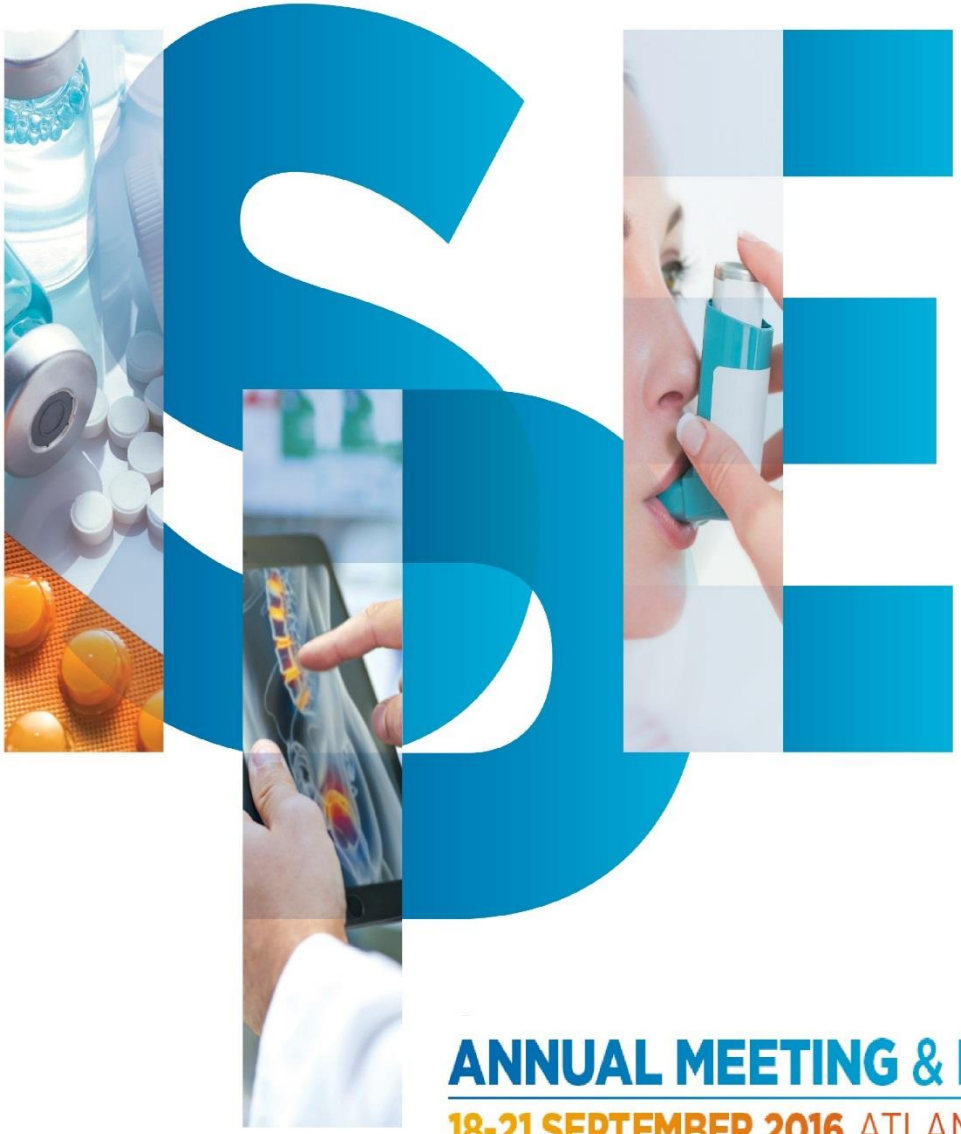

Introducing an Innovative, Advanced Aseptic Filling Technology to a New Manufacturing Facility

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ANNUAL MEETING & EXPO
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DPS

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‘Despite increasing recalls, contamination events, and shortages, drug companies continue to rely on outdated manufacturing plants and processes’

W. Nicholson Price II, Making Do in Making Drugs: Innovation Policy and Pharmaceutical Manufacturing 55 B.C.L. Rev. 491 (2014), http://lawdigitalcommons.bc.edu/bclr/vol55/iss2/5

Desired State

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

Ashley Boam, FDA Acting Director Office of Policy for Pharmaceutical Quality – FDA/PDA Joint Regulatory Conference, Sept 2015.

