Date of This Update: April 30, 2024

Compendial Forum Updates Relevant to Microbiological Issues

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Compendium	Proposal Type	Title	New[N] / Revised[R]	Synopsis [requirements or description]	BG
EP 36.2	general chapter	5.32. Cell-based Preparations for Human Use	N	"**Bacterial endotoxins** (2.6.14 or 2.6.32). It complies with the predefined requirements. **Sterility** (2.6.1). The substance complies with the test. **Use of antimicrobial preservatives** Preparation and processing of cells must not have a negative impact on microbiological quality. While starting materials may be washed with antimicrobial solutions, the use of antimicrobial preservatives in later steps of the manufacturing process is to be avoided. The use of antibiotics in expansion or storage media or in other solutions must be justified and authorised. s (2.6.7). The substance complies with the test." "Microbiological examination of cellular material, waste media and rinse solutions is included at suitable processing steps and complies with Ph. Eur. general chapters on microbiological examination or sterility (2.6.27, 2.6.1 or via alternative microbiological methods validated according to the principles of general chapter 5.1.6. Alternative methods for control of microbiological quality), mycoplasmas (2.6.7) and mycobacteria (2.6.2), where relevant." TESTS "Microbiological examination. Depending on the preparation, the final lot complies with the test for microbiological examination (2.6.27), sterility (2.6.1), microbiological examination of non-sterile products: microbial enumeration (2.6.12) or specified micro-organisms (2.6.13). Alternative microbiological methods can be used and are validated according to general chapter 5.1.6. The principles of general chapter 2.6.39. Microbiological examination of human tissues apply where relevant. Pyrogenicity. The final lot complies with a suitable test for pyrogenicity. Guidance for the selection of a test is given in general chapter 5.1.13(2). It complies with the limit approved for the particular preparation. Mycoplasmas (2.6.7). The final lot complies with the test. Depending on the cell-based preparation and where relevant, the following additional tests are required as approved by the competent authority. Mycobacteria (2.6.2). The final lot complies with the test."	
EP 36.2	general chapter	5.36. mRNA Vaccines for Human Use	N	TESTS "5-10. Bacterial endotoxins (2.6.14 or 2.6.32): less than the limit approved for the particular preparation. 5-11. Sterility (2.6.1). It complies with the test."	
EP 36.2	general chapter	5.37. Recombinant Viral Vectored vaccines for Human Use	N	PURIFICATION AND PURIFIED HARVEST "Bacterial and fungal contamination. The microbiological quality is controlled either through a sterility test or a bioburden test (as indicated in general monograph Vaccines for human use (0153)). The purified harvest complies with the test for sterility (2.6.1) or with a low bioburden limit, as approved by the competent authority."	
EP 36.2	general chapter	5.39. mRNA Substances for the Production of mRNA Vaccines for Human Use	N	TESTS "4-8. Bacterial endotoxins (2.6.14 or 2.6.32): less than the limit approved for the particular preparation. 4-9. Microbiological examination (2.6.12). It complies with the limit approved for the particular preparation."	
EP 36.2	general chapter	5.40. DNA Template for the Preparation of mRNA Substances	N	TESTS "4.8. Bacterial endotoxins (2.6.14 or 2.6.32): less than the limit approved for the particular preparation. 4.9. Microbiological examination (2.6.12). It complies with the limit approved for the particular preparation."	
EP 36.2	monograph	Aprotinin	R	"Bacterial endotoxins (2.6.14): less than 0.14 IU per European Pharmacopoeia Unit of aprotinin, if intended for use in the manufacture of parenteral preparations without a further appropriate procedure for the removal of bacterial endotoxins."	

