September 22, 2021 FDA-NRC Workshop

Presenter Biographies

Enhancing Development of Targeted Alpha Emitting Radiopharmaceuticals

Special Session on Actinium-225

Welcome and Introductions

Louis Marzella, MD, PhD
Director, FDA

Dr. Louis Marzella is the Director of the Division of Imaging and Radiation Medicine (DIRM) in the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration (FDA). DIRM regulates imaging drugs including contrast agents and radiopharmaceuticals as well as therapeutic drugs for use in radiation injury.

Before joining FDA, Dr. Marzella did research and taught at the University of Maryland school of medicine. He trained at the University of Maryland (M.D. and Family Medicine residency), and Karolinska Institutet (Ph.D., Experimental Pathology).

Kevin Williams
Director, NRC

Mr. Kevin Williams serves as the Director, Division of Materials Safety, Security, State, and Tribal Programs, Office of Nuclear Material Safety and Safeguards (NMSS).

Mr. Williams joined the U.S Nuclear Regulatory Commission (NRC) in September 2002, as a technical reviewer in the Office of Nuclear Reactor Regulation, Division of Inspection and Program Management. In 2004, he transitioned to a technical reviewer position in the Office of Nuclear Security and Incident Response (NSIR), Division of Preparedness and Response, and subsequently progressed through positions of increased responsibility focused on emergency preparedness-related licensing, guidance, outreach, rulemaking and policy development, and oversight programs. Mr. Williams has also successfully completed assignments as the acting Chief, Spent Fuel Storage and Transportation Branch, NMSS; Chief, New Reactor Licensing Branch, NSIR; Acting Deputy Director, Division of Preparedness and Response, NSIR; Director, Program Management, Policy Development and Analysis, NSIR; Acting Deputy Director, Division of Nuclear Materials Safety, Region IV; and Acting Deputy Controller, Office of the Chief Financial Officer. In June 2017, Mr. Williams joined the Senior Executive Service (SES) in the position of Deputy Director, MSST/NMSS.

Before joining the NRC, Mr. Williams began his nuclear career at the Duane Arnold Energy Center, Palo, Iowa, where he worked for over 16 years. He held various positions in the areas of Radwaste, Health Physics, Shift Technical Advisor, and Emergency Preparedness. Mr.

Williams earned a bachelor's degree in Business Administration with a Chemistry Minor from Coe College in Cedar Rapids, Iowa.

Session I: Targeted Alpha Emitters with Focus on Actinium-225 Radiotherapies

The Clinical Evolution of Alpha Particle Radiopharmaceutical Therapy: Focus on Actinium-225

Richard Wahl, MD
President, Society of Nuclear Medicine and Molecular Imaging

Dr. Richard Wahl is the Elizabeth E. Mallinckrodt Professor and head of radiology at Washington University School of Medicine in St. Louis, director of the university's Mallinckrodt Institute of Radiology and professor of radiation oncology. Dr. Wahl earned his medical degree from Washington University School of Medicine and completed training there in diagnostic radiology and nuclear medicine.

Dr. Wahl is a pioneer in the use of PET scans to diagnose and assess treatment of a broad array of human cancers and other diseases, and he is at the forefront of efforts to combine quantitative data from PET scans with computerized tomography (CT). Dr. Wahl and colleagues developed the PERCIST 1.0 criteria for assessing treatment response in cancer. He is the primary author of several textbooks, including Principles and Practice of PET and PET/CT.

Dr. Wahl is also a world-renowned leader in molecular imaging and his research and clinical interest contributions in radionuclide therapy led to the development of radiolabeled antibodies for the treatment of lymphoma.

Dr. Wahl is an elected member of the National Academy of Medicine. Awards include a U.S. Department of Energy Achievement Award; the de Hevesy, Tetalman, Berson and Yalow and two Alavi-Mandel awards from SNMMI; and the Academy of Molecular Imaging's Distinguished Scientist Award. He has given many named lectureships including the Marie Curie Lecture at the European Association of Nuclear Medicine. He is the recipient of the SNMMI Georg Charles de Hevesy Nuclear Pioneer Award and the Saul Hertz, MD Lifetime Achievement Award. Dr. Wahl is currently President of the SNMMI.

