Beginning with the End in Mind – Study Endpoints: Targeting Patient-Centered Outcomes

March 18-20 | North Bethesda, MD

PROGRAM CO-CHAIRS:

Linda S. Deal, MS
Head of Patient-Reported Outcomes
Shire

Elektra Papadopoulos, MD, MPH
Medical Officer
Study Endpoints and Labeling Development
CDER, FDA

PROGRAM COMMITTEE:

Dianne (Dee) Kennedy, MPH, RPh
Consumer Safety Officer
Study Endpoints and Labeling Development
CDER, FDA

Annabel Nixon, PhD
Director, Patient Reported Outcomes
PRMA Consulting

James Stansbury, PhD, MPH
Consumer Safety Officer
Study Endpoints and Labeling Development
CDER, FDA

Ashley Slagle, MS, PhD
Endpoints Reviewer
Study Endpoints and Labeling Development
CDER, FDA

Jessica Voqui, PharmD, MS
Regulatory Review Officer
Study Endpoints and Labeling Development
CDER, FDA

Keith Wenzel
Senior Director
Global Alliances
Perceptive Informatics

OVERVIEW:

Study endpoint measures in clinical trials determine what conclusions can be made about treatment benefit, medical differentiation, and value. For medical product developers, this evidence plays a critical role in drug development futility decisions as well. Measure selection varies depending upon the development phase and the specific objectives of the trial. Balancing the measurement objectives with various drug development stakeholder interests requires thoughtful planning and consideration. Evidence requirements to support labeling and promotion claims can require substantial time and effort to coordinate, especially when endpoint measures must be developed de novo.

During this meeting, you will gain insight into the tradeoffs and various stakeholder perspectives for developing a study endpoint measurement strategy, including detailed and practical tips for ensuring that measurement tools are adequate to support the targeted objectives with a focus on establishing instrument content validity for the specified clinical trial context of use.

AGENDA:

- Day One/Day Two AM: Review the scientific methods, issues, and execution challenges for internal and external stakeholders
- Day Two PM: Discuss measurements to achieve labeling and promotion claims
- Day Three: FDA will present good measurement principles ensuring that the measure is meaningful and interpretable

LEARNING OBJECTIVES:

At the conclusion of this conference, participants should be able to:

- Recognize the challenges sponsors face with setting an endpoint strategy and prioritizing the endpoint objectives across multiple internal stakeholders
- Discuss the scientific methods, issues and execution challenges for each of the respective internal and external stakeholder's endpoint goals
- Populate and employ strategic drug development tools such as the Target Product Profile to facilitate study endpoint objectives and regulatory interactions
- Discuss the characteristics of a clinically meaningful measurement instrument
- Apply good measurement principles to the development of clinical trial endpoints
- Discuss why the "context of use" is important to developing, evaluating, and interpreting meaningful measurements and appropriate measurement procedures
- Describe the key steps in meaningful measurement starting with establishing the conceptual basis for a patient-focused clinical outcome measure of treatment benefit

Register at **diahome.org/studyendpoints**

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TUESDAY, MARCH 18

8:30-8:45AM WELCOME AND OPENING REMARKS I

How Study Endpoints are Used and Why

Linda S. Deal, MS
Head of Patient-Reported Outcomes
Shire

8:45-9:30AM

Commercial Interest in Study Endpoints

Joseph Caminiti
President and Chief of Staff
BQ6 Media Group

Topics presented in this session include:

- The value of pharmaceutical agents and treatments depends on the proven efficacy, safety, and quality of care versus an accepted comparator
- There are potential differences in demonstrating efficacy and safety vs. suitability for P&T inclusion and/or reimbursement
- Commercialization involves leveraging the intrinsic properties of a compound to develop promotional strategies around the unique product attributes that provide value for physicians, patients, and payers
- Exploiting these "unique" properties with product promotion and sales support activities that support successful market launch and growth needs to be supported by data

9:30-10:15AM

Translational Medicine: The Bridge Between the Beginning and the End

Francisco Leon, MD, PhD
Vice President
Translational Medicine, Immunology Development
Janssen R&D (Pharmaceutical Companies of Johnson & Johnson)

Translational Medicine bridges preclinical and clinical development. "Reverse Translation" planning often results in recommendations for the development of patient-reported outcomes and biomarkers in early development. Challenges and case studies will be discussed.

