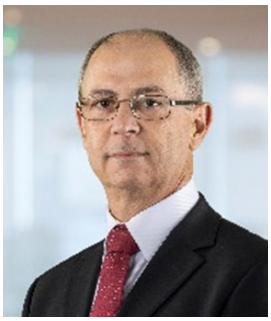
USP Workshop

Identifying and Addressing Barriers to Continuous Manufacturing Adoption

Speaker Profiles and Abstracts

July 18–19, 2023



Olivier Dapremont, Ph.D.

Executive Director for Process Technologies, AMPAC Fine Chemicals

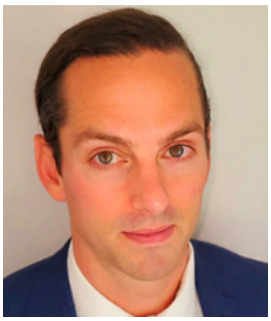
Dr. Dapremont has over 30 years of experience in developing continuous processes for pharmaceutical active ingredients and intermediates. He started his career in 1992 developing Simulated Moving Bed (SMB) technology for Prochrom R&D, France while doing in parallel his Ph.D. on SMB and chiral applications at the University of Pierre and Marie Curie in Paris, France (ESPCI – Paris VI). In 1997, he joined Chiral Technologies Europe, near Strasbourg, to manage the kilo scale SMB chiral separations service. He later joined Aerojet Fine Chemicals, now AMPAC Fine Chemicals (AFC) in California, in 2001. At AFC, Dr. Dapremont leads the R&D engineering group, which supports the development of continuous processes for APIs and intermediates in a regulated environment. With his team, he has developed and implemented over 50 chiral and non-chiral separations using SMB from gram to multi-ton scale (GMP manufacturing) including continuous solvent recycling and continuous racemization of the undesired enantiomer.

Dr. Dapremont is author and co-author of several articles in various scientific journals and magazines as well as multiple chapters in reference books. He is co-inventor on a dozen patents using SMB for API purification and he is a recognized expert in the field. Dr. Dapremont is a member of the Organizing Committee of the Prep Symposium conference and a member of the Scientific Committee of the SPICA conference. He is also a member of the Scientific Advisory Board to the Chemistry Today magazine. He has a Ph.D. in chemical engineering and applied chemistry from ESPCI – Paris VI.

Presentation: Development of a modular platform for a rapid implementation of continuous manufacturing for clinical material production under c-GMP

ABSTRACT: The adoption of flow processes in the pharmaceutical industry is gaining momentum and significant progresses have been made at the bench scale to evaluate, optimize, and demonstrate the feasibility of the technology to provide a safe and cost attractive process. However, the scale-up of the process to the c-GMP suite for clinical phase supply can be significantly delayed as the equipment is not always available and often a dedicated “skid” must be designed and built. This major hurdle is responsible for the slow implementation of continuous manufacturing in the pharmaceutical industry.

By using a modular approach, AFC has now demonstrated capabilities to rapidly set up a c-GMP continuous process to supply kilo quantities for clinical trials in a matter of days. This technology platform is accelerating the delivery of material to patients by bridging the gap between process development and commercial scale manufacturing. As an added benefit, the flexibility of the modular platform also provides rapid adaptation of the manufacturing tools to address process changes while minimizing downtime and CAPEX requirements while maintaining a c-GMP status.



Adam Fisher, Ph.D.

Director, Science Staff - Office of Pharmaceutical Quality, CDER, FDA

Dr. Fisher is the director of Science Staff in the Office of Pharmaceutical Quality in the Center for Drug Evaluation and Research at the U.S. FDA. He focuses on engaging FDA stakeholders and supporting advanced pharmaceutical manufacturing technologies. At FDA, he has served as a primary and secondary reviewer of Abbreviated New Drug Applications (generics) and Drug Master Files, team lead, subject matter expert on complex drug substances and advanced biomanufacturing, and liaison to the U.S. Pharmacopeia BIO1 Expert Committee. He joined FDA in 2014 as a chemical engineer with expertise in the synthesis of biomolecules. Prior to FDA, he was co-founder and chief science officer of a biotechnology startup company. He earned his Ph.D. in chemical and biomolecular engineering at Cornell University, and a B.S. in chemical engineering at the University of Maryland College Park.

