Lonza

Amylin's Improved Aseptic Gowning and Monitoring Program Using MODA™ Solution

Today's Presenters

- **Bob Toal**
  Segment Manager, Informatics
  Lonza Wayne

- **Dominick Villani**
  Manager of QC Microbiology
  Amylin Pharmaceuticals

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60-Minute Agenda

- Lonza Overview

- 45-min Presentation

- 15-min Interactive Q&A

- Upcoming News/Events

- Wrap-up

A copy of this presentation will be made available through a follow up email.
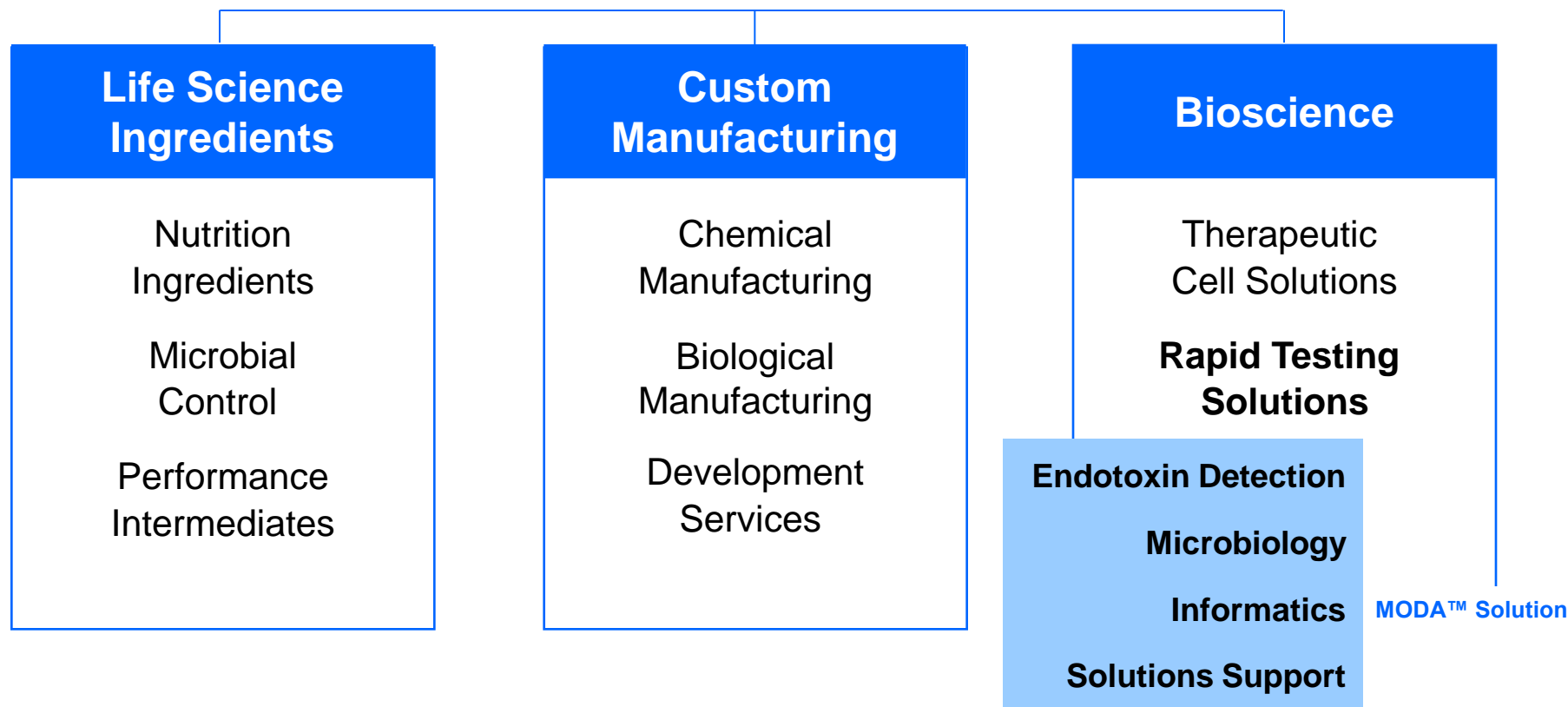
Webinar Focus Areas

- Industry best practices, strategies, and regulatory guidelines

- Definitions of qualification, re-qualification and routine monitoring

- Use of automation and the MODA™ Solution to meet requirements

- Tracking, trending, and report generation compliance using MODA™ Solution

# Lonza

Lonza and MODA™ Solution Overview

B. Toal / Lonza / 07 Jun 2011

Lonza's Life-Science Platform

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Life Science Ingredients	Custom Manufacturing	Bioscience
Nutrition Ingredients	Chemical Manufacturing	Therapeutic Cell Solutions
Microbial Control	Biological Manufacturing	**Rapid Testing Solutions**
Performance Intermediates	Development Services	**Endotoxin Detection**
		Microbiology
		Informatics — MODA™ Solution
		Solutions Support

MODA™ Solution Value Proposition

- **More science. Less paper.™**
  - Quickly move from paper-intensive QC Monitoring & Analysis

