Development and Validation of Clinical Trial Endpoints

1. Introduce and define concept of endpoints
2. Discuss development & validation of clinical endpoints, for efficacy clinical trials

- improved survival
- improvement in symptoms or functioning
- [illegible] symptom [illegible]

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

- Biologic, physiologic, symptomatic, functional

- Improve? Stabilize? Prevent?

1,3,7, 9

- Meaningful to patients?
- Is the measurement…?

  survival, disease exacerbation, clinical event, etc.

  symptom score, “health related quality of life”, etc.

1, 3,6, 9

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

- Weekly? Monthly? Once a year?

1, 4-


Office of New Drugs
http://www.fda.gov/Drugs

FDA Patient-Reported Outcomes Guidance – Published in December 2009[1]

"Claim"

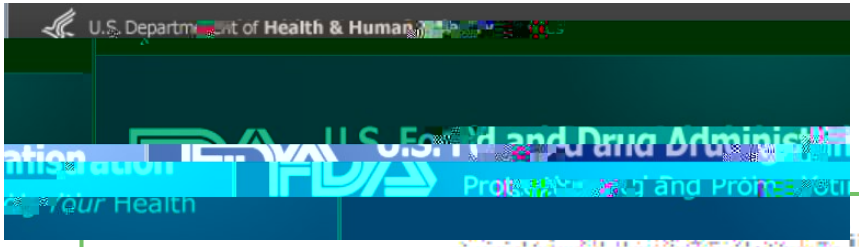
...

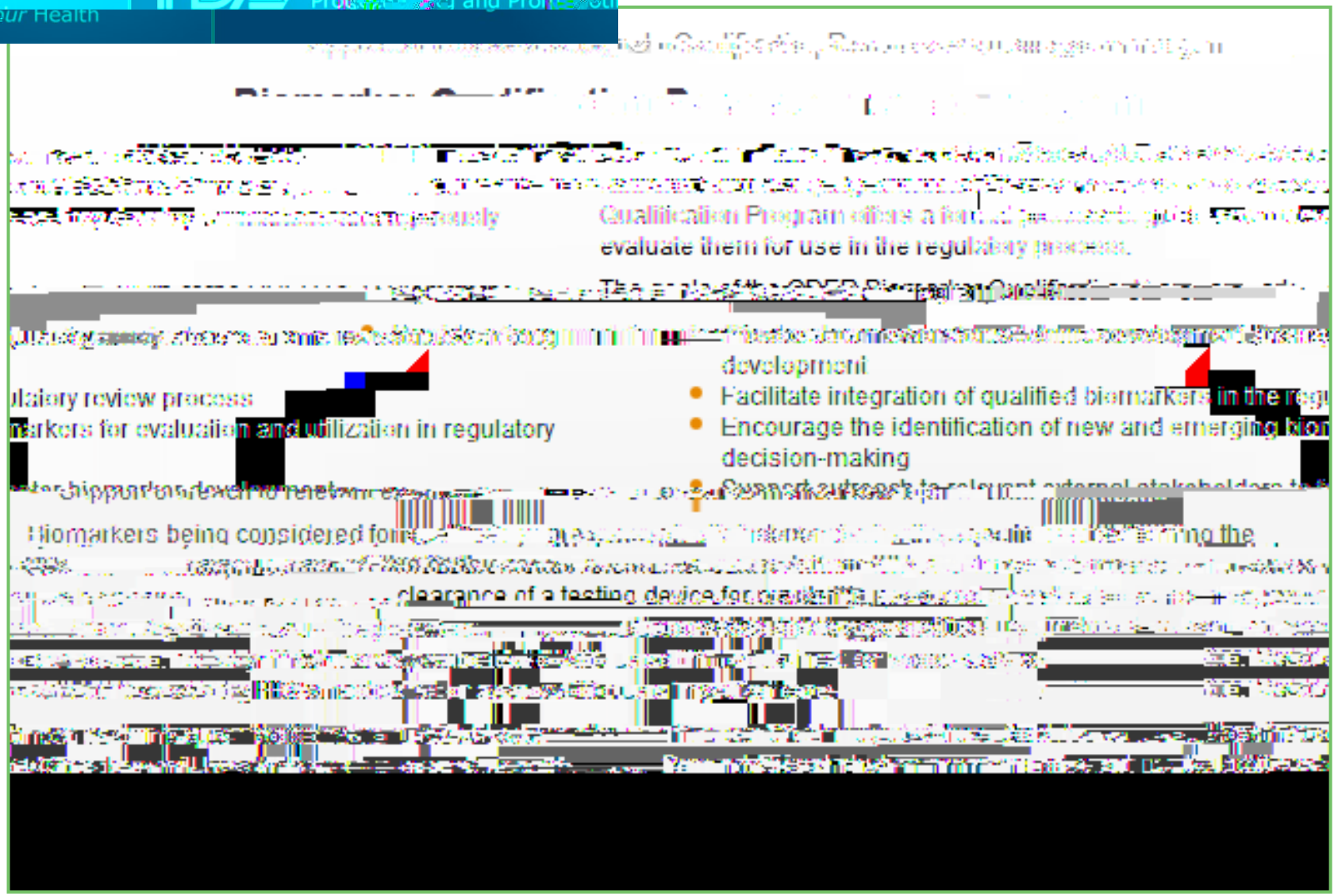
http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM193282.pdf

