A Role for Public-Private Partnerships in Advancing Biopharmaceutical Manufacturing Innovation

Kelvin H. Lee Professor of Chemical & Biomolecular Engineering, University of Delaware Director, National Institute for Innovation in Manufacturing Biopharmaceuticals KHL@udel.edu

Disclosures:

NIIMBL supported by awards 70NANB17H002 & 70NANB20H037 from U.S. Dept of Commerce, National Institute of Standards and Technology. KHL also PI on awards from NSF, State of Delaware, a number of companies and nonprofits in, or related to, the biopharmaceutical industry. KHL also a member of the FDA Pharmaceutical Science and Clinical Pharmacology Advisory Committee



Our Mission

The NIIMBL mission is to accelerate biopharmaceutical manufacturing innovation, support the development of standards that enable more efficient and rapid manufacturing capabilities, and educate and train a world-leading biopharmaceutical manufacturing workforce, fundamentally advancing U.S. competitiveness in this industry.







AMERICAN INNOVATION AT WORK

IMPACT

domestic industry

Regional economic

Secure, integrated

Access to new and

Flexible, adaptive

manufacturing innovation

Accelerated development

manufacturing

De-risked

Lower costs

and approval

improved medicines

development

supply chain

Growth of globally-competitive

NATIONAL

+

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E

INDUSTRY



3





At a February 2020 workshop, distinguished R&D and supply chain technical leaders from 14 major manufacturers & suppliers met and agreed:

- Significant opportunity to impactfully transform CMC development & manufacturing through E2E integration and technology advancement.
- Collaboration in consortium will significantly accelerate transformation
- Success enabled by expertise, leadership & capability of committed industry leaders
- We will advocate for <u>our</u> companies to participate
- High level goals/strategy agreed: priorities/details to be refined after participants identified



Vision: By 2029 invent, design, build and commercialize drug substance and product manufacturing capability enabling:

- Flexibility to supply extremely diverse and changing portfolio of products in the face of uncertainty and changing demand
- Improved Control, Robustness and Security of Supply
- Faster Product Development and Supply Chain Velocity
- Sustainable plastic and energy use
- Capital & Operating Cost dramatically reduced
 - No longer barrier to availability of capacity, innovation or change
- DS & DP expertise and thinking integrated vial to vial





High Program Level Strategy

- Accelerate adoption of intensified processes already developed (1st gen)
- Collaborate to develop process technology and equipment (2nd gen) in use in commercial production in 6 years.
- Design hypothetical 3rd gen facility to determine what technology needs to be developed
- 4. Technology will be developed with platform processes and demonstrated with collaborators and in NIIMBL test bed.



NIIMBL Active Listening Meeting

Overview

- NIIMBL piloted a new type of conversation between the regulated industry and FDA, while reducing risk of participation by both groups
- We sought to better understand the reasons behind the challenges in implementing new technologies in biopharmaceutical manufacturing
- Participants were asked to consider the following question as prework ...

NIIMBL-facilitated Active Listening Meeting between industry and FDA identifies common challenges for adoption of new biopharmaceutical manufacturing technologies

Mantle and Lee <u>PDA Journal of Pharmaceutical Science and Technology</u> May 2020 DOI: https://doi.org/10.5731/pdajpst.2019.011049





NIIMBL Active Listening Meeting

Overview

There are significant challenges in implementing new technologies in manufacturing. With respect to the regulatory landscape, what changes would you like to see implemented that would enable your company to deploy innovative technology for manufacturing or continuous improvement?

Guiding questions:

What is not working well today? Process, tools, and/or technology?

What do you need that you don't have?

Is there sufficient awareness at all critical points within your organization about these challenges? Is there any disconnect between what is perceived as the hurdle and the actual impediments? What competencies, skills, experiences, and knowledge exist in staff/managers/suppliers? What are the written or unwritten "rules"?

How much of a concern are post-approval changes?





NIIMBL Active Listening Process Overview

Interview Question: There are significant challenges in implementing new technologies in manufacturing. With respect to the regulatory landscape, what changes would you like to see implemented that would enable your company to deploy innovative technology for manufacturing or continuous improvement?



NOTE: The scope of the meeting was limited to topics of relevance to the Center for Drug Evaluation and Research (CDER) at the FDA (i.e. specifically, biotechnology products).

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Consensus Areas Identified in Company Interviews

CONSENSUS AREA	#
Interaction between industry and the FDA	11
Transparency	10
Collaboration	10
Early interaction and the Emerging Technologies Team	9
Case Studies	9
Changes to approved manufacturing processes	11
Approaches to comparability	10
Post approval changes	10
Operating in a global regulatory environment	11
Consistency across the FDA	8
Between individuals (reviewers or inspectors)	7
Between leadership/policy and reviewers/inspectors	3
Guidance documents	8
ICHQ12	3
Manufacturing process development	7
Specification setting	4
Using prior knowledge in regulatory filings	6
Additional regulatory pathways/tools	7
Education and training	5

General Reflections

- The industry has had a broad spectrum of experiences and perspectives in their interactions with FDA CDER
- Under the current system, there is rarely a business case for implementing new manufacturing technologies. While new technologies may offer some process improvements, those are weighed against business risks associated with speed to market.