Presentation: FDA Updates and the Regulatory Landscape Regarding CM

ABSTRACT: Continuous manufacturing can bring potential advantages to many drug substance and drug product manufacturing processes: better efficiency, reduced costs, and improved process control. Not widely adopted in the pharmaceutical industry, continuous manufacturing initially challenged regulators' expectations and regulatory frameworks. FDA has addressed regulatory hurdles related to CM to broaden its adoption through engagement, regulatory science, guidance, and international harmonization.

Judy Frels, Ph.D.

Senior Fellow, Executive Development Programs,
Academic Director of the MS Marketing Analytics,
Clinical Professor, University of Maryland – Robert H. Smith School of Business

Dr. Frels is a clinical professor of marketing with a background in technology development at IBM, smaller tech firms and consulting. She is an award-winning instructor with multiple years' experience teaching in the U.S. as well as France, Italy, England, Beijing, Tianjin, and Cairo. From 2014 through 2019, Dr. Frels led Smith's online programs effort in establishing the school's Online MBA and leading it to be ranked in the top 10 for several years.

Dr. Frels has taught executive education and consulted with multinational organizations including Prysmian Group, W. R. Grace, U.S. AID, Marriott International, Black and Decker, Northrop Grumman, Microstrategy, Sprint Nextel, Hughes Network Systems, SAIC, Imation, Bay Networks, and Input-Output, Inc. She has designed executive education programs for Lockheed Martin, Black and Decker, Hughes Network Systems, and MedChi: Maryland State Medical Society, among others. She holds a B.A. in computer science, an M.B.A. in information systems management, and a Ph.D. with a focus on marketing strategy, all from the University of Texas at Austin.

Presentation: How to Survive and Thrive in the Face of Disruptive Change

Dennis Hall

Vice President, Advanced Manufacturing Technologies, U.S. Pharmacopeia (USP)

As vice president for advanced manufacturing technologies at USP, Dennis Hall leads a team charged with identifying new manufacturing or other enabling technologies and deploying services and solutions to support adoption of these advanced manufacturing technologies. Through these solutions, USP can help detect where complications or problems exist, deploy our best science to solve these problems, and then scale those solutions through USP's broad reach to industry, regulators, and academia.

Mr. Hall has been a key leader at USP since 2001 in a variety of areas including strategy, marketing, and leading USP's global growth initiative focused on Asia, Europe, and Latin America. He holds an M.B.A. in strategic management and marketing from the University of Maryland – Robert H. Smith School of Business, a M.A. in education from the College of William and Mary, and a B.S. in physics from Clarion University of Pennsylvania.

Eric Jayjock, Ph.D.

Director, Process Engineering, Technical Operations Drug Product,
Vertex Pharmaceuticals

Dr. Jayjock is director of Process Engineering, Technical Operations Drug Product, at Vertex Pharmaceuticals. He performed his graduate studies and received his Ph.D. at Rutgers University, where he was a part of the NSF Center for Structured Organic Particulate systems (C-SOPS). During his time at Rutgers, his main area of research was the development of scalable manufacturing processes for oral solid dosage products. His graduate work culminated in the design and construction of the C-SOPS continuous direct compression line in collaboration with Janssen, a Johnson & Johnson company. Upon completion of this work, Eric joined the Janssen team and worked on bringing the continuous manufacturing approach to the industry. After the successful production of a continuously manufactured registration batch, Eric moved on to join Patheon to develop a continuous manufacturing program for the CDMO industry. The Patheon program was built around the concept of being able to modularly configure an integrated continuous process to meet the diverse needs of the pharmaceutical industry. The centerpiece of the program was a highly flexible continuous manufacturing facility deployed in Greenville, North Carolina. Next, Eric went on to do independent consulting work counseling both pharmaceutical companies and suppliers on the complexity of innovative projects within a CGMP space. In the past year, Eric has joined the small molecule Technical Operations team at Vertex. Here he is focused on improving operational efficiency while defining how novel technology, such as continuous manufacturing, can be leveraged to improve the pharmaceutical industry.

Presentation: Barriers to Continuous Manufacturing: Why Batch is Often Preferred Over CM

Todd D. Maloney, Ph.D.

