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Dockets Management Staff
U.S. Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Docket No. FDA-2022-N-2316

**Discussion Paper: Distributed Manufacturing and Point-of-Care Manufacturing of Drugs;
Request for Information and Comments**

To Whom It May Concern,

Biotechnology Innovation Organization (BIO) welcomes the opportunity to comment on the Food and Drug Administration (FDA or Agency) discussion paper for stakeholders entitled "Distributed Manufacturing and Point-of-Care Manufacturing of Drugs".

We appreciate the complexities associated with the development, use, and regulation of advanced and innovative manufacturing tools and approaches throughout medical product development. BIO applauds FDA's work to realize the potential of advanced manufacturing through regulatory guidance and programs to collaborate with industry on finding solutions for these unique challenges that may benefit both industry and regulators alike, and ultimately, our patients.

BIO is the world's largest trade association representing biotechnology companies, academic institutions, state biotechnology centers and related organizations across the United States and in more than 30 other nations. BIO's members develop medical products and technologies to treat patients afflicted with serious diseases, to delay the onset of these diseases, or to prevent them in the first place.

BIO recognizes the impact distributed manufacturing (DM) and point-of-care (POC) manufacturing can bring to drug supply chain reliability and robustness, especially in time-sensitive scenarios such as public health emergencies. We are pleased to provide the general comments below on this discussion paper.

(1) General

First, we commend FDA for the development of this paper and consider it an important step for the Agency and other stakeholders to start discussing DM and POC. We note its timeliness as other regulatory authorities (e.g., China's National Medical Products Administration, or NMPA) are proposing a regulatory framework for products manufactured at the POC. While more technological advances in the area might be needed to inform potential policy related to DM and POC, we agree that the timing is appropriate to harmonize terminology and concepts around DM and POC. In general, we recommend that FDA collaborates with other health authorities to ensure harmonization of the concepts involved in DM and POC strategies to incorporate a

global perspective at this early stage and anticipate the impact that implementation might have on emergent markets with less maturity in their regulations and infrastructure.

BIO notes the impact that introducing DM and POC will have on current regulations, and we look forward to collaborating with the Agency on revisions potentially needed. Lessons learned from cell therapy products currently manufactured at POC can inform the regulatory framework for DM and POC.

Due to the high risk involved in the introduction of these innovative manufacturing strategies, it will be important to clearly state in the paper the benefits of implementing DM and POC manufacturing as well as their frameworks for products other than cell and gene therapies (CGT). BIO understands that improving patient access and creating personalized medicines are key benefits of pursuing these innovative strategies, but we note that different business models for POC and DM will generate different levels of risks.

For example, the use of highly replicable modular systems, placed in different locations as part of a fleet of manufacturing units (scale-out model) for several target molecules, has the potential to reduce costs, increase efficiency, agility, and flexibility without the need to create a complex regulatory framework.

Next, it might be challenging to replicate current activities in central plants at a more local level. Approaches would need to be changed, and as such, BIO recommends that FDA consider developing new guidances discussing potential enablers, e.g., digital twins of processes for real time release (RTR), digital assets, predictive maintenance, guided worker, digitalization of process interactions, fully parameterized recipes, data standards for data exchange, etc.

Enabling regulation for ancillary technologies to support filing tools such as imaging, PAT, biopharmaceutics modeling, and stability modeling will improve the quality and safety of DM and POC platforms as well as traditional products and processes. Similarly, we recommend considering whether additional risk can be mitigated for POC scenarios, but limiting shelf life (e.g., 30 to 90-day supply) and changing the nature of the persistence of product rather than considering it as the same as a 2+ year shelf-life product.

(2) Distributed Manufacturing

In general, there are practical elements that need to be considered to support DM that may impact the ability to deploy the same approaches in different regions. As previously noted, these differences may be solved through international harmonization.

In addition to the list of DM discussion questions provided, BIO recommends that the Agency collect stakeholder input on the following points and consider:

- Whether remote inspections will be considered for multiple locations once the pre-approval inspection has been completed. FDA should consider the need to evaluate and/or inspect units after they move to new locations.
- Whether review of any changes to a manufacturing unit's movement will be an expedited review (if it constitutes a manufacturing site change requiring the submission of an amendment or a supplement to the application). A DM-specific regulatory framework with different rules for moves of DM-registered units would be especially helpful.

- Whether there could be benefit in development protocols for remote inspections guided by telepresence tools, e.g., augmented reality (AR) glasses, to monitor batches at external vendors.

