Microbial Contamination and Control Conference

Case Study: Expediting Mold Investigations with Biofluorescent Particle Counting (BFPC) Technology

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PDA® Parenteral Drug Association Midwest Chapter

Agenda

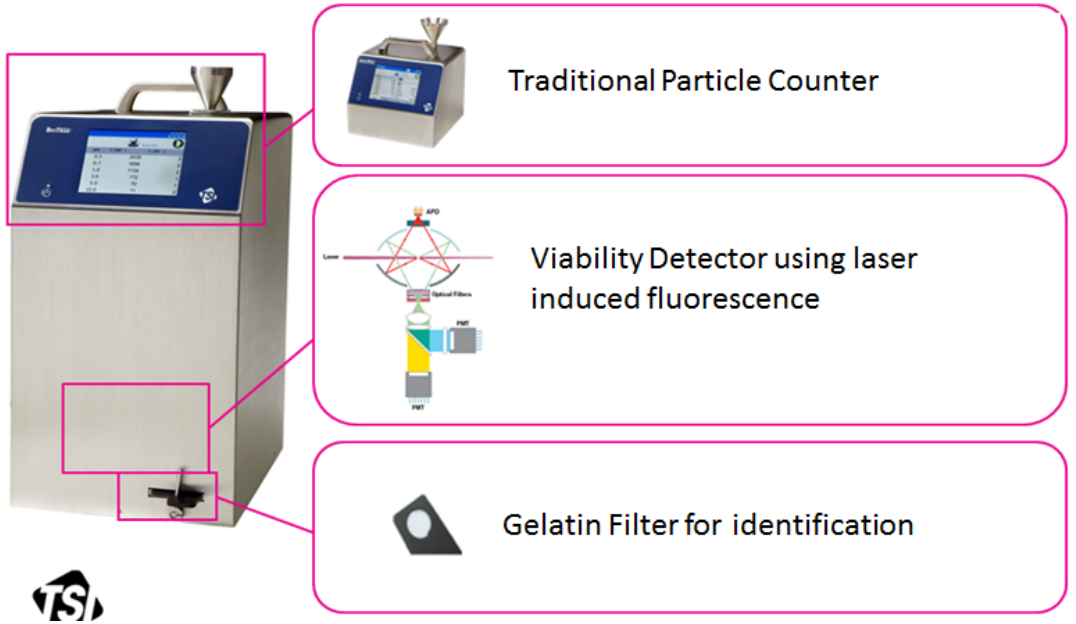
- BFPC Technology Overview
- Integration of BFPC into Root Cause Analysis
- Case Study
- Additional Applications Beyond Investigations
- Overall Conclusions

BFPC Technology Overview

Biofluorescent Particle Counter (BFPC)

- BFPC is a real-time rapid alternative method for traditional EM for measuring airborne viable particle counts
- Laser excitation of particles results in bio-fluorescence of biological compounds allowing for real time detection

Image of BioTrak (BFPC)



BFPC System Operation

Scanning Mode:

Scan a source and supply immediate feedback on airborne viable levels from a specific location

Continuous Mode:

Will provide time related results that can be used to correlate increased contamination levels with such things as manufacturing activities, shift changes, cleaning, equipment operations, HVAC cycles, etc.

Comparison of Technologies

Traditional EM

- 5-7 days time to result
- Difficult to determine root cause
- Delays product batch release
- On-risk manufacturing
- Human manipulation in classified areas

BFPC

- Real time results
- Enables fast root cause analysis
- Real time results enable quicker batch release
- Improves manufacturing quality decisions
- Reduces operator manipulation assuring product quality

Integration of BFPC into Root Cause Analysis (RCA)

