Capital Hilton

Oct 28, 2024 8:30 AM - Oct 30, 2024 12:40 PM

1001 16th Street NW, Washington, DC 20036-5794

DIA/FDA Oligonucleotide-Based Therapeutics Conference

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00 DAYS 09 HOURS 29 MINUTES 30 SECONDS

Print Agenda

Day 1 Oct 28, 2024

8:30 AM — 4:45 PM — Capital Terrace

Registration

9:15 AM — 9:30 AM — Presidential Ballroom

Welcome and Opening Remarks

Speaker(s)

Sorcha McCrohan, MS

Scientific Projects Manager
DIA, United States

Sorcha McCrohan is a Specialist of Scientific Programs for the Americas Region at DIA. In her current role, she focuses on content development and strategy for DIA's meetings to improve and facilitate innovation in clinical research, drug development, and the fields of devices and diagnostics. Before joining DIA, she conducted COVID-19 research in Chiapas, Mexico, and worked in marketing within Pfizer's Global Vaccines Meningococcal franchise. Sorcha holds a BA in Sociology from Mount Holyoke College and an MSc in Global Health, Disease Prevention & Control from Georgetown University.

Scott Henry, PhD

Senior Vice President, Nonclinical Development
Ionis Pharmaceuticals, Inc., United States

Dr. Henry received a PhD in Biochemistry form North Dakota State University. He was a post-doc fellow at Parke Davis, Ann Arbor MI, depart. of toxicology. He joined Isis Pharmaceuticals, Inc. as a Sr Scientist in toxicology. He helped characterized and studied mechanisms of various toxicities e.g. the effects of oligonucleotide treatment on clotting time prolongation, alternative complement pathway activation, proinflammatory effects in rodents, platelet alterations and the effects related to the accumulation of oligonucleotide in kidney. As VP of Non-Clinical Development he has participated in the development of ~8 different phosphorothioate oligodeoxynucleotides and 30+ different 2'-MOE modified phosphorothioate oligonucleotides.

Ronald Wange, PhD

Associate Director for Pharm/Tox OND
FDA, United States

Dr. Wange is an Associate Director for Pharmacology & Toxicology within the Office of New Drugs in CDER at the FDA, and has over 19 years of experience reviewing small molecule drugs, biotherapeutic proteins and oligonucleotide-based therapeutics. He is a founding member of OND's Pharmacology/Toxicology Oligonucleotide Subcommittee, which considers issues specifically related to the safety review of oligonucleotide-based therapeutics. In addition, he was the primary author of the recently published draft guidance on Nonclinical Testing of Individualized ASOs for Severely Debilitating or Life-Threatening Diseases. Prior to joining FDA, he was the head of the T-lymphocyte Signaling Unit at the National Institute on Aging at the NIH.

9:30 AM — 10:30 AM

Presidential Ballroom

Session 1: Keynote Address

Session 1: Keynote Address

Track: General Session

Session Chair(s)

Jeffrey Foy, PhD

Senior VP, Toxicology
PepGen Inc., United States

Speaker(s)

Speaker

Peter P. Stein, MD

Director, Office of New Drugs, CDER
FDA, United States

Peter Stein, MD, is the Director of CDER's Office of New Drugs (OND). OND is responsible for the regulatory oversight of investigational studies during drug development and decisions regarding marketing approval for new (innovator or non-generic) drugs, including decisions related to changes to already marketed products. OND provides guidance to regulated industry on a wide variety of clinical, scientific, and regulatory matters. A nationally-recognized leader in pharmaceutical research and development, Dr. Stein joined CDER in 2016 as the OND Deputy Director. Before coming to FDA, he served as Vice President for late stage development, diabetes, and endocrinology at Merck Research Laboratories.

10:30 AM — 11:00 AM Capital Terrace

Refreshment and Networking Break

11:00 AM — 12:30 PM South American AB

Session 2 Track 1: Extra-Hepatic Delivery – Clinical Experience: Emerging

Track 1: Extra-Hepatic Delivery – Clinical Experience: Emerging

Track: Track 1: Clinical

Session Chair(s)

Xing Jing, PhD, MBA

Reviewer
FDA, United States

Dr. Xing Jing is an expert in oligonucleotide-based therapeutics. He possesses a broad range of experiences from biology to clinical trials. He was trained as a structural biologist in academia. After training, he worked in the field of R&D and bioinformatics in industry. Dr. Jing has been a clinical pharmacology reviewer at FDA since 2020. Initially, Dr. Jing was a reviewer in CDER at the FDA, where he reviewed oligonucleotide therapeutics and published a summary of clinical pharmacology for siRNA therapeutics. Currently, he is a reviewer of cell and gene therapies in CBER at the FDA. Dr. Jing's regulatory review experience covers a wide range of therapeutic areas including oncology, CNS, autoimmune, virology, etc.

Arthur A. Levin, PhD

Distinguished Scientist
Avidity Biosciences, United States

Speaker(s)

Pulmonary Delivery Platform and Clinical Programs

James Hamilton, MD, MBA

Chief of Discovery and Transitional Medicine
Arrowhead Pharmaceuticals, United States

Dr. Hamilton currently serves as Vice President, Clinical Development at Arrowhead Pharmaceuticals and previously served as Medical Director at Arrowhead. In these roles, he has designed and managed multiple clinical studies with a wide range of siRNA compounds and has led clinical programs in various disease areas including hepatitis B, alpha-1 antitrypsin deficiency and dyslipidemia. He is the global medical lead on the AROAAT2001 (SEQUOIA) study evaluating the siRNA compound, ARO-AAT for the treatment of liver disease in the setting of alpha-1 antitrypsin deficiency. Dr. Hamilton holds an MD and an MBA from The Ohio State University and is board certified in Emergency Medicine.

Cardiac Delivery of Oligonucleotides

Thomas Thum, MD, PhD, FACC

CSO/CMO
Cardior Pharmaceuticals GmbH, Germany

Thomas Thum, Founder and CSO/CMO of Cardior Pharmaceutials (a Novo Nordisk company), is a key opinion leader in cardiac diseases and the development of RNA-based therapeutics and has received numerous awards for his work. Thomas is a member of the editorial boards of the world's most prestigious journals for cardiovascular research and an executive member of national and international research committees in the cardiovascular field. Thomas is Director of the Institute of Molecular and Translational Therapeutic Strategies (IMTTS) at Hanover Medical School (MHH) and visiting professor at the National Heart and Lung Institute at Imperial College London.

Delivery of siRNA to Placenta for Treatment of Preeclampsia

Allison August

Chief Medical Officer
Comanche Biopharma, United States

Delivery of Oligonucleotides to Muscle in Patients

Steve Hughes, MD, MBA

Chief Medical Officer
Avidity Biosciences, United States

Dr Hughes trained in general internal medicine and has been in the biotech/pharma sector for over 25 years. He has been involved in more than 60 clinical trials with more than 30 drugs across multiple therapeutic areas including multiple rare diseases, neurology, cardiac and oncology. Dr Hughes is currently Chief Medical Officer at Avidity BioSciences, an RNA focused company developing treatments for rare neuromuscular and cardac diseases. Prior to joining Avidity he has held senior drug development positions at several other RNA therapeutics companies.

11:00 AM — 12:30 PM Presidential Ballroom

Session 2 Track 2: Pro-Arrhythmic Risk of Oligonucleotide Therapeutics: Is New Guidance Needed?

To date, the proarrhythmic assessment of oligonucleotide therapeutics has been influenced by existing International Conference on Harmonization (ICH) E14 and S7B guidance. However, oligonucleotide therapeutics exhibit distinctive physiochemical characteristics that may impact their proarrhythmic risk profile. Accumulating nonclinical and clinical data in this space may further inform future guidance development and regulatory decisions. This session will provide 1) a retrospective overview of the past practices used to conduct proarrhythmic assessment of oligonucleotide therapeutics in both nonclinical and clinical studies; 2) potential future recommendations to evaluate pro-arrhythmic risk of oligonucleotide therapeutics; and 3) FDAs perspective and experience with proarrhythmic risk assessment of oligonucleotide therapeutics.

Learning Objective :

- Recognize practices previously used to evaluate pro-arrhythmic risk both in nonclinical and clinical studies, and their correlation
- Debate the need for harmonized recommendations for evaluation of pro-arrhythmic risk of oligonucleotide therapeutics
- Discuss considerations for future recommendations to evaluate pro-arrhythmic risk of oligonucleotide therapeutics

Track: Track 2: Nonclinical

Session Chair(s)

Xuan Chi, PhD

Supervisory Pharmacologist
CDER, FDA, United States

Dr. Chi is a Supervisory Pharmacologist in the Office of Cardiology, Hematology, Endocrinology and Nephrology, CDER FDA. Prior to that, she was a senior consultant in the Federal Healthcare Practice at Deloitte Consulting LLP and her projects were focused on post-marketing drug safety, data warehouse and review modernization effort. She had also worked as a staff fellow at Office of Blood Review and Research, CBER FDA. She is specialized in analyzing data from toxicological, pharmacological and clinical studies of original NDAs, BLAs, INDs, and 510(k)s. She had Ph.D. in molecular genetics from Baylor College of Medicine and had postdoctoral training in molecular genetics and pathology at Columbia University Medical Center.

Tod Harper, PhD

Scientific Associate Director
Amgen, United States

Speaker(s)

A Scientific Review of the Low Proarrhythmic Risk of Oligonucleotide Therapeutics

Hugo Vargas, PhD

Executive Director
Amgen Inc., United States

I am an Executive Director in Translational Safety & Bioanalytical Sciences an integral group within Amgen Research that is responsible for nonclinical safety evaluation of our pipeline molecules. I also lead the Translational Safety Research group, which is a diverse group of scientists with safety pharmacology, immunology, drug safety and toxicology expertise. My team is located at the Thousand Oaks and San Francisco sites in California. I have been in the pharm industry since 1991. I am actively involved with several industry-wide activities and serve at the Deputy Technical Lead (PhRMA representative) to the ICH E4/S7B Implementation Working Group. I have a PhD in Pharmacology (Rutgers) and did postdoctoral research at UCLA.

Future Recommendations: Update from ICH E14/S7B IWG

Derek Leishman, PhD

Vice President, Translational and Quantitative Toxicology
Eli Lilly and Company, United States

FDA Clinical and Nonclinical Perspectives and Experience with Evaluation of Pro-arrhythmic Risk After Exposure to Oligo-based Products

Wendy Wu, PhD

Pharmacologist
FDA, United States

FDA Clinical and Nonclinical Perspectives and Experience with Evaluation of Pro-arrhythmic Risk After Exposure to Oligo-based Products

Lars Johannessen, MSc

Senior Clinical Analyst
FDA, United States

11:00 AM — 12:30 PM

Federal AB

Session 2 Track 3: Regulatory Experiences with Clinical/ Commercial Oligonucleotides

Recent filings of siRNAs and ASOs have come with interesting challenges for regulators and industry alike. Hot topics and learnings from recent filings will be discussed with two talks from industry, one on experiences with siRNA molecules and the other on the subject of Solution API, followed by a panel discussion with regulatory agency and industrial participants.