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

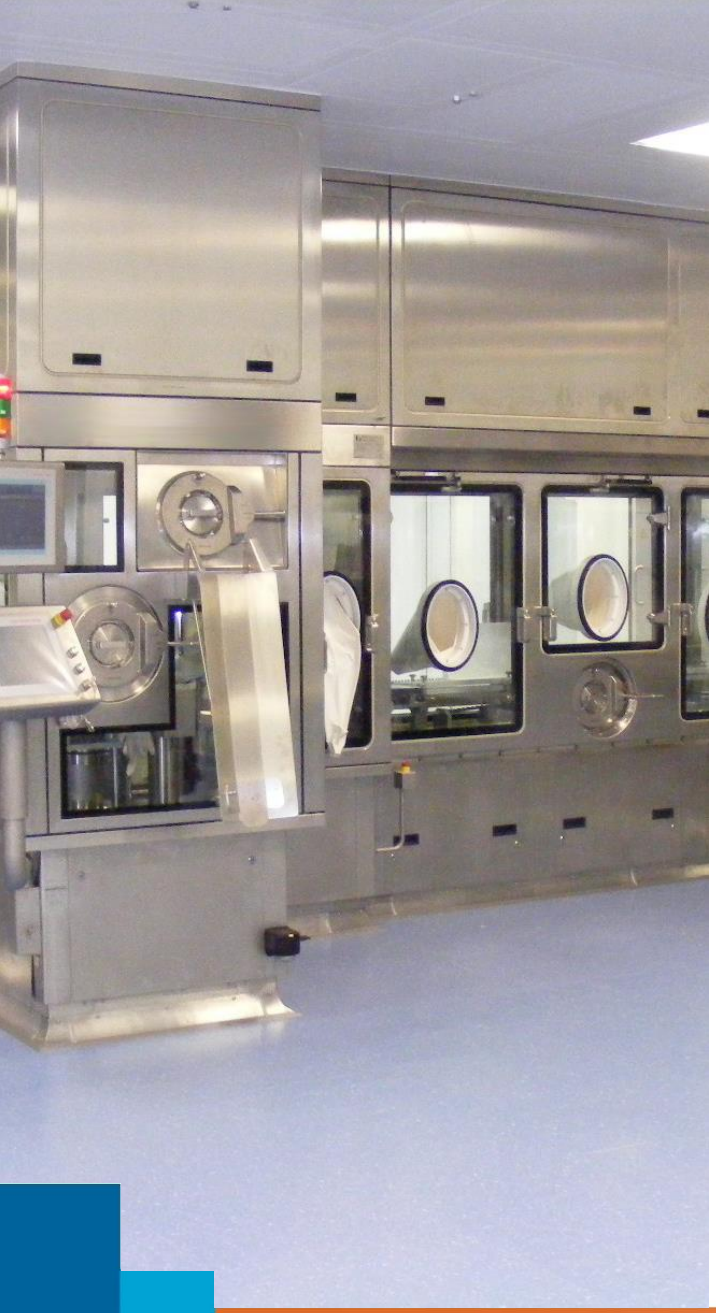
FDA Draft Guidance for Industry

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'

Akers, J, Agalloco, J, Madsen, R. What is Advanced Aseptic Processing? Pharm. Manuf. 2006: 4(2) 25 – 27.

