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 Information

1. \*\*Date and time of sample collection:

(MM/DD/YYYY):

(HH:MM, 24 hr clock):

1. Date last had an alcoholic drink:

(MM/DD/YYYY):

N/A – has not consumed an alcoholic drink within the past year

1. Date of last tobacco use (cigarette, cigar, chewing tobacco or pipe):\*\*

(MM/DD/YYYY):

N/A – has not used tobacco products in the past year

1. Date and time last ate:

(MM/DD/YYYY):

(HH:MM, 24 hr. clock):

1. \*\*Sample source:

Biological tissue  Unknown

Biological fluid

1. \*\*Living or Deceased at time of collection:

Living  Deceased

1. \*\*Type of sample:

Venous blood: (Further indicate venous type)

Whole  Plasma

Serum  Platelets

Buffy coat

Arterial blood: (Further indicate arterial type)

Whole  Plasma

Serum  Platelets

Buffy coat

Tissue (Further indicate type and specific area):

Clot  Cardiac

Blood vessel  Other

Saliva  Cerebral Spinal Fluid

Buccal swab  Newborn cord blood

Brain tissue  Placenta

Amniotic fluid  Other, specify:

Dura Tissue

1. \*\*Reason(s) sample excluded:

Nervous system infection  Inflammatory conditions

Infection at site of sample  Malignancy

Nervous system neoplasm  Renal failure

Paraneoplastic conditions  Liver failure

Demyelinating conditions  Participant declined to provide specimen

Exclusionary medication being taken

1. \*\*Baseline specimen collected:

Yes  No  Unknown

## Blood Sample Collection Information

1. \*\* Normal/Control samples collected:

Yes  No  Unknown

1. Patient position during sample collection:

Seated  Lying

Standing

1. \*\*Method of blood collection:

Routine venipuncture w/ tourniquet  Routine venipuncture w/o tourniquet

Drawn through peripheral venous catheter  Drawn through central venous catheter

Drawn through PICC (peripherally inserted central catheter)  Drawn through peripheral arterial puncture

Drawn through arterial peripheral line  Drawn through arterial central line

Special procedures  Other, specify:

Unknown

1. \*\*Was sample hemolyzed (Gross hemolysis, microscope not required)?

Yes  No  Unknown

1. \*\*Needle gauge size:

16 gauge 18 gauge

20 gauge  Unknown

Other, specify:

1. \*\*Type and volume/number of collection tubes used:

Blood cultures- SPS  Citrate Tube

Serum Tube Vacutainer SST/ Gel Separator Tube

Vacutainer PST  Heparin Tube

Gel Separator Tube with Heparin  EDTA tube

Fluoride (glucose) Tube  Polypropylene

Other, specify:

**Cerebral Spinal Fluid (CSF) Sample Collection Information**

1. Normal/Control samples collected:

Yes  No  Unknown

1. \*\*Method of CSF acquisition:

Collection catheter  Sample collected from bag/reservoir

Lumbar puncture  Other, specify:

1. \*\*Site of CSF acquisition:

Ventricular cistern  Lumbar cistern

Other, specify:

1. \*\*Type and volume/number of collection tubes used:

Coated with EDTA  Polystyrene tubes

Coated with heparin  Polypropylene tubes

Coated with citrate  No coating

Other, specify:

1. \*\*CSF and serum collected simultaneously?

Yes  No

Unknown

\*\*If Yes, laboratory test(s) conducted:

Glucose  Oligoclonal bands

IgG  Other, specify:

1. \*\*CSF and plasma collected simultaneously?

Yes  No

Unknown

If Yes, laboratory test(s) conducted:

Glucose  Oligoclonal bands

IgG  Other, specify:

1. \*\*Collection grossly bloody?

Yes  No  Unknown

**Sample Shipping Information**

1. \*\*Sample shipped?

Yes No (Skip Q2) Unknown(Skip Q2)

1. \*\*Shipping conditions (choose all that apply):

Dry ice  Overnight

Other, specify:

## Sample Processing

1. \*\*Sample protected from ambient light?:

Yes  No  Unknown

1. \*\*Sample kept cooler than room temperature?:

Yes  No  Unknown

1. \*\*Sample centrifuged?:

Yes No (Skip to Q6)Unknown (Skip to Q6)

1. \*\*Time sample centrifuged

(MM/DD/YYYY):

(HH:MM, 24 hr clock):

1. \*\*Centrifugation methods:

RPM:

Temperature:

Duration:

1. \*\*Date and time of sample freezing:

(MM/DD/YYYY):

(HH:MM, 24 hr clock):

1. Method of freezing:

Snap- frozen  Dry ice-ethanol

Slowly cooled  Storage at -20°C

Storage at -80°C  Other, specify:

1. \*\*Type of sample stored:

Venous blood: (Further indicate venous type)

Whole  Plasma

Serum  Platelets

Buffy coat

Arterial blood: (Further indicate arterial type)

Whole  Plasma

Serum  Platelets

Buffy coat

Tissue (Further indicate type and specific area):

Clot  Cardiac

Blood vessel  Other

Saliva  Cerebral Spinal Fluid

Buccal swab  Newborn cord blood

Brain tissue  Placenta

Amniotic fluid  Other, specify:

Dura tissue

1. Additives used to store sample (Choose all that apply):

EDTA  Heparin

Citrate  None

Other, specify:

1. \*\*Sample storage temperature: (Co)
2. \*\*Number of Aliquots:
3. \*\*Volume of Aliquots (µL):
4. \*\*Date of sample expiration:

(MM/DD/YYYY):

N/A – no expiration

1. \*\*Date and time of analysis:

(MM/DD/YYYY):

(HH:MM, 24 hr clock):

## Supplemental Data Element Recommendations

1. \*\*Convalescent samples collected:

Yes  No  Unknown

1. \*\*Serial specimens collected (over time):

Yes  No  Unknown

1. \*\*Sample storage bar-code system (automated date/time) method used:

Yes  No  Unknown

1. \*\*Number of freeze/thaw cycles the sample went through prior to biomarker assay:
2. \*\*Selective inhibitors used (depending on target analyte):

Yes  No

If YES,

Protease inhibitor  RNAase inhibitor  Unknown

1. \*\*Condition of shipping (if samples shipped prior to biomarker assay):
   1. Potentially hazardous biological materials are triple packaged to withstand leakage, shocks, temperature and pressure changes that occur during handling and transportation:

Yes  No

* 1. Samples surrounded by dry ice to maintain temperature -80C or below throughout shipment:

Yes  No

* 1. \*\*Use insulated bio-shipment box:

Yes  No

1. \*\*\*For cerebral microdialysis specimens:
2. Location of probe placement:
3. Number of probes:
4. Probe molecular weight cut-off:
5. Membrane length:
6. Manufacturer:
7. Model #:
8. Time from ictus to monitoring:
9. Composition and source of the microdialysate:
10. Analyte values (mmol/l):
    1. Glucose:
    2. Pyruvate:
    3. Lactate:
    4. L/P ratio:
11. Any novel target analytes?

Yes  No

1. For multiplex platforms (proteomics, metabolomics, luminex assays):
   1. \*\*\*Normalization techniques:
   2. \*\*\*Presence of batch-effect?

Yes  No

* 1. Statistical methodology used to address multiple hypothesis testing:

## General Instructions

Important note: This case report form (CRF) contains data elements that are recommended for biospecimen methodology. Some of the data elements included on this CRF Module are classified as Core, Supplemental – Highly Recommended or Exploratory, as indicated by asterisks below:

\*\*Element is classified as Supplemental-Highly Recommended for biomarker/biospecimen studies. Tobacco/alchohol/food intake questions are Supplemental-Highly Recommended for observational studies.

\*\*\*Element is classified as Exploratory

All other elements are Supplemental and should only be collected if the research team considers them appropriate for their study. Please see the Data Dictionary for element classifications. Elements that are classified as Exploratory are those emerging molecular targets that may be recommended for more advanced and extended studies directed at a molecular mechanism that the biomarker measures.

## Specific Instructions

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

* Sample source: Biological fluid includes CSF, plasma, microdialysate, urine, etc.
* Reason(s) sample excluded: Certain conditions may alter normal biomarker composition and inclusion/exclusion should be carefully considered.
  + Infections of the nervous system or the target organ system from which samples are collected
  + Inflammatory conditions, (e.g., vasculitis, nervous system involvement of systemic autoimmune disorders).
  + Malignancy: changes serum/plasma analyte composition
* Baseline specimen collected: Collected within 12 hours of initial hospital presentation.
* Site of sample acquisition (for blood/plasma/serum samples): Vascular access includes arterial or central venous catheters.
* Method of CSF acquisition: Collection catheters include external ventricular and lumbar drain catheters. Other methods can include VP shunt tap.
* Date of sample acquisition: relative to disease/event onset
* Type of collection tubes: Recommended to use polypropylene tubes, rather than polystyrene.
* Sample processing:
  + For RNA, protein, metabolite targets: Sample should be immediately processed and frozen following sample collection. Recommend storage at -80⁰C or below, with minimal freeze/thaw cycles.
  + CSF samples: Recommend centrifugation for separation of supinate from cellular debri and storage of cell-free supinate.
* Normal/control samples: should be collected and analyzed to establish “normal” level for target biomarker.
* Convalescent samples from study subjects should be collected to establish the changes in biomarker level following acute illness/recovery.
* Collect serial specimens over time to determine the kinetics of the target biomarker of interest.
  + If serial collections used, the use of consistent method and site acquisition of serial CSF biospecimens is recommended.
* If samples are shipped prior to biomarker assay, report condition of shipping. Recommend samples be shipped frozen with abundant amount of dry ice to maintain temperature of -80 Co or below.
* For cerebral microdialysis specimens:
  + Probe placement should be in at-risk but viable tissue. Avoid placement in hematoma or infarcted tissue.
  + Recommendation: use concentric configuration commercially-available probes.
  + Microdialysate flow rate should be 0.3 uL/min over 1 hr. Avoid sample evaporation.
  + First hour microdialysate after probe placement should not be used.
  + Stored samples may be assayed using the batch analysis systems. However, if the low volume samples sit for too long in the analyzer prior to analysis, unacceptable evaporation may occur. Calibration samples should be interspersed in the batch to detect a systematic elevation in analyte levels due to evaporative loss.