AMENDMENT TO FDA BROAD AGENCY ANNOUNCEMENT FOR THE ADVANCE RESEARCH AND DEVELOPMENT OF REGULATORY SCIENCE AND INNOVATION

Broad Agency Announcement Number: FDA BAA-15-00121
Amendment Number: Three (2)
Amendment Posting Date: September 18, 2015

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SUMMARY OF CHANGES

PURPOSE: The purpose of this amendment is to add an additional sub area of research interest to “Part I: Research Areas of Interest, Research Area 3. Support New Approaches to Improve Product Manufacturing and Quality” of the announcement document.

The following research area is hereby added to Part I of FDA’s Broad Agency Announcement No. FDABAA-15-00121.

3.1 Enable development and evaluation of novel and improved manufacturing methods

3.1.1 Investigate the effects of continuous manufacturing (manufacturing using a continuous process, rather than a batch approach) on product quality

The FDA and the HHS Biomedical Advanced Research and Development Authority (BARDA) which has identified continuous manufacturing (CM) as an emerging technology within the pharmaceutical industry that has significant potential to improve agility, flexibility, cost, and robustness in the development of manufacturing processes. Although the continuous input of active pharmaceutical ingredient in the manufacturing of small-molecule drug products has been met with some success, as has the production of biotechnology products (e.g. monoclonal antibodies) by means of continuous perfusion bioreactors, end-to-end continuous manufacturing from reagents to drug product at a commercial scale has not been realized.

3.1.1.1 Enabling Technologies for Continuous Manufacturing

This research will advance continuous manufacturing by developing and making technologies accessible to industry in the near term (1-3 years), by bridging the gap between discoveries in academia or industry and implementation by industry. Results of this research will support the control of integrated end-to-end continuous processes (raw materials to final dosage form) as well as continuous process for the manufacture of drug substance and/or drug product. Additionally, this research is intended to support advances in regulatory science that allow for development of science and risk based guidelines to facilitate faster CM adoption. Some specific CM
enabling areas of research could include the following, but proposals should clearly describe the potential impacts of the proposed enabling technology on readiness for broad implementation in pharmaceutical industry, control strategy, and/or regulatory evaluation of CM:

- Continuous processing equipment (e.g., crystallizers, coaters, and viral clearance)
- Enhanced in-line process analytical technologies
- Integrated data management and plant-wide control systems
- Process modeling and simulation
- Advanced process control (e.g., feedback, feedforward or plant-wide control)

3.1.1.2 Continuous Manufacturing Innovation

Research aimed towards new processes or process improvements that may have an impact in 3-5 years, for example towards capabilities where CM can afford improvement that would not be achievable by batch production. Some specific research areas for CM innovations could include the following, but the proposal should clearly quantify the improvement metric for implementation of CM at commercial scale as compared to batch or pilot production if relevant:

- Synthetic processes that would benefit from flow processing; syntheses that could be affected through a reduced number of steps or that would not be feasible by batch production; highly selective chemistries that allow use of simple and effective continuous workup technologies, etc.
- Modular or plug and play type equipment with re-usable or flexible, interchangeable parts that allows the development of platform technologies for drug substance, drug product or end-to-end continuous manufacturing processes.
- Non-column based chromatography and alternative purification techniques (e.g. continuous precipitation)
- Continuous processes for homogeneous production of final dosage forms (e.g., strip film manufacturing system, injection molding, and printing).
- Alternatives to inherently batch unit operations (e.g. viral and sterile filtration)
- Process control systems with improved user interface (e.g. GUI) and capability for integration with new unit operations and ancillary equipment, with reduced need for programmer hours