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EP 36.2	monograph	Aprotinin Concentrated Solution	R	"Bacterial endotoxins (2.6.14): less than 0.14 IU per European Pharmacopoeia Unit of aprotinin, if intended for use in the manufacture of parenteral preparations without a further appropriate procedure for the removal of bacterial endotoxins."	
EP 36.2	monograph	Danaparoid Sodium	R	"Bacterial endotoxins (2.6.14): less than 0.02 IU per unit of anti-factor Xa activity, if intended for use in the manufacture of parenteral preparations without a further appropriate procedure for the removal of bacterial endotoxins."	
EP 36.2	monograph	Daunorubicin Hydrochloride	R	"Bacterial endotoxins (2.6.14): less than 4.3 IU/mg, if intended for use in the manufacture of parenteral preparations without a further appropriate procedure for the removal of bacterial endotoxins."	
EP 36.2	monograph	Ear Preparations	R	"Sterility (2.6.1). Where the label states that the preparation is sterile, it complies with the test."	
EP 36.2	monograph	Foot-and-mouth Disease (Ruminants) Vaccine (Inactivated)	R	"3-2. Bacteria and fungi. The vaccine and, where applicable, the liquid supplied with it, comply with the test for sterility prescribed in the monograph Vaccines for veterinary use (0062)."	
EP 36.2	monograph	Heparin Calcium	R	"Bacterial endotoxins (2.6.14): less than 0.01 IU per International Unit of heparin, if intended for use in the manufacture of parenteral preparations without a further appropriate procedure for the removal of bacterial endotoxins. The addition of divalent cations may be necessary in order to fulfil the validation criteria."	
EP 36.2	monograph	Heparin Sodium	R	"Bacterial endotoxins (2.6.14): less than 0.01 IU per International Unit of heparin, if intended for use in the manufacture of parenteral preparations without a further appropriate procedure for the removal of bacterial endotoxins."	
EP 36.2	monograph	Kanamycin Acid Sulfate	R	**THIS SECTION REMOVED:** "Pyrogens (2.6.8). If intended for use in the manufacture of parenteral preparations without a further appropriate procedure for the removal of pyrogens, it complies with the test for pyrogens. Inject per kilogram of the rabbit's mass 1 mL of a solution in water for injections R containing 10 mg per millilitre of the substance to be examined."	
EP 36.2	monograph	Kanamycin Monosulfate Monohydrate	R	**THIS SECTION REMOVED:** "Pyrogens (2.6.8). If intended for use in the manufacture of parenteral preparations without a further appropriate procedure for the removal of pyrogens, it complies with the test for pyrogens. Inject per kilogram of the rabbit's mass 1 mL of a 10 mg/mL solution of the substance to be examined in water for injections R."	
EP 36.2	monograph	Pressurised Pharmaceutical Preparations	R	"Sterility (2.6.1). Where the label states that the preparation is sterile, it complies with the test."	
EP 36.2	monograph	Rifamycin Sodium	R	"Bacterial endotoxins (2.6.14): less than 0.50 IU/mg, if intended for use in the manufacture of parenteral preparations without a further appropriate procedure for removal of bacterial endotoxins."	
EP 36.2	monograph	Streptomycin Sulfate	R	"Bacterial endotoxins (2.6.14): less than 0.25 IU/mg, if intended for use in the manufacture of parenteral preparations without a further appropriate procedure for removal of bacterial endotoxins."	
EP 36.2	monograph	Tobramycin	R	"Bacterial endotoxins (2.6.14): less than 2.0 IU/mg, if intended for use in the manufacture of parenteral preparations without a further appropriate procedure for the removal of bacterial endotoxins."	

