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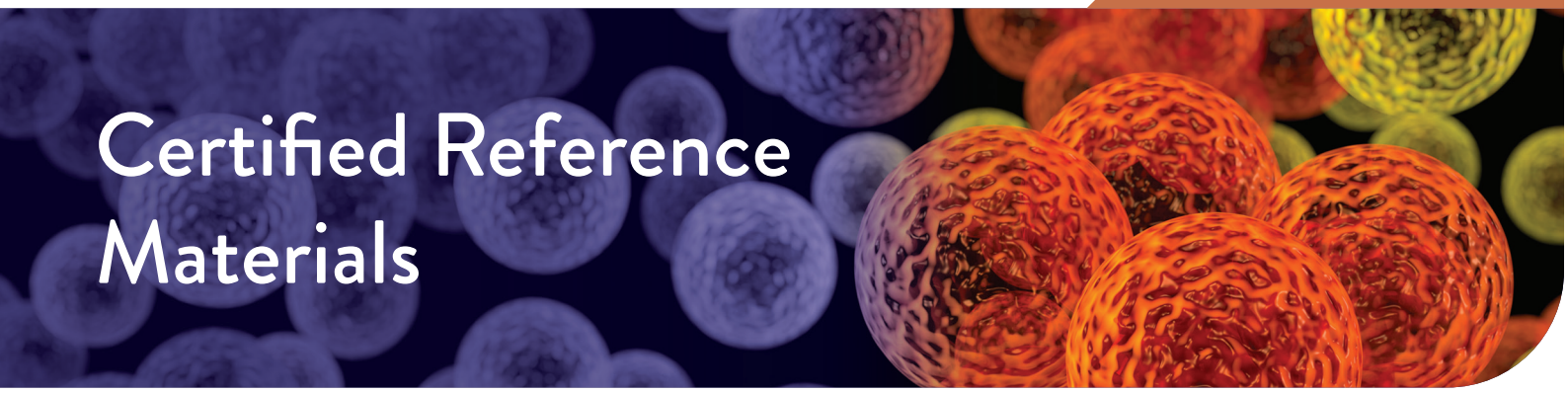
Application Note

Certified Reference Materials



Enhance Pharmaceutical Sterility Testing Using ATCC Certified Reference Materials

Contamination of non-sterile medicinal products by objectionable microorganisms is a major concern among the pharmaceutical industry, affecting patient morbidity and mortality as well as product integrity and stability. To combat this problem, the Food and Drug Administration (FDA) requires licensed pharmaceutical manufacturing companies to adhere to strict government regulations and testing protocols. These regulatory processes include quality control methods such as microbiological testing protocols described in the United States Pharmacopeia (USP) and the addition of antimicrobial preservatives. When properly followed, these processes prevent the distribution of products contaminated with objectionable microorganisms.

An example of a microbiological assessment process performed by pharmaceutical manufacturers is the Microbial Enumeration Test described in USP chapter <61>. This is a bioburden test used to determine the viable microbial load in raw pharmaceutical materials, in-process samples, and finished products through membrane filtration, direct plating, or the most-probable-number method[1]. If a product contains more than the allowable concentration of an objectionable organism, it is deemed unfit for distribution.

In addition to determining product contamination through microbiological assessment protocols, many pharmaceutical manufacturing companies supplement their non-sterile products with antimicrobial preservatives. To ensure these preservatives function properly, the preservative stability, minimum inhibitory concentration, chemical interactions with the product, and optimum pH must be considered[2], [3]. Once the appropriate conditions have been established, pharmaceutical manufacturing companies must test the efficacy of each antimicrobial preservative using the Antimicrobial Effectiveness Test (AET) described in USP chapter <51>. This analysis provides a general gauge for determining the lowest concentration the antimicrobial preservative can be used that still ensures an effective level of antimicrobial activity[4], [5].

To properly perform the protocols listed in USP chapters <61> and <51>, the USP has set forth strict guidelines regarding the quality of reference standards. These guidelines can be met using ATCC certified reference materials (CRM) prearranged in the Microbial Enumeration Testing Panel (ATCC® MP-17™) and the Antimicrobial Effectiveness Testing Panel (ATCC® MP-16™) (Tables 1, 2). Both panels, which were generated based on federal guidelines and regulations, are composed of bacterial and fungal strains produced under an ISO Guide 34:2009 process. This ensures that each strain has confirmed identity, well-defined characteristics, and an established chain of custody.

There are many advantages to using the CRM strains organized in the ATCC® MP-16™ and ATCC® MP-17™ panels. Each strain is analyzed for purity, viability, and identity through a comprehensive polyphasic approach that combines phenotypic and genotypic testing. Additionally, as CRM strains, each biomaterial has a documented chain of custody that is traceable to the original seed lot. Cultures are accompanied by a certificate of analysis, which states the results of each assessed property value, the expiration date of the material, and proper use, confirming all necessary procedures were performed to determine both purity and authenticity of the strain. As an added advantage, each pre-selected panel is offered at bulk discount pricing, providing members of the pharmaceutical industry with valuable cost savings when compared to purchasing CRM strains individually.

ATCC microbial CRM strains included in the ATCC® MP-16™ and ATCC® MP-17™ panels are ideally suited as reference standards for the microbiological analysis of pharmaceutical products. For additional information please contact ATCC Technical Services at Tech@atcc.org.

Table 1. Antimicrobial Effectiveness Testing Panel (ATCC® MP-16™)

ATCC® Number	Product Description	Strain
CRM-6538™	*Staphylococcus aureus*	FDA 209
CRM-8739™	*Escherichia coli*	Crooks
CRM-9027™	*Pseudomonas aeruginosa*	R Hugh 813
CRM-10231™	*Candida albicans*	3147
CRM-16404™	*Aspergillus* brasiliensis	WLRI 034 (120)

Table 2. Microbial Enumeration Testing Panel (AT CC® MP-17™)

ATCC® Number	Product Description	Strain
CRM-6538™	*Staphylococcus aureus*	FDA 209
CRM-6633™	*Bacillus subtilis* subsp. *spizizenii*	NRS 231
CRM-9027™	*Pseudomonas aeruginosa*	R Hugh 813
CRM-10231™	*Candida albicans*	3147
CRM-16404™	*Aspergillus* brasiliensis	WLRI 034 (120)

References

1. The United States Pharmacopeia. 2012. <61> Microbiological Examination of Nonsterile Products: Microbial Enumeration Tests.
2. Meyer B.K., Ni A., Hu B., Shi L. Antimicrobial preservative use in parenteral products: past and present. J. Pharm. Sci. 96: 3155-3167, 2007.
3. Meyer B.K., Shi L. Antimicrobial preservative use in parenteral products: an overview. Eur. J. Parent. Pharm. Sci. 14: 115-117, 2009.
4. Sutton S.V., Porter D. Development of the antimicrobial effectiveness test as USP Chapter <51>. PDA J. Pharm. Sci. Technol. 56: 300-311, 2002.
5. The United States Pharmacopeia. 2012. <51> Antimicrobial Effectiveness Tests.

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