FDA/PQRI Workshop on

The Regulatory Framework for Distributed and Point-of-Care Pharmaceutical Manufacturing

An Opportunity for DM/POC Stakeholder Engagement

pqri.org/fda_pqri_poc_dm_workshop

PQRI Product Quality Research Institute

FDA U.S. FOOD & DRUG ADMINISTRATION

Virtual Event | **November 14-16, 2022**

U.S. FOOD & DRUG ADMINISTRATION

VIRTUAL EVENT

PQRI Product Quality Research Institute

FDA/PQRI Workshop on the Regulatory Framework for Distributed and Point-of-Care Pharmaceutical Manufacturing

Monday - Wednesday, November 14 – 16, 2022

Day 1 – Monday, November 14, 2022
10:00 AM – 3:00 PM US ET

9:45 – 10:00 AM US	Pre-Workshop Attendees Check Connections
10:00 - 10:10 AM	***Welcome and Introductory Remarks*** **Glenn Wright**, Chair - PQRI Board of Directors; Chief Operating Officer, Parenteral Drug Association (PDA)
10:10 – 10:30 AM	***A Regulatory Perspective on Innovations in Pharmaceutical Manufacturing*** **Michael Kopcha**, Ph.D., R.Ph., Director, Office of Pharmaceutical Quality (OPQ), Center for Drug Evaluation and Research (CDER), US Food and Drug Administration (FDA) Future drug manufacturing may be more distributed, flexible, and portable than it is today. Distributed manufacturing (DM) platforms may even enable localized point-of-care (POC) manufacturing, which could allow for better response to patient demand but also challenge the current approach for regulating pharmaceutical quality. Appreciating the potential benefits of these advanced technologies for U.S. patients, FDA started an initiative of collaborative engagement to proactively develop a regulatory framework for DM and POC technologies.
SESSION 1: Harmonizing Terminology Among All Stakeholders *Session 1 will provide an introduction to DM and POC technologies, summarize critical areas for consideration as FDA evaluates a potential framework to regulate these technologies, and discuss DM/POC terminology harmonization among all stakeholders.*	
Moderator: Adam C. Fisher, Ph.D., Director, Science Staff, OPQ/CDER/FDA	
10:30 – 11:15 AM	***Keynote: An Introduction to Distributed Manufacturing and Point-of-Care Manufacturing Technologies and Terminology*** **Thomas O'Connor**, Ph.D., Deputy Director, Office of Testing and Research, OPQ/CDER/FDA **Riley Myers**, Ph.D., Emerging Technology Team, OPQ and Lead Biologist, Office of Biotechnology Products (OBP), CDER/FDA
11:15 – 11:45 AM	***Panel Discussion Q&A*** • **Thomas O'Connor**, Ph.D. • **Riley Myers**, Ph.D. • **Carolyn Yong**, Ph.D., Associate Director for Policy, Office of Tissues and Advanced Therapies (OTAT), Center for Biologics Evaluation and Research (CBER)/FDA
11:45 AM – 12:15 PM	**BREAK**

SESSION 2: Operating/Business Models between DM/POC Applicants and DM/POC Sites

Session 2 will explore potential operating/business models between a DM/POC applicant and DM/POC sites, discuss the roles and responsibilities of the applicant and the site user(s) based on various operating/business models, and identify regulatory challenges associated with these models.

Moderator: Cat Vicente, Associate Director, Enterprise Regulatory Outreach, Johnson & Johnson

12:15 – 12:40 PM	***Operating Models for Distributed and Point-of-Care Manufacturing*** **John J. Lewin** III, Pharm.D., MBA, Chief Medical Officer, On Demand Pharmaceuticals, Inc. We will explore various potential models for distributed/point-of-care manufacturing operations. In addition to evaluating the potential benefits to patients, we will discuss implications for different approaches as it relates to the applicant and the site user(s) as well as regulatory challenges and opportunities.
12:40 – 1:05 PM	***3D Printing Operating/Business Models*** **Alvaro Goyanes**, Ph.D., Co-Founder and CEO, FabRx; Honorary Lecturer, UCL School of Pharmacy
1:05 – 1:30 PM	***Panel Discussion and Q&A*** • **John J. Lewin** III, Pharm.D, MBA • **Alvaro Goyanes**, Ph.D. • **Joel Welch**, Ph.D., Chair, Emerging Technology Program, Associate Director for Science & Biosimilar Strategy, OBP/OPQ/CDER/ FDA
1:30 – 3:00 PM	***Breakouts*** *Registrants will breakout into several concurrent breakout sessions to facilitate small group discussions*
3:00 PM	***Wrap up and End of Day 1***

