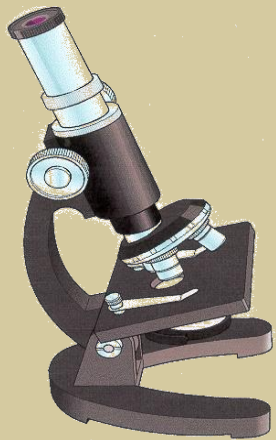


Making Sense of Your Environmental Monitoring Data



*Presented by
Dawn McIver
MicroWorks, Inc.*

Objectives

- Environmental Monitoring Basics
- Importance of Tracking and Trending EM Data
- Techniques for Tracking Data
- What is a trend?
- Techniques for Trending
- Objectionable Organisms
- Summary Report Contents

Types of Environmental Monitoring

Static and Dynamic

- Airborne Non-Viable (Particulate Monitoring)
- Airborne Viable Monitoring
- Surface Monitoring – floors, walls, equipment, etc.
- Personnel Monitoring – gowns and glove
- Some firms include water testing

Particulate Monitoring



Airborne Viable- SAS



Airborne Viable-SMA

IT'S ONETOUCH AWAY™
SMA™ Microbial Air Sampling Systems

SMA OneTouch™ Modules
1 to 10 location flush mount or table top units provide remote start capabilities up to 150 ft. away and eliminate the electronics from the aseptic area.

SMA Control Centers
Enables 1 to 10 location testing to be performed simultaneously or independently with sampling data recorded to PC or Network System. (SMA-CC-10 shown)

The SMA Atrium can
be steam sterilized and located up to 150 ft. away from the control center.

The advertisement features a central image of a control center unit with multiple ports. To its left, a hand points to a wall-mounted module. Below the control center, several circular atrium units are connected to the system by cables. The background is dark, and the text is in a bold, sans-serif font.

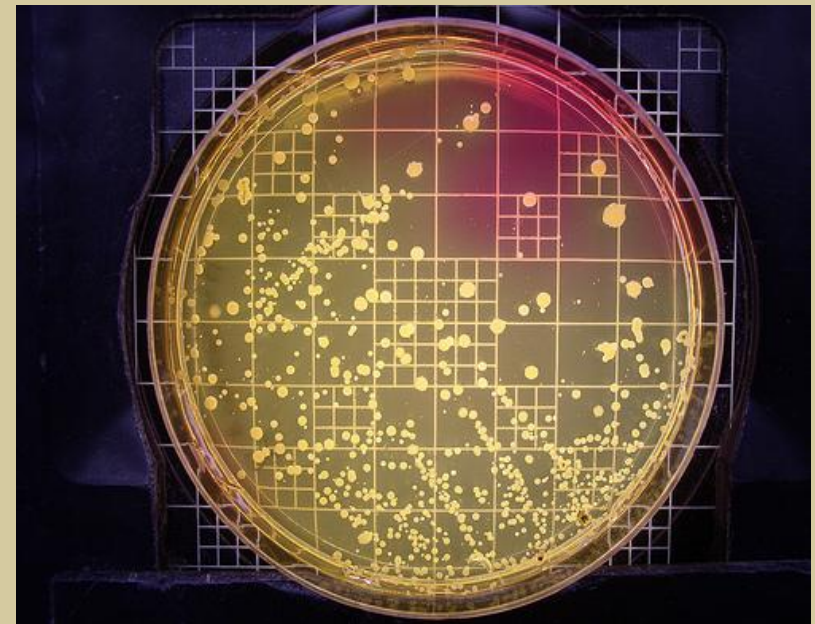
Passive Air-Settle Plates

- Simple and inexpensive way to monitor
- Any type of media can be used
- Small size allows easy placement in a variety of locations
- Allows “continuous” monitoring
- No power connection needed
- Semi-quantitative



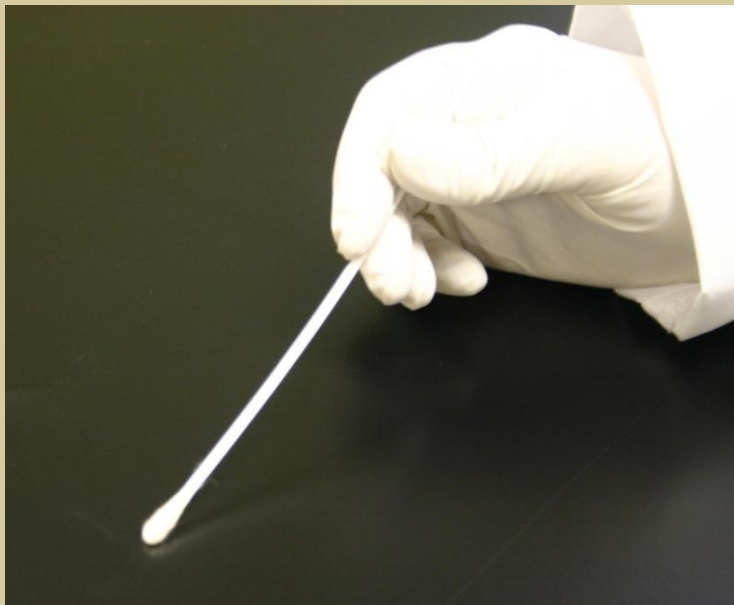
Contact Plates

- Flat, non-porous surfaces
- Standard surface area of 4 sq. in. (25.8 sq. cm.)
- Contact plates are designed to allow contact of the agar with the surface that is being sampled.
- Contact plates should have neutralizers in case sanitizers are picked up during sampling
- Contact plates are placed on the surface to be sampled so that media picks up any organisms that are on the surface.



Swabs

- Cracks, crevices, irregular surfaces, large surface area
- Quantitative or Qualitative



Importance of Trending EM Data

- Input from the participants was as follows:
- Graphical Representation “A picture is worth a thousand word.”
- Assures state of control
- Identify problems before they are to big
- How can you manage If you can't measure?

Importance of Trending EM Data

- Input from the participants was as follows:
- Hard to see day to day
- Proof of control (GMP)
- To set alert limits
- Help identify process improvements
- Help determine if process improvements are effective

Importance of Trending EM Data

- Input from the participants was as follows:
- Because it is required for compliance
- Provides the FDA something to look at to show control/prevention monitoring
- Satisfies regulatory requirements as well as business needs to maintain control of critical production areas
- Allows us to be proactive in cleaning

Importance of Trending EM Data

- 21 CFR 211.113(b): Firms must follow appropriate written procedures designed to prevent microbiological contamination of drug products claiming to be sterile.
- Without tracking and trending it is difficult to show that procedures for preventing contamination are effective.

Importance of Trending EM Data

- FDA 483s and warning letters continuously state issues with review of environmental monitoring data.
- March, 2004 warning letter to a veterinary manufacturing facility: We require to see the data and the analysis of data generated from this monitoring including any trending data.