Session II: Novel Radiopharmaceuticals: Standards Development, Product Quality Considerations, Supply and Demand

Moderator: Danae Christodoulou, PhD
Branch Chief, FDA

Dr. Danae Christodoulou is a Branch Chief in the Office of New Drug Products. She joined the FDA in 1998. Prior to the FDA, Dr. Christodoulou worked at Johnson Matthey Inc. R&D Drug Discovery as a Senior Research Chemist and at the National Cancer Institute in Frederick, MD.

Dr. Christodoulou has a background in Inorganic Chemistry and received her Ph.D. from the University of Michigan, Ann Arbor, MI.

Product Quality Considerations in Actinium-225 Radiopharmaceuticals

Ravindra Kasliwal, M.Sc., PhD
Chemist, FDA

Dr. Ravindra Kasliwal is CMC expert in radiopharmaceutical drug products in the Office of New Drug Products in Office of Pharmaceutical Quality at CDER/ FDA. He has been at FDA since 1994. During his career at FDA he has been involved in the review of many diagnostic and therapeutic radiopharmaceuticals. He has served on many FDA committees as well as USP standards committees dealing with radioactive drugs, where he has been involved with writing regulations, guidance documents, as well as USP standards.

High Energy Accelerator Production of Actinium-225 to Meet Clinical Demand

Cathy Cutler, PhD
MIRP Director, Brookhaven National Laboratory

Dr. Cathy Cutler is Director of the Medical Isotope Research Production and Development group (MIRP) at Brookhaven National Laboratory. Dr. Cutler moved to the University of Missouri Research Reactor Centre's Radiopharmaceuticals Group in 1998. There she developed reactor processing methods for radioisotopes such as Lutetium-177 and developed targeting molecules such as nanoparticles for selective delivery. She worked there till June 2015. The MIRP group at Brookhaven operates the LINAC Isotope Producer (BLIP) that produces radioisotopes for commercial production as well as several research radioisotopes and is currently evaluating the accelerator production of Ac-225. Additionally, she directs the Radiopharmaceutical Research and Production Labs (RRPL) that processes targets from the BLIP. Dr. Cutler's research focuses on developing production and separation methods for high specific activity radioisotopes, creating a suite of diagnostic and therapeutic agents tailored for individual needs which has been funded by the DOE, NIH, NSF and public foundations. She brings more than 28 years of experience in the development and evaluation of radiopharmaceuticals, utilizing bioinorganic and radioanalytical chemistry to develop and evaluate radiopharmaceuticals for both diagnosis and therapy.

Realizing the Becquerel for Actinium-225: The Current Landscape and the Road to a New National Activity Standard in the U.S.A.

Denis Bergeron, PhD
Research Chemist, NIST

Dr. Denis Bergeron is a research chemist in the Radiation Physics Division at the National Institute of Standards and Technology (NIST) in Gaithersburg, MD. He earned a B.S. in Chemistry from Loyola University New Orleans and a Ph.D. in Physical Chemistry from the Pennsylvania State University. Following a postdoctoral fellowship at the University of Nottingham, Dr. Bergeron came to NIST as a National Research Council (NRC) Fellow in 2006 and joined the Nuclear Medicine Project team in 2008.

Much of Dr. Bergeron's current research focuses on the basic measurement science behind activity standards for medically important radionuclides. In other words, he works to define, realize, and disseminate the SI unit for activity, the becquerel.

He is active in the international radionuclide metrology community and serves on various AAPM, RSNA (QIBA), and IEC committees. He has published more than 80 research papers and is Editor-in-Chief of Applied Radiation and Isotopes. His research has been recognized with awards including the Department of Commerce Silver and Bronze medals and the William P. Slichter Award.

