Introducing an Innovative, Advanced Aseptic Filling Technology to a New Manufacturing Facility

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Agenda

• Introducing New Manufacturing Technologies – Perceived Barriers to Entry

• Current State of Advanced Aseptic Processing

• Our Business Case and Progress to Date
Barriers to Innovation

“Large corporations welcome innovation and individualism in the same way the dinosaurs welcomed large meteors.”

Scott Adams - Dilbert
Current State?

‘Despite increasing recalls, contamination events, and shortages, drug companies continue to rely on outdated manufacturing plants and processes’

‘Desired State: A maximally efficient, agile, flexible pharmaceutical sector that reliably produces drug products without extensive regulatory oversight’

Barriers to Innovation

Reluctant or Frustrated Innovators?

- Innate Conservatism
- Lack of Process Understanding
- If it’s not broken....no issues from last audit
- Perceived Regulatory Hurdles
Regulatory Support

FDA Draft Guidance for Industry

Advancement of Emerging Technology Applications to Modernize the Pharmaceutical Manufacturing Base, Dec. 2015
Advanced Aseptic Processing

‘An Advanced Aseptic Process is one in which direct intervention with open product containers or exposed product contact surfaces by operators wearing conventional cleanroom garments is not required and never permitted’

What are we seeing?

- Isolator technology is almost exclusively the pathway
- RABS becoming limited to debagging and capping operations
- Enhanced sterility assurance thanks to aseptic transfer systems and use of single-use technologies
Market Projections

Top 10 Therapy Areas in 2020, Market Share & Sales Growth

Sales lost from Angiotensin II segment
- Diovan (NVS): $1.6bn
- Benicar (Daiichi Sankyo): $1.6bn
- Exforge (NVS): $1.0bn
- Micardis (Boehringer): $0.9bn

Key growth drivers:
- Opdivo (BMY), Imbruvica (PCYC, JNJ), Xtandi (Astellas), Keytruda (MRK), Ibrance (PFE), Perjeta (Roche)

Key patent expiries:
- Gleevec (NVS) in 2015, Rituaxan (Roche) 2015+, Herceptin (Roche) 2014+

Source: EvaluatePharma® 22 May 2015
What we are seeing?  

Micro Lot Sizes

- Growth in personalized medicines
- Lot sizes range from 50 – 500 vials
- Need for very rapid turnaround
- Actual filling can go slower to go faster
Where do we need to go?

- Reliable Robotics
- Minimal Handling, Minimal Damage
- Simple to use Components
- Gloveless
- Flexible
- Minimal Environmental Monitoring
- Fast Turnaround – high OEE
- Supplier CQV that works for all
Business Case/Drivers for New AP Facility

- De-Risk the Supply Chain
- Low Volume, High Value Products
- Flexible, Agile, Reduced Cycle Times – Vials / Cartridges / Syringes
- Advanced Aseptic Technology
Technical Due Diligence

- Specific Closure Requirements – Availability
- VHP Technology & Robustness
- Viable and Non – Viable EM Media Fill Data
Sterility Assurance with Advancing Technologies

Significantly Increased Sterility Assurance

- Conventional A/B arrangement
- Restricted Access Barrier
- Isolator with gloves

Enhanced Sterility Assurance

- Remove the Operator
- Remove the Gloves
- Isolator with no gloves

Contamination Risks

- Operator interventions
- Material transfer
- Operator interventions
- Glove integrity failure
- Operator interventions
- Glove integrity failure
Gloves and Regulations

The transfer of materials into and out of the unit is one of the greatest potential sources of contamination – Annex 1

A program to minimize the risk of loss of integrity of gloves, sleeves and suits should be present – PICS

A faulty glove or sleeve assembly represents a route of contamination and a critical breach of isolator integrity - FDA
Gloves

How Risky are Pinholes in Gloves?

A Rational Appeal for the Integrity of Gloves for Isolators

By removing operator interventions and removing gloves, the biggest risk to sterility failure is removed.

By removing operator interventions and removing gloves, conventional environmental monitoring is not possible.

Options:

Re-engineer the system to allow environmental monitoring. However, this then invalidates the concept of removing interventions and gloves.

Provide an alternative to conventional environmental monitoring which is at least equivalent to the convention.
While acknowledging the step change in Aseptic Control, a form of EM is warranted during the Critical operation.

EM – New Technologies
Regulatory Expectation

Article 23 of Directive 2001/83/EC

‘...the authorization holder must, in respect of the methods of manufacturing and control...take account of scientific and technical progress’
While acknowledging the step change in Aseptic Control, a form of EM is warranted during the Critical operation. EM – New Technologies
Successful collaboration between vendor / user / regulatory authorities

This (Advanced)$^2$ Aseptic Processing platform has the potential to deliver to the lean, flexible and agile desired state

Open your mind

We’re almost there!