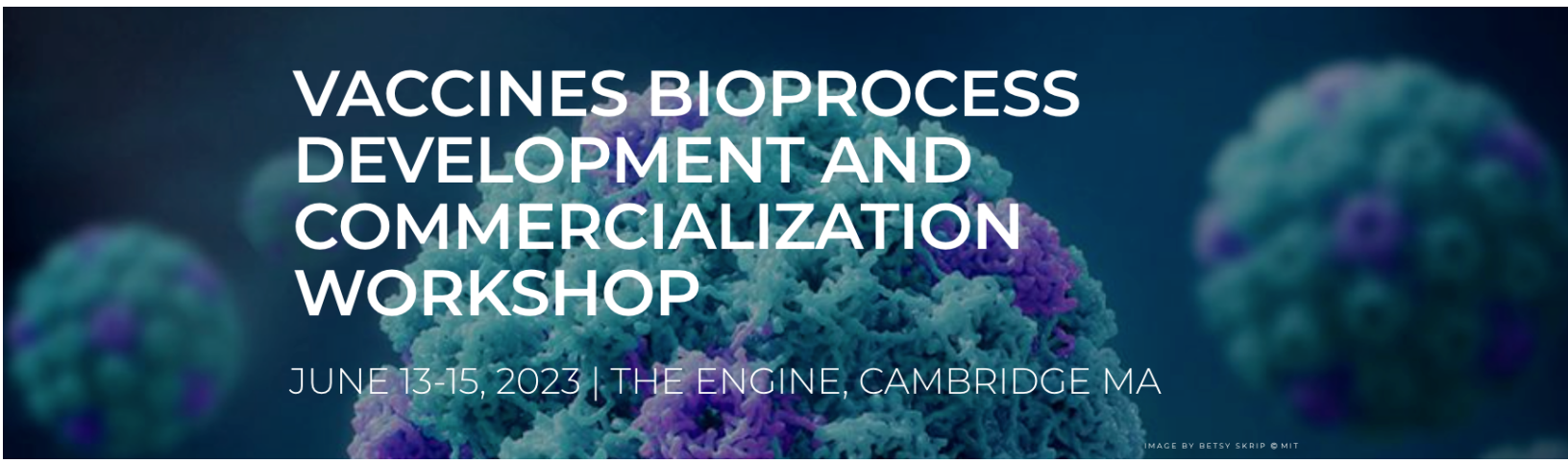
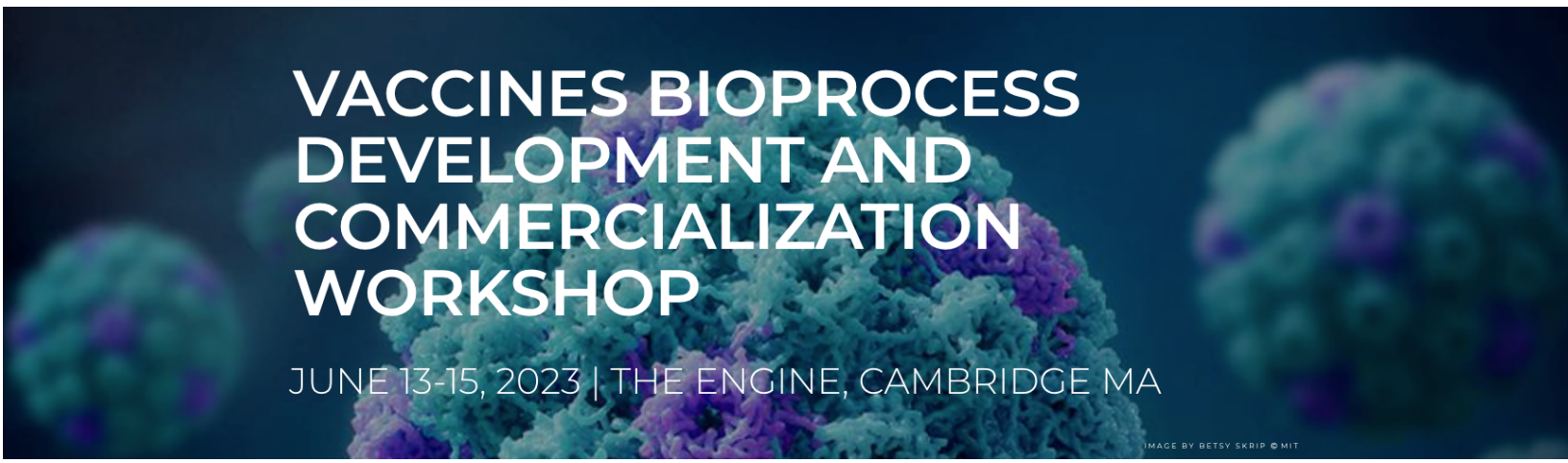


Agenda for Day 1: June 13, 2023

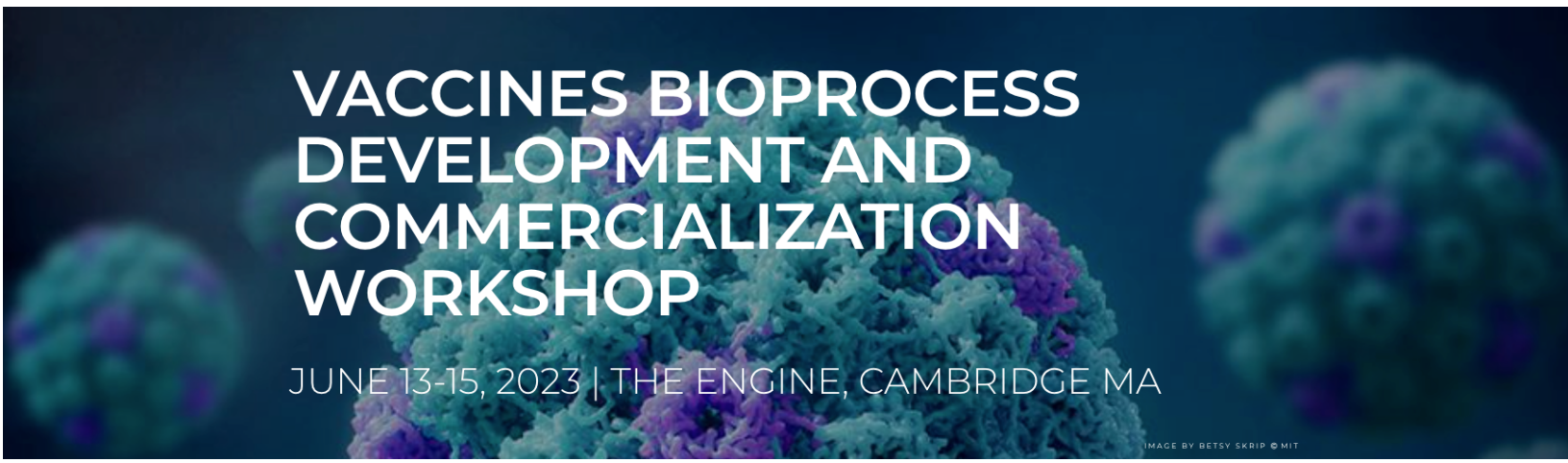
Day 1 Session Chairs:

