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Environmental Monitoring

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Paul Moody,
Inspector

Scope of this Presentation

- Inspection Expectations for an EM Program
  - Personnel Training
  - Clean Area Monitoring
  - Clean Area Sanitisation
  - Laboratory Considerations
  - EM Program Review and Evaluation

- Out of scope
  - Equipment Qualification
  - Product Monitoring
  - Utility Monitoring
  - Sterilisation

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Personnel Training

- Looking at Annex 1 Principle:
  - …minimise risks of microbiological contamination. Much depends on the skill, training and attitudes of the personnel involved.

- Personnel involved include
  - Employees
  - Contractors
  - Cleaners
  - Anyone else?

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Personnel Training

- Robust training process is required.

- It should include:
  - Theoretical and Practical Elements
    - Basic Microbiology
    - GMP
    - Hygiene
    - Garbing
    - Clean Room Behaviour (Activities & Interventions)

  - Mode of Assessment
    - E.g. Observation and Process Sim. /Monitoring
  - Mode of Disqualification
  - Periodic Requalification

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- Established Environmental Monitoring Program should have SOPs:
  - Adequately detailed
  - Map of area indicating sites
  - Frequency
  - Include at rest monitoring

- Specifications
  - Action Limits – Annex 1
  - Alert limits – Historical data
  - Counts should not be averaged

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- What sites should be monitored?
  - Initial basis for approach should include
    - Qualification activities
      - Smoke studies
    - Risk Assessment
  - Subsequent basis should include
    - EM Review and Evaluation
    - Investigations & CAPA
    - Risk Assessment

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- Risk Assessment should consider
  - Activities in the areas such as
    - Personnel Flows
    - Set up/MFG procedures and flows
    - Hot spots of activity
    - Material and Waste Flows
  - Sites where microbial contamination would most likely have an adverse effect on product quality.
    - E.g. Areas of exposed product or components
  - Inaccessible/Difficult Areas to clean or sanitise

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- Risk Assessment should also consider
  - Relevant Investigations and CAPAs
  - Periodic surveillance monitoring at additional sites during and/or after operations
    - E.g. surface of intervention tools etc.
- Give consideration to Annex 1 Paragraph 18: Sampling methods used in operation should not interfere with zone protection.

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Cleaning and Sanitisation Program

- Detailed documentation
  - Procedures
  - Contact time
  - Record of make up & sterilisation
- Program should be Qualified
  - Efficacy Demonstrated
  - Justified Expiration Period
- Subject to Monitoring
- Control of Disinfectants
  - Movement within the facility
  - Rotation of disinfectants

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EM: Laboratory Considerations

- Laboratory Design
  - Sample flows
  - Appropriate Segregation
- Preparation and control of culture media
- Validated Procedures
  - Recovery studies – full exposure time
  - Use of inactivating agents within media
- Sampling & testing
  - Monitoring program, Raw materials, water, clean steam, process gas (air, N2), environment, bioburden

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EM: Laboratory Considerations

- Investigation System
  - Action limit excursions
  - System for handling Alert limit excursions
  - Organism identification

  - Remember... Annex 1 Principle:
    Sole reliance for sterility or other quality aspects must not be placed on any terminal process or finished product test.

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EM: Review and Evaluation

- Procedures for review and evaluation
- Trending
  - Defined within procedures
  - Scientifically Based
- Alert Limits
  - Based on historical data
  - Appropriate model used

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EM: Review and Evaluation

- Critical Assessment of EM program
  - Results obtained
  - Holistic View of results
  - Investigations and CAPA effectiveness
  - Assessment of the type and significance of organisms isolated and identified

- Review and Evaluation should feed back to the Risk Assessment
  - a living document
  - re-evaluated at least annually

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Some Considerations

- Looking at the types of deficiencies issued:
  - Do zero counts in Grade A mean EM program is functioning satisfactorily
    - Appropriateness of locations?
  - Has anything changed in the process?
    - Is the design of the process optimal?
    - Re-observation and reconsider EM sites?
    - Process simulation results?
    - Product/Material Results?

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Some Considerations

- Personnel behaviour changes?
- Has anything else changed affecting the area?
  - Change in HVAC parameters?
  - Change in cleaning agents?
  - Personnel Flows?
- Are additional monitoring sites required?

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In Summary

- Documented EM Program
- Adequate Personnel Training
- Defined Limits & Investigation Processes
- Justification for EM sites selected
- Map of EM sites
- Periodic Critical Evaluation of EM Program
- Holistic view of the program

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Questions

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Thank You for Listening

Paul.Moody@imb.ie
Compliance@imb.ie
+353 (0)1 676 4971

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