Learning Objective :

- Identify key regulatory challenges associated with siRNA molecules
- Recognize benefits and concerns of liquid API for oligonucleotide molecules
- Compare perspectives of US /EU regulators and industrial practitioners on the above topics in the panel discussion

Track: Track 3: CMC

Session Chair(s)

Firoz Antia, PhD

Vice President, Oligonucleotide and Small Molecule CMC
Denali Therapeutics, United States

A PhD Chemical Engineer by training, Dr. Antia has spent over 30 years in the pharmaceutical industry carrying out process development with roles at Sandoz, J&J, Merck and Palatin

Technologies, before joining Biogen in 2012, where he is now Head of Oligonucleotide Development

Speaker(s)

Oligonucleotide Solution API: Navigating the Regulatory Landscape

Chris Chorley

Associate Director, Regulatory Affairs CMC
Biogen, United Kingdom

Chris has worked in the pharmaceutical industry for approximately 17 years, beginning his career at AstraZeneca as a synthetic organic chemistry research scientist, before moving into regulatory affairs in 2011. He held positions of increasing responsibility with Genpact and Ipsen, before joining Biogen in 2020 where he currently leads regulatory CMC activities for oligonucleotide programs at various stages of development. Chris holds a master's degree in chemistry from the University of York, UK.

Regulatory CMC Learnings and Perspectives from recent RNAi Filings

Erik McKinney, MS

Senior Director, CMC Regulatory Affairs
Alnylam Pharmaceuticals, United States

Eric McKinney is a Senior Director of CMC, Regulatory Affairs at Alnylam Pharmaceuticals. In his role, he leads the development and implementation of Alnylam's global regulatory CMC strategy for developmental programs. Eric has over twenty years of experience in the pharmaceutical industry, and prior to Alnylam, he spent eleven years with Boehringer Ingelheim. Initially, Eric started his career on the technical track with positions in Quality Control & Analytical Development before transitioning into Regulatory Affairs. While at Alnylam, Eric designed and implemented programs for stability, specifications, and extractables & leachables. He serves on the Board of Directors for the International Consortium for Innovation and Quality.

Panel Discussion

René Thürmer, PhD

Quality Assessor
Federal Institute for Drugs and Medical Devices, Germany

Dr. René Thürmer received his diploma in chemistry and his Ph.D. in biochemistry from the University of Tübingen. He joined the BfArM (Federal Institute for Drugs and Medical Devices, Bonn, Germany) in 2000. He currently serves as a CMC reviewer and is Deputy Head of the Unit Pharmaceutical Biotechnology. His experience is in the field of formulation, manufacture and control of medicinal products, in particular in the field of peptides, proteins, liposomes, sustained release polymer drug products, depot formulations, polymer-conjugated drug products, natural and synthetic surfactants, nanomedicine and others. His special focus lies on oligonucleotide preparations.

Panel Discussion

Katharine Duncan, PhD

Senior Pharmaceutical Quality Assessor (SPQA), Office of Product Quality Assessm
FDA, United States

Katharine Duncan is a Senior Pharmaceutical Quality Assessor with the Office of Product Quality Assessment III within the Office of Pharmaceutical Quality at the Food and Drug Administration. Dr. Duncan joined the FDA in 2019 after several years working in small molecule drug discovery at a pharmaceutical company in San Diego. Her Ph.D. research was conducted in the laboratory of Dr. Dale Boger at the Scripps Research Institute in La Jolla, California. She received her undergraduate degree in chemistry from Amherst College in Amherst, Massachusetts.

12:30 PM — 1:30 PM Capital Terrace

Networking Luncheon

1:30 PM — 3:00 PM South American AB

Session 3 Track 1: Safety Observations in Late Clinic Development and Early Commercial Surveillance

Oligonucleotide therapeutics have become mainstream tools for regulation of rare and genetic diseases through their ability to modulate gene expression across a variety of processes. Generational advances in chemistry, delivery and targeting have positively impacted their safety profile. While challenges remain, cell-specific targeting has significantly decreased effective dose and reduced off-target effects, leading to improved safety. This session will address some of the strategies that have contributed to these improvements in safety.

Learning Objective : At the conclusion of this session, participants should be able to:

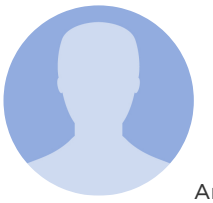
- Understand the underlying advances that have contributed to the Safety of oligonucleotide-based therapeutics
- Understand the impact of specific targeting on exposure reduction and resulting Safety
- Hear about the expansion of oligonucleotide-based therapeutics to broader disease populations as a result of their improved benefit-risk profile

Track: Track 1: Clinical

Session Chair(s)

Louis St. L. O'Dea, MD

Independent Consultant
United States



Anuradha Ramamoorthy, PharmD, PhD

Policy Lead, OCP, OTS, CDER
FDA, United States

Anuradha Ramamoorthy, Ph.D. is a Policy Lead at the Office of Clinical Pharmacology (OCP), Food and Drug Administration (FDA). She received her Ph.D. in Medical and Molecular Genetics from Indiana University and was a postdoctoral fellow at the NIH and FDA. In her current role, she contributes to regulatory policy development, stakeholder engagement, and regulatory research focused on clinical pharmacology. Prior to this role, she was a Reviewer in the Genomics and Targeted Therapy, OCP contributing to the regulatory review of investigational new drug (IND), new drug application (NDA), and biologic licensing application (BLA).

Speaker(s)

The Evolution of Safety in Oligonucleotide-based Therapeutics; the Roles of Chemistry, Formulation and Targeting

Richard Geary, PhD

EVP, Chief Development Officer
Ionis, United States

Dr. Geary is Chief Development Officer and Executive Vice President of Antisense Drug Development at Ionis Pharmaceuticals. He is responsible for preclinical development, global clinical development and regulatory, and manufacturing for Ionis' antisense drugs. Since joining Ionis in 1995, Dr. Geary has been involved in discovery and development including the regulatory submission of more than forty investigational new drug applications and five successful antisense medicine late stage development programs through approvals in multiple jurisdictions. Dr. Geary received his Ph.D. in Biopharmaceutics from the University of Texas, College of Pharmacy, Austin, Texas and his B.S. in Biology from Texas A&M University, College Station, Texas.

Clinical Case Study in Oligo Safety, TTR Amyloidosis Comparative Safety of Systemic vs Targeted Oligonucleotide Therapeutics

Elena Yureneva, MD, MHS

Executive Director, Head Medical Safety and Risk Management
Alnylam Pharmaceuticals, United States

Elena Yureneva MD, MHSA is a cardiologist by training, with 10 years of pharmacovigilance experience, serving as an Executive Director, Head of Medical Safety and Risk Management at Alnylam Pharmaceuticals. Prior to Alnylam Elena worked at Merck and Cubist. Before pursuing her career in the industry, Elena served as a Chief of Staff to the Chief Medical Officer at Children's National Health Systems in Washington, DC. Elena acquired her MD at the First Moscow State Medical University in Russia, and completed her Master's Degree in Health Systems Administration at Georgetown University.

1:30 PM — 3:00 PM Presidential Ballroom

Session 3 Track 2: Translatability of CNS Safety and Pharmacology

This session will focus on current research efforts in the area of neurological diseases. The focus of the session will be improved oligonucleotide delivery to the CNS, pharmacokinetics/interspecies scaling for neurological assessment based on age and exposure levels, and safety observations following administration of oligonucleotides to the CNS.

Learning Objective : At the conclusion of this session, participants should be able to:

- Describe the mechanisms and drivers for CNS uptake and pharmacokinetics
- Identify nonclinical study design considerations and translatability for nonclinical studies in the CNS
- Understand safety considerations for oligonucleotide therapeutics in the CNS

Track: Track 2: Nonclinical

Session Chair(s)

Aimee L. Jackson, PhD

Chief Scientific Officer
Atalanta Therapeutics, United States

Aimee has been working in the field of RNA interference and microRNAs for >15 years and has authored/co-authored >20 publications. She received her PhD from Univ of Colorado Health Science Cntr and performed post-doc research at Univ of Washington. Aimee joined Rosetta Inpharmatics/Merck, where she established the use of RNAi combined with expression profiling technologies for target identification, target validation, elucidation of drug mechanism-of-action, and patient stratification. She investigated the therapeutic application of siRNAs. Aimee leads the discovery/development of new therapeutic targets in diverse disease indications, pioneering the implementation of translational biomarkers for mechanistic proof-of-concept in patients.

Lois Freed, PhD

Director, Division of Pharmacology/Toxicology-Neuroscience (DPT-N), CDER
FDA, United States

Lois Freed earned her undergraduate and Master's degrees from the University of Kansas and her Ph.D. from the University of Maryland. Prior to working at the FDA, Lois worked at the National Institute on Aging/NIH in the Laboratory of Neurosciences. Lois has been at the FDA since 1992, joining the Division of Neuropharmacological Drug Products as a nonclinical reviewer. She was the Supervisory Pharmacologist in this Division and then the Division of Neurology Products. Lois is currently the Director of the Division of Pharmacology/Toxicology in the Office of Neuroscience (OND/CDER).

Speaker(s)

Acute Transient Neurobehavioral Changes in NHPs

Hao Chen, PhD

Toxicologist
Ionis Pharmaceuticals, Inc., United States

Rugonersen Pediatric Trial: How Did Nonclinical Studies (not) Translate?

Katharine Bray-French, PhD, MS

Toxicology Project Lead / Distinguished Scientist
F. Hoffmann La-Roche, Switzerland

Katharine is a pharmacologist and toxicologist with more than 30 years experience in nonclinical research and drug development. She has a proven track record in leading and empowering teams in large strategic initiatives e.g. immunogenicity. Her comprehensive experience spans various modalities (including large molecules, small molecules, and oligonucleotides), routes of administration, and disease areas including oncology. More recently she has been involved in the development of oligonucleotides in a number of neurological and rare diseases.

Safety and Biodistribution of both IT/ICV and Conjugated IV ASOs and siRNAs targeting CNS indications

Kendall Frazier, DVM, PhD

Retired, United States

Dr. Ken Frazier has a BS from WSU, DVM from KSU and PhD from the U of Miami. He did a residency in comparative pathology at UM Jackson Memorial Hosp and is board certified in pathology and toxicology, and is one of only a few veterinary nephrology experts in the world. He has over 100 scientific articles and book chapters and has extensive experience in the safety of antisense oligonucleotides as a faculty member at U of Georgia and 18 years as a sr. science fellow/safety liaison for GSK. Since retiring he has consulted with over 25 companies on ASO toxicology and lectures widely, including safety workshops for CDER, CBER & CFSAN. He has chaired many committees and meetings for STP, ESTP, ACVP and is incoming president of the IATP.

1:30 PM — 3:00 PM Federal AB

Session 3 Track 3: Emerging Oligonucleotide CMC Guidance

This session will provide updates on emerging regulatory guidances from key global regulators such as FDA and EMA. Special emphasis will be placed on the forthcoming EMA guidance on synthetic oligonucleotides given the 2023 publication of the concept paper and feedback from industry. A panel discussion including both regulator and industry perspectives will follow to address audience questions and any future directions that will impact the global regulatory landscape for oligonucleotides.

Learning Objective : At the conclusion of this session, participants should be able to:

- Identify key emerging global oligonucleotide guidance and standards
- Apply concepts from the session to establishing regulatory strategies for meeting the requirements of global regulators for oligonucleotides
- Analyze and discuss new or evolving elements of the emerging regulatory landscape for oligonucleotides, particularly potential risks or gaps

Track: Track 3: CMC

Session Chair(s)

Benjamin Stevens, PhD, MPH

Director CMC Policy and Advocacy
GlaxoSmithKline, United States

Ben Stevens is a Director of CMC Policy and Advocacy at GlaxoSmithKline and has nearly 15 years of drug discovery and regulatory experience. Prior to GSK, Ben was a Director of Regulatory Affairs CMC at Alnylam, a Principal Consultant at PAREXEL and an acting Branch Chief in the Office of New Drug Products (ONDP) at the FDA. Before FDA, Ben spent seven years in pharmaceutical R&D at Pfizer and Merck. Ben received a Ph. D. in Chemistry from the University of Pittsburgh, a M.P.H. from the Johns Hopkins and is a co-author of over 20 publications and patents.

