Participants:
Ray Anton, Medical University of South Carolina, Chair
Hardean Achneck, Dicerna
Arnie Aldridge, RTI
Henri-Jean Aubin, Hôpitaux Universitaires Paris-Sud
Kathleen Davenport, Dicerna
Heather Davidson, Otsuka
Deborah Hasin, Columbia University
Keith Isenberg, Blue Cross Blue Shield
Justin Knox
Henry Kranzler, University of Connecticut Health
William Martin, Alkermes
Roger Meyer, Penn State Hershey College of Medicine
Charles O’Brien, University of Pennsylvania
Stephanie O’Malley, Yale University School of Medicine
Bernard Silverman, Independent Consultant
Maria Sullivan, Alkermes
Celia Winchell, FDA
Katie Witkiewitz, University of New Mexico
Gary Zarkin, RTI
Susan Shreve, Parthenon Management Group
Lindsay Snyder, Parthenon Management Group

Summary of the Meeting:
1. New members and guests were welcomed to the meeting.

2. FDA Clinical Outcome Qualification Plan: R. Anton discussed an overview of the FDA Clinical Outcome Qualification (COQ) Plan, including summarizing historical background that ACTIVE previously met with the FDA to discuss the WHO risk drinking level metric as an outcome for AUD clinical trials. R. Anton explained that the next step for the FDA COQ Plan is to submit a plan which is essentially taking the initial dossier and removing the data. If accepted, the data will be added back in and submitted to the FDA. R. Anton summarized what NIAAA staff was going to submit to the FDA in regards to the use of the Timeline Followback (TLFB) drinking calendar interview as the basis for all drinking metrics, including the WHO Risk Drinking Levels in clinical trials. R. Anton also emphasized the need to define trial length during this WHO RDL process. NIAAA has added this to their submission plan.

3. WHO Drinking Level Change and Economic Issues in the COMBINE Trial – Review and Update of Paper: Given his expertise in this area, Dr. Isenberg provided suggestions on the paper and has been included as an author. A. Aldridge discussed that the paper is being edited to include Keith Isenberg’s suggestions. The article is
currently being re-worked to be submitted to *The Journal of Managed Care and Specialty Pharmacy*. A. Aldridge explained that the current paper is focused on solely self-reported healthcare costs, including ER visits, inpatient visits, outpatient visits, behavioral health visits, and wellness healthcare visits.

a. **ACTION ITEM:** A. Aldridge will share final edits with co-authors by Monday, March 30, 2020 to get feedback and submit next week.

4. **The Relationship between Reductions in WHO Drinking Risk Levels during Treatment and Labor Market Outcomes:** A. Aldridge discussed that the objective of the analyses is to evaluate the relationship between reductions in WHO risk drinking levels from baseline (pre-COMBINE treatment) to the treatment period and subsequent labor market outcomes.

   a. **ACTION ITEMS:** A. Aldridge will monetize labor market outcomes and might work with Dr. Witkiewitz to include the relationship between employment changes and QOL measurements.

   b. **ACTION ITEM:** J. Knox will share the NESARC population data paper with K. Isenberg.

5. **Review/Highlights of NESARC – WHO Shift Data – New Findings:** D. Hasin discussed WHO Drinking Risk Levels NESARC and NESARC-III analyses. D. Hasin explained that she became involved with ACTIVE not only to analyze the clinical data but to also provide support to see how generalizable some of the finding were about reductions in WHO Risk drinking levels if we looked at the risks in the general population, not limited to just clinical samples. Starting early in the study, differences in risks for various outcomes cross sectionally across the levels of the NESARC datasets were reviewed. NESARC and NESARC-III are national surveys that were conducted of alcohol, drug and psychiatric conditions that had very detailed measures of alcohol consumption which enabled the creation of the WHO risk drinking levels precisely for men and women.

   a. **ACTION ITEM:** D. Hasin will do a final review, once done the paper will be sent out to everyone to review and will resubmit to a high impact journal, possibly the *American Journal of Psychiatry*.