Techniques for Tracking Data

- Input from the participants was as follows:
- Manual/Paper
- Excel/Minitab
- Legacy LIMS
- Novatek System
- MODA

Techniques for Tracking Data

- Input from the participants was as follows:
- MIMS
- EMS
- Custom system

Techniques for Tracking Data

- Excel Spreadsheet
- MODA™ System
- NOVATEK Software
- LIMS Systems
- Custom Systems

Tracking of Deviations

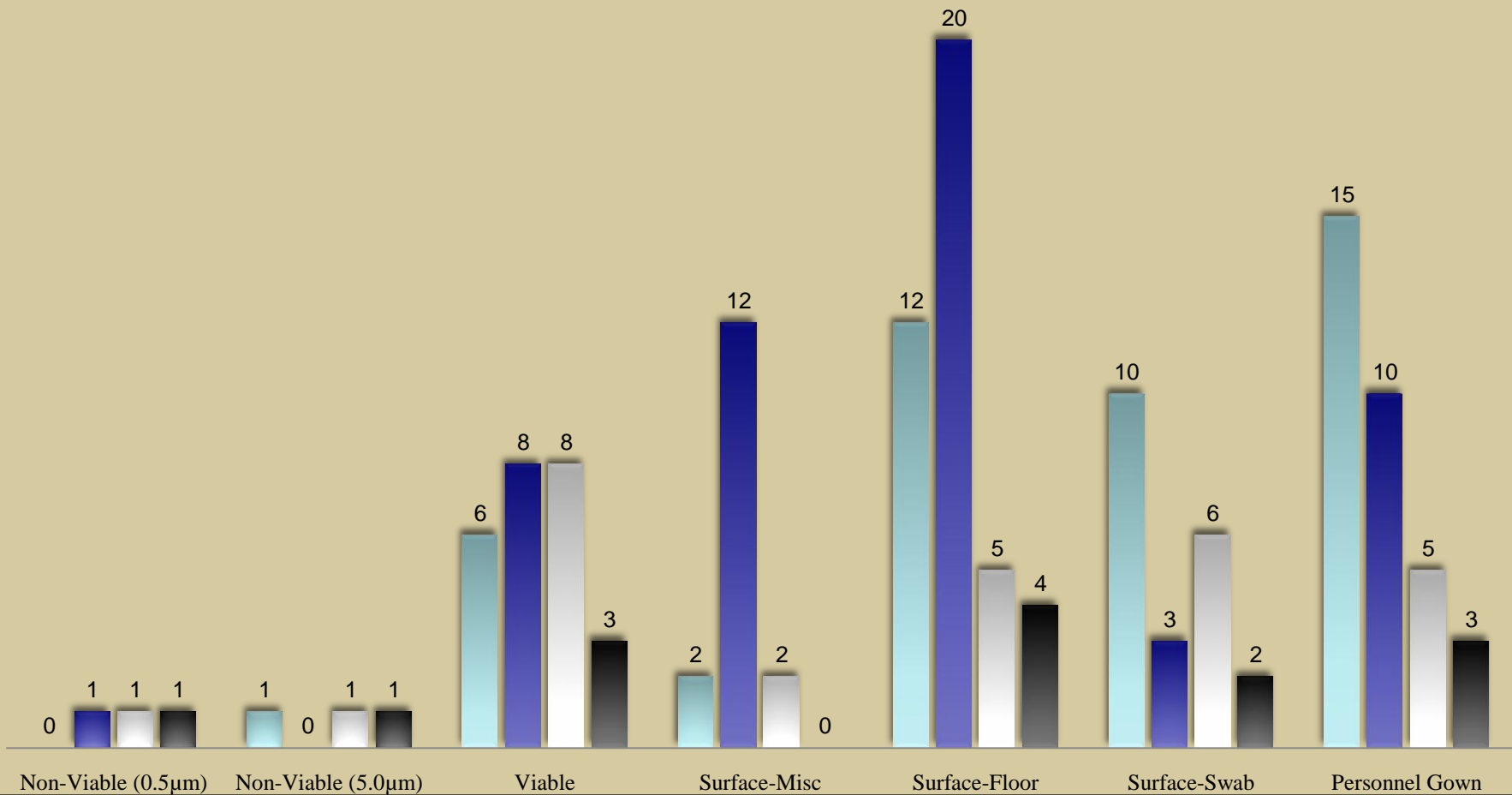
Summary of Deviation Investigations

Deviation	Room	Probable Root Cause	Root Cause Category	Adverse Trend?	Ingress?	Corrective Actions
12345	1	Floor may have become contaminated in the off-season due to floor installation.	Facility/Utility/Equipment	Yes	No	Not applicable. Subsequent sampling revealed no additional excursions.
12346	Personnel	Possible lapse in gowning technique.		Yes	No	CAPA 345. Awareness training and requalification
12347	1	Floor walked on without proper footwear.	Facility/Utility/Equipment	Yes	No	Footwear evaluated.
12348	2	Ingress due to transport of materials into the area.	Materials	Yes	No	CAPA 4346. Create a procedure.
12349	Personnel	Lapse in aseptic technique .	Environment; Operator Error	No	No	CAPA 4347. Awareness training on the incident and proper aseptic technique.
12350	3	Mishandling of 100mm plates after exposure in the fill enclosure.	Method (Process); People	Yes	No	CAPA 4047 Effectiveness Check Assessment.
12351	Personnel	Aseptic technique	People	No	No	CAPA 4100. Awareness training.
12352	Personnel	Operator error. Contamination from surrounding area.	People	Yes	No	CAPA 41030. Change work instructions to wipe bags and tank with SporKlenz prior to use.

Graph from Excel Spreadsheet

Alert and Action Limit Excursions
by Test Type.

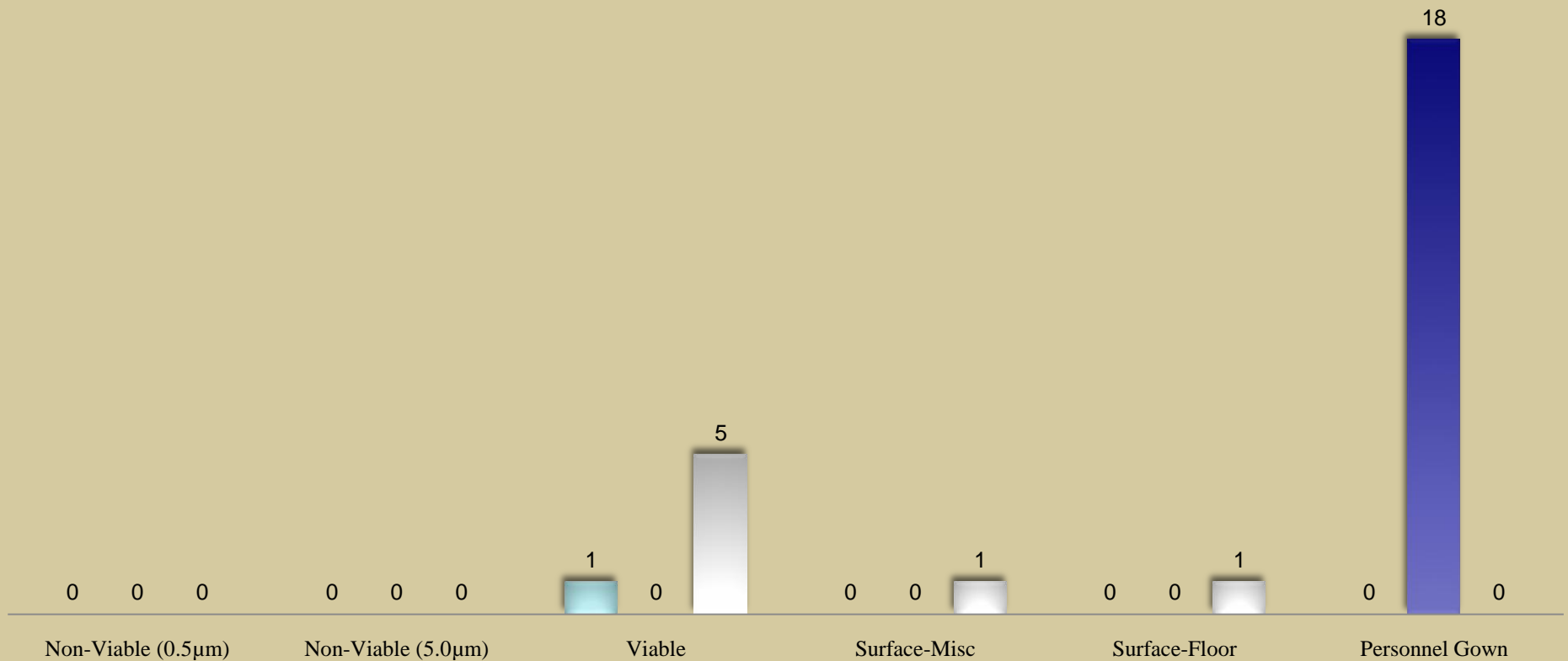
■ Action ■ Alert ■ Alert (Mold) ■ Action (Mold)



