Speaker Biographies & Abstracts (listed alphabetically)

Fouad Atouf, Ph.D.
Vice President, Science-Global Biologics
U.S. Pharmacopeia

Fouad Atouf is Vice President, Science—Global Biologics, for USP. He leads all scientific activities related to the development and maintenance of documentary and reference standards for biologics and antibiotics and oversees the biologics laboratories in USP–U.S. and USP–India. His department supports the work of the associated USP Expert Committees. Dr. Atouf has been at USP for over 10 years and served in a variety of scientific leadership roles including being the regional champion for the Middle East and North Africa Region, where he helped facilitate programs designed to enhance the understanding of the role of regulations and standards in the registration of medicinal products. Dr. Atouf has strong background and experience in the development and regulation of *cellular and tissue-based products*. Prior to joining USP in 2006, his research at the U.S. National Institutes of Health focused on developing methods for the *in vitro* generation of cell-based therapies for diabetes. Dr. Atouf is the author of numerous publications in peer-reviewed journals and a frequent speaker at national and international scientific conferences. Dr. Atouf earned his Master's degree in Biochemistry and his Ph.D. in Cell Biology from the Pierre & Marie Curie University, Paris, France.

Presentation
USP Welcome

Judith Arcidiacono, Ph. D.
U.S. Food and Drug Administration, Center for Biologics Evaluation and Research,
Office of Tissues and Advanced Therapies (OTAT)

Judith earned her B.S. in biology from West Virginia University in 1987 and M.S. in genetics from Clarion University in 1990. After receiving her MS degree, she continued her education by taking 30 hours of course work in immunology at the Foundation for the Advancement of Education in the Sciences (FAES) at the National Institutes of Health, Bethesda, Maryland, and the George Washington University, Washington, D.C. Judith has 30 years of experience at FDA. For the first 18 years of her career at FDA she served as a research/reviewer. In this role she performed research on the human immunological response to xenotransplantation products and reviewed clinical trial applications for NK cell and T cell therapies and xenotransplantation products. Ms. Arcidiacono is currently working in the Immediate Office of the Director, OTAT, where she is responsible for developing regulatory policy with respect to international harmonization efforts, collaborations with global regulatory authorities. She serves as the secretariat for the International Pharmaceutical Regulators Programme (IPRP), Cell Therapy Working Group and Gene Therapy Working Group. Judith serves as the FDA Subject Matter Expert for the APEC/RHSC Priority Work Area for Advanced Therapies and is a faculty member at the Northeastern University Center of Excellence for Advanced Therapies. As an expert in standards development, she represents FDA in ISO Technical Committee 276, Biotechnology, American Society for Testing Materials (ASTM) F04 Committee on Medical and Surgical Materials and Devices, Tissue Engineering Medical Products, and the Parenteral Drug Association Standards Committee.

Session V – Standards to Facilitate Gene Therapy Product Development and Quality
Global Harmonization and Standards for Regenerative Medicine Therapies

Harmonized regulatory approaches for Regenerative Medicine Advanced Therapies (RMTs) are essential to increasing patient access to cell therapy, gene therapy and tissue engineered products globally. Although it is difficult to harmonize regulations among regulators, there are multiple international venues where regulators and industry can work towards regulatory harmonization and convergence. Such venues include Discussion Clusters, the International Pharmaceutical Regulators Programme (IPRP), Cell Therapy Working Group and Gene Therapy Working Group, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), and the Asia Pacific Economic Cooperation (APEC) Regulatory Harmonization Steering Committee (RHSC). Global harmonization can also be achieved by regulator's participation in standards development activities and the use of standards to meet regulatory expectations. Standardized methodologies for testing RMTs, standardized reference materials and data standards are a few examples of such standards.
Information sharing between regulators and sponsors of regulatory applications can facilitate global marketing of RMTs. Collaborations between international regulators on the review of regulatory submissions for RMTs ensure that regulatory expectations can be met across regions.

James Brown
Steering Committee Member, Aldevron

James Brown has over 25 years of biotechnology industry experience and has spent the last decade in gene and cell therapy. In 2015 he joined Aldevron where he serves as Vice President, Corporate Development and Chief of Staff. His responsibilities include developing and implementing strategies for expanding Aldevron's products and services. In this capacity he heads the product management function, which enhances existing product features and develops new products. As Chief of Staff Brown works with the CEO to execute on his strategic priorities. Prior to joining Aldevron, Brown was Vice President, Technical Operations, at REGENXBIO Inc., a gene therapy company. In this role he was responsible for contract manufacturing, vendor management, operations, quality assurance and biological reagent sales. Prior to REGENXBIO Dr. Brown served in roles of increasing responsibility in operations and quality assurance at MedImmune, Meso Scale Discovery and IGEN International, Inc. Brown holds a Ph.D. in chemistry from Stanford University and a B.S. in chemistry from Butler University.

