Food and Drug Administration
Center for Drug Evaluation and Research

Final Summary Minutes of the Medical Imaging Drugs Advisory Committee Meeting
August 1, 2023

Location: All meeting participants joined this advisory committee meeting via an online teleconferencing and/or video conferencing platform.

Topic: The committee discussed dosimetry data needed to support the initial clinical study in an original investigational new drug (IND) application for certain new positron emission tomography (PET) drugs. FDA obtained the committee's input on the following: (1) the sufficiency of available data from animal or human studies involving certain positron emitting radionuclides (e.g., C11, F18) to allow a reasonable calculation of radiation-absorbed dose to the whole body and critical organs upon administration of a new PET drug containing certain radionuclides to a human subject in first-in-human studies; and (2) the reasonableness of a proposed list of numerical radioactivity thresholds for new PET drugs containing these radionuclides, such that Phase 1 studies that will both (a) administer sub-threshold activities and (b) obtain sufficient human data for dosimetry calculations may be found safe-to-proceed in the absence of dosimetry data based on prior animal administration of the new PET drug under investigation.

These summary minutes for the August 1, 2023 meeting of the Medical Imaging Drugs Advisory Committee (MIDAC) of the Food and Drug Administration were approved on October 24, 2023.

I certify that I attended the August 1, 2023 meeting of the MIDAC of the Food and Drug Administration and that these minutes accurately reflect what transpired.

/s/	/s/
Rhea Bhatt	Henry D. Royal, MD
Acting Designated Federal Officer, MIDAC	Chairperson, MIDAC

Final Summary Minutes of the Medical Imaging Drugs Advisory Committee Meeting
August 1, 2023

The Medical Imaging Drugs Advisory Committee (MIDAC) of the Food and Drug Administration, Center for Drug Evaluation and Research, met on August 1, 2023. The meeting presentations were heard, viewed, captioned, and recorded through an online teleconferencing platform. Prior to the meeting, the members and temporary voting members were provided the briefing materials from the FDA. The meeting was called to order by Henry Royal, MD (Chairperson). The conflict of interest statement was read into the record by Rhea Bhatt (Acting Designated Federal Officer). There were approximately 105 people online. There were no Open Public Hearing (OPH) speaker presentations.

A verbatim transcript will be available, in most instances, at approximately ten to twelve weeks following the meeting date.

Agenda:

The committee discussed dosimetry data needed to support the initial clinical study in an original investigational new drug (IND) application for certain new positron emission tomography (PET) drugs. FDA obtained the committee's input on the following: (1) the sufficiency of available data from animal or human studies involving certain positron emitting radionuclides (e.g., C11, F18) to allow a reasonable calculation of radiation-absorbed dose to the whole body and critical organs upon administration of a new PET drug containing certain radionuclides to a human subject in first-in-human studies; and (2) the reasonableness of a proposed list of numerical radioactivity thresholds for new PET drugs containing these radionuclides, such that Phase 1 studies that will both (a) administer sub-threshold activities and (b) obtain sufficient human data for dosimetry calculations may be found safe-to-proceed in the absence of dosimetry data based on prior animal administration of the new PET drug under investigation.

Attendance:

Medical Imaging Drugs Advisory Committee Members Present (Voting): Wesley E. Bolch, PhD; David B. Hackney, MD; Peter Herscovitch, MD, FACP, FSNMMI; Paula M. Jacobs, PhD; M. Elizabeth Oates, MD, FAAWR, FACR; Rupa Sanghani, MD, FACC, FASNC

Medical Imaging Drugs Advisory Committee Member Not Present (Voting): Eben L. Rosenthal, MD

Medical Imaging Drugs Advisory Committee Member Present (Non-Voting): Mark Mintun, MD (*Industry Representative*)

Temporary Members (Voting): Kimberly E. Applegate, MD, MS, FACR; Yuni Dewaraja, PhD; Terry Gillespie (*Patient Representative*); Steven M. Larson, MD; Jessie R. Nedrow, PhD; Henry D. Royal, MD (*Chairperson*); Chengjie Xiong, PhD

FDA Participants (Non-Voting): Charles Ganley, MD; Alex Gorovets, MD; Libero Marzella MD, PhD; Ira Krefting, MD; August (Alex) Hofling, MD, PhD

