An Analysis of Clinical Outcome Assessment (COA) Trends for Neurological and Psychiatric Drug Approvals

Steven Brettler, Elektra Papadopoulos

Division of Clinical Outcomes Assessment, Office of Drug Evaluation Sciences, Office of New Drugs, Center for Drug Evaluation and Research
FDA White Oak Campus, 10903 New Hampshire Ave, White Oak, MD 20903
Steven.Brettler@fda.hhs.gov; Elektra.Papadopoulos@fda.hhs.gov

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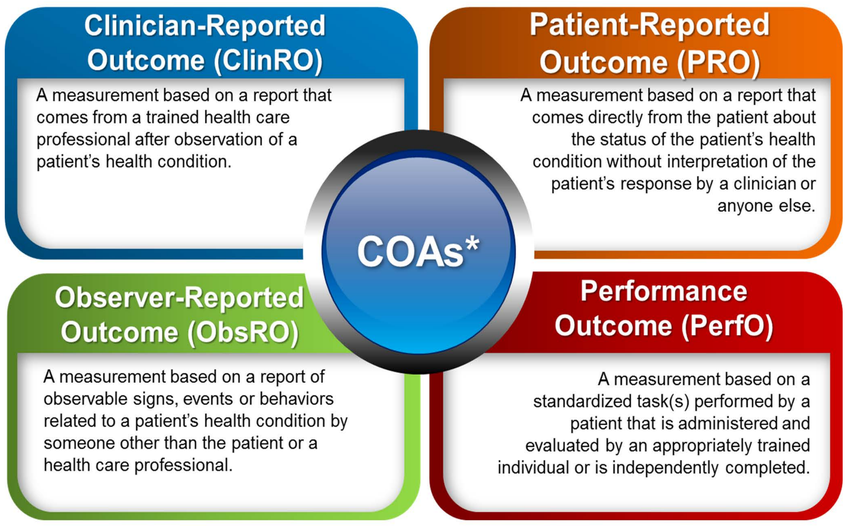
Introduction

COA Compendium

The COA Compendium is part of FDA's efforts to foster patient-focused drug development. The Compendium is a living document intended to facilitate communication and to provide clarity and transparency to drug developers and researchers by collating and summarizing clinical outcome assessment (COA) information for many different diseases and conditions into a single resource.

A COA is a measure used to assess how patients feel, function, or survive. Currently, there are four major types of COAs as shown in Figure 1.



*Digital health technology (e.g., activity monitors, sleep monitors) can also be used to collect clinical outcomes.

Figure 1: Major types of COA diagram

The COA Compendium is a table that[1]

- Describes how certain COAs have been used in clinical trials to measure the patient's experience and to support FDA labeling claims
- Identifies COAs that have been qualified under the CDER Drug Development Tool (DDT) Qualification Program to assess clinical concepts of interest within a specific context of use

COA Trends for Neurology & Psychiatry

The COA Compendium collates COAs from approved drug labels dating back to 2003. There is an opportunity to review potential trends of COAs from New Molecular Entities (NMEs) that can span more than a decade. NMEs can be approved under a New Drug Application (NDA) via *type 1* (New Molecular Entity) or *type 1,4* (New combination with at least one of the active moieties as an NME) as well as Biologics License Applications (BLA).[2,3] The COA Compendium also describes and references COAs qualified through CDER's DDT Qualification Program.

Project objective

To explore trends over time in COA types included in NME labeling for drugs approved by the Neurology and Psychiatry review divisions within FDA.

Methods

Phase 1: Catalog NME Approvals from 2003 to 2018

- Utilized Drugs@FDA database via Drug Approvals by Month
  - Searched database from January 2003 to December 2018
    - Selected all BLAs, Type 1s and Type 1/4s for consideration
    - Categorized approvals to each division based on indications and/or clinical trials from labeling (Drugs@FDA & DailyMed)

Phase 2: Quantify COA types via COA Compendium

- Per drug and disease/COA Context of Use, each COA tool type was tallied
  - COA types that were recurrent in each drug approval and disease/COA Context of Use were counted only once
- Efficacy supplements (ES) were excluded, as the focus is only on NME labeling

Results

There were over 1500 NDA and BLA approvals during the analysis period, which included 494 NME approvals. Of the 494 NME approvals, 56 were considered to be from either neurological or psychiatric therapeutic areas. Figures 2, 3, & 4 describe each COA tool type utilized per NME approval and disease/COA Context of Use combinations described in the COA Compendium. Some entries within the COA Compendium had multiple diseases and/or COA Contexts of Use described within a single NME approval. Therefore, a larger number of COAs were tallied than NME approvals as reflected in the data presented. Some of the entries within the COA Compendium were considered either ES or did not fall under the search parameters and thus were excluded from analysis.