Graph from Excel Spreadsheet

Alert and Action Limit Excursions
by Test Type

■ Action ■ Alert ■ Alert (Mold)

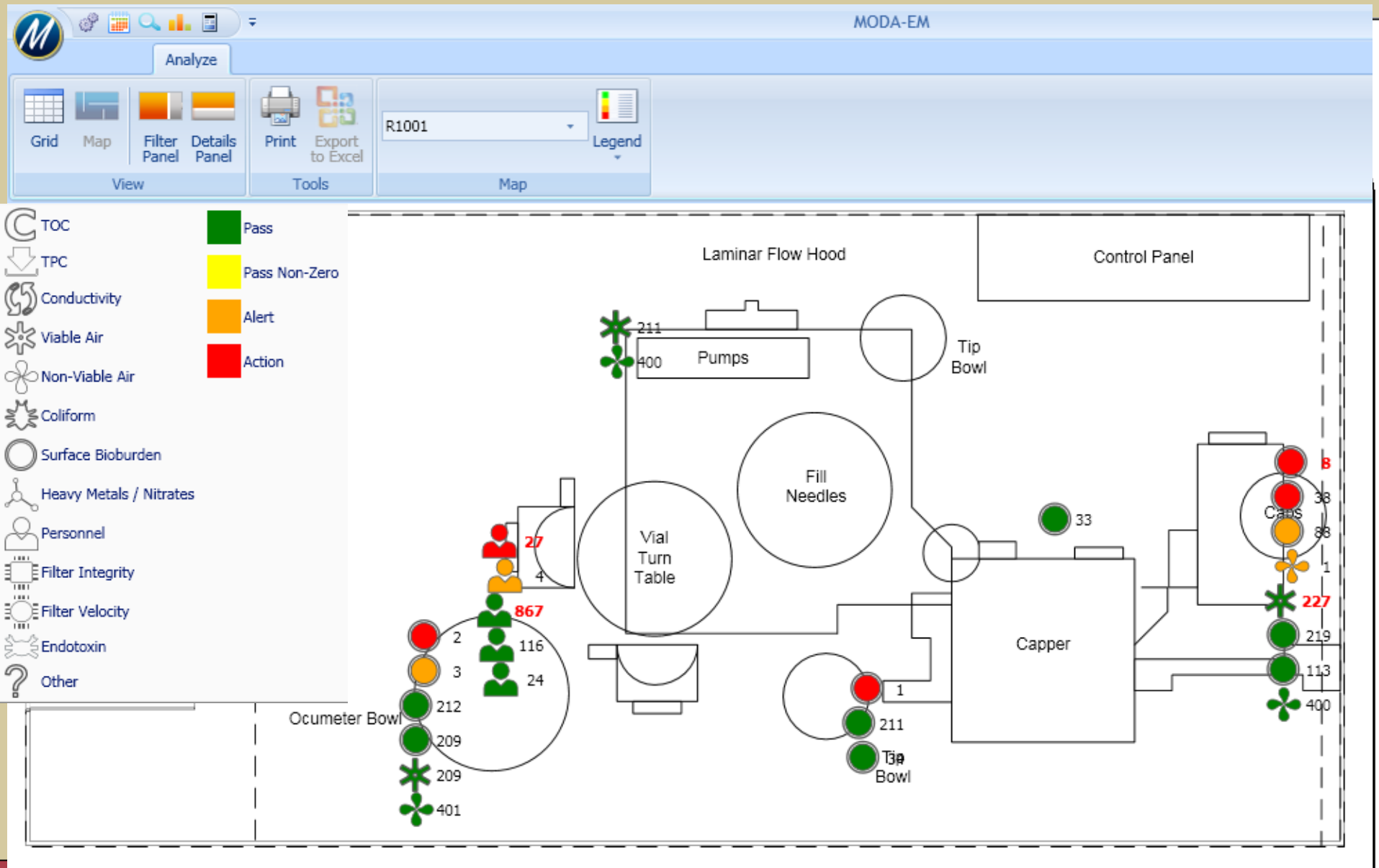


Trending with MODA System

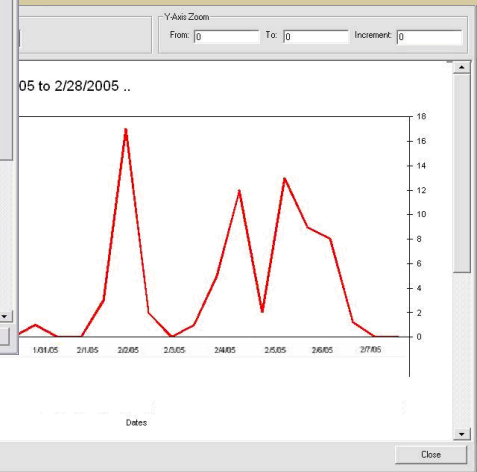
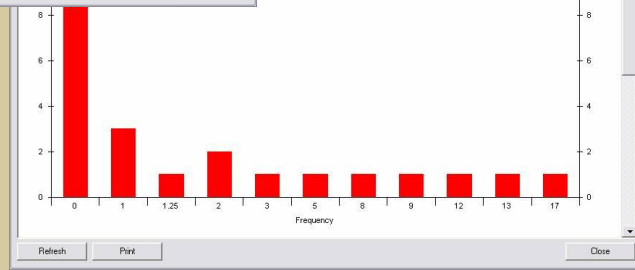
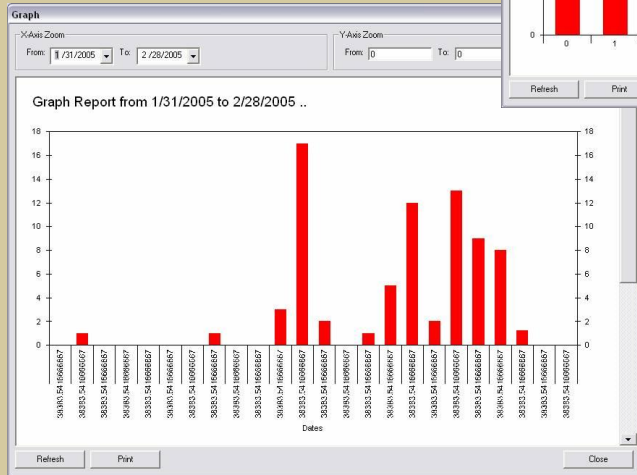
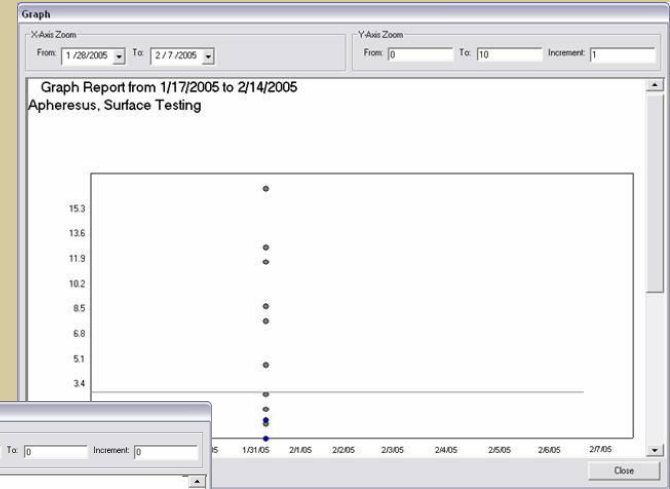
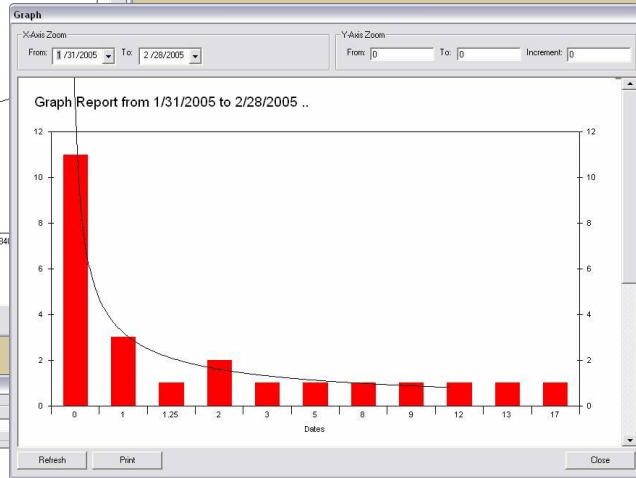