DM Discussion Questions

BIO's answers to FDA's questions are bulleted below.

1. *Are there any additional aspects of the current regulatory framework (e.g., aspects not listed above) that may affect DM and should be considered by FDA?*
 - Because DM does not necessarily mean mobile manufacturing, static installations of DM equipment should be considered and defined. Although static installations do not necessarily require changes to the regulatory framework, we recommend including parameters by which the equivalency of DMs can be maintained, whether they are mobile or stationary single units, which could reduce burden on both the Agency and sites. The discussion paper does address several possibilities but having a "fleet of equivalent systems" or a scale-out business model in which a platform is not movable but replicated in multiple regions is not yet discussed. Points to consider for a fleet concept are:
 - "Fleet control strategy (FCS)" which uses globally maintained pharmaceutical quality systems (PQS) to design, build, qualify, conduct vendor management, technology transfer, and maintain DMs. This can potentially remediate or help manufacturers and regulators with challenges in DM sections 3, 4, and 5 of the document.
 - The fleet approach can be considered as a lower risk entry point in certain situations, within a defined environment and with minimal "movement". This situation might create even benefits for FDA in terms of inspection frequency or update of documents where FDA can provide flexibility instead of inspecting all single units.
 - The FDA could consider an approach where sponsors file by facility or DM unit. The Agency can also consider inspecting the initial production facility/DM unit for pre-licensure inspections (PLI) only, and for other facility/DM units making the same product, or consider doing minimal inspection as long as the fleet concept has been approved.
 - The discussion paper describes the potential impact upon first move or manufacturing facility change but there is no discussion on ongoing requirements (e.g., periodic revalidation, annual stability testing per fill line, etc.). It discusses multiple DM locations impacting FDA but the impact on the applicant should be considered as well.
 - Discussion of how the Agency would conduct an inspection at a DM site when the host PQS is located at a different location would be helpful.
 - The different scenarios for DM listed would require different levels of controls commensurate with their risks, e.g., level of PQS oversight. We suggest including more discussion of such different levels of controls taking into account the respective risks of each scenario.
 - It would be helpful to clarify justification that may be acceptable to satisfy product bioequivalence through process evaluation rather than product testing if bioequivalence support is an expectation.
 - The approach for developing a mechanism by which the manufacturing platform, or a subset of the platform in the form of a

manufacturing module, can be approved outside of the product approval process is necessary to support the business case for establishing a DM/POC network.

- If the driver for establishing a DM network is either (1) to ensure access of drugs and biologics to populations that otherwise would be unable to acquire them because of cost or logistics or (2) to ensure rapid availability of a drug or biologic during a global health crisis, then harmonization with global Health Authorities during development of DM and POC approval pathways is necessary. The white paper could more thoroughly consider implications of obtaining global acceptance of DM and POC and differing regional requirements for post-approval maintenance, both of which must be considered to create a business case for developing advanced manufacturing technologies.
- It would be helpful to distinguish the risks from the facility and the region. We suggest that FDA consider updating current regulations and guidances to separate these two categories of risks. Both would apply to a static facility, but mobile facilities could have regulations addressed once comprehensively and as needed around the geography following a move.

2. *Are there new regulations or guidances that would be helpful for providing transparency on DM, and if so, what aspects of DM should be considered?*

- Guidance on specific considerations for mobile (or portable) units would be helpful.
- Detailed guidance on what constitutes equivalency of units.
- Global harmonization on terminology and technical principles for DM and POC are needed.
- Introduction of Fleet Control for DM concept of static assets would be helpful. It could be done under the same regulations as mobile assets or create a separate guidance for the scale-out, fleet concept. The guidance should include expectation for control of the fleet for initial and future qualifications.
- Guidance on the use of DM for multiproduct manufacturing (i.e., when different products are made at each DM site).
- Future guidances and discussion papers should include case scenarios of different types of DM and POC.
- We encourage FDA to progress the acceptance of in silico biopharmaceutics models in lieu of clinical bioequivalence (BE) studies to facilitate mitigating this risk without incurring the large cost and delay to patients of conducting clinical BE studies. The level of understanding of in silico models, where they can be applied, and what rigor/validation should be applied to them could be articulated to ensure the risks here are sufficiently mitigated.
- We encourage FDA to progress the acceptance of flexibility around in silico stability models in lieu of real time stability data.