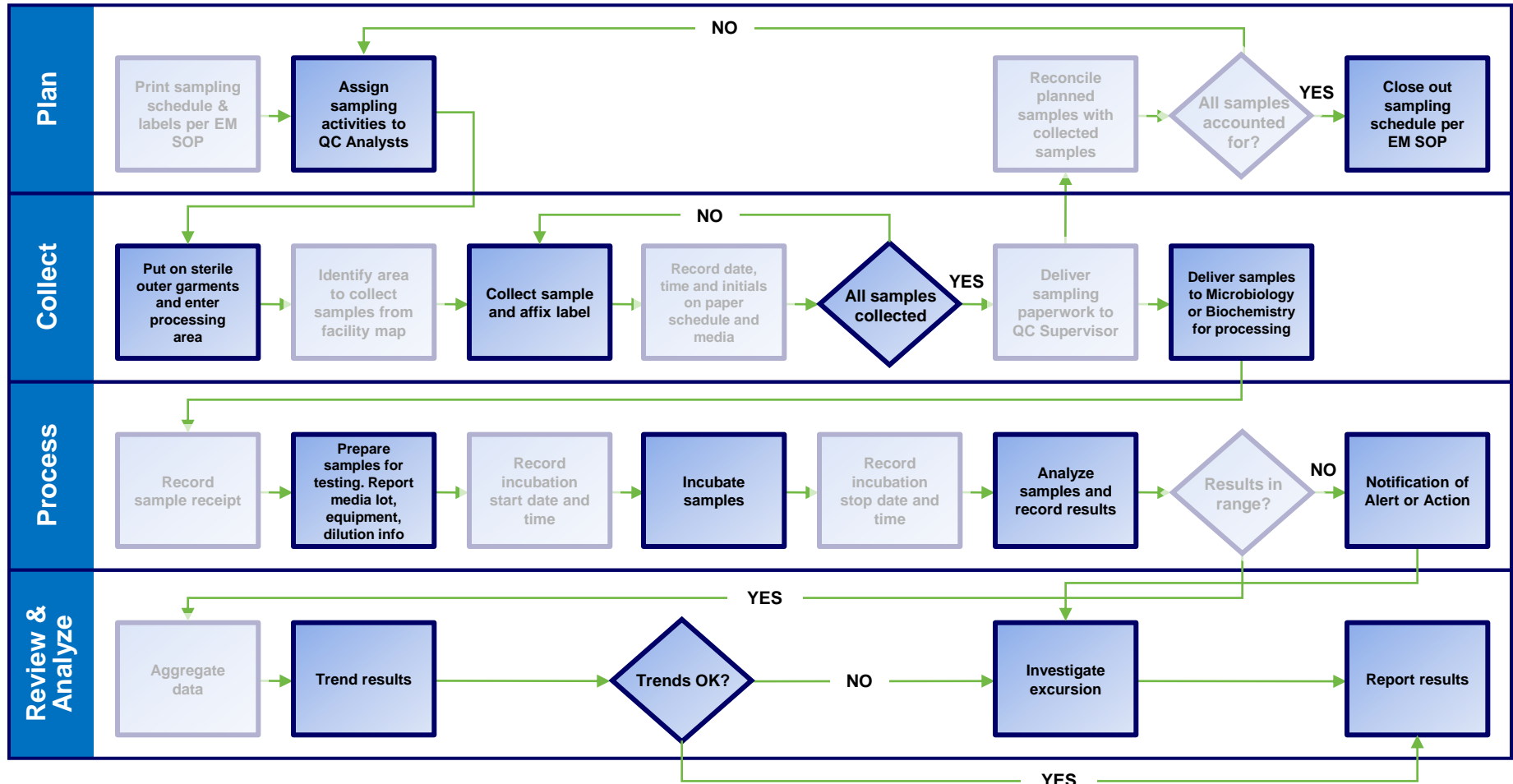- **Increase operational efficiency, improve quality, reduce costs**
  - MODA-EM™ platform offers mobile computing technology & advanced visualization tools