Paresma (Pinky) Patel, PhD

Division Director, Office of Product Quality Assessment III
FDA, United States

Paresma (Pinky) Patel, Ph.D. is a Division Director in CDER's Office of Pharmaceutical Quality, Office of Product Quality Assessment III. In this role, she leads groups responsible for the evaluation of chemistry, manufacturing, and controls (CMC) information with a focus on drug substance quality throughout clinical development to submission of marketing applications. She served as a Branch Chief, supporting the oncology and anti-viral clinical divisions, prior to transitioning to her current role. Prior to FDA, she worked as a medicinal chemist at the National Institutes of Health. Dr. Patel completed her Ph.D. in organic chemistry at The Scripps Research Institute and a postdoctoral fellowship at the California Institute of Technology.

Speaker(s)

Update on the EMA Draft Guideline on the Development and Manufacture of Oligonucleotides

René Thürmer, PhD

Quality Assessor
Federal Institute for Drugs and Medical Devices, Germany

Dr. René Thürmer received his diploma in chemistry and his Ph.D. in biochemistry from the University of Tübingen. He joined the BfArM (Federal Institute for Drugs and Medical Devices, Bonn, Germany) in 2000. He currently serves as a CMC reviewer and is Deputy Head of the Unit Pharmaceutical Biotechnology. His experience is in the field of formulation, manufacture and control of medicinal products, in particular in the field of peptides, proteins, liposomes, sustained release polymer drug products, depot formulations, polymer-conjugated drug products, natural and synthetic surfactants, nanomedicine and others. His special focus lies on oligonucleotide preparations.

Speaker

Katherine Windsor, PhD

Senior Pharmaceutical Quality Assessor, CDER
Food and Drug Administration, United States

Dr. Katherine Windsor is a Senior Pharmaceutical Quality Assessor (Drug Substance Lead) in the Office of Pharmaceutical Quality within the Center for Drug Evaluation and Research (CDER) at FDA. Katherine has 10 years of experience assessing CMC aspects of drugs in several therapeutic areas, particularly anti-infectives and antivirals, and a wide variety of APIs, including oligonucleotides, peptides, antibody-drug conjugates, and small molecules. Katherine conducted postdoctoral research at Vanderbilt University and obtained her Ph.D. in Organic Chemistry from the University of Wisconsin-Madison and her B.S. in Chemistry from the University of Notre Dame.

Quality Attributes of Starting Materials for Therapeutic Oligonucleotides

Kevin Carrick, PhD

Senior Director, Science and Standards, Biologics
United States Pharmacopei, United States

Dr. Kevin Carrick is a Senior Director of Science & Standards in USP's Global Biologics Department. Dr. Carrick and his team work with the five USP Expert Committees and multiple Expert Panels in the area of biologics to develop standards that support biopharmaceutical quality assessment. These standards include documentary (monographs and general chapters) and physical reference standards for varied products from oligonucleotides to gene therapies.

Speaker

Brian Pack

Principal Research Scientist
Eli Lilly & Company, United States

3:00 PM — 3:30 PM Capital Terrace

Refreshment and Networking Break

3:30 PM — 5:00 PM Presidential Ballroom

Session 4 Track 1 and 2: Applying Toxicology Testing to the Clinic

Due to the unique pharmacokinetic properties of some oligonucleotide-based therapeutics, it can be challenging to compare the exposure achieved in animal pharmacology or toxicology studies to humans. Furthermore, understanding the relevant concentration of drug at the site of action (on and off target pharmacology and DDI) is key to the prediction of clinical outcomes. With a lack of clear guidance, several strategies have been employed to assess the relevance of nonclinical findings and predict clinical efficacy or safety. This session will share case examples of how programs have navigated from preclinical to clinical development including strategies used to calculate safety margins and DDI Liability with the goal of better predicting clinical outcomes.

Learning Objective : At the conclusion of this session, participants should be able to:

- Define different parameters including pharmacokinetic metrics that can be used to calculate safety margins
- Describe how in silico PK/PD models can be used in combination with cellular and subcellular kinetics to predict drug concentrations at the site of action

Track: Track 1 and 2: Clinical/Nonclinical

Session Chair(s)

Elena Braithwaite, PhD

Toxicologist
FDA, United States

Dr. Elena Braithwaite is a toxicologist at the US Food and Drug Administration and a Diplomate of the American Board of Toxicology. She has a broad background in various aspects of basic research including DNA repair, mutagenesis and signal transduction.

Andrew Slugg, MBA, MS

Senior Vice President, Global Head of Regulatory Affairs
Alnylam Pharmaceuticals, United States

Andrew began his career in industry over 20 years ago and has spent the last 17 years in Regulatory Affairs. He's had the fortune of being a part of many great teams who have brought seven novel therapies to market for a variety of conditions. This includes the first four RNAi therapeutics. Andrew holds degrees from Bates College, Massachusetts College of Pharmacy and Health Sciences, and Babson College.

Speaker(s)

Refinement of PKPD Models and DDI Assessment

Steve Hood, PhD

Senior Director, Oligo ADME Strategy
GlaxoSmithKline, United Kingdom

Steve Hood received a PhD in Molecular Toxicology from the University of Surrey in 1993 and joined Glaxo Group Research as an Industrial Post doc. Steve is now a senior Scientific Director in Bioimaging, responsible for external imaging collaborations in the Bioimaging Expertise Network (BEN). As part of this network, Steve is also Co-Director of the GSK Centre for Molecular Imaging (COMI) at the University of Illinois at Urbana Champaign, where he works closely with Professor Stephen Boppart and his team. Steve has spent most of the last 2 decades working on GSK's diverse oligo portfolio and has supported projects ranging from inhaled SiRNAs, TLR antagonists, DMD exon skippers (Prosensa) and ASOs for TTR and HBV with Ionis.

Considerations for Determining Safety Margins for Oligonucleotides During Clinical Development

Meena Meena, PhD

SVP of Translational DMPK and Clinical Pharmacology
Stoke Therapeutics, United States

Meena is the Senior Vice President of Translational DMPK and Clinical Pharmacology at Stoke Therapeutics. Prior to joining Stoke in 2018, Meena served as senior director of bioanalytical, pharmacology and biomarker development at Wave Life Sciences. She played a pivotal role in building Wave's stereopure oligonucleotide chemistry platform and in guiding the clinical entry of three antisense oligonucleotide programs. Earlier in her career, Meena worked at Alnylam Pharmaceuticals on siRNA chemistry and targeted siRNA delivery. Meena received her Ph.D. in chemistry with Dr. K.N. Ganesh at the National Chemical Laboratory in Pune, India, and did her postdoctoral research on nucleic acid analogs with Professor Larry W. McLaughlin at Boston Colle

Harnessing ASO Platform Technology: A Precise Approach to the Design, Development and Administration of Individualized Therapies

Julie Douville, PhD, MS

Executive Director, ASO Discovery and Development
N-Lorem Foundation, United States

Julie Douville is the Executive Director of ASO Discovery and Development at n-Lorem, where she oversees ASO design, in vitro screening, manufacturing, toxicology, and regulatory aspects. Prior to this, she spent 15 years at Charles River Laboratories where she led hundreds of programs for CNS indications such as ALS, Alzheimer's, Parkinson's, Angelman's Syndrome, Duchenne's Muscular Dystrophy, and many others. Of note, she oversaw the toxicology program for milasen, the first individualized antisense oligonucleotide customized for a mutation in a single patient, which was approved by the FDA in 2018. In continuation with this work, she joined n-Lorem in 2022 to lead nonclinical development and has since contributed to >20 IND applications.

3:30 PM — 4:45 PM Federal AB

Session 4 Track 3: Demonstrating Comparability for Oligonucleotides Therapeutics

Oligonucleotide therapeutics are larger and more complex than traditional small molecule drugs. Consequently, the task of demonstrating comparability of materials made by different manufacturing processes, may be more challenging for oligonucleotide therapeutics than for small molecule drugs. The session will include presentations from regulatory authorities, and industry scientists. The presentations will be followed by a panel discussion. Topics for discussion may include how to define comparability, the types of chemical and physicochemical characteristics that should be evaluated, analytical methods for assessing comparability, and the potential impact of observed differences in chemical and physicochemical properties.

Learning Objective : At the conclusion of this session, participants should be able to:

- Define comparability requirements for oligonucleotide therapeutics
- Discuss how to evaluate the impact of manufacturing changes on oligonucleotide therapeutics
- Discuss how to demonstrate comparability between generic and brand name oligonucleotide therapeutics

Track: Track 3: CMC

Session Chair(s)

Daniel Capaldi, PhD

Vice President, Analytical and Process Development
Ionis Pharmaceuticals, Inc, United States

Daniel received a B.Sc in chemistry and biology and a Ph. D in chemistry from King's College, London. In March 1996, Daniel joined Ionis Pharmaceuticals, Inc. as a process chemist where he spent four years working on process improvements in large-scale oligonucleotide synthesis. In his current position as Vice President, Analytical and Process Development, Daniel is contributing to the development of antisense therapeutics and has responsibility for a variety of process chemistry and CMC functions including supply chain

improvements and process optimization, analytical method development and validation, release and stability testing and impurity characterization

Fran Wincott, PhD

President
Wincott & Associates, LLC, United States

Dr. Fran Wincott is President of Wincott & Associates, LLC, a consulting firm focused on providing assistance in the area of oligonucleotide manufacturing and development. Prior to founding Wincott & Associates, Dr. Wincott was Vice President of Oligonucleotide Manufacturing & Development at Eyetech Pharmaceuticals, Inc. (2002-2005). Prior to joining Eyetech Pharmaceuticals, Dr. Wincott served as Senior Director of Manufacturing Operations at Ribozyme Pharmaceuticals, Inc. From 1989-1993 she worked as a scientist at Merck, Inc. and Cortech, Inc. Dr. Wincott received her B.A. in Chemistry at the University of Pennsylvania in 1984 and a Ph.D. in Organic Chemistry in 1989 from Yale University

Speaker(s)

Comparability in Generic Oligonucleotide Drug Development: Regulatory Considerations and Case Studies

Deyi Zhang, PhD, MS

Senior Chemist, Office of Generic Drugs
FDA, United States

Dr. Deyi Zhang is a senior chemist in the Office of Research and Standards (ORS), Office of Generic Drugs (OGD) at FDA specializing in complex active ingredients, including peptides, oligonucleotides and complex mixtures. He provides scientific inputs for regulatory policy and actively involves in pre-ANDA meetings, product-specific guidance development of such products, and manages related research activities. Dr. Zhang received his Ph.D. in organic chemistry from the University of Notre Dame. He had a two-year NIH postdoctoral fellowship training at the University of Pennsylvania before joining Eli Lilly in 2000. After 15 years in pharmaceutical industry, he joined FDA. He has over 50 publications and presentations.

Demonstrating Comparability of Oligonucleotide Therapeutics Following Manufacturing Changes

Carolyn Mazzitelli, PhD

Executive Director, Analytical Development and Quality Control
Ionis Pharmaceuticals, United States

Carolyn is an Executive Director in the Analytical Development and Quality Control department at Ionis Pharmaceuticals. She is responsible for the analytical activities for oligonucleotide therapeutics in all phases of development. Her expertise includes method development, validation, stability testing, establishing specifications, authoring and defending regulatory submissions, and supporting commercial supply chains. Prior to joining Ionis, she

worked at Dart NeuroScience, Gilead Sciences, and Vertex Pharmaceuticals. She received a B.S. in Chemistry from the University of North Carolina at Chapel Hill and Ph.D. in Chemistry from the University of Texas at Austin.

