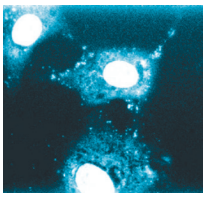
BioReliance

Biologics Safety Testing Services

USP 63 Compliant Mycoplasma Detection Assays



Introduction

Mycoplasma are the smallest self-replicating organisms known to exist. More than 100 distinct species have been identified to date. Therapeutic products for human or veterinary use require mycoplasma screening at a variety of stages in their production, such as: cell banking, virus seed stock preparation, unprocessed bulk harvesting, raw material use and final product release.

Mycoplasma contamination of cell culture is a serious concern for the biopharmaceutical industry. The organism can compromise the safety of a eukaryotic cell culture derived product and result in expensive withdrawals or loss of productivity. Contamination usually originates from components of cell culture medium, such as serum, or is introduced via an individual working in the laboratory or manufacturing facility. All animal species from which biological products are derived are known to be permissive for mycoplasma infection. In fact, according to Hay *et al*, 5-35% of cell cultures worldwide are potentially contaminated with at least one species of mycoplasma[1].

USP 63 Compliant Mycoplasma Testing

All biologics manufactured in cell substrates (e.g., viral vaccines, monoclonal antibodies and similar products) must be tested to ensure the absence of mycoplasma contamination. This is true regardless of whether the material is produced for clinical testing or as a marketed product. Tests for the presence of mycoplasma contamination in Master Cell Banks (MCB) and Working Cell Banks (WCB) originating from metazoan cells should also be conducted as part of purity testing. Guidance for this testing is detailed in the PTC[4-6], EP[2], and USP[8] publications referenced. Live viral vaccines produced from *in vitro* living cell cultures prior to clarification or filtration and inactivated viral vaccines produced from living cell cultures prior to inactivation must also be tested to ensure the absence of mycoplasma per 21 CFR 610.30[7].

The recently published USP chapter on "Mycoplasma Tests" represents a step forward in bringing requirements in the US closer to those outlined in the EP. BioReliance now announces the availability of its new USP 63 compliant mycoplasma detection assay family. These new assays, all performed to cGMP standard, will meet or exceed USP, EP, and PTC requirements. In addition to the combined USP/EP/PTC test, a 21 CFR 610.30 compliant assay will be available separately for viral vaccines, as well as a JP-compliant test for those clients who must conform to Japanese regulations[3, 9].

One assay satisfies three regulatory requirements (USP, EP and PTC)

Global harmonization of assay procedures

Assays delivered to GMP specifications ensure quality

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For more detailed information about the various mycoplasma regulations, please refer to the recently published White Paper, "BioReliance's Approach to Mycoplasma Testing: Introduction of United States Pharmacopeia 63 Regulation". (This paper is available through the BioReliance website or by contacting your Program Manager or Account Manager.)

BioReliance Mycoplasma Protocols include:

- Agar and broth cultivation to detect low level contamination
- Use of indicator cell lines and fluorochrome stain

Additional protocols are available for:

- Inclusion of avian controls
- Spiroplasma testing for insect cells
- Testing large volume samples
- Testing FBS and trypsin

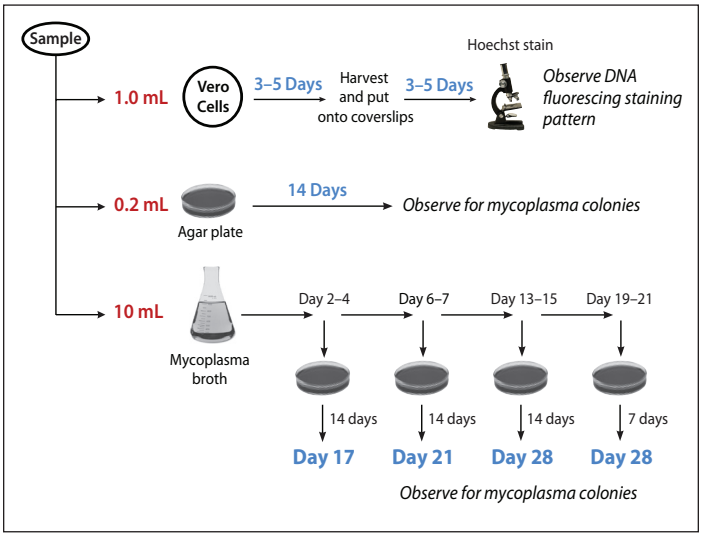

Figure 1 – Schematic depicting basic mycoplasma testing principles.

Ordering Information

Assay Number	Assay Description	Regulatory Compliance	Sample Requirements*
102063GMP.BSV (US Labs) 102063GMP.BUK (UK Labs)	Test for Agar Cultivable and Non-Agar Cultivable Mycoplasma	USP, EP, PTC	1 × 12 ml plus 1 × 2 ml recommended (12 ml minimum)
102062GMP.BSV (US Labs) 102062GMP.BUK (UK Labs)	Mycoplasmastasis Assay	USP, EP, PTC, JP	2 × 26 ml plus 1 × 2 ml recommended (26 ml minimum)
102064GMP.BSV (US Labs) 102064GMP.BUK (UK Labs)	Test for Agar Cultivable Mycoplasma	USP, EP, PTC	1 × 12 ml plus 1 × 2 ml recommended (12 ml minimum)
102065GMP.BSV (US Labs) 102065GMP.BUK (UK Labs)	Test for Non-agar Cultivable Mycoplasma	USP, EP, PTC	2 × 1 ml recommended (1 ml minimum)

** Additional sample volume needed when avian controls are required, please inquire..*

References

1. Hay, R.J., Macy, M.L., and Chen, T.R. Mycoplasma Infection of cultured cells. Nature (London), 229: 487-488, 1989.
2. European Pharmacopoeia, 7th Edition, Section 2.6.7, Mycoplasmas, 01/2008:20607 corrected 6.1.
3. Japanese Pharmacopoeia XV, 14. Mycoplasma Testing for Cell Substrates used for the Production of Biotechnological/Biological Products.
4. Center for Biologics Evaluation and Research. Food and Drug Administration. Points to Consider in characterization of cell lines to produce biologicals, 1993.
5. Center for Biologics Evaluation and Research. Food and Drug Administration. Points to Consider in the Manufacture and testing of monoclonal antibody products for Human use, 1997.
6. Center for Biologics Evaluation and Research. Food and Drug Administration. Guidance for Industry: Characterization and Qualification of Cell Substrates and Other Biological Materials Used in the Production of Viral Vaccines for Infectious Disease Indications, Feb 2010.
7. *Code of Federal Regulations*, Title 21: Food and Drugs, Part 610. General Biological Product Standards, Section 610.30. Test for Mycoplasma.
8. General Chapter 63, "Mycoplasma Tests," USP 33–NF 28 Reissue. (US Pharmacopoeial Convention, Rockville, MD, 2010), pp. 88-91.
9. Japanese Pharmacopoeia XV, 14. Mycoplasma Testing for Cell Substrates used for the Production of Biotechnological/Biological Products. Supplement II (September 30, 2009)

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