can therefore be applied to any situation in which an extractables assessment is required for pharmaceutical application. **Not intended to convey requirements enforceable by regulatory agencies.**
<1664> Assessment of Drug Product Leachables Associated With Pharmaceutical Packaging/ Delivery Systems	This general chapter presents a framework for the design, justification and implementation of assessments for drug product leachables derived from pharmaceutical packaging and delivery systems. A scientifically sound leachables assessment is important to manufacturers and their various suppliers primarily as a means of establishing the suitability for use of pharmaceutical packaging/delivery systems, as leachables can potentially affect drug product efficacy, safety and quality. **Not intended to convey requirements enforceable by regulatory agencies.**
<1787> Measurement of Subvisible Particulate Matter in Therapeutic Protein Injections	Parenteral products are designed and manufactured to minimize particulate matter, which is differentiated into two broad categories: visible and subvisible. The absolute limit of visibility, or detectability, depends on the test conditions and the nature of the particulate matter. This general information chapter covers subvisible particles in the range of 2-100 µm. This chapter will focus on enumeration, characterization and, when possible, identification of inherent particles, distinguishing them from extrinsic and intrinsic particles. The chapter does not cover formulations that are suspensions or emulsions, or those that contain adjuvants or similar intended particle components. **Not intended to convey requirements enforceable by regulatory agencies.**
<1790> Visual Inspection of Injections	This chapter provides guidance on the inspection of injections for visible particles. The terms “particle,” “particulates” and “particulate matter” are equivalent and do not have different meanings when used in this chapter. “Particulate matter” is defined in 788 Particulate Matter in Injections as “mobile undissolved particles, other than gas bubbles, unintentionally present in the solutions.” The methods discussed in this chapter are also applicable to the detection of other visible defects not the subject of 790 Visible Particulates in Injections but critical to a qualified, comprehensive inspection process. The primary focus of this chapter is a manual reference inspection method; however, semi-automated and automated methods are also discussed and permitted by the pharmacopeia. **Not intended to convey requirements enforceable by regulatory agencies.**