Panelist

Lawrence Perez, PhD

Senior Pharmaceutical Quality Assessor, CDER
FDA, United States

Lawrence Perez has been a CMC Reviewer for new drugs with the FDA since 2015 and in 2021 he became a Senior Pharmaceutical Quality Assessor for API New Drugs. Before that, Lawrence was a discovery chemist with Novartis Oncology. Lawrence has been active in the areas of pharmaceutical regulations and medicinal chemistry, with his most notable work being the discovery and development of the oncology drug Farydak®.

Panelist

Lubo Nechev, PhD

Chief CMC Officer
Alnylam Pharmaceuticals, United States

After Ribozyme Pharmaceuticals (RPI) and the Nucleic Acids Synthesis unit of Transgenomic, Inc., in March 2004 Dr. Nechev joined Alnylam Pharmaceuticals. In the last 18 years, he has led the development and implementation of the CMC strategy for siRNA therapeutics used in four approved products – ONPATTRO®, GIVLAARI®, OXLUMO® and Leqvio®(Novartis). ONPATTRO® is the first approved siRNA therapeutic and the first approved lipid nanoparticle (LNP) formulated oligonucleotide. GIVLAARI® is the first approved GalNAc-conjugated siRNA. Dr. Nechev received his Ph.D. degree in Organic Chemistry from St. Kl. Ohridski University, Sofia, Bulgaria and completed his post-doctoral training at Vanderbilt University, Nashville, Tennessee.

Panelist

Lori Troup

Director, Analytical Development
Novo Nordisk, United States

Lori is the Director of Analytical Development for Novo Nordisk Global Nucleic Acid Therapies, where her team is responsible for method development and validation activities for custom starting materials, drug substance and drug product, as well as drug substance characterization, drug substance and drug product release and stability studies, and CMC regulatory authoring. Prior to joining Novo Nordisk (formerly Dicerna Pharmaceuticals) in 2018, Lori spent 12 years at Agilent Technologies in a number of different roles within Quality Control, Analytical Development, and Analytical Services. Lori holds a B.S. in Chemistry from Abilene Christian University.

5:00 PM — 6:00 PM

Capital Terrace

Networking and Poster Reception

Day 2 Oct 29, 2024

8:00 AM — 8:30 AM Capital Terrace

Networking Breakfast

8:00 AM — 4:15 PM Capital Terrace

Registration

8:30 AM — 9:30 AM Presidential Ballroom

Welcome to Day Two and Session 5: Plenary Session: CRISPR Cures

CRISPR-Cas gene editing is unique among all genetic therapy modalities in relying on an RNA oligonucleotide to target a number of clinical-need-determined molecular genetic outcomes to any native gene. Definitive clinical evidence illustrates the curative potential of gene editing in the hemoglobinopathies, TTR amyloidosis, and hereditary angioedema. Further progress of this oligonucleotide-based therapeutic modality is hampered by lack of a platform approach to the design, development, and delivery of an on-demand, patient-specific gene editor at a time and a cost commensurate with benefit-risk considerations. Robust efforts to address these challenges are underway, with clinical trial evidence from the deployment of such platform approaches being critical to essential streamlining of the nonclinical and CMC path.

Track: General Session

Session Chair(s)

Scott Henry, PhD

Senior Vice President, Nonclinical Development
Ionis Pharmaceuticals, Inc., United States

Dr. Henry received a PhD in Biochemistry form North Dakota State University. He was a post-doc fellow at Parke Davis, Ann Arbor MI, depart. of toxicology. He joined Isis Pharmaceuticals, Inc. as a

Sr Scientist in toxicology. He helped characterized and studied mechanisms of various toxicities e.g. the effects of oligonucleotide treatment on clotting time prolongation, alternative complement pathway activation, proinflammatory effects in rodents, platelet alterations and the effects related to the accumulation of oligonucleotide in kidney. As VP of Non-Clinical Development he has participated in the development of ~8 different phosphorothioate oligodeoxynucleotides and 30+ different 2'-MOE modified phosphorothioate oligonucleotides.

Speaker(s)

Speaker

Fyodor Urnov, PhD

Scientific Director
Innovative Genomics Institute , United States

9:30 AM — 10:00 AM Capital Terrace

Refreshment and Networking Break

10:00 AM — 11:30 AM South American AB

Session 6 Track 1: Extra Hepatic Delivery – Clinical Experience in CNS

Oligonucleotides are an emerging class of drugs with potential for the treatment of a wide range of central nervous system conditions. To date, there are two approved oligos for brain diseases and a large number of ongoing clinical trials. This session will review recent advances in chemical modifications and delivery techniques of oligonucleotides in clinical testing that are intended to enhance brain exposure and clinical efficacy.

Learning Objective : At the conclusion of this session, participants should be able to:

- Compare various methods of delivery of oligos to the brain
- Understand the targets of new oligos for CNS diseases
- Evaluate the challenges and risks of clinical testing of oligos for brain diseases

Track: Track 1: Clinical

Session Chair(s)

Barry Ticho, MD, PhD

Chief Medical Officer

Stoke Therapeutics, United States

As Chief Medical Officer Dr. Ticho is responsible for Stoke's efforts to develop first-in-class RNA based disease-modifying medicines to treat severe genetic diseases. He is also co-founder and former CEO of Verve Therapeutics which is developing therapies to edit the genome and confer protection from cardiovascular disease. Prior to joining Stoke Barry was Head of R&D for Cardiovascular and Metabolic Diseases at Moderna Therapeutics. He was previously Head of External R&D Innovation for Cardiovascular and Metabolic Diseases at Pfizer and was Vice President of Clinical Development at Biogen. Barry obtained his MD and PhD degrees from the University of Chicago. He was on staff at Harvard Medical School and Massachusetts General Hospital

Amy Kao, MD

Medical Officer, Division of Neurology 2, OND, CDER
FDA, United States

Dr. Amy Kao is a clinical reviewer in the Division of Neurology 2 in the Office of Neuroscience at the FDA (Office of New Drugs/Center for Drug Evaluation and Research) and a Diplomate of the American Board of Pediatrics and American Board of Psychiatry and Neurology. She earned her medical degree from Northwestern University and completed residency and fellowship training at the Children's Hospital of Philadelphia/Hospital of the University of Pennsylvania. Areas of interest include oligonucleotide therapies in developmental and epileptic encephalopathies.

Speaker(s)

Targeting Central Nervous System Disease with a Conjugated siRNA Platform

Andrew H Ahn, MD, PhD

SVP Clinical Research
Alnylam Pharmaceuticals, United States

Andrew Ahn, MD PhD is Senior Vice President of Clinical Research and leads a clinical team focused on the CNS-directed portfolio at Alnylam Pharmaceuticals. With training as a neurologist and neuroscientist, in prior roles he led clinical and scientific drug development teams at Lilly Research Laboratories and Teva Pharmaceuticals, featuring both small molecule and antibody programs for a range of neurology, psychiatry, and pain indications. Prior to working in industry, he was an NIH-funded investigator at the University of Florida and the University of California San Francisco.

Transferrin Receptor-Mediated Brain Delivery of Enzymes and Oligonucleotides Using Transport Vehicle Technology

Kirk Henne, PhD

Senior Vice President, Development Sciences

Denali Therapeutics, United States

Kirk serves as Head of Development Sciences at Denali Therapeutics. In this role he supports Pharmacokinetics, Quantitative Clinical Pharmacology, Safety Assessment, Multi-omics, and Bioanalytical teams to advance Denali's portfolio. Prior to Denali, Kirk was Director of DMPK and Project Team Lead at Assembly Biosciences, Principal Scientist and Group Leader at Amgen, and Principal Scientist at Pfizer. He has contributed to successful candidate identification, IND-enabling, and early clinical development activities for more than 20 molecules representing multiple modalities across therapeutic areas. Kirk has authored/co-authored >30 peer-reviewed publications. He obtained his Ph.D. in Medicinal Chemistry from the University of Washington.

10:00 AM — 11:30 AM Presidential Ballroom

Session 6 Track 2: Off Target Safety Assessment

Hybridization-dependent off-target effects are a potential safety concern for both oligonucleotide and gene editing therapeutics. This session will start with updated recommendations from Industry on identification, verification and risk assessment of off-target sites for oligonucleotides. This will be followed by a presentation with concrete examples illustrating how the recommendations could be used. The final presentations will focus on assessment of off-target editing for in vivo gene editing approaches.

Learning Objective : At the conclusion of this session, participants should be able to:

- Describe the different steps in the recommended approach to identify and evaluate potential off-target effects
- Compare and contrast off-target assessments for oligonucleotides and gene editing applications
- Discuss specific considerations for different oligonucleotide and gene editing applications, classes, and delivery systems

Track: Track 2: Nonclinical

Session Chair(s)

Patrik Andersson, PhD

Senior Director, RNA Therapeutics Safety
AstraZeneca R&D, Sweden

I received my PhD in toxicology from Karolinska Institutet, Stockholm in 2003. Joined AstraZeneca R&D in Gothenburg in 2004 as a toxicologist supporting Cardiovascular and Metabolic drug projects in the Discovery phase. Since 2012 focusing on nucleotide drugs, including oligonucleotides and mRNA therapeutics. Currently leading the preclinical safety activities for oligonucleotides and targeted drug delivery in AstraZeneca as well as different mRNA applications.

James Wild, PhD, MS

Pharmacologist, CDER
FDA, United States

James Wild received a MS and PhD in Pharmacology and Toxicology at the University of California, Davis. Areas of study included idiopathic pulmonary fibrosis and characterization of a novel, ryanodine-sensitive receptor in the lung. Subsequently he completed two postdoctoral fellowships specializing in asthma research. In later career positions, James conducted discovery pulmonary disease research at EpiGenesis Pharmaceuticals, Schering-Plough Research Institute, and Johnson and Johnson PRDUS. Currently, James is a Senior Pharmacologist at the FDA supporting the Division of Anti-Infectives. Areas of interest include anti-infective drugs, oligonucleotide therapies, pulmonary research, and drug regulation.

Speaker(s)

Discerning the Off-target Effects of RNase H-Dependent Antisense Oligonucleotides by Sequence Analysis and Transcriptomics

Peter Hagedorn, PhD, MSc

Scientific Director, Head of Bioinformatics
Contera Pharma, Denmark

Peter Hagedorn is a Scientific Director and Head of Bioinformatics at Contera Pharma. Peter has worked with drug design and development of nucleic acid therapeutics for more than 15 years. He holds a master's degree in Biophysics from the Niels Bohr Institute, University of Copenhagen, Denmark, and a PhD in Molecular Biology and Bioinformatics from the University of Southern Denmark.

Assessing the Potential for Off-target Editing with in Vivo Liver-directed Base Editing Therapies

Joseph Bidenkapp, PhD

Vice President, Editing Development
Verve Therapeutics, United States

Joe Biedenkapp is Vice President of Editing Development at Verve Therapeutics, a clinical-stage genetic medicines company pioneering a new approach to the care of cardiovascular disease, potentially transforming treatment from chronic management to single-course gene editing medicines. In this role, Joe leads a team of scientists and computational biologists developing off-target data packages to support regulatory submissions for Verve's gene editing programs. Prior to joining Verve, Joe served in numerous cross-functional leadership positions at Shape Therapeutics, bluebird bio and Dyax, working across early and late-stage drug development, basic and clinical research, medical affairs, alliance management and product commercialization.