Capture

Track

Visualize

Trend

LONZA
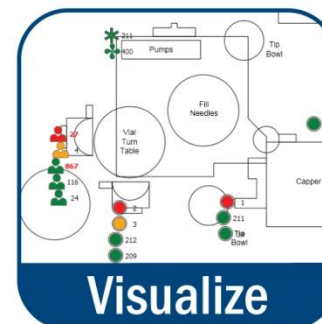
The Paper-based QC Process

Example: QC Sampling and Lab Processing
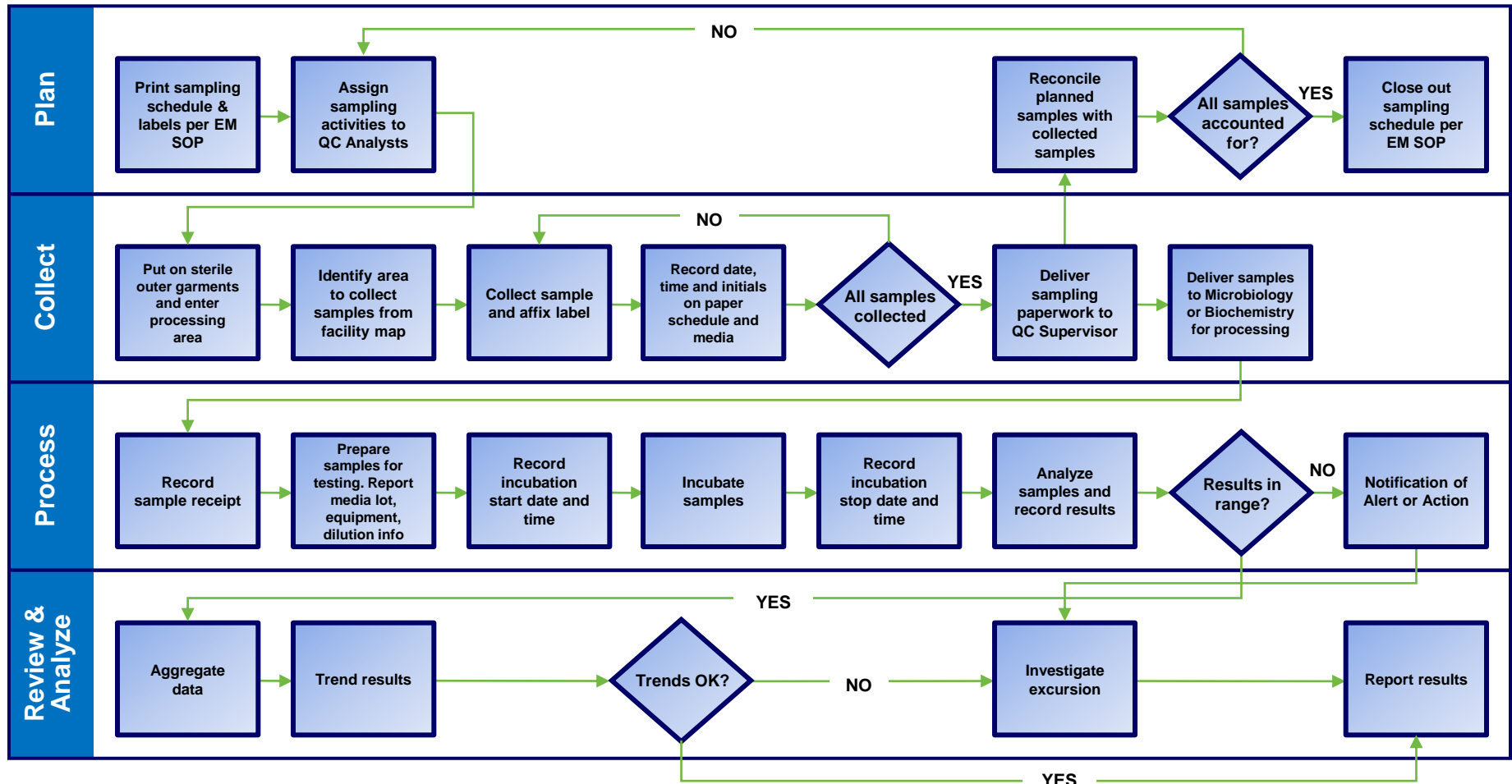
The **Paperless** QC Process—*11 Steps Removed*

Paperless Efficiency Example

Record on paper template	Record on plate	Reconcile media and template	Enter data into Excel/LIMS
1: BB50, SS43, Water, IE5 2: BB50, SS43, RODAC, IP72/IP82 3: BB50, SS44, Water, IE5/IE7 4: BB50, SS44, Water, IE9/SP2 5: BB50, SS65, RODAC, IP74			
6 hours		1 hour	1 hour

Scan room or site	Select sample and print labels	Send to repository	
	P1106-1107		Paper 8 hours
4 hours		Finished	− Paperless 4 Hours
			= **Savings 4 Hours**

