JOHN STERLING: Welcome to GENCast, a sponsored podcast series brought to you by *Genetic Engineering and Biotechnology News*. I'm John Sterling, Editor-in-Chief of *GEN*, and I will be serving as the moderator.

I want you all to know that there is a new sheriff in town. No, I am not referring to the old Wild West. I'm speaking about the world of biomanufacturing, which is undergoing a major paradigm shift. It's known as Biopharma 4 or Industry 4.0.

The biopharma industry as a whole has recognized the need to advance the industry by applying the principles of Industry 4.0. The Biopharma Operations Group (BPOG) has developed a ten-year Technology Roadmap with the objective of increasing speed, quality, and flexibility in biopharma manufacturing while reducing cost.

Collaboration and partnerships are a critical element in adapting to this paradigm shift and moving toward the facility of the future.

To learn more, let's meet our panel. Gentlemen, can you introduce yourselves?

JOHN CYGANOWSKI: Hi. I'm John Cyganowski. I'm the Director of Manufacturing Sciences and Technologies in the Americas for MilliporeSigma.

JIM NEVILLE: Hi. My name is Jim Neville. I'm the Director of Technology Management for the Americas at MilliporeSigma.

JOHN STERLING: One of the hottest trends in 2020 will be the advancement of Industry 4.0 in biopharmaceutical manufacturing. What is it, and how is it being applied to the biopharma industry? Jim or John?

JIM NEVILLE: This is Jim. What it is is the current biopharma vision that would utilize digital technologies and capabilities to proactively use process modeling as well as collection of process data by sensors and process analytical technology. And this would really enable an understanding of the process data and predict optimization for path-forward processing by the industry.

JOHN CYGANOWSKI: So in the BPOG Roadmap, which we will be discussing today, Technology Roadmap, Industry 4.0 concepts are addressed within that document, so these two concepts are very much related.

JOHN STERLING: A lot of what's involved in Bioprocess 4.0 revolves around data and analytics. How much of a drastic change is this from the way, say, biopharmaceutical manufacturing was done ten or 15 years ago or longer?

JOHN CYGANOWSKI: So, ten or 15 years ago, the state of manufacturing control, there was a lot of local control, and then it fed into a supervisory control and data acquisition system. I think nowadays, these systems have become much more powerful, and the data is being fed directly into the data system, and the data system is controlling process.

I think the hope is that, as we learn more, we can analyze more data and actually use some of these data to anticipate process upsets and avoid them.

JIM NEVILLE: Yeah, and I would also add that, as John pointed out, having that valuable data can be fed back real time to optimize the process as the process continues.

JOHN STERLING: Do you anticipate any hurdles to accomplishing this mission?

JIM NEVILLE: A few hurdles that people in the industry have pointed out are regulatory implications-- really, what we see as fewer hurdles for data acquisition and analysis, which we were speaking to, but more validation required for the internal and external regulatory partners on control approaches going forward.

JOHN CYGANOWSKI: I think currently, some analytics can be done online, but additional work is needed to develop sensors and systems for real-time analysis and control.

JOHN STERLING: So you mentioned a moment ago about regulatory implications. Since a lot of these technologies, as we mentioned earlier, are so new compared to how biomanufacturing was done 15 or more years ago, how is the FDA handling all of this? Are they

comfortable with these technologies? Do they seem up to date on what these things can do?

JOHN CYGANOWSKI: The Agency has published a guide for the continuous manufacturer of, say, solid dosage forms. And I think much of what's happening, the processes are changing. The unit operations are similar or the same, but they are operated in a different way. And I think this is a learning that the entire industry and the Agency is currently engaged in. I fully anticipate that the Agency will have guidance documents for us later on.

I think one of the big topics on the minds of people in the industry is that, well, say, in a continuous process, how do I define a lot, because in a batch process, it is pretty obvious, but in a continuous process, it is not that obvious. And I think there really needs to be some sort of consensus and a regulatory blessing before people can move forward.

JIM NEVILLE: John makes a great point here. What it is going to need is, between the regulatory bodies and the industry, is this collaboration of how to do validation here. What is the best practice of validation for that particular lot, for that particular batch, which could be one and the same?

JOHN STERLING: Now, you both represent the M Lab Collaboration Center Network of Technical Expertise. How is the M Lab Collaboration Center Network participating in the advancement of Biopharma 4.0 and helping overcome the barriers you just mentioned?

JOHN CYGANOWSKI: The M Lab is a proving ground for new ideas and concepts for innovative and cutting-edge methods and technologies. Connected unit operations and orchestrations will be tested this year. Linking studies for different unit operations are being

performed and will culminate in the continuous manufacturing process model.

JIM NEVILLE: Yeah, and also, you know, the manufacturers can simulate connecting processes in the M Lab in a non-GMP environment. It gives really the freedom of use or exploration or testing, and this is in the mode of intensified, linked, and continuous processes. This really allows industry colleagues to collaborate with us to do this exploration, and that really will address the current and future needs going forward.

JOHN STERLING: So, within M Lab, I know there is also this platform called BioContinuum. Can you talk about the BioContinuum and how it intersects or interacts with the M Lab system?

JOHN CYGANOWSKI: So the BioContinuum platform is a platform that looks at intensified processing,

linked process steps and continuous processes. The M Lab, as Jim mentioned, is a non-GMP environment, yet it is a facility where scale-up and scale-down experiments can be performed, and so we can work things out at the bench scale and then validate how these unit operations behave at scale in the M Lab. All of this is to reduce the risk when these processes go into industry use.

JOHN STERLING: Now, if the industry could accomplish at least one key milestone in 2020 for the advancement of Biopharma 4.0, what do you think it should be?

JIM NEVILLE: Yeah, really, what we believe is every industry organization should have at least one milestone this year related to digital transformation of their related capabilities that addresses the BPOG group and

other collaborators' priorities with the aligned goals towards manufacturing optimization for the future.

JOHN CYGANOWSKI: When I think about some of the recent initiatives in biopharma, the QbD initiative really changed the way drugs are developed and submitted for approval. I think the BPOG Technology Roadmap is a very timely document, and I feel that the industry should look at this document and adopt it as a guide in order to drive progress in 2020.

JOHN STERLING: Well, Jim and John, I want to thank you for sharing your expertise and experience in biomanufacturing and talking about Biopharma 4.0. And thanks to our audience for joining us for this discussion on this rapidly evolving area of biomanufacturing. Be sure to follow *GEN* in print and online for the latest advances in biomanufacturing and Biopharma 4.0.

Thanks for listening to GENCast. For *Genetic Engineering and Biotechnology News*, I'm John Sterling.

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