Session III. Clinical Considerations for Development of Novel Radiopharmaceuticals

Alpha-emitting Therapeutic Radiopharmaceuticals: Nonclinical Studies Prior to Initiating a Human Study, Dose Selection, and Impact of Impurities

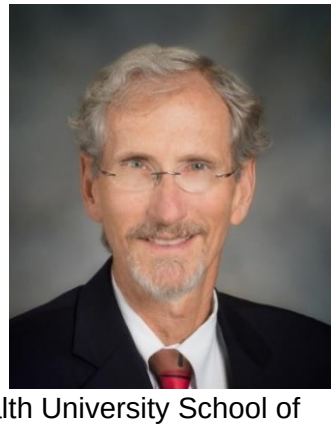
Haleh Saber, PhD, MS
Deputy Director, FDA

Dr. Haleh Saber is the Deputy Director in the Division of Hematology Oncology Toxicology (DHOT), in the Office of Oncologic Diseases, in CDER. In this role she provides leadership for day-to-day activities, leads and coordinates scientific research, and participates in guidance development. Dr. Saber has extensive industry and regulatory experience. She served as a Subject Matter Expert assisting pharmaceutical companies worldwide in nonclinical drug development and served many roles at the FDA over 15 years.

Dr. Saber is recognized for her efforts in establishing acceptable approaches in first-in-human dose selection for new classes of products. She was the lead author of the guidance Oncology Therapeutic Radiopharmaceuticals: Nonclinical Studies and Labeling Recommendations. Dr. Saber received her PhD in Biochemistry from Lehigh University and conducted her post-doctoral studies at Fox Chase Cancer Center, PA.

Challenges to Safety Assessments in Early Phase Clinical Trials for Radiopharmaceuticals

Mitchell S. Anscher, MD
Medical Officer, FDA

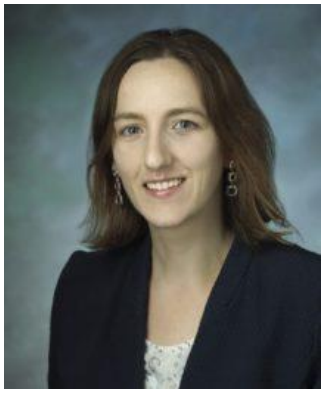


Dr. Mitchell Anscher is a Medical Officer in the Division of Oncology 1 in the Center for Drug Evaluation and Research at the FDA. Prior to joining the FDA, Dr. Anscher served as Professor and Genitourinary Section Chief in the Department of Radiation Oncology at the University of Texas M.D. Anderson Cancer Center, Florence and Hyman Meyers Professor and Chair of the Department of Radiation Oncology at Virginia Commonwealth University, and Professor in the Department of Radiation Oncology at Duke University. He received his BS from Stanford University and his MD from Virginia Commonwealth University School of Medicine. He completed his residency in Internal Medicine at St. Mary's Hospital in Waterbury, CT and his residency in Radiation Oncology at Duke University Medical Center. He is board certified in both Internal Medicine and Radiation Oncology.

His funded research interests included clinical trials in Genitourinary malignancies and molecular and translation research into normal tissue injury following cancer therapies. He is the recipient of the R. Wayne Rundles Award for Excellence in Cancer Research from Duke University and was named one of America's Top Doctors for 20 consecutive years. He has been awarded fellowships in the American College of Radiology, American Society for Radiation Oncology and the American College of Radiation Oncology. He has served on numerous national and international grant review committees, and on the Program Committees for the Annual Meetings of the Radiation Research Society and the American Society of Radiation Oncology for which he has chaired the Genitourinary Subcommittee.

Dosimetry for Radiopharmaceutical Therapy

Donika Plyku, PhD
Senior Staff Fellow, Nuclear Medical Physicist, FDA



Dr. Donika Plyku is a medical physicist and a senior staff fellow at the Food and Drug Administration's (FDA's) Division of Imaging and Radiation Medicine. She leads a research team that focuses on regulatory challenges regarding radiation dosimetry of diagnostic and therapeutic radiopharmaceuticals. She provides subject matter expertise to review decisions throughout FDA on questions related to radiation dosimetry. She has worked at the Johns Hopkins Hospital PET Center and Division of Nuclear Medicine and at MedStar Health Research Institute and Medstar Washington Hospital Center as a medical physicist after completing a post-doctoral fellowship at the Radionuclide Therapy and Dosimetry Laboratory, Johns Hopkins University, Radiological Physics Division.