Overview of Current Genomic Analytical Tools to Enable Advancement of Investigational In Vivo Genome Editing Products into Clinical Studies

Jessica Lynn Seitzer

Vice President, Head of Genomic Operations
Intellia Therapuetics, United States

Jessica Seitzer is the Vice President of Genomic Operations at Intellia Therapeutics with over 20 years of industry experience in the development of oligonucleotide therapies as well as cell and gene therapies. She joined Intellia during the beginning of company's inception where she built out their genomics and high throughput screening core with a focus on next generation sequencing and genomics infrastructure. Jessica has supported genomics analysis for all Intellia's Development programs including their clinical programs for Transthyretin Amyloidosis (NTLA-2001) and Hereditary Angioedema (NTLA-2002). More recently Jessica has been focusing on genomics strategy to support Intellia's regulatory and clinical development programs.

10:00 AM — 11:30 AM Federal AB

Session 6 Track 3: CMC Considerations in Development of mRNA-based Therapeutics

The breadth of mRNA-based vaccines in clinical and commercial development has continued to mature beyond SARS-CoV-2 vaccines, with the platform nature of mRNA supporting common CMC principles between products. As the landscape of mRNA-based therapeutics in development expands and evolves, thoughtfully adapting principles from mRNA-based vaccines to meet the unique CMC requirements of therapeutic development across diverse therapeutic areas will be needed. This session will include industrial and regulatory perspectives on CMC challenges specific to mRNA-based therapeutics and opportunities to efficiently support their development.

Learning Objective :

- Compare differences in technical requirements and regulatory expectations between vaccines and therapeutics which warrant differentiated development strategies
- Discuss how platform principles which have accelerated the development of mRNA-based vaccines can be adapted to the development of mRNA-based therapeutics

Track: Track 3: CMC

Session Chair(s)

Brian Doyle

Senior Director, Technical Development
Moderna, United States

Brian Doyle has over 15 years of experience in technical and CMC development for vaccines and therapeutics. Since joining Moderna in 2019, Brian has led organizations focused on late-stage and commercial process development and CMC technical writing, with a particular interest at the interface between process and regulatory science related to platform-based approaches. Prior to joining Moderna, Brian held roles in roles in cell culture and fermentation process development at Gilead Sciences and Merck. Brian holds a B.S. in Chemical-Biological Engineering from the Massachusetts Institute of Technology.

Speaker(s)

Expanding Horizons: Navigating CMC Challenges and Opportunities for mRNA Therapeutics Beyond Vaccines

Xin (Jack) Yu, PhD

Vice President, CLinical Development
Moderna, United States

Advancing mRNA Vaccine Specifications to Support mRNA Therapeutics

Eric A Levenson, PhD, MS

Biological Reviewer
FDA, United States

Eric is a biological reviewer in the Office of Gene Therapy (OGT) / CBER/ FDA. He reviews a wide range of direct acting gene therapy products including DNA or RNA therapeutics delivered by nanoparticles carriers, including lipid nanoparticles. An interdisciplinary scientist, he has degrees in biochemistry (M.S., Ph.D. University of Delaware) with extensive training in virology, immunology, and chemical biology. His dissertation included developing novel polymer-oligonucleotide conjugates to study innate cellular response. Postdoctoral studies included whole genome siRNA and miRNA screens to find host gene targets of noroviral infection. Prior to joining OGT, Eric was a reviewer of allergenic products and studied host antiviral response.

Panelists

Andreas Kuhn, PhD

Senior Vice President RNA Biochemistry & CMC Development
Biontech SE, Germany

Andreas Kuhn, Senior Vice President RNA Biochemistry & CMC Development, has worked in the field of RNA biochemistry and molecular biology for about 30 years. His work on RNA-based immunotherapies began in 2007 with Ugur Sahin and Andreas joined BioNTech SE shortly after its founding in 2008. His main focus is expanding BioNTech's proprietary technologies to increase the efficacy of RNA immunotherapies and to optimize GMP-compatible manufacturing processes for RNA. He has co-authored several publications and patents ranging from basic research on RNA to its application as a therapeutic agent and vaccine.

Panelists

Silke Schüle, PhD

Scientific Assessor
Paul-Ehrlich-Institute, Federal Agency of Vaccines and Biomedicines, Germany

Dr. Schüle is a Senior Assessor for Advanced Therapy Medicinal Products (ATMPs, gene and cell therapy as well as tissue engineering products) and the respective regulatory procedures focusing on quality issues. This includes the experience in the evaluation of marketing authorization applications for ATMPs on the EU level. Dr. Schüle started her career in 2006, assessing ATMPs at the Paul-Ehrlich-Institute. During this period she participated in different EMA drafting groups developing ATMP specific guidelines. Since 2022 Dr Schüle is a permanent member of the EMA Quality Innovation Group (QIG).

11:30 AM — 12:45 PM Congressional/Senate Rms

Networking Luncheon featuring Roundtable Discussions

12:45 PM — 2:15 PM Presidential Ballroom

Session 7 Track 1 and 2: Gene Editing

This will be a joint clinical and non-clinical session on gene editing. The session will begin with an overview of the FDA guidance on human genome editing to provide an overview of the recommendations for sponsors developing such products. The subsequent talks will be from sponsors actively working in this space and will include two presentations on nonclinical development topics and one presentation on clinical development.

Learning Objective : At the conclusion of this session, participants should be able to:

- Understand the latest guidance from FDA on the development of gene editing products
- Gain insight into unique nonclinical considerations for the development of gene editing products
- Understand how sponsors are approaching clinical development of gene editing products

Track: Track 1 and 2: Clinical/Nonclinical

Session Chair(s)

Scott Vafai, MD

Vice President, Translational Medicine
Verve Therapeutics, United States

David Cantu, PhD

Biological Reviewer, CBER
FDA, United States

Speaker(s)

The Modularity of an In Vivo CRISPR-based Therapeutic Platform

Jonathan Phillips, PhD

Vice President, Pharmacology & Toxicology
Intellia Therapeutics, United States

Dr. Jonathan Phillips leads nonclinical strategy as Vice President of Pharmacology & Toxicology at Intellia Therapeutics in Cambridge, MA. His experience developing gene editing therapies began at Vertex where he co-authored first-in-human applications for CTX001 (CASGEVY), in partnership with CRISPR Therapeutics. He also built and led several translational and investigative safety teams during his time with Boehringer Ingelheim. Prior to industry, Dr. Phillips was a Bioastronautics Fellow at NASA Ames Research Center in Mountain View, CA investigating mechanobiology in space travel environments. He holds a PhD in cell biology from UMass-Worcester and has dozens of peer reviewed publications, book chapters, and invited presentations.

Evaluation of Reni-cel, an Investigational AsCas12a Gene-edited Autologous Cell Therapy, in Patients with Severe Sickle Cell Disease Treated in the TUBY Trial

Olubunmi Afonja, MD, MBA

Vice President, Clinical Development
Editas Medicine, United States

Dr. Olubunmi Afonja is Vice President of Clinical Development at Editas Medicine, Cambridge, MA. She joined Editas in 2021 as the medical lead for an investigational gene therapy medicine for hemoglobinopathies. Prior to joining industry, she spent 13 years at NYU Lagone, NY, serving as a clinical attending and faculty in the pediatric hem/onc program. Thereafter, she joined Bayer where she spent ~ 13 years in various roles within medical affairs and clinical development. Dr. Afonja received her MBBS at the University of Ibadan , completed a pediatric residency at SUNY, Brooklyn, and pediatric hem/onc fellowship at NYU College of Medicine. Dr. Afonja obtained her MBA from GWU, and is first and co-author on several peer-reviewed publication

12:45 PM — 2:15 PM Federal AB

Session 7 Track 3: Challenges Around Oligonucleotides Control Strategies

Close to a decade ago, pioneering papers were written on how to set up oligonucleotide control strategies, including proposed impurity grouping. Since then, industry and regulators have expanded their knowledge and their experience in this area. At the same time, the complexity of the oligonucleotide landscape is increasing, in particular because of the

development of conjugates and new modifications. Because of the reached level of maturity, oligonucleotides are in scope of new or to-be-revised guidelines. The current session aims at exchanging on experiences and challenges pertaining to oligonucleotide control strategies in general and in view of the changing guideline landscape.

Learning Objective : At the conclusion of this session, participants should be able to:

- Understand the current trends pertaining to oligonucleotide control strategies
- Understand the current challenges and how they could influence the content of new guidelines

Track: Track 3: CMC

Session Chair(s)

Christian Wetter, PhD

Senior Regulatory Portfolio Director
Roche, Switzerland

Christian Wetter is an organic chemist and holds a Ph.D. from the University of Marburg. He started his professional career at Roche in 2004 in Chemical Development before moving to Novartis to Regulatory CMC in 2009. In 2020 he joined Roche again and currently acts as a Senior Regulatory Portfolio Director. Christian has worked on small molecule, peptide, oligonucleotide and device development projects in various phases of development and commercial lifecycle. He is part of the European Pharma Oligonucleotide Consortium (EPOC) and is currently leading its regulatory subteam.

Katherine Windsor, PhD

Senior Pharmaceutical Quality Assessor, CDER
Food and Drug Administration, United States

Dr. Katherine Windsor is a Senior Pharmaceutical Quality Assessor (Drug Substance Lead) in the Office of Pharmaceutical Quality within the Center for Drug Evaluation and Research (CDER) at FDA. Katherine has 10 years of experience assessing CMC aspects of drugs in several therapeutic areas, particularly anti-infectives and antivirals, and a wide variety of APIs, including oligonucleotides, peptides, antibody-drug conjugates, and small molecules. Katherine conducted postdoctoral research at Vanderbilt University and obtained her Ph.D. in Organic Chemistry from the University of Wisconsin-Madison and her B.S. in Chemistry from the University of Notre Dame.

Speaker(s)

Senior Pharmaceutical Quality Assessor (SPQA), Division of New Drug API, Office of New Drug Products Katharine Duncan, PhD

Senior Pharmaceutical Quality Assessor (SPQA), Office of Product Quality Assessm
FDA, United States

Katharine Duncan is a Senior Pharmaceutical Quality Assessor with the Office of Product Quality Assessment III within the Office of Pharmaceutical Quality at the Food and Drug Administration. Dr. Duncan joined the FDA in 2019

after several years working in small molecule drug discovery at a pharmaceutical company in San Diego. Her Ph.D. research was conducted in the laboratory of Dr. Dale Boger at the Scripps Research Institute in La Jolla, California. She received her undergraduate degree in chemistry from Amherst College in Amherst, Massachusetts.

Evaluating the Requirements for Multiple Identity and Purity Methods

Lori Troup

Director, Analytical Development
Novo Nordisk, United States

Lori is the Director of Analytical Development for Novo Nordisk Global Nucleic Acid Therapies, where her team is responsible for method development and validation activities for custom starting materials, drug substance and drug product, as well as drug substance characterization, drug substance and drug product release and stability studies, and CMC regulatory authoring. Prior to joining Novo Nordisk (formerly Dicerna Pharmaceuticals) in 2018, Lori spent 12 years at Agilent Technologies in a number of different roles within Quality Control, Analytical Development, and Analytical Services. Lori holds a B.S. in Chemistry from Abilene Christian University.