Executive Director, Eli Lilly and Company

Dr. Maloney is executive director in the Synthetic Molecule Design and Development group at Eli Lilly – a company he joined in 2007 – and currently leads teams developing process analytical technologies and integrated process control strategies for synthetic oligonucleotides, peptides, and small molecules. He started his career in 2001 with Pfizer Global Research and Development in Ann Arbor, MI. While at Pfizer, he was a member of the Chemical R&D and Analytical Sciences R&D organizations, where he was involved in early phase analytical development, automation technologies, and in-silico method development strategies for pharmaceutical analysis. Dr. Maloney earned his Ph.D. in Chemistry from the University at Buffalo, The State University of New York, and also holds a B.S. in Chemistry from the State University of New York at Oswego.

Presentation: Implementing Process Analytical Technology for Advanced Process Understanding and Control: Case Studies in Synthetic Drug Substance Processes

ABSTRACT: Pharmaceutical processes utilizing flow chemistry and continuous manufacturing are rapidly emerging as the future of pharmaceutical manufacturing. Successful installations of continuous processes have leveraged process analytical technology (PAT) to increase process understanding and enable process control. This presentation will focus on the implementation of process analytical technology in continuous drug substance processes. Drivers for implementing PAT, overcoming challenges from paradigm shifts, and successful case studies will be presented. Strategies for transferring data to distributed control systems, process models, and data historians will also be discussed.

Srividya Ramakrishnan, Ph.D.

Vice President and Head – API Process Engineering, Dr. Reddy's Laboratories

Dr. Ramakrishnan is vice president and head-API Process Engineering, at Dr. Reddy's Laboratories Limited, in Hyderabad, India. Her nearly two decades of experience in the pharmaceutical industry includes working on crystallization development at Bristol-Myers Squibb, followed by process engineering at Dr. Reddy's. She is passionate about advanced manufacturing technologies and has delivered talks on emerging frontiers in this area. Dr. Ramakrishnan has several publications and patents to her credit and is an ASQ-certified Six Sigma Black Belt. In addition, as the chief diversity officer at Dr. Reddy's, she is championing diversity (gender and beyond) within the organization. She holds a Ph.D. in chemical engineering from Princeton University, and a B.Tech from Indian Institute of Technology, Madras.

Presentation: Flow Chemistry; Issues, Adaptation and Path Forward

Frank Witulski

Director of Engineering, Merck & Co.

Frank Witulski is a director of engineering in Merck's Pharmaceutical Commercialization Technology department. He has over 23 years of experience in process and packaging development, and commercialization of oral solid dosage products. He did preliminary process development work on continuous manufacturing processes in 2005, then returned to continuous manufacturing in 2015 as the drug product commercialization lead for Merck's first fully continuous drug product process. He has also sponsored Merck's Technology Development Teams on the development of continuous manufacturing and twin screw wet granulation. He holds a B.S. and M.S. in chemical engineering from Drexel University.

Presentation: Commercializing a Continuous Direct Compression Product with a Novel Control Strategy

ABSTRACT: A case study will be presented on Merck's first fully continuous drug product process. This case study involves a continuous direct compression process with the novel use of a residence time distribution-based process control model as the primary control of drug product potency without the redundant use of NIRS of the drug product blend. The case study will touch on the business case and approach that Merck took towards CM development, development of the control strategy, and regulatory interactions during the development of the process.

Facilitator Profiles

Matthew G. Beaver, Ph.D.

Director, Process Development, Pivotal and Commercial Synthetics, Amgen

Dr. Beaver joined Amgen's Process Development organization in 2012 to deliver improved synthetic processes and advanced technologies for small-molecule programs spanning pre-clinical to commercial stages. He is currently a director of process development within Amgen's Pivotal and Commercial Synthetics group, where he leads efforts in process intensification, including development and implementation of continuous manufacturing.

Prior to joining Amgen, Dr. Beaver was an NIH postdoctoral fellow working with Prof. Timothy F. Jamison, where he made contributions to two distinct areas of research: the development of nickel-catalyzed C–C bond forming reactions and natural product synthesis utilizing endo-selective epoxide-opening cascades. He earned his Ph.D. from the University of California, Irvine, under the guidance of Prof. Keith A. Woerpel, where his research focused on the elucidation of factors that govern stereoselectivity in the reactions of oxocarbenium ion intermediates. He also holds a B.A. from the College of the Holy Cross.