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Company Interviews January – February 2019	Written Document March – April 2019	Active Listening Meeting May 23, 2019	Outputs Jun – Jul 2019
11 Companies Amgen, AstraZeneca, BMS, Celgene, Genentech, GSK, Janssen, Merck, MilliporeSigma/EMD Serono, Novartis,	NIIMBL anonymized & compiled feedback Identified 8 consensus areas	Morning : Prioritization of consensus areas for afternoon discussion; attended by industry representatives and NIIMBL staff.	NIIMBL synthesized the survey responses and the discussion into a whitepaper
and Pfizer	[Section 2.2.]	[Section 3.1]	FDA staff took issues back for internal discussions
Regulatory Affairs, CMC, and/or Process Development groups were represented		Afternoon: Readout of briefing at FDA and discussion; attended by industry representatives, FDA staff, NIST staff, and NIIMBL staff.	(No expectation of formal response)
[Section 2]		[Section 3.2]	

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Morning Industry-only Session

Anonymous, real-time poll results

How does your current company view and approach interactions with the FDA, on a spectrum from conservative to progressive? (14 Responses)

How do you, based on your individual experiences, view and approach interactions with the FDA, on a spectrum from conservative to progressive? (16 Responses)



Topic Prioritization for Afternoon Discussion

- Interaction between industry and the FDA
- Changes to approved manufacturing processes
- Consistency across the FDA

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Afternoon Readout & Discussion

Business Case for adoption of new technologies

- Discussion of the business case in early and late stage projects
- Considerations of the global regulatory environment
- Timeline is a key driver

Changes to approved manufacturing processes

• There was discussion around comparability protocol as a tool for post-approval process changes

Interaction between industry and the FDA

- Desire for more informal interactions with the FDA
- Relationship between specificity of a question and formality of response
- Case studies, collaboration, shared learnings

Consistency across the FDA

Consistency of reviewer questions during information requests – context



Summary from Advanced Manufacturing Technology Workshop held at 6th Accelerating Biopharmaceutical Development Meeting in 2019

Lee and Mantle 2020, under revision (a different publication from Active Listening)

Imagine a future state for the industry that allows for manufacturing of biologics, vaccines, and/or advanced therapies in a flexible-use facility and where diverse biopharmaceuticals could be manufactured rapidly (e.g. in response to a public health threat, in an effort to be proactively prepared to address dynamic needs, etc.). This vision could be realized through advances in end-to-end continuous manufacturing, improved automation and robotics, innovations in host cells, development of sensors to monitor and control processes, new/better/faster release tests, assays and integrated technologies for monitoring quality attributes, approaches to faster changeover, and other technological achievements.

What do you think are the top 10 technological barriers or bottlenecks that need to be addressed to help realize this vision?





Summary from Advanced Manufacturing Technology Workshop held at 6th Accelerating Biopharmaceutical Development Meeting in 2019

Lee and Mantle 2020, under revision





What are drivers for adoption of NEW technology?

supply need economics competition new modalities quality improvement funding patient patient need enabling technology problems patients simplicity relevant cost education simplify trust product adds real value agility data analytics reliability Speed quality robustness supply internal cool factor project specific need business case manufacturingspped solution cost reduction secure digitization specifications new challenges reducing cogm pressing efficiency diversity increase glexibility convincing consistency computational models

Lee and Mantle 2020, under revision

Policy suggestions for consideration by the committee (1)

The CDER ETT provides a mechanism for companies to get early engagement with the Agency on issues related to innovative manufacturing technologies.

As with all matters, discussions between the Agency and sponsors is confidential.

Such confidentiality is important to protect intellectual property, but also works to slow the adoption of new approaches by multiple organizations.

Would a policy that required <u>some form</u> of public dissemination of the types of technologies and approaches being considered by the ETT (or outputs from discussions), help other companies understand the which innovative approaches being considered by Agency staff?

Could such a practice, if done with understanding by all parties about what might be disclosed, help accelerate adoption of approaches across the industry? Could it lead to improved submissions by helping nucleate discussions around certain approaches and leading to collaborative activities for demonstrating innovative manufacturing technologies?





Policy suggestions for consideration by the committee (2)

Janet Woodcock, Michael Kopcha Quality: The Often Overlooked Critical Element for Assuring Access to Safe and Effective Drugs https://www.healthaffairs.org/do/10.1377/hblog20200311.912049/full/

Incentives – A key missing ingredient

"The FDA's Drug Shortages Task Force's October 2019 report, Drug Shortages: Root Causes and Potential Solutions, identifies root causes of drug shortages and makes recommendations for effectively resolving them. For one, <u>there are few incentives in today's manufacturing market</u> to support investment in advancing the technologies used in manufacturing. Furthermore, payers are not equipped with the necessary information to reward a manufacturer by paying more for a product made using a more mature quality management system that is less susceptible to a shortage. In short, we need to recognize the higher value of drugs manufactured using advanced technologies and mature quality management systems." ...







Policy suggestions for consideration by the committee (3)

Frameworks that allow the FDA (CDER and other Centers) to interact 'informally' (not in the context of a review) to discuss, learn, and engage in a dialogue regarding manufacturing innovations can help all parties – ultimately benefiting patients.

Build trust between the Agency and the regulated industry Create a mechanism to interact more deeply with suppliers and vendors Establish mechanisms for Agency staff technical development Lead to improved quality of submissions

We've experienced it within NIIMBL, but:

it takes time to bring stakeholders together it isn't easy for one type of stakeholder to understand the perspective of others one must learn the vocabulary

