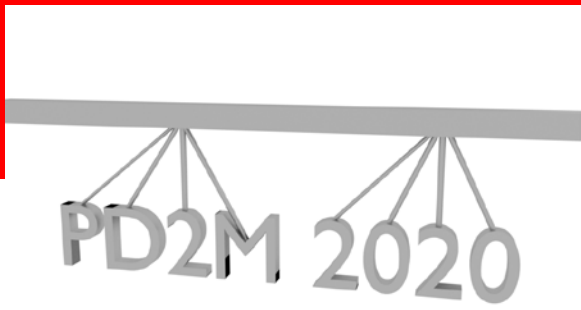
PD2M Newsletter

March 2020



Note from the Editor

Our first issue of the PD2M Newsletter 2020 highlights two interesting topics:

- **Pharma 4.0:** The term “Industry 4.0” was first used in Germany to incentivize modernization of manufacturing. The International Society for Pharmaceutical Engineering (ISPE) adapted it 2017 and the concept of “Pharma 4.0” was born. The vision of highly efficient, vastly automated, self-driven manufacturing processes is extremely appealing to practitioners. But separating hype from reality is important. Get a feel of what is going on from Nima Yazdanpanah (Procegence), Shujauddin Changi (Vertex), Moiz Diwan (Abbvie), and Christopher Burcham (Eli Lilly) who reported Pharma 4.0 Highlights from the last AIChE Annual Meeting.

- **Connect @ AIChE:** Meet candidates in a poster session & reception at the 2020 AIChE Annual Meeting in San Francisco. If you are a graduate student/postdoc who are available for employment by summer 2021 or you work in industry and want to meet new talent and grow connections, this is a great event to do so. Learn everything you need to know here.

There is still more to come on PD2M programming and activities. Don’t miss future issues of the PD2M Newsletter.

Carla Luciani

Pharmaceutical Discovery, Development and Manufacturing Forum, Newsletter Chair

RNA-Tx, Lilly Research Laboratories, Eli Lilly & Co.

In this issue:

It is all about connectivity…

Pharma 4.0

Highlights from AIChE Annual Meeting 2019

The Pharma 4.0 paradigm, analogous to the Industry 4.0, intends to utilize enabling technologies in the pharmaceutical and biopharmaceutical industries. Process digitalization, utilizing big data, robotics and cyber-physical hybrid system in manufacturing, process automation, modular and distributed manufacturing, predictive maintenance and modeling, supply chain management, digital twin, and application of new data streams in continuous process verification will be the center of the Pharma 4.0 discussion to expedite process development and commercial manufacturing.

The Pharma 4.0 was topic of two plenary sessions in the AIChE Annual meeting 2019 in Orlando, FL, held by PD2M and Next-Gen Manufacturing Topical Conference. The invited keynote speakers provided their visions on the topic and shared their insights on applications of the corresponding technologies in the industry.

This report is intended to provide an overview of the talks and share some key messages from the sessions with the PD2M community. Interested readers are referred to the AIChE Annual meeting 2019 proceeding and whitepapers that will be published soon.

Authors:
Nima Yazdanpanah, Principal, Procegence
Shujauddin Changi, Associate Director, Vertex Pharmaceuticals
Moiz Diwan, Director, Pharmaceutical Development, AbbVie Inc.
Christopher Burcham, Senior Engineering Advisor, Eli Lilly and Company

Subject matter experts were invited from big-pharma companies, technology vendors, management consulting, and academia to address different aspects of the topic as keynote speakers. Current status and future trend of the Industry 4.0 in pharma and biopharma manufacturing facilities, case studies, technological potentialities and needs, challenges and complexities, and quality and economical studies were discussed. Diverse applications and technologies were covered, such as, continuous processing, automation, predictive modeling, as well as machine learning in an integrated fashion to develop quality and cost-effective pharmaceutical products. These technologies play an important role in developing holistic control strategies along with product/process life cycle management. Being a relatively new area, it is drawing a lot of interest from academic and industrial folks, over the last few years.