Session I – Regulatory and Raw Material Considerations
Considerations for nucleic acids and enzymes in gene therapy: evaluating the impact of how materials are used on design, characterization and specifications

Recent advances in gene therapy have made treatments based on reprogramming cells to treat disease a reality. Researchers are developing a wide array of modalities to address an ever-growing list of diseases. Viral vectors are addressing monogenic defects with protein replacements, delivering therapeutic proteins, and reprogramming T cells to target cancer. Nucleic acids and gene editing nucleases are being used to manipulate various stem cells. Genetic payloads are being developed for individual patients based on the unique proteins and peptides in a tumor, resulting in a truly personalized therapy. Each of these approaches needs a variety of nucleic acids and enzymes to achieve the therapeutic benefit. How each of these are used, their proximity to the patient, the route of administration, and other factors impact the requirements of these materials. We will review examples of how raw materials are used in these therapies and how best to evaluate the design, characterization and specifications in the context of their use. We will present some of the key requirements that drive cost and timeline with a goal to optimize production and ensure the safety and efficacy of the product. We will discuss the spectrum of needs that must be addressed, from off-the-shelf products to enable large scale production of a single therapy to "off-the-shelf production methods" to enable small scale production of many individual therapies.

Session IV – Novel Approaches for Characterization
Session Chair

Heath Coats BS, MS.
PAREXEL

Heath Coats, Principal Consultant at PAREXEL Consulting, Strategic Consulting Services, has over 25 years of industry and consulting experience in parenterals and biologics. Heath worked previously for seven years as a Biologist with the Division of Manufacturing and Product Quality (DMPQ) in CBER, gaining extensive knowledge of administrative and regulatory review procedures for INDs and CMC sections of biologics license applications. While at the Agency, Heath reviewed applications and supplements for cell therapy products, HPC cord blood, plasma fractionated products, vaccines, allergenics, aseptic processing, and in vitro diagnostics. Heath performed and led numerous pre-license and pre-approval inspections while a member of DMPQ. Heath's involvement on inspections has included compilation and review of relevant information from new applications or previous inspections for discussion during pre-inspection meetings and during the inspection. During these inspections, Heath observed and documented deviations in product manufacture, facility qualification, and quality systems. Heath has also prepared inspection reports and reviewed manufacturer's responses to observations during inspections. Heath would also routinely participate in pre-submission meetings with sponsors in order to evaluate facility design, operation, manufacturing and testing procedures, and compliance with Good Manufacturing Practices. Prior to his tenure at FDA, Heath was a hands-on manager of the validation program for eight years at a cell therapy contract manufacturing company that also manufactured endotoxin detection products and cell culture media. His department was responsible for all validation activities at the site including facility, equipment, computer, process, and cleaning. His department documented, investigated, and facilitated corrective actions for deviations when encountered. Heath and his department also participated in factory acceptance testing of capital equipment, statement of work generation for cell therapy clients, and customer and Agency audits as facility and technical subject matter experts. Heath also has over ten years hands on industrial experience in manufacture of biologically active proteins. This experience includes protein expression through fermentation, protein purification and quality control testing. Heath's responsibilities included development and optimization of procedures and then creating accompanying procedures and batch records. Mr. Coats holds a BS in Biology from Mount St. Mary's University and an MS in Biomedical Science from Hood College.

Session I – Regulatory and Raw Material Considerations
Current Good Manufacturing Practices (CGMP) Compliance Issues for Gene Therapy Products

- Phase specific GMPS
  - Phase I
    - Chain of Custody/Chain of Identity
    - GMPs to ensure patient safety
  - Phase II and III
    - Phase 2 and 3 manufacturing will continue to be subject to parts 210 and 211.
- Raw material appropriate quality and grade – vendor and material qualification
- If contract manufacturer used, adequate management and oversight of CMO
  - Appropriate experience with product type by CMO
  - Appropriate KSA (Knowledge, Skill, Ability) of sponsor personnel to adequately oversee CMO
  - Appropriate segregation of different products if multi-product facility
    - Dedicated/Shared/Single use equipment
    - Understanding boundaries of shared/dedicated equipment
    - PCR use for carryover assessment
  - CMO may not disclose all products manufactured due to proprietary information - reference a contract manufacturing facility's Master Files for submissions

        - CBER Drug Master File Guidance information https://www.fda.gov/vaccines-blood-biologics/new-drug-application-nda-process-cber/drug-master-files-cber-regulated-products
        - Drug Master Files Guidance for Industry (DRAFT) https://www.fda.gov/media/131861/download
    - Appropriate viral vector containment mitigation strategies
    - Appropriate review (and approval) of CMO documentation – sponsor review of CMO final product
- Quality agreements with suppliers, CMOs, and CTLs
- ALCOA data integrity
- Capacity throughput studies if Gene Therapy product will be introduced into patients cells then administered to patient
- Example 483 items

Benjamin E Draper, Ph.D.
Megadalton Solutions

Benjamin Draper completed his doctoral work in 2018 under Martin Jarrold at Indiana University working on the development of charge detection mass spectrometry (CDMS). As part of his doctoral work he streamlined CDMS data acquisition and analysis to achieve a 100x speedup, which allowed data analysis to occur in real time. This revolutionized CDMS and opened the window to the analysis of a wide range of high molecular weight samples including gene therapies. Benjamin also contributed to sensitivity improvements such that CDMS can now measure down to femtomolar concentrations of megadalton sized species. Such improvements have also substantially reduced the time required for a CDMS measurement. Recognizing the need for CDMS measurements to be commercially available, Benjamin joined Megadalton Solutions in 2018 to begin the commercialization of instrumentation and provide accurate mass measurements for gene therapies to the pharmaceutical community.