Speaker

Carolyn Mazzitelli, PhD

Executive Director, Analytical Development and Quality Control
Ionis Pharmaceuticals, United States

Carolyn is an Executive Director in the Analytical Development and Quality Control department at Ionis Pharmaceuticals. She is responsible for the analytical activities for oligonucleotide therapeutics in all phases of development. Her expertise includes method development, validation, stability testing, establishing specifications, authoring and defending regulatory submissions, and supporting commercial supply chains. Prior to joining Ionis, she worked at Dart NeuroScience, Gilead Sciences, and Vertex Pharmaceuticals. She received a B.S. in Chemistry from the University of North Carolina at Chapel Hill and Ph.D. in Chemistry from the University of Texas at Austin.

Speaker

Lubo Nechev, PhD

Chief CMC Officer
Alnylam Pharmaceuticals, United States

After Ribozyme Pharmaceuticals (RPI) and the Nucleic Acids Synthesis unit of Transgenomic, Inc., in March 2004 Dr. Nechev joined Alnylam Pharmaceuticals. In the last 18 years, he has led the development and implementation of the CMC strategy for siRNA therapeutics used in four approved products – ONPATTRO®, GIVLAARI®, OXLUMO® and Leqvio®(Novartis). ONPATTRO® is the first approved siRNA therapeutic and the first approved lipid nanoparticle (LNP) formulated oligonucleotide. GIVLAARI® is the first approved GalNAc-conjugated siRNA. Dr. Nechev received his Ph.D. degree in Organic Chemistry from St. Kl. Ohridski University, Sofia, Bulgaria and completed his post-doctoral training at Vanderbilt University, Nashville, Tennessee.

2:15 PM — 2:45 PM Capital Terrace

Refreshment and Networking Break

2:45 PM — 4:15 PM Presidential Ballroom

Session 8: Hot Topics

Session 8: Hot Topics

Track: General Session

Session Chair(s)

Emily Place, PhD, MPH

Senior Consultant
Aclairo Pharmaceutical Development Group, United States

Emily is a co-chair of FDA's Pharmacology/Toxicology Oligonucleotide Subcommittee. She received a BS in Biology from State University of New York, a PhD in Cell Biology from University of Connecticut, and her MPH in Epidemiology at University of California at Berkeley. She was an Associate Investigator at San Francisco VA Medical Center where her research focused on miRNA dysregulation in prostate cancer. She completed post doctoral research at Stanford School of Medicine on miRNAs in NHL and was a Cancer Prevention Fellow at the National Cancer Institute in the Laboratory of Human Carcinogenesis where her research involved examining the role of extracellular plant small RNA communication in human carcinogenesis.

Ronald Wange, PhD

Associate Director for Pharm/Tox OND
FDA, United States

Dr. Wange is an Associate Director for Pharmacology & Toxicology within the Office of New Drugs in CDER at the FDA, and has over 19 years of experience reviewing small molecule drugs, biotherapeutic proteins and oligonucleotide-based therapeutics. He is a founding member of OND's Pharmacology/Toxicology Oligonucleotide Subcommittee, which considers issues specifically related to the safety review of oligonucleotide-based therapeutics. In addition, he was the primary author of the recently published draft guidance on Nonclinical Testing of Individualized ASOs for Severely Debilitating or Life-Threatening Diseases. Prior to joining FDA, he was the head of the T-lymphocyte Signaling Unit at the National Institute on Aging at the NIH.

Speaker(s)

Presentation Title: Harnessing RNA Exon Editing to Rewrite the Underlying Causes of Genetic Diseases

Robert Bell, PhD

CSO
Ascidian, United States

siRNA Manufacturing with Engineered Enzymes

Stefan Lutz, PhD

SVP, Head of Research
Codexis, Inc. , United States

Dr. Stefan Lutz joined Codexis in 2020 as the Senior Vice President of Research to lead the company's research team advancing the technology platform, as well as the discovery and engineering of novel enzymes for the Life Sciences and Pharma Manufacturing markets. Prior to his arrival in Redwood City, he was a Professor and Chair of the Chemistry Department at Emory University, Atlanta GA, having joined the university in 2002 and ascending to Chemistry Department Chair in 2014. He received a B.Sc. in chemistry/chemical engineering from the Zurich University of Applied Sciences, Switzerland, an M.Sc. in Biotechnology from the University of Teesside UK and a Ph.D. in chemistry from the University of Florida.

4:15 PM — 5:15 PM Presidential Ballroom

Oligonucleotide Safety Working Group (OSWG) – Open Meeting

Oligonucleotide Safety Working Group (OSWG) – Open Meeting

Session Chair(s)

Jeffrey Foy, PhD

Senior VP, Toxicology
PepGen Inc., United States

Day 3 Oct 30, 2024

7:30 AM — 8:00 AM Capital Terrace

Networking Breakfast

7:30 AM — 12:40 PM

Capital Terrace

Registration

8:00 AM — 9:15 AM

South American AB

Session 9 Track 1: Advantages & Challenges of Early Phase Clinical Studies with Oligos

Phase 1 and 2 clinical trials of oligonucleotide therapeutics offer valuable opportunities as well as important challenges. In this session we will explore the unique features of the design and execution of early phase oligo trials, including: study duration and the operational challenges posed by long-acting drugs for rare diseases; gaining early clinical insights into potency and safety and the value of non-clinical data in informing study design; challenges of predicting and measuring drug accumulation; the importance of engagement with healthy participants and patients to support trial success.

Learning Objective : At the conclusion of this session, participants should be able to:

- Recognize the opportunities and challenges of early phase clinical trials with oligonucleotides
- Formulate the designs of their own clinical programs to maximize those opportunities and address the challenges
- Interpret the findings of early phase oligonucleotide trials
- Identify the challenges associated with long oligo pharmacodynamic half-life and predicting optimal dose selection

Track: Track 1: Clinical

Session Chair(s)

Dan Swerdlow, MD, PhD

Senior Director, Early Clinical Development
GSK, United Kingdom

Dan trained on the MD PhD programme at UCL, completing a PhD in genetic epidemiology. Thereafter he worked in London as a clinical academic in internal medicine and clinical pharmacology. In his academic research he led international human genetics consortia for drug target discovery in cardiometabolic disease, with findings published in the Lancet and Nature Communications. Before joining GSK in 2022, Dan led oligonucleotide clinical development programmes and a computational genomics group at Silence Therapeutics, prior to which he worked in AI-enabled translational and precision medicine at BenevolentAI. At GSK, Dan is a clinical lead on translational and early clinical development projects. He is an honorary associate professor at UCL.

Sydney Stern, PhD, MS

Pharmacokineticist
FDA, United States

Dr. Sydney Stern is a clinical pharmacology reviewer in the Division of Translational and Precision Medicine (DTPM) in the Office of Clinical Pharmacology (OCP) at the FDA. She is a primary reviewer for oligonucleotide programs and rare diseases in OCP and she has extensive experience with in vitro/in vivo extrapolation. Dr. Stern has led several data projects in the rare disease space and research projects investigating strategies for selecting safe starting doses in oligonucleotide-based therapeutic. Her research interests are focused on the pharmacology of synthetic oligonucleotides and rare diseases. She received her Master of Science in Clinical Research and a Ph.D. in Pharmaceutical Sciences at University of Maryland Baltimore.

Speaker(s)

Speaker

Malcolm James Boyce

Managing & Clinical Director
Hammersmith Medicines Research, United Kingdom

Speaker

Keyvan Yousefi, PharmD, PhD

Associate Director of Clinical Development
Ionis Pharmaceuticals, United States

Keyvan Yousefi is an Associate Director in Clinical Development at Ionis Pharmaceuticals. Keyvan holds a Doctor of Pharmacy degree and also completed a PhD in Pharmacology at the University of Miami-Miller School of Medicine. After several years of clinical pharmacy practice and translational research, Keyvan transitioned into clinical research space in 2020 as Clinical Scientist at Longeveron Inc. Keyvan Joined Ionis in 2022. He has extensive experience with executing clinical trials as clinical scientist and medical monitor in various therapeutic areas including cardiovascular, cardiorenal, hematology, and metabolic disease.

8:00 AM — 9:15 AM Presidential Ballroom

Session 9 Track 2: Extra/Non-Hepatic Delivery

This session will describe strategies for targeting extra-hepatic organs and will feature data from sponsor programs. Delivery technologies, nonclinical study design considerations, and pharmacology, ADME, and toxicology data will be discussed.

Learning Objective : At the conclusion of this session, participants should be able to:

- Recognize current efforts to deliver oligonucleotide-based products to cells or organs outside of the liver
- Have a greater understanding of the challenges associated with delivering oligos to muscle, lung, and brain

Track: Track 2: Nonclinical

Session Chair(s)

Jeffrey Foy, PhD

Senior VP, Toxicology
PepGen Inc., United States

Sree Rayavarapu, DVM, PhD

Toxicologist
FDA, United States

Speaker(s)

Development of a Novel Muscle-targeted Antibody Oligonucleotide Conjugate for the Treatment of Myotonic Dystrophy Type 1: Toxicology and Regulatory Approaches and Considerations

Eileen Blasi, MS, MSc

Senior Director of Toxicology
Avidity Biosciences, United States

Eileen Blasi, Sr Director, Avidity Biosciences, San Diego, CA: Eileen leads toxicology and regulatory strategy of multiple development programs in rare disease using antibody oligonucleotide conjugate platform. Prior to Avidity, Eileen was at Pfizer, Pharmacia & Upjohn, and Searle where she held various positions in toxicology and regulatory strategy, safety pharmacology, and cardiovascular pharmacology. Over 20+ yrs, Eileen has worked in cardiovascular, oncology and rare disease areas covering small molecule, antibodies, ADCs, and oligonucleotide modalities. Eileen received undergraduate degree from Ithaca College and graduate degrees from Miami University and University of Illinois. Eileen received her DABT in 2013.

Nonclinical Development of Inhaled Oligonucleotides: Nothing Good Comes Easily

Jessica Grieves, DVM, PhD

Director, Pathology and Nonclinical Development

Ionis Pharmaceuticals, United States

Jessica Grieves is a toxicologic pathologist at Ionis Pharmaceuticals where she is involved with the nonclinical development of ASOs, siRNAs, and gene editing modalities with a focus on pulmonary, neurology, and cardiometabolic therapeutic areas. Prior to Ionis, Jessica was a toxicologic pathologist at Takeda Pharmaceuticals.

Speaker

Vignesh Narayan Hariharan, PhD

Instructor
University of Massachutes Medical School, United States

Vignesh (Viggy) is a molecular biologist with expertise in siRNA discovery and pre-clinical pharmacology from the Khvorova Lab at the University of Massachusetts Chan Medical School. The focus of his work is the exploration of chemical space of siRNA conjugates for the purpose of characterization and improvement of extra-hepatic delivery. His contributions include optimization of siRNA chemistry for several clinically relevant organs, modulation of siRNA potency through backbone chemical modifications and the discovery of clinical quality lead sequences for novel siRNA targets. He is currently Instructor at UMass Chan Medical School and Director of Biology at Comanche Biopharma Corp.

8:00 AM — 9:15 AM Federal AB

Session 9 Track 3: Innovative Manufacturing Approaches and Regulatory Implications

Continuous improvement in manufacturing of nucleic acid-based modalities requires innovative approaches, with the potential for introduction of new challenges, including the regulatory implications. This session will feature some of the recent innovative manufacturing approaches, along with a panel discussion to highlight the current regulatory landscape and identify prospects in closing potential gaps in understanding.

