The Pandemic-Caused Process Changes and Lessons for the Future

The Bioprocessing Summit
Bioproduction: Scale, Bioreactors & Digitalization
Boston, MA
16-19 August 2021

James Blackwell, Ph.D. M.B.A.
Bryan Monroe
The Windshire Group, LLC

Comprehensive Life Science CMC and Management Consulting™

Overview- Lessons Learned

- Drivers for Speed- COVID-Vaccine
- Process Development/Technology
- Manufacturing, Facility, and Operations
- CDMO/Partnerships
- Organizational
- Regulatory
- Conclusions

Drivers for Speed- COVID-Vaccine

Windshire

COVID-19

- COVID-19 Vaccine Launch = Commercialization of Routine Therapeutics/Vaccines
- What lessons learned can guide development for other therapeutics?
  - Hyper-speed forces out inefficiencies and elucidates things that could be best practices
- Content here-in incorporates insights garnered from virtually all the major players in the news, however…
- ***Nothing herein is revolutionary or new***

Windshire

Process Development/Technology

Windshire

PD is the foundation

- Platform technologies and processes
  - Prior learning already incorporated- “don’t re-invent the wheel”
    - Process understanding and characterization
    - Previous process efficiencies and productivities
    - Procedure templates established
    - Personnel already familiar with and trained
    - Make your Phase 2 process your Phase 3/Commercial process
      - Examples: Aby/peptides/oligo platform- many Ph. 1 processes are nearly commercial enabling today
  - May have had previous regulatory scrutiny

Windshire

- Process intensification
  - E.g., some *E.coli* processes at beginning of pandemic needed intensification
  - Intensification has several benefits:
    1. Cycle times per unit dose is decreased and capacity is increased
    2. More efficient use of capital and COGS (and Cost per Unit Capital) is lowered
    3. Lower equipment capacity utilization makes it easier to command surge or excess capacity to meet unexpected demand
       - Increasing production requires less expense and time
         - E.g., increase through-put just be increasing cycles; facility expansion issues are minimized
         - Risk reduction for commercial launch
  - Continuous processing is one means of process intensification

Windshire

- Look for lean and process simplification
  - E.g.
    - Frozen *E. coli* inocula in bags to reduce seed train cycle time
    - DS formulation for direct DP fill with no additions and dilutions
  - Lean and simplification improve quality
    - Can’t have all three: speed, lower cost and quality is a lie

- Process technology makes a difference in development times and time to market
  - E.g., mRNA was easier and faster than conventional vaccine technology
- Transiently expressed material was used for Phase 1
  - Can significantly shorten time to clinic
  - Health Authorities learned this is “OK”
  - No significant problems or issues known to date
  - Some want to use for Phase 2 too
  - Scientifically there is not reason this can’t continue as a practice going forward
    - Thought leader companies should lead the way until Health Authority thinking changes and is common knowledge

Windshire

- Process validation (PPQ) did not occur for any of the COVID processes- 100s of millions have been injected
  - How many people have died or had adverse events due to a lack of process validation?
- Regulatory expectations for what constitutes justification for number of successive PPQ runs needs to be simplified
  - "***You state that you will perform a minimum of 3 consecutive PPQ runs to support your process performance qualification. Since testing should be adequate to provide sufficient statistical confidence of quality both within a batch and between batches, note that 3 consecutive PPQ runs may not be sufficient to support your process performance qualification.***"