Flora J. Keumurian & Jacqueline Wolfrum
MIT Center for Biomedical Innovation

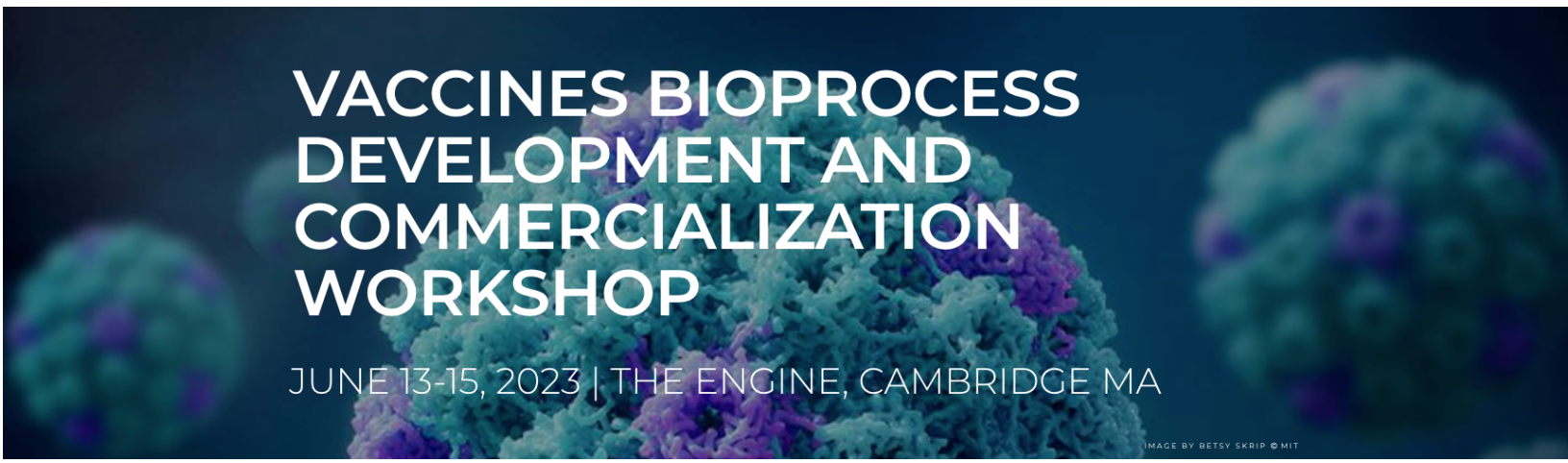
8:30-9:15 AM	***REGISTRATION & BREAKFAST***
9:15-9:50 AM	**Welcome, Introduction, and Framing of the Workshop** **Stacy L. Springs & Stefanie Frank** *Executive Director* *MIT Center for Biomedical Innovation* *Lecturer in Synthetic Biology* *University College London*
9:50-10:40 AM	**Introduction to Vaccine Bioprocess Development** **Barry C. Buckland** *Visiting Professor* *University College London* Following a survey of the main different vaccine technology platforms examples will be given for specific case studies. Gardasil® vaccine for prevention of cervical cancer is a great example of a Virus Like Particle (VLP) vaccine. Rotateq® vaccine for prevention of Rotavirus infection is an example of a live virus vaccine. Flublok quadrivalent is a protein-based vaccine for protection against Influenza. For protection against COVID-19 both the Moderna mRNA vaccine and the Pfizer mRNA vaccine are great examples.
10:40-11:30 AM	**Vaccine platforms to enable speed and innovation** **Tara Tagmyer** *Executive Director, Vaccine Process Development* *Merck & Co., Inc.* The biopharmaceutical industry mounted an impressive response to the COVID-19 pandemic, but it was the companies that previously invested in platform-based technologies, such as mRNA and viral vectors, that were successful in gaining Emergency Use Authorization (EUA) and eventual approval most quickly. As a result, multiple safe and efficacious vaccines were authorized for emergency use, resulting in significant declines in severe disease and mortality, however, durable immunity to COVID-19 has not yet been achieved. While many biopharmaceutical companies have launched independent efforts to develop mRNA vaccines, it is important to reflect on efficacy and durability of legacy vaccines and what those platforms have to offer.