3. *Are there DM use scenarios that are not captured in the discussion paper? Do the areas of consideration still apply? Are there additional areas of consideration?*

- It would be helpful to clarify situations where release of intermediates and finished product remain the responsibility of the licence holder and not HCF personnel.
- For marketed product there will be an impact on serialisation to maintain integrity of the supply chain. It would be helpful to clarify whether product at DM or POC would need to be serialised.
- For N-of-1 type therapies, the concept of “process validation” will need to be significantly re-envisioned, particularly for complex therapeutics (e.g., oligonucleotides). It is not possible to follow traditional process validation paradigms (i.e., 3 concurrent DS/DP lots) in cases of highly distributed and/or POC manufacturing suites that are generating individualized therapies.
- It would be helpful to clarify whether reach DM site will be assigned an FDA Establishment Identifier (FEI) number, whether the DM site would carry the same FEI number after relocation, whether DM sites would be allowed to relocate to a different region/country, how the Agency would conduct adverse event or quality related for-cause inspections if the DM site has been relocated, etc.

4. *How could the DM unit resemble or differ from that of a manufacturing facility at a fixed location?*

- In general, a specific guidance on point of considerations for mobile (or portable) unit manufacturing would be helpful.
- Core manufacturing equipment elements should not be any different.
- Additional attention will need to be paid to validation of moves – assurance that equipment functionality is not impacted (or that any impact is readily detectable) over a range of potential move scenarios. A situation is feasible where installation qualification, operational qualification, and performance qualification (IQ/OQ/PQ) are carried out in one location and a wider package shows that subject to repeat IQ (e.g., service connections)/abridged OQ (confirmatory checks on operation following installation at the new location), PQ is not impacted.
- Environmental monitoring and microbial control would need to be considered, e.g., if mobile, the common isolates for the facilities, training of operators, utilities, etc.
- The manufacturing unit and what it includes would need to be considered, i.e., whether the environment is part of the manufacturing unit.
- All input materials (including starting materials and packaging materials), batch documentation, electronic systems (for material management, deviation management and customer complaints), procedures and training should be common amongst facilities and should all feed into an overarching QMS.
- Environmental monitoring (viable and non-viable) could be different depending on local layout and conditions. Each DM/POC site will have a different environmental profile that would need to be assessed in each case. This would present challenges especially in the manufacture of sterile product though it is likely that a DM scenario would involve isolator technology rather than traditional restricted access barrier systems (RABS), thereby minimising risk.

5. *How should an applicant report the installation or relocation of a DM unit to the Agency?*

- We recommend as simple a solution as possible, e.g., a global positioning system (GPS) tracker. Automated tracking of the unit could eliminate the need for applicant reporting.
- FDA may want to consider a risk-based framework on reporting installation/relocation of DM units, similarly to scale-up and the post-approval changes (SUPAC) for centralized manufacturing site changes. Establish higher risk criterion that would warrant a reporting requirement and minimize administrative burden for reporting of low-risk installations/relocations.

6. *How often would a DM unit be projected to move to a new location?*

- While this would be dependent on the technology and intended use, “typical” scenarios could indicate less than 10 moves per year.
- However, any guidance should anticipate worst case, i.e., frequent, moves, and facilitate this to ensure that technology is able to fully advance for patient benefit.

7. *How should an applicant demonstrate comparability of product quality following a DM unit move to a new location?*

- Given that the manufacturing unit and process remain unchanged when moving to a new location, the local parameters (such as background environment, process utilities, operator training) would need to be verified in order to confirm equivalency. Initial process performance qualification (PPQ) strategy (typically triplicate batches are expected) should be amended to allow for distribution of PPQ batches across multiple DM units as appropriate provided documented rationale.
- There would need to be consideration of operator training. The simplest scenario would be if there is a pool of operators who move with the unit, in which case no further action would be required. Training could be addressed as for multiple individuals at a fixed manufacturing site. Another alternative might be a set of trained operators at each of a number of regularly used locations which could be covered in a similar manner. If the operators change at each location and will not be regularly using the unit, then this will be more challenging and will depend on the nature of the unit and the extent of operator activities from ‘push start’ to high dependency.
- Guided worker and Just in Time training through digital delivery means are also options.
- Ultimately, this should be flexible and should be weighed against patient risk-benefit rather than product modality. The extent of comparability studies should be reduced as the license holder has demonstrated repeatedly that there is no impact for new distributed sites and should shift to more routine verification/qualification activities.

