Blinding – Codes and Code Breaking		
VCU/VCU Health CLINICAL RESEARCH STANDARD OPERATING PROCEDURES		
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1. PURPOSE

This Standard Operating Procedure describes the processes for using and/or breaking codes in blinded clinical trials. It is important to note that externally-sponsored studies and studies where an Independent Data Monitoring Committee is in place may implement separate procedures that should be followed, which may differ from the general procedures outlined within this document.

2. REQUIREMENTS

When a trial is blinded, the assigned intervention should remain indistinguishable from the comparator throughout the term of the study. It is normally the sponsor of the clinical trial who plans and organizes the procedures for blinding and unblinding by using coding and code-breaking. However, in cases where the investigator is also the sponsor, there must still be a clear procedure for blinding and unblinding by using coding and code-breaking.

3. DEFINITIONS

Blinding- Blinding is a procedure in which one or more participants and/or members of the research team are kept unaware of the assigned intervention.

Single-blind- Single-blind is where the participants remain unaware of the assigned intervention.

Double-blind- Double-blind is where both the participants and the investigators are unaware of the assigned intervention.

Triple-blind- Triple-blind is where the participants, investigators, and the data analysts involved are unaware of the assigned intervention.

4. PROCESS

Procedures for breaking codes vary from study to study. The procedures must be established and reviewed before the first participant begins treatment.

- Ensure that a 24-hour contact number for the sponsor's delegate is available. Obtain the names and telephone numbers for key contacts and keep them in a location easily accessible by all study personnel.

- Study codes may be available directly from the sponsor or may be stored at the study site. If stored at the study site, the study codes may be contained on the Study Drug Label or in individual envelopes depending on direction from the sponsor. The code must be stored in a secure area, with access being provided by keys assigned to the designated member of the clinical research team.

- The code must only be broken in accordance with the protocol or in the case of an adverse event, where it is necessary for the investigator to know which treatment the patient is receiving before the condition can be treated. The code may also have to be broken if someone not in the study uses the investigational agent. For example, if a child in the participant's household takes a study medication, the blind may be broken to determine treatment for the child. The principal investigator of the study should be notified immediately if the code must be broken.

- When the code is broken for an individual participant, this must be clearly documented, along with reasons for breaking the code. For a study using code envelopes for emergency unblinding, the code envelope that was opened should be signed, dated and annotated with the reasons for breaking the blind.

- The IRB of record must be notified in the case of unblinding due to an unanticipated problem, such as an adverse event

- Unless it is an emergency or if there is any doubt as to whether a code should be broken, contact the sponsor or sponsor designee to determine if the code may be broken.

5. REFERENCES

A. Good Clinical Practice

- ICH Harmonised Guideline Guideline For Good Clinical Practice E6(R3)
    - Section 4 – Investigator
        - Section 4.5 – Compliance with Protocol
        - Section 4.6 – Investigational Product(s)
        - Section 4.7 – Randomization Procedures and Unblinding

B. VCU HRPP Policies and Guidance; HRPP Toolkit

- HRP-103; Investigator Manual

Review/Revision History CR-CO-500		
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CR-CO-500.3	08/04/2025	● Aligned with HRPP toolkit ● Aligned with ICG E6(R3) ● Biennial review performed ● Minor formatting edits ● Reference links updated
CR-CO-500.2	06-01-2021	● Biennial review performed ● Minor formatting edits ● Reference links updated
CR-CO-500.1	06-01-2018	● Original