Automated Field Data Capture

Featured: MODA-FDC™ platform, used for field data capture in clean room areas

- Stainless steel cart
- Ergonomic tablet PC
- Docking station
- Thermal label printer
- Barcode scanner gun
- Proximity reader for RF badges
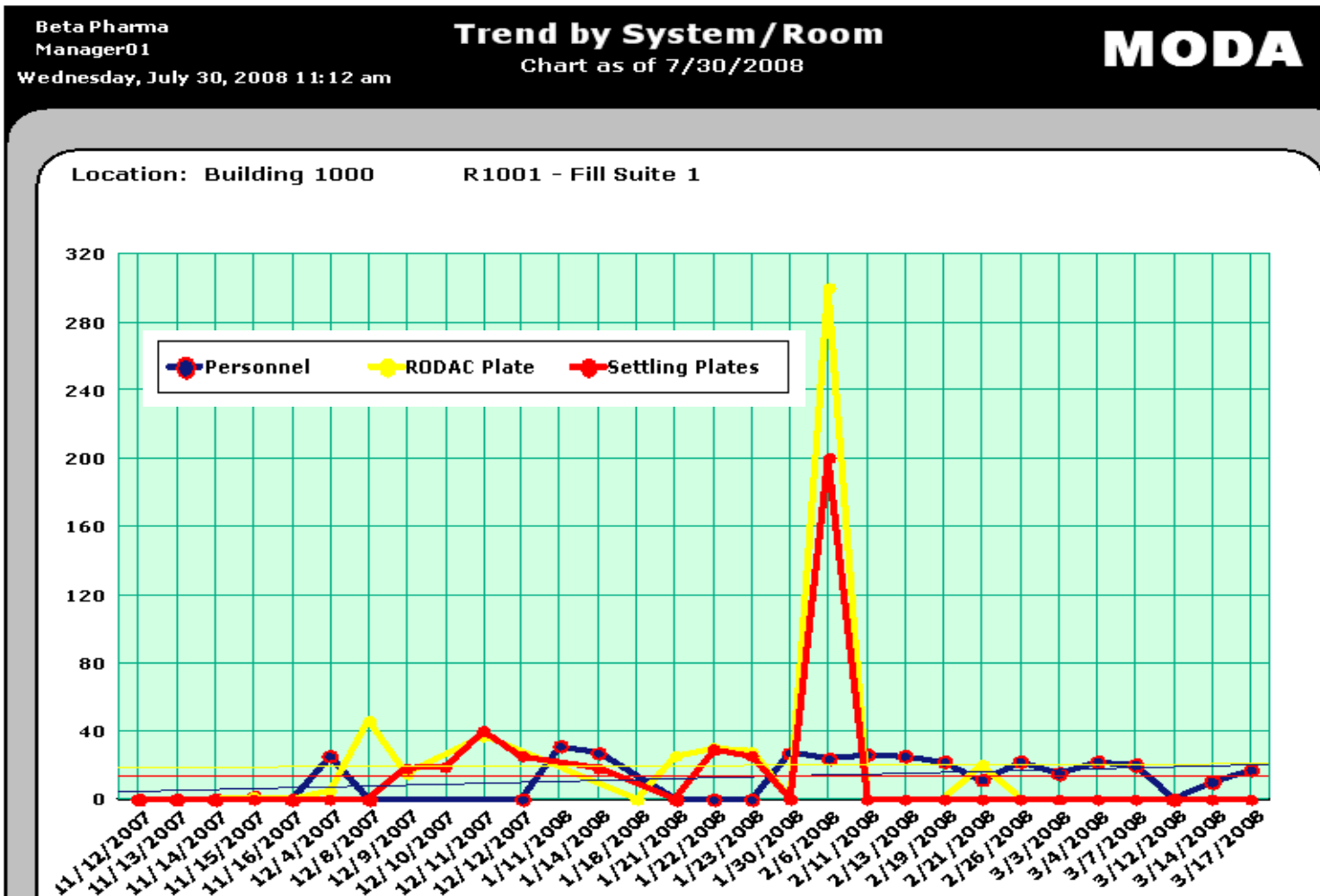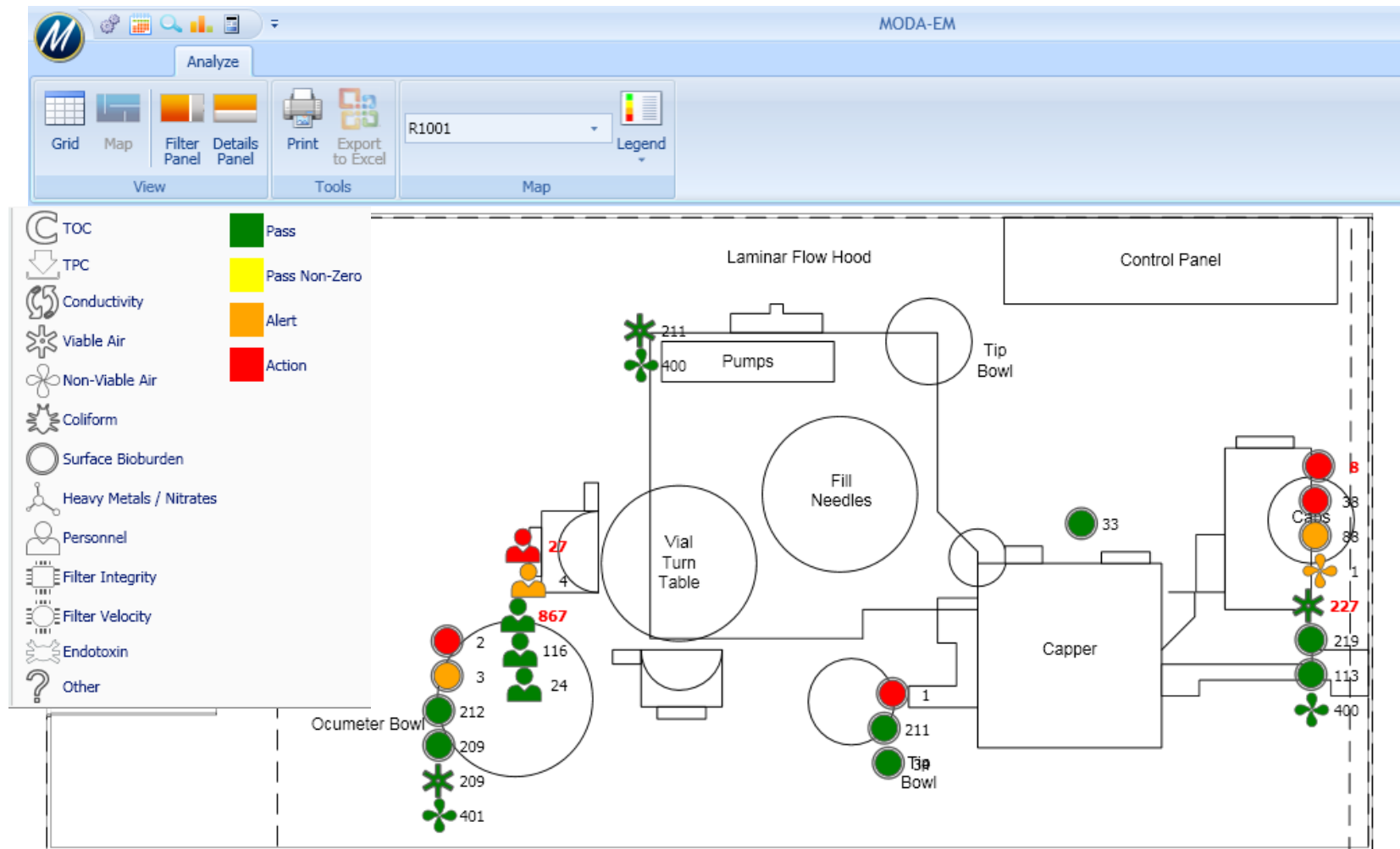- Space for equipment
- Space for growth media

Automated Lab Processing and Reporting

Automated Reporting and Analytics

Automated Reporting and Analytics

Automated Reporting and Analytics

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Our Featured Speaker:
Dom Villani – Amylin Pharmaceuticals

USING MODA™ SOLUTION TO IMPLEMENT AND MAINTAIN A ROBUST AND COMPLIANT ASEPTIC GOWNING QUALIFICATION, RE-QUALIFICATION, AND ROUTINE MONITORING PROGRAM

