NINDS Common Data Element (CDE) Project

Stroke Version 2.0 Public Review

Biospecimens, Biomarkers, and Laboratory Tests Subgroup Materials

Guidance Documents:

- Appendix 1: Biomarker Targets in Stroke
- Appendix 2: Biospecimen SOP Guidance

Case Report Forms:

- Biospecimen Collection and Processing
- Laboratory Tests

Appendix 1: Biomarkers Targets in Stroke

~~NINDS Stroke Common Data Element (CDE) Project~~
~~Biospecimens and Biomarkers Subgroup: Recommendations~~

The Stroke Biospecimens ~~and~~, Biomarkers, and Laboratory Tests Subgroup recommended that stroke clinical studies consider collecting the ~~FDA approved~~Recommended biomarkers. They also listed other emerging biomarkers~~, which are not yet FDA approved,~~ that studies may want to collect.

~~FDA approved~~Recommended biomarkers:

- **Protein assays:**
  - Alipoprotein A (ApoA)
  - Alipoprotein B (ApoB)
  - **Brain natriuretic peptide** (BNP)
  - C-reactive protein (CRP)
  - D-dimer
  - Fibrinogen
  - Lipoprotein(a) [Lp(a)]
  - Lipoprotein-associated phospholipase A2 (Lp-PLA2)
  - Troponin
  - Von Willebrand factor (VWF)
- **Genotyping assays:**
  - Cytochrome P450 2C19 (CYP2c19)
  - Factor V Leiden
- **Metabolite assays:**
  - Homocysteine (homoCYS)
  - Uric acid

~~Non FDA approved, e~~Emerging biomarkers:

- **Protein assays:**
  - Inter-Cellular Adhesion Molecule 1 (ICAM-1)
  - Interleukin-6 (IL-6)
  - Matrix-metalloproteinase (MMP)
  - Neuron-specific enolase (NSE)
  - Plasminogen activator inhibitor type 1 (PAI)
  - P-selectin
  - S100 calcium binding protein B (S-100B)
  - Soluble CD40 ligand (sCD40 ligand)
  - Tumor necrosis factor (TNF)
  - Vascular cell adhesion molecule 1 (VCAM-1)

Genotyping assays:

- Activated Protein C Resistance (APC-R)
- Angiotensin converting enzyme (ACE)
- Alipoprotein E (ApoE)
- E-selectin
- ~~Methylenetetrahydrofolate reductase (MTHFR)~~
- Phosphodiesterase 4D (PDE4D)
- Prothrombin G20210A

The subsequent pages provide a short synopsis on each of the ~~FDA approved~~Recommended biomarkers.

Alipoprotein A (ApoA)

Appendix 1: Biomarkers Targets in Stroke

~~NINDS Stroke Common Data Element (CDE) Project~~
~~Biospecimens and Biomarkers Subgroup: Recommendations~~

Type of Assay
Protein

Annotation
Apo A-I is thought to be anti-atherogenic. It transports high density lipoprotein. ApoB-to-Apo A I ratio is associated with carotid plaque and with fatal and nonfatal ischemic stroke. One potential practical advantage of this ratio over conventional lipid markers, like LDL cholesterol, is that fasting is not be required for a reliable assessment. Apo A-I has also been associated with young adult stroke in some series (Erquo et al 2010).

References
(1) Gardener, H., Morte, D.D., Elkind, M., Sacco, R.L., Rundek, T. (2009). Lipids and carotid plaque in the Northern Manhattan Study (NOMAS). BMC Cardiovascular Disorders, 9, 55-63.
(2) Holme, I., Aastveit, A.H., Niklas, H., Jungner, I., Walldius, G. (2009). Inflammatory markers, lipoprotein components and risk of major cardiovascular events in 65,005 men and women in the Apolipoprotein MOrtality RISk study (AMORIS). J Internal Med., 265, 275-287.
(3) Walldius G, Aastveit AH, Jungner I. (2006). Stroke mortality and the apoB/apoA-I ratio: Results of the AMORIS prospective study. J Intern Med., 259, 259-266.
(4) Di Angelantonio E, Sarwar N., Perry P., Kaptoge, S., Ray, K.K. et al. (2009) Major Lipids, Apolipoproteins, and Risk of Vascular Disease Jama, 302(18), 1993-2000.
(5) Erqou S, Thompson A, Di AE et al. (2010). Apolipoprotein(a) isoforms and the risk of vascular disease: systematic review of 40 studies involving 58,000 participants. J Am Coll Cardiol, 11(19), 2160-2167.