	Vaccine platforms offer speed of development and flexibility in manufacturing, however, not all antigens are amenable to a specific platform, and there are strategic trade-offs in developing a vaccine for rapid emergency use deployment vs. a long-term product for endemic prophylaxis. Here we will present case studies from live viral and subunit vaccine platforms, and how continued investment in these established platforms have enabled speed and innovation to support both EUA and long-term commercial manufacturing.
11:30-11:50 AM	***REFRESHMENT BREAK***
11:50-12:40 PM	**Quality Control of Human Viral Vaccines** **Alison Armstrong - Virtually** *Senior Director, Global Head Technical and Scientific Solutions* ***MilliporeSigma*** Global Health agencies have relied on vaccination as one of the most effective treatment options during epidemics and more recently pandemics associated with viral disease. Vaccination campaigns have been shown to significantly reduce the number of deaths caused by infectious agents. With the introduction of cell culture and DNA recombinant technologies vaccine design has changed dramatically. Permissive cell lines have allowed the production of attenuated and inactivated vaccines. The advent and use of newer manufacturing technologies to produce vaccines though the use of, for example, virus like particles, vectored vaccines and chimeric vaccines bring specific quality and safety issues which need to be addressed. The overall safety of vaccines is still of paramount importance and this presentation will focus on regulatory expectations from a global view. In addition, we will address the impact of new vaccine developments which are now being used to supply high quality and effective products.
12:40-1:40 PM	***LUNCH***
1:40-2:30 PM	**Lessons from the CAACB on the Prevention and Control of Adventitious Agent Contamination** **Stacy L. Springs** *Executive Director* ***MIT Center for Biomedical Innovation*** Adventitious agent contamination of cell culture-based biomanufacturing operations for the production of protein and monoclonal antibody biotherapeutics are infrequent, but when they do occur, they are very costly, impact manufacturing operations, and can potentially impact patient safety and product supply. In response to this need, the MIT Consortium on Adventitious Agent Contamination in Biomanufacturing (CAACB) began the confidential collection and analysis of industry-wide viral contamination data with an emphasis on "lessons learned". The mission of

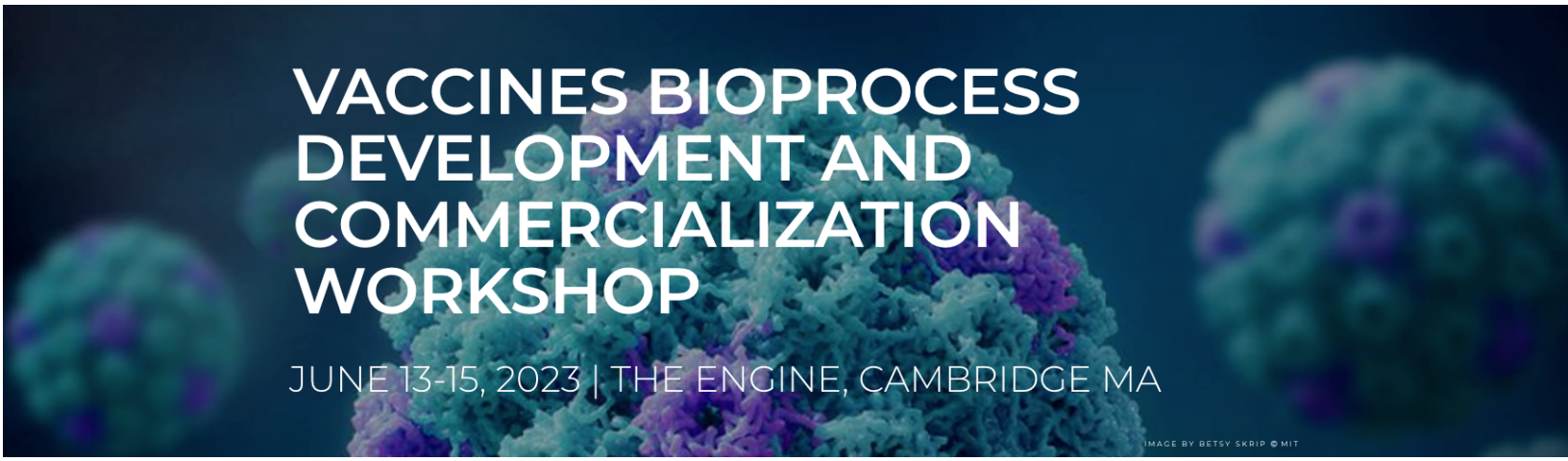


	the CAACB is to pool and to share knowledge, experience and practices in the area of adventitious agent contamination in biomanufacturing. The Consortium is providing a safe and collaborative environment for networking and information exchange focused on identifying best industry practices in contamination response, corrective and preventive actions, and promoting the development of new technologies to detect adventitious agents and mitigate risk of contamination. This presentation will cover the learnings from this study, including identified industry risks and best practices to mitigate those risks. This talk will discuss some of the lessons learned from the collaborative work done by the CAACB and their implications for vaccine manufacture.
2:30-3:20 PM	**Future Vaccine Manufacturing Research Hub (Vax-Hub) developments** **Stefanie Frank** *Lecturer in Synthetic Biology* ***University College London*** The Future Vaccine Manufacturing Research Hub (Vax-Hub) is an academic collaboration led by UCL Biochemical Engineering and the University of Oxford. Vax-Hub comprises world-leading experts in vaccinology, synthetic biology, biochemical, materials, and system engineering working on integrated discovery through to bioprocess manufacture of next-generation vaccines. This presentation will provide an overview of developments within Vax-Hub, from innovative tools and technologies to outreach activities.
3:20-3:40 PM	***REFRESHMENT BREAK***
3:40-4:30 PM	**Designing and building the next generation of vaccine adjuvants** **Derek O'Hagan** *Associate Vice President, Regulatory CMC* ***GSK*** Adjuvants are vaccine components that enhance the magnitude, breadth, and durability of the immune response. Since its introduction in the 1920s, insoluble Alum remained the only adjuvant licensed for human use for the next 70 years. However, since the 1990s, a further five adjuvants have been included in licensed vaccines. Yet, the molecular mechanisms by which adjuvants work remains only partially understood. A revolution in our understanding of the molecular pathways of activation of the innate immune system through pattern recognition receptors (PRRs) has allowed a mechanistic understanding of adjuvants. The intervening period has witnessed many conceptual advances, including the notion that tissue damage, different forms of cell death, and metabolic regulators and nutrient sensors, can all profoundly activate the innate immune system and adaptive immunity. Also, recent advances in the use of systems biology to probe the molecular networks driving immune response to vaccines in humans is revealing new mechanistic insights and