Lawrence De Belder

Continuous Manufacturing Practice Lead, Pharmatech Associates, Inc.

Lawrence De Belder leads the continuous manufacturing consulting group at Pharmatech Associates, Inc. In his previous role at Johnson and Johnson, he was responsible for oversight of all continuous manufacturing projects and activities of the Janssen Supply Chain, and initiated multiple collaborations with academics and other pharma companies. In addition to his 15-plus years of project management, equipment design, and validation experience in the pharmaceutical industry, De Belder started the International Society for Pharmaceutical Engineering (ISPE) Working Group on Continuous Manufacturing (CM), and chaired the CM and Process Analytical Technology (PAT) working groups at the International Consortium for Innovation and Quality in Pharmaceutical Development (the IQ Consortium) for several years. He holds a M.S. degree in industrial engineering from Group-T Belgium.

Maggie Gallagher

Program Associate, RESOLVE

Maggie Gallagher is a program associate at RESOLVE, based in Washington D.C. She supports collaborative processes and consensus-building dialogues across RESOLVE's Healthy Communities and Collaborative Ecosystem Stewardship teams. She focuses primarily on environmental challenges, public health issues, and the intersections between them, and brings a background in qualitative research, community engagement, and program management to her work at RESOLVE.

Ernie Hillier

Principal Owner at EJH Consulting

After 39 years at analytical instruments and software firm Waters Corporation, Ernie Hillier retired and formed EJH Consulting in 2019 with a focus on helping the industry continue to evolve in process analytical technology (PAT) to implement continuous manufacturing. During his career, his roles have included work with new High Performance Liquid Chromatography (HPLC) systems and chemistry evaluation, product marketing for detectors, and operations as manager of the Waters Technical Product Management Group responsible for quality. His experience in this last role led to a better understanding of process and his final role as principal systems product manager for Waters' PATROL (PAT), Alliance and Breeze Systems.

Mr. Hillier is on the Scientific Board of the International Forum on Process Analytical Chemistry (IFPAC) and chair of the Advanced Separations Session, and he is on the International Scientific Advisory Board for *Chemistry Today*. He is also working with a technical team supporting separation science, and on organizing and moderating conferences and expert panel discussions focused on Quality by Design (QbD), PAT and continuous manufacturing. Lastly, he is also part of the technology team for Optimal Industrial Technologies' sales and implementation of the SynTQ PAT knowledge management software solution, and further expanding system offerings in the QbD/PAT space. Mr. Hillier has a B.S. in chemistry and biology from Northeastern University.

Mason Hines

Senior Program Manager and Mediator, RESOLVE

An experienced facilitator and collaborative process designer, Mason Hines works primarily on issues related to health and the myriad intersecting social factors that affect it, including drug, food and water safety and access, community preparedness and resiliency, employment, housing, and education. The underlying goal of his work is to improve wellness at the individual, community, and population levels, particularly for those whom current health systems underserve. Mr. Hines is based out of RESOLVE's headquarters in Washington, D.C. He holds a master's degree in conflict and dispute resolution from the University of Oregon.

Riley Myers, Ph.D.

Chief, Advanced Pharmaceutical Manufacturing Laboratory,
Office of Testing and Research, FDA

Dr. Myers is chief of FDA's Advanced Pharmaceutical Manufacturing Laboratory in the Office of Testing and Research, and a member of the Emerging Technology Team. Dr. Myers is also a member of the Framework for Regulatory Advanced Manufacturing Evaluation (FRAME) working group where he is evaluating approaches for regulating future advanced manufacturing technologies. He was previously a lead biologist in the Office of Biotechnology Products where he led a team responsible for the quality assessment of Biologics License Applications for therapeutic proteins, and a microbiologist in the Center for Devices and Radiological Health where he assessed medical devices that contain antimicrobial agents. Prior to joining FDA, Dr. Myers studied mechanisms to program anti-pathogenic immune responses at Boston Children's Hospital. He received his Ph.D. in immunology from the University of Alabama at Birmingham.