Alipoprotein B (ApoB)

Type of Assay
Protein

Annotation
ApoB is thought to be atherogenic. ApoB is a transporter of very low density lipoprotein, intermediate-density lipoprotein and LDL particles. ApoB-to-Apo A-I ratio is associated with carotid plaque and with fatal and nonfatal ischemic stroke. One potential practical advantage of this ratio over conventional lipid markers, like LDL cholesterol, is that fasting is not be required for a reliable assessment. Apo B levels are reduced by statin use. Apo B is predictive of ischemic stroke in patients with previous transient ischemic attack. It has also been associated with young adult stroke and ApoB/ApoA is an independent predictor (Sabino 2008).

References
(1) Gardener, H., Morte, D.D., Elkind, M., Sacco, R.L., Rundek, T. (2009). Lipids and carotid plaque in the Northern Manhattan Study (NOMAS). BMC Cardiovascular Disorders, 9, 55-63.
(2) Holme, I., Aastveit, A.H., Niklas, H., Jungner, I., Walldius, G. (2009). Inflammatory markers, lipoprotein components and risk of major cardiovascular events in 65,005 men and women in the Apolipoprotein MOrtality RISk study (AMORIS). J Internal Med., 265, 275-287.

(3) Bhatia M, Howard SC, Clark TG, Neale R, Qizilbash N, Murphy MFG, Rothwell PM (2006). Apolipoproteins as Predictors of Ischaemic Stroke in Patients with a Previous Transient Ischaemic Attack. Cerebrovasc Dis 2006;21:323-328.
(4) Sabino AP, De Oliveira SM, Moreira LL et al. (2008). ApoB/ApoA-I ratio in young patients with ischemic cerebral stroke or peripheral arterial disease. Transl Res, 152(3),113-118.

Brain natriuretic peptide (BNP)

Type of Assay
Protein

Annotation
Brain natriuretic peptide (BNP) is a sensitive marker of cardiac contractile dysfunction. Levels of BNP have been shown to predict atrial fibrillation. BNP has been measured subacutely in patients with ischemic stroke, and levels associated with cardioembolic stroke mechanism and atrial fibrillation. Levels of BNP are also increased in congestive heart failure and renal failure.

References
No references

C-reactive protein (CRP)

Type of Assay
Protein

Annotation
High sensitivity C-reactive protein (hsCRP) is an inflammation-related biomarker related to risk of stroke in several studies. A meta-analysis including 54 prospective cohort studies (n=160,309) found an increased risk of ischemic stroke (RR per SD logCRP 1.44, 95% CI 1.32-1.57) adjusted for age and sex; this attenuated (RR 1.27, 95% CI 1.15-1.40) when further adjusted for other risk factors. Those with hsCRP>2 mg/L and <1 other risk factor may benefit from treatment with rosuvastatin or other statins, based on the results of a large RCT. CDC/AHA guidelines recommend considering measuring hsCRP for primary preventive purposes only in patients at intermediate risk of vascular disease. The role of hsCRP in secondary prevention after stroke remains uncertain, though some studies suggest hsCRP predicts mortality and recurrent events. Furthermore, hsCRP is acutely elevated in children with stroke that is associated with non-moyamoya arteriopathy (Bernard et al 2010).

References
(1) The Emerging Risk Factors Collaboration. (2010). C-reactive protein concentration and risk of coronary heart disease, stroke, and mortality: an individual participant meta-analysis. Lancet, 375, 132-140.
(2) Everett, B.M., Glynn, R.J., MacFadyen, J.G., Ridker, P.M. (2010). Rosuvastatin in the Prevention of Stroke Among Men and Women With Elevated Levels of C-Reactive Protein: Justification for the Use of Statins in Prevention: An Intervention Trial Evaluating Rosuvastatin (JUPITER). Circulation, 121, 143-150.
(3) Pearson, T.A., Mensah, G.A., Alexander, R.W., et al. (2003). Markers of inflammation and cardiovascular disease. Application to clinical and public health practice. A statement for

healthcare professionals from the Centers for Disease Control and Prevention and the American Heart Association. Circulation, 107, 499-511.
(4) Di Napoli, M., Schwaninger, M., Cappelli, R., et al. (2005). Evaluation of C-reactive protein measurement for assessing the risk and prognosis in ischemic stroke: a statement for health care professionals from the CRP Pooling Project members. Stroke, 36, 1316-1329.
(5) Bernard, T.J., et al., Biomarkers of hypercoagulability and inflammation in childhood-onset arterial ischemic stroke. J Pediatr., 156(4), 651-656.