Session III – Novel Approaches for Characterization
Charge detection mass spectrometry for characterization of AAV capsids at Megadalton Solutions

- Charge Detection Mass Spectrometry (CDMS) is capable of making mass and charge measurements of AAV vectors.
- CDMS quantifies empty/partial/full ratios, impurities and high mass aggregates of AAV formulations.
- CDMS measurements are fast, sensitive, and comprehensive allowing measurement of low concentration and heterogeneous samples.
- CDMS can characterize AAV vectors from early to late stage development

Lauren Drouin, Ph.D.
LogicBio Therapeutics

Lauren M. Drouin leads the Analytical Development group at LogicBio Therapeutics, where she supports the development and implementation of analytical methodologies needed to progress LB-001 and other pipeline products from preclinical development into the clinic. Previously, Lauren worked at Voyager Therapeutics where she was responsible for both analytical method development and overseeing CMC analytics operations for the Phase II VY-AADC02 program. Lauren received her PhD in Biochemistry and Molecular Biology from the University of Florida where she utilized biophysical and structural techniques to characterize the AAV capsid for improved gene delivery

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Session II – Analytical and Control Strategies
Developing a Potency Assay for GeneRide Products: an AAV-based Genome Editing Platform

Authors: Chris Cummings, Ryan Hayes, **Lauren M. Drouin**, Matthias Hebben

The GeneRide platform utilizes the natural process of homologous recombination to achieve targeted genome editing without the use of exogenous nucleases or promoters. Developing a potency assay for this unique technology poses additional challenges over those for canonical gene therapy products, including the requirement of a highly sensitive detection method to measure low levels of genome integration. The first GeneRide candidate, LB-001, is currently under clinical development for the treatment of methylmalonic acidemia. LB-001 targets site-specific integration into the albumin locus to allow the gene of interest (*MMUT)* to be expressed concomitantly with albumin. In order to control LB-001 product activity and assess lot-to-lot consistency, a cell-based assay was developed to measure fused mRNA expression as a surrogate of biological activity. The assay was developed in a cell line that naturally expresses albumin and can thus drive expression of the *MMUT* gene upon site-specific integration. Fused mRNA is quantified using primers overlapping the host genome and the transgene DNA to ensure that only the integrated product is detected. The results show that AAV-driven homologous recombination is reproducible in vitro, which allows for the qualification of assay control material. The method was tested for linearity, repeatability, and specificity. Examination of the assay data demonstrates that this method is suitable for assessing the relative potency of integrating GeneRide vectors.

Marina Feschenko Ph. D.
Biogen

Dr. Marina Feschenko is currently a Director in Analytical Development at Biogen. She has been with the company for 9 years. Marina leads activities for development, qualification, and transfer of strategic Gene Therapy assays for dosing, potency, and other critical quality attributes. She also oversees evaluation and implementation of new technologies. Marina is a member of USP expert panel on Fc function assays. She previously worked for Pfizer and Adolor Corporation. Marina holds Ph.D. from Shemyakin Institute of Bioorganic Chemistry in Russia where her work was focused on monoclonal antibody generation and characterization. Dr. Feschenko underwent postdoctoral training in cell biology and signaling at MGH and Harvard Medical School.

Session II – Analytical and Control Strategies
Potency assessment for novel AAV-based drugs: Exploration of different biological activities and stability indicating properties of the assays

Gene therapies, including AAV-based vectors, are novel types of drugs, which require development of many new analytical assays and implementation of additional regulatory guidelines. Potency of gene therapy drugs can be assessed in animal models and cell-based assays. The lack of relevant animal models for human diseases coupled with large variability and high cost of testing makes them a rare choice for drug release. The cell-based assays can measure three different activities of the viral vector: ability to penetrate cells (infectivity), target protein expression, and functional potency. Do we need to have all three or we can justify selecting one or two assays for release? Our approach for two different programs and exploration of stability indicating properties of several potency assays will be presented.

Mohammad (Mo) Heidaran, Ph.D
Chair, USP Gene Therapy Workshop Steering Committee, and Member, USP BIO3 – Complex Biologics Expert Committee

(Mo)hammad Heidaran, Ph.D, Vice President – Technical, PAREXEL Consulting - Dr. Heidaran joined PAREXEL International as Vice President of Technical in December of 2018. He has close to 9 years prior experience as a Biologist and as a Master Reviewer in OTAT, and as a facility reviewer and inspector in the Division of Manufacturing and Product Quality (DMPQ). During his tenure at OTAT, in addition to his review responsibilities, he also served as Acting Team Lead and Branch Chief briefly and as a DCGT representative to several FDA and CBER wide working groups and outside organizations such as USP. He has also been involved in various standard development activities, cell-based product manufacturing initiatives and various compliance activities. Dr. Heidaran has a multidisciplinary academic and industrial background in basic and applied cell biology and innovative cell therapy and tissue engineering product development. He also has hands-on industrial experience in manufacturing of cell therapy and tissue engineering products for about 15 years in small and large size Biotech companies. Mo received his formal training at the National Cancer Institute where he served as a Senior Staff Scientist for about 6 years and 3 years as an IRTA fellow studying signal transduction by receptor tyrosine kinases. Dr. Heidaran holds a Ph.D. in biochemistry from the University of South Carolina and received his formal training at the National Cancer Institute. Prior to FDA, he served as R&D Director at both Celgene and Becton Dickinson. He has been an adhoc reviewer and member of editorial boards of several peer reviewed publications. He also holds 25 issued patents and 54 pending patents and his work has appeared in more than 50 scientific publications.