Presenter: Dominick C. Villani III

07JUN2011

AMYLIN PHARMACEUTICALS

- Amylin produces sterile products through aseptic processing
- Amylin implemented and qualified MODA™ in Q1 2009
- Amylin utilizes MODA™ to track, monitor, and manage all sample plans, sample frequencies, and excursions for classified cleanrooms and critical utilities (i.e. WFI, Clean Steam, Compressed Gases, etc.)
- Amylin currently uses MODA™ 2.3 and is in the process of upgrading to MODA™ 3.0

PRESENTER BIOGRAPHY

Dominick Villani

Manager of Quality Control Microbiology at Amylin OH LLC

- Current responsibilities: Laboratory method development and validation; environmental and utilities monitoring qualifications and routing maintenance programs; and overall Sterility Assurance Programs

- 13+ years experience with GMP manufacturing operations, QC microbiology activities, and QA oversight of GMP facilities at Amgen, Bioport Corporation, Bristol-Myers Squibb, and Amylin

  - 4 years dedicated to the development and management of EM programs, including aseptic gowning, and sterility assurance programs for sterile products

- B.S. in Biological Sciences, with an emphasis in Microbiology

AGENDA AND OBJECTIVES
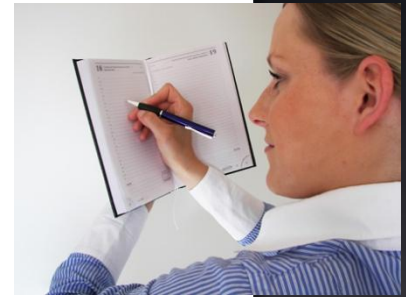
- Regulatory requirements for a compliant aseptic gowning monitoring program

- Industry best practices, guidances and standards for a compliant aseptic gowning monitoring program

- Definitions of qualification, re-qualification, and routine monitoring for aseptic gowning

- Requirements and guidelines for investigations, immediate actions, and corrective actions

- MODA™ Solution advantages and solutions for implementing and managing a compliant aseptic gowning monitoring program

ASEPTIC GOWNING INTRODUCTION

- The quality of a company's product(s) can be directly defined and assessed based on:
    - Robustness of its aseptic gowning program
    - Data produced from that program
- Good aseptic gowning results signify that:
    - The company and its employees are committed to quality
    - The site and process are in a state of control

ASEPTIC GOWNING INTRODUCTION

- Aseptic gowning is by far the most important and critical operation for manufacturers of sterile products using aseptic operations. The program must be:
  - Intensive, robust, and rigid, with defined actions and consequences
  - Balanced to manage business and compliance expectations
  - Evolutionary and current
  - Timely

ASEPTIC GOWNING INTRODUCTION

- The aseptic gowning program must be monitored, managed, and updated in the same way critical utility systems (e.g. WFI) are treated.
  - Sample plans
  - Sample frequencies
  - Sampling methods
  - Timely reporting
  - Data trending

ASEPTIC GOWNING INTRODUCTION

- Who defines the requirements and components of an aseptic gowning program?
  - Regulatory bodies
  - Industry best practices, guidances, and standards
  - Company management
- Who defends the requirements and components of an aseptic gowning program?
  - Company management
- Who is responsible for the requirements, components, and data of program to inspectors?
  - Company management

REGULATORY REQUIREMENTS

- Regulatory requirements:
  - Legal requirements
  - Based on the drug market
  - Are *minimum* requirements

REGULATORY REQUIREMENTS

United States

21CFR 210 & 211, "cGMP in Manufacturing, Processing, Packing, or Holding of Drugs and Finished Pharmaceuticals"
- 21CFR 211.25 (a) – Personnel Qualifications
- 21CFR 211.28 (a), (b), and (d) – Personnel Responsibilities
- 21CFR 211.113 (b) – Control of Microbiological Contamination

European Union

Eudralex Volume 4, "Good Manufacturing Practice Medicinal Products for Human and Veterinary Use"
- Chapter 2, "Personnel"
  - 2.10, "Training"
  - 2.13, 2.15, 2.18, "Personnel Hygiene"
- Chapter 5, "Production"
  - 5.18 "Prevention of Cross-Contamination in Production"

REGULATORY REQUIREMENTS

Japan

Japanese GMPs, "GMP Guideline for Drugs and Quasi-Drugs (Drug Products) 2005"
- Section 3, "Personnel"
  - 3.10, "Personnel Qualifications"
  - 3.20, 3.22, "Education and Training"
  - 3.30, 3.31, 3.3, "Personnel Hygiene Control"
- Section 7, "Production and In-Process Control"
  - 7.6, "Microbiological Contamination Control"

Harmonization

ICH Harmonised Tripartite Guideline Q7, "Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients"
- Section 3, "Personnel"
  - 3.10, 3.12, "Personnel Qualifications"
  - 3.20, 3.21, 3.24, "Personnel Hygiene"

REGULATORY REQUIREMENTS

- Common themes with most observations are:
  - Sample frequency
  - Sample site rationale
  - Sample techniques
  - Data tracking and trending
  - Employee training

REGULATORY REQUIREMENTS

- What are the consequences for not implementing and maintaining a robust and compliant aseptic gowning qualification, re-qualification, and routine monitoring program?
  - Observations
  - Warning letters
  - Recalls
  - Consent decrees

INDUSTRY BEST PRACTICES, GUIDANCES AND STANDARDS

- Industry best practices that are applicable to implementing and managing a compliant aseptic gowning program are:

  - FDA Guidance for Industry section V, "Sterile Drug Products Produced by Aseptic Processing – Current Good Manufacturing Practice"

  - PDA Journal of Pharmaceutical Science and Technology, Technical Report No.13, "Fundamentals of an Environmental Monitoring Program"

  - ISPE, Pharmaceutical Engineering Guides for New and Renovated Facilities, Volume 3, "Sterile Manufacturing Facilities"

