Continuous Manufacturing
PMDA’s Perspective

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A Background – ICH(1)

- One of the Future ICH Topics proposed by FDA
  - Continuous Manufacturing of Pharmaceuticals

- Problem Statement:
  - Continuous manufacturing of pharmaceuticals is a rapidly growing approach for production of both active ingredients and finished products.
  - There is a lack of guidance for regulators and industry on how to implement and regulate continuous pharmaceutical manufacturing.
A Background – ICH(2)

- **Desired State:**
  - Clear expectation of scientific and regulatory approaches for continuous manufacturing which will lower perceived barriers and encourage implementation of this emerging technology.

- **Timelines:**
  - Start in the Spring of 2018
  - The target completion is in the Fall of 2020
A Background – MIT(1)

- International Symposium on Continuous Manufacturing of Pharmaceuticals
- MIT on May 20-21, 2014
- This meeting was brought about by FDA CDER Dr. Janet Woodcock to open up Novartis-MIT Center for Continuous Manufacturing vision to a wider industry view.
- 8 white papers were finally published after discussion at the symposium.
A Background – MIT(2)

- (White Paper #3) Regulatory and Quality Considerations for Continuous Manufacturing
  - Continuous manufacturing (CM) provides multiple opportunities for improvements in pharmaceutical manufacturing → Agree
  - The current regulatory environment supports advancing regulatory science and innovation, including CM → Agree
  - Traditional concepts need to be further explored or modified, to advance the implementation of continuous processes → Agree

(Reference: https://iscmp.mit.edu/sites/default/files/documents/ISCMP2014_WP3_Slides.pdf)
A Background – MIT(3)

- The regulatory expectations for assurance of quality and reliable and predictive processing, are the same for batch and continuous processing → Agree
- CM provides additional opportunities to design the appropriate controls into the system, rather than current industry practice on relying mostly on testing materials at the end of the process → Agree
A Background – MIT(4)

- The flexibility of cGMPs supports new manufacturing technologies including CM → Agree

- Risk analysis techniques and/or modeling tools should be employed to fully understand the process, the impact on product quality, and to develop the appropriate controls → Agree

- Continuous Quality Verification is well suited to the validation of CM processes → Agree

- Regulatory expectations for cleaning and cleaning validation are the same → Agree
Approaches to CM at PMDA(1)

- Before ICH activity for CM, we have a lot to learn regarding CM.

- Collaboration with AMED sponsored Study Group.

- Communication between PMDA and Industries who are studying CM.

- Collaboration with other regulators.

(AMED: Japan Agency for Medical Research and Development)
Approaches to CM at PMDA(2)

- Professional Training together with GMP Inspectors.
  - External specialists/scientists give us lectures.
- Collaboration with a society, e.g. JSPME (Japan Society of pharmaceutical Machinery and Engineering).
  - PAT, Multivariate analysis etc.
Innovative Manufacturing Technology Working Group (IMT-WG)

- Has been established in PMDA since July, 2016.
- Purpose
  - To establish PMDA’s perspective on the latest technologies of pharmaceutical quality control
  - To propose a new regulatory framework for the pharmaceutical quality control by the new technologies
  - To draft guidelines
- Members
  - Senior Scientist (for Quality); Dr. Yoshihiro Matsuda
  - From Office of New Drugs
  - From Office of Manufacturing/Quality and Compliance
  - From Office of Regulatory Science
IMT-WG Activity Plan (J-FY 2016*)

- To organize face-to-face meeting(s) with FDA and EMA
- To visit continuous manufacturing sites
- To discuss with stakeholders including industries and academia
- To collaborate with a national research project on pharmaceutical quality control
- To publish points-to-consider about CM

*; April, 2016 – March, 2017
Opportunities:
- To avoid poor quality product with PAT etc.
  → Prevention of drug shortage problem
- To avoid scale-up issues
  → Rapid development
- To operate multiple scales and dosage manufacturing
  → Personalized medicine
- To reduce inventory
  → Cost reductions
Perspective on CM(2)

- PMDA is positive towards CM
- Issues to solve
  - Definition of Batch/Lot
    - How to determine reference/representative batch/lot for PV or Stability Test?
  - Handling deviations
    - How to restart manufacturing?
  - Cleaning Strategies
    - How to set a timing of Cleaning

Strongly Recommend to have PMDA consultations prior to submission!
Potential Regulatory Benefits for Industries

- Benefits
  - To communicate with PMDA IMT-WG
  - To gain PMDA’s confidence

- Expectations for industries
  - What can industries commit to?
    - Continuous verification for CM
    - To return profits to patients?
Thank you for your attention