	providing a new paradigm for the vaccine discovery-development process. I will discuss the emerging concepts in adjuvant science, and highlight how our expanding knowledge about innate immunity and systems immunology are revitalizing the science and development of adjuvants.
4:30-5:20 PM	**Conjugate Vaccine Structure, Development, and Manufacture** **Steven Kolodziej** *Associate Research Fellow, Bioprocess Research & Development* ***Pfizer*** The manufacture of conjugate vaccines is very complex. Carrier proteins and capsular polysaccharides are produced by fermentation processes, while capsular polysaccharide activation and conjugation to the carrier protein are chemically mediated. Process development requires a cross-discipline team of scientists with backgrounds in analytical chemistry, biochemistry, bioprocess, chemistry, engineering, statistics, and vaccines research. Throughout the development process, care must be taken to ensure that the physicochemical, biochemical, and immunogenic properties of the conjugate are consistently maintained across production scales. This talk will highlight some of the manufacturing and development challenges encountered with conjugate vaccines and potential mitigations.
5:20-5:30 PM	**Day 1 Closing Remarks** **Stacy L. Springs** *Executive Director* ***MIT Center for Biomedical Innovation***

5:30-7:30 PM — Networking Reception

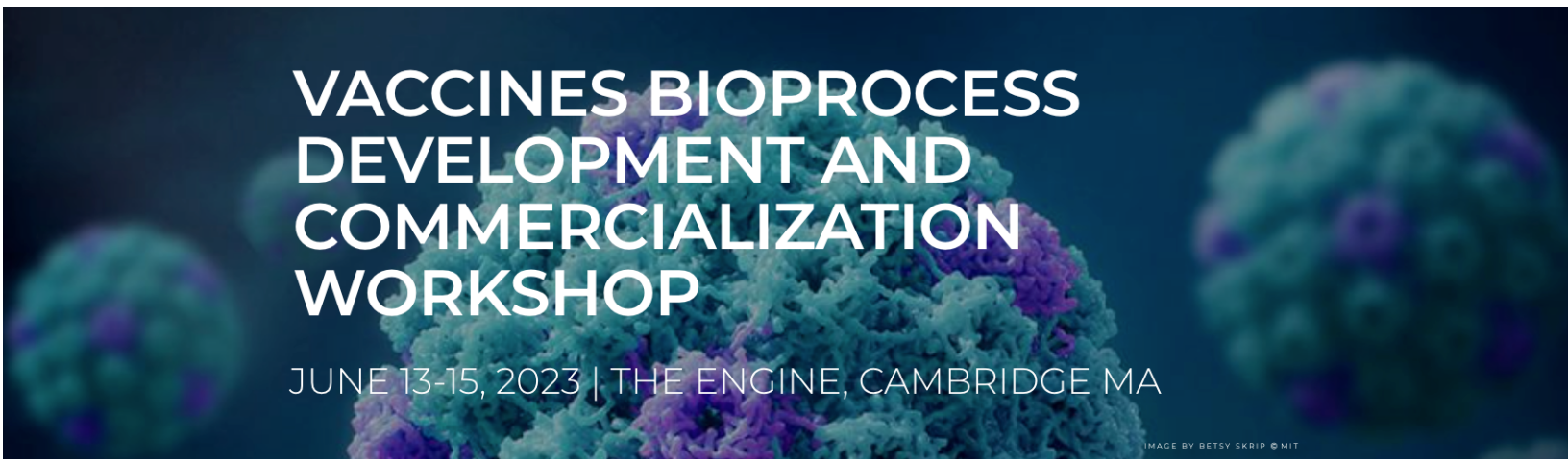


Agenda for Day 2: June 14, 2023

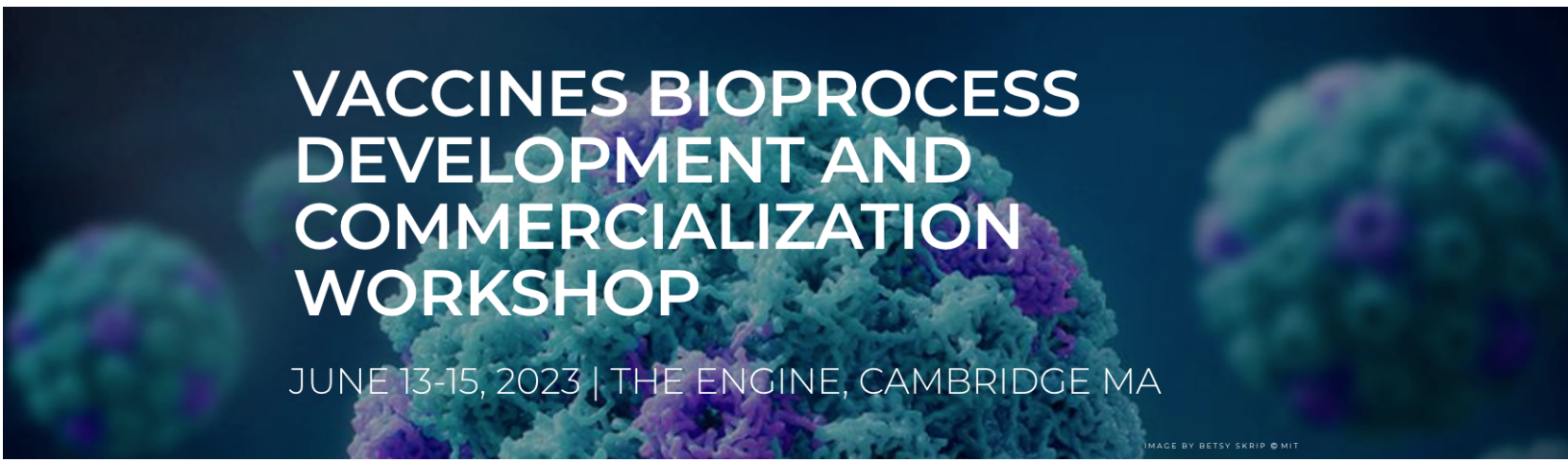
Day 2 Session Chair:

Barry C. Buckland
University College London

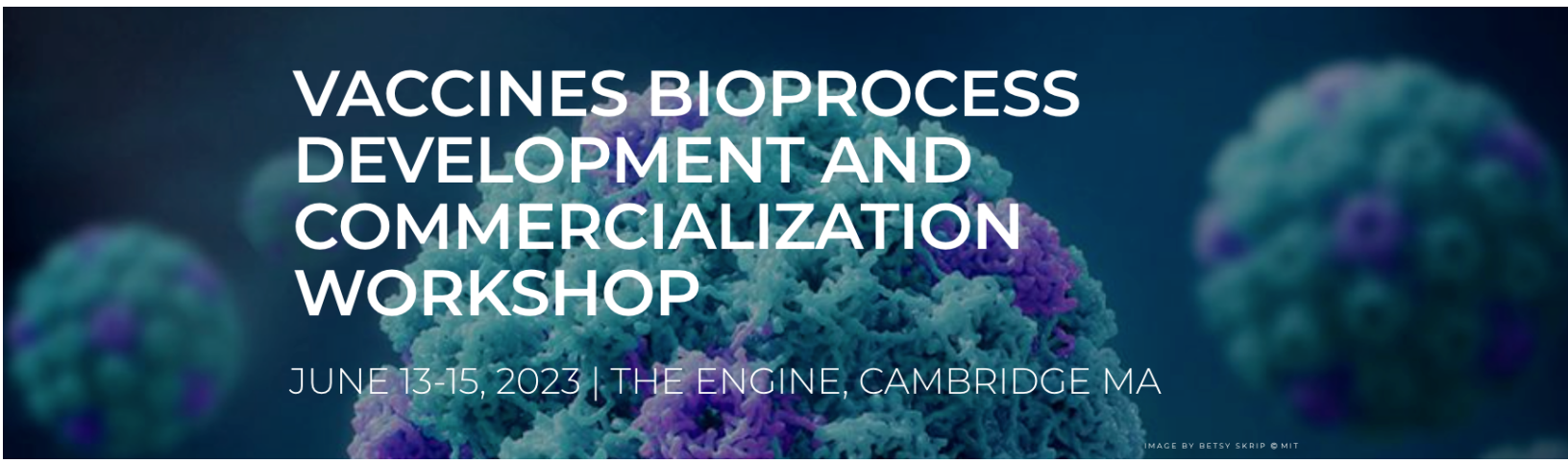
8:00-8:50 AM	***BREAKFAST***
8:50-9:00 AM	**Welcome Remarks**
9:00-9:50 AM	**Keynote Presentation: Regulatory Considerations for the Expedited Development of Vaccines During a Public Health Emergency** **Robin Levis** *Deputy Director, Division of Viral Products* *U.S. Food and Drug Administration* Current regulations and guidance define several pathways that facilitate expedited product development. These regulatory mechanisms allow for enhanced interaction between the sponsor and the FDA review team, flexible submission schedules, and, in some case, shortened review timelines. These pathways were created to better support development of new products where a defined unmet medical need exists. In response to the emergence of viruses that have caused regional and global public health emergencies, Ebola virus in 2014 and SARS-CoV-2 in 2020, respectively, the Agency conducted expedited reviews based on existing review mechanisms, but also utilized additional regulatory resources to facilitate the availability of safe and effective vaccines to help prevent disease from each of these viruses. This presentation will highlight the history of regulations related to vaccine development, review activities associated with vaccine development during an ongoing pandemic, and how lessons learned will be used to facilitate vaccine development and availability in the event of future public health emergencies.



9:50-10:40 AM	**The development of the Oxford AstraZeneca Covid-19 vaccine** **Dame Sarah Gilbert** *Saïd Professor of Vaccinology at the Pandemic Sciences Institute, Nuffield Department of Medicine* ***University of Oxford*** The 2014 outbreak of Ebola virus disease in West Africa highlighted the lack of preparedness for combating infectious disease outbreaks. Since 1976, vaccine development had proceeded slowly and no candidate vaccines had progressed further than phase I trials. Ebola is only one of many known viruses with the potential to cause outbreaks. With the support of the WHO in identifying priority pathogens, and the formation of CEPI to provide funding, vaccine development was initiated with the aim of having vaccines available in readiness for future disease outbreaks. 'Disease X', to represent a disease caused by a previously unknown pathogen, was also considered. In the first days of 2020, the first 'Disease X' outbreak, caused by a virus later named SARS-CoV-2 occurred. Vaccine developers found ourselves attempting to put into place plans that were at an early stage of development, had not been funded and had not therefore been tested. Rather than working to produce a vaccine which could then be deployed in the 'outbreak area' we found ourselves attempting to develop a vaccine against a novel pathogen that was causing a pandemic whilst we ourselves were in the grip of that pandemic with every aspect of our work affected.
10:40-11:00 AM	***REFRESHMENT BREAK***
11:00-11:50 AM	**Mechanistic Modeling and Control of Vaccine Manufacturing** **Richard D. Braatz** *Edwin R. Gilliland Professor, Chemical Engineering* ***Massachusetts Institute of Technology*** This presentation describes the mechanistic modeling and control of the manufacturing of viral, virus-like particle, subunit protein, and mRNA vaccines. After an overview of the progress for all of these vaccine types, the use of perfusion or continuous culture to increase productivity is discussed. Then a detailed description is provided on mechanistic models, sensor development, and control for continuous viral vaccine manufacturing in suspension culture. Results demonstrate smooth quasi-steady continuous operation over an extended period of time and good agreement between a mechanistic model and data for experiments carried out at a local contract manufacturing organization.