  - International Standard (ISO) 13408-1

  - United States Pharmacopeia <1116>

INDUSTRY BEST PRACTICES, GUIDANCES AND STANDARDS

- Industry best practices and standards highlight:
  - Training
  - Personal hygiene and health habits
  - Gowning control
  - Facilities control
  - Aseptic gowning monitoring
  - Tracking and trending

- Major phases of the program should include:
  - Qualification
  - Routine monitoring
  - Re-qualification

ASEPTIC GOWNING DEFINITIONS OF QUALIFICATION, RE-QUALIFICATION, AND ROUTINE MONITORING PROGRAM

- Routine monitoring activities should include:
  - Routine monitoring
  - Audits

- Batch critical interventions
  - Sample locations
  - Frequency of sampling
  - Limits
  - Microbiological assessments
 - Actions and consequences
  - Security

Aseptic Gowning Definitions of Qualification, Re-Qualification, and Routine Monitoring Program

- Audits
  - Sample locations
  - Frequency of sampling
  - Limits
  - Microbiological assessments
  - Actions and consequences
  - Security

ASEPTIC GOWNING DEFINITIONS OF QUALIFICATION, RE-QUALIFICATION, AND ROUTINE MONITORING PROGRAM

- Re-qualification activities should include:
  - Sample locations
  - Frequency of sampling
  - Limits
  - Microbiological assessments
  - Actions and consequences
  - Security

RATIONALE FOR SAMPLE LOCATIONS, SAMPLE FREQUENCY, SAMPLE LIMITS

- Definitions of particular importance:
  - Alert
  - Action
  - % Positives
- Predecessors to defining locations, frequencies, and limits:
  - Sample methods
  - Media type
  - Equipment type
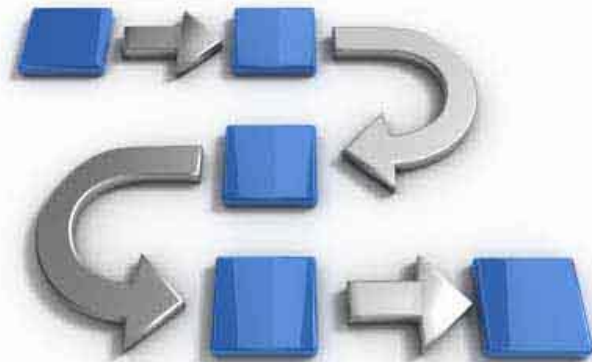
RATIONALE FOR SAMPLE LOCATIONS, SAMPLE FREQUENCY, SAMPLE LIMITS

- Sample location selection is based on the following factors:
  - Likelihood for contamination
  - Likelihood for contamination transfer
  - Gown attachment points
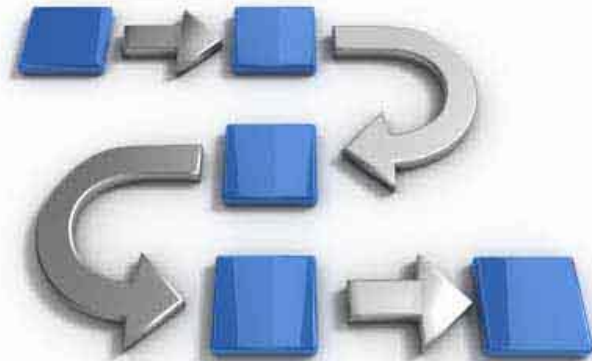
RATIONALE FOR SAMPLE LOCATIONS, SAMPLE FREQUENCY, SAMPLE LIMITS

- Sample frequencies should be based on:
  - Criticality of tasks
  - Frequency of tasks
  - Trends
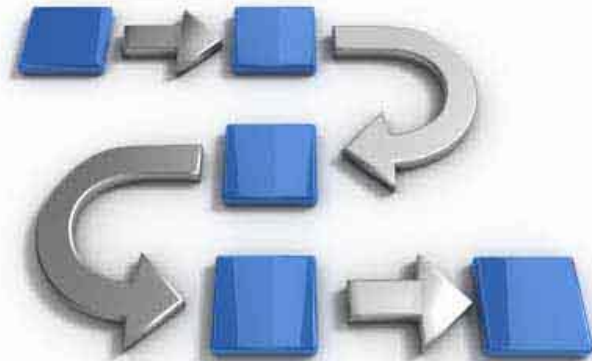
RATIONALE FOR SAMPLE LOCATIONS, SAMPLE FREQUENCY, SAMPLE LIMITS

- Sample limits should be defined and justified:
  - Absence of objectionable microorganisms
  - Alert
  - Action
  - % Positives
  - Total body count
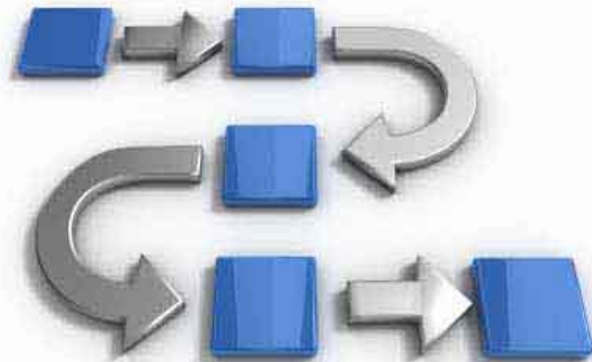
INVESTIGATIONS, IMMEDIATE ACTIONS, AND CORRECTIVE ACTIONS

- Investigation types include:
  - Alerts
  - Actions
  - % Positives
  - Total body count
- Investigations into aseptic gowning excursions should include:
  - Immediate response
  - Timely closure
  - Approved by all key stakeholders