Integrating BFPC into RCA

Response to an Excursion

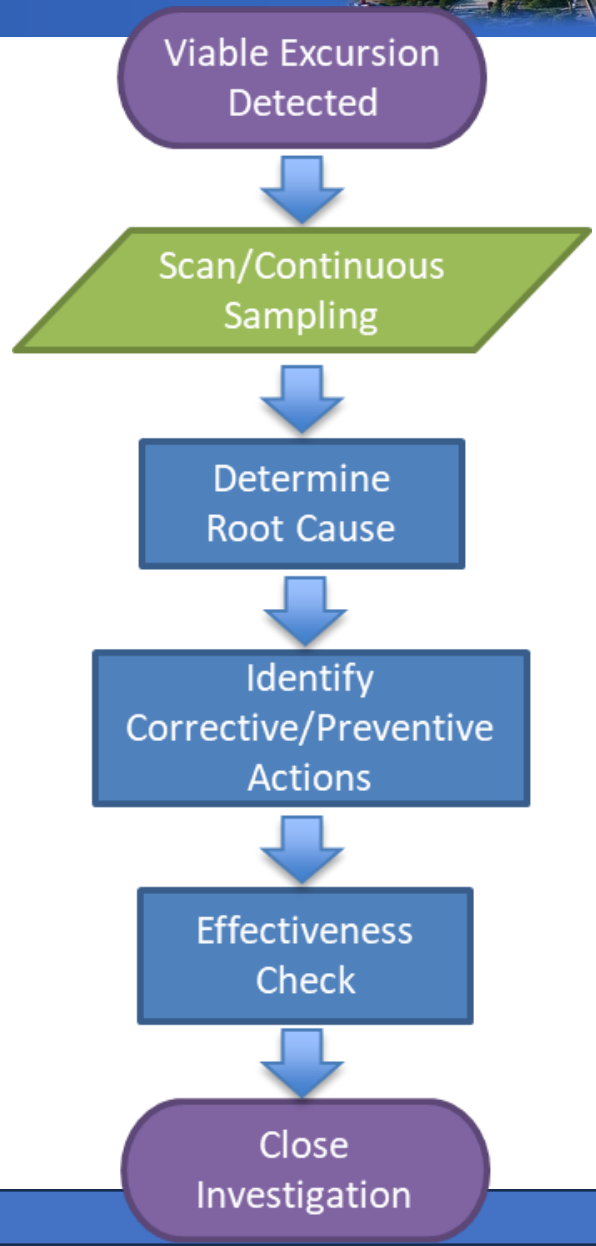
•Sample at additional locations in the area where the excursion occurred to gather more data

Source Identification

•Scan specific sources and/or allow it to run continuously to see if actions/process cause increase in viable particles

Effectiveness Check

•Confirm successful remediation activities



Use Considerations

Getting Started

- Training for how to use unit
- Safety
- Confirm calibration
- Pilot/test unit to ensure functionality and for general familiarity
- Cross contamination considerations
- Disinfection for material transfer
- Set-up data capture
- Outline sampling locations and type of sampling – scan or continuous
- Estimate of time needed to sample areas

Use Considerations

Protocol

- Purpose for use
- Sampling locations/Type of sampling
- Establish baseline
- Documentation of observations
- How data will be used

Case Study

Event Description

- An increase in mold excursions (viable air and surface) was observed
- Excursions occurred in a Grade D, component wash/prep room
- Primary locations for excursions included a transfer cart, floor sample near floor drain and eyewash station

