Compendial Forum Updates Relevant to Microbiological Issues

Because some of the proposals of the various forums often rely on linkages to general chapters, at times guesses based on dosage form need to be made as to whether the specific proposal makes a reference to microbiological requirements. When such a guess has been made, this is indicated with an X in the BG column. Remember that no guarantees are made relative to completeness of this update, and you should make reference to the respective pharmacopeial form if in doubt. BP: https://www.pharmacopoeia.com EP: https://pharmeuropa.edqm.eu/home IP: https://ipcmline.ipc.gov.in/ipqa/indian-pharmacopoeia JP: https://www.pmda.go.jp/english/ USP: https://www.usp.org. WHO: https://digicollections.net/phint/2025/index.html#p/home. A hyperlink in the Sidecar column indicates that there is a YouTube video associated with the item. "Sidecars" videos are designed to be thought provoking, as per the white paper "Critical Scientific Thinking, SOPs and "Sidecars" at https://microbiologyforum.org/Articles_White_Papers/Critical_Scientific_Thinking_and_SOPs.pdf. Side cars will be added periodically and listed here, at the PMF web site Training Tab [https://microbiologyforum.org/Training.html], and via online PMF Forum postings [https://microbiologyforum.org/Forum.html].

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Compendium	Proposal Type	Title	New[N] / Revised[R]	Synopsis [requirements or description]	BG	Side Car
BP	monograph	Copper Sulfate Sterile Concentrate	N	*The concentrate complies with the requirements for Concentrates for Injections or Infusions stated under Parenteral Preparations and with the following requirements. Where appropriate, the concentrate also complies with the requirements stated under Unlicensed Medicines.*		
BP	monograph	Brimonidine Eye Drops	N	Brimonidine Eye Drops are a sterile solution of Brimonidine Tartrate.		
BP	monograph	Clarithromycin for Infusion	R	Clarithromycin for Infusion is a sterile material consisting of *Clarithromycin* with or without excipients. It is supplied in a sealed container. *The contents of the sealed container comply with the requirements for Powders for Injections or Infusions stated under Parenteral Preparations and with the following requirements.*		
BP	monograph	Bleomycin Powder for Injection	R	Bleomycin Powder for Injection is a sterile material consisting of Bleomycin Sulfate with or without excipients. It is supplied in a sterile container. The contents of the sealed container comply with the requirements stated under Parenteral Preparations and with the following requirements.		
EP	monograph	Croscarmellose Sodium	R	Microbial contamination TAMC: acceptance criterion 10^3 CFU/g (2.6.12). TYMC: acceptance criterion 10^2 CFU/g (2.6.12). Absence of Escherichia coli (2.6.13).		
EP	monograph	Parenteral preparations	R	Sterility (2.6.1). Parenteral preparations comply with the test. Pyrogenicity. Parenteral preparations for human use, if applicable after reconstitution or dilution, comply with a suitable test for pyrogenicity. Guidance for the selection of a test is given in general chapter 5.1.13. The limit, when not indicated in the individual monograph, is determined in accordance with the recommendations of general chapter 5.1.10 when a test for bacterial endotoxins is selected or general chapter 2.6.30 when a monocyte-activation test is selected. The limit for intravitreal preparations for intraocular use is expressed per eye. Where the label states that the preparation is free from bacterial endotoxins, the preparation complies with the test for bacterial endotoxins (2.6.14 or 2.6.32). Where the label states that the preparation is apyrogenic, the preparation complies with the monocyte-activation test (2.6.30). Parenteral preparations for veterinary use comply with a suitable test for pyrogenicity when the volume to be injected in a single dose is 15 mL or more and is equivalent to a dose of 0.2 mL or more per kilogram of body mass. Guidance for the selection of a test is given in general chapter 5.1.13.		
EP	monograph	Sorbitol, Liquid, Partially Dehydrated	R	Microbial contamination TAMC: acceptance criterion 10^3 CFU/g (2.6.12). TYMC: acceptance criterion 10^2 CFU/g (2.6.12). Absence of Escherichia coli (2.6.13). Absence of Salmonella (2.6.13).		