INVESTIGATIONS, IMMEDIATE ACTIONS, AND CORRECTIVE ACTIONS

- Investigations for personnel excursions can be:
  - Difficult and challenging
  - Subjective
  - Adversarial
- Use the Program
  - Sample locations
  - Frequencies
  - Locations
  - Isolate information

INVESTIGATIONS, IMMEDIATE ACTIONS, AND CORRECTIVE ACTIONS

- Immediate actions:
  - Actions implemented to prevent nonconforming events from having or continuing to have impact to the process or product
- Immediate actions should be:
  - Timely
  - Diligent
  - Be based on a point system

INVESTIGATIONS, IMMEDIATE ACTIONS, AND CORRECTIVE ACTIONS

- Corrective actions:
  - Actions taken to prevent recurrence of the defined root cause
  - A corrective action will always relate to the determined root cause
- Preventive Actions:
  - Actions taken to prevent the occurrence of an issue

INVESTIGATIONS, IMMEDIATE ACTIONS, AND CORRECTIVE ACTIONS

- Incomplete investigations and root cause determinations may lead to:
  - Implementation of ineffective CAPAs
  - Recurring excursions
  - Compliance vulnerabilities
  - Negative impact to the product and processes

OBJECTIONABLE MICROORGANISMS

- Know your micro flora:
  - Frequent microbial identifications
  - Define objectionable microorganisms
  - When to act and when not to
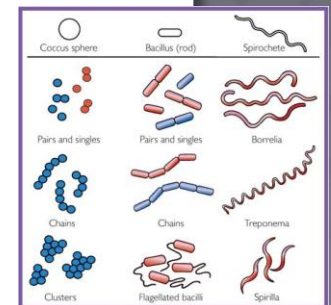
TRACKING AND TRENDING CRITICAL DATA FOR ASEPTIC GOWNING

- The tracking and trending system must be qualified

- Examples of data that should be tracked and reported include:

  - Excursion rate by area or by person

  - % Positive rate by area or by person

  - Most commonly recovered isolates by area, by person, and by quarter
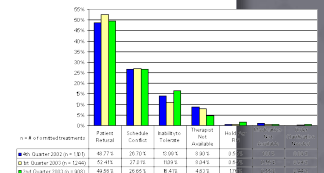
HOW DOES THE MODA™ SOLUTION AID IN IMPLEMENTING AND MAINTAINING A GOOD ASEPTIC MONITORING PROGRAM?

KEY FUNCTIONALITY FOR AMYLIN

- MODA™ Solution provides an automated and compliant solution for:
  - Defining, Controlling, and Managing Sample Plans
  - Defining, Controlling, and Managing Sample Frequencies
  - Defining and Controlling Security Roles and Rights
  - Forcing and maintaining structured and consistent work flows for samples. Sample Chain of Custody is controlled!
  - Tracking and Controlling Materials, Equipment, Results, and Personnel
  - Assistance in Investigating Aseptic Gowning Excursions
  - Tracking and Trending Critical Data points specific to:
    - Qualifications
    - Batch Monitoring
    - Audits
    - Re-Qualifications

QC PROCESS CHALLENGES

Disparate Data Points

Air, Surface, Water
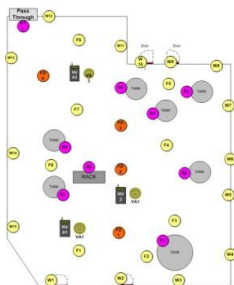
Personnel

Media
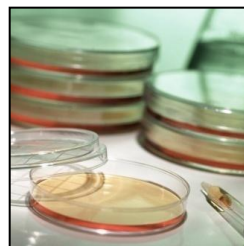
Equipment

"Islands" of Information

Sample Records

Laboratory

Spreadsheets
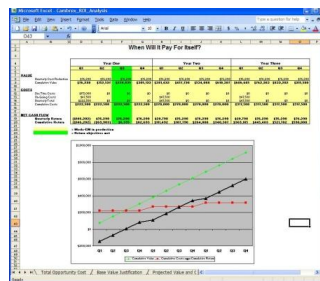
Management

WHY IT MATTERS

- Paper-based, redundant data recording & reconciliation

- Increased labor and time costs & delays in data analysis/reporting

- Ineffective data analysis and trending

- Impacts overall effectiveness of QC program

AUTOMATION IN CLEANROOM

"…cleanroom touch pads or computer terminals that allow for automated data entry IN THE ROOM."

"…palm-pilot-type of data collection devices… that can directly download to the computer system and allow for direct data transfer without risk of contamination."

"…real time data for many of the chemistry and microbiology tests that must be performed."

PDA
Parenteral Drug Association

Source: Environmental Monitoring A Comprehensive Handbook, Volume 1

AUTOMATION IN QC MICRO LAB

"…analysis and trending of environmental data is essential to aid in the interpretation of process stability and assess overall control performance."

EM Reports must be "…accurate, traceable, timely, and well-documented."

Source: Environmental Monitoring A Comprehensive Handbook, Volume 1

21 CFR PART 11 COMPLIANCE

Paper-Based System

Access database for data storage is not validated

No control of changes in access database

No electronic signature for changes

All users have all privileges

Data stored in binders that are stored on and off site

MODA™ Solution

✓ **Validated system**

✓ **Audit trail tracks all changes/records**

✓ **Electronic signature for all major steps to enable quick and clear traceability**

✓ **Varying levels of access to system dependent upon job function**

✓ **Data stored on servers that are backed up on a routine basis**

TRENDING/REPORT GENERATION COMPLIANCE

Paper-Based System

5 Analysts 8-10 hours per month after data entry

Limited Scope of Trending Reports

No Formal way of tracking flora

Difficult to extract client-specific data

All trending performed by QC for QA and Manufacturing

MODA™ Solution

✓ Quick and efficient trending in real time

✓ Wide array of trend report formats

✓ Flora can be trended by person, site, room, facility

✓ Client-specific reporting for Contract Manufacturing

✓ Ease of trending allows others (QA, Manufacturing) to perform their own trending

FROM THIS…..

