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COMMON DEFICIENCIES

IMB GMP Information Seminar, Crowne Plaza, Santry.

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Scope

Deficiencies in the following areas:

- Deviations, Investigations, Complaints
- Autoclaves
- Isolators
- Sterilisation in Place
- Environmental Monitoring
- Process Simulations

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Scope cont'd.

- Smoke Studies
- Gowning
- Clean room behaviour
- Disinfectants
- Sterility Testing
- Environmental Monitoring

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Inspections 2011 to 2012

- 2011 -Total of 98 GMP Inspections

  57 – Non- sterile

  41 – Sterile

- 2012 -Total of 126 GMP Inspections

  90 – Non- sterile

  36 – Sterile

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Deviations, Investigations & Complaints

- Incorrectly classified
- No system to reclassify where appropriate
- The root cause was not established
- No trends or inadequate trends
- Not processed in a timely manner
- No assessment or inadequate assessment for recurrence

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Deviations, Investigations & Complaints

- Purpose of assessment for recurrence and trending was not clearly defined and understood
- Trends were not critically assessed and compared with previous trends
- Appropriate CAPAs were not established
- Effectiveness checks were not performed

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Planned deviations/Temporary changes

- There was no requirement to perform a validation impact assessment as a result of a temporary change
- There was no system in place to return a system to its validated state following a temporary change
- There was no formal approval to ensure systems were returned to their validated state

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Autoclaves

- Air detector functionality tests were not performed weekly
- Qualification of autoclave was performed with Max and Min loads - but no air detector in place
- Empty chamber mapping had not been considered since initial qualification
- The worst case item was not considered for min load validation

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Autoclaves

- A daily steam penetration test was not performed
- Changes made during validation were not adequately documented
- Equipment was not dry prior to wrapping
- Excessive autoclave tape was used for wrapping

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Isolators

- VHP:

  -Items were not positioned as per the validated loading pattern

  -Gloves were not fully extended

- Transfer of items within the isolator was performed over exposed vials

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Sterilisation In Place (SIP)

Section taken from a 'Critical Deficiency'

- *The slopes of all pipe work in the system had not been assessed with respect to potential for condensate accumulation. E.g. Spool pieces in the aseptic filling room.*
- *Validation protocol X indicated an engineering assessment was to be undertaken to identify likely worst case areas; however, this assessment was not documented.*
- *Pressure was not monitored or assessed during validation cycles or routine cycles for the equipment Sterilisation In Place (SIP) process.*

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Process Simulations

- All elements of the manufacturing process were not simulated
- Worst case scenarios were not simulated
- Max bulk hold time were not used
- There was no control of interventions by operators
- Processed media was discarded

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Smoke Studies

- Smoke studies were not available, no record and no documentation of patterns observed
- Smoke studies did not adequately demonstrate air patterns
- Failed smoke studies were not adequately documented

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Gowning

- No check or inadequate check of garb packaging for integrity
- No initial integrity check of garb for rips or tears
- Excessive handling of outside of garb
- Inadequate sanitisation of surfaces, packaging, hands
- No integrity check of garb on exit

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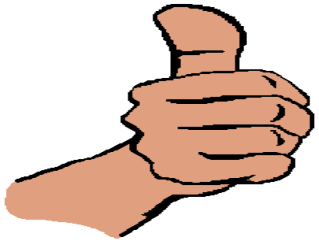
Clean room behaviour

- Inadequate procedures and performance of glove/gauntlet checks
- Gloves were sanitised prior to performing EM glove dabs
- No finger dabs were taken prior to glove change
- Inadequate sanitisation of hands and gloves



Rule of Thumb!

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Clean room behaviour

- Cleaning and wiping of surfaces was not conducive to good clean room practice
- Entire surface of items being transferred into the critical zone were not appropriately sanitised

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Clean room behaviour

- The following was noted:

  - Erratic movements
  - Throwing objects into bins
  - Multiple use of sanitising wipes

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Disinfectants

- In use expiration dates were not justified
- Disinfectants were non-sterile
- There was no rotation of disinfectants
- There was no routine monitoring of disinfectants for microbial contamination

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Sterility Testing

- Sterility test failures were not adequately investigated
- Contaminants were incorrectly identified
- Invalidation of tests was not performed as per Ph. Eur.

You must prove unequivocally that there is association between the environmental & test isolate

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Environmental Monitoring

- There was no inactivating agent in media
- Growth promotion of media was not performed
- There was inadequate documentation regarding description of monitoring locations
- Identification of all isolates in Grade A was not performed
- There was no assessment of identified microorganisms

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Environmental Monitoring

- Trend reviews did not include all room grades
- There was no system for checking the adequacy of the Environmental Monitoring program

All 0's is not necessarily a sign of a controlled environment

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Justification & Rationalisation

- The ……was not appropriately justified or rationalised.
- There was insufficient information regarding...

It may be at the nth degree you realise a failure in the concept so ask all questions

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Don’t wait until the inspection to answer the questions...

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Have the answers documented and there should be no additional questions...

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Thank You for Listening

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