Jean Tom and Jose Tabora (BMS) presented "Approaches to Knowledge Management and Data Transformations in Pharmaceutical Process Invention". The talk covered some current work in the knowledge management space and its potential to drive innovation in pharmaceutical development in the future. They addressed some approaches on overcoming challenges that require innovations in tools supporting data generation and curation, and new approaches to data metrics and modeling. They presented success stories and implemented projects for knowledge management and digital transformation that enhanced the pharmaceutical process invention capabilities.

Lucas Vann (Applied Materials) presented on smart factories and advanced manufacturing software solutions. His presentation title was "Leading the Way to Pharma 4.0". An integrated suite of advanced manufacturing software solutions can provide a real-time, data-driven plant environment that senses factory activity, predicts performance, and prescribes effective actions. He demonstrated some applications of the advanced manufacturing software on:

- *Analytics & Control*: Increase yield, prevent deviations, and assure quality
- *Operations Productivity*: Reclaim capacity, maximize throughput, providing real-time adaptive scheduling
- *Predictive Maintenance*: Prevent costly unscheduled downtime
- *Knowledge Advisor:* Convert operator know-how & experience into process understanding & stability

John Mack (Perceptive Engineering) presented "Machine Learning in Pharmaceutical Process Development: Where Are We up to in Pharma 4.0?". His presentation explored and compared the current AI, Machnie Learning (ML) approaches with alternative techniques which are already well established within the chemical industries, and now also in many of the innovative Pharmaceutical companies. He provided case studies from the Pharmaceutical industry to demonstrate the application of several forms of ML for process control and optimization. He demonstrated, by comparing these ML based algorithms with other tools in the process optimization toolbox, how to examine the benefits and challenges in implementing this technology within the industry.

Cameron Brown (University of Strathclyde, CMAC) covered the research and workforce development (education) with presentation title "Machine Learning in Pharmaceutical Process Development: Where Are We up to in Pharma 4.0?". He highlighted his team's recent work in 1) creating digital twins that sit across multiple model types with an interface accessible for a non-modeler, 2) undertaking end to end manufacturing of an API mirrored by an end to end process model and 3) developing and delivering training to researchers to provide them with the skills needed to design, build and operate digital twins and microfactories across pharmaceutical manufacturing.

Paul Jones (PwC) shed a light on the enterprise level and C-suite aspect of the digitalization in pharma by his talk titled "The Art of the Possible When Digitizing Your Pharmaceutical Operations". The core of his talk was on integrating business understanding and human insights with technology innovation. He provided a look at the manufacturers who have embarked on digital transformation and are leading the way, discussed what's holding some companies back, and discussed what can be done now to stay ahead of the global competition. With a lens on emerging Industry 4.0 technologies, how Continuous Manufacturing can be an enabler of the Digitization agenda, he framed some of the immediate challenges and the future opportunities that will deliver 'real' business benefit and ultimately patient value.

Venkat Venkatasubramanian (Columbia University) talk focused on "artificial intelligence" challenges and opportunities. The pharmaceutical industry is drawing its version of Pharma 4.0 from the learnings of Industry 4.0 due to the urgency to increase productivity, shorten development cycle time, reduce costs, and get it right the first time needs for its processes. A typical New Drug Application (NDA) contains more than 100,000 pages of data, information, and knowledge. The amount and complexity of information of different types, ranging from raw experimental data to lab reports to sophisticated mathematical models, that need to be stored, accessed, validated, manipulated, managed, and used for decision-making is staggering. Recent progress in machine learning, natural language processing, ontology engineering, etc., offers potential solutions to these challenges. Case studies in structure-property prediction, hybrid-AI models, and a Watson like system for pharmaceutical manufacturing were discussed.