Dr. Plyku has research and clinical experience on radiation dosimetry, quality assurance and instrumentation in nuclear medicine. She received her PhD from Old Dominion University, Norfolk, VA after completing her research in the nuclear/high-energy physics at the Relativistic Heavy Ion Collider, Brookhaven National Laboratory, Long Island, NY. Dr. Plyku has published in peer-reviewed journals in both nuclear and medical physics fields. Her contributions in nuclear medicine have focused on patient-specific radiobiological dosimetry for radiopharmaceutical therapy and on dose reduction in pediatric molecular imaging. She is an active member of the Society of Nuclear Medicine and Molecular Imaging, Women in Nuclear Medicine, and the American Association of Physicists in Medicine. In her free time, she enjoys spending time in nature, swimming and reading or listening to audiobooks.

Dosimetry of Alpha Emitters and Caution for Extravasation.

Kish Chakrabarti, PhD, FAAPM
Senior Health Physicist, FDA

Dr. Kish Chakrabarti is with FDA for more than 27 years. He is nationally and internationally known for his contributions in diagnostic imaging especially digital mammography and digital breast tomosynthesis. He has written regulations and guidance for FDA. He also supervised students and research fellows that generated several peer reviewed publications. He was considered as one of the top 100 name in health imaging by the Health Imaging magazine. He was awarded senior expert scientist position by FDA's peer reviewed committee because of his contributions in the field. American Association of Physicists in Medicine (AAPM) selected him as a fellow of the organization. Since joining DIRM in 2019 he is active in theranostic reviews and consulting.

Session IV. User and Industry Perspective

Moderator: Michelle Hammond, M.Sc.
Health Physicist, NRC

Ms. Michelle Hammond is a Health Physicist in the Materials Safety and Tribal Liaison Branch of the Office of Nuclear Materials Safety and Safeguards, U.S. Nuclear Regulatory Commission (NRC). Ms. Hammond received her M.Sc. in Health Physics from Georgetown University and her B.Sc. in Physics from Southern University A&M College, Baton Rouge, Louisiana.

Ms. Hammond has over 20 years of federal government service and worked as a physical scientist at the National Institute of Standards and Technology in Gaithersburg, MD. Her research interests included: nuclear medicine measurements and standards, alpha-emitting radiopharmaceuticals, and measurement assurance for radiological threats in homeland security.

In 2009, Ms. Hammond joined the NRC Region IV as a nuclear materials inspector and license reviewer. She has supported the NRC Technical Training Center (TTC) as an instructor for the Licensing Practices and Procedures Course and contributed to the Integrated Materials Performance Evaluation Program (IMPEP) by evaluating the technical quality of licensing for agreement states.

Ms. Hammond is an active member of Alpha Kappa Alpha Sorority, Inc. and in her spare time she enjoys community service projects, dancing, camping, fishing, and cooking for family and friends. She is a wife and mother of two sons, Cameron (16) and Dillon (13).

Targeted Alpha Therapy (TAT) Use of Actinium-225: Regulatory Interactions Now and Tomorrow

Victor Paulus, PhD
Senior Vice President of Regulatory Affairs, Fusion Pharmaceuticals, Inc.

Dr. Victor Paulus is currently the Senior Vice President of Regulatory Affairs at Fusion Pharmaceuticals. He has over 30 years experience in the pharmaceutical industry, including 20 years specializing in Regulatory Affairs.

Prior to joining Fusion, Dr. Paulus served as Senior Vice President, Regulatory Affairs at the clinical-stage gene therapy company Abeona Therapeutics. Previously, he was Global Head of Regulatory Affairs for Advanced Accelerator Applications where he secured orphan drug designations, fast track designation for Lutathera, priority review and approvals for NETSPOT and Lutathera. Earlier in his career, he served as Director of Regulatory Affairs for pediatric vaccines at GlaxoSmithKine and Senior Director of Regulatory Affairs for biosimilar drug development at Dr. Reddy's. He also held roles of increasing responsibility at Organon, Elusys Therapeutics, and the Population Council.

Dr. Paulus began his career as a laboratory technician at the Salk Institute, then managed a cell culture laboratory at Centocor and viral vaccine production at what is now Sanofi Pasteur. He has BS degrees in biology and biochemistry, an MSc in biology and a Ph.D. in public health.

Industry Experience in the Development and Clinical Testing of Actinium-225- based Radio-conjugates

Mark S. Berger, MD
Chief Medical Officer, Actinium Pharmaceuticals, Inc.

