DATE: November 04, 2011

TO: PBMC Processing Laboratories

FROM: IMPAACT Laboratory Steering Committee

SUBJECT: Change of Viable PBMC Shipping in IMPAACT

The ACTG and IMPAACT Networks have adopted different methods for storing and shipping viably cryopreserved peripheral blood mononuclear cells (PBMCs) based mainly on issues related to feasibility and cost. The ACTG protocol requires that PBMCs be processed and stored on site at -70/-80°C for no more than 4 weeks before sending all of them on dry ice to the central repository at BRI for long-term storage in liquid nitrogen (LN2). At the end of the study or upon request, BRI ships selected PBMCs in LN2 shippers to the testing site. The remaining PBMCs stay at BRI in LN2 storage. In contrast, IMPAACT typically requires PBMCs to be processed and stored long term in LN2 at the sites, and only some of the aliquots are eventually shipped to the BRI (NIAID sites) or Fisher (NICHD sites) repositories or to the testing laboratory

Why didn't IMPAACT adopt the ACTG method?

- There would be very few aliquots of cells/site sent per shipment. Unlike the ACTG where virtually all stored aliquots of all sample types from all studies are sent to BRI for storage, IMPAACT has approved only a few high priority protocols for long term storage at the repository. In addition, IMPAACT protocols typically store only 2-4 aliquots/time point since volumes of blood collected from children and pregnant women are much smaller than from non-pregnant adults.
- Since the ACTG is storing all specimens (serum, plasma, urine, genital secretions, CSF, etc) from all participants from all studies, the sites can include one box of PBMCs with their other monthly dry ice shipments. IMPAACT sites might only be sending one partial box of PBMCs/month.
- Expense of monthly shipping to BRI from the domestic sites would be $1500-1800/yr, but for international sites would be $15,000-20,000/yr.
- We would have to increase the amount of money allocated to BRI if we adopted the ACTG method.

Problems with the current IMPAACT method:

- Many international (and some domestic) sites have no or only a very tenuous access to reliable supplies of LN2. This lack of a reliable source of LN2 has the potential to compromise the viability of the PBMCs. An acceptable alternative adopted by a few sites is to use a -150°C freezer.
- Shipping on LN2 dry shippers can be very expensive - $1500 - $2500/shipment from the international sites, plus the cost of returning the dry shipper to the site (perhaps another 500 - $1000).

Given the lack of reliable sources of LN2 at many of our sites and given the considerable costs to make monthly shipments to the BRI repository, the IMPAACT Lab Steering Committee (ILSC) has the following recommendations:

- Pilot testing of the assay that will be used in the study with frozen and fresh PBMCs to insure that the assay will work and provide consistent results when frozen cells are employed. These data would also be reviewed by the ILSC prior to approving the collection of viable PBMCs for an IMPAACT study.
- Limit the number of protocols, subjects, and time points for viable PBMC collection and storage. Any study that wants to collect and store viable PBMCs would have to provide compelling justification and both the ILSC and the Finance and Budget Office would have to review this information prior to approval.
- Limit the number of sites approved to process and store viable PBMCs to those sites that can assure a reliable, un-interrupted supply of LN2 or in -150°C mechanical freezer and are in good standing with the IQA's Cryopreservation Proficiency Testing program. If a site cannot guarantee a reliable supply, they would not be approved for viable PBMC processing and storage. Try to use as few sites as possible for each protocol to reduce shipping costs.
- **Viable PBMCs from all studies would be shipped twice a year to BRI, Fisher, or the testing laboratory in LN2 dry shippers.**

The ILSC believes that these changes will limit the number of PBMCs collected, stored, shipped and tested to only those critical to the success of the study and only at those sites which can guarantee safe storage of the vials. In addition, by shipping samples twice a year, shipping costs can be minimized while enhancing the integrity of the samples.

Please note that this change of shipping method has also been incorporated in the Cross-Network PBMC Processing SOP version 4.0 which can be found on the HANC website at http://www.hanc.info/labs/labresources/procedures/Pages/pbmcSop.aspx