Workshop Overview

Session Chair: Session II – Analytical and Control Strategies

Workshop Wrap-up and Next Steps

Sophia Kenrick, Ph.D.
Wyatt Technology Corporation

Sophia Kenrick received her Ph.D. in Chemical Engineering from the University of California, Santa Barbara, where she utilized a variety of biophysical techniques to characterize combinatorial protein-binding ligands. Sophia joined Wyatt in 2010 and has provided support to the Sales and Marketing teams and R&D product development efforts. She supports multiple applications for Wyatt instrumentation, especially in the field of molecular recognition and biomolecular interactions.

Session IV – Novel Approaches for Characterization
Characterize and Quantify AAV by DLS and SEC-MALS

To ensure the safety and efficacy of viral vector-based drug products, robust and reliable characterization tools are essential throughout the production and manufacturing process. In this presentation, we discuss a size exclusion chromatography (SEC) method coupled with UV, multi-angle light scattering (MALS), and differential refractive index (dRI) detectors to measure the following three important AAV quality attributes (QAs): total number of viral capsid particles, relative capsid content, and percentage of monomer or aggregates. In addition, orthogonal screening and characterization with dynamic light scattering (DLS) and field flow fractionation (FFF) will be compared.

Maura Kibbey, **Ph. D.**
U.S. Pharmacopeia

Dr. Maura Kibbey is a Senior Scientific Fellow for Education and Training in USP's Global Biologics Department. Dr. Kibbey leads development of courses, workshops, and forums to engage USP's biologics stakeholders. This role builds on her previous responsibilities directing USP scientists developing compendial standards. Before joining USP, Dr. Kibbey worked for several biotechnology and diagnostic companies in the Washington DC area in scientific, management, marketing, and business development roles, as well as performing cancer research at the National Institutes of Health. She has published over 40 peer-reviewed articles and has been an invited speaker or workshop organizer for numerous scientific conferences.

Session Chair: Session V – Standards to Facilitate Gene Therapy Product Development and Quality

Hui-wen Liu, Ph.D.,
Biogen

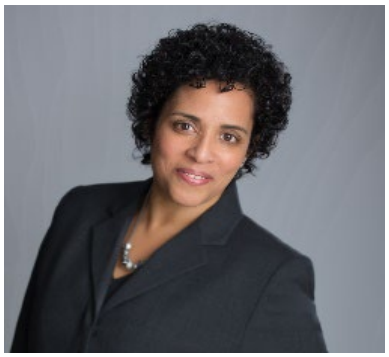
Hui-wen Liu joined Biogen as scientist I at bioassay development group since 2018. She finished her PhD degree in molecular biology at Ohio State University and post-doctoral training at Vollum Institute in Portland, OR. Her current work focuses on characterization of rAAV genome using NGS and other molecular tools. “

Session III: Novel Approaches for Characterization
Encapsidated rAAV genome characterization by next generation sequencing (NGS)

Authors: Hui-wen Liu[1,3], Dongdong Lin[2], Thomas Carlile[2], Jenny Shupe[1], Chao Sun[2], Baohong Zhang[2], Svetlana Bergelson[1], Meisam Bakhshayeshirad[1], Terrence Dobrowsky[1], Wei Zhang[1]

1. Technical Development, Biogen
2. Computational Biology & Genomics, Biogen
3. Contact information: huiwen.liu1@biogen.com

Recombinant adeno-associated virus (rAAV) is one of the promising therapeutic strategies to deliver long-term gene expression *in vivo*. While AAV-based gene therapy products have achieved positive clinical outcomes, one of the risks is genome integrity, as mutations/truncations/insertions may occur in the gene-of-interest, and rAAVs are known to internalize residual DNA fragments along with the gene-of-interest. Therefore, a full characterization of encapsidated DNA to ensure product safety and quality is imperative. Here, we demonstrate that next generation sequencing (NGS) is a method suitable for profiling rAAV genome integrity including mutations and contaminants.



Martiza McIntyre, Ph.D.
USP Gene Therapy Workshop Steering Committee member;
Advanced Therapies Partners