10:15-10:30AM REFRESHMENT BREAK

10:30-11:15AM

Addressing Study Endpoints for Clinical Relevance

Debra Silberg, MD, PhD
Senior Director
Clinical Development
Shire

Diseases can be evaluated by changes in physiology, signs, and symptoms. When performing a clinical study, it is important to determine the endpoint that is most clinically relevant, discussing with both clinicians and patients what they are looking for from the treatment. The view may not always be the same, but should be taken into consideration when evaluating efficacy. This talk will discuss different endpoints from the viewpoint of both the patient and clinician.

11:15AM-12:00PM

Study Endpoints: A Market Access Perspective

Mohan Bala, PhD
Head
Oncology Value & Access
Sanofi

Topics presented in this session include:

- Overview of market access process and evolving concept of value
- Relevance of study endpoints for market access
- Payer perspective on endpoints from key countries: a few illustrative examples
- Study endpoints and market access: What does the future hold?

12:00-1:00PM LUNCH

1:00-1:45PM PANEL DISCUSSION

What Does Differentiation Mean to You and How You Select Endpoints?

MODERATOR

Linda S. Deal, MS
Head of Patient-Reported Outcomes
Shire

Topics discussed in this session include:

- All stakeholders want differentiation – are we talking about the same thing?
- What is(are) the priority(ies)? How are these determined/traded off? Are there specific scenarios that influence this e.g. first in class, best in class, second generation of same mechanism of action (i.e. potential generic competition), etc.?
- Speaker representatives of the stakeholder functions to participate
- The regulatory tight rope

1:45-2:30PM

Tools to Help Gain Alignment in the Project Team

Charles Gombar, PhD
Senior Vice President, Project Management and Pharmaceutical Development
Endo Pharmaceuticals

There is more than one way to develop most new drugs. A key challenge in pharmaceutical R&D is establishing and maintaining alignment on the development strategy and plan in the project team. This session will highlight some tools that can be used to ensure that a development plan is aligned with the value proposition for the new product.

2:30-2:45PM REFRESHMENT BREAK

2:45-3:30PM

Beginning with the End in Mind – Who Should Care?

Evan Loh, MD
Chairman
Board of Directors
Chief Medical Officer
Paratek Pharmaceuticals

As project teams advance products during development, there is a natural tension between the merits of any single project and "the portfolio" views considered by executive governance. As project teams move forward passionately, who should care about the merits and applicability of the strategy to achieve the endpoints demonstrating diferentiation as well as the strength of the clinical data that enables teams to learn and confirm whether a given compound will become a medicine of tomorrow. That all being said, will the internal company culture of decision-making, governance and leadership truly result in bold and courageous commitments on which compounds will ultimately possess the greatest value for patients, physicians, and other stakeholders.

3:30-4:00PM WRAP UP AND SUMMARIZE THE DAY

WEDNESDAY, MARCH 19

8:30-8:45AM WELCOME, REFRESH OF DAY 1, AND INTRODUCTION OF DAY 2 AGENDA

What Does it Take to Achieve the Study Endpoint Goals Discussed in Day 1?

Linda S. Deal, MS
Head of Patient-Reported Outcomes
Shire

8:45-9:30AM

Adaptive Designs and Endpoint Selection

Scott Berry, PhD
President and Senior Statistical Scientist
Berry Consultants

The selection of endpoints in the learn phases of trials can be a very difficult problem typically involving the time of the trial, the relevance of the endpoint, and the power of the study. Many times decisions to select short term endpoints, for the sake of speed of getting to phase III can create poor dose selection, incorrect go/no-go decisions, and inefficient drug development. The issue can be more complex in an adaptive trial design because of the need to provide information for the adaptations. A strength of the adaptive design is that it can utilize endpoints in different ways — early markers can be used as possibly correlated to the more appropriate long-term endpoint, and this correlation can be modeled and informed by the trial, and thus the design can be made more efficient and yet the focus is on the more relevant long-term clinical endpoint.

In this talk the selection of endpoints, the modeling of different endpoints, within the building and simulation of an adaptive clinical trial will be discussed. Real examples of endpoint selection within adaptive designs will be presented.

9:30-10:15AM

Overcoming Regulatory Challenges in Targeting Patient-Centered Outcomes in Psychiatric Drug Development

Thomas Laughren, MD
Director
Laughren Psychopharm Consulting, LLC.

Selecting the primary measure for a definitive trial and defining the primary study endpoint are critical steps in any drug development program. There is increasing interest in using patient-reported outcome (PRO) measures in registration trials, and these measures present many challenges, including regulatory challenges. Included among the regulatory challenges are redundancy with investigator rated measures and pseudo-specificity. This session will discuss possible approaches to overcoming these and other regulatory challenges associated with PROs.

