# Development and Validation of Clinical Trial Endpoints



## Goals of Talk

- Introduce and define concept of endpoints
- Discuss development & validation of clinical endpoints, for efficacy clinical trials

## What is an endpoint?



# <u>Why</u> do we need endpoints in efficacy clinical trials?

- improved survival
- improvement in symptoms or functioning



## Endpoint terms

What are we measuring?

Concept of Interest COI

How are we measuring it?

Clinical Outcome Assessment

COA

Why, where, when, & with whom are we measuring it?

Context of Use COU



# Concept of Interest (COI)<sup>6</sup>

What are we measuring?

What

• Biologic, physiologic, symptomatic, functional

What

What

• Improve? Stabilize? Prevent?



# Clinical Outcomes Assessment (COA) 1,3,7,9

#### How are we measuring it?

How

- Meaningful to patients?
- Is the measurement...? survival, disease exacerbation, clinical event, etc.

symptom score, "health related quality of life", etc.

Context of Use<sup>1, 3,6,9</sup>

#### Why, Where, When, & with Whom are we measuring it?

Why

#### Where

- Geographic location? Language / culture?
- Clinical practice variations

When

• Weekly? Monthly? Once a year?

With Whom?

# Other characteristics of endpoints<sup>1, 4-</sup>



#### FDA Patient-Reported Outcomes Guidance -Published in December 2009<sup>1</sup>



"Claim"

http://www.fda.gov/downloads/Drugs/GuidanceCompliance RegulatoryInformation/Guidances/UCM193282.pdf

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# What is a biomarker?<sup>10</sup>

- A lab measure
- Objectively measured
- - Normal biologic process
  - Disease
  - Response to treatment

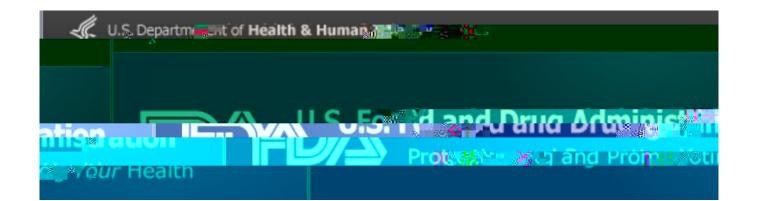
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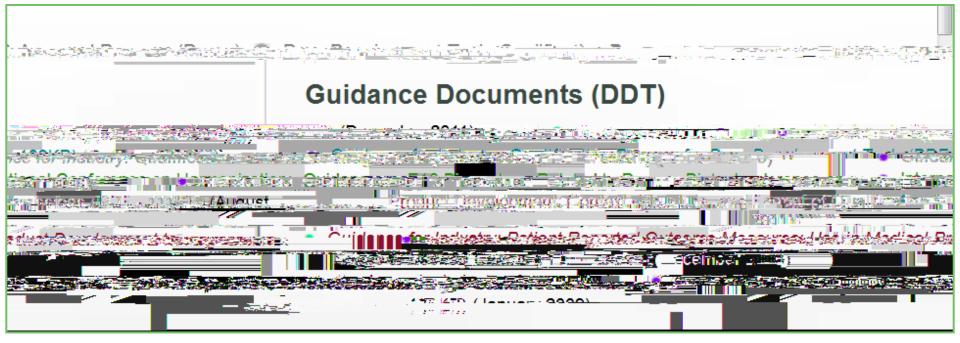
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## Features of Validated, Surrogate Biomarker Endpoints for Efficacy Trials<sup>11</sup>

- <u>Indirect</u> endpoints
- Ideally, should exist within the therapeutic pathway between the drug and meaningful benefit
- Expected to reflect changes in a clinically meaningful endpoint

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# Conclusions

#### ...use <u>validated</u> Clinical Outcome Assessments, to measure a specific Concept of Interest, for a specific Context of Use.

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#### Source Material

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- 2. Drug Development Tools Qualification Program: Clinical outcome Assessment (COA) Glossary of Terms. <u>http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DrugDevelopment</u> <u>ToolsQualificationProgram/ucm370262.htm</u>
- "Exploring Clinical Outcome Assessments in Rare Disease Trials" Presented by Laurie B. Burke PhD, Associate Director for Study Endpoints and Labeling, Office of New Drugs, CDER, FDA, *Rare Disease Workshop Series,* June 14-15, 2011. Sponsored by: EveryLife Foundation for Rare Diseases
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- Nancy Kline Leidy, PhD, VP Scientific Affairs, United BioSource Corporation, Bethesda, MD. Addressing Content Validity of PRO Measures: The Unique Case of Rare Diseases. Rare Disease Workshop Series – Improving the Clinical Development Process. Everylife Foundation.
- 7. Nunnally, J (1978). Psychometric Theory. New York: McGraw-Hill.
- 8. EveryLife Foundation: Workshop 3, November 2011: Use of surrogate endpoints in rare disease treatment development



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