1. PURPOSE

1.1 This document describes the Division of Microbiology and Infectious Diseases (DMID) policy for unblinding individual participants during the conduct of clinical trials.

- This document does not cover unblinding of all participants after database lock.

2. SCOPE

2.1 This policy applies to:

- Blinded clinical trials where DMID is the IND sponsor (regardless of funding type);
- Blinded non-IND clinical trials funded under contract;
- Blinded non-IND clinical trials funded under cooperative agreement and implemented through a DMID funded network.

2.1.1 For IND trials where the IND sponsor is not DMID, the IND sponsor makes determination about unblinding.

2.1.2 For non-IND trials funded under grant or cooperative agreement other than those specified above, the grantee makes determination about unblinding.

3. DEFINITIONS

3.1 Adverse event - Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product.

3.2 Blinding - A procedure in which one or more parties to the trial are kept unaware of the treatment assignment(s). Single blinding usually refers to the subject(s) being unaware, and double¬ blinding usually refers to the subject(s), investigator(s), monitor, and, in some cases, data analyst(s) being unaware of the treatment assignment(s).

For additional definitions, see DMID glossary.

4. RESPONSIBILITIES

Responsibilities are delineated in the policy.

5. POLICY

5.1 Unblinding in response to a medical emergency or immediate hazard.

5.1.1 Unblinding in response to a medical emergency or immediate hazard to participants do not require approval from DMID.

5.1.2 The site PI may take any steps necessary including unblinding to eliminate hazards and ensure the participant safety.

5.1.3 Any such unblinding needs to be reported to DMID as soon as practical, and no later than 48 hours.

5.2 Unblinding in response to an unexpected medical event (but not a medical emergency or immediate hazzard).

5.2.1 The Principal Investigator (PI) must notify DMID if there is a need to unblind an individual study participant and get DMID's concurrence prior to any unblinding. Reasons to unblind include but are not limited to:

- An adverse event for which knowing the study assignment is necessary to direct or manage current or future care of the participant, interpret the event, or provide critical safety information that could impact the ongoing conduct of the trial.
- A participant becomes pregnant while receiving the investigational product or intervention, and there is concern the fetus may be at risk as a result of having received the investigational product or intervention.
- An unexpected adverse event of a unique nature where knowledge of the assignment may impact decisions on enrollment or continuation.

5.2.2 The DMID Medical Officer (MO) or the Medical Monitor (MM) can make the determination to unblind.

- For time sensitive situations if the MM and MO are not available, the Associate Director for Clinical Research or the Director of any of the clinical offices (OCRR, OCRA, or ORA) may make the determination to unblind on behalf of DMID.

5.3 Unblinding for independent data and safety oversight (including Safety Monitoring Committees (SMCs) and Data and Safety Monitoring Committees (DSMBs)).

5.3.1 The use of any independent data and safety oversight and their access to unblinded data must be described in the protocol. As long as it is stated in the protocol, no additional approvals by the sponsor are needed for unblinding.

5.4 Unblinding required by regulatory agencies.

5.4.1 Unblinding in response to a request by a regulatory agency should be communicated to DMID prior to unblinding.

5.4.2 These requests will be allowed. However, as part of due diligence as regulatory requests to unblind are unusual during an active trial, DMID reserves the right to question/clarify with the regulatory authority as to the purpose of unblinding, which must be answered prior to unblinding.

5.4.3 The Associate Director for Clinical Research or the Director of any of the clinical offices (OCRR, OCRA, or ORA) may make the determination to unblind.

5.5 Accidental unblinding

5.5.1 If the PI becomes aware of an intentional or unintentional breaking of the blind, they must report the unblinding through the protocol deviation reporting process.

6. REFERENCES

Not applicable.

7. APPENDICES

Not applicable

8. REVISION HISTORY

8.1 This is the original version of this Policy within the eQMS. It replaces DMID Policy-015 – NCRS 2.3 v 2, which was revised prior to incorporation into the eQMS.

9. ADDITIONAL INFORMATION

9.1 Document Lead: Associate Director for Clinical Research

9.2 Posting externally: Yes