10:15-10:30AM REFRESHMENT BREAK

10:30-11:15AM

Patient-Centered Outcomes Targeting Payers and Regulators

Ethan M. Basch, MD
Director
Cancer Outcomes Research Program
Associate Professor of Medicine
University of North Carolina at Chapel Hill

Payers seek information about the comparative value of products, and increasingly consider the patient experience as an important component of value. Patient-reported outcome (PRO) data may be desired or requested by payers including information about symptoms, functional status, harms of care, treatment preferences, and/or quality of life. There is some overlap with the informational needs and published guidance of regulators. New standards for PROs have also emerged from several entities involved with evaluating comparative effectiveness and quality of care.

11:15AM-12:00PM

Study Endpoints and Patient-Centered Outcomes: Payer Needs vs Regulatory Limits

Paul Radensky, MD
Partner
McDermott Will & Emery LLP

Payers are increasingly asking for value information to support coverage and pricing decisions about new drugs and medical devices. Sometimes the data payers want do not fit squarely within the labeling of the medical product. Many were hopeful that Section 114 of FDAMA and the guidance on patient-reported outcomes would reduce uncertainty about what manufacturers could communicate to payers about their products, but much uncertainty—and potential risk—remains. This talk will explore the regulatory landscape for payer communications and consider some options to bridge payer needs and regulatory limits.

12:00-12:15PM **Q & A**

12:15-1:15PM **LUNCH**

1:15-1:30PM **RECAP OF MORNING SESSION AND INTRODUCTION TO AFTERNOON SESSION**

Linda S. Deal, MS
Head of Patient-Reported Outcomes
Shire

Elektra Papadopoulos, MD, MPH
Medical Officer
Study Endpoints and Labeling Development
CDER, FDA

Measurement to Achieve Labeling and Promotion Claims

Good measurement principles form the foundation for clinical outcome measurement. Investment in measurement will ultimately benefit people with diseases, drug developers, clinical trialists, and regulatory authorities. This session will provide an overview of the comprehensive process of creating and implementing a new outcome measure or modifying an existing instrument. The development of a patient-based, clinical outcome measure that will support a labelling claim requires advance planning in the early phases of product development. Establishing the context of use and planning the protocol for qualitative research that thoroughly explores the conceptual basis for measurement are fundamental. This session emphasizes the importance of identifying what is meaningful to be measured based on the context of use for measurement, getting the content right, and finally, ensuring that the measure is meaningful and interpretable.

1:30-3:00PM

Navigating Instrument Development Using the Wheel and Spokes

Session Chair

Jessica Voqui, PharmD, MS
Regulatory Review Officer
Study Endpoints and Labeling Development
CDER, FDA

This session will give an overview of the process of instrument development as illustrated by the Wheel and Spokes diagram. Responses by EMA and OPDP representatives will explain the relevance of this diagram to their regulatory settings.

Roadmap to Patient-Focused Outcome Measurements in Clinical Trials

Elektra Papadopoulos, MD, MPH
Medical Officer
Study Endpoints and Labeling Development
CDER, FDA

EMA Response (Via Telecommunications)

Maria Isaac, MASc, MD, PhD
Scientific Administrator
European Medicines Agency (EMA), European Union

OPDP Response

Elaine Hu Cunningham, PharmD
Senior Regulatory Review Officer
OPDP
CDER, FDA

Panel Discussion

Moderator

Jessica Voqui

Panelists

Elaine Hu Cunningham

Maria Isaac

Elektra Papadopoulos

3:00-3:15PM **REFRESHMENT BREAK**

3:15-4:30PM

Spoke 1: Defining the Clinical Trial Context of Use

SESSION CHAIR

Ashley F. Slagle, MS, PhD
Endpoints Reviewer
Study Endpoints and Labeling Development
CDER, FDA

Good measurement depends on a clearly defined context of use, including explicit consideration of the targeted disease definition, patient population, clinical trial design and objectives, clinical practice, and other aspects of the study setting.