TO THIS.....

Organism Characterization
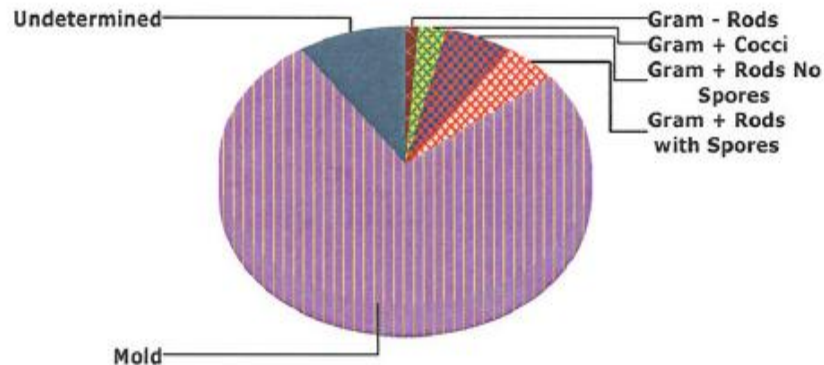
⊞	0	0.0%
Gram - Rods	1	1.2%
Gram + Cocci	2	2.4%
Gram + Rods No Spores	5	5.9%
Gram + Rods with Spores	4	4.7%
Mold	65	76.5%
Undetermined	8	9.4%
Total:	85	100.0%

Organism Description
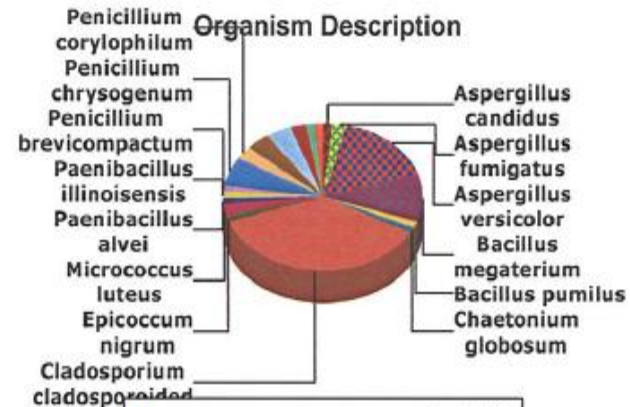
⊞	0	0.0%
Aspergillus candidus	1	1.3%
Aspergillus fumigatus	2	2.7%
Aspergillus versicolor	12	16.0%
Bacillus megaterium	8	10.7%
Bacillus pumilus	1	1.3%
Chaetonium globosum	1	1.3%
Cladosporium cladosporoided	27	36.0%
Epicoccum nigrum	1	1.3%
Micrococcus luteus	2	2.7%
Paenibacillus alvei	1	1.3%
Paenibacillus illinoisensis	1	1.3%
Penicillium brevicompactum	1	1.3%
Penicillium chrysogenum	5	6.7%
Penicillium corylophilum	2	2.7%
Penicillium glabrum	3	4.0%
Rhodococcus equi	3	4.0%
Staphylococcus hominis hominis	2	2.7%
Staphylococcus warneri	1	1.3%
Stereum hirsutum	1	1.3%
Total:	75	100.0%

THIS.....

THIS.....

AND THIS

PAPERLESS QC MICRO AT AMYLIN

- MODA™ Solution provides the ability to:
  - Regulate and control existing and new sample locations
  - Define and set sample frequencies (discrete or standardized)
  - Immediately report nonconforming values
  - Define and control equipment and materials required for sampling and testing activities
  - Track the lifecycle of samples
  - Monitor and track plant flora by rooms, locations, and systems
  - Paperless – barcode scanning

AUTOMATED REPORTING AND TRENDING AT AMYLIN

- MODA™ Solution makes investigations into aseptic gowning excursions easy. Specifically,
  - Gathers and reports the data (trends overtime, specific areas where microorganisms were recovered, etc.)
  - Removes the human element and reports the facts
  - Data for the classified rooms and systems are housed in the same system

SUMMARY - WHAT DOES SUCCESS LOOK LIKE?

- A robust and compliant aseptic gowning qualification program is a program that utilizes:
  - A fully qualified 21CFR Part 11 compliant system
  - A system where all data can be tracked and trended together and timely
  - A system that tracks Samples Frequencies, Sample Locations, Sample Plans, Chain of Custody, Materials, and Equipment
  - Standardizes the Requirements and Guidelines for Investigations, Immediate Actions, and Corrective Actions

To submit a question, use the "Q&A" feature of WebEx (bottom right of your screen). If we do not answer a question online, we will be sure to follow up with an e-mail.

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Questions & Answers

Upcoming News & Events

See Lonza and MODA™ solution in action

- Jun 21-23: IVT ACE, Philadelphia, PA
- Jun 28 – Irish Cleanroom Society, Dublin, Ireland
- Jun 29-Jul 1: Interphex Japan 2011 – Tokyo, Japan
- Aug 1-3 : International Assoc of Food Protection, Milwaukee, WI

Upcoming Webinars (topics under consideration)

- Non-sterile Manufacturing Quality Control
- Advancements in Automated Water Testing
- Process optimization – making the business case
- Client Case Studies

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Wrap-up

Personal Consultation

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Learn more about MODA Solution: www.lonza.com/moda

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Thank You