IP [no new relevant items as of this report date]						
JP [no new relevant items as of this report date]						
USP [5105]	chapter	〈71〉 Ophthalmic Products—Quality Tests	R	**STERILITY** Ophthalmic dosage forms•All ophthalmic drug products• USP 1 Feb 2027 must meet the requirements of *Sterility Tests* 〈71〉. •Sterility is considered a critical quality attribute for ophthalmic drug products. • USP 1 Feb 2027 If the specific ingredients used in the formulation do not lend themselves to validation of sterilization techniques, ingredients that meet the sterility requirements described in 〈71〉, along with aseptic manufacture, may be used. The immediate-container•primary container–closure system• USP 1 Feb 2027 for ophthalmic •Drugs• USP 1 Feb 2027 products shall be sterile at the time of filling and •container• USP 1 Feb 2027 closing. **antimicrobial preservatives** •Multidose drug products shall contain a suitable antimicrobial preservative, and the effectiveness of the preservative during the use period of the drug product must be verified. The efficacy of the preservative must also be maintained for the shelf life of the product. Alternatively, preservative-free multidose drug products require a packaging system that has been demonstrated to maintain sterility during the use period of the drug product. The efficacy of the preservative-free packaging system must also be maintained for the shelf life of the drug product. • USP 1 Feb 2027 Antimicrobial agents must be added to products that are packaged in containers that allow for the withdrawal or administration of multiple doses, unless one of the following provisions prevails: 1) there are different directions in the individual monograph; 2) the radiopharmaceutical drug product contains a radionuclide with a physical half-life of <24 h; 3) the drug product, without additional agents, is sufficiently microbicidal to meet the requirements of *Antimicrobial Effectiveness Testing* 〈51〉, or 4) the container–closure system is capable of maintaining sterility of the product throughout its shelf life until opened or accessed. Once opened or accessed, it must maintain antimicrobial effectiveness during the intended use period. Antimicrobial agents must meet the requirements of 〈51〉, and *Antimicrobial Agents—Content* 〈341〉. Acceptance criteria for antimicrobial preservative content in multidose products should be established. **bacterial endotoxins** All injected ophthalmic drug products shall be prepared in a manner designed to minimize bacterial endotoxins as defined in *Bacterial Endotoxins Test* 〈85〉. The limits are not more than 0.5 EU/mL for ophthalmic irrigation products and not more than 2.0 EU/dosevolume for injected or implanted drug products. Typically, this test is not required for topically applied ophthalmic •Drug• USP 1 Feb 2027 products. This chapter does not address the endotoxin limits for devices that are injected or implanted.		
USP [5105]	chapter	〈825〉 Radiopharmaceuticals—Preparation, Compounding, Dispensing, and Repackaging.	R	from Briefing] • Clarify in 1.2 Sterile Radiopharmaceuticals that 70% isopropyl alcohol (IPA) must be allowed to dry, prior to initial needle puncture, when wiping vial septa. Revise 3. Immediate Use of Sterile Radiopharmaceuticals as follows: • Add the requirement that intrathecally administered radiopharmaceuticals not be dispensed according to the immediate use standards. • Revise 3. Immediate Use of Sterile Radiopharmaceuticals as follows: • Add the requirement that intrathecally administered radiopharmaceuticals not be dispensed according to the immediate use standards. • Add requirements that nondirect infusion generators may not be used according to the immediate use standards and that nondirect infusion generators are required to be stored and eluted in a segregated radiopharmaceutical processing area (SRPA) in ISO 8 total airborne particles or better. Garbing and aseptic qualifications for the environment must be performed. • Clarify requirements in 4.1 Aseptic Qualifications under *Gloved Fingertip and Thumb Sampling*. • Revise in 4.2 Revisalidation, Retraining, and Requalification: • Clarify the requirement that gloved fingertip and thumb sampling is not required but may be allowed to be in conjunction with media-fill testing. • Clarify the requirement for revisalidation and requalification after a pause in sterile radiopharmaceutical processing. • Clarify the requirements for ancillary individuals with regard to whether or not they handle sterile radiopharmaceuticals directly. • Clarify the expectation for all personnel entering ISO classified areas to meet the requirements for the specific classified area that they access. • In 6. Microbiological Air and Surface Monitoring, delete requirements for incubation of samples in separate incubators. Make the following changes to 7. Cleaning and Disinfecting: • Update the frequency requirement for cleaning and disinfecting surfaces. • Update Table 5 to include a requirement for cleaning and disinfecting the surfaces of handwashing sink(s) used as part of aseptic garbing. • Update 7.2 Cleaning Supplies to add a requirement for cleaning, disinfecting, and sporicidal agents used within the PEC to be sterile with the exception of tool handles and holders. • In 7.6 Cleaning and Disinfecting Items from Patient Care Area, update to include syringe-carrying containers.		
USP [5105]	chapter	〈1155〉 Injectable Iron Colloidal Products—Characterization Methods	N	Sterility Tests 〈71〉 Bacterial endotoxins (Bacterial Endotoxins Test 〈85〉 and Guidelines for Bacterial Endotoxins Testing 〈1085〉)		
USP [5105]	chapter	〈1156〉 LG Polymer Microparticle Drug Products—Characterization Methods	N	• Bacterial endotoxins (*Bacterial Endotoxins Test* 〈85〉 and *Guidelines For Bacterial Endotoxins Testing* 〈1085〉) • *Sterility Tests* 〈71〉 **Sterility** Sterility should be determined both within and on the surface of the LG polymer microparticles. Thus, during method development, studies should be conducted to detect any organisms inside the test sample.		
USP [5105]	chapter	〈1225〉 Validation of Compendial Procedures	R	This chapter is always of general importance.		
