Pilot Clinical Outcome Assessment Compendium (COA Compendium) Webinar

March 8, 2016

Objectives

This webinar will:

1. Familiarize the audience with the Pilot COA Compendium
2. Address questions about the Pilot COA Compendium.

You may submit your questions at any time during the webinar. Questions will be addressed after the presentation during the Q&A session.

Please submit your questions to:
CDERSBIA@fda.hhs.gov

Webinar Agenda

1. Introductions by Forest (Ray) Ford, PharmD, CDR, USPHS
2. Background/Overview of COA Compendium by Elektra Papadopoulos, MD, MPH
3. COA Compendium Demo by Nikunj B. Patel, PharmD
4. FDA Panel Discussion
   - Elektra Papadopoulos, MD, MPH
   - Paul Kluetz, MD
   - Christina Fang, MD, MPH
   - Andrew Mulberg, MD, FAAP, CPI
5. Q & A Session
6. Wrap-up

Background & Overview

Purpose of the COA Compendium

FDA's effort to foster patient-focused drug development by collating and summarizing COA information for many different diseases and conditions into a single resource intended to:

- **facilitate communication**
- **provide clarity and transparency**
- **be used as a starting point for early drug development**

Clinical Outcome Assessment

Assessment of a clinical outcome can be made through report by a clinician, a patient, a non-clinician observer or through a performance-based assessment. There are four types of COAs.

- clinician-reported outcome
- observer-reported outcome
- patient-reported outcome
- performance outcome

Please visit following website with a complete list of Glossary of Terms:
http://www.ncbi.nlm.nih.gov/books/NBK338448/pdf/Bookshelf_NBK338448.pdf

What is the Pilot COA Compendium?

A collaborative initiative by the COA Staff & OND Review Divisions

The *COA Compendium* is a table that

1. **Describes how certain *clinical outcome assessments* have been used in clinical trials to measure the patient's experience (such as disease-related symptoms) and to support labeling claims.**

2. **Identifies clinical outcome assessments that have been qualified for potential use in multiple drug development programs under the COA type of the Drug Development Tool (DDT) Qualification Program of the Center for Drug Evaluation and Research (CDER).**

3. **Recognizes ongoing qualification projects to encourage community collaboration in the development of clinical outcome assessments for unmet measurement needs.**

How were COAs Selected for the Pilot COA Compendium?

COA Qualification Program

1. Collation of qualified and ongoing qualification projects
2. Permissions obtained from the qualification instrument developers for public posting

Approved Drug Labeling

1. Retrospective Review of Approved Drug Labeling (NMEs only 2003 – 2014)
2. Collaboration with OND review divisions

Pilot COA Compendium

NME = New Molecular Entity

What is in the COA Compendium and what is not?

The pilot version is limited in scope to enable FDA to obtain public input.

The pilot includes:

- **Labeled COAs from a retrospective review of a small subset of approved new molecular entity (NME) drug labeling between 2003 and 2014**
- **Qualified COAs and ongoing qualification projects as of December 31, 2015**

The pilot does not include:

- **Labeled COAs from efficacy supplement drug labeling**
- **Labeled COAs from approved drug labeling prior to 2003 or after 2014**
- **Labeled COAs in certain cases such as where FDA has issued guidance that provides recommendations for using different outcome measure(s)**

Sponsors are strongly encouraged to seek the relevant Office of New Drug (OND) review division's advice early (e.g., pre-IND meeting) and throughout drug development to discuss COA selection and implementation specific to their program, irrespective of whether the disease, condition, indication, claim, or COA is included in the COA Compendium.