Day 2 – Tuesday, November 15, 2022 10:00 AM – 3:00 PM US ET	
9:45 – 10:00 AM US	Pre-Workshop Attendees Check Connections
10:00 – 10:15 AM	***Welcome to Day 2 and Recap of Day 1*** *FDA/PQRI Workshop Organizing Committee – Cat Vicente*
Session 3: DM/POC Location and Sizes of Spaces at Sites *Session 3 will explore the regulatory challenges, risks, and opportunities associated with the location, size, and mobility of the DM/POC site as compared to traditional manufacturing sites. The speakers will also discuss the strategies to demonstrate comparability of product quality between different DM/POC locations.*	
Moderator: Cat Vicente, Associate Director, Enterprise Regulatory Outreach, Johnson & Johnson	
10:15 – 10:40 AM	***Distributed Manufacturing Spaces – Options and Considerations*** **Dennis Powers**, M.S., Vice President, Business Development & Design Consulting, G-CON Changes in the global manufacturing and supply chain landscape coupled with advances in personalized medicine and process innovation are driving the biopharm industry to consider decentralized strategies including both distributed and point of care manufacturing. The realization of this capability is dependent upon the adoption of innovative transportable process and facility platforms which are currently being utilized and advanced within the industry. The presentation will provide an overview of the industry drivers for distributed manufacturing, the modalities that are considering this capability, as well as examples of various transportable technology options that are available and can be leveraged to support to support distributed manufacturing. The benefits and considerations for implementation will also be addressed.
10:40 – 11:05 AM	***Modular Robotic Systems for the Distributed Manufacturing of Personalized Drug Products*** **Fred Parietti**, Ph.D., CEO and Co-Founder, Multiply Labs This talk focuses on an automated production process for the manufacturing of personalized drug products in a consistent and controlled way. Particularly, we developed a modular system able to fulfill the needs of a small-batch, high-mix, personalized, or even on-demand, production thanks to a fully automated architecture (*i.e.* hardware and software). In this respect, we have developed a robotic cluster, consisting of i) different manufacturing modules, each of them performing specific fabrication steps, and ii) a transfer system that moves work-in-progress units (WIPUs) from module to module in a distributed and parallelized way. WIPUs are shuttled into a given module, which performs a specific step of the process and then conveyed out of the module for the next operations, including quality controls. This sequence can be performed in a fully-planned manner, fixed-scheduled manner, a flexible-scheduled manner, or a dynamic manner, being everything monitored locally and in the cloud. The strategy pursued not only ensures security of the manufacturing systems but increase its versatility and flexibility while making the proposed architecture suitable for scaling, being able to deploy many clusters at the same time in different distributed points.

