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ENVIRONMENTAL ISOLATES AND PHARMACEUTICAL QC TESTING

ENVIRONMENTAL MONITORING DOESN'T STOP AT DETECTION

Pharmaceutical auditors and regulators are increasingly issuing observations related to the use of environmental isolates in microbiological quality control testing. Though regulations and industry standards are somewhat limited on guidance for the proper use of environmental isolates, there is a clear expectation to use them in some microbiology laboratory testing applications.

Key regulations and standards that mention the use of environmental isolates:

- **European Pharmacopoeia (Ph. Eur.) Chapter 5.1.4:** Microbiological Quality of Non-Sterile Pharmaceutical Preparations and Substances for Pharmaceutical Use
- **Parenteral Drug Association (PDA) Technical Reports 70:** Fundamentals of Cleaning and Disinfection Programs for Aseptic Manufacturing Facilities
- **United States Pharmacopeia (USP) Chapter <1116>:** Microbiological Control and Monitoring of Aseptic Processing Environments
- **U.S. Food and Drug Administration:** Compliance Program Guidance Manual Program 7356.002A, Chapter 56 – Drug Quality Assurance
- **U.S. Food and Drug Administration:** FDA Guidance for Industry for Sterile Drug Products Produced by Aseptic Processing
- **U.S. Food and Drug Administration:** Guide to Inspections of Microbiological Pharmaceutical Quality Control Laboratories
- **United States Pharmacopeia (USP) Chapter <1072>:** Disinfectants and Antiseptics
- **United States Pharmacopeia (USP) Chapter <1117>:** Microbiological Best Laboratory Practices
- **United States Pharmacopeia (USP) Chapter <51>:** Antimicrobial Effectiveness Testing
- **World Health Organization (WHO):** Environmental Monitoring of Clean Rooms in Vaccine Manufacturing Facilities

OBJECTIONABLE ORGANISMS AND PHARMACEUTICAL QC TESTING

A LEADING CAUSE OF PHARMACEUTICAL PRODUCT RECALLS

Objectionable organisms are a leading cause of regulatory observations and recalls for sterile and non-sterile pharmaceutical products. Determining which organisms should be considered objectionable is one of the biggest challenges facing non-sterile pharmaceutical and personal care laboratories today. In the case of sterile products, all organisms are considered objectionable. When it comes to non-sterile products, a thorough risk assessment must be completed to ascertain the objectionable status of a particular organism.

Key regulations and standards regarding objectionable organisms:

- **U.S. Food and Drug Administration Code of Federal Regulations Title 21:** 211.84(d)(6), 211.113(a) and 211.165(b)
- **Parenteral Drug Association (PDA) Technical Report 67:** Exclusion of Objectionable Microorganisms from Nonsterile Pharmaceuticals, Medical Devices, and Cosmetics
- **United States Pharmacopeia (USP) Chapter <61>:** Microbial Enumeration Tests
- **United States Pharmacopeia (USP) Chapter <62>:** Tests for Specified Microorganisms
- **United States Pharmacopeia (USP) Chapter <1111>:** Acceptance Criteria for Pharmaceutical Preparations and Substances for Pharmaceutical Use
- **United States Pharmacopeia (USP) Chapter <1112>:** Application of Water Activity Determination to Nonsterile Pharmaceutical Products
- **Japanese Pharmacopoeia (JP) Chapter 4.05:** Microbiological Examination of Non-sterile Products
- **European Pharmacopoeia (Ph. Eur.) Chapter 2.6.12:** Microbial Enumeration Tests
- **European Pharmacopoeia (Ph. Eur.) 2.6.13:** Tests for Specified Micro-organisms

DETERMINING WHICH ORGANISMS TO USE IN ROUTINE MICROBIOLOGY TESTING

GOING BEYOND PHARMACOPEIA REQUIRED SPECIFIED MICROORGANISMS

Determining which microorganisms to include in your pharmaceutical microbiology testing is a complex undertaking. The objectionable status of an organism or appropriate use for an environmental isolate is dependent on many variables. Auditors and regulators expect manufacturers to know and document all the variable information about their product and its intended use to make appropriate decisions regarding batch release. A formal risk assessment will help laboratories establish a list of objectionable organisms and environmental isolates to include in their microbiological assay.

