## Specimen Collection from Adult Subjects/Participants

1. \*Sample source:

Biological tissue

Biological fluid

Unknown

1. \*Reason(s) sample excluded:

Nervous system infection  Inflammatory conditions

Target organ infection  Malignancy

Nervous system neoplasm  Renal failure

Paraneoplastic conditions  Liver failure

Demyelinating conditions

1. \*Site of sample acquisition (blood/serum/plasma samples):

Arterial blood source

Venous blood source

Peripheral venipuncture

Vascular access

Unknown

1. \*Baseline specimen collected:

Yes

No

Unknown

1. \*Method of CSF acquisition:

Collection catheter

Lumbar puncture

Other, specify:

1. \*Site of CSF acquisition:

Ventricular cistern

Lumbar cistern

Other, specify:

1. \*Date of sample collection:
2. \*Type of collection tubes used:

Coated with EDTA  Polystyrene tubes

Coated with heparin  Polypropylene tubes

Coated with citrate

No coating

Other, specify:

## Sample Processing

1. \*Centrifugation methods:
   1. RPM:
   2. Temperature
   3. Duration
2. \*Time lapse between sample collection and initial processing:
3. \*Type of sample stored:

Serum

Plasma

Buffy coat

Other, specify:

1. \*Sample storage temperature: (Co)

## Supplemental Data Element Recommendations

1. Normal/Control samples collected:

Yes

No

Unknown

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):

Potentially hazardous biological materials are triple packaged to withstand leakage, shocks, temperature and pressure changes that occur during handling and transportation:

Yes

No

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

Yes

No

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 Core

\*\*\*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.
* Conditions 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 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.