Shailendra Bordawekar (Abbvie) emphasized on speed being of essence in early development and the need to focus more on flexible design concepts involving smaller footprints, shorter cycle times, high degree of automation, digitalization, and improved process control. Abbvie's small molecule division has created Center for Excellence (CoEs) to adopt novel concepts and technologies to accelerate pharmaceutical development and manufacturing. Abbvie's efforts in Pharma 4.0 was discussed through multiple examples utilizing novel technologies and engineering solutions to enable chemistry such as photochemistry, impinging jet, flow processing, and automation (high and medium throughput screening) incorporating PAT, SWIFT (Synthesis with Integrated Flow Technology) for process design and optimization, solid form development, and machine learning.

Costas Pantelides and Sean Bermingham (PSE) focused on their company's vision of developing a Systems-based Pharmaceutics (SbP) engineering methodology for the pharmaceutical industry that encompasses drug substance drug product manufacturing, as well as in vivo drug performance. The approach aims to capture available relevant knowledge in the form of validated mathematical models. They discussed different phases of their vision being delivered through collaboration with multiple pharma companies (e.g. Eli Lilly & Co., Pfizer, GSK, Roche, Sanofi) and delivering gPROMS as an end-to-end modeling tool with unrestricted and immediate access to all pharmaceutical company. By integrating knowledge across the product lifecycle, SbP allows the quantification of the impact of critical process parameters and other decisions and environmental factors on the product's critical quality attributes and the process key performance indicators.

Cathal Strain (Neo PLM Inc.) presented his viewpoints on impending challenges slowing down the progress of Pharma 4.0, primarily because of a compliance culture that has fed an ultra-conservative approach to adopting new, innovative approaches to enabling the manufacturing supply chain. In today's IT system, an integration layer founded on a Structured Digital Process Design Core is currently missing and PLM technology can be a core enabler. Pharma 4.0 should be built on process modeling and simulation, but a critical component to be successful in implementing the data for empowering artificial intelligence or higher level analysis, is the instant availability of this information to scientists and engineers. His vision discussed creation of electronic batch records and that would suffice as an acceptable quality system.

References:

https://www.aiche.org/conferences/aiche-annual-meeting/2019/proceeding/session/pharma-40-invited-talks
https://www.aiche.org/conferences/aiche-annual-meeting/2019/proceeding/session/forum-plenary-opportunities-and-challenges-journey-industry-40-pharma-40-invited-talks

Declaimer:

This report prepared from publicly available materials that are accessible via the links in the reference list. The content should not be construed to represent authors' affiliation views. Nima Yazdanpanah was a research Scientist at the Food and Drug Administration at the time of the conference.

Connect at AIChE

Sponsored by The Pharmaceutical Discovery, Development and Manufacturing Forum

Meet industry candidates at the Poster Session & Reception at the 2020 AIChE Annual Meeting in San Francisco (Nov 15-20). This session will be a great opportunity for:

- **INDUSTRY CANDIDATES** to:
  - Showcase your research to a targeted pharmaceutical audience
  - Learn about employment opportunities across multiple pharma companies in one session
  - Build your network to bridge from academia to industry
- **PHARMA COMPANIES/ORGANIZATIONS** to:
  - See the latest and greatest research from top universities
  - Meet new talent across the entire AIChE community coming out of academia in one setting
  - Grow connections or increase collaborations with academic partners

Presenting authors should be graduate students/postdocs who are available for employment by Summer 2021. Interested applicants are asked to submit their resume (2 pages) and research abstract (<400 words) through Confex '*PD2M Meet the Industry Candidates Poster Session*'

For further questions, contact the session chairs: Moiz.Diwan@abbvie.com, jasmine.rowe@merck.com, or jean.tom@bms.com

This session is designed to facilitate pharmaceutical industry scientists and recruiting teams to network with potential industry candidates. Come show off your research!

Confirmed participants (plus more to come):

Bristol-Myers Squibb, abbvie, AMGEN, gsk, MERCK, Lilly, Lyndra