Common questions that factor into a comprehensive risk-assessment include:

THE DATA

- How often has the organism been found?
- Does trending data show an increase in instances?

THE LOCATION

- Where was the organism found?
- Was it found in a critical zone such as a cleanroom?

THE ORGANISM

- What are the characteristics of the organism?
- What is the pathogenicity of the organism?
- What is the organism's infectious dose?

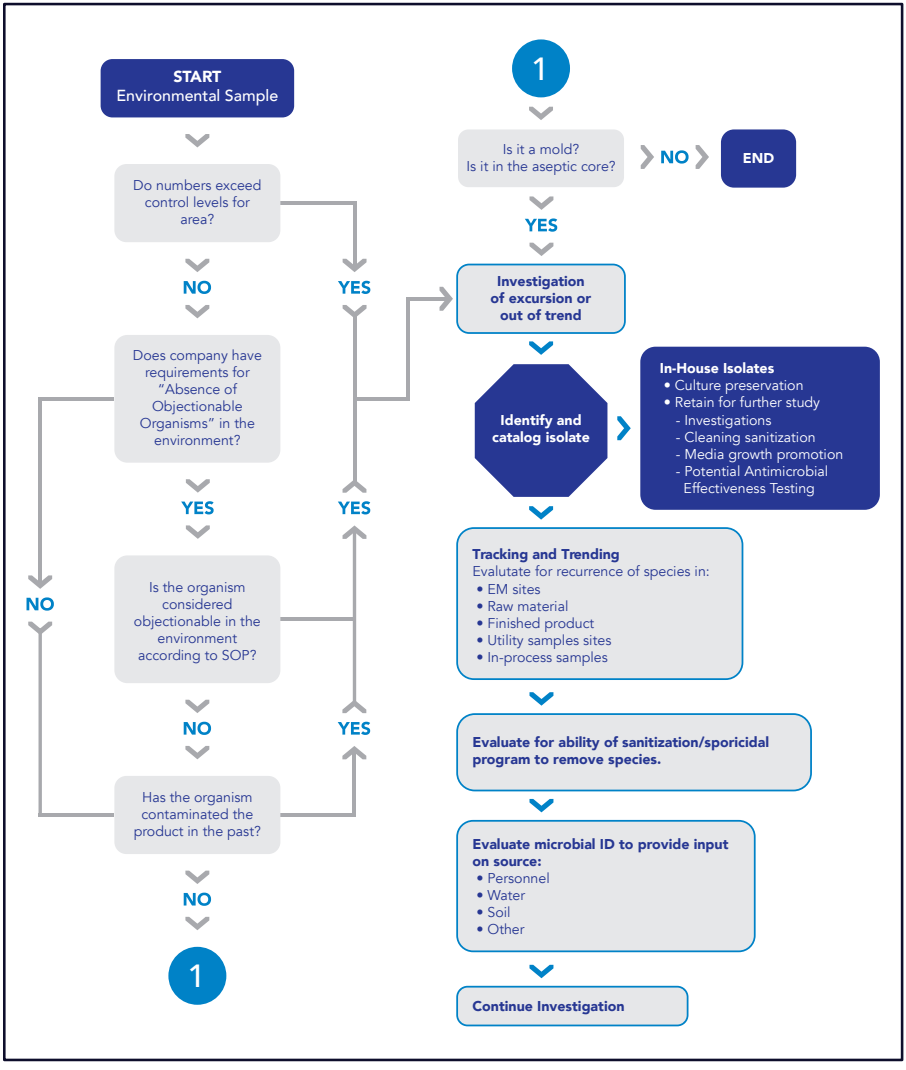
THE PRODUCT

- What is the pH and water activity of the product?
- What nutrients are in the product?
- Does the organism use these nutrients?
- What is the product's method of application?
- Can the organism cause spoilage or degrade the drug or component?