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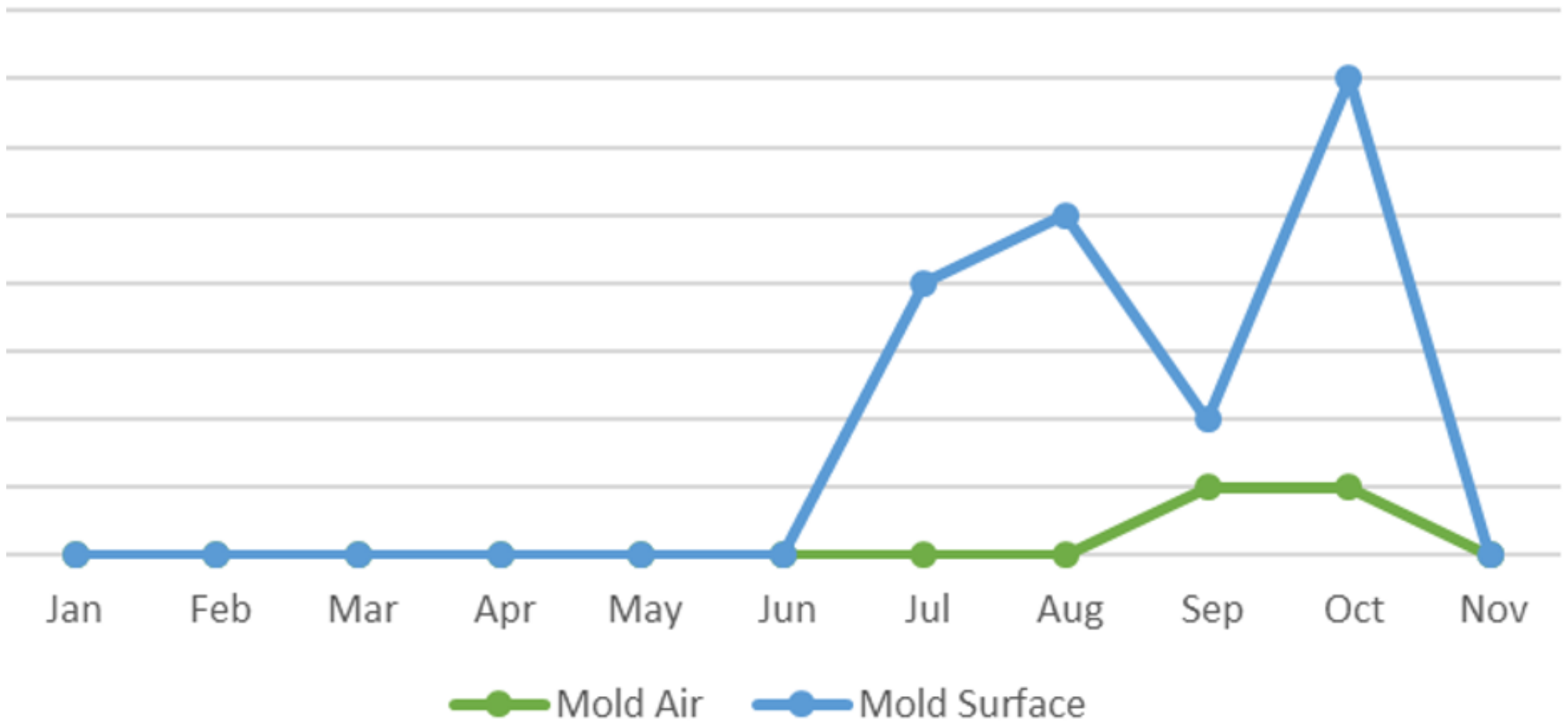
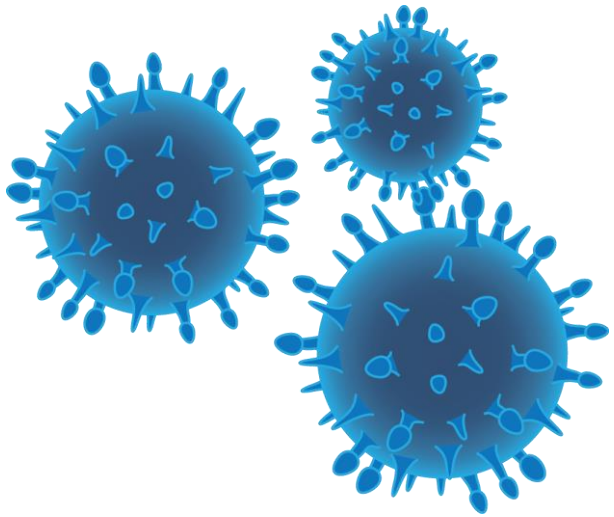
Mold Recoveries in Grade D Wash Room



