The Emerging Environment of Aseptic Filling

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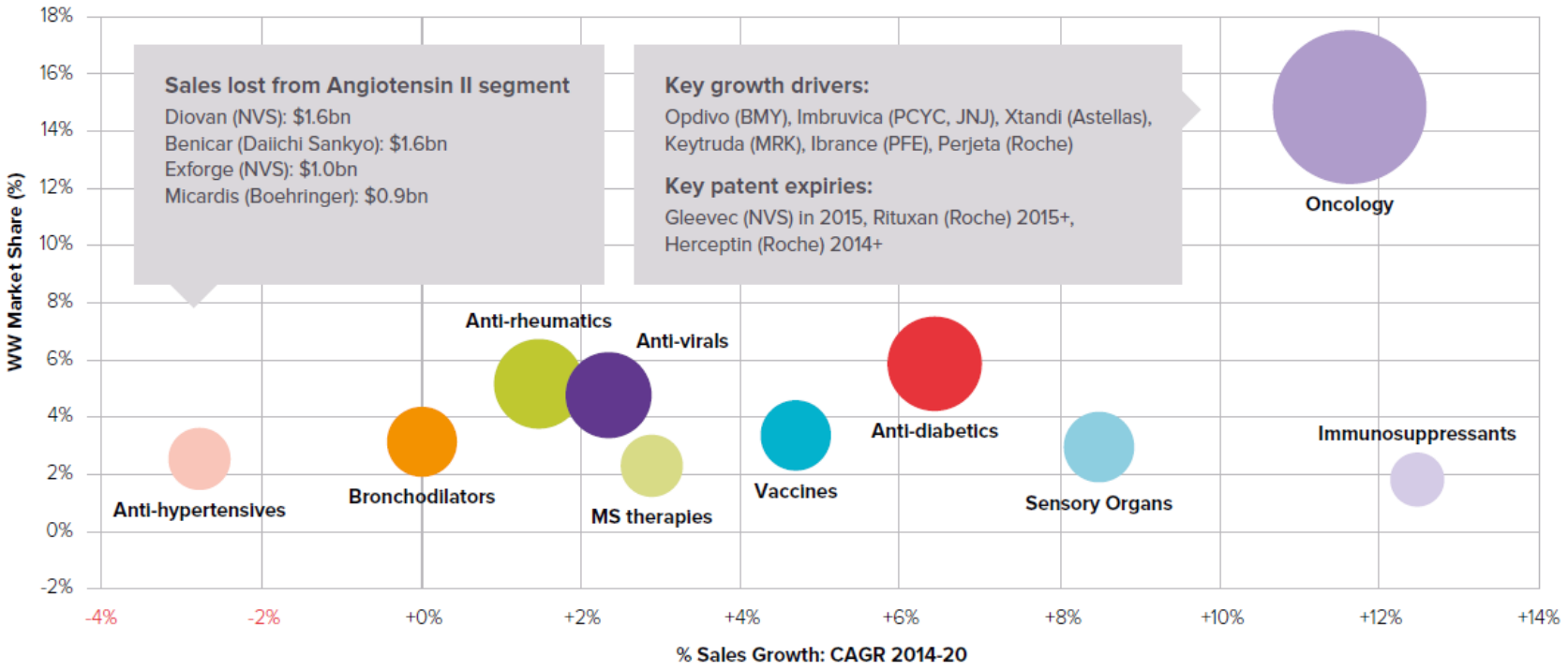
New Biotech Startups and Technologies Coming of Age

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

Advanced Aseptic Processing

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

Source: EvaluatePharma® 22 May 2015



Barriers to Innovation

Reluctant or Frustrated Innovators?

- Innate Conservatism
- Lack of Process Understanding
- If its not broken….no issues from last audit
- Perceived Regulatory Hurdles

Where are we?

‘Despite increasing recalls, contamination events, and shortages, drug companies continue to rely on outdated manufacturing plants and processes’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

Where are we?

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

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

What are we seeing?

Compact Spaces

- $$$ 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

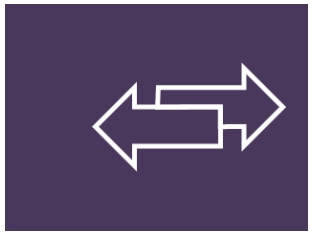
LIQUID AND LYO ON THE SAME MACHINE

- Lyo requires autoloading in an isolator

What we are seeing? Micro Lot Sizes

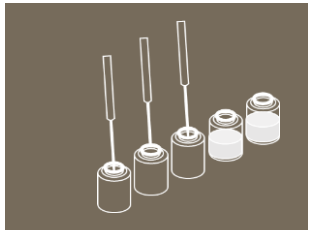
New area of growth in personalized medicines

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

What are we seeing?

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’

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

- 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

Questions???

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