Cytochrome P450 2C19 (CYP2c19)

Type of Assay
Genotyping

Annotation
This test is only FDA approved in the context of its inclusion in the Roche AmpliChip P450, which allows for the identification of genetic variants in CYP2d6 and CYP2c19 genes. Genetic variation in 2c19 allows for the identification of poor metabolizers of medications that are metabolized through the 2c19 pathway, including anti-epileptics, anti-convulsants, and psychotherapeutic drugs. Although CYP2c19 variants can also identify poor metabolizers of Clopidogrel (Plavix), there is no specific mention of this intended use.

References
DNA Direct. (n.d.) Drugs Metabolized by CYP450. Retrieved September 15, 2010

D-dimer

Type of Assay
Protein

Annotation
As products of fibrinolysis, serum D-dimer concentrations are acutely elevated in adult ischemic stroke patients, but serum D-dimer concentrations do not independently have the necessary sensitivity nor specificity to singularly serve as a reliable diagnostic marker (Haapaniemi 2009). In other studies, D-dimer levels have been associated with early clinical deterioration, stroke severity, poor clinical outcomes in patients with both ischemic and hemorrhagic stroke. However, D-dimer levels alone lack the robustness to serve as independent predictors of these endpoints (Barber 2006; Delgado 2006). D-dimer is elevated in acute childhood stroke and decreases over time in non-cardioembolic stroke (Bernard et al 2010). It is persistently elevated in childhood cardioembolic stroke (Bernard et al 2010).

References
(1) Bernard, T.J., Fenton, L.Z., Apkon, S.D., Broda, R., Wilkening, G.N., et al. (2009) Biomarkers of hypercoagulability and inflammation in childhood-onset arterial ischemic stroke. J Pediatr., 156(4), 651-656.
(2) Haapaniemi, E., Tatlisumak, T. (2009). Is D-dimer helpful in evaluating stroke patients? A systematic review. Acta Neurol Scand., 119, 141-150.
(3) Barber, M., Langhorne, P., Rumley, A., et al. (2006). D-dimer predict early clinical progression in ischemic stroke. Stroke, 37, 1113-1115.

(4) Delgado, P., Alverez-Sabin, J., Abilleira, S., et al. (2006). Plasma D-dimer predicts poor outcome after acute intracerebral hemorrhage. Neurology, 67, 94-98.

Fibrinogen

Type of Assay
Protein

Annotation
Controlling for diabetes and hypertension, higher fibrinogen levels are associated with the development of ischemic stroke (Fibrinogen Studies Collaboration 2005). After controlling for age and initial stroke severity, higher initial fibrinogen levels have been associated with poor outcomes in adults (del Zoppo et al 2009). Fibrinogen is also associated with childhood stroke that is associated with arteriopathy and cardiac disorders (Kopyta et al 2010).

References
(1) Kopyta, I., Sarecka-Hujar, B., Emich-Widera, E., Marszal, E., Zak, I. (2010). Association between lipids and fibrinogen levels and ischemic stroke in the population of the Polish children with arteriopathy and cardiac disorders. Wiad Lek, 63(1), 17-23.
(2) Fibrinogen, S.C. (2005). Plasma fibrinogen level and the risk of major cardiovascular diseases and nonvascular mortality: an individual participant metaanalysis. JAMA., 294, 1799 –1809.
(3) del Zoppo, G., Levy, D.E., Wasiewski, W.W., et al. (2009). Hyperfibrinogenemia and functional outcome from acute ischemic stroke. Stroke, 40, 1687-1691.

Factor V Leiden

Type of Assay
Genotyping

Annotation
The factor V (Leiden) mutation (1691G→A) occurs primarily in Caucasian populations and is a major risk factor for venous thrombosis and a lesser risk factor for arterial thrombosis. Factor V mutation analysis is also recommended to confirm positive APCR (activated Protein C resistance) tests. It is associated with stroke in childhood (Barrierinho et al, 2003; Duran et al, 2005; Kenet et al, 2007; Nowak-Gottl et al, 1998).

