## *Note:* please complete the Headache Diary alongside this form

## Relationship to Headache and Other Pertinent Covariates

1. Was sample obtained while the participant was having a headache?

[ ]  Yes [ ]  No

1. What was the headache diagnosis at the time of sample collection?
	1. Was headache ictal? [ ]  Yes [ ]  No
2. Record *severity* of last headache prior to sample collection on a scale of 0-10: (0 = Least severe, 10 = Most severe)
3. \*Record 28-day headache days frequency prior to sample collection:

[ ]  No headaches in the past 28 days

[ ]  <1 day per month in the past 28 days

[ ]  1-4 days in the past 28 days

[ ]  5-9 days in the past 28 days

[ ]  10-14 days in the past 28 days

[ ]  15 or more days in the past 28 days

1. Indicate whether any medication changes have recently occurred prior to the sample?

 [ ] Yes [ ] No [ ]  Unknown

* 1. If yes, specify timeframe window between medication changes and specimen collection:

[ ]  Less than 1 week

[ ]  1-2 weeks

[ ]  3-4 weeks

[ ]  1-3 months

[ ]  >3 months

1. Respond to one *or* both of the following questions:
	1. In relationship to the blood sample, what time was the last acute abortive was taken?
	2. Indicate any medications that have been adjusted or taken within 5 half lives of the biomarkers being assessed:
2. Is participant a current smoker? [ ]  Yes [ ]  No
	1. If yes, specify how many cigarettes were smoked in the past week: (in units)
	2. Provide time since last cigarette was smoked before sample collection:
3. Specify how many alcoholic drinks were consumed in the past week: (in units)
4. How many of the following medication(s) was taken in the past week:
	1. Prescription medication:

Name:

Dose:

Quantity:

* 1. Over-the-counter medication and/or supplements:

 Name:

Dose:

Quantity:

* 1. Recreational substances:

Name:

Dose:

Quantity:

*To be answered for Women only*

1. \*\*Is the participant/subject currently:

[ ] Premenopausal

[ ] Perimenopausal

[ ] Postmenopausal

1. Please indicate the start date of the last or most recent menstrual bleeding (menstruation):
	1. If premenopausal or perimenopausal, specify day of cycle (e.g. first day of menses is day 0) at time of sample collection: (#)
	2. If postmenopausal, specify date of last menstruation:

Note: At time of sample, consider inquiring from all reproductive age women the first day of last known menses.

1. Is the participant/subject currently pregnant? [ ]  Yes [ ]  No [ ]  Unknown

If Yes, specify number of gestational week(s): (#)

1. Is the participant/subject currently postpartum? [ ]  Yes [ ]  No [ ]  Unknown

If Yes, specify the number of days/weeks the participant/subject is postpartum:

(#) [ ]  Days, (#) **[ ]** Weeks

## Complete for Pediatric-studies ONLY

1. Is the participant/subject premenarchal? [ ]  Yes [ ]  No [ ]  Unknown

This document provides guidance on the types of specifications that should be documented in the protocol if the study involves collection of biospecimens. As the majority of the items that follow will be dictated on the protocol level and NOT collected for each and every specimen, CDEs are not associated with these guidelines.

## Specimen Collection

1. \*\*Did the subject/participant have any specimen(s) collected for biomarkers?

[ ]  Yes [ ]  No (STOP) [ ]  Unknown (STOP)

1. Date and time of specimen collection:
2. \*\*Date and time the participant last ate or drank fluids:
3. Please indicate time between collection and storage:
	1. CSF:
	2. Blood:
	3. Temperature before centrifugation or storage: (i.e. was the sample collected at room temperature or on ice)
4. Please indicate time between storage and analysis:
	1. CSF:
	2. Blood:
	3. Temperature before centrifugation or storage: (i.e. was the sample collected at room temperature or on ice)
5. \*\*What type of specimen was collected from the participant/subject?– (complete this form for each type of specimen collected)

[ ]  Blood, specify type: *(Choose one)* [ ]  Platelet-rich plasma [ ]  Platelet-free plasma [ ]  Serum

[ ]  Specify collection tube: *(Choose one)* [ ]  Polypropylene [ ]  Polystyrene [ ]  Other, specify:

[ ]  CSF, complete the following:

1. Opening pressure:
2. Amount of mL taken:
3. Speed and duration of centrifugation: (in G force or speed and name centrifugation):
4. WBC Cell count (include units):
5. RBC Cell count (include units) :
6. Total Protein (include units) :
7. Glucose (include units):
8. Method of testing for hemoglobin contaminants:
9. Specify collection tube: *(Choose one)* [ ]  Polypropylene [ ]  Polystyrene [ ]  Other, specify:

[ ]  Urine

[ ]  Saliva

[ ]  Other, specify:

## Specimen Processing

Please note that if *both* blood and CSF was collected, please complete this section twice

1. \*\*Was centrifugation performed? [ ]  Yes [ ]  No [ ]  Unknown
	1. If yes, were there any substances added before or after centrifugation?

[ ]  Yes, specify: [ ]  No [ ]  Unknown

1. \*\*Temperature of centrifugation: (please specify in 0 C)
2. \*\*Were any other processing methods performed? [ ]  Yes, specify: [ ]  No [ ]  Unknown
3. \*\*Was the specimen frozen? [ ]  Yes [ ]  No (Skip to next section) [ ]  Unknown (Skip to next section)
	1. \*\*Has the original specimen been repeatedly re-frozen or re-thawed?