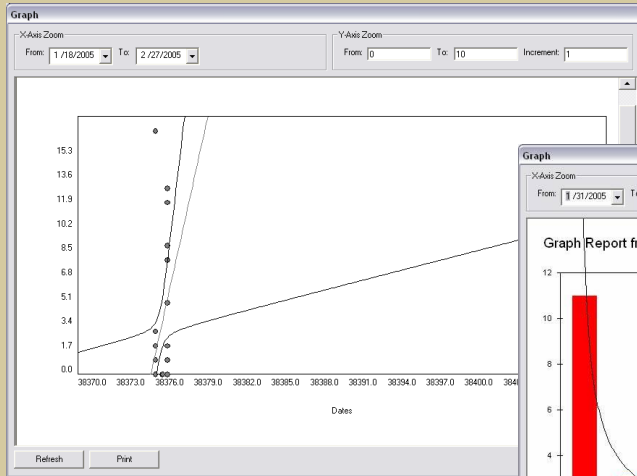


MODA System

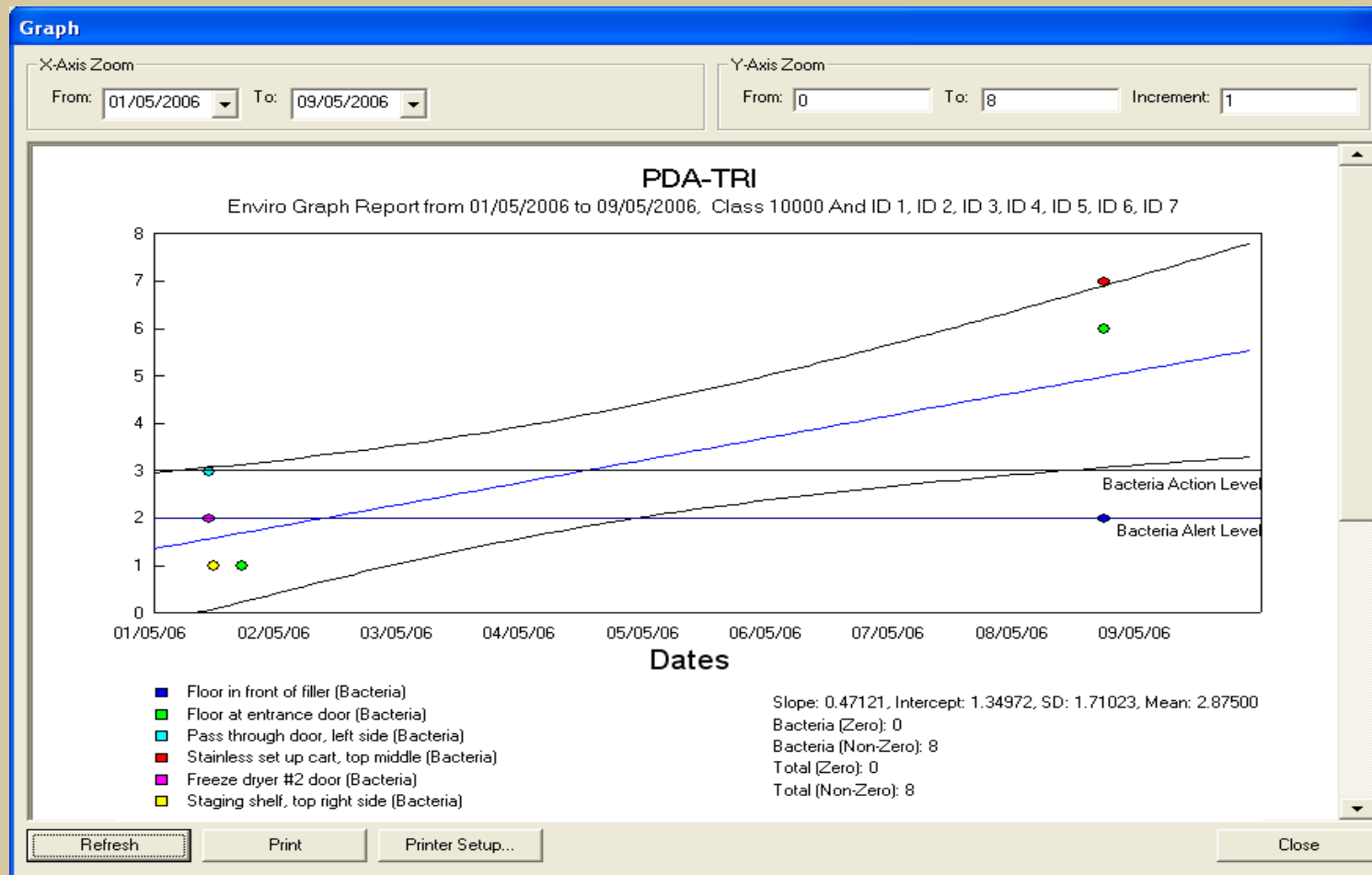
Automated Reporting and Analytics with MODA



Trending with Novatek System



Trend line with Novatek System



- An example of a linear regression showing bacteria found in all Class 10,000 areas grouped by location description for sampling done 8 days apart.