IND = Investigational New Drug

The *COA Compendium* includes the following six columns

COLUMNS	ELEMENTS	DESCRIPTION OF CONTENT
1	Disease/Condition	Lists disease or condition and any relevant FDA disease-specific guidance.
2	Indication and/or Claim(s) Description	Lists key elements of indication and/or claim (either labeled or qualified). For ongoing COA qualification projects, targeted labeling or promotional claim(s) may not be yet known and may be described as "to be determined." **Inclusion of a clinical outcome assessment in the COA Compendium is not intended to indicate that the measure is or should be the sole (or primary) determinant of a clinical benefit in a particular clinical trial.*
3	Outcome of Interest	Describes an outcome of interest that was assessed (labeled) or could be assessed (in our qualification program) by clinical outcome assessment(s) displayed in Column 4.
4	COA (COA Type)	• Lists a labeled, qualified, or ongoing qualification project clinical outcome assessment name and/or description. • Includes the clinical outcome assessment type (i.e., a patient-reported outcome, observer-reported outcome, clinician-reported outcome, or performance outcome).
5	COA Context of Use	Describes circumstances under which the outcomes of interest and the clinical outcome assessment have been used (i.e., labeled) or are targeted for use (i.e., they have been qualified or are part of an ongoing qualification).
6	COA Qualification Information	Lists ongoing and completed clinical outcome assessment qualification project information, if applicable.

COA Compendium

What it is:

- **A communication tool to promote transparency between FDA and drug developers**
- **Method to improve collaboration by describing ongoing qualification efforts**
- **Method to encourage the development and use of COAs (especially those that are important to patients)**

What it is not:

- **All-inclusive list**
- **A way to stifle innovation**
- **A replacement for existing communication channels with review divisions (e.g., pre-IND, EOP 2 meetings)**
- **A replacement for existing disease-specific guidances or qualification**

IND = Investigational New Drug
EOP2 = End of Phase 2

Future Directions

- **Review of public comments**
- **Scope expansion**
- **Manual of Policies & Procedures (MAPP)**
- **Draft guidance**

COA Compendium Demo

www.fda.gov

www.fda.gov/coacompendium

(http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/UCM459231.htm)

FDA Panel Discussion

- **Elektra J. Papadopoulos, MD, MPH**
  Acting Associate Director, Clinical Outcome Assessments Staff (COA Staff)
- **Paul Kluetz, MD**
  Associate Director, Division of Hematology and Oncology Products
- **Christina Fang, MD, M.P.H.**
  Medical Officer, Division of Anesthesia, Analgesia, and Addiction Products
- **Andrew Mulberg, MD, FAAP, CPI**
  Deputy Division Director, Division of Gastroenterology and Inborn Errors Products

FDA Panel Discussion

- **Impact on FDA communication with drug developers**
- **Spur innovation and development of well-defined and reliable COAs in areas of unmet measurement need by encouraging collaborative efforts (e.g., COA Qualification Program)**
- **Potential advantages and disadvantages**

Q & A Session

Please submit your questions to: CDERSBIA@fda.hhs.gov

We encourage you to submit written comments to the Docket No. FDA-2015-N-5106
(Public Comment Period Ends by March 14, 2016)

Link to the Docket: https://www.federalregister.gov/articles/2016/01/13/2016-00529/clinical-outcome-assessment-compendium

Key Takeaways

- **The FDA encourages the development and implementation of patient-focused clinical outcome assessments (COAs) in clinical trials to support drug approvals and labeling claims.**
- **The COA Compendium is intended to facilitate communication and to provide clarity and transparency to drug developers and the research community.**
- **The FDA seeks public feedback on the initial release and suggestions for future expansion of the COA Compendium.**

Relevant Resources

- **FDA COA Staff Website:** http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm349031.htm#Endpoints
- **COA Qualification Website:** http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DrugDevelopmentToolsQualificationProgram/ucm284077.htm
- **COA Compendium Website:** http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/ucm459231.htm
- **PRO Guidance:** http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM193282.pdf
- **DDT COA Qualification Guidance:** http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM230597.pdf

THANK YOU!

We encourage you to submit written comments to the Docket No. FDA-2015-N-5106
(Public Comment Period Ends by March 14, 2016)

Link to the Federal Register Notice & Docket:
https://www.federalregister.gov/articles/2016/01/13/2016-00529/clinical-outcome-assessment-compendium

ADDITIONAL SLIDES

What are key considerations of the COA Compendium?

