

## **Addendum to the collection of blood samples for HRRC#0902: Study to Investigate Use of Tobacco Snus Compared to Smoking Usual Brand Cigarettes.**

HRRC Proposal #0902, as written, states that 117 mL of blood will be collected from each participant. We collect and **keep** 117 mL of blood from each participant, but our procedure for drawing blood from a catheter requires a small amount of blood to be drawn before we draw the sample we keep and use for biomarker analysis. The volume collected in the draw-off tubes was not included in the above calculation. We estimate that approximately 1.5 mL of blood is drawn off and discarded before each time point at visits 1 and 4; therefore, the total blood drawn and discarded in the study is 48 mL.

## **Changes/Additions Proposed for HRRC#0902: Study to Investigate Use of Tobacco Snus Compared to Smoking Usual Brand Cigarettes.**

- We propose to change the time at which blood samples are drawn for the assessment of COHb levels and the time at which expired CO is measured.

**Reason:** Under the current protocol, expired CO and blood COHb are measured at 25 minutes following smoking at visit 1 and 25 minutes following alternative tobacco product use at visits 2, 3, and 4. We compare the CO and COHb measurements taken at visits 2, 3, and 4 to the measurements taken at visit 1 to calculate a percent reduction in CO and %COHb over the course of the study. Because the measurements at visit 1 are taken after a smoking session required by the study (not *ad libitum*), we may be falsely elevating the reductions seen following visit 1. To rectify this, we propose taking baseline CO and COHb measurements prior to the smoking session at visit 1 in addition to the 25 minute samples stated in the current proposal. Continuing to measure COHb and expired CO at 25 minutes will allow us to determine whether the baseline measurements are necessary and will allow us to estimate falsely elevated reductions that may have been seen in previous studies that employed the same study protocol (HRRC#0811, HRRC#0812).

**Exact changes:** Expired CO samples will be taken at baseline and 25 minutes at visits 1, 2, 3, and 4. Percent COHb in whole blood will be calculated in samples taken at baseline and 25 minutes following product use at visits 1 and 4, and will be calculated in samples taken at baseline only at visits 2 and 3. (Blood samples will **not** be taken at 25 minutes post product use at visits 2 and 3.) The informed consent form will be modified to include these changes.

- We propose to collect 2 additional tubes of blood for future biomarker development.

**Reason:** The clinical studies division is currently working to develop additional biomarkers of tobacco harm. This method development requires plasma samples, ideally

from product migration studies, to look for changes in biomarker levels from baseline smoking to product migration.

**Exact changes:** Two additional tubes of whole blood will be collected prior to product use at visits 1 and 4. The informed consent form will be modified to include this addition and to include the updated total volume of blood to be drawn.

**Taking into consideration the above addendum and the two proposed changes, the total volume of blood to be drawn in this study is 183 mL. (183mL is 0.77 cups, which is 0.39 pints.)**

- We propose to obtain medical history information for participants in this study.

**Reason:** It is important to have accurate, documented medical history information for participants (rather than asking them to deny certain medical conditions by signing the informed consent form) to ensure participant safety upon entering our studies involving new-to-market products and to accurately assess adverse events that occur during the study.

**Exact Changes:** We will obtain medical history information for each participant in this study. An example of the medical history form will be included in the proposal. We will amend the informed consent form to state the confidential nature of this information and explain how this information will be handled. Information regarding staff training in the confidential treatment of personal information and collection of medical history information will also be added to the proposal.