Dr. McIntyre has 20 years of experience in the development, evaluation and regulation of biological and small molecule products within startup biotech firms, the Food and Drug Administration (FDA), and as a consultant. Dr. McIntyre was a product reviewer and ultimately Branch Chief in the Division of Cellular and Gene Therapies at FDA/CBER, where she was actively involved policy development and liaison activities to stakeholder groups. She has since worked in regulatory affairs and product development at Bavarian Nordic, REGENXBIO, Inc., and NanoCor Therapeutics. She served as Executive Vice President of Regulatory Affairs and Product Development at Bamboo Therapeutics where, as part of the senior management team, she participated in portfolio selection, product development and fundraising that resulted in an initial $50 million finance round and ultimate the sale of the company to Pfizer. As president of Advanced Therapies Partners LLC Dr. McIntyre provides strategic regulatory and product development advice to biotech companies, academics, and venture capital firms. She has proven success in defining development strategies for products with complex regulatory challenges including special designations (orphan, RMAT, pediatric orphan drug designation), endpoint selection, accelerated approval, complete response letters, and dispute resolution. She has also been involved in the preparation of some of the first BLA and MAA submissions for gene therapy products to FDA and EMA. She has multidisciplinary experience, including chemistry manufacturing and control (CMC), preclinical, and clinical with a wide range of product types, including novel gene and cell therapy products, vaccines, biological products and small molecules at varied stages of product development. Through her participation in industry associations, including ASGCT and the Standards Coordinating Body she has continued to contribute to gene therapy regulatory policy development. She has been elected to the ASGCT Board of Directors with a term starting in 2019. Dr. McIntyre received a Ph.D. in virology from the University of Chicago and graduated magna cum laude with an Honors B.S. in biology from Wayne State University. She performed postdoctoral research in the laboratories of Dr. Christian Bréchot, INSERM, and Dr. Eda Bloom, FDA/CBER.

Session Chair: Session I – Regulatory and Raw Material Considerations

Sahana Mollah, Ph.D.
SCIEX

Sahana Mollah completed her PhD in Bioanalytical chemistry from the University of Virginia. She has more than 20 years of experience in analytical development and mass spectrometry for biological analysis. Her early work involved in utilizing LCMS for epigenetic and immunology studies including cancer research. In 2004, she started as an application scientist at SCIEX focusing on protein characterization and quantitation. Later, she led the team of applications scientists for Academics and Biopharma. She currently manages the SCIEX global biopharma scientific collaborations as well as technical marketing for capillary electrophoresis. In the past couple of years, she has been heavily involved in the gene therapy analytical assay development at SCIEX using capillary electrophoresis and mass spectrometric tools.

Session IV – Novel Approaches for Characterization
Analytical Methodologies for Analysis of AAV Viral Vector and Nucleic Acids for Gene Therapy

Fast growth in cell and gene therapy industry has generated an urgent need for fast and robust analytics for characterization and impurity determination for both viral vectors and various types of nucleic acid biotherapeutics such as oligonucleotides, plasmid DNA, small RNA, mRNA and double stranded DNA. Although there are efforts to develop analytical assays for characterization of the nucleic acids and vectors, there are still limitations and drawbacks to some of these analysis. In addition, the different workflows are done on different platforms. Capillary electrophoresis is a widely used technique for analysis of protein and nucleic based therapeutics. Here, we present results for multiple key gene therapy analytical workflows performed using capillary electrophoresis (CE) based platform. These methods not only provide characterization of various nucleic acid and vectors, but also analysis of impurities in raw material and drug products. Analytical methodologies included in this presentation are i) fast, easy, orthogonal method for AAV capsid purity analysis (VP1, VP2 and VP3) with ultra-high sensitivity using capillary electrophoresis sodium dodecyl sulfate (CE-SDS) with laser induced fluorescence detection (LIF), ii) method for analysis of plasmid purity and stability using capillary gel electrophoresis (CGE) with LIF detection, iii) sizing and purity analysis of transgenes with CGE-LIF and iv) purity analysis of single guide RNA (sgRNA) and cas9 mRNA for CRISPR analysis with CGE-LIF.

Sushma Ogram, Ph. D.
Viral Vector Services (VVS), Thermo Fisher Scientific

Sushma Ogram has over 25 years of experience working on DNA and RNA viruses. She has been directly involved in developing methods for viral vector analytics for VVS, a CDMO that specializes in the manufacture of viral vectors used in gene therapy. She received her Ph.D. in microbiology with a concentration in molecular virology from the University of Tennessee, Knoxville and post-doctoral training at Cold Spring Harbor Laboratories.

Session III – Novel Approaches for Characterization
Analytical Methods for the quantification of residual DNA and empty capsids in gene therapy vectors

Authors: Sushma A. Ogram, Diego Matayoshi, Laure Kairawicz, Steve Milian and Susan D'costa

Gene therapy viral vectors continue to show great promise for the delivery of therapeutic DNA to treat a variety of monogenic genetic diseases and cancer. There is a significant increase in the number of clinical trials using this novel therapeutic platform, and the number of gene therapy products in the pipeline continue to increase. These biotherapeutic agents being viruses add a significant level of complexity for their production compared to recombinant proteins. This in turn leads to challenges for product characterization with the need for continuous improvement of analytical methods to ensure the safety, quality and potency of the product. In particular, characterization of process impurities remains a challenge. Innovative approaches to quantify two such process impurities, residual DNA (host cell and plasmid DNA) and empty capsids will be discussed. Case studies using duplex ddPCR to quantify residual DNA and analytical ultracentrifugation (AUC) to quantify empty capsids will be presented. Accurate determination of these impurities is critical to product quality as well as lot to lot consistency of gene therapy vectors.