Learning Objective : At the conclusion of this session, participants should be able to:

- Understand the critical risk factors associated with innovative manufacturing approaches
- Recognize and identify the relevant CMC challenges during the development stages
- Learn about developmental and regulatory considerations in mitigating the CMC risks

Track: Track 3: CMC

Session Chair(s)

Ramin Darvari, PhD, MS

Research Fellow
Pfizer Inc., United States

Ramin Darvari is a Research Fellow in Drug Product Design & Development group at Pfizer; contributing to the strategic and tactical planning for evaluation of external delivery technologies and internal delivery formulation & process development, with a focus on collaborative partner engagement. Ramin has lent his expertise in particle engineering and matrix-based drug delivery systems to evaluation and development of variety of applications, including his role as the drug product project lead for Pfizer-BioNTech Covid-19 Vaccine.

Rohit Tiwari, PhD

Director, Global Regulatory Affairs-CMC
Eli Lilly & Company, United States

Rohit is a Director at Eli Lilly & Company and is responsible for developing CMC regulatory strategies for oligonucleotides and oligonucleotide conjugates. Previously, he was a senior CMC reviewer at FDA for 5 years where he reviewed small molecules, oligonucleotides and ADCs. Rohit received his Ph.D. in Medicinal Chemistry from The Ohio State University working on the design and syntheses of nucleoside analogues. This was followed by a post-doctoral work at University of Notre Dame and ORISE research fellowship at FDA where he learned about oligonucleotide chemistry.

Speaker(s)

Solvent and Reagent Reuse in Solid Phase Oligonucleotide Synthesis

Martin "Marty" Johnson, PhD

Vice President, Engineering
Eli Lilly, United States

Martin D. Johnson works for Eli Lilly and Company in Synthetic Molecule Design and Development. He received his dual doctorate in chemical engineering and environmental engineering from the University of Michigan in 2000. Dr. Johnson was awarded the 2016 ACS Award for Affordable Green Chemistry for work with continuous aerobic oxidations, the 2016 AIChE Award for Outstanding Contribution to QbD for Drug Substance for implementation of continuous processes, and the 2021 AIChE CRE Practice Award for design and implementation of continuous reactors in the pharmaceutical industry. Recently his group has been applying chemical engineering concepts to improve oligonucleotide syntheses.

A Ligation Platform Approach to Enzymatic Oligonucleotide Assembly

Doug Fuerst, PhD

Senior Director Drug Substance Development
GSK, United States

Doug Fuerst is a Senior Director in Drug Substance Development at GSK. Doug leads the Enzyme Engineering and Biocatalysis department responsible for the discovery and development of novel enzyme-based processes for pharmaceutical manufacture. Doug holds a Ph.D. in Organic Chemistry from Yale University and has completed

postdoctoral studies in organocatalysis at Harvard University. His recent work focuses on leading internal oligonucleotide strategy drug substance efforts spanning enzymatic, liquid phase, and solid phase synthesis approaches, with an emphasis on developing novel convergent enzyme-catalyzed approaches for oligonucleotide manufacture.

Revolutionizing Nucleic Acid Manufacturing: Showcasing a Cutting-Edge Platform for Fully synthetic Cell-free Production of Nucleic Acids

Joe Russo

Senior Principal Scientist/Group leader
Pfizer, Inc. , United States

Speaker

René Thürmer, PhD

Quality Assessor
Federal Institute for Drugs and Medical Devices, Germany

Dr. René Thürmer received his diploma in chemistry and his Ph.D. in biochemistry from the University of Tübingen. He joined the BfArM (Federal Institute for Drugs and Medical Devices, Bonn, Germany) in 2000. He currently serves as a CMC reviewer and is Deputy Head of the Unit Pharmaceutical Biotechnology. His experience is in the field of formulation, manufacture and control of medicinal products, in particular in the field of peptides, proteins, liposomes, sustained release polymer drug products, depot formulations, polymer-conjugated drug products, natural and synthetic surfactants, nanomedicine and others. His special focus lies on oligonucleotide preparations.

Speaker

Paresma (Pinky) Patel, PhD

Division Director, Office of Product Quality Assessment III
FDA, United States

Paresma (Pinky) Patel, Ph.D. is a Division Director in CDER's Office of Pharmaceutical Quality, Office of Product Quality Assessment III. In this role, she leads groups responsible for the evaluation of chemistry, manufacturing, and controls (CMC) information with a focus on drug substance quality throughout clinical development to submission of marketing applications. She served as a Branch Chief, supporting the oncology and anti-viral clinical divisions, prior to transitioning to her current role. Prior to FDA, she worked as a medicinal chemist at the National Institutes of Health. Dr. Patel completed her Ph.D. in organic chemistry at The Scripps Research Institute and a postdoctoral fellowship at the California Institute of Technology.

9:25 AM — 10:40 AM South American AB

Session 10 Track 1: Clinical Pharmacology of Oligonucleotides

This session will explore the various clinical pharmacology aspects that are primarily unique to RNA-oligonucleotides. Topics will include: regulatory considerations regarding clinical pharmacology studies, transitioning to first-in-human studies, and the importance of pharmacodynamic biomarkers. Overall, this session will provide various viewpoints on the unique challenges encountered in the clinical development of oligonucleotides.

Learning Objective : At the conclusion of this session, participants should be able to:

- Distinguish between EMA and FDA Clinical Pharmacology Guidelines in relation to oligonucleotides
- Recognize the various challenges in the development of pharmacodynamic biomarkers in clinical studies
- Appraise the clinical pharmacology issues unique to oligonucleotides compared to small molecules and biologics

Track: Track 1: Clinical

Session Chair(s)

Hobart Rogers, PharmD, PhD

Pharmacologist
FDA, United States

Dr. Bart Rogers is a reviewer in the Division of Translational and Precision Medicine in the Office of Clinical Pharmacology (OCP) at the FDA. Dr. Rogers also serves as an active duty officer with the United States Public Health Service. He serves as the lead for OCPs review of all synthetic oligonucleotides. His research interests are focused on the pharmacology of synthetic oligonucleotides, orphan disease drug development, and pharmacogenomics. Dr. Rogers completed his Pharm.D. degree from the University of Maryland, School of Pharmacy in 2004. He went on to obtain his Ph.D. in Clinical Pharmaceutical Sciences with a focus on cardiovascular pharmacogenomics from the same institution.

Mark Rogge

Adjunct Professor
University of Florida, United States

Speaker(s)

An Overview of EMA's Clinical Pharmacology Assessment of Oligonucleotides

Carolien Versantvoort, PhD

Senior Clinical Pharmacokinetics Assessor
Medicines Evaluation Board, Netherlands

Bio – Carolien Versantvoort I have over 20 years experience as senior clinical pharmacology assessor and scientific expert at Medicines Evaluation Board in the Netherlands for new medicines and generics. Since 2014, I am a member of the Pharmacokinetic Working Party / Product Specific Bioequivalence Guidance Drafting Group at EMA, currently as Chair. In addition, I am member of the leadership team for the Clinical Pharmacology Special Interest Area group at EMA's Methodology Working Party. Further, I was member of the ICH-M12 team as EU expert on the harmonisation of the drug interaction guideline.

Application of Model Informed Drug Development in Clinical Pharmacology for Oligonucleotides

Xiao Hu, PhD, MSc

Vice President, DMPK and Clinical Pharmacology
Wave Life Sciences, United States

Dr. Xiao Shelley Hu, Ph.D., is a VP at Wave Life Sciences, leading the DMPK and Clinical Pharmacology department. Her group is responsible for ADME and PK/PD studies and analyses in preclinical and clinical stages in various disease areas. Prior to joining Wave Life Sciences, she was a Director at Akebia Therapeutics, leading the Bioanalytical and Clinical Pharmacology. Shelley joined Akebia from Biogen, where she supported DMPK, Clinical Pharmacology, and Pharmacometrics for small and large molecules from discovery to post-market in Neurology, Rheumatology, Oncology, and Immunology. Shelley received her Ph.D. in Pharmaceutical Sciences from the Ohio State University, MS from Chinese Academy of Sciences, and BS from Peking University.

9:25 AM — 10:40 AM Presidential Ballroom

Session 10 Track 2: Non-Clinical Safety Assessment of Oligonucleotides

This session will provide updates on two areas of regulated nonclinical safety assessment (genotoxicity and developmental and reproductive toxicology (DART) evaluation) and experience of characterizing these hazards for therapeutic oligonucleotides (ONTs), as well as a novel application of Artificial Intelligence (AI) to improve the safety of this modality.

Learning Objective :

- Describe the typical approaches taken for evaluating the genotoxicity and carcinogenicity of therapeutic oligonucleotides
- Explain the characteristics of therapeutic oligonucleotides that warrant consideration for whether typical small molecule approaches to Developmental and Reproductive Toxicology (DART) evaluation are appropriate
- Describe the structural determinants of therapeutic oligonucleotides that are amenable to employing AI/ML models

Track: Track 2: Nonclinical

Session Chair(s)

Joel D Parry, PhD

Director, Nonclinical Safety Project Specialist
GlaxoSmithKline R&D, United Kingdom

I have worked in nonclinical safety within GSK R&D for 30+ years, conducting/directing mechanistic work for 20 of those. Over the last 15 years I have provided project toxicologist support, working on a range of modalities, although mainly oligonucleotides, both in discovery and development. In 2023 I joined the Nonclinical Safety Project Specialists department and lead a matrix team, accountable for implementation of a safety screening cascade for GSK's internal oligonucleotide discovery programs. Since being involved in oligonucleotide projects within GSK I have participated in cross industry working groups (e.g., chairing the EFPIA Oligo Safety Group and member of DruSafe Oligo Safety group and various sub-committees of the OSWG).

Paul C. Brown, PhD

Associate Director for Pharmacology and Toxicology, OND, CDER
FDA, United States

Dr. Brown's responsibilities include development and implementation of guidance and policy related to the nonclinical assessment of human pharmaceuticals. He has been at the FDA since 1996 when he joined the Division of Dermatology and Dental Drug Products as a Pharmacology/Toxicology reviewer. He was supervisor for Pharmacology/Toxicology in this Division from 2003 to 2008. Prior to coming to the FDA he was a Pharmacology Research and Training Fellow in the National Cancer Institute from 1991 to 1996. He worked on multidrug resistance gene structure and function in the Laboratory of Experimental Carcinogenesis. He received his Ph.D. in toxicology from the University of Maryland in 1991.

Speaker(s)

Key Considerations for DART Assessment of Oligonucleotides

Bethany Hannas, PhD

Senior Director, Toxicology
Eli Lilly and Company, United States

Artificial Intelligence and Machine Learning Utility in Safety Assessments of Therapeutic Oligonucleotides

Chris Hart, PhD

CEO & Co-Founder
Creyon Bio, Inc. , United States

Chris is the CEO and co-founder of Creyon Bio and an experienced leader leveraging computational methods, ML/AI, and deep biological insights to solve problems. He has extensive experience in pharma and biotech, including building and leading the functional genomics department at Ionis where he was responsible for company-wide genomics and bioinformatics efforts as well as execution and strategic leadership of exploratory drug discovery programs for rare and common diseases. He also worked at the Science and Technology Policy Institute advising the

White House Office of Science and Technology Policy on biomedical research and health policy issues. Chris earned his PhD from Caltech and conducted post-doctoral training at Yale University.

9:25 AM — 10:40 AM Federal AB

Session 10 Track 3: Streamlining Oligonucleotide Development with Platform Approaches Roundtable

This session will discuss the benefits of using platform approaches in the development of therapeutic oligonucleotides, including streamlining processes and expediting regulatory submissions. The session will feature mini talks on platform strategies, where experts will share their insights and experiences. Following the talks, there will be a round table discussion with regulators and industry experts on the challenges and opportunities of implementing these strategies. The discussion will provide a forum for an open exchange of ideas and perspectives, and participants will have the opportunity to engage with the experts and learn from their experiences.