Microbial Contamination

Source



Origin of Microbial Contaminant

Point of Entry

Location where microbial contaminant entered manufacturing area

Vector

Mechanism that combined point of entry and source resulting in contamination

Investigation

SOURCE	POINT OF ENTRY	VECTOR
- Investigational Sampling + **BioTrak®***	- Facility Walk Throughs	- Personnel Flow/Activity
- EM Trending	- Process Reviews	- Material Transfer
- Historical Data	- Recent Changes	
- Cleaning/Disinfectant/ Decontaminant Review		

***BioTrak® – Specific biofluorescent particle counter used to support investigation**

Investigation

- Initial Investigation utilized traditional EM sampling
- Multiple rounds of EM sampling were performed and yielded some information to support root cause, but ultimately did not result in remediation
- Limitations in pinpointing areas of contamination included:
    1. Lack of real time feedback due to required incubation period
    2. Inability to completely survey entire area due to predefined sample locations

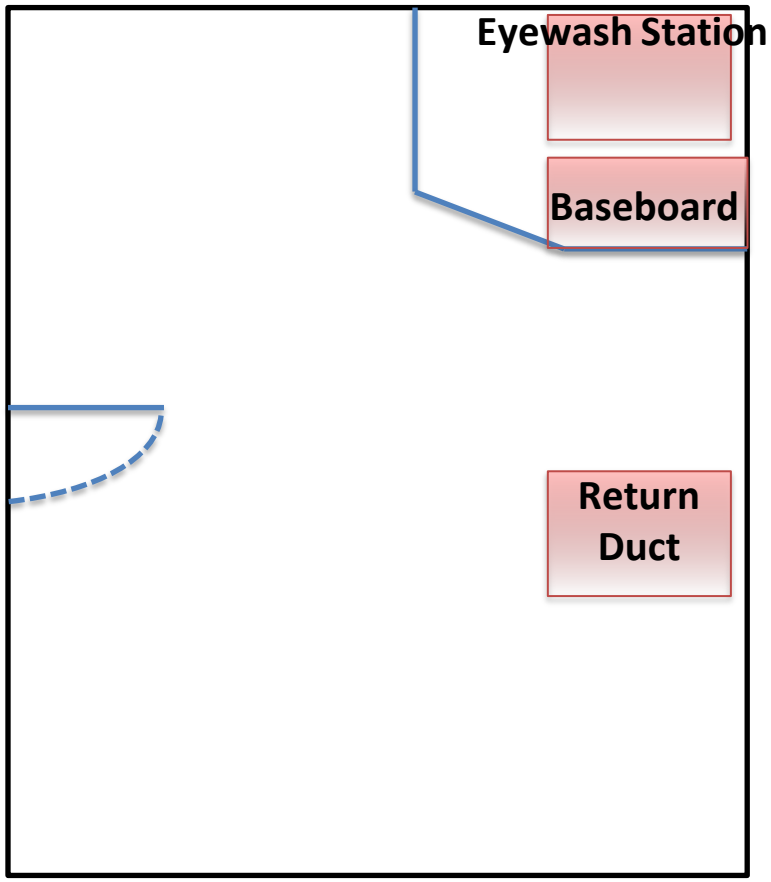
Investigation

- BioTrak® was added to the investigation toolkit after lack of success with EM sampling
  - Analogous to a metal detector, the BioTrak® provided real time feedback, but in this case for potential microorganisms present in the area
  - It provided an immediate signal and visibility to areas that may not have been previously considered a concern
  - Parallel EM samples (surface) were taken with the BioTrak® to confirm contamination and support ID of the microorganism of concern