- **The *COA Compendium* is not a comprehensive list of clinical outcome assessments and is not intended to replace either existing disease-specific guidance or key interactions with FDA concerning drug development (e.g., during pre-IND meetings). Inclusion of a clinical outcome assessment in the *COA Compendium* is not intended to indicate that the measure is or should be the sole (or primary) determinant of a clinical benefit in a clinical trial.**
- **Drug sponsors are strongly encouraged to seek advice from the relevant Office of New Drug (OND) review division early in drug development to discuss the selection and implementation of the clinical outcome assessment specific to their program, irrespective of whether the disease, condition, indication, claim, or clinical outcome assessment is included in the *COA Compendium*.**
- **Some of the clinical outcome assessments listed in the *COA Compendium* may be protected by proprietary rights, and in some cases, a royalty and fee may be charged by the copyright owners for their authorized use. The inclusion of a clinical outcome assessment in the *COA Compendium* does not equate to an endorsement by FDA**

Select Glossary of Terms

Clinician-reported outcome

A type of clinical outcome assessment. A measurement based on a report that comes from a trained health-care professional after observation of a patient's health condition. Most ClinRO measures involve a clinical judgment or interpretation of the observable signs, behaviors, or other manifestations related to a disease or condition. ClinRO measures cannot directly assess symptoms that are known only to the patient. ClinRO measures include:

- **Reports of particular clinical findings (e.g., presence of a skin lesion or swollen lymph nodes) or clinical events (stroke, heart attack, death, hospitalization for a particular cause), which can be based on clinical observations together with biomarker data, such as electrocardiogram (ECG) and creatine phosphokinase (CPK) results supporting a myocardial infarction**
- **Rating scales, such as:**
  - **Psoriasis Area and Severity Index (PASI) for measurement of severity and extent of a patient's psoriasis**
  - **Hamilton Depression Rating Scale (HAM-D) for assessment of depression**

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Select Glossary of Terms

Observer-reported outcome

A type of clinical outcome assessment. A measurement based on a report of observable signs, events or behaviors related to a patient's health condition by someone other than the patient or a health professional. Generally, ObsROs are reported by a parent, caregiver, or someone who observes the patient in daily life and are particularly useful for patients who cannot report for themselves (e.g., infants or individuals who are cognitively impaired). An ObsRO measure does not include medical judgment or interpretation. ObsRO measures include:

- **Rating scales, such as:**
  - **Acute Otitis Media Severity of Symptoms scale (AOM-SOS), a measure used to assess signs and behaviors related to acute otitis media in infants**
  - **Face, Legs, Activity, Cry, Consolability scale (FLACC), a measure used to assess signs and behaviors related to pain**
- **Counts of events (e.g., observer-completed log of seizure episodes)**

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Select Glossary of Terms

Patient-reported outcome

A type of clinical outcome assessment. A measurement based on a report that comes directly from the patient (i.e., study subject) about the status of a patient's health condition without amendment or interpretation of the patient's response by a clinician or anyone else. A PRO can be measured by self-report or by interview provided that the interviewer records only the patient's response. Symptoms or other unobservable concepts known only to the patient can only be measured by PRO measures. PROs can also assess the patient perspective on functioning or activities that may also be observable by others. PRO measures include:

- **Rating scales (e.g., numeric rating scale of pain intensity or Minnesota Living with Heart Failure Questionnaire for assessing heart failure)**
- **Counts of events (e.g., patient-completed log of emesis episodes or micturition episodes)**

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Select Glossary of Terms

Performance outcome

A type of clinical outcome assessment. A measurement based on a task(s) performed by a patient according to instructions that is administered by a health care professional. PerfOs require patient cooperation and motivation. PerfO measures include:

- **Measures of gait speed (e.g., timed 25 foot walk test)**
- **Measures of memory (e.g., word recall test)**

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http://www.ncbi.nlm.nih.gov/books/NBK338448/pdf/Bookshelf_NBK338448.pdf