Peter Reczek, Ph.D.
SBC

Peter Reczek, PhD is the Executive Director of the Standards Coordinating Body for Gene Therapy, Cell Therapy, Regenerative Medicines, and Cell-based Drug Discovery (SCB). He comes to SCB with over 30 years of leadership experience in academics, industry, and government serving most recently as AAAS Science and Technology Policy Fellow in the Directors' Office of Science Policy at NIH. Prior to that, he served as Director of Drug Discovery at Bristol Myers Squibb Company where he headed the first drug discovery program dedicated to stem cell targets in a major pharmaceutical company. In addition, he has founded several biotechnology companies. In government, Peter served as the Chief Science and Technology advisor to Gov. Jon S. Corzine of New Jersey where he was a trustee of the New Jersey Stem Cell Institute and served as a founding member of the US National Academy of Science Interstate Alliance for Stem Cell Research. Founded in 2017, SCB is an unbiased, not-for-profit, consensus building organization dedicated to the development of manufacturing standards for advanced therapeutics. Working closely with the U.S. Food and Drug Administration (FDA) and the National Institute of Standards and Technology (NIST), SCB's mission is to "coordinate the accelerated advancement and improved awareness of the standards and best practices that address the rapidly evolving needs of the global regenerative medicine advanced therapy community" SCB's stakeholders represent a cross-section of the global regenerative medicine community and encompasses industry, professional societies, patient advocates, and academic entities. A major portion of SCBs efforts at developing standards involves outreach to the regenerative medicine community through direct communications with stakeholder's, a regularly updated web page, regularly published case studies, blogs, and newsletters, organization and participation in national and international workshops, and the publication of the widely referenced reports, "The Regenerative Medicines Standards Landscape" and "Community Perspectives: Needed Standards in Regenerative Medicine". SCB continues to expand its outreach to volunteers and subject matter experts who are interested in joining us in influencing the future of medical care. More information is available at www.standardscoordinatingbody.org

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Session V – Standards to Facilitate Gene Therapy Product Development and Quality
Update from the Standards Coordinating Body in Support of Gene Therapy

The Standards Coordinating Body for Regenerative Medicine (SCB) is a non-profit that responds to the requests of the regenerative medicine community and their identified standards needs. To support standards advancement SCB engages, coordinates, and eventually educates regenerative medicine stakeholders. Focusing the expertise of subject matter experts on common challenges has the potential to transform product development and spur innovation. Consensus standards and best practices help to reduce the costs of developing regenerative medicine products, and, as a result, accelerate a new therapy's pathway to patients. Because SCB has no vested interests in any particular scientific, commercial, clinical, or policy approach, it occupies a unique and beneficial niche within the regenerative medicine ecosystem.

Current standards under development with application to gene therapy treatments, where input from the regenerative medicine community is valuable, include several ISO standards (TC 276): these include ancillary materials present during the production of cellular therapeutic products, risk based approach for design and validation of methods for rapid microbial detection in bioprocesses, and autologous cell and tissue therapy labeling standards. Other standard areas in development are evaluating preexisting immunity to AAV Vectors, and SCB is currently investigating standards advancement opportunities for therapies that utilize lentiviral vectors. Additionally, SCB regularly updates two canonical documents/reports for the community. The first is *Community Perspectives: Needed Standards in Regenerative Medicine* which outlines more than 30 areas identified and prioritized by the regenerative medicine community where standards could yield significant benefits to the field. The second document/report is *The Regenerative Medicine Standards Landscape*, a list of standards by sector and functional area that can be used as a comprehensive reference for determining what and how current standards apply to an organization's needs.

Jim Richardson, Ph. D.
U.S. Pharmacopeia

Dr. Richardson is in the standards pipeline development group within global biologics at USP, leading efforts to develop standards for emerging technologies such as cell and gene therapy. Jim has been involved in the development of cell and gene therapies for over 20 years, working on retrovirally mediated ex vivo gene therapies at Enzo Therapeutics as well as Adenoviral and AAV-based products at Genovo/Targeted Genetics. Trained as a virologist, Jim has also held positions in process and analytical development, Quality Control, and Translational Science.

Session V – Standards to Facilitate Gene Therapy Product Development and Quality
USP Standards and Best Practices for Gene Therapy

Gene therapies offer tremendous promise to address human disease but their complexity and diversity present unique challenges to those seeking to standardize materials and methods. USP is engaging with stakeholders to identify and develop documentary and physical standards to support gene therapy. This presentation will provide an overview of existing USP documentary and physical standards as well as an update on standards under development.

Richard Snyder, Ph.D.
Thermo Fisher Scientific

Richard O. Snyder, Ph.D. is the Vice President for Science and Technology, Pharma Services, Viral Vector Services at Thermo Fisher Scientific. Dr. Snyder has been investigating virus biology, vector development, cGMP vector manufacturing and analytical technologies, and viral vector-mediated gene transfer for over 33 years and was a member of teams who developed novel viral vector-based human gene therapies. Dr. Snyder was an Associate Professor of Molecular Genetics and Microbiology, and Director of Biotherapeutic Programs at the University of Florida; an Assistant Professor of Pediatrics at Harvard Medical School; and was previously employed by Cell Genesys, Somatix, Merlin, and Avigen where he was engaged in the development of gene transfer vector and vaccine technology, along with therapeutic applications. Dr. Snyder was a postdoctoral fellow at Johns Hopkins University School of Medicine, received his doctoral degree in Microbiology from The State University of New York at Stony Brook, and obtained his B.A. in Biology from Washington University in St. Louis.