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EP 36.2	monograph	Trypsin	R	**Microbial contamination** "TAMC: acceptance criterion 10^4 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)."	
EP 36.2	monograph	Vaccines for Human Use	R	**"Test for sterility of intermediates prior to final bulk.** Individual monographs on vaccines for human use may prescribe a test for sterility for intermediates. In agreement with the competent authority, replacement of the sterility test by a bioburden test with a low bioburden limit based on batch data and process validation may be acceptable for intermediates, provided that a sterile filtration is performed later in the production process. It is a prerequisite that the intermediate is filtered through a bacteria-retentive filter prior to storage, that authorised pre-filtration bioburden limits have been established for this filtration, and that adequate measures are in place to avoid contamination and growth of micro-organisms during storage of the intermediate. "Final bulk. For vaccines that do not undergo final sterile filtration, the final bulk is prepared by aseptically blending the ingredients of the vaccine. For vaccines that undergo final sterile filtration, the final bulk can be prepared by blending the ingredients of the vaccine under controlled low bioburden conditions before final sterile filtration, in agreement with the competent authority. For non-liquid vaccines for administration by a non-parenteral route, the final bulk is prepared by blending the ingredients of the vaccine under suitable conditions. Final lot. The final lot is prepared by aseptically distributing the final bulk into sterile, tamper-evident containers, which, after freeze-drying where applicable, are closed so as to exclude contamination. For non-liquid vaccines for administration by a non-parenteral route, the final lot is prepared by distributing the final bulk under suitable conditions into sterile, tamper-evident containers. Where justified and authorised, certain tests prescribed for the final lot may be carried out on the final bulk, if it has been demonstrated that subsequent manufacturing operations do not affect compliance."	
EP 36.2	monograph		R	**THIS SECTION REMOVED:** "Bacterial endotoxins. Unless otherwise justified and authorised, a test for bacterial endotoxins is carried out on the final product. Where no limit is specified in the individual monograph, the content of bacterial endotoxins determined by a suitable method (2.6.14) is less than the limit approved for the particular product." **THIS SECTION ADDED:** "Pyrogenicity. Vaccines for parenteral administration comply with a suitable test for pyrogenicity. Guidance for the selection of a test is given in general chapter 5.1.13. Where no limit is specified in the individual monograph, the vaccine complies with the limit approved for the particular product. For vaccines containing inherently pyrogenic components, the method described in general chapter 2.6.40 may be used."	
IP 07/2/2024	monograph	Aciclovir Intravenous Infusion	N	"Bacterial endotoxins (2.2.3). Not more than 4.37 Endotoxin Units per ml of acyclovir, determined on 25 mg per ml solution of Aciclovir."	
IP 07/2/2024	monograph	Bendamustine Hydrochloride	N	"Bacterial endotoxins (2.2.3). Not more than 1.125 Endotoxin Units per mg of bendamustine hydrochloride. Microbial contamination (2.2.9). Total aerobic viable count is not more than 1000 CFU per g and total moulds and yeasts is not more than 100 CFU per g."	
IP 07/2/2024	monograph	Dicyclomine Injection	N	"Bacterial endotoxins (2.2.3). Not more than 17.2 Endotoxin Unit per mg of Dicyclomine Hydrochloride."	

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IP 07/2/2024	monograph	Ketorolac Tromethamine Injection	N	"Bacterial endotoxins (2.2.3). Not more than 5.8 Endotoxin units per mg of ketorolac tromethamine."	
IP 07/2/2024	monograph	Sulphacetamide Eye Drops	N	"Sterility (2.2.11). Complies with the test for sterility."	
IP 07/2/2024	monograph	Temozolomide Capsules	N	"Microbial contamination (2.2.9). Total aerobic microbial count is not more than 1000 CFU per g and total fungal count is not more than 500 CFU per g and it is free from *Escherichia coli*."	
JP Vol. 33 No. 1	general chapter	Rapid Microbial Methods	R	text not available for free	X
JP Vol. 33 No. 1	general chapter	Rapid Identification of Microorganisms Based on Genetic Analysis	R	text not available for free	X
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				https://www.rapidmicrobiology.com/subscribe	
	Giles Scientific, Inc.			https://www.biomic.com/trinity-v3.html	
	Special Process Services, LC			https://www.linkedin.com/in/joseph-connaghan-b663929	
	Becton Dickinson Integrated Diagnostic Solutions			https://www.bd.com/en-us/products-and-solutions/solutions/diagnostic-solutions	