LIMS System

- LabVantage Micro/EM Module

What is a Trend?

- Input from the participants was as follows:
- Data over time which allows the use of statistical data to demonstrate deviations and conformance to established limits.
- Demonstration of product quality
- Should be defined in the company EM policy

What is a Trend?

- Input from the participants was as follows:
- A tendency or drift in condition or performance.
- A number of consecutive readings in a negative direction (i.e. increase in bioburden).
- Consecutive readings equal to or greater than the alert limits.

What is a Trend?

- Definitions should be given in the company environmental monitoring policy to ensure consistency.

How often do you trend?

- Input from the participants was as follows:
- Monthly
- Quarterly
- Annually
- Weekly

Trend Definitions Seen

- Multiple recoveries of the same organism in several locations on the same day or over the course of several days.
- Results that are typically around a known value but are moving upward.
- Alert or action level counts that are generated when re-sampling for previous excursions.

Trend Definitions Seen

- Three or more action level excursions for a sample type on the same day.
- Three or more consecutive action level excursions for a sample type in a room from any sample site on different days.
- Three or more excursions for a sample type in a room from four consecutive samplings.

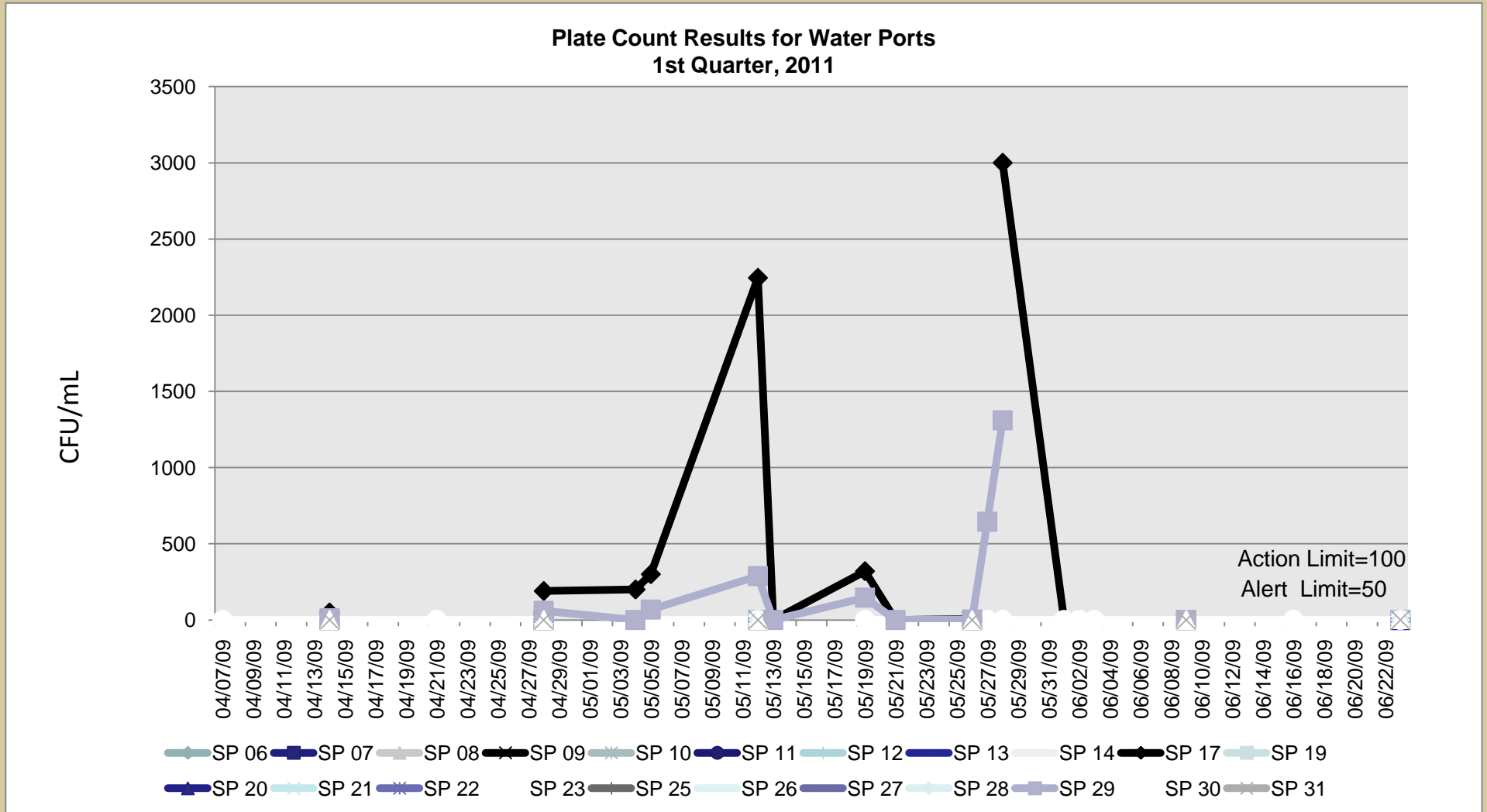
Techniques for Trending

- Input from the participants was as follows:
- Watching closely the data for three months prior to when samples are obtained and identified.
- Trending is performed by comparing the number of colonies during monitoring as well as evaluating recurrences of the same species.

Techniques for Trending

- Prepare a simple line graph of the data collected each month and look for any upward slopes of the lines.
- Graph the data with bar graphs and look for obvious spikes.