6. **WHO Drinking Risk Levels & Cardiovascular Disease NESARC Waves 1 and 2:** J. Knox updated the group on the analyses looking at WHO Drinking Risk Levels and Cardiovascular Disease using NESARC waves 1 and 2.

7. **Update on PRO Measures – What Can Be “Promised”:** S. O’Malley gave a brief overview of patient rated outcomes and whether there is a good alcohol consequences measure that could be validated for a secondary outcome for clinical trials. S. O’Malley discussed the Impact of Beverage Intake on Behavior – ImBIBE and the Patient-Reported Outcomes Measurement Information System – PROMIS.

   a. **ACTION ITEM:** S. O’Malley will email the NIAAA to see if we can reach out to funded clinical trial recipients for studies to suggest that they collect these PROMIS measures, as well as the NIAAA intramural research program, as they
have a screening battery. It was suggested to contact David Goldman and/or BJ Song.

8. **Review of Data on Trial Length and Sustainability, including gabapentin six-month study analyses:** K. Witkiewitz presented on the Stability of WHO Risk Drinking Level Over Time in the COMBINE, Vivitrol, and Horizant (gabapentin encarbil) Studies with the goal of Informing Trial Length. The following questions were examined:
   
   **a.** What is the stability of the WHO risk drinking levels in alcohol clinical trials over time?
   
   i. In a 4-month trial
   
   ii. In a 6-month trial

   **b.** What are the associations between 4-month versus 6-month WHO risk level reductions and long term outcomes?

   **c.** **ACTION ITEM:** K. Witkiewitz will look at MATCH data with the Kappa and Markov models. It was discussed that it would be helpful to see if a 1 month sample of behavior is sufficient, or if it is important to see sustained 2-3 month samples.

9. **Alkermes Educational Efforts Update:** W. Martin provided an update on Alkermes research and collaborations with ACTIVE. Based on feedback from the last ACTIVE meeting, W. Martin discussed updates on Vivitrol.

10. **Alkermes Research Update:** M. Sullivan provided an overview of Alkermes research updates, including explaining the resurgence in commitment to research for AUD. M. Sullivan discussed the following items:

   **a.** Health Economics Outcome Research (HEOR) Studies in AUD, including the historical context of AUD treatment, as well as design and key findings.

   **b.** The ongoing study of AUD treatment outcomes in the VHA.

   **c.** Investigator-Sponsored Studies (ISS) Program, Early-career investigator Awards Program, and Collaborative Research.

11. **Future ACTIVE Considerations:** The group discussed future ACTIVE considerations and projects, including:

   **a.** Alcohol Consequence Reporting (PROMIS) – as translational concept and work toward the FDA.

   **b.** Combining Biomarkers with Verbal Report as Outcome Measures – R. Anton published a Gabapentin trial in which CDT was used to recategorize people. Verbal reporting was combined with CDT measures to strengthen some of the findings. This had been recently distributed to the ACTIVE members but is also accessible here: [https://www.ncbi.nlm.nih.gov/pubmed/32150232](https://www.ncbi.nlm.nih.gov/pubmed/32150232)

12. **Future ACTIVE Meetings:**

   **a.** **ASAM 2020 Meeting:** This meeting was cancelled secondary to COVID-19 but has turned virtual and a live, online presentation will be delivered to the ASAM membership. This symposium will also be recorded and available afterwards. R.
Anton, D. Falk, S. O’Malley, and Richard Saitz (ASAM member and editor of their journal) and will be participating in this online symposium.

b. RSA 2020 Meeting – June 20-24, 2020 in New Orleans, Louisiana: An ACTIVE symposium organized by S. O’Malley and will be in collaboration with ISBRA. This meeting was also cancelled because of COVID-19 and will likely not be rescheduled. Accepted presentations will likely be carried over till the next meeting in June 2021.