11:50-12:40 PM	**Vaccine manufacturing perspectives for process and technology developers through the product life cycle. Insights and approaches from different case studies.** **Mireli Fino** *Executive Vice Chancellor* ***MassBiologics*** The development and manufacturing of vaccines has rich history and evolution, driving, adopting or adapting the science and technology boundaries of the time. As a vaccine progresses through the life cycle, from discovery to stablished product to end of life cycle, different factors dictate the decisions and paths organizations take. From the constraints of the scientific and technical knowledge, to the economics of production and distribution, our industry achieves a careful balance to ensure the continued delivery of life-saving vaccines. In this presentation, we will look through the lens of the manufacturer at factors playing significant roles as a vaccine candidate transitions from development to commercial manufacturing, from launch to mature product incorporating advances in science, technology and regulatory science and to a final transition at the end of the product life cycle.
12:40-1:40 PM	***LUNCH***
1:40-2:30 PM	**Accelerated process development and industrialization of mRNA-LNP based vaccines- current status and challenges** **Kumar Namdev** *Global Head, CMC Product development and industrialization, mRNA Center of Excellence* *Sanofi* Significant investment is being made in developing mRNA-based vaccines for infectious diseases such as Influenza and RSV with an expectation of speedy development with high efficacy. There are, however, several CMC pre-requisites to enable these expectations. • Standardize mRNA and LNP design platforms to maximize therapeutic index while ensure manufacturability. • Continuously build product understanding through analytical and biological characterization in pre-clinical and clinical settings. • Establish phase appropriate control strategy that incorporates latest product understanding and regulatory expectations. • Develop and standardize designs of manufacturing process and formulations that meets control strategy while retains flexibility to capture innovation in product and process platforms. • Establish end to end manufacturing & QC footprints for clinical and commercial launch of a dynamic product portfolio; This network should



	include external sourcing and/or internal manufacturing of special raw materials at appropriate levels of quality, scale, and cost. This presentation will summarize status of CMC platforms and describe specific elements of mRNA-LNP to consider in designing control strategy, manufacturing process, thermostable formulation, and associated technologies. Additionally, the requirement to build a deep understanding of critical materials will be emphasized. The enabling role of data continuum infrastructure and data science tools to efficiently optimize processes will be noted.
2:30-3:20 PM	**Case Study: Supplying mRNA COVID 19 Vaccine at Unprecedented Pace & Scale** **Kevin Doyle** *Director, Sterile Injectables and Biotech Technology* *Pfizer* Here to be presented is case study on Pfizer's journey to supplying COVID 19 Vaccine at unprecedented pace & scale. Kevin will give a high-level overview of Pfizer's and BioNTech's mRNA vaccine technology and bring us through us some of the key process innovations which facilitated rapid process development and scale up which were required to provide COVID 19 vaccine at a pandemic supply level.
3:30-3:45 PM	**Day 2 Closing Remarks** **Jacqueline Wolfrum** *Director, BioMAN* *MIT Center for Biomedical Innovation*

5:00-8:00 PM — Networking Reception & Dinner
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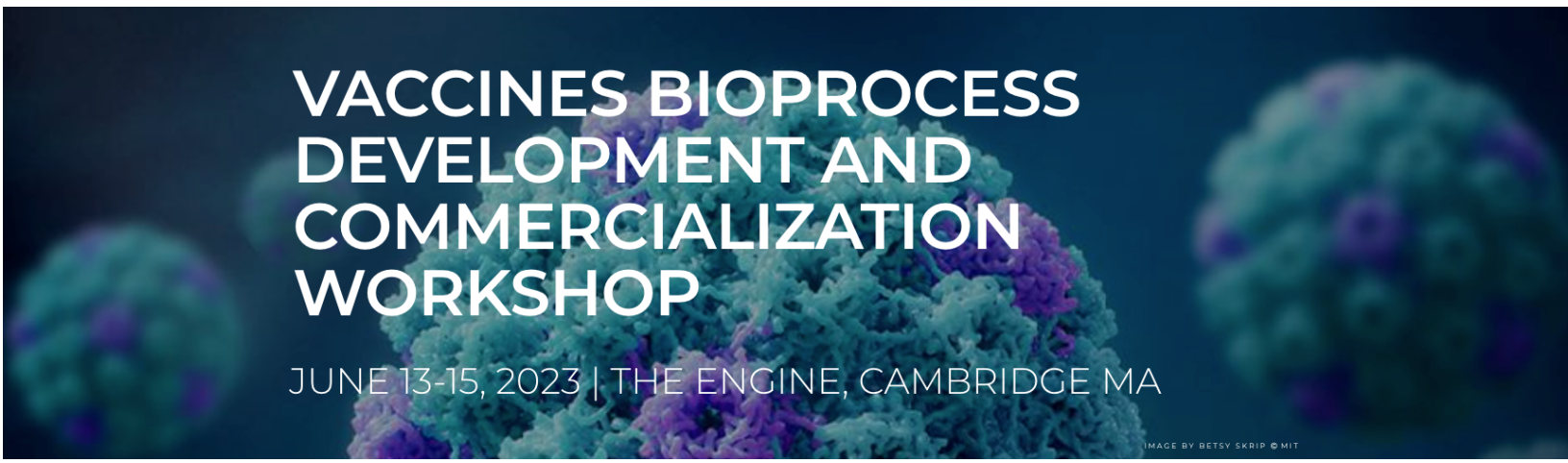
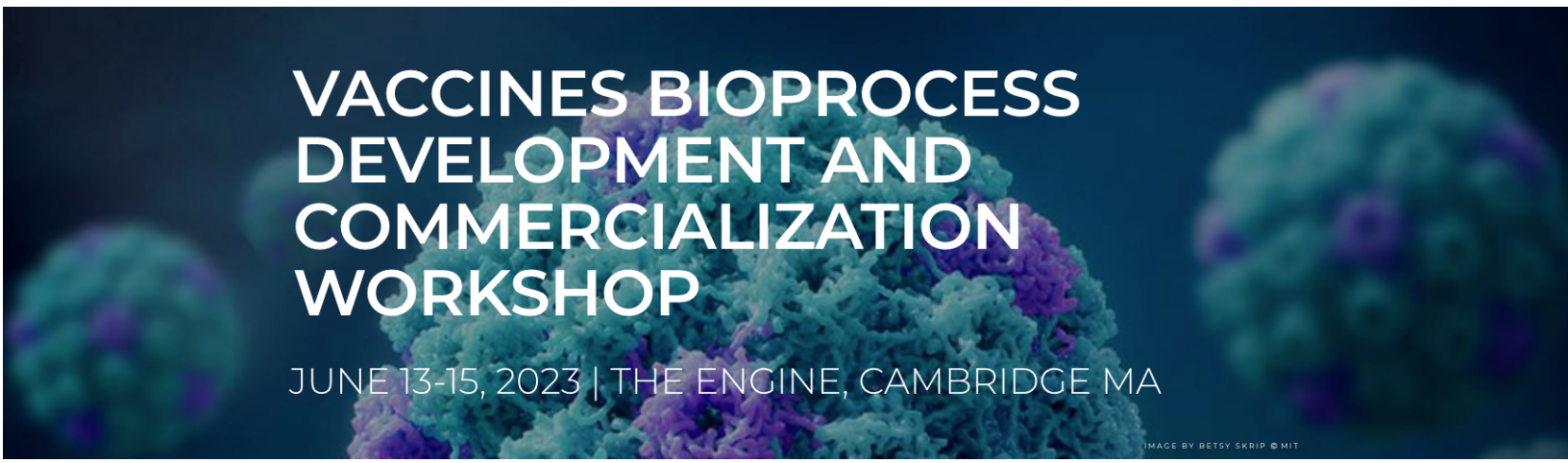