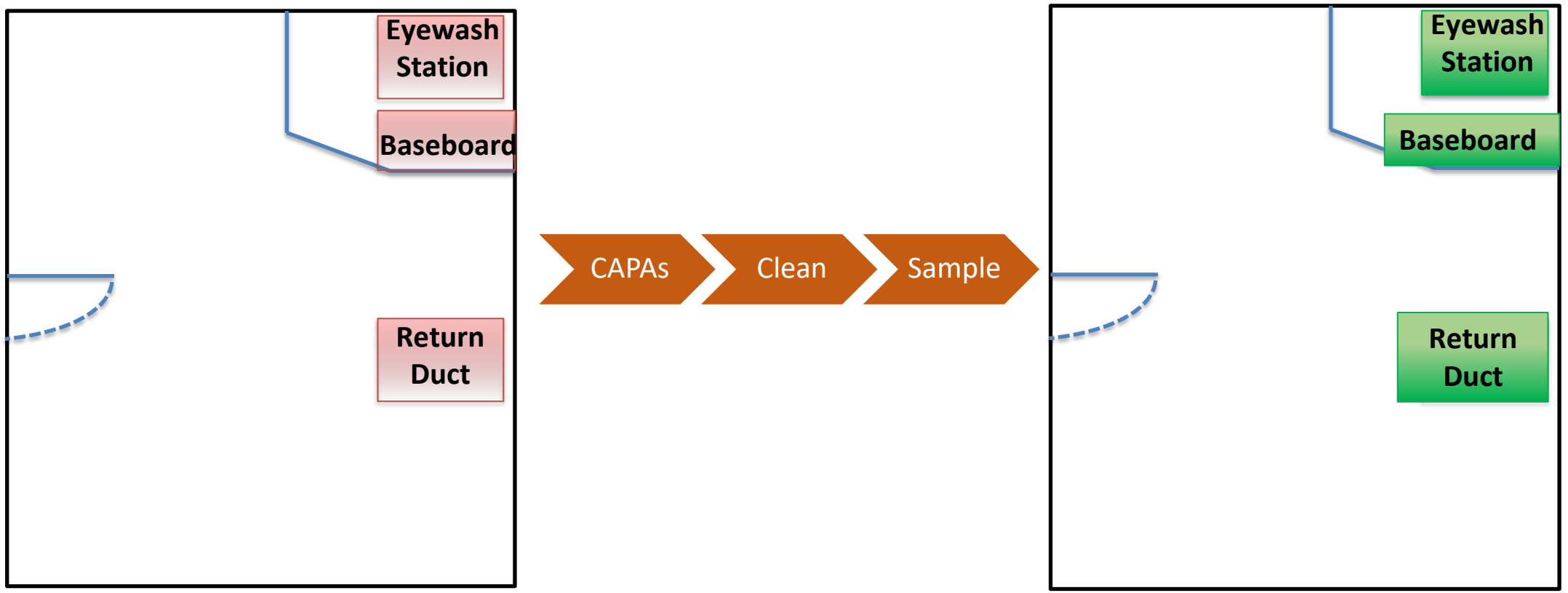
Incorporation of BioTrak® alleviated limitations of traditional EM methods and enabled pinpointing of areas of contamination

BioTrak® Results – Grade D Wash Room

- Sampling of Grade D Component Prep/Wash Room
- Detected areas of potential **VIABLE** particles
  - Baseboard
  - Return Duct
  - Emergency Eyewash Station



Grade D Wash Room Remediation



BioTrak® supported identification of sources of contamination and provided immediate feedback for effective remediation