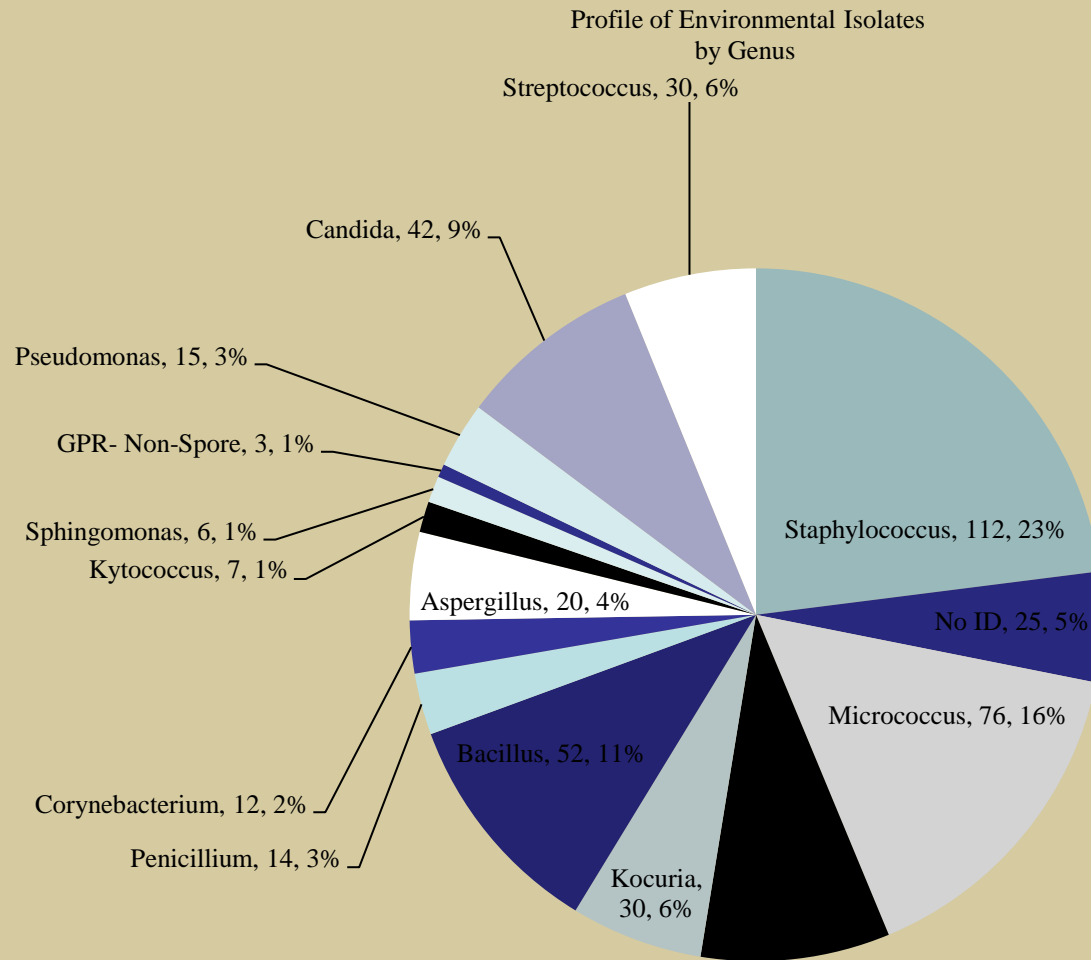
Line Graph of Data



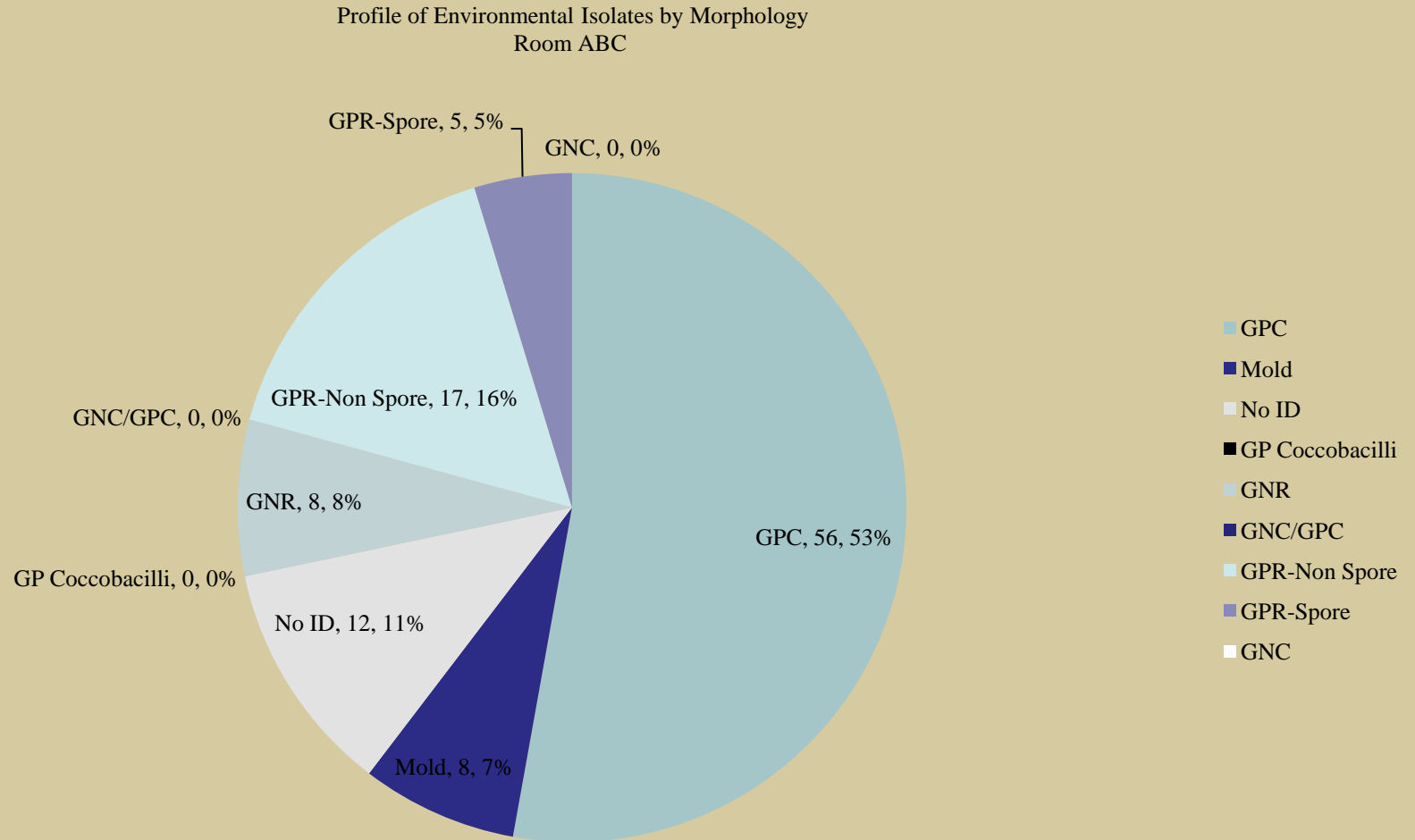
Techniques for Trending Isolates

- Keep a list of all the isolates recovered and identified in the facility.
- Prepare a graph that groups the isolates by Genus.
- This gives you a good idea what the predominant flora are in your facility and shows you if changes are occurring over time.