Agenda for Day 3: June 15, 2023

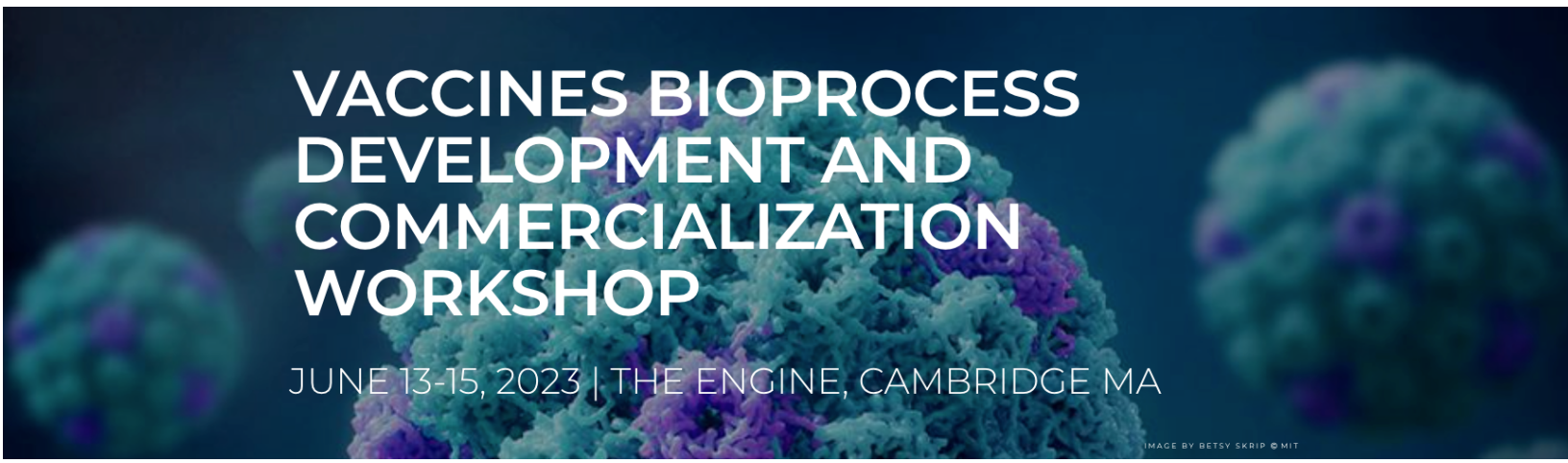
Day 3 Session Chair:

Stefanie Frank
University College London

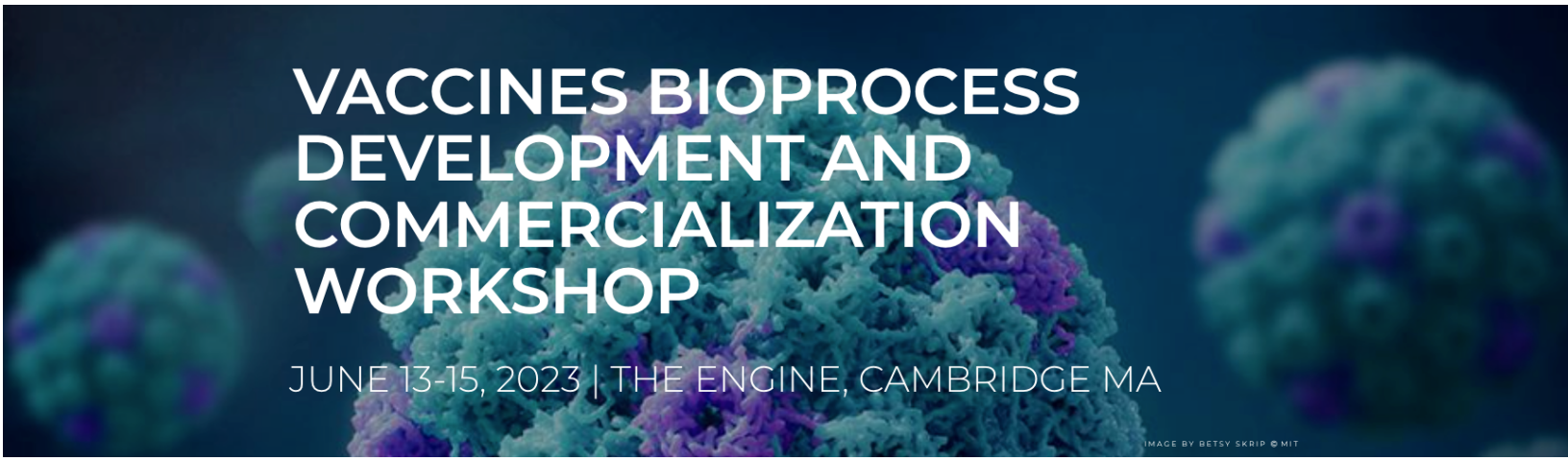
8:00-8:50 AM	***BREAKFAST***
8:50-9:00 AM	**Welcome Remarks**
9:00-9:50 AM	**Integrated Design and Development of Recombinant Vaccines** **J. Christopher Love** *Raymond A. (1921) and Helen E. St. Laurent Chair of Chemical Engineering, David H. Koch Institute for Integrative Cancer Research* ***Massachusetts Institute of Technology*** Translational development of new concepts for vaccines from discovery to the clinic has required unique processes tailored to the characteristics of each immunogen and final vaccine product. For recombinant vaccines, each immunogen may have its own properties and specifications that confer immunogenicity, and development usually begins with optimizing production of a selected sequence, followed by serial development of steps for recovery of the antigen. With these materials in hand, product development follows formulation development and stability studies. This approach to process development is linear, with limited feedback into prior stages including discovery and early evaluation of candidate vaccines. Iterative learning from one vaccine to another can be also limited and process development often starts new each time. This talk will present an integrated platform-like approach to recombinant vaccine development that incorporates an iterative design process emphasizing molecular design of antigens, strain engineering and integrated straight-through purification for recombinant proteins with examples for rotavirus and SARS-CoV-2 vaccine candidates.
9:50-10:40 AM	**Applying intensification and continuous processing to streamline vaccines development** **Mathias Garny** *Chief Executive Officer* ***Univercells Technologies*** Delivering effective viral vaccines to the market on time is critical for preventing and controlling infectious diseases. Traditional manufacturing processes are highly complex, require extensive process development efforts, and tend to suffer from a lack of scalability to rapidly reach commercial scale capacity. Advances in integrated and automated manufacturing technologies result in cost-effective, scalable, and highly productive processes. Those technologies are considered as flexible by design



