# 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**
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Study Endpoints and Labeling Development
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## 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
- Explain how to 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**
Executive Vice President, Director Client Services-Professional
H4B Catapult, a division of Havas Health Inc.

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

**William Jacobson, PhD**
Medical Director, CNS, Clinical Science
Takeda Development Center Americas

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 Differentiation in Mind – Easier Said than Done

**Linda S. Deal**
Head of Patient-Reported Outcomes
Shire

Because yesterday's blockbuster is today's generic, the complexity of the development process for new drugs includes raised approval, adoption and reimbursement hurdles. To be competitive and truly groundbreaking, pharmaceutical and biotech companies must be willing to begin earlier in development to evaluate an asset's potential to differentiate. And, because developing a new endpoint/outcomes measure takes time and investment, an early understanding of the end target(s) is critical when evaluating whether an existing clinical outcomes measure will be sufficient, whether it will need to be adapted, or whether a new measure needs to be developed, for addressing the program goals. The current state of regulatory challenges for study endpoints requires early planning and must be integrated into and accounted for within the overall development strategy. Internal company infrastructure, processes and governance may also present a challenge and may need to be reengineered to meet patient-centric objectives while still adhering to competitive timelines that optimize return on research and development investment and patent terms. This session further emphasizes the case for beginning early with the intention to differentiate, and discusses some of the internal and regulatory challenges to carrying out this objective.

**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** (Via Telecommunications)
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**
Senior Scientific Officer
Product Development Scientific Support Department
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 P. Stansbury, PhD, MPH**
Social Science Analyst
Division of Non-Prescription Clinical Evaluation
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 P. Stansbury, PhD, MPH**
Social Science Analyst
Division of Non-Prescription Clinical Evaluation
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**
Senior Principal Scientist
AstraZeneca

## 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