Session II – Analytical and Control Strategies
Virus Manufacturing and Control Strategies

Viral gene transfer vector manufacturing for in vivo and ex vivo applications has largely been in support of early phase clinical trials, but as product candidates move to later development stages, demand is rapidly increasing for commercial grade vectors at a variety of scales. Decisions regarding vector design, manufacturing platform, product configuration, process control, and regulatory strategy have an impact on timelines and resources, raw materials sourcing, and analytical testing. Developing a strategy that supports an efficient path to commercialization while reducing risk helps to bring these cutting-edge cell and gene therapies to patients in need.

Angela Whatley, Ph.D.,
CBER, FDA

Angela Whatley, Ph.D. is a Product/ CMC Reviewer in the Division of Cellular and Gene Therapies at the FDA's Center for Biologics Evaluation and is responsible for review of the CMC sections of various pre-IND, IND, and BLA submissions for gene therapy products. Dr. Whatley patriciates in several inter and intra-agency working groups, meetings, and conferences focused on advancing cell and gene therapy products. Dr. Whatley has reviewed various BLAs for gene therapy products and is an expert in the use of AAV for gene therapy products. Dr. Whatley is also a member of the Society for Cell and Gene Therapy and serves on the Genome Editing committee. Prior to joining FDA, Dr. Whatley was a Presidential Management Fellow in the Office of Research and Development at the US Department of Veterans Affairs. As a fellow, Dr. Whatley collaborated with the Chief Research and Development Officer to analyze scoring variations between scientific review committees, how academic rank and gender impact merit review success rates and health disparities in comparative effectiveness research. Dr. Whatley received her Ph.D. in Microbiology from the University of Missouri and has a strong record of leading the next generation of scientist.

Session I – Regulatory and Raw Material Considerations
Suitable Raw Material Qualification for Gene Therapy Products

ABSTRACT NOT AVAILABLE

Eric Yearly, Ph. D.
BridgeBio Gene Therapy

Eric Yearley has over 8 years of experience in the biopharmaceutical industry. Eric began his career at Genentech, Inc./University of Delaware where he held a postdoctoral position studying the reversible cluster formation of monoclonal antibodies at high concentrations. Eric then continued to advance his career in analytical development at MacroGenics, Inc., GlaxoSmithKline Vaccines and Precision Biosciences. During this time, he obtained broad knowledge and experience with the analytical development and characterization of vaccines, biopharmaceuticals and gene therapy products. Eric is presently serving as a Principal Scientist in the Analytical Development department at BridgeBio Gene Therapy in Raleigh, North Carolina.

Session II – Analytical and Control Strategies
Phase-Appropriate Analytical Control Strategies for Recombinant AAV-Based Gene Therapy Products: Case Studies in the Characterization of a Process-Related Impurity and Development of an In-Vitro Potency Assay

Authors: Eric Yearley, Daniel Gall, Frederick Porter, and Zi Wang

Analytical control including both in-process and release testing remains challenging for gene therapy product development due to shorter clinical trial timeframes, the definition of new and unique critical quality attributes (CQAs), the lack of standard analytical methods and control strategies for each of the critical attributes and sampling issues due to lack of appropriate reference standards. Hence, significant effort is exerted to develop phase-appropriate analytical control strategies and assays for identity, potency and purity along with other CQAs to ensure that these attributes of gene therapy candidates are within strict specifications to establish that they are safe and efficacious. Here, we will discuss the analytical control strategies employed at Bridgebio Gene Therapy for the development of a rAAV product targeting an ultra-rare genetic disease. Case studies including the characterization of a process-related impurity and the development of a stability-indicating in-vitro potency release assay will be presented.

Frank Zhang Ph. D.
GlasxoSmithKline

Currently Scientific Leader in GSK Vaccine. Acquired 18+ years in drug/vaccine development of molecules at various stages in NIH, Otsuka Pharmaceutical, BeneVir, and GSK. His expertise spans antibody/recombinant protein, oncolytic virus/cancer vaccine (Adenovirus, HSV), small molecules and mRNAs vaccines

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Session II – Analytical and Control Strategies
Analytical Control Strategy for mRNA-based Vaccines

Authors: Frank Zhang, Xiangzhi Zhou, Jingning Li, Kunal Bakshi, Richard Buckholz, Dong Yu, Nicolas Moniotte, Varnika Roy

The emerging messenger RNA (mRNA) vaccine is demonstrating the potential as a disruptive technology to the industry. It offers a broad range of quick and effective immune response to many infectious diseases. It holds the promise to deliver clinical trial material (CTM) within weeks during disease outbreak. To realize that potential, it's essential to develop robust analytical assays that provide solid foundation for process/product development and quality understanding. Given that mRNA is a novel biological molecule in vaccine/pharmaceutical field, conventional analytical technologies and assays used in the industry require significant adaptation or even re-development. New technologies need to be applied to evaluate the distinct physico-chemical and biological properties of mRNA. Additionally, since mRNA has inherent adjuvant activity, analytical assays must address not only process and product performance, but also issues of clinical safety and efficacy related to inflammation. GSK is developing this novel technology to the vaccine field to address unmet medical needs and other challenges. Over the past decade, we have achieved significant understanding about this modality. We will be sharing our current approach regarding the analytical control strategy.