Trending Microflora by Genus



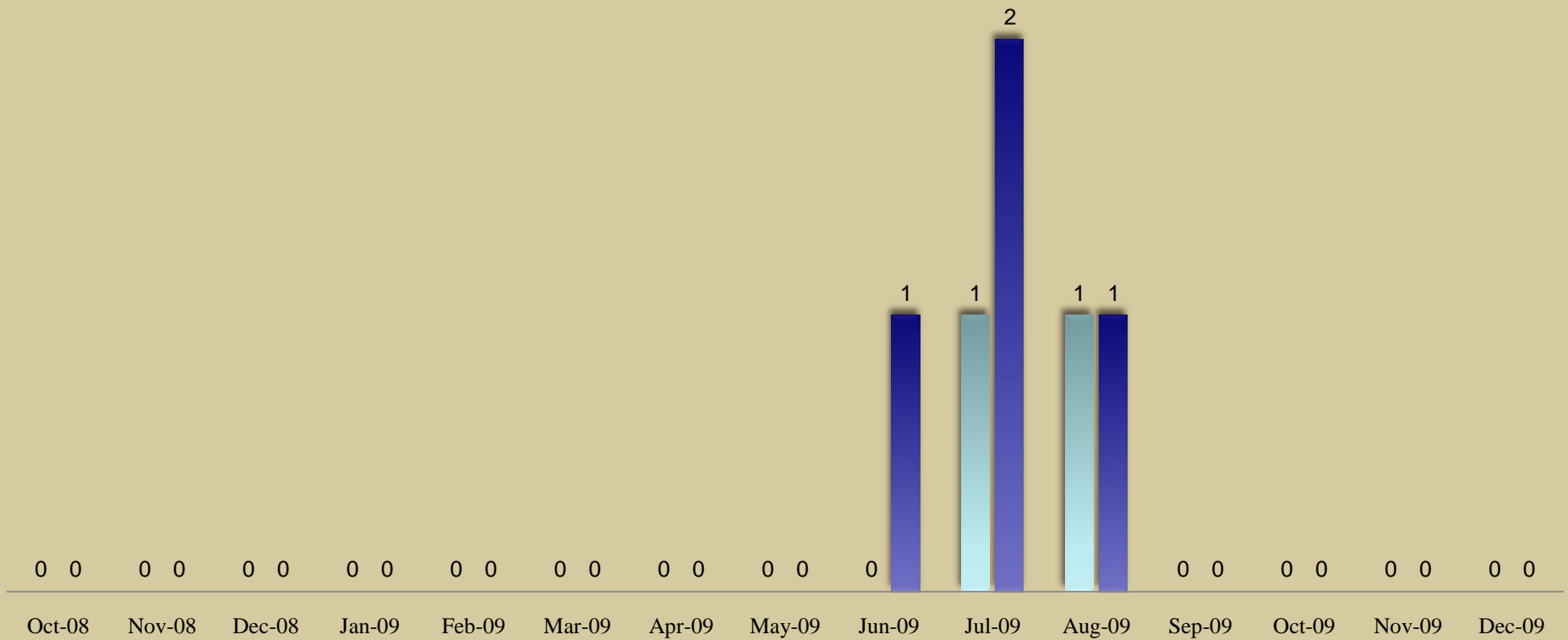
Trending Microflora by Room



Trending Particular “Issues”

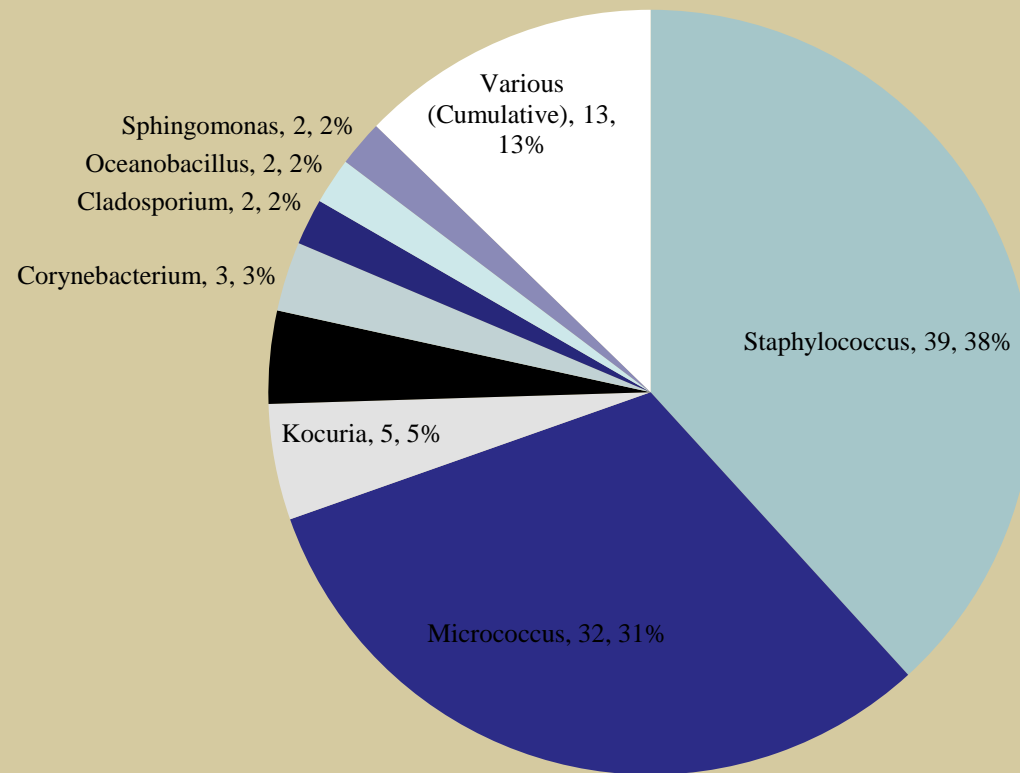
Chronological Incidence
of Spore-Forming Organisms, Class 100