8. *How could a “centralized” quality system (i.e., at the “parent location”) ensure that each DM unit would comply with CGMP requirements and biological product quality standards?*

- Manufacturer QMS and quality assurance (QA) oversight could address this.
- Many quality system elements can be readily centralized across multiple sites. The fundamental ICH Q10 objectives of product realisation, establishing and

maintaining a state of control and facilitating continual improvement remain, as do the associated enablers of knowledge and quality risk management.

- 21 CFR 210/211 fundamentals (i.e., sub-parts that need to be covered) are also largely unaffected.
- In general, we recommend that FDA elaborate on this topic, specifically on the types of regulatory actions that would be taken if one DM unit fails to comply with GMP requirements and how the other DM units managed under the same centralized PQS would be impacted.

9. *Are there additional areas of consideration that should be addressed for DM units capable of manufacturing multiple, different drug products compared to DM units capable of manufacturing a single product?*

- Change-over and cleaning validation.
- Safety, Health, and Environment (SHE) should be harmonized across sites to the extent allowed by local regulations.

(3) Point-of-Care Manufacturing

In general, BIO recommends that FDA clarify whether finished drug products, devices, and testing would be in scope of point-of-care (POC) manufacturing. In addition, it would be helpful to provide the requirements that apply to the POC 'provider' and clarify who is the responsible entity during an inspection.

In addition to the list of DM discussion questions provided, BIO recommends that the Agency collect stakeholder input on the following points and consider:

- Whether there will be specific requirements as to the types of activities or type of products that will be permitted to be conducted or manufactured at the POCs. We also recommend adding a question concerning the expectations of the POC host site during an inspection.

POC Discussion Questions

BIO's answers to FDA's questions are bulleted below.

1. *Are there additional aspects of the current regulatory framework (e.g., aspects not listed above) that may affect POC and should be considered by FDA?*

- Responsibilities and accountabilities of the POC platform manufacturer and Health Care Facility (HCF) should be defined.
- Details on the development of Risk Management Plans (RMPs) between the POC platform manufacturer and HCF should be defined.
- Creation, maintenance, and review responsibilities for Master Production Records (MPRs), Batch Production Records (BPRs), etc. should be defined.
- Advancement of imaging and PAT tools and methods may be necessary in ensuring quality at host sites. The Agency may consider investing in regulations and guidance for these technologies in general, facilitating their use for POC applications.

- POC units may fit under device regulations rather than manufacturing regulations, e.g., resembling an auto-injector than a manufacturing facility. Such equipment should depend more on testing and validation when manufactured rather than inspection at each location that the device is deployed.
2. *Are there new regulations or guidances that would be helpful for providing transparency on POC, and if so, what aspects of POC should be considered?*
 - POC could be used for DP with short stability, and requirements for instant release/conditional release are relevant. Requirements for reconstitution are relevant to explain, e.g., whether a washing step is minimal handling.
 - More guidance on the molecules or DP candidates that can be considered would be helpful. Examples may include but are not limited to advanced therapy medicinal products (ATMPs), drugs with short shelf life, final formulation unit operation, etc.
 - We suggest that FDA consider a concept where the patient comes to the sponsors in specific locations instead of sponsors going to the patient in different HCFs with different capabilities to absorb manufacturing processes.
 3. *What type of business relationships are envisioned between companies developing POC platforms and health care facilities (HCFs)?*
For example:
 - a. *POC platform manufacturer co-located at HCF and operates platform locally*
 - b. *POC platform manufacturer operates platform remotely with qualified HCF staff as end users*
 - c. *HCF purchases and operates POC manufacturing platform*
 - An alternative scenario could be where a POC platform manufacturer operates the platform remotely with manufacturer staff. A contract would be needed to define responsibility split between manufacturer and HCF.
 - Likewise, batch release algorithms could potentially be built in that would allow site staff to routinely make decisions on use. Through digital enabling, the POC platform manufacturer could be able to monitor operations remotely in real time (AI in preference to human, for greater data capability) and be able to intervene (AI notification to human) as required.
 4. *What mechanisms are needed for the maintenance and validation of the POC unit at the host site?*
 - The fundamentals would be the same as DM, but with POC there would be different units at different locations, rather than the same unit moving to different locations. This then brings in the question of comparability between the different units. There is potentially more variation in the operation of different units (because there will be different staff at each location), though the variation associated with each unit should be minimal due to same pool of staff being used at each location. It will be necessary to understand unit robustness across as wide a range of environments as possible given that the variability between different HCF locations may be high.
 - Calibration and maintenance status of equipment must always be established and recorded. Requalification of the equipment is needed after relocation or product change, or requalification on a periodically basis. A risk-based approach should be

used to evaluate need for calibration, maintenance, and re-validation. Evaluation of trends - trends in performance must be monitored. This is difficult when manufacturing is decentralized. Periodic system evaluation should be performed. Process automation could be a way to ensure process control and product quality. Other elements to ensure control of the POC unit are e.g., manufacturer QMS, training, and room classification/environmental monitoring.

