Clinical Outcome Assessments (COA) Qualification Program
DDT COA #000138: Opioid Craving

Administrative Structure:

Description of the submitter including, but not limited to, principal investigator(s), working group member(s), institutions, and contact information not contained within the cover letter.

Principal Investigators:

Cecilia Bergeria, Ph.D.
Behavioral Pharmacology Research Unit
Departments of Psychiatry and Behavioral Sciences
Johns Hopkins University School of Medicine
Email: cberge21@jhmi.edu
Phone Number: 410-550-1979
Address: 5510 Nathan Shock Drive, Baltimore, MD 21230

Kelly Dunn, Ph.D., M.B.A.
Behavioral Pharmacology Research Unit
Departments of Psychiatry and Behavioral Sciences
Johns Hopkins University School of Medicine
Email: kdunn9@jhmi.edu
Phone Number: 410-550-2254
Address: 5510 Nathan Shock Drive, Baltimore, MD 21230

Eric C. Strain, M.D.
Behavioral Pharmacology Research Unit
Departments of Psychiatry and Behavioral Sciences
Johns Hopkins University School of Medicine
Email: estrain1@jhmi.edu
Phone Number: 410-550-1191
Address: 5510 Nathan Shock Drive, Baltimore, MD, 21230

Concept(s) of Interest (COI) for Meaningful Treatment Benefit:

A description of the meaningful aspect of patient experience that will represent the intended benefit of treatment (e.g., presence/severity of symptoms, limitations in performance of daily activities).

National epidemiological surveys report that approximately 5% (*n*=12,258,000) of people in the United States misused heroin or a prescription opioid in 2018 and that 68% of those individuals wanted help abstaining from opioids[1]. Opioid craving is a recalcitrant element of opioid use disorder (OUD) that is inadequately treated by existing opioid pharmacotherapies and remains a significant area of concern for persons seeking opioid treatment or in recovery from OUD. We propose to develop a

novel Clinical Outcome Assessment (COA) for opioid craving that can be subsequently used as the basis for approving medications and behavioral approaches that have a specific indication for reduction of opioid craving.

In 2018, under the Patient-focused Drug Development Initiative that was authorized as part of the Prescription Drug User Fee Act V the FDA held a patient listening session focused on drug development goals for persons with opioid use disorder. A theme that emerged as part of this session was that craving served as a primary barrier to recovery and treatment success in persons with OUD[2]. Opioid craving that has been assessed via Ecological Momentary Assessments – a novel way to collect real time data in people's natural environments- provides initial evidence that craving is predictive of future illicit opioid use among individuals receiving long-term medications for opioid use disorder [3-5]. Despite patient concern and association with relapse, none of the currently approved OUD pharmacotherapies explicitly address craving.

Moreover, the complete lack of validated opioid craving measures has significantly impeded efforts to use craving as a primary outcome for opioid pharmacotherapy trials. There is therefore a critical need to develop a reliable and valid opioid craving assessment that can be used in phased clinical trials, as formal evaluations of medications for an opioid craving indication are developed. This will address a gap in the opioid use disorder continuum of care.

Provide a conceptual framework for the COA(s)

A recent scoping review, assisted in part by members of our research team, found a total of 15 opioid craving assessments that were used within 85 different studies [6]. While there is no widely accepted measure of opioid craving, domains that were commonly included within the existing opioid craving assessments included:

(1) *Control*- will power, ability to cope with craving, degree of control over use, self-efficacy, resistance to drug use
(2) *Negative Reinforcement* -the anticipation of relief from negative states or feelings
(3) *Thoughts/preoccupations with craving*- psychological reactions to craving, desire, intention to use, thoughts and interference, mental preoccupation with drugs, effects of desire for drug and drug related thoughts on patient's work and life, resistance to thoughts and intentions

Context of Use for COA Qualification:

Targeted study population including a definition of the disease and selection criteria for clinical trials (e.g., baseline symptom severity, patient demographics, comorbidities, language/culture groups).

Persons currently using opioids, person meeting criteria for mild-to-severe OUD or individuals who are in recovery from opioids (licit and illicit use).

OUD is defined by the American Psychiatric Association (APA) in the Diagnostic and

Statistical Manual of Mental Disorders – 5th Ed as a problematic pattern of opioid use leading to problems or distress with at least two of the following occurring within a 12-month period:

1. Taking larger amounts or taking drugs over a longer period than intended.
2. Persistent desire or unsuccessful efforts to cut down or control opioid use.
3. Spending a great deal of time obtaining or using the opioid or recovering from its effects.
4. Craving, or a strong desire or urge to use opioids
5. Problems fulfilling obligations at work, school or home.
6. Continued opioid use despite having recurring social or interpersonal problems.
7. Giving up or reducing activities because of opioid use.
8. Using opioids in physically hazardous situations.
9. Continued opioid use despite ongoing physical or psychological problem likely to have been caused or worsened by opioids.
10. Tolerance (i.e., need for increased amounts or diminished effect with continued use of the same amount)
11. Experiencing withdrawal (opioid withdrawal syndrome) or taking opioids (or a closely related substance) to relieve or avoid withdrawal symptoms

***Targeted study design and statistical analysis plan (includes the role of the planned COA in future drug development clinical trials, including the planned set of primary and secondary endpoints with hierarchy, if appropriate*).**

The final COA will be available for use in assessing the degree to which an intervention (pharmacotherapy or other) changes opioid craving, either as a primary or secondary outcome measure. Therefore, the COA should be used in the context of clinical trials with appropriate control conditions.

Applicable study settings for future clinical trials

- ***Geographic location with language/culture groups***
- ***Other study setting specifics (e.g., inpatient versus outpatient)***

  This COA will be used with English-speaking populations in laboratory, remote, or clinical research assessments, as well as inpatient and outpatient treatment settings. The questions will be collected with pen/pencil and paper or on an electronic device (e.g., computer, tablet). The questionnaire is intended for completion by a patient or study participant, or can be completed with the patient/participant through an interviewer/clinician

<u>COA Type:</u> Patient-Reported Outcome (PRO)