■ GPR-Spore ■ Mold



Personnel Data

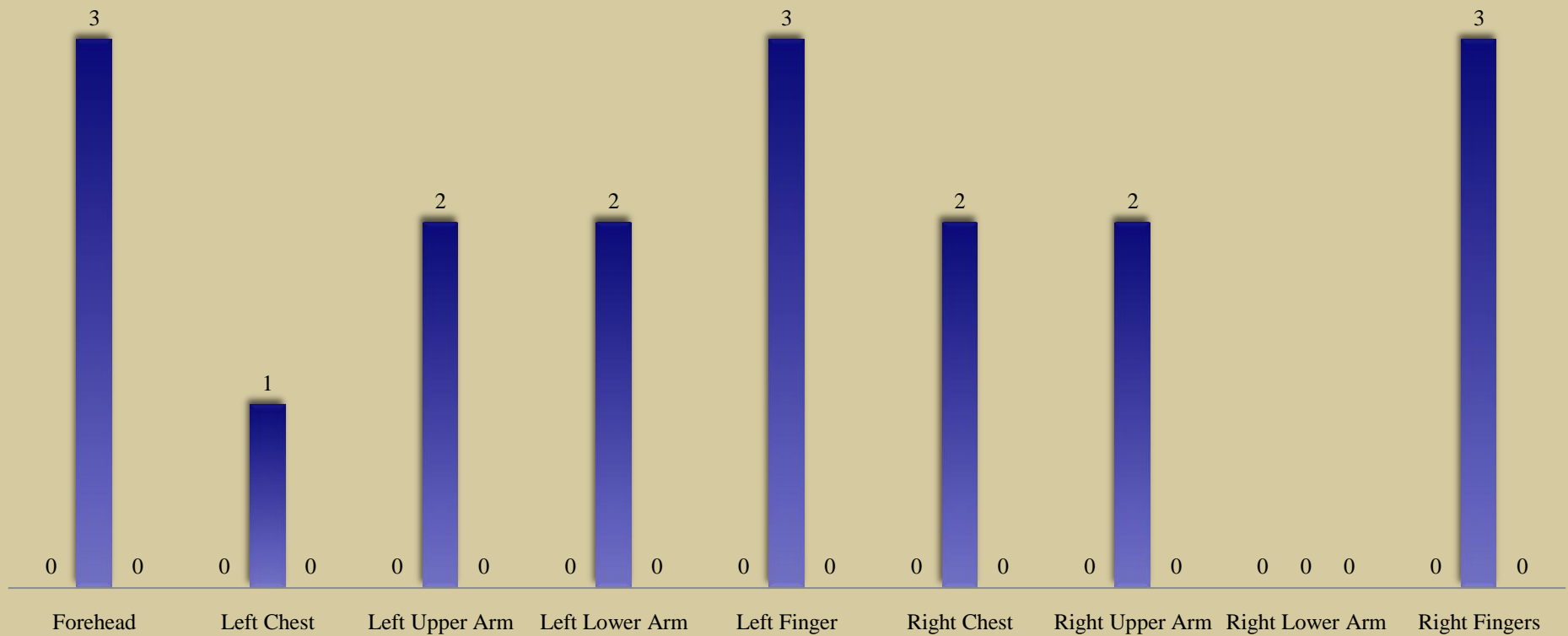
Personnel Microbial Isolates
by Genus



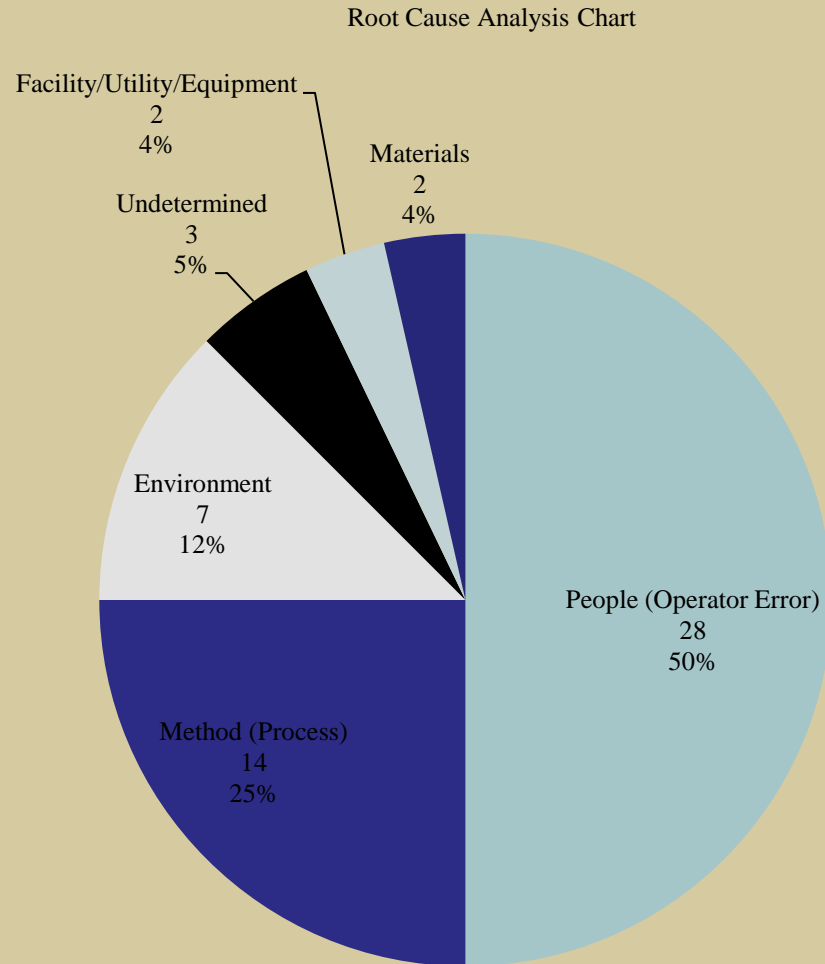
Personnel Data

Alert and Action Limit Excursions
by Personnel Gown Location

■ Action ■ Alert ■ Alert (Mold)



Root Cause Analysis



Summary Report Contents

- List of applicable references for EM SOPs, Personnel and material flow SOPs, Cleaning SOPs
- Facility Description and map
- List of rooms including classification of each room
- Description of facility cleaning
- Types of EM performed

Summary Report Contents

- Summary of Alert and Action levels
- Summary of procedure for response to excursions
- Summary of excursions experienced during the time period being summarized
- Excursion responses and CAPAs
- Changes in procedures during time period

Summary Report Contents

- Tables presenting data for each room including the number and % excursion rate for each type of monitoring
- Comparison to the same table from the previous month or year
- Discussion of significance of any differences seen.

Objectionable Organisms

- Input from the participants was as follows:
- Undesirable
- Detectable
- Harm to patient/customer
- Degradation of product and product stability
- Affect to processing/manufacturing

Objectionable Organisms

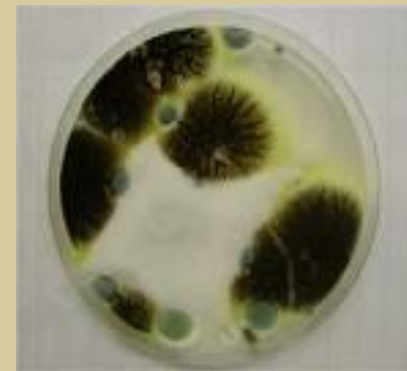
- Input from the participants was as follows:
- As a terminal sterilizer, we define our challenge organisms, *G. sterothermophilus* and *B. atrophaeus*
- Seasonal organisms that come up.
- Any organism having been determined to have an adverse effect on product, based on risk assessment.

Objectionable Organisms

- Input from the participants was as follows:
- Based on compendial requirements
- Organisms that are not normal for your product
- *E. coli* indicates a breakdown in gowning/handwashing

Objectionable Organisms

- Each firm needs to accumulate a list of “objectionable” organisms that are important in their environment or product.
- Each organism recovered needs to be evaluated to determine if it is objectionable.



Objectionable Organisms

- Gram-negative bacteria in high numbers are objectionable in injectable product due to potential for production of endotoxin.
- Mold is objectionable due to the possibility of spreading and resistance to certain sanitizers.

Objectionable Organisms

- Food poisoning organisms such as *Salmonella*, *Listeria*, *E. coli*, *B. cereus*, *Staphylococcus aureus*, *Clostridium botulinum*, *Shigella*, *Campylobacter*, *Vibrio cholerea*, *Clostridium perfringens*, *Yersenia enterocolitica* should raise red flags and warrant further investigation and confirmation.

Objectionable Organisms

- Organisms that are the causative agents in STDs should raise red flags and warrant further investigation and confirmation.
- *Neisseria gonorrhoeae*, *Chlamydia trachomatis*

Objectionable Organisms

- *Legionella* species (Legionnaires disease)
- *Helicobacter pylori* (Gastric ulcers)
- *Borrelia burgdorferi* (Lyme disease)

Objectionable Organisms

- FDA Guide to Inspections of Microbiological Pharmaceutical QC Labs states, “The significance of microorganisms in non-sterile pharmaceutical products should be evaluated in terms of the use of the product, the nature of the product, and the potential hazard to the user”.

Objectionable Organisms

- FDA Guidance continues, “For example, natural plant, animal and mineral products should be tested for *Salmonella*, oral liquids for *E. coli*, topicals for *Pseudomonas aeruginosa* and *S. aureus* and articles intended for rectal, urethral, or vaginal administration for yeast and mold”.

Objectionable Organisms

- FDA Guidance document states, “It is widely recognized that *Pseudomonas cepacia* is objectionable if found in a topical product or nasal solution in high numbers...”
- Microbiological testing may include an identification of colonies found during the Total Plate Count test. Identification should not be limited to USP indicator organisms.

Conclusions

- What regulators are looking for is that the facility is running in a state of control.
- Management is expected to know what EM data means, what the issues have been, what organisms are present in the environment.
- Summaries, tracking and trending are essential to keeping management informed.

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“Mold Art”