11:05 – 11:30 AM	***Panel Discussion and Q&A*** • **Dennis Powers**, M.S. • **Fred Parietti**, Ph.D. • **Rakhi Shah**, Ph.D., Associate Director for Science and Communication, Office of Pharmaceutical Manufacturing Assessment (OPMA)/ OPQ/CDER/FDA • **Christine Moore**, Ph.D., Executive Director, Organon
11:30 AM – 12:00 PM	**BREAK**
Session 4: Structure of DM/POC Pharmaceutical Quality Systems and Assuring Quality Oversight *Session 4 will explore how the PQS can assure oversight of DM and POC technologies and the sites to which they are deployed to ensure compliance with CGMP. Additionally, this session will probe what changes, if any, are necessary to a PQS if DM and POC technologies are employed.*	
Moderator: **Dave Schoneker**, President/Owner, Black Diamond Regulatory Consulting, LLC	
12:00 – 12:30 PM	***Distributed Manufacturing Pharmaceutical Quality Systems*** **Celeste Frankenfeld Lamm**, Ph.D., Director, Global Regulatory Affairs, CMC, Merck & Co., Inc. Distributed manufacturing is a shift from traditional drug product manufacture, that enables the same manufacturing process to occur in multiple different locations. When the same equipment, process, controls, and quality systems are used, risk that may arise due technology transfer to a new location is reduced. A critical factor in the reduction of risk is quality systems; this talk will share perspectives regarding how a manufacturer can ensure compliance with CGMPs, approach Quality Risk Management, generate-maintain-and-access batch records, and control raw materials for distributed manufacturing.
12:30 – 1:00 PM	***Point-of-Care Pharmaceutical Quality Systems*** **Paul Smolenski**, Regulatory Director, DEKA Research and Development Point-of-Care pharmaceutical manufacturing is a nearly self-contained manufacturing system located in virtually any healthcare setting and operated as "vendor equipment" by the host site end user where requirements are limited to providing minimal utilities and support. This vision requires a site agnostic approach to quality and compliance. The vision is enabled by robust process validation and a central quality unit that monitors Point-of-Care fleet performance. This presentation will discuss quality and compliance attributes necessary to enable point-of-care pharmaceutical quality system implementation.
1:00 – 1:30 PM	***Panel Discussion and Q&A*** • **Celeste Frankenfeld Lamm**, Ph.D. • **Paul Smolenski** • **Ashley Boam**, Ph.D., Director, Office of Policy for Pharmaceutical Quality/OPQ/CDER/FDA
1:30 – 3:00 PM	***Breakouts*** *Registrants will breakout into several concurrent breakout sessions to facilitate small group discussions*
3:00 PM	***Wrap up and End of Day 2***

Day 3 – Wednesday, November 16, 2022 10:00 AM – 4:00 PM US ET	
9:45 – 10:00 AM US	Pre-Workshop Attendees Check Connections
10:00 – 10:15 AM	***Welcome to Day 3 and Recap of Day 2*** *FDA/PQRI Workshop Organizing Committee – Diane Paskiet*
Session 5: Strategies to Ensure that Drugs and Biologics Meet Established Specifications *The current regulatory framework includes requirements intended to ensure product quality, such as the testing of input components (e.g., raw materials) prior to manufacture and testing of the finished product. Challenges may arise if a DM or POC technology or host site do not contain a traditional quality control laboratory. This session will explore potential strategies for ensuring drugs and biologics manufactured using DM/POC technologies meet the established specifications and potential alternatives to traditional analytical testing approaches.*	
Moderator: Diane Paskiet, MS, Director of Scientific Affairs, West Pharmaceutical Services	
10:15 – 10:50 AM	***Ensuring the Quality of Therapeutics Proteins*** **J. Christopher Love**, Ph.D., Professor, Massachusetts Institute of Technology (MIT); Chairman Sunflower Therapeutics Therapeutics and vaccines that rely on proteins as the active drug substance are conventionally produced in large manufacturing facilities designed to segregate individual production steps and require many operators to implement processes. As a result, control strategies to assure quality of the protein emphasize elements of the building, the process controls, and final measurements of quality attributes. This talk with consider 1) how control strategies may differ for distributed and point-of-care manufacturing, 2) what technologies, biologies, processes and analytical approaches could enable alternative, fit-for-purpose control strategies, and 3) provide examples of support for these new paradigms that can enable high-quality protein production with new manufacturing capabilities.
10:50 – 11:25 AM	***Ensuring the Quality of Small Molecules*** **Thomas D. Roper,** Ph.D., Professor, Department of Chemical and Life Sciences Engineering, School of Engineering, Virginia Commonwealth University The current regulatory framework for small molecule supply to patients assumes a traditional approach wherein a central manufacturing facility produces the material and ensures the quality meets the specification prior to distributing to patients. The realization of the potential for small, modular, and mobile production facilities as well as the need to protect against supply chain risk offers the opportunity for a much more distributed pharmaceutical supply chain than in the past. This presentation will focus on the options for modifying the current product control strategies and product testing regimes to a more distributed paradigm. Examples of how traditional release testing may be re-envisioned will be presented for discussion.
11:25 AM – 12:45 PM	***Breakouts*** *Registrants will breakout into several concurrent breakout sessions to facilitate small group discussions*
12:45 – 1:15 PM	**BREAK**

Session 6: DM/POC Suitability for Center for Biologics Evaluation and Research (CBER) Regulated Products

CBER has encountered the rapid emergence of advanced manufacturing technologies in various investigational biological products, such as cell-based and tissue-based advance therapy products, intersecting with critical areas associated with DM and POC manufacturing. While CDER & CBER both regulate biological products, CBER biologics are generally more complex with undefined critical quality attributes and often have different manufacturing paradigms. This is particularly true for cellular and gene therapy products and tissue-engineered products. The aim of this session is to discuss the unique challenges and considerations that apply to these products.