- Pharmaceutical Inspection Co-operation Scheme (PIC/S) Annex 2A (Manufacture of advanced therapy medicinal products for human use) states that the process performed at the POC should maintain its validated status in accordance with PIC/S Annex 15 (Qualification and validation), PIC/s Annex 20 (Quality Risk Management), and PIC/S Annex 2A.
5. *What are the necessary steps and elements for the qualification and training of end users? What safeguards should be in place to ensure that only the qualified, trained end user operates the POC platform?*
 - Access control, segregation of roles under a quality agreement, on-site training, training in the PQS, etc. should be considered.
 6. *What steps are necessary to ensure the quality of materials (APIs, excipients, processing aids, container-closure systems) distributed or sold to POC end users and that only qualified components are used in the POC platform?*
 - Local receiving control, traceability, tamper proofing, IT solutions, segregated storage (release/quarantine), etc. should be considered. The manufacturer could provide and release all materials, or the local site could source and release materials in a defined manner.
 7. *What mechanisms are needed to ensure deviations will be identified and prevented, and nonconforming drug is rejected or segregated?*
 - In general, this will depend on the platform and the modality of the product being manufactured at POC.
 - A service level agreement (SLA) with local operators should exist. A central quality digital system (e.g., cloud-based system) linked to POC would be helpful. Training of operators, technicians and other users, QA oversight/presence/review, dose control, batch record, etc. would be needed.
 - The establishment of a recognized Pharmaceutical Quality System (ICH Q10) with a defined oversight (manufacturing authorization holder or MAH) will capture deviations, change control corrective and preventive actions (CAPAs), etc.
 - The PQS will be subject of periodic audits of systems and sites carried out by the POC platform manufacturer
 8. *A POC unit may be operated in a designated location at the host site (e.g., hospital pharmacy) or be moved to different locations (e.g., a patient's bedside). What additional potential locations are envisioned for the POC unit operation, if any?*

- The location could also be a Good Manufacturing Practice (GMP) facility at the hospital.
9. *How might records of the drug manufactured in the POC platform and dispensed by the end user be created, maintained, and made available?*
- Batch records (paper-based or electronic) could be used. Ideally, records would be digital enabling with appropriate access control at the HCF and central POC platform owner.
 - The manufacturer should be able to record and store all data digitally and internally, for the end of monitoring, maintaining, and improving the POC platform. Such data access and management should be regulated on a global and not local/country basis. Digital twins in DM and POC pose questions on data management regulations which currently could differ by country and region.
10. *Do the areas of consideration apply to POC for biological products where end users would be expected to perform extensive preparation or substantial manipulation (e.g., cell isolation, cell processing, combining with scaffolds, etc.) of the product at the HCF? Are there additional unique areas of consideration for these products?*
- The same fundamental considerations apply. Requirements for control and staff training will differ case-by-case. Many HCF facilities already have a wide range of highly skilled staff who may be well placed to do these activities. We note that much of the early work on CGT was driven by HCFs with strong academic clinical credentials rather than traditional industry.
 - If users perform, e.g., extensive preparation or substantial manipulation of cells, it could be considered DM. Reconstitution of frozen cells for cell therapy could be considered.
11. *Are there aspects of POC platforms that have not been considered in the discussion above?*
- Cross contamination strategy is needed (including procedures for sufficient cleaning) as well as a procedure for line clearance.
 - Implications to regulations from approaches such as “N of 1” therapies should be considered.

In addition to our general comments and question responses, please consider the following table outlining comments on specific language in the discussion paper. While we understand that FDA may not intend to revise the paper, we suggest that the feedback below is an extension of BIO's responses to the Agency's questions.