Acting Designated Federal Officer (Non-Voting): Rhea Bhatt

Open Public Hearing Speakers Present: None

The agenda was as follows:

Call to Order	**Henry Royal, MD** Chairperson, MIDAC
Introduction of Committee and Conflict of Interest Statement	**Rhea Bhatt** Acting Designated Federal Officer, MIDAC
FDA Introductory Comments	**Anthony Fotenos, MD, PhD** Clinical Team Leader Division of Imaging and Radiation Medicine (DIRM) Office of Specialty Medicine (OSM) Office of New Drugs (OND), CDER, FDA
GUEST SPEAKER PRESENTATION	
PET Dosimetry Preclinical and Human Experience for Clinical Research	**William Hallett, DPhil** Head of Imaging Physics Invicro, LLC London
SPEAKER PRESENTATION	
Dosimetry for first-in-human PET studies The NIH experience	**Paolo Zanotti Fregonara, MD, PhD**
Clarifying Questions to Speakers	
FDA PRESENTATIONS	
Medical Physics Presentation	**Donika Plyku, PhD** Senior Staff Fellow DIRM, OSP, OND, CDER, FDA
Nonclinical Perspective on Biodistribution and Dosimetry Studies	**Jonathan Cohen, PhD** Supervisory Pharmacologist Division of Pharm/Tox, Office of Rare Diseases, Pediatrics, Urologic, and Reproductive Medicine (DPT-RDPURM) DIRM, OSP, OND, CDER, FDA

FDA PRESENTATIONS (CONT.)

Pharmacovigilance in CDER	**Samantha Cotter, PharmD** Division of Pharmacovigilance (DPV) II Office of Pharmacovigilance and Epidemiology (OPE) Office of Surveillance and Epidemiology (OSE) CDER, FDA
Clarifying Questions to Presenters	

BREAK

OPEN PUBLIC HEARING

Questions to the Committee/Committee Discussion

ADJOURNMENT

Questions to the Committee:

1. **DISCUSSION**: Discuss the sufficiency of reviewed data from animal or human studies involving F 18, C 11, Ga 68, Cu 64, Rb 82, or N 13 to allow a reasonable calculation of radiation-absorbed dose to the whole body and critical organs upon first-in-human administration of a new PET drug containing one of these radionuclides.

   Committee Discussion*: The majority of panel members agreed that there are sufficient reviewed data from animal or human studies involving F 18, C 11, Ga 68, Cu 64, Rb 82, or N 13 to allow a reasonable calculation of radiation-absorbed dose to the whole body and critical organs upon first-in-human administration of a new PET drug containing one of these radionuclides. While most panel members agreed with including the aforementioned six radionuclides within the scope defined by the Agency, some committee members expressed concerns about Cu 64 given the paucity of data and its longer half-life. The consideration of the pharmacokinetics of these agents, especially for Cu 64, was mentioned as being a factor in determining if animal dosimetry is needed. Please see the transcript for details of the Committee's discussion.*

2. **DISCUSSION**: Discuss the reasonableness of the approach under consideration involving administered activity values for new PET drugs containing F 18, C 11, Ga 68, Cu 64, Rb 82, and N 13, such that Phase 1 studies that will both (a) initially administer one or more activity levels ≤ value and (b) collect sufficient human data for dosimetry calculations may generally be found safe-to-proceed from a radiation safety perspective in the absence of dosimetry data based on prior animal administration of the new PET drug under investigation.

Committee Discussion: *Most committee members were comfortable with the reasonableness of the approach under consideration involving administered activity values for new PET drugs containing F 18, C 11, Ga 68, Cu 64, Rb 82, and N 13, such that Phase 1 studies that will both (a) initially administer one or more activity levels ≤ value and (b) collect sufficient human data for dosimetry calculations may generally be found safe-to-proceed from a radiation safety perspective in the absence of dosimetry data based on prior animal administration of the new PET drug under investigation.*

One member mentioned that in general, prescribing information doses are based on the ability of the radiopharmaceutical to be useful as a diagnostic to detect disease, whereas initial human dosimetry studies can often require lower doses since radioactivity from whole organs is being measured. Committee members mentioned they are more comfortable with the human administration of a new PET drug containing Cu 64 knowing how the Agency plans to apply the limits. Please see the transcript for details of the Committee's discussion.

The meeting was adjourned at approximately 4:10 p.m. ET.