Moderator: Carolyn Yong, Ph.D., Associate Director for Policy, OTAT/CBER/FDA

1:15 – 1:40 PM	***CBER's Perspective on Distributed Manufacturing and Point-of-Care Manufacturing of Complex Biologics*** **Laura M. Ricles**, Ph.D., Chief, Tissue Engineering Branch, Division of Cellular and Gene Therapies (DCGT), Office of Tissues and Advanced Therapies (OTAT), CBER/FDA This presentation will discuss CBER's experience with distributed manufacturing and point-of-care manufacturing of complex biologics, including cellular and gene therapy products and tissue-engineered products. The current regulatory framework for these CBER-regulated medical products will be presented and discussed in the context of distributed manufacturing and point-of-care manufacturing.
1:40 – 2:00 PM	***Distributed and Point of Care Manufacturing – Ensuring the Quality of Autologous Cell Therapy Products*** **Laura Sands**, MSc, Head of Regulatory Affairs, Bioscience and Personalized Medicine, Lonza For autologous cell therapies, proximity to patients matters; however, the complexity of Cell and Gene Therapies as compared to traditional biologics and small molecules creates unique product quality considerations during implementation of distributed manufacturing models. This talk will review some of the challenges specific to autologous cell therapies and highlight industry needs for successful application of distributed manufacturing.
2:00– 2:20 PM	***Design of Quality Systems and Oversight for CGT Products under DM/POC Manufacturing Models*** **Richard McFarland**, Ph.D. MD, Chief Regulatory Officer, Advanced Regenerative Manufacturing Institute (ARMI) Cell and Gene Therapy (CGT) products constitute a diverse group of products in commercial use with many more in research and development. This group is heterogeneous and includes most of the products classified under regenerative medicine including both in vitro and in vivo gene therapies, cell therapies of all types, and tissue engineered medical products and engineered organs. In addition, unlike traditional biotech products where the cells and gene are 'biofactories' and the therapeutic products are either secreted or extracted from the cells, the cells and genetic material are the final products. This situation tends to make in process control during manufacturing even more challenging than traditional biotech as a result of the fact that given our current understanding of ex vivo biology it is often not possible to control their responses to seemingly trivial changes of their microenvironments. As a result it is difficult to offer precise, well-defined proscriptive solutions to the design of quality systems for CGT manufacturing under conventional conditions, much less distributed and point of care manufacturing models (DM/POC). However the general tenets of distributed PQS with respect to data integrity, security, and degree of centralized control that are being established for other drug and biologic products should also be applicable. There are many logistic and patient care benefits of DM/POC that should lead to increased use in CGT manufacturing as increased process analytical technology allow for more robust application of QbD principles to CGT manufacturing.

2:20 – 2:45 PM	***Panel Discussion and Q&A*** • **Laura M. Ricles, Ph.D.** • **Laura Sands, MSc** • **Richard McFarland, Ph.D., MD** • **Steven Oh**, Ph.D., Deputy Director, DCGT/OTAT/CBER/FDA
2:45 – 4:00 PM	***Breakouts*** *Registrants will breakout into several concurrent breakout sessions to facilitate small group discussions*
4:00 PM	***Wrap up and End of Workshop***

PQRI Members

- U.S. Food and Drug Administration (FDA)
- Health Canada (HC)
- Consumer Healthcare Products Association (CHPA)
- International Pharmaceutical Aerosol Consortium on Regulation & Science (IPAC-RS)
- International Pharmaceutical Excipients Council of the Americas (IPEC-Americas)
- Parenteral Drug Association (PDA)
- United States Pharmacopeia (USP)
- Extractables and Leachables Safety Information Exchange (ELSIE)

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The Product Quality Research Institute (PQRI) is a non-profit consortium of organizations working together to generate and share timely, relevant, and impactful information that advances drug product quality, manufacturing, and regulation. To learn more or to join, contact us at **PQRISecretariat@pqri.org**, call, **+1 (202) 230-5607** or visit **www.PQRI.org**.