New Biotech Startups and Technologies Coming of Age

- More parenteral products in the clinic
- Trend toward in-house supply
- The "tougher, rarer" diseases - smaller cohorts
- Higher velocity to clinic
- More control of their destiny
- Use of clinical manufacturing facility for launch
- Availability of CMO's
- New technology initiatives by regulators
- Willingness to try new technologies
- New parenteral products in the clinic
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, Rituxan (Roche) 2015+, Herceptin (Roche) 2014+

**Graph:**
- **Axes:**
  - Y-axis: WW Market Share (%)
  - X-axis: % Sales Growth: CAGR 2014-20

- **Therapy Areas:**
  - Oncology
  - Anti-rheumatics
  - Anti-virals
  - Anti-diabetics
  - Vaccines
  - Sensory Organs
  - Immunosuppressants
  - Anti-hypertensives
  - Bronchodilators
  - MS therapies

**Source:** EvaluatePharma® 22 May 2015
PROTESTING AGAINST NEW TECHNOLOGY - THE EARLY DAYS
Reluctant or Frustrated Innovators?

- Innate Conservatism
- Lack of Process Understanding
- If it's not broken....no issues from last audit
- Perceived Regulatory Hurdles
‘Despite increasing recalls, contamination events, and shortages, drug companies continue to rely on outdated manufacturing plants and processes’

‘Pharmaceutical Manufacturing lags far behind the innovative techniques found in other industries due to high regulatory barriers and ineffective intellectual property incentives’

What are we seeing?

- Compact Spaces
- $$\text{per square foot}
- Compact filling machines
- Use of ready to fill components means less equipment
- E-Beam reserved for high throughput facilities
- Manual debagging is ok
- Space needed for handling tubs since they are mostly air
What are we seeing?

**Isolators… Isolators… Isolators**

- Isolator technology is almost exclusively the pathway
- Extraordinary performance over the last 20 years
- Need to understand VPHP compatibility with new biotech products
  - MABS seem to be reasonably stable
  - Some experiences with problems with hormones and live virus indicate need for extra care, lower residuals
- RABS limited to debagging and capping operations
- Do robotics require gloves? A next paradigm shift?
What are we seeing?

**LARGE VARIATIONS IN LOT SIZES**

**VARIOUS COMPONENTS ON THE SAME MACHINE**
- Syringes
- Cartridges
- Vials
- Made possible by tub/nest innovations

**LIQUID AND LYO ON THE SAME MACHINE**
- Lyo requires autoloading in an isolator
New area of growth in personalized medicines

Lot sizes range from 50 – 500 vials

Need for very rapid turnaround
- Pushing the envelope of aeration technology
- Rapid clean-up, set-up and line clearance
- Exclusive use of single-use, disposable wetted path components

Actual filling can go slower to go faster
- Up-time/reliability is critical
- Precision of movements may be more important than higher speeds
- Use of intelligent sensors to aid in machine movements and alignments
What are we seeing?

Maximize Yield

- Extraordinary costs for personalized medicines
- No room for error or patient treatment is delayed
- Use of 100% IPC to limit overfills and maximize fill quantities
- Use of IPC to eliminate wasted vials at beginning and end of fill
- Gravity feed using disposable technologies to eliminate hold-up
What are we seeing?

Human Vial Inspection

- Small, ever changing lots preclude automated inspection
  - Validation for each product with automated inspection is prohibitive
  - Humans can make subjective judgments to maximize yield
- Certain filling technologies can all but eliminate glass damage
- Excellent training and validation of human inspection is mandatory
- The key is designing quality into the process, not inspecting it in
The “New” CQV Paradigm*

Outsourcing of CQV is becoming more common

Clients would love to use vendor packages, but......

Focus on the risk based-approach to a point – ASTM E2500

“Beginning with the end in mind”

* “At least that’s what people are saying!”
Where do we want to go?

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

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 want to go?
Questions???

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