USP [5105]	chapter	〈1771〉 Ophthalmic Products—Performance Tests	R	**Sterilization** Ophthalmic drug products must be sterile, and the sterilization methods used for the manufacturing process should be appropriately justified. (For example, see Ref. 3.) During the sterilization step of the manufacturing process, degradation and morphological changes can occur in the drug product. These changes depend on the formulation, container–closure system, and sterilization process. Such changes should be minimized to ensure product integrity and efficacy. • **Autoclaving:** The high temperatures required for this moist heat sterilization method can cause irreversible damage to certain dosage forms, especially those containing heat-sensitive components. • **Filtration:** While sterile filtration through a 0.2-µm filter is effective, it is only applicable to formulations that can be successfully filtered without impacting their quality or performance. It may not be suitable for suspensions or viscous solutions. • **Dry heat sterilization:** This method requires prolonged exposure to high temperatures, which can also degrade heat-sensitive materials and is generally unsuitable for ophthalmic preparations. • **Ethylene oxide (EtO):** Although useful for terminal sterilization, EtO may leave harmful residuals if not carefully removed, posing safety concerns. • **Gamma irradiation:** Exposure to radiation can lead to chemical changes in the formulation and container materials, potentially affecting the product's safety and stability. An alternative approach is to manufacture the drug product using sterile ingredients in an aseptic environment. This method avoids exposing the formulation to conditions that may lead to degradation, but it requires meticulous control and compliance with stringent aseptic techniques to prevent contamination.		
USP [5105]	monograph	Acrocia malincarpa Fruit Aqueous Dry Extract	N	•**Microbial Enumeration Tests** 〈2021〉 :The total aerobic bacterial count does not exceed 10^4 cfu/g, and the total combined molds and yeasts count does not exceed 100 cfu/g. •**Absence of Specified Microorganisms** 〈2022〉 , *Test Procedures, Test for Absence of Salmonella Species*[illegible] *Test for Absence of Escherichia coli*:Meets the requirements		
USP [5105]	monograph	Arsenic Trioxide	N	•**Bacterial Endotoxins Test** 〈85〉 :Where the label states that Arsenic Trioxide must be subjected to further processing during the preparation of injectable dosage forms, the level of bacterial endotoxins are such that the requirement under the relevant dosage form monograph(s) in which Arsenic Trioxide is used can be met. •**Microbial Enumeration Tests** 〈61〉 :The total aerobic microbial count does not exceed 10^3 cfu/g. The total molds and yeasts count does not exceed 50^1 cfu/g.		
USP [5105]	monograph	Arsenic Trioxide Injection	N	•**Bacterial Endotoxins Test** 〈85〉:Meets the requirements •**Sterility Tests** 〈71〉:Meets the requirements		
USP [5105]	monograph	Cordyceps sinensis Fruiting Body	N	•**Microbial Enumeration Tests** 〈2021〉 :The total aerobic bacterial count does not exceed 10^4 cfu/g, and the total combined molds and yeasts count does not exceed 10^2 cfu/g. •**Absence of Specified Microorganisms** 〈2022〉 , *Test Procedures, Test for Absence of Salmonella Species*[illegible] *Test for Absence of Escherichia coli*:Meets the requirements		
USP [5105]	monograph	Cordyceps sinensis Fruiting Body Powder	N	•**Microbial Enumeration Tests** 〈2021〉 :The total aerobic bacterial count does not exceed 10^4 cfu/g, and the total combined molds and yeasts count does not exceed 10^2 cfu/g. •**Absence of Specified Microorganisms** 〈2022〉 , *Test Procedures, Test for Absence of Salmonella Species*[illegible] *Test for Absence of Escherichia coli*:Meets the requirements		
USP [5105]	monograph	Latanoprost Ophthalmic Solution	N	•**Sterility Tests** 〈71〉:Meets the requirements		
USP [5105]	monograph	Palonosetron Injection	N	•**Bacterial Endotoxins Test** 〈85〉:Meets the requirements •**Sterility Tests** 〈71〉:Meets the requirements		
USP [5105]	monograph	Phosphatidylserine	N	•**Microbial Enumeration Tests** 〈2021〉 :The total bacterial count does not exceed 10^3 cfu/g, and the total combined molds and yeasts count does not exceed 10^2 cfu/g. •**Absence of Specified Microorganisms** 〈2022〉 , *Test Procedures, Test for Absence of Salmonella Species*[illegible] *Test for Absence of Escherichia coli*:Meets the requirements		
USP [5105]	monograph	Scaffold Bovine Dermis	R	•**Sterility Tests** 〈71〉 :It meets the requirements as directed •**Bacterial Endotoxins Test** 〈85〉 :It meets the requirements as directed in *Medical Devices—Bacterial Endotoxin and Pyrogen Tests* 〈161〉.		
WHO [no new relevant items as of this report date]						

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