Yuan Zhao Ph. D.
NIBSC

Dr. Yuan Zhao is a principal scientist and the head of gene therapy section at NIBSC/ Medicines and Healthcare Products Regulatory Agency (MHRA), United Kingdom. Dr Zhao obtained her PhD at Manchester University/UK and gained her postdoctoral experiences at the University of Oxford, CR-UK Cancer Institute and UCL. She has a background in gene therapy, virology and cancer biology. As an expert member of EDQM/Gene Therapy Working Group, EDQM/OMCL/Gene Therapy network, EMA/CAT and previous EMA/Gene Therapy Working Party, her role includes developing WHO international standards and European official control tests for gene therapy products and, contributing to the development of European and International Guidance on Advance Therapies.

Session IV – Impurities and Immunogenicity
Purge-based Risk Assessment for Solvent and Small Molecule Impurities Generated During Oligonucleotide Manufacture

Through the European Pharmaceutical Oligonucleotide Consortium, a team of companies is exploring opportunities to justify the exclusion of small molecule impurities and solvents from release testing through the use of risk-based purge arguments. To support the theoretical purge arguments, spike and purge studies have been performed in different processes and by multiple companies. Results show that process related impurities generated during the synthesis are well purged by the downstream unit operations and justify the exclusion of testing.

Qin Zou Ph. D.
Pfizer

Qin “Chinn” Zou is currently the group leader and associate research fellow at Pfizer, responsible for product and process characterization using various biophysical and biochemical techniques. Before joining Pfizer, he was with Eli Lilly and Co. and worked on formulation development, analytical research and biophysical analysis for biotherapeutics. Qin has a PhD in physical biochemistry from University of Iowa College of Medicine, specifically on thermodynamics of protein stability, protein unfolding and protein interaction. He was also a postdoctoral fellow at Indiana University School of Medicine studying enzymology and protein crystallography.

Session IV – Novel Approaches for Characterization
Holistic Characterization of AAV Capsid Particles Using Advanced Analytical Tools

AAV contains both DNA and proteins. It is the fully assembled AAV capsid particle with the correct genome that act as a gene therapy agent to infect the cells and to deliver the biological function to the desired areas of patients. Characterization of intact AAV particles is critical to understand the product quality attributes that potentially impact the potency and safety of the product, which may include the particle content, integrity, size and morphology. Many analytical tools are available to evaluate these attributes with different pros and cons and should be used complementarily to provide a more comprehensive picture of the AAV capsid as a whole. This talk will strive to demonstrate the use of several different analytical techniques for this purpose.

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Nate Weinstock Ph. D.
Steering Committee Member, Biogen

Nate is currently a Senior Scientist at Biogen where he is primarily responsible for leading the assay transfer team for their gene therapy programs. Prior to joining Biogen, he was the Assistant Director of Quality Control at AGTC. During his time at AGTC he was responsible for analytical development, testing, and stability, for all cell banks, viral banks, and AAV products. Prior to AGTC he worked at Brammer Bio where he led the analytical development and QC testing group, supporting all gene therapy clients. Nate has a Bachelor's, Master's, and Ph.D. in Behavioral Neuroscience from the University of Florida.

Session Chair: Session III – Novel Approaches for Characterization

Catherine (Katie) Zander, PhD.
SCB

Catherine (Katie) Zander, PhD is the SCB Technical Program Manager for gene therapy. Katie holds a PhD in Chemistry from Binghamton University, where she studied the kinetics of neurotransmitters. Her past experience includes researching rare blood clotting diseases at the University of Alabama at Birmingham, founding a patient education program, working in the U.S. House of Representatives Committee on Energy and Commerce as an American Society of Hematology & American Association for the Advancement of Science (AAAS) Science & Technology Policy Fellow, and co-chairing the National Postdoctoral Association's Advocacy Committee..

Session V – Standards to Facilitate Gene Therapy Product Development and Quality
Update from the Standards Coordinating Body in Support of Gene Therapy

The Standards Coordinating Body for Regenerative Medicine (SCB) is a non-profit that responds to the requests of the regenerative medicine community and their identified standards needs. To support standards advancement SCB engages, coordinates, and eventually educates regenerative medicine stakeholders. Focusing the expertise of subject matter experts on common challenges has the potential to transform product development and spur innovation. Consensus standards and best practices help to reduce the costs of developing regenerative medicine products, and, as a result, accelerate a new therapy's pathway to patients. Because SCB has no vested interests in any particular scientific, commercial, clinical, or policy approach, it occupies a unique and beneficial niche within the regenerative medicine ecosystem.

Current standards under development with application to gene therapy treatments, where input from the regenerative medicine community is valuable, include several ISO standards (TC 276): these include ancillary materials present during the production of cellular therapeutic products, risk based approach for design and validation of methods for rapid microbial detection in bioprocesses, and autologous cell and tissue therapy labeling standards. Other standard areas in development are evaluating preexisting immunity to AAV Vectors, and SCB is currently investigating standards advancement opportunities for therapies that utilize lentiviral vectors. Additionally, SCB regularly updates two canonical documents/reports for the community. The first is *Community Perspectives: Needed Standards in Regenerative Medicine* which outlines more than 30 areas identified and prioritized by the regenerative medicine community where standards could yield significant benefits to the field. The second document/report is *The Regenerative Medicine Standards Landscape*, a list of standards by sector and functional area that can be used as a comprehensive reference for determining what and how current standards apply to an organization's needs.