# Medical Imaging:

# CDER's Perspective

**Janet Woodcock, M.D.**
**Director, Center for Drug Evaluation and Research**

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# 2 Topics: 2 Days

- **Standardization of imaging in clinical trials**

*and*

- **Current Good Manufacturing Practices (CGMPs) for PET drugs…**

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# Not Disparate Topics…

**Day one**:

- **Standardization** of image acquisition, interpretation, and management of data in multicenter clinical trials is essential for accurate **diagnosis and to assess response to therapies**

**Day 2**:

- **Standardization of PET Radiopharmaceuticals** production under CGMP 21 CFR 212

This workshop will help us all achieve our goals of facilitating the public access to important, safe and effective products

# Imaging in Clinical Trials

- **Long history of use in exploratory and confirmatory clinical trials, e.g.,**
  - ***coronary arteriographic patency important to the development of thrombolytic agents in the 1980's and early 90's***
  - ***Changes in tumor size widely used to detect oncologic drug efficacy***
- **Imaging: essential for accurate diagnosis and in most therapeutic area clinical trials**

# Importance of Standardization in Trials

- Rapid advances in imaging technology-- increased potential for site-to-site variability in imaging data
- Variability may obscure treatment effects and complicate data verification
- Multiple challenges given wide role for imaging
  - Selection of patients (eligibility)
  - Safety (e.g., decreased ejection fraction)
  - Efficacy (e.g., change in joint architecture or tumor size)

# Importance of Standardization in Trials

- **Emphasized in the 2007 PDUFA agreements where FDA agreed to develop (by end of 2011) a guidance document on *"Imaging Standards for Endpoints in Clinical Trials"***

- **In this workshop, FDA wants to hear your thoughts on standardization**

- **Your feedback will inform the imaging guidance:**
  - **What do you regard as important?**
  - **How is this standardization best accomplished?**

# PET CGMP *(day 2)*

- **Publication of PET CGMP (12/2009) has implications for the use of PET drugs in trials *as well as* clinical practice**
- **Law requires NDA or ANDA submission for any PET drug used in clinical practice (i.e., non-investigational use) within 2 yrs of CGMP publication (12/2011)**
- **Investigational PET drug use continues under IND or RDRC pathways**
- **FDA working to facilitate the submission of NDA and ANDAs for most commonly used PET drugs, e.g., F18-FDG**

# PET CGMP

- PET producers may find NDA/ANDA submission challenging, particularly the development of the PET drug production and testing information

- CGMP standards for PET drug production: focus of tomorrow's sessions

- PET drug production "on site" necessitates consistency in the manufacturing process—an "added" standardization consideration for imaging in clinical trials

# Imaging as a Biomarker

- **Concept: Biomarker qualification is a conclusion that within the stated context of use, the results of biomarker measurements (e.g. imaging) or can be relied upon to have a stated interpretation and utility**

- **Context of use must be clearly specified**

- **Regulatory implication: Industry relies upon use of the biomarker in the qualified manner in IND, NDA and BLA submissions, without a need to resubmit data for the relevant CDER review group to consider and reconfirm the biomarker usage**

# Qualified Biomarker Usage

- The use of a qualified imaging biomarker can be applied in drug development and evaluation if there are NO:
  - **Serious study flaws (e.g., unverifiable data, improper performance of assays, etc.)**
  - **Intention to apply the imaging biomarker outside the qualified context of use**
  - **New and conflicting scientific facts not known at the time the qualification was determined**

# Qualification Process in General

- **A framework for interactions between CDER and sponsors so that CDER can provide guidance towards compiling comprehensive evidence to support qualification of the selected biomarker(s), including imaging biomarkers**

- **A mechanism enabling CDER to have a well-organized, multi-discipline, CDER-unified, formal review of the data supporting a biomarker, eventually leading to a CDER decision on qualification**

- **Enables a scientifically well-supported statement by CDER of qualification providing confidence that the evaluation has been comprehensive and the conclusions can be relied upon**

# Qualification Process within CDER

- Formalized process still under development
- 'Sponsor' brings imaging biomarker concept/information package to CDER
- Interdisciplinary working team assembled within CDER & other FDA components
- Information Package reviewed
- Advice given on how to further progress development for intended use
  - Consultation and advice
  - Continued until development is complete
- Full detailed CDER review and decision on qualification
- Formal statement of qualification if appropriate

# Points of Contact at CDER

## For Biomarker Qualification:

Marianne Noone
Regulatory Project Manager
Office of Translational Sciences (CDER)
(301) 796-7495
Marianne.noone@fda.hhs.gov

## For Regulatory Submissions (IND, NDA):

Kyong “Kaye” Kang
Chief, Project Management Staff
Division of Medical Imaging Products (CDER)
(301) 796-2050 (o)
kyong.kang@fda.hhs.gov

# Summary

- Standardization of production and use of imaging technologies will facilitate use in drug (and device) development trials, and uptake in clinical practice
- FDA intends to work with the community in standards development

# Summary

- The biomarker qualification process will be useful when considering use of an imaging technology as an important component in a drug development process
- Initiating qualification of an imaging biomarker will be contingent upon adequate standardization of the particular imaging process