1. PURPOSE

1.1 To delineate the requirements for the use of the DMID peripheral blood mononuclear cells (PBMC) processing Standard Operating Procedure (SOP) in clinical trials and clinical research from which PBMC alone or PBMC and plasma will be collected.

1.2 Specimen collection is an integral component of clinical trials/research, and the availability of high-quality specimens are important for clinical research. PBMCs are commonly collected in DMID-funded clinical research. However, collection of PBMCs poses challenges. Numerous publications have shown that multiple parameters, such as PBMC processing time and temperature, can impact cell viability. This can result in either insufficient quantity of cells to perform protocol related assay(s) and/or generation of data that are inaccurate or irreproducible.

1.3 The Office of Clinical Research Resources (OCRR) established the PBMC Processing SOP to optimize and standardize the processing of whole blood to separate plasma and isolate PBMC for cryopreservation for both the DMID clinical trials/research and secondary research.

2. SCOPE

2.1 This policy applies to:

- Trials funded by NIAID/DMID when DMID is the IND/IDE sponsor;
- If requested by the Contracting Officer's Representative (COR) or Program Officer (PO), clinical trials that utilize DMID clinical support contracts.

3. DEFINITIONS

3.1 **Protocol –** Formal description and design for a specific research project. A protocol involving human subject research must be reviewed and approved by an Institutional Review Board (IRB) if the research is not exempt, and by an IRB or other designated institutional process for exempt research.

3.2 **Standard Operating Procedures (SOPs) –** Detailed, written instructions to achieve uniformity of the performance of a specific function.

For other definitions, see DMID glossary.

4. RESPONSIBILITIES

4.1 OCRR provides oversight for the Vaccine and Treatment Evaluation Units (VTEUs), the Early Phase Clinical Trial Units (EPCTUs) clinical site contracts, and the Infectious Diseases Clinical Research Consortium cooperative agreements, which are DMID central resources for the conduct of clinical trials and clinical research.

4.2 The Respiratory Diseases Branch provides oversight of the Collaborative Influenza Vaccine Innovation Centers contracts.

4.3 The Bacteriology and Mycology Branch provides oversight of the Antibacterial Resistance Leadership Group cooperative agreement.

5. POLICY

5.1 Use of the DMID PBMC Processing SOP, entitled "Peripheral Blood Mononuclear Cells (PBMC) and Plasma Collection" is required for the collection and cryopreservation of all PBMC/plasma for DMID-funded clinical trials/research listed under the scope above.

5.2 The DMID PBMC Processing SOP provides systematic and detailed instructions for processing whole blood to separate plasma and isolate PBMCs for cryopreservation at clinical site-affiliated laboratories. By following the SOP, this approach will:

5.2.1 Reduce the risk of introduction of site-specific variations in specimen preparation;

5.2.2 Increase the probability of obtaining cryopreserved cells with high recovery/viability across sites and studies;

5.2.3 Facilitate the comparison of data and results across sites and studies; and

5.2.4 Improve the ability to train site staff on PBMC processing.

5.3 The most current version of the DMID PBMC Processing SOP should be utilized at the beginning of the trial/research. If the DMID PBMC Processing SOP is revised during ongoing clinical trial/research, the Study Team will discuss and determine if the sites should continue using the previous version of the SOP or implement the subsequent revision. If the revision is implemented, the change of version number should be documented in the clinical trial/research database.

5.4 The Principal Investigator (PI) is responsible for the implementation of the DMID PBMC Processing SOP and for ensuring that all appropriate laboratory personnel are trained and demonstrate proficiency in the SOP. Best practice to document proficiency includes participation and good standing in a PBMC proficiency program.

5.4.1 Criterion of proficiency: The target PBMC post-thawing viability is ≥90%, while the minimum acceptable target is >80%.

5.5 Requests for exceptions to this policy must be submitted in writing to the OCRR Director for review and approval.

6. REFERENCES

6.1 Optimization and Limitations of Use of Cryopreserved Peripheral Blood Mononuclear Cells for Functional and Phenotypic T-Cell Characterization: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2725535/

6.2 Optimization of storage and shipment of cryopreserved peripheral blood mononuclear cells from HIV-infected and uninfected individuals for ELISPOT assays: http://www.sciencedirect.com/science/article/pii/S0022175910002863

6.3 Isolation and preservation of peripheral blood mononuclear cells for analysis of islet antigen- reactive T cell responses: position statement of the T-Cell Workshop Committee of the Immunology of Diabetes Society:

https://www.ncbi.nlm.nih.gov/pubmed/20939860

6.4 DMID PBMC Processing SOP - Peripheral Blood Mononuclear Cells (PBMC) and Plasma Collection

7. APPENDICES

Not applicable

8. REVISION HISTORY

8.1 DMID-LB-POL-00001 rev 01 is the first version of this policy in eQMS and replaces the previous Policy-010 effective 01Feb2017.

9. ADDITIONAL INFORMATION

9.1 Document Lead: OCRR

9.2 Posting externally: Yes