Figure 2: COA types for Neurology

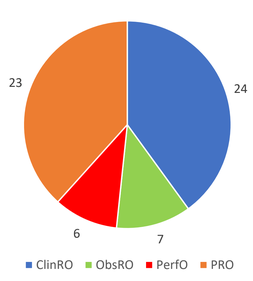


Figure 3: COA types for Psychiatry

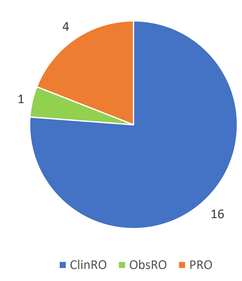
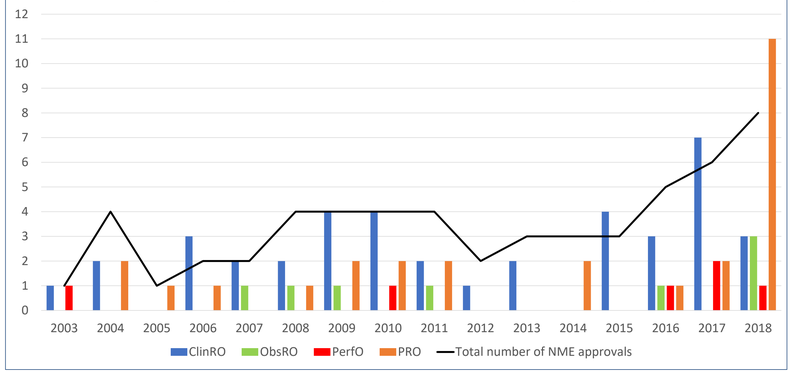


Figure 4: COA type trends with total NME approvals & combinations (Neurology + Psychiatry)



Discussion

The total number of NME approvals for neurological and psychiatric indications has increased in recent years, most notably from 2015 to 2018 as shown in Figure 4. Among the 56 NME approvals, most labels included ClinRO measures or PRO measures while other COA types were less commonly included. While the data displayed do not show any sustained trends in COA types in labeling over time, in 2018 there was an increase in NME labeling including PRO measures. The approval of new drugs for the treatment of migraine headache and seizure disorders contributed to this increase in PRO measures. Analyses of subsequent years' labeling data will be needed to evaluate whether this increase is sustained. One limitation to this study is that only NMEs were analyzed; ES were not reviewed but could add more clarity on COA trends. Another limitation to this study is that while it provides an overview of COA trends, it does not provide the number of COAs labeled within each COA type, which can be of interest.

PRO measures have played an important role in demonstrating the clinical benefit from medications used to treat CNS disorders, such as migraine headache and seizure disorders. CDER is piloting a new grant program, the Standard Core Clinical Outcome Assessments and their Related Endpoints, to support development of COAs for migraine drug development [Migraine Clinical Outcome Assessment System].[4] Under the CDER DDT Qualification Program, CDER has qualified the Symptoms of Major Depressive Disorder Scale, a PRO measure of the overall symptoms of major depressive disorder.[5]

Conclusion

In neurology and psychiatry, NME approvals have increased from 2015 to 2018, with a notable increase in PRO use for 2018. Ultimately, the COA Compendium is a useful tool for assessing how COAs have been used in clinical trials to support labeling claims and to present COAs that have been qualified for use through the CDER DDT Qualification Program.

References

1. Clinical Outcome Assessment Compendium. *FDA.gov*. https://www.fda.gov/drugs/development-resources/clinical-outcome-assessment-compendium. Updated as of April 27, 2020. Accessed on June 29, 2020.
2. NDA Classification Codes. *FDA.gov*. https://www.fda.gov/media/94381/download. Accessed on July 6th, 2020.
3. New Drugs at FDA: CDER's New Molecular Entities and New Therapeutic Biological Products. *FDA.gov*. *https://www.fda.gov/drugs/development-approval-process-drugs/new-drugs-fda-cders-new-molecular-entities-and-new-therapeutic-biological-products*. Updated as of January 10, 2020. Accessed on July 6th, 2020.
4. CDER Pilot Grant Program: Standard Core Clinical Outcome Assessments (COAs) and their Related Endpoints. *FDA.gov*. https://www.fda.gov/drugs/development-approval-process-drugs/cder-pilot-grant-program-standard-core-clinical-outcome-assessments-coas-and-their-related-endpoints. Updated as of January 9, 2020. Accessed on June 29, 2020
5. Qualified Clinical Outcome Assessments (COA). *FDA.gov*. https://www.fda.gov/drugs/development-approval-process-drugs/qualified-clinical-outcome-assessments-coa. Updated as of April 14, 2020. Accessed on June 29, 2020.

Acknowledgements

We would like to thank all of the FDA ORISE Fellows and the Division of Clinical Outcomes Assessment (DCOA) for developing and maintaining the COA Compendium for public dissemination and discussion. We would also like to thank Michael Davis of the Division of Psychiatry (DP) within the FDA for his contributions to the project.

This project was supported in part by an appointment to the Research Participation Program at the U.S. Food and Drug Administration administered by the Oak Ridge Institute for Science and Education through an interagency agreement between the U.S. Department of Energy and the U.S. Food and Drug Administration

The authors report no conflicts of interest for this work.