References
(1) Barreirinho, S., Ferro, A., Santos, M., et al. (2003) Inherited and acquired risk factors and their combined effects in pediatric stroke. Pediatr Neurol., 28(2), 134-138.
(2) Duran, R., Biner, B., Demir, M., Celtik, C., Karasalihoglu, S. (2005). Factor V Leiden mutation and other thrombophilia markers in childhood ischemic stroke. Clin Appl Thromb Hemost, 11(1), 83-88.
(3) Kenet, G., Sadetzki, S., Murad, H., et al. (2000). Factor V Leiden and antiphospholipid antibodies are significant risk factors for ischemic stroke in children. Stroke, 31(6), 1283-1288.

(4) Nowak-Gottl, U., Strater, R., Heinecke, A., et al. (1999). Lipoprotein (a) and genetic polymorphisms of clotting factor V, prothrombin, and methylenetetrahydrofolate reductase are risk factors of spontaneous ischemic stroke in childhood. Blood, 94(11), 3678-3682.

Homocysteine (homoCYS)

Type of Assay
Metabolite

Annotation
Extensive data supports a role for hyperhomocysteinemia as an independent risk factor for cerebrovascular atherosclerosis, leukoaraiosis, and ischemic stroke. Levels of homocysteine can be affected by folate or vitamin B12 deficiency, metabolic derangements, and many medications. In addition, levels of homocysteine increase after protein-rich meals. Methylenetetrahydrofolate reductase (MTHFR) is a key enzyme involved in degradation of plasma homocysteine. A common MTHFR substitution, 677C→T, causes reduced enzyme activity and increases plasma levels of homocysteine. Despite strong epidemiological data linking homocysteine to the pathogenesis of cerebrovascular disease, two secondary stroke prevention studies targeting homocysteine have failed to show a benefit to vitamin therapy. Homocysteine levels have been associated with stroke in children (Ganesan et al, 2003). MTHFR is no longer recommended as a first line test as homocysteine is preferred.

References
(1) Ganesan, V., Prengler, M., McShane, M.A., Wade, A.M., Kirkham, F.J. (2003). Investigation of risk factors in children with arterial ischemic stroke. Ann Neurol., 53(2), 167-73.

Lipoprotein(a) [Lp(a)]

Type of Assay
Protein

Annotation
Lp(a) consists of a protein moiety, apolipoprotein B-100 (LDL) linked, on a 1:1 molar basis, by a disulfide bond to apolipoprotein (a). Lp(a) decreases systemic fibrinolytic activity through multiple mechanisms. Lp(a) inhibits binding of plasminogen to annexin, preventing the conversion of plasminogen to plasmin. Lp(a) increases circulating levels of plasminogen activator inhibitor (PAI), thus lowering levels of tPA. Epidemiological studies in cerebrovascular disease have provided conflicting evidence regarding the role lp(a) plays in stroke risk, recurrence, or outcome. Published studies have used different assays, making comparisons difficult. Aspirin and niacin, commonly used in a stroke-prone population, can affect lp(a) levels. Lp(a) has been associated with stroke in children with cardiac disease (Strater et al, 1999). It has also been associated with recurrent stroke in childhood (Strater et al, 2002). Furthermore, it has shown to be a risk factor for stroke (Nowak-Gottl et al, 1999).

References
(1) Strater, R., Vielhaber, H., Kassenbohmer, R., von, K.R., Gobel, U., Nowak-Gottl, U. (1999). Genetic risk factors of thrombophilia in ischaemic childhood stroke of cardiac origin. A prospective ESPED survey. Eur J Pediatr., 158(Suppl 3), S122-S125.

(2) Strater, R., Becker, S., von, E.A., et al. (2002). Prospective assessment of risk factors for recurrent stroke during childhood--a 5-year follow-up study. Lancet, 360(9345), 1540-1545.
(3) Nowak-Gottl, U., Strater, R., Heinecke, A., et al. (1999). Lipoprotein (a) and genetic polymorphisms of clotting factor V, prothrombin, and methylenetetrahydrofolate reductase are risk factors of spontaneous ischemic stroke in childhood. Blood, 94(11), 3678-3682.