Context of Use: An FDA Perspective

Ashley F. Slagle
Endpoints Reviewer
Study Endpoints and Labeling Development
CDER, FDA

Context of Use: Industry Perspective

Debra Silberg, MD, PhD
Senior Director
Clinical Development
Shire

Context of Use: Patient Advocate Perspective

Cynthia Bens, MBA
Vice President
Public Policy, Accelerate Cure/Treatments for Alzheimer's Disease (ACT-AD)
Alliance for Aging Research

Panel Discussion

MODERATOR

Ashley F. Slagle

PANELISTS

Cynthia Bens

Debra Silberg

4:30-4:45PM WRAP-UP AND ADJOURNMENT OF THE DAY

4:45-5:45PM NETWORKING RECEPTION

THURSDAY, MARCH 20

8:30-8:45AM WELCOME, REFRESH OF DAY 2, AND INTRODUCTION OF DAY 3 AGENDA

Attention to Measurement in Clinical Trials: Why it Matters

Elektra Papadopoulos, MD, MPH
Medical Officer
Study Endpoints and Labeling Development
CDER, FDA

8:45-10:15AM

Conceptualization and Generation of a Draft Measure

Session Chair

Elektra Papadopoulos, MD, MPH
Medical Officer
Study Endpoints and Labeling Development
CDER, FDA

Along with a clearly defined context of use, clear conceptualization provides the foundation for the process of instrument development. This is particularly important in clinical trials for regulatory purposes because the concept of interest becomes the labeling claim. Once there is clarity in conceptualization, the qualitative research process may begin.

Spoke 1: Conceptualization and Making the Case for Content Validity

Donald Patrick, PhD, MPH
Professor
Health Services, School of Public Health
University of Washington

Spoke 2: Interview, Qualitative Analysis, and Item Development Techniques

Ashley Slagle, PhD, MS
Endpoints Reviewer
Study Endpoints and Labeling Development
CDER, FDA

James Stansbury, PhD, MPH
Consumer Safety Officer
Study Endpoints and Labeling Development
CDER, FDA

10:15-10:30AM REFRESHMENT BREAK

10:30-11:45PM

Spoke 2: Interview, Qualitative Analysis, and Item Development Techniques continued

Ashley Slagle, PhD, MS
Endpoints Reviewer
Study Endpoints and Labeling Development
CDER, FDA

James Stansbury, PhD, MPH
Consumer Safety Officer
Study Endpoints and Labeling Development
CDER, FDA

Panel Discussion

Moderator

Elektra Papadopoulos

Panelists

Cynthia Bens

Donald Patrick

Ashley Slagle

James Stansbury

11:45AM-12:45PM LUNCH

12:45-2:15PM

Confirming Content Validity: Finalizing a Measure with an Interpretable Score

Session Chair

Jessica Voqui, PharmD, MS
Regulatory Review Officer
Study Endpoints and Labeling Development
CDER, FDA

This session builds from the basis of the well-conceptualized draft instrument, looking at methods for finalizing a clinically meaningful instrument that provides interpretable measurement in a specific context of use. The session focuses on exploratory use of mixed methods that incorporate quantification to refine meaning and content.

Spoke 2 continued:

Jeremy Hobart, PhD, FRCP
Professor
Clinical Neurology and Health Measurement
Peninsula College of Medicine and Dentistry
United Kingdom

Panel Discussion

Moderator

Jessica Voqui

Panelists

Cynthia Bens

Jeremy Hobart

Ashley Slagle

James Stansbury

2:15-2:30PM REFRESHMENT BREAK

2:30-3:45PM

Spoke 3 and 4: Completing the Dossier: Reliability, Construct Validity, Ability to Detect Change, and Interpretation Metrics

Session Chair

Paivi Miskala, MSPH, PhD
Endpoints Reviewer
Study Endpoints and Labeling Development
CDER, FDA

After content validity is demonstrated, other measurement properties specific to the context of use, need to be demonstrated. This session is dedicated to research methods for identifying the other measurement properties—reliability, construct validity, and the ability to detect change. In addition the metrics of clinically meaningful change in the particular context of use will be discussed.

Practical Consideration when Planning the Evaluation of Measurement Properties

Patrick Marquis, MD, MBA
President
TwoLegs Consulting, LLC

Longitudinal Psychometric Evaluation

Laura Lee Johnson, PhD
Statistician
National Center for Complimentary and Alternative Medicine
National Institutes of Health

Interpretation of Scores

Lisa Kammerman, PhD
Master Reviewer
Office of Biostatistics
CDER, FDA

Panel Discussion

Moderator

Paivi Miskala

Panelists

Cynthia Bens

Jeremy Hobart

Laura Lee Johnson

Lisa Kammerman

Patrick Marquis

Elektra Papadopoulos

3:45-4:00PM WRAP UP

Elektra Papadopoulos, MD, MPH
Medical Officer
Study Endpoints and Labeling Development
CDER, FDA

4:00PM MEETING ADJOURNED