Root Cause Analysis

Source

Water Leak Event

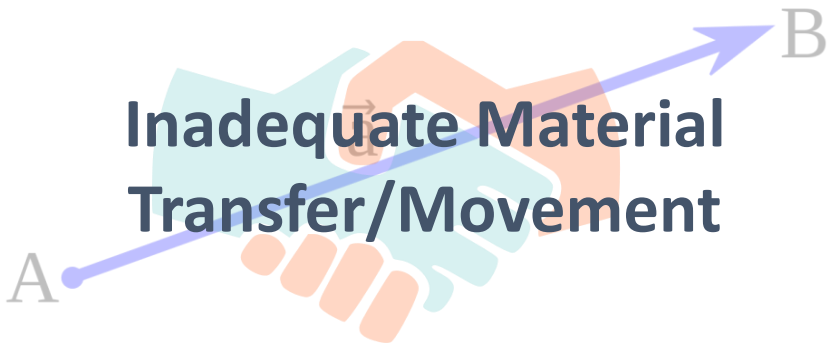
Origin of Microbial Contaminant

Point of Entry

Ingress in Grade D Room

Location where microbial contaminant entered manufacturing area

Vector



Inadequate Material Transfer/Movement

Mechanism that combined point of entry and source resulting in contamination

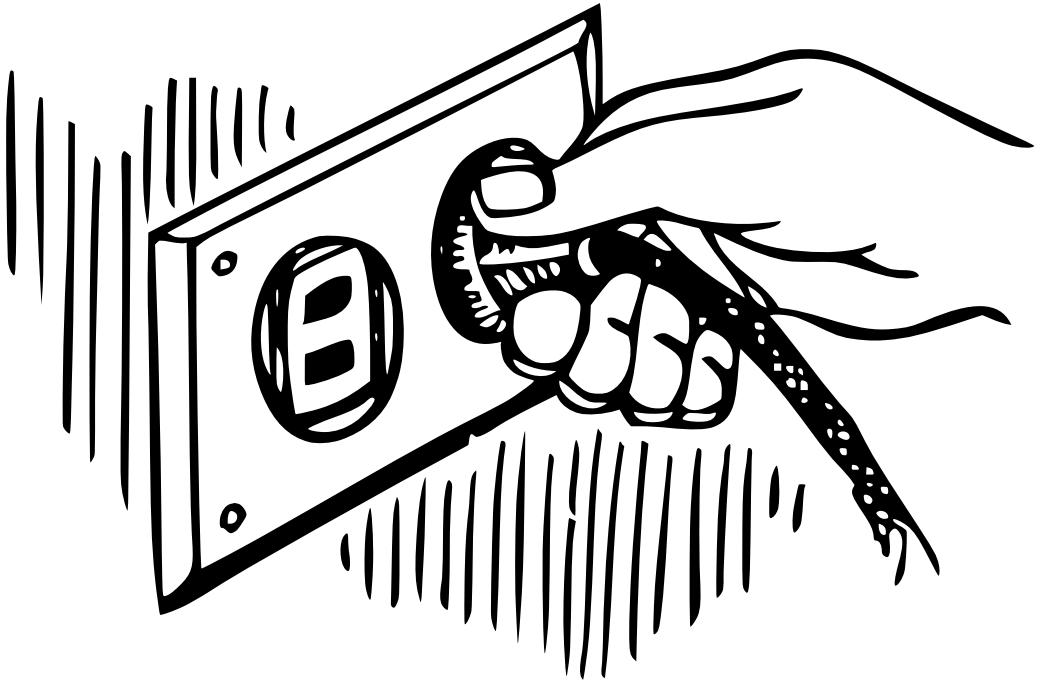
Regulatory Feedback

- Investigation reviewed during FDA audit
- Feedback from auditor was positive
- Use of the BioTrak to support root cause analysis was acknowledged and appreciated