Dr. Berger has 25 years of experience in oncology drug development in the pharmaceutical and biotech industries, with agents ranging from small molecules to antibody radioconjugates. For the past 4 years he has served as the Chief Medical Officer at Actinium Pharmaceuticals where he has played a leading role in the development of antibody radioconjugates for use as conditioning prior to allogeneic hematopoietic cell transplant for AML patients, and for use as therapeutic agents in patients with AML. This work has included clinical development of the anti-CD33 antibody lintuzumab labeled with Actinium-225. His previous experience includes playing a key role in the clinical trials that led to approval for Mylotarg (gemtuzumab ozogamacin) for relapsed AML, as well as the approval of Tykerb (lapatinib) for metastatic breast cancer.

Dr. Berger obtained a BA degree at Wesleyan University and an MD degree at the University of Virginia. His medical training continued as a Medical Resident and Chief Medical Resident at Thomas Jefferson University, and as a Hematology-Oncology fellow at University of Pennsylvania.

Clinical Utilization of Actinium-225 Alpha for Targeted Therapies: Potential and Challenges

Neeta Pandit-Taskar, MD
Attending Radiologist, Molecular Imaging & Therapy Svc, Dept of Radiology.
***Member*, Memorial Hospital.**
Memorial Sloan Kettering Cancer Center, NY
***Professor*, Dept of Radiology**
Weill Cornell Medical Center, NY
***Clinical Director*, Center for Targeted Radioimmunotherapy and Theranostics**
Ludwig Center for Cancer Immunotherapy, MSK
Member, Parker Institute of Cancer Immunotherapy, MSK

Dr. Pandit-Taskar is a nuclear medicine faculty at Memorial Sloan Kettering Cancer Center, with extensive experience in Diagnostic and therapeutic nuclear medicine. She is particularly interested in molecular imaging and development of novel techniques in diagnosis and treatment of cancer, with special focus on novel targets including radioimmunotargeted imaging and therapy as well as use of alpha and beta radioisotopes in theranostics. She has special interest in radiopharmaceutical therapy and immune targeting agents. Dr. Pandit-Taskar has been intricately involved and lead clinical trials involving imaging and therapy using radiolabeled monoclonal antibodies and small molecules to treat a variety of cancers including lymphoma, renal cancer, prostate cancer and pancreatic cancers and development of novel therapeutic approaches for pediatric cancers. As a clinical director of Ludwig center of radioimmunotargeted imaging and theranostics of LCCI at MSK and a Research member of Parker institute of cancer immunotherapy at MSK, Dr. Pandit-Taskar closely works with oncologists, scientists and physicists in methods to optimize targeted delivery of radiolabeled agents and dosimetry approaches.

Radiation Safety Considerations for Novel Radionuclide Therapies

Megan Shober
Advanced Nuclear Safety Specialist, Wisconsin Department of Health Services

Ms. Megan Shober is an Advanced Nuclear Safety Specialist with the Wisconsin Department of Health Services and has been licensing and inspecting the use of radioactive material since 2003. For the past five years, Ms. Shober has been actively involved in developing radiation safety controls for actinium-225 and currently oversees nine licensees using or pursuing actinium-225 for research or medical use.

Since 2018, Ms. Shober has been the State Representative on NRC's Advisory Committee on the Medical Uses of Isotopes. Ms. Shober holds a master's degree in Geophysics from the University of Wisconsin and a bachelor's degree in Geology from the College of Wooster, in Ohio.

Closing Remarks

Lisa Dimmick, MBA
Medical Team Leader, NRC

Ms. Lisa Dimmick is the Team Leader for the Medical Radiation Safety Team at the U.S. Nuclear Regulatory Commission. Previously she was a Senior Health Physicist in the Agreement State Program Branch coordinating the Integrated Materials Performance Evaluation Program.

Ms. Dimmick received undergraduate degrees in Biology and Nuclear Medicine Technology from Old Dominion University in Norfolk, VA, and graduate degrees in Health Physics from Georgetown University in Washington, D.C., and in Business Administration from The Johns Hopkins University in Baltimore, MD.

Before joining the NRC, Ms. Dimmick was the regulatory affairs manager and radiation safety officer for an international medical device company, and a health physics consultant.