THE CONSUMER

- Who is the intended recipient of the product?
- Is the consumer immunocompromised or otherwise at risk?
- Is the organism harmful for the intended consumer?

ENVIRONMENTAL ISOLATE DECISION TREE



With all the necessary information, microbiologists can make a scientifically-sound, risk-based decision about the appropriate use for environmental isolates. Microbiologics created this decision tree, in partnership with the late Scott Sutton, Ph.D., as a quick reference for charting a course of action when isolates are recovered from an environmental sample.

COMMON APPLICATIONS FOR ENVIRONMENTAL ISOLATES & OBJECTIONABLE ORGANISMS

The following are common assays where environmental isolates and objectionable organisms may be included:

United States Pharmacopeia (USP)

- Antimicrobial Effectiveness Testing – USP <51>
- Aseptic Processing Environment – USP <1116>
- Disinfectant Qualification – USP <1072>
- Growth Promotion Testing – USP <61> | <62> | <71>
- Suitability Testing – USP <51> | <61> | <62> | <71>
- Validation of Neutralization Methods – USP <1227>
- Water for Pharmaceutical Purposes – USP <1231>

European Pharmacopoeia (Ph. Eur.)

- Antimicrobial Effectiveness Testing – Ph. Eur. 5.1.3
- Growth Promotion Testing – Ph. Eur. 2.6.1 | 2.6.12 | 2.6.13
- Suitability Testing – Ph. Eur. 2.6.1 | 2.6.12 | 2.6.13 | 5.1.3

Japanese Pharmacopoeia (JP)

- Antimicrobial Effectiveness Testing – JP 19
- Growth Promotion Testing – JP 4.05, I.3 | 4.05, II.2 | 4.06, III.02
- Suitability Testing – JP 4.05, I.3 | 4.05, II.2 | 4.06, III.02

TEST-READY FORMATS FOR COMMON APPLICATIONS

QUICK AND EASY TEST-READY FORMATS

We have an extensive portfolio of microbial control kits designed for the most common pharmaceutical microbiology test methods. Many times, customers look for these same formats to use in their environmental monitoring and quality control programs. The product formats listed in this section serve as a starting point. Additional customization can be done to meet your needs.

KITS FOR GROWTH PROMOTION TESTING

Product	Packaging/Contents	Enumeration	Specifications
EZ-Accu Shot™	Kit containing 5 vials of lyophilized microorganism pellets and 5 vials of hydrating fluid. Packaged in a plastic container.	Delivers 10-100 CFU per 0.1 ml	- Instant dissolve - No dilutions - 50 tests per kit - 8 hour stability at 2-8°C
EZ-CFU™ One Step	Kit containing 2 vials of 10 lyophilized microorganism pellets and 10 vials of Hydrating Fluid. Packaged in a plastic container.	Delivers 10-100 CFU per 0.1 ml	- No dilutions - 190 tests per kit
EZ-CFU™	Kit containing 2 vials of 10 lyophilized microorganism pellets and 10 vials of Hydrating Fluid. Packaged in a plastic container.	Delivers 10-100 CFU per 0.1 ml	- Requires a 1:10 dilution step - 900+ tests per kit

KIT FOR DISINFECTANT QUALIFICATION, METHOD SUITABILITY & WATER TESTING

Product	Packaging/Contents	Enumeration
Epower™	Vial of 10 lyophilized microorganism pellets. Packaged in a plastic container.	Available in concentrations ranging from 10^2 to 10^8 CFU per pellet

KIT FOR ANTIMICROBIAL EFFECTIVENESS & PRESERVATIVE EFFICACY TESTING

Product	Packaging/Contents	Enumeration
EZ-PEC™	Kit containing 2 vials of 10 lyophilized microorganism pellets and 10 vials of Hydrating Fluid. Packaged in a plastic container.	Final concentration of 10^5 to 10^6 CFU per ml of product tested

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