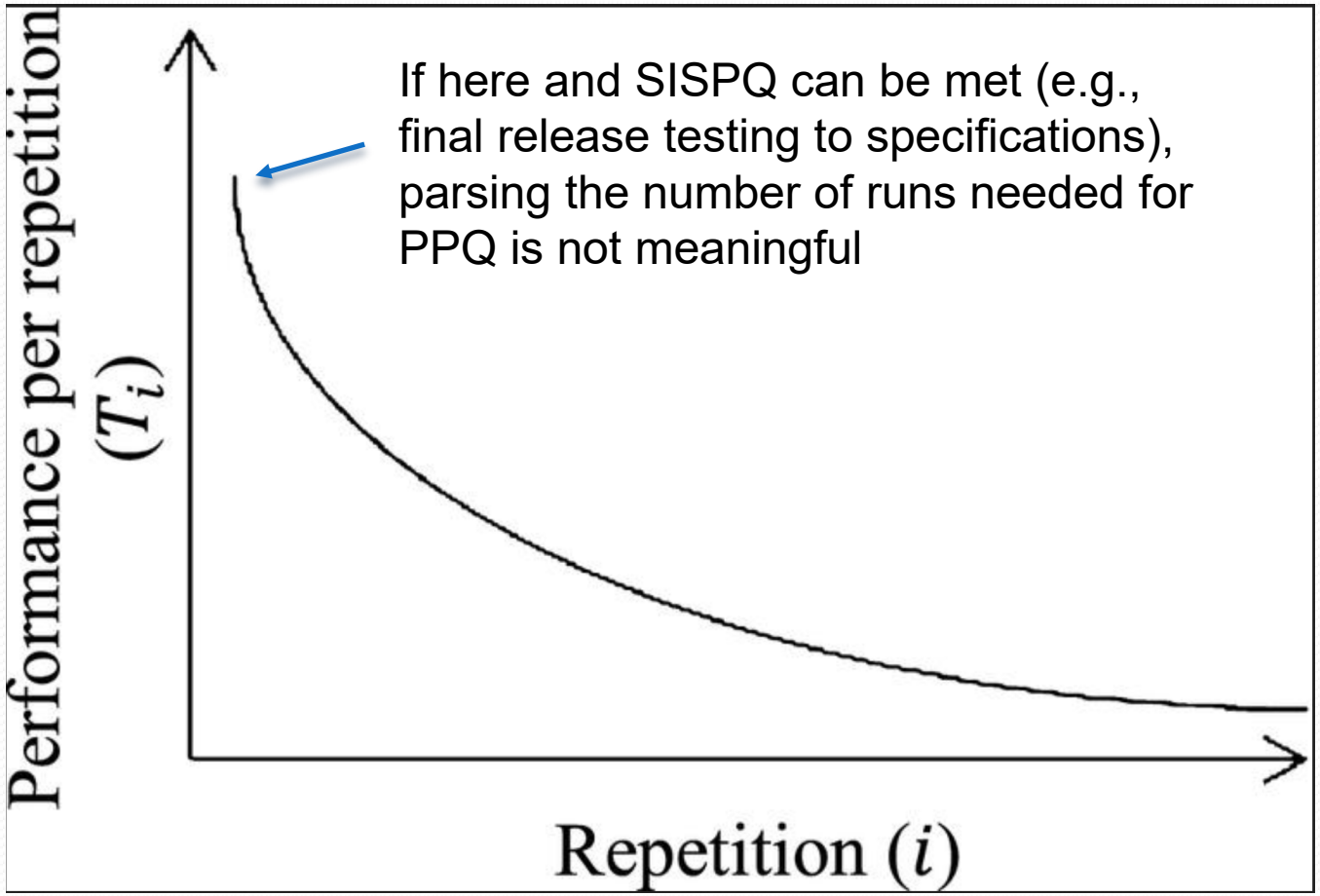
Windshire

PDA TR 60: Process Validation- A Lifecycle Approach

Windshire

Wright's Learning Curve (1936)

Cost (mistakes)
Per unit (batch)



Windshire

- My position: **three runs and you're done**
  - Use statistical justification for less than that or more if your process is not well characterized using a lifecycle approach to Design
  - Design, process characterization, process parameter justification, DOE, risk assessments, technical reports, and related activities are far more important than number of PPQ runs
- Processes do not need to be perfect or completely optimized for time-to-market
  - They just need to meet the requirements of stake-holders- patients, health authorities, commercial

Manufacturing, Facility and Operations

Windshire

Manufacturing execution is critical

- New or updated procedures sign-offs were accelerated
  - Verify, verify, verify, verify
    - **Batch record is the most important control!**
    - Thorough reviews, walk-down on floor, use for mock/engineering runs
  - Group reviews/sign-offs
    - Issues/communications dealt with/occurred in real-time
- In-process samples had QC on the floor to receive
  - Communications and coordination to expedite and eliminate mistakes
- QA on the floor at all times
  - Sign-off on batch records before they left the floor
  - Investigations triaged, completed or started on the floor
    - Investigations and batch release expedited

Windshire

- Flexible facility design can allow for easy expansion
  - Available grey space allow easy expansion of foot-print
  - Modular and flexible spaces can accommodate change quickly
  - Think about future expansion with existing foot-print and how this can be done to meet GMP

CDMOs/Partnerships

Windshire

Partner relationships are critical

- Communications and coordination were un-paralleled
- Can't "throw it over the wall". Significant time and effort need in overseeing and working with your partner
- PIP (person-in-plant) is a recipe for success
  - Look for partners that recognize the mutual value of PIP and don't consign PIP to an office and play obfuscation games
- CRO testing laboratory testing was done stat. When sample was going on test and result would be available was transparent

Regulatory

Windshire

FDA showed they can get it done!

- Review cycles needing weeks before FDA responds or asks questions needs to change
- Can rolling submissions used for accelerated pathway approvals be used for all approvals?
- Evaluate what process changes make sense now versus what can be done post-approval using a comparability protocol

Windshire

Organizational

Windshire

People make the difference

- People that believe in and are dedicated to the cause
- Tear down bureaucracy- empower people, give them the resources they need
- Training, training, training…
  - Not all training is LMS or classroom
  - Extend training to the floor
    - E.g., Genba spirit: first few times process is run, swarm the process with experienced personnel **on the floor** with junior or less experienced people
  - Mock and engineering runs are great for training
- People sacrificed, were flexible and put in extra-ordinary hours. Organizations need to reciprocate in kind, reward and appreciate effort

Windshire

- Big Pharma know-how to do it “right” and small company creativity and flexibility can be a potent combination if managed judiciously
- People focused and dedicated to clear and important outcomes can’t be stopped
- It’s not about “we’ve always done it this way” it’s about “how we can do it better”
- To get things done quickly, risks need to be taken
  - Control risks with planning/communications/coordination
- Correct mid-stream: when going very fast, learn when going off course and correct immediately

Windshire

Conclusions

Windshire

Final thoughts

- Get off your  and get on the floor!
- Platform technologies, process intensification and lean/simplification
- Treatment modality/technology can make a difference
- Transiently expressed material should be allowed in early clinical trials
- Industry guidance on how to approach number of PPQ runs needs to change- simplify
- Integrate with partners: clear two-way communications
- People power: communication/coordination, training, focus, “how can we do better”

Windshire

Thank you!

Contact Information

James Blackwell, Ph.D. M.B.A.

Principal Consultant and Founder

The Windshire Group, LLC

info@windshire.com

+1 844-868-5750

windshire.com

Windshire