Learning Objective : At the conclusion of this session, participants should be able to:

- Identify benefits of using platform approaches in the development of therapeutic oligonucleotides
- Recognize the regulatory challenges associated with using platform approaches
- Apply concepts from the session to enable the use of platform approaches

Track: Track 3: CMC

Session Chair(s)

Dominik Altevogt, PhD

Associate Director Regulatory Affairs CMC
Novartis, Switzerland

Dominik Altevogt is an experienced professional in the pharmaceutical industry, with over 15 years of experience leading regulatory submissions and health authority interactions for small molecule drugs, with a special focus on synthetic peptides and oligonucleotides. He started his career in CMC regulatory affairs at Bachem AG and has since worked for F. Hoffmann-La Roche AG and Novartis AG. Dominik holds a Ph.D. in organic chemistry from the University of Freiburg, Germany, and is an active member of the European Pharma Oligonucleotide Consortium (EPOC), where he currently leads the platform strategies subteam.

Speaker(s)

A Novel Approach to Stability Platform Definition In Support of Clinical Trial Dating

Brian Pack, PhD

Associate Vice President

Eli Lilly, United States

Dr. Brian W. Pack received his Ph.D. in analytical chemistry from Indiana University and joined Eli Lilly as a senior analytical chemist in 2001. He has contributed regulatory specifications to all phases of development, from first in human studies to marketing applications. He is an Executive Director in early phase analytical development, overseeing control strategy development for small organic molecules, peptides, and oligonucleotides. Dr. Pack is responsible for specification review for all synthetic molecules in the portfolio and is passionate about this topic. He has over 25 publications, including three book chapters, mainly focused on the issues of cleaning verification and chromatographic applications.

Platform Approach to siRNA Drug Substance Manufacturing Process Validation

Joshua Leo Brooks, PhD

Director of Process Validation
Alnylam Pharmaceuticals, United States

Josh is a Director at Alnylam Pharmaceuticals and leads the process validation group. He received his Ph.D. in organic chemistry in the lab of Alison Frontier at the University of Rochester in 2012, and then completed his postdoctoral training working with Derek Tan at Memorial Sloan Kettering. He then joined the process chemistry group at Ionis pharmaceuticals before moving to the process sciences group at Alnylam in 2017.

Speaker

Lawrence Perez, PhD

Senior Pharmaceutical Quality Assessor, CDER
FDA, United States

Lawrence Perez has been a CMC Reviewer for new drugs with the FDA since 2015 and in 2021 he became a Senior Pharmaceutical Quality Assessor for API New Drugs. Before that, Lawrence was a discovery chemist with Novartis Oncology. Lawrence has been active in the areas of pharmaceutical regulations and medicinal chemistry, with his most notable work being the discovery and development of the oncology drug Farydak®.

Operational Range Assessment for Oligonucleotide Characterization

Yannick Fillon, PhD

Head of Oligonucleotide Process Chemistry
Biogen, United States

Yannick Fillon obtained his PhD in Organic Chemistry in Purdue University in 2006. He started his career at Millipore Sigma in Houston Texas with the Custom Product division where he focused his efforts on the process development and improvement to produce peptides and oligonucleotides. In 2012 he moved to Boston to work for Cubist Pharmaceuticals, but subsequently joined the ASO group at Biogen in 2014 as a Senior Scientist. Since then, he has accumulated experience in several roles, all related to oligonucleotides development. He currently is the Product

Technical Lead, overseeing the development, launch and ongoing commercial performance of Biogen's portfolio of Oligonucleotides.

Panel Discussion:

Brian Dooley, MPharm, MSc

Pharmaceutical Quality Senior Specialist
European Medicines Agency, Netherlands

Brian Dooley has worked as a quality specialist in the Pharmaceutical Quality Office of EMA since 2016, working mostly on centralised marketing authorisations and scientific advice, and supporting the development of scientific guidelines by the CHMP, QWP and BWP. From 2008 to 2016, Brian worked as a pharmaceutical assessor in the IMB/HPRA (Ireland). He holds a B.Sc. in Pharmacy (2005) and M.Sc. in Pharmaceutical Medicine (2015) both from Trinity College Dublin, Ireland. Areas of interest: lifecycle management, assessment-inspection interface, synthetic peptides, oligonucleotides, mRNA technology, sterilisation processes, radiopharmaceuticals.

Towards a Bracketing / Matrix approach for PPQ Covering a Defined mRNA Sequence and Process Space

Andreas Kuhn, PhD

Senior Vice President RNA Biochemistry & CMC Development
Biontech SE, Germany

Andreas Kuhn, Senior Vice President RNA Biochemistry & CMC Development, has worked in the field of RNA biochemistry and molecular biology for about 30 years. His work on RNA-based immunotherapies began in 2007 with Ugur Sahin and Andreas joined BioNTech SE shortly after its founding in 2008. His main focus is expanding BioNTech's proprietary technologies to increase the efficacy of RNA immunotherapies and to optimize GMP-compatible manufacturing processes for RNA. He has co-authored several publications and patents ranging from basic research on RNA to its application as a therapeutic agent and vaccine.

10:40 AM — 11:10 AM Capital Terrace

Refreshment and Networking Break

11:10 AM — 12:25 PM Presidential Ballroom

Session 11: Grand Q&A Panel

Speaker(s)

Session 11: Grand Q and A Panel

Ramesh Raghavachari, PhD

Supervisor, Unit 3/DPQA IV/OPQA I/OPQ/CDER
FDA, United States

Ph.D - Temple University, Philadelphia, PA Currently a Chemist at FDA/CDER, has been with FDA since 2003.

Speaker

Barry Ticho, MD, PhD

Chief Medical Officer
Stoke Therapeutics, United States

As Chief Medical Officer Dr. Ticho is responsible for Stoke's efforts to develop first-in-class RNA based disease-modifying medicines to treat severe genetic diseases. He is also co-founder and former CEO of Verve Therapeutics which is developing therapies to edit the genome and confer protection from cardiovascular disease. Prior to joining Stoke Barry was Head of R&D for Cardiovascular and Metabolic Diseases at Moderna Therapeutics. He was previously Head of External R&D Innovation for Cardiovascular and Metabolic Diseases at Pfizer and was Vice President of Clinical Development at Biogen. Barry obtained his MD and PhD degrees from the University of Chicago. He was on staff at Harvard Medical School and Massachusetts General Hospital

Speakers

Hobart Rogers, PharmD, PhD

Pharmacologist
FDA, United States

Dr. Bart Rogers is a reviewer in the Division of Translational and Precision Medicine in the Office of Clinical Pharmacology (OCP) at the FDA. Dr. Rogers also serves as an active duty officer with the United States Public Health Service. He serves as the lead for OCPs review of all synthetic oligonucleotides. His research interests are focused on the pharmacology of synthetic oligonucleotides, orphan disease drug development, and pharmacogenomics. Dr. Rogers completed his Pharm.D. degree from the University of Maryland, School of Pharmacy in 2004. He went on to obtain his Ph.D. in Clinical Pharmaceutical Sciences with a focus on cardiovascular pharmacogenomics from the same institution.

Speaker

Firoz Antia, PhD

Vice President, Oligonucleotide and Small Molecule CMC
Denali Therapeutics, United States

A PhD Chemical Engineer by training, Dr. Antia has spent over 30 years in the pharmaceutical industry carrying out process development with roles at Sandoz, J&J, Merck and Palatin Technologies, before joining Biogen in 2012, where

he is now Head of Oligonucleotide Development

Speaker

Andreas Kuhn, PhD

Senior Vice President RNA Biochemistry & CMC Development
Biontech SE, Germany

Andreas Kuhn, Senior Vice President RNA Biochemistry & CMC Development, has worked in the field of RNA biochemistry and molecular biology for about 30 years. His work on RNA-based immunotherapies began in 2007 with Ugur Sahin and Andreas joined BioNTech SE shortly after its founding in 2008. His main focus is expanding BioNTech's proprietary technologies to increase the efficacy of RNA immunotherapies and to optimize GMP-compatible manufacturing processes for RNA. He has co-authored several publications and patents ranging from basic research on RNA to its application as a therapeutic agent and vaccine.

Speaker

Jeffrey Foy, PhD

Senior VP, Toxicology
PepGen Inc., United States

Speaker

Ronald Wange, PhD

Associate Director for Pharm/Tox OND
FDA, United States

Dr. Wange is an Associate Director for Pharmacology & Toxicology within the Office of New Drugs in CDER at the FDA, and has over 19 years of experience reviewing small molecule drugs, biotherapeutic proteins and oligonucleotide-based therapeutics. He is a founding member of OND's Pharmacology/Toxicology Oligonucleotide Subcommittee, which considers issues specifically related to the safety review of oligonucleotide-based therapeutics. In addition, he was the primary author of the recently published draft guidance on Nonclinical Testing of Individualized ASOs for Severely Debilitating or Life-Threatening Diseases. Prior to joining FDA, he was the head of the T-lymphocyte Signaling Unit at the National Institute on Aging at the NIH.

12:25 PM — 12:40 PM Presidential Ballroom

Closing Remarks

Speaker(s)

Sorcha McCrohan, MS

Scientific Projects Manager
DIA, United States

Sorcha McCrohan is a Specialist of Scientific Programs for the Americas Region at DIA. In her current role, she focuses on content development and strategy for DIA's meetings to improve and facilitate innovation in clinical research, drug development, and the fields of devices and diagnostics. Before joining DIA, she conducted COVID-19 research in Chiapas, Mexico, and worked in marketing within Pfizer's Global Vaccines Meningococcal franchise. Sorcha holds a BA in Sociology from Mount Holyoke College and an MSc in Global Health, Disease Prevention & Control from Georgetown University.

Scott Henry, PhD

Senior Vice President, Nonclinical Development
Ionis Pharmaceuticals, Inc., United States

Dr. Henry received a PhD in Biochemistry form North Dakota State University. He was a post-doc fellow at Parke Davis, Ann Arbor MI, depart. of toxicology. He joined Isis Pharmaceuticals, Inc. as a Sr Scientist in toxicology. He helped characterized and studied mechanisms of various toxicities e.g. the effects of oligonucleotide treatment on clotting time prolongation, alternative complement pathway activation, proinflammatory effects in rodents, platelet alterations and the effects related to the accumulation of oligonucleotide in kidney. As VP of Non-Clinical Development he has participated in the development of ~8 different phosphorothioate oligodeoxynucleotides and 30+ different 2'-MOE modified phosphorothioate oligonucleotides.

Ronald Wange, PhD

Associate Director for Pharm/Tox OND
FDA, United States

Dr. Wange is an Associate Director for Pharmacology & Toxicology within the Office of New Drugs in CDER at the FDA, and has over 19 years of experience reviewing small molecule drugs, biotherapeutic proteins and oligonucleotide-based therapeutics. He is a founding member of OND's Pharmacology/Toxicology Oligonucleotide Subcommittee, which considers issues specifically related to the safety review of oligonucleotide-based therapeutics. In addition, he was the primary author of the recently published draft guidance on Nonclinical Testing of Individualized ASOs for Severely Debilitating or Life-Threatening Diseases. Prior to joining FDA, he was the head of the T-lymphocyte Signaling Unit at the National Institute on Aging at the NIH.

12:40 PM — 12:40 PM

Conference Adjourns