LINE #	COMMENT w/RATIONALE	PROPOSED CHANGE (Using strikethrough text for deletions and <u>underline text</u> for additions)
Introduction		
Scope		
Background		
Page 4; Terminology of "Manufacturer"	We note that a manufacturer is typically an entity rather than a person.	BIO recommends the following revision: " A person <u>An Entity</u> who owns or operates a facility: [...]"
Page 5; Terminology of "Manufacturing Unit"	BIO notes that the definition should not be specific to mobile systems and should apply to more permanent approaches.	BIO recommends the following revision: " A mobile manufacturing process: [...]"
Page 5; Terminology of "Distributed Manufacturing (DM)"	We note close similarity between the first two bullets in the definition of DM. Also, the second bullet includes a requirement for units to be "manufactured and installed to the same specifications", which is not included in the first bullet.	BIO recommends the following revision to combine the first two bullets: "Units located within one manufacturing facility or multiple manufacturing facilities installed to the same specification, networked and operated by a central PQS."
Page 5; Terminology of "Point-of-Care Manufacturing (POC)"	Original text: "Point-of-Care Manufacturing (POC) A subset of DM that uses manufacturing units distributed to host sites in proximity to patient care (e.g., health care facilities) where: [...]" BIO recommends that the discussion paper differentiate POC from contract manufacturing and compounding.	BIO recommends the following revision: "Point-of-Care Manufacturing (POC) A subset of DM, <u>excluding contract manufacturing</u> , that uses manufacturing units distributed to host sites in proximity to patient care (e.g., health care facilities) where: [...]"

LINE #	COMMENT w/RATIONALE	PROPOSED CHANGE (Using strikethrough text for deletions and <u>underline text</u> for additions)
Areas of Consideration Associated with DM		
Page 10; 5. Each new location of a DM unit may cause the applicant to be required to generate analytical comparability, method transfer and validation, and stability data	Original text: "Each new location of a DM unit may cause the applicant to be required to generate analytical comparability, method transfer and validation, and stability data" We recommend that the Agency provide additional details regarding the above statement. Specifically, it is unclear what will be the driver for the need for additional data: the location or the type of unit.	We recommend further specifying the factors that influence when additional data will be expected.
Page 10; 5. Each new location of a DM unit may cause the applicant to be required to generate analytical comparability, method transfer and validation, and stability data	Original text: "Each new location of a DM unit may cause the applicant to be required to generate analytical comparability, method transfer and validation, and stability data" This statement appears to conflate a manufacturing unit with a testing unit. There is no regulatory or practical requirement for testing to be co-located with manufacturing.	Method transfer and validation requirements should be out of scope of this discussion unless limited to the narrow scope of "at line," "in line" or "on line" testing that is integral to the modular manufacturing unit design and operation. BIO recommends the following revisions: "Each new location of a DM unit may cause the applicant to be required to generate analytical comparability, method transfer and validation, and stability data. <u>Analytical method transfer and validation data may also be required if testing will be located with the DM unit.</u> "
Page 10; 5. Each new location of a DM unit may cause the applicant to be required to generate analytical comparability, method transfer	Original text: "Each new location of a DM unit may cause the applicant to be required to generate analytical comparability, method transfer and validation, and stability data. [...] The need for these additional data (especially stability data) would burden applicants making multiple	We recommend that FDA consider addressing risk and experience-based considerations that would lead to a reduction in the extent of analytical data and reporting categories for subsequent DM units or relocated DM units.

LINE #	COMMENT w/RATIONALE	PROPOSED CHANGE (Using strikethrough text for deletions and <u>underline</u> text for additions)
and validation, and stability data; Paragraph 1; Lines 4-6	and/or frequent location changes and increase FDA’s assessment responsibility.” Data for subsequent DM unit additions, or for existing DM unit relocations, could be considered confirmatory subject to a protocol. This would reduce reporting categories (e.g., confirmatory comparability with CBE+30, confirmatory stability that is annually reportable).	
Page 11; 6. A central PQS for multiple units and locations may affect the Agency’s ability to evaluate the PQS	BIO proposes reconsidering the interpretation of the ICH Q10 guideline to account for DM and POC setup.	BIO recommends the following revision: “[...] ICH Q10, recommends that a PQS is primarily assessed at facility level and in alignment with corporate PQS policies <u>the effectiveness of the PQS can normally be evaluated during a regulatory inspection at the manufacturing site.</u> ”

Conclusion

BIO appreciates this opportunity to submit comments regarding FDA’s discussion paper entitled “Distributed Manufacturing and Point-of-Care Manufacturing of Drugs”. As FDA continues to innovate and invest in novel approaches for drug manufacturing, we would welcome future opportunities to partner with the Agency and discuss this topic.

Sincerely,



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Biotechnology Innovation Organization