Today’s Presenters

- Bob Toal
  Segment Manager, Informatics
  *Lonza Wayne*

- Dominick Villani
  Manager of QC Microbiology
  *Amylin Pharmaceuticals*
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 and MODA™ Solution Overview

B. Toal / Lonza / 07 Jun 2011
Lonza’s Life-Science Platform

Lonza

**Life Science Ingredients**
- Nutrition Ingredients
- Microbial Control
- Performance Intermediates

**Custom Manufacturing**
- Chemical Manufacturing
- Biological Manufacturing
- Development Services

**Bioscience**
- Therapeutic Cell Solutions
- Rapid Testing Solutions
  - Endotoxin Detection
  - Microbiology
  - Informatics
  - Solutions Support

MODA™ Solution
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
Example: QC Sampling and Lab Processing

The Paper-based QC Process

**Plan**
- Print sampling schedule & labels per EM SOP
- Assign sampling activities to QC Analysts
- Reconcile planned samples with collected samples
- Close out sampling schedule per EM SOP

**Collect**
- Put on sterile outer garments and enter processing area
- Identify area to collect samples from facility map
- Collect sample and affix label
- Record date, time and initials on paper schedule and media
- All samples collected
- Deliver sampling paperwork to QC Supervisor
- Deliver samples to Microbiology or Biochemistry for processing

**Process**
- Record sample receipt
- Prepare samples for testing. Report media lot, equipment, dilution info
- Record incubation start date and time
- Incubate samples
- Record incubation stop date and time
- Analyze samples and record results
- Results in range?
- Notification of Alert or Action

**Review & Analyze**
- Aggregate data
- Trend results
- Trends OK?
- Investigate excursion
- Report results
- YES
- NO

YES
- YES
- NO
- YES
Example: QC Sampling and Lab Processing

The Paperless QC Process—11 Steps Removed

1. **Plan**
   - Print sampling schedule & labels per EM SOP
   - Assign sampling activities to QC Analysts
   - Reconcile planned samples with collected samples
   - Close out sampling schedule per EM SOP

2. **Collect**
   - Put on sterile outer garments and enter processing area
   - Identify area to collect samples from facility map
   - Collect sample and affix label
   - Record date, time and initials on paper schedule and media
   - All samples collected
   - Deliver sampling paperwork to QC Supervisor
   - Deliver samples to Microbiology or Biochemistry for processing

3. **Process**
   - Record sample receipt
   - Prepare samples for testing. Report media lot, equipment, dilution info
   - Record incubation start date and time
   - Incubate samples
   - Record incubation stop date and time
   - Analyze samples and record results
   - Results in range?
   - Notification of Alert or Action

4. **Review & Analyze**
   - Aggregate data
   - Trend results
   - Trends OK?
   - Investigate excursion
   - Report results

   All samples collected?
   - YES
   - NO

   All samples accounted for?
   - YES
   - NO
# Paperless Efficiency Example

<table>
<thead>
<tr>
<th>Record on paper template</th>
<th>Record on plate</th>
<th>Reconcile media and template</th>
<th>Enter data into Excel/LIMS</th>
</tr>
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<tbody>
<tr>
<td>1: BB50, SS43, Water, IE5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2: BB50, SS43, RODAC, IP72/IP82</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>3: BB50, SS44, Water, IE5/IE7</td>
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<tr>
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<td></td>
</tr>
<tr>
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<table>
<thead>
<tr>
<th>Scan room or site</th>
<th>Select sample and print labels</th>
<th>Send to repository</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 hours</td>
<td></td>
<td>Finished</td>
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</tbody>
</table>

- Paper 8 hours
- 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

### Deviation Summary

Report Period From 11/1/2007 12:00:00AM to 3/31/2008 12:00:00AM

<table>
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<tr>
<th>Deviation</th>
<th>Sample</th>
<th>Sample Date</th>
<th>Sampled By</th>
<th>Test</th>
<th>Result</th>
<th>Alert Limit</th>
<th>Action Limit</th>
<th>Organism</th>
<th>Deviation Type</th>
<th>Environment</th>
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</table>
Automated Reporting and Analytics

Trend by System/Room
Chart as of 7/30/2008

Location: Building 1000  R1001 - Fill Suite 1

- Personnel
- RODAC Plate
- Settling Plates
Automated Reporting and Analytics
Our Featured Speaker:
Dom Villani – Amylin Pharmaceuticals

B. Toal / Lonza / 07 Jun 2011
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 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
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
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 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
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:
- Legal requirements
- Based on the drug market
- Are minimum 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
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 that are applicable to implementing and managing a compliant aseptic gowning program are:

- International Standard (ISO) 13408-1
- United States Pharmacopeia <1116>
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
Re-qualification activities should include:

- Sample locations
- Frequency of sampling
- Limits
- Microbiological assessments
- Actions and consequences
- Security
Definitions of particular importance:
- Alert
- Action
- % Positives

Predecessors to defining locations, frequencies, and limits:
- Sample methods
- Media type
- Equipment type
Sample location selection is based on the following factors:

- Likelihood for contamination
- Likelihood for contamination transfer
- Gown attachment points
Sample frequencies should be based on:
- Criticality of tasks
- Frequency of tasks
- Trends
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 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
Incomplete investigations and root cause determinations may lead to:

- Implementation of ineffective CAPAs
- Recurring excursions
- Compliance vulnerabilities
- Negative impact to the product and processes
Know your micro flora:

- Frequent microbial identifications
- Define objectionable microorganisms
- When to act and when not to
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?
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
“…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.”

Source: Environmental Monitoring A Comprehensive Handbook, Volume 1
“...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.....
THIS....
THIS.....
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
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
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.
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
Wrap-up

Personal Consultation
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Email: robert.toal@lonza.com

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