[ ]  Yes [ ]  No (Skip to next section)[ ]  Unknown (Skip to next section)

1. \*\*Frozen aliquot volume: (please specify) [ ]  milliliters (mL) [ ]  microliters (µL)
2. \*\*Time of specimen freezing:
3. \*\*Storage temperature: (please specify) 0 C

## Assay Information

(Assay Information should be collected for each assay performed and result obtained. This CRF should be completed multiple times to accommodate multiple assays and results)

1. \*\*\*Date and time of assay:
2. \*\*\*For each assay, where proven report:
3. assay sensitivity and specificity
4. upper and lower limit of detection of assay
5. intra assay and inter assay variability
6. \*\*\*Results of assay: (Choose only one)

[ ]  Normal

[ ]  Abnormal

[ ]  Clinically Significant

[ ]  Other, specify:

[ ]  Unknown

**History of Headaches after Sample Collection**

**Note: these questions should be answered with an interview 48 hours after collection**

### \*\*\*State the length of time participant was VERIFIED to be headache free after specimen collection:

### \*\*\*Specimen collection date and time:

### \*\*\*Time at onset of first headache following specimen obtained (date and time):

### \*\*\*Time of end of first headache (date and time):

### \*\*\*Type of headache, specify

### \*\*\*Treatment for this headache:

[ ]  Bed rest [ ]  Blood patch for post puncture headache [ ]  Other, specify:

### General Instructions

This form contains data elements that are collected for biomarkers. This form is to be used for each type of specimen collected. Most data elements on this CRF are classified as Supplemental (should only be collected if the research team considers them appropriate for their study). The remaining elements are classified as indicated by asterisks below:

\*Elements are classified as Core

\*\*Elements are classified as Supplemental Highly Recommended

\*\*\*Elements are classified as Exploratory

### Specific Instructions

*Please see the Data Dictionary for definitions for each of the data elements included in this CRF Module.*

* **Date/Time** – Record the date/time according to the ISO 8601, the International Standard for the representation of dates and times (http://www.iso.org/iso/home.html). The date/time should be recorded to the level of granularity known (e.g., year, year and month, complete date plus hours and minutes, etc.).
* **Did the subject/participant have any specimen(s) collected for biomarkers?** – If there was no specimen collected for biomarkers or it is unknown that a specimen was collected for biomarkers, discontinue obtaining information from participant/subject
* **What type of specimen was collected from the participant/subject?** – Choose only one specimen type per CRF. If more than one specimen type collected, additional form(s) should be completed.
	+ Blood, specify type – No additional instructions.
	+ CSF, complete the following – Complete as appropriate and include units where applicable.
* **Elapsed time since last headache** – This element should be included on other study-specific source documentation (e.g. Headache Diary). This item should be pre-populated if initially collected elsewhere in order to avoid redundant collection of data.
* **Elapsed time from last headache to today’s sample collection** – This element should be included on other study-specific source documentation (e.g. Headache Diary). This item should be pre-populated if initially collected elsewhere in order to avoid redundant collection of data.
* **Record severity of last headache prior to sample collection on a scale of 0-10**– The use of a standard numerical scale is recommended. If a more detailed scale is required per the study, then a different scale could be used.
* **Did the participant/subject’s medication history change around time of specimen collection?** *–* Medication history should be included on other study-specific source documentation (e.g. Prior and Concomitant Medications*).* This item should be pre-populated if initially collected elsewhere in order to avoid redundant collection of data.
	+ **More specific question proposed on previous call:** Specify timeframe window between any medication changes and specimen draw
* **Was centrifugation performed?** – No additional instructions.
	+ If Yes, were there any substances added before or after centrifugation? Specify the substances\* – No additional instructions.
* **Speed of centrifugation** – No additional instructions.
* **Temperature of centrifugation** – No additional instructions.
* **Were any other processing methods performed? If yes, specify** – *No additional instructions.*
* **Was the specimen frozen?** – No additional instructions.
	+ Has the original specimen been repeatedly re-frozen or re-thawed? – If repeated samples were done, then questions 6-8 need to be repeated for each cycle.
* **Frozen aliquot volume** – Record and indicate which unit of measure is being used (mL or µL).
* **Storage temperature** – No additional instructions.
* **Assay Information –** Assay information should be collected for each assay performed and results obtained. Multiple CRFs should be completed if multiple assays are performed and collected.
* **Assay method used** – Report Assay sensitivity and specificity and upper and lower limits of detection
	+ **Difference between sensitivity and detection limit**
	+ *Sensitivity* is a measure only of signal magnitude, the solution concentration or weight of an element that produces a signal
		- *Detection limit* is a measure of the smallest concentration which can be determined with a specified precision or reproducibility.
		- Most frequently, the specified precision is defined in terms of the concentration producing a signal equivalent to three times the standard deviation of a series of blank (baseline) readings or readings for a standard with a concentration close to the anticipated detection limit.
		- As defined, the detection limit is a function of both signal strength (or sensitivity) and signal reproducibility.
* **Results of assay** – Choose only one.
* **Is the participant/subject currently premenopausal? –** If the participant/subject is currently premenopausal, specify day of cycle (e.g. first day of menses) during collection. To be answered for female participant’s/subject’s only.
	+ If Yes, specify day of cycle (e.g. first day of menses is day 0) at time of sample collection – No additional instructions.
* **Is the participant/subject currently pregnant?** – If the participant/subject is currently pregnant, specify number of gestational weeks. To be answered for female participant’s/subject’s only.
	+ If Yes, specify number of gestational week(s) – No additional instructions.
* **Is the participant/subject currently postpartum? –** If the participant/subject is postpartum, specify the number of weeks the participant/subject is postpartum. To be answered for female participant’s/subject’s only.
	+ If Yes, specify the number of days/weeks the participant/subject is postpartum – No additional instructions.
* **Is the participant/subject premenarchal?** – To be used in pediatric studies ONLY.