Additional Investigation Examples

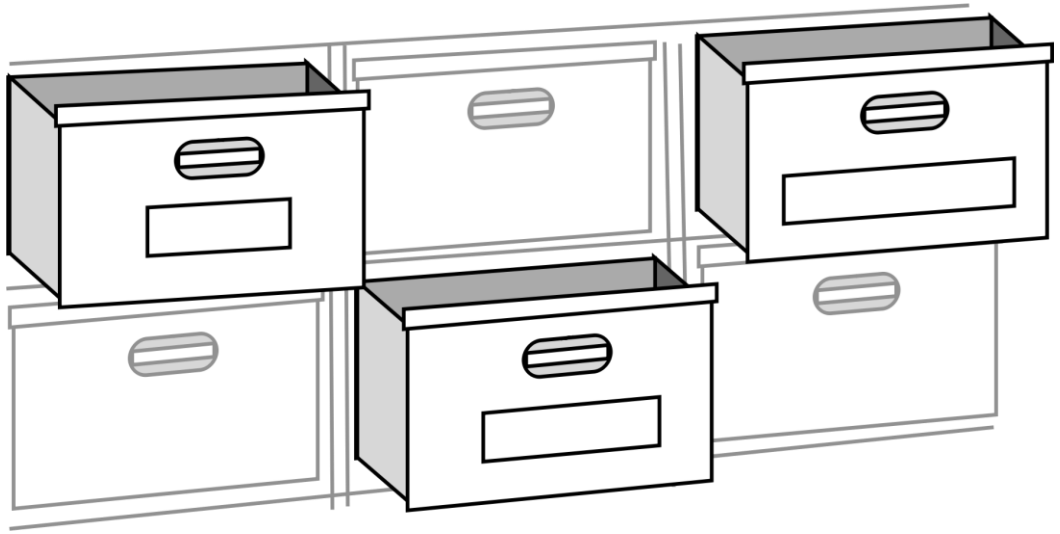
Investigation Examples

- Example 1 – Containment facility pressure cascades altered due to adjacent construction leading to increased mold recoveries
  - BioTrak® detected ingress at electrical outlets



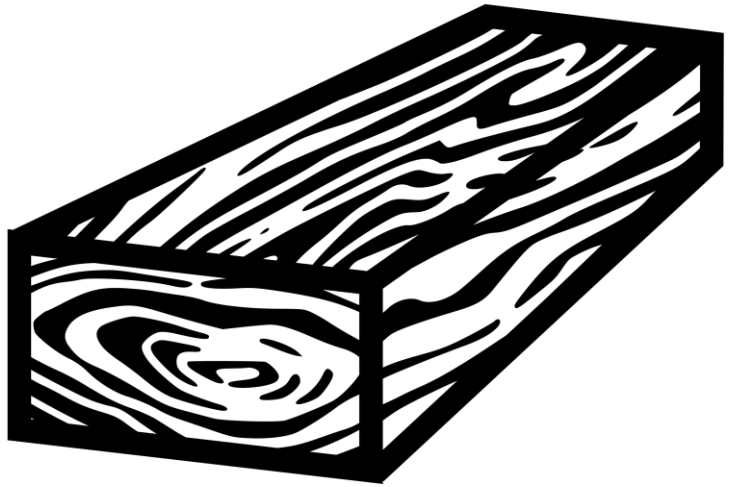
Investigation Examples

- Example 2 – Increased mold recoveries identified with fixed furnishing in room
  - Signal detected when drawers/storage were open



Investigation Examples

- Example 3 – Construction spacer made of wood left behind within ceiling from construction
  - Signal from Biotrak® at ceiling location



Investigation Examples

- Example 4 – Confirmation that environment had no signal encouraged site to consider other modes of introduction
  - Management of sampling identified as source

Investigation Examples

In all cases, successful remediation could be immediately confirmed with the BioTrak®!

Applications Beyond Investigations

Applications Beyond Investigations

Applications to proactively utilize BFPC to avoid production downtime and prevent excursions

- Shutdowns – sampling of typical areas that have historical excursions and/or scan of facility to confirm absence of contamination post shutdown
- Facility Modifications – scan of area following modifications to establish baseline and confirm no change
- Breaches – sampling of area following mitigation of breach to confirm effectiveness of actions and ensure state of control

Conclusion

Conclusions

- BFPC systems enable an expedited and more efficient investigative process for EM excursions
  - Enables immediate root cause determination and CAPA effectiveness through real time feedback
  - Avoids multiple rounds of sampling and incubation
  - Reduces burden on lab
- BFPC systems can be used proactively to limit risk to production, e.g. post shutdown, breaches or modifications

Acknowledgements

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QUESTIONS