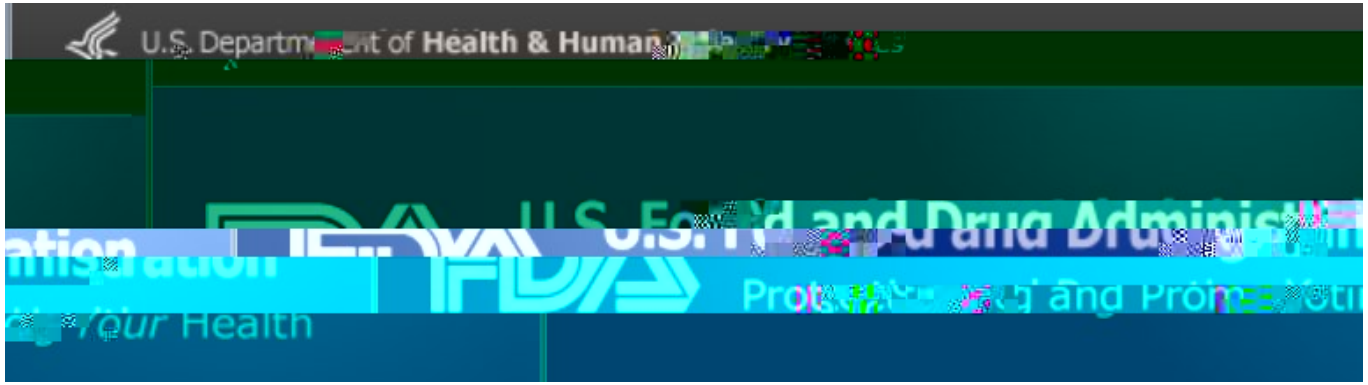
- A lab measure
- Objectively measured
- ...
  - Normal biologic process
  - Disease
  - Response to treatment

Features of Validated, Surrogate Biomarker Endpoints for Efficacy Trials[11]

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


U.S. Department of Health & Human
U.S. Food and Drug Administration
Protecting and Promoting
Your Health


Qualification Program allows a for
evaluate them for use in the regulatory process.
developmen
Facilitate integration of qualified biomarkers in the reg
Encourage the identification of new and emerging bion
decision-making
clearance of a testing device for



Guidance Documents (DDT)

...use validated Clinical Outcome Assessments,
to measure a specific Concept of Interest,
for a specific Context of Use.

~

Source Material

1. **ñClinical trial endpoints: Development and validation of measures to support claims in labeling**" Presented by Laurie B. Burke PhD, Associate Director for Study Endpoints and Labeling. At Office of New Drugs, CDER, FDA. *Accelerating Therapies for Rare Diseases Workshop,* October 19, 2010

2. **Drug Development Tools Qualification Program**: Clinical outcome Assessment (COA) Glossary of Terms. http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DrugDevelopmentToolsQualificationProgram/ucm370262.htm

3. "**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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Source Material

5. Thomas R Fleming, PhD. "**Introduction to some important issues in evaluating efficacyò.** June 14, 2011, Rare Disease Workshop Series – Improving the Clinical Development Process. Everylife Foundation.

6. 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**

9. Sullivan, EJ. **Clinical Trial Endpoints.** FDA, CPI, CTTI

10. BIOMARKERS DEFINITIONS WORKING GROUP: BIOMARKERS AND SURROGATE ENDPOINTS: PREFERRED DEFINITIONS AND