I. PURPOSE AND SCOPE

The purpose of this SOP is to describe procedures to protect the health and welfare of research participants in a blinded clinical research study.

This SOP applies to all blinded clinical research studies conducted at Loyola University Chicago (LUC) and Loyola University Medical Center (LUMC).

II. DEFINITIONS

A. **Blinding:** The procedure in which one or more parties in the study are kept unaware of the treatment assignment to prevent conscious and unconscious bias when comparing the investigational treatment's safety and efficacy.
B. **Treatment Code:** The code which identifies the intervention to which the research participant is assigned.
C. **Unblinding:** Identification of the treatment code of a participant or grouped results in studies where the treatment assignment is unknown to the research participant and investigators. Also referred to as "breaking the blind."

III. PROCEDURES

1. Before the study is initiated, the Principal Investigator (PI) and his/her designated research personnel ("Study Team") ensures the study sponsor provides, or, if LUC is the sponsor, ensures the protocol specifies:
    a. the randomization procedure.
    b. the circumstances for unblinding.
    c. 24-hour contact information of the unblinded personnel including names, telephone numbers and e-mail addresses.
        (1) The Study Team maintains this information in a location that is readily accessible to the complete Study Team in the event of a medical emergency that requires an emergency need to unblind.
        (2) For external sponsors, the medical officer and monitor are typically the unblinded personnel.
        (3) For LUC-sponsored (PI initiated) studies, LUMC Investigational Pharmacy is typically the unblinded personnel. Therefore the 24-hour contact information of LUMC Investigational Pharmacy personnel must be readily available.
2. Throughout the study, the Study Team is responsible for:
    a. discussing blinding with the potential research participant during the initial informed consent process and throughout their participation utilizing the most current IRB approved informed consent and in accordance with the study protocol.
    b. ensuring that the randomization schedule is followed to ensure the Treatment Code is broken only in accordance with the protocol.

3. **Non-Emergency Unblinding**
    a. The PI may request the sponsor's approval to unblind a research participant when knowing the Treatment Code will directly impact the research participant's next line of treatment.
    b. The sponsor's approval must be obtained prior to unblinding if the study is externally sponsored.
    c. The Study Team retains copies of the documented correspondence with the PI and study sponsor's approval to unblind in the study record.

4. **Emergency Unblinding**
    a. Emergency unblinding is only appropriate during a medical emergency (as determined by the PI or treating physician) where knowledge of the Treatment Code

is likely to have a significant effect on the clinical management of the research participant and would be necessary in immediate treatment decisions.

b. In an emergency, it may not be feasible to obtain prior approval from the PI or sponsor. In this case, after the research participant is successfully unblinded, the Study Team creates clear documentation explaining why unblinding was necessary. The Study Team notifies the PI, sponsor, and IRB as soon as possible.

5. **Accidental Unblinding**
   a. If a research participant is accidentally unblinded, the Study Team creates clear documentation of events, as well as communication with the sponsor and PI.
   b. Those who were accidentally unblinded must not reveal the Treatment Code to any other members of the Study Team, pharmacy staff, or to the research participant, unless written approval from the study sponsor is obtained. Every effort should be made to maintain what remains of the blind.
   c. The Study Team reports a protocol deviation to the IRB of Record.

IV. REFERENCES AND ASSOCIATED DOCUMENTS AND FORMS

Guidance for Industry E6: Good Clinical Practice, section 4.7 *Randomization Procedures & Unblinding*.

V. APPROVALS

Allison M. Fitzgerald, MD, MS — 12/14/2020
Loyola University Chicago Clinical Research Office — Date

Katherine von Meurs — 12/3/2020
LUMC Clinical Research Manager — Date