	as they can accommodate various expression systems, vaccine applications and capacity requirements, while streamlining the vaccine development process. Structured fixed-bed bioreactors can achieve high cell densities with superior specific cell productivities through homogeneous cell distribution and media flow. They sustain reproducible results from small to large scale in a reduced volume and simplify the time to scale-up. Additionally, the integration of upstream and midstream process units with a highly intensified fixed-bed bioreactor provides automated continuous processing, drastically reducing the complexity, footprint and CAPEX while meaningfully reducing the cost per dose. In this presentation, the speaker will focus on technology innovations leveraging process intensification and continuous processing to deliver capacity at low footprint, process flexibility and accelerated development and scale-up timelines.
10:40-11:30 AM	**Accelerating Process Changes Through Comparability Protocols – Two Case Studies** **Penny Post** *Head of Regulatory Affairs Development, US Vaccines* ***Sanofi*** Post approval changes are common for licensed vaccines. Such changes to the license may be done to implement cost-saving process improvements, change a formulation, or put a new manufacturing site into service. Use of a comparability protocol can speed implementation of changes. This presentation will introduce the concept of comparability protocols and discuss two vaccine case studies that used comparability protocols to implement changes to the license.
11:30-11:50 AM	***REFRESHMENT BREAK***
11:50-12:40 PM	**Process Development and Manufacturing of mRNA/LNP Products: The Catalent Experience** **Jingtao Zhang** *Scientific Director, Biologics Group* ***Catalent*** mRNA/Lipid Nanoparticle (LNP) technology has evolved rapidly over the last decade, significantly changed the vaccine and therapeutics landscape, and recently proven its technology potential with commercial successes in two COVID-19 vaccines. Catalent has contributed to the evolution of this exciting technology field since 2016, by helping clients to develop, manufacture, and test vaccines or drugs for cancer, infectious disease, or genome editing applications. In this presentation, we will share our process development and manufacturing experience in the workflow from DNA, mRNA, LNP, to fill finish. Unique challenges in developing and manufacturing this nascent technology will be covered. Outlook on further evolution of DNA and mRNA technology to increase product quality and reduce development time will be



	discussed. Challenges and opportunities in LNP processing and stabilization will be discussed.
12:40-1:40 PM	***LUNCH***
1:40-2:30 PM	**Keynote Presentation: The Role of Vaccines in Addressing a Looming Global Health Crisis** **Judith Maxwell Silverman** *Program Officer, Chemistry Manufacturing & Controls* *Vaccine Development & Surveillance, Global Health* ***The Bill & Melinda Gates Foundation*** At the Bill & Melina Gates Foundation we envision a world where every person has the opportunity to live a healthy, productive life. To that end the foundation invests heavily in vaccines, from discovery, to manufacturing, delivery and policy, an effort that has aided the reduction of global measles, paralytic polio, and COVID-19 disease burden. We are currently facing the looming existential threat of climate change, which affects the most basic requirements of health: clean air, safe water, sufficient food and adequate shelter. Vaccine discovery, development and commercialization can all play a role in mitigating the risk of climate change related health crises. Maximizing manufacturing efficiency, by producing a higher yield per unit of each input, has potential to dramatically reduce cost of the final product. New and evolving tools in computation, materials science, and vaccine delivery similarly provide opportunities for efficiency gains across multiple dimensions, including minimizing development time, streamlining tech transfer activities, and maximizing protective responses and vaccine coverage while minimizing injection pain and adverse events. New technologies that control vaccine release may be deployable to maximize efficiency for existing vaccines and achieve robust protection against intractable infections like HIV and malaria.



2:30-3:30 PM	**Panel Discussion on Accessibility & Platformability** **Discussion Moderator:** **Barry C. Buckland** *University College London* **Discussion Panelists:** **Dame Sarah Gilbert** *University of Oxford* **Robin Levis** *U.S. Food and Drug Administration* **Judith Maxwell Silverman** *The Bill & Melinda Gates Foundation* **Tara Tagmyer** *Merck & Co., Inc.*
3:30-3:45 PM	**Day 3 Closing Remarks** **Stacy L. Springs** *Executive Director* *MIT Center for Biomedical Innovation*