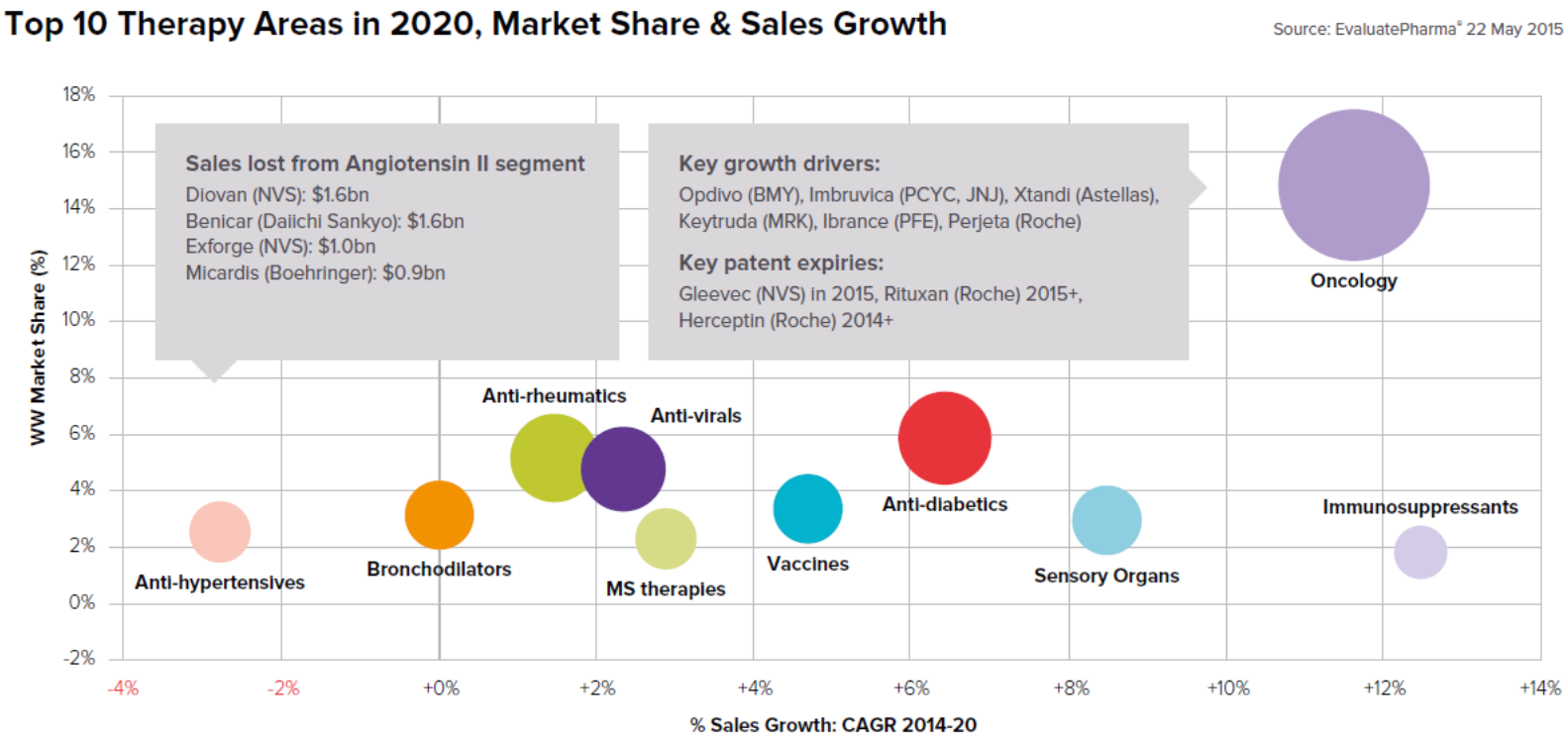


What are we seeing?

Isolators…. Isolators…. Isolators

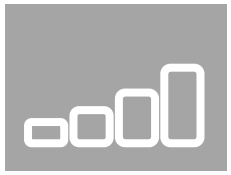
- Isolator technology is almost exclusively the pathway
- RABS becoming limited to debagging and capping operations
- Enhanced sterility assurance thanks to aseptic transfer systems and use of single-use technologies

Market Projections



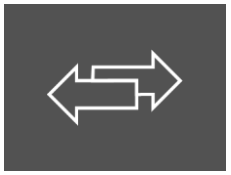
What we are seeing?

Micro Lot Sizes

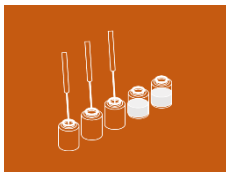


Growth in personalized medicines

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


vanrx

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

- Isolator with no gloves

Contamination Risks

- Operator interventions
- Material transfer

- Operator interventions
- Glove integrity failure

- Operator interventions
- Glove integrity failure

- **Remove the Operator**
- **Remove the Gloves**

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

Gessler, A. ; Stark, A.; Sigwarth, S. & Moirandt, C. PDA J. Pharm Sci and Tech 2011 65: 227-241

EM Proposal

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

Regulatory Feedback

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'

Regulatory Feedback

While acknowledging the step change in Aseptic Control, a form of EM is warranted during the Critical operation

EM – New Technologies

Conclusion

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 !

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