Lipoprotein-associated phospholipase A2 (Lp-PLA2)

Type of Assay
Protein

Annotation
Lp-PLA2 is a macrophage-derived enzyme involved in metabolism of LDL that is responsible for release of inflammatory mediators. Relative elevations in serum levels of Lp-PLA2 are associated with increased risk of incident ischemic stroke, independent of the effect of hsCRP. A large meta-analysis found evidence that LpPLA2 predicts risk of a first stroke. LP-PLA2 may also predict risk of recurrent stroke and other vascular events after a first stroke.

References
(1) Oei, H.H., van der Meer, I.M., Hofman, A., et al. (2005). Lipoprotein-associated phospholipase A2 activity is associated with risk of coronary heart disease and ischemic stroke: the Rotterdam Study. Circulation, 111, 570-575.
(2) Ballantyne, C.M., Hoogeveen, R.C., Bang, H., et al. (2005). Lipoprotein-associated phospholipase A2, high-sensitivity C-reactive protein, and risk for incident ischemic stroke in middle-aged men and women in the Atherosclerosis Risk in Communities (ARIC) study. Arch Intern Med., 165, 2479-2484.
(3) Lp-PLA(2) Studies Collaboration, Thompson, A., Gao, P., Orfei, L., Watson, S., (2010). Lipoprotein-associated phospholipase A2 and the risk of coronary disease, stroke and non-vascular mortality. Individual data analysis of 78,989 participants from 32 prospective studies. Lancet, 37, 1536-1544.
(4) Elkind, M.S.V., Tai, W., Coates, K., Paik, M.C., Sacco, R.L. (2006). Lipoprotein-associated phospholipase A2, C-reactive protein, and outcome after ischemic stroke. Arch Int Med., 166, 2073-2080.

Troponin

Type of Assay
Protein

Annotation
Cardiac troponins classically are associated with acute coronary syndrome and heart failure. Elevations in troponin have also been observed after stroke. This post-stroke elevation in cardiac troponins is associated with sympathoadrenal activation and is associated with electrocardiogram changes suggestive of acute coronary syndrome and with death. Troponin T has been associated with large infarcts involving the MCA distribution. Troponin I elevations have been associated with new onset atrial fibrillation soon after stroke.

References

(1) Kerra, G., Raya, G., Wub, O., Stotta, D.J., Langhornea, P., (2009). Elevated Troponin after Stroke: A Systematic Review. Cerebrovascular Diseases, 28(3), 220-226.
(2) Bugnicourta, J.M., Rogezb, V., Guillaumontc, M.P., Rogezd, J.C., Canapleb, S., et al. (2010). Troponin Levels Help Predict New-Onset Atrial Fibrillation in Ischaemic Stroke Patients: A Retrospective Study Euro Neuro, 63, 24-28
(3) Jensen, J.K., Kristensen, S.R., Bak, S., Atar, D., Høilund-Carlsen, P.F., Mickley, H. (2007). Frequency and significance of troponin T elevation in acute ischemic stroke. Am J Cardiol., 99, 108-112
(4) Chalela, J.A., Ezzeddine, M.A., Davis, L., Warach, S. (2004). Myocardial injury in acute stroke A troponin I study Neurocritical Care, 1, 343-6

Uric acid

Type of Assay
Metabolite

Annotation
Uric acid, a product of purine metabolism, is fairly abundant in human plasma, with normal concentrations ranging from 3.5 mg/dL to 8.3 mg/dL, and serves as one of the most important antioxidants in plasma. Compared to other biomarkers presented here, less data are available for uric acid in acute stroke. Increasing levels of uric acid have been associated with increasing risk of ischemic stroke and acute myocardial infarction (Bos 2006). In the setting of acute ischemic stroke, uric acid levels are increased and decline gradually over the course of days post-stroke. Declines in uric acid levels have been associated with stroke progression, increased morbidity and mortality (Brouns 2010). The potential neuroprotective effect of uric acid, serving as an antioxidant, in the setting of acute ischemic stroke is currently under study (Amaro 2007).

References
(1) Bos, M.J., Koudstaal, P.J., Hofman, A., et al. (2006). Uric acid is a risk factor for myocardial infarction and stroke: the Rotterdam study. Stroke, 37, 1503-1507.
(2) Brouns, R., Wauters, A., Van De Vijver, G. (2010). Decrease in uric acid in acute ischemic stroke correlates with stroke severity, evolution and outcome. Clin Chem Lab Med., 48, 383-390.
(3) Amaro, S., Soy, D., Obach, V., et al. (2007). A pilot study of dual treatment with recombinant tissue plasminogen activator and uric acid in acute ischemic stroke. Stroke, 38, 2173-2175.

Von Willebrand factor (VWF)

Type of Assay
Protein

Annotation
Megakaryocytes and endothelial cells synthesize von Willebrand factor. Clot stabilization is achieved once vWF becomes activated at the site of vascular injury, leading to binding of fibrin, transglutamination by factor XIII, and covalent crosslinking. vWF mediates the incorporation of platelets into thrombus. Elevations in von Willebrand factor have been associated with an

increased risk of ischemic stroke. Levels of vWF have been shown to be higher in patients with a greater burden of small vessel/lacunar strokes. vWF levels are also associated with many stroke risk factors such as atrial fibrillation, high grade carotid stenosis, and hyperhomocysteinemia. Single nucleotide polymorphisms in the promoter region of the vWF gene, affecting vWF levels, have been identified.

References

No references

Appendix 2: Biospecimen standard operating procedure (SOP) guidance~~elines~~:

1. Plasma and Serum

I. Acquisition of Blood Biospecimens

A. For patients with vascular access catheters (arterial line, central venous access devices) that have been placed as part of the patients' routine medical care, venous or arterial blood samples can be collected via these vascular access devices. Beware that certain biomarkers may have different levels depending on arterial vs. venous sampling (e.g., lactate). For patients without vascular access devices, trained personnel should collect blood through standard venipuncture.

B. For most purposes ~~for SAH research studies~~, whole blood will be collected using a vacutainer system. Standard vacutainer tubes for plasma collection may contain different anticoagulants (EDTA, citrate, heparin). It should be noted that if a vacutainer tube contains liquid anticoagulant (typically citrate), the vacutainer should be fully filled, otherwise the presence of liquid anticoagulant may cause differential dilution and alter the concentration of target biomarker. For studies requiring measurement of platelet function, vacutainers should not be used.

C. Quantity of blood taken at each collection depends on the total number of serial collections required for your study. Table 2 provides sample guideline on maximum allowable volume of blood draw for research purposes based on the research subject's total body weight and hemoglobin.

D. It should be noted that the use of glass tubes can lead to low values for certain analytes. For the most generalizable purposes, polypropylene vacutainers and subsequent storage tubes are recommended.

II. Local Processing (Serum)

A. Blood samples should be collected in vacutainers that contain no anticoagulant for the processing of serum.

B. Samples should be sat upright at room temperature for 15-20 minutes to allow for clotting. They then should be spun at 3900 RPM at room temperature for 5-7 minutes. The cleared serum should be pipetted and stored in small aliquots.

C. Record the volume of each aliquot.

III. Local Processing (Plasma)

A. Blood samples should be collected in vacutainers that contain EDTA, citrate, or heparin when preparing plasma. Note that the anticoagulant agent may interfere with analyte detection. It is important to select a collection vacutainer that does not contain chemicals that may interfere with the planned biomarker assay. EDTA may be the most versatile anticoagulant as it is less likely to interfere with analyte detection compared with other anticoagulants.

B. Transport the original, unfrozen blood sample to the designated local laboratory as soon as possible. Freezing has significant adverse effects on plasma and its proteomic elements.

C. As soon as possible, samples should be spun at 3900 RPM at room temperature for 10 - 15 minutes. Plasma should be immediately pipetted and stored in small aliquots.

D. Record the volume of each aliquot.

IV. Local Documentation and Storage

A. Appropriate and complete documentation surrounding biospecimen collection, processing, and storage are essential and will influence the quality of research data to be obtained.

B. Bar code identification of samples with an automated date and time stamp is recommended.

C. Samples should be placed in non frost-free freezers at or below -80^{0}C. Frost-free freezers go through freeze-thaw cycles that further damage the specimen.

D. Centers at which samples are stored should institute a back-up plan for freezer failure (e.g., dry ice or liquid nitrogen). An appropriate alarm system to support freezers for longtime storage is essential.

E. An inventory system should be established for tracking provenance of samples, including the time of collection, processing, storage, and quality-control procedures carried out on each sample.

V. Shipping

A. Dry ice or cold packs must accompany the frozen specimen during air shipment. When dry ice is used, the transport time should be minimized given that dry ice sublimates at a rate of 5-10lbs per 24 hours, depending on the insulation of the shipment container.
B. Consult the local agency for proper shipping options and certified transport materials. The International Air Transportantion Association (IATA, International Air Transportation Assosciation Website) and the U.S. Department of Transportation (DOT, United States Department of Transportation Website) have legal requirements governing the packaging, labeling, and shipping of biospecimen.
    b. Category A Infectious Substances are capable of causing permanent disability, life threatening or fatal disease in humans or animals when exposure occurs.
    c. Category B Infectious Substances (also “diagnostic specimens” or “clinical specimens”) are infectious but do not meet the standard for Category A inclusion.
    d. Exempt Patient Specimens have a minimal likelihood of containing pathogens.
D. Temperature loggers can be used to monitor temperature in shipments of samples to provide confirmation and assurance that samples have been maintained at appropriate temperatures.

VI. Central Storage

A. Appropriate and complete documentation surrounding biospecimen collection, processing, storage, and shipping from the individual sites is essential and will influence the quality of the multicenter research data to be obtained.
B. Bar code identification of samples with an automated date and time stamp is recommended.
C. A formal plan for sharing the central biospecimen resource is recommended.
D. The Central Bank should maintain information of laboratories where the samples have been sent to avoid duplicative analyses and inadvertent repetitive reporting of data from the same patient.
E. The Central Bank should also maintain information regarding any stipulations on informed consent for the use of the samples. For example, in some studies participants may provide permission for their samples to be used only for studies on SAH.

2. Cerebrospinal Fluid (CSF)

I. Acquisition of CSF from an external ventricular drain (EVD) or lumbar drain (LD):

A. Document whether CSF drainage is continuous or intermittent (catheter opened only in response to intracranial hypertension). Drainage method has been shown to alter CSF protein concentration (Shore et al, 2004).
B. Recommend the use of full sterile technique for all access to the CSF collection system for CSF sampling.
C. Draw CSF directly from ventriculostomy catheter or sample from other portions of the EVD setup (e.g., below the collection cylinder) for large volume collection.
D. For larger volume collection, can let CSF collect over 30 – 60 mins in the collection cylinder, and then collect the accumulated fluid from below the cylinder, before CSF is drained into the large collection bag. Do not sample from the collection bag as it contains CSF and cell debri over time and may not represent CSF composition surrounding the brain.
E. Target CSF collection within the first 24 hours of admission, recording time of collection from SAH onset and time of day. Ideally, the first collection should be as close to the SAH onset as feasible.
F. If CSF is available through external collection system, recommend repeated sampling for at a minimum frequency of every 24 h for biokinetic studies.
A. Clearly document source of CSF collection (EVD v.s. LD). Note that there may be a 2.5-fold difference in protein concentration in ventricular CSF compared to lumbar CSF (Hühmer et al, 2006). Comparison of CSF from different sources is generally discouraged. If a comparison must be made, the difference in CSF composition by region should be taken into account in the interpretation of results.

Acquisition of CSF from a Lumbar Puncture (LP)

B. In patients who are unlikely to receive ventriculostomy. CSF can be collected via lumbar puncture (LP) with informed consent. However, comparison with EVD CSF is discouraged given a 2.5-fold lower protein concentration than in LP CSF (Hühmer et al, 2006).
C. Atraumatic spinal needle LP kits should be used to minimize risk of post-LP headache. Draw with a sterile polypropylene syringe, or allow flow under gravity.

D. Target CSF collection within the first 24 hours of admission, recording time of collection from SAH onset and time of day. Ideally, the first collection should be as close to the SAH onset as feasible.
E. Collect 1-mL fractions and place in ice bath, with a maximum of 25 mL per time point. Send the first 2 mL for clinical laboratory analysis. It is important to match fractions when comparing across patients, as protein concentration varies depending on the draw volume (Blennow et al, 1993).
F. Patient should rest in a recumbent position for 1 h post-LP receive liberal fluid intake, and avoid exertion for 24-48 h to minimize risk of headache.

II. Processing and Storage of CSF

A. Transport and process CSF immediately after collection as significant cell lysis contamination will occur within 1 hour.
B. Collect CSF samples into low protein binding polypropylene tubes (e.g., Eppendorf brand LoBind® tubes). Avoid polystyrene and glass tubes, which will result in significant protein loss (Hesse et al, 2000).
C. Centrifuge CSF at 3900 RPM at room temperature for