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

PDA Europe
Current Trends in Aseptic Fill & Finish of Pre-filled Syringes
Lindau | 26. - 27. April 2017
Introducing New Manufacturing Technologies – Perceived Barriers to Entry

Current State of Advanced Aseptic Processing

Our Business Case and Progress to Date
“Large corporations welcome innovation and individualism in the same way the dinosaurs welcomed large meteors.”

Scott Adams
aka Dilbert
‘Despite increasing recalls, contamination events, and shortages, drug companies continue to rely on outdated manufacturing plants and processes’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
Advancement of Emerging Technology Applications to Modernize the Pharmaceutical Manufacturing Base, Dec. 2015
‘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?

Isolators.... Isolators.... Isolators

- 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 2022, Market Share & Sales Growth

Key growth drivers:
- Descovy (GILD), Genvoya (GILD), Bictegravir/F/TAF (GILD), Triumeq (GSK)
- Key growth brakes:
  - Harvoni (GILD), Sovaldi (GILD), Truvada (GILD), Atripla (GILD)

Key growth drivers:
- Opdivo (BMY), Revlimid (CELG), Keytruda (MRK), Ibrance (PFE), Perjeta (Roche), Tecentriq (Roche)

Key patent expiries:
- Gleevec (Novartis) 2016; Rituxan (Roche) 2016+
- Altima (LLY) 2015+; Herceptin (Roche) 2014+

Key contributors to CAGR growth:
- Stelara (JNJ); dupilumab (SAN) – expected 2017 WW launch
- Ozanimod (CELG) - expected 2018 launch

Source: EvaluatePharma® August 2016
Micro Lot Sizes

Growth in personalized medicines

Lot sizes range from 50 – 500 vials

Need for very rapid turnaround
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

Where do we need to go?
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
Vanrx SA25 Aseptic Filling Workcell
Technical Due Diligence

- Specific Closure Requirements – Availability
- VHP Technology & Robustness
  - Challenge of operating without gloves – corrective interventions
- 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
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 by additional robotic arms or adding 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
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’
• EM – New Technologies
• Not necessarily settle plates
• NVP Monitoring is useful – but vials behave in a completely different way
  • Consequence of equipment failure
  • Ability to clean system prior to VHP
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!
Acknowledgements