PQRI Workshop:

Managing Excipient and API Impact on Continuous Manufacturing

Breakout Session 1: May 17, 2022

What are the Challenges You've Experienced Related to Material Impact on CM Processes?

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What are the challenges you have experienced related to material impact on CM processes?

1. Have you observed an excipient impact on the residence time distribution?
    a. If so, what excipient(s)/type(s) had the greatest impact?
    b. Does excipient variability have an impact?
2. How does the number of entry points impact excipient selection?
3. Do lower dose ingredients (excipients and APIs) pose a greater challenge?
4. What is the impact of excipient variability on continuous verification?
5. What is the best approach in engaging suppliers to discuss CMAs?

What are the challenges you have experienced related to material impact on CM processes?

6. What is the impact of head pressure on feed hoppers, and how does one control the change in feed as the hopper empties?
    a. Is hopper design important (mass flow vs funnel flow)?
7. How important is “PATability”/signal quality of excipient and its impact for process control?
    a. Does signal quality become a CMA?
    b. Have you used process compensation versus exclusionary specification for excipient attributes requiring additional control to ensure finished product quality (CMAs).
8. What is the inter- versus intra-lot and supplier-to-supplier variability impact on CM process?
9. Has fouling ever interfered with defined run-time and/or run-time extension?
    a. What are some of the contributing factors to process fatigue?
    b. Should lubricants be used to reduce build-up? If so, is that the right choice?
    c. Would it be helpful for suppliers to demonstrate extended runs with their excipients?

What are the challenges you have experienced related to material impact on CM processes?

10. Can equipment/tooling design help in circumvent issues related to raw material processing in CM?
11. The focus has been on solids; what about liquids, semisolids, biologics? Are there examples?
12. Is anyone attempting integrated DS/DP continuous manufacture?
    a. Are there additional excipient requirements for composite APIs?
        i. Amorphization of APIs?
13. Will CM drive the transition from QbD to QbC (Quality by Control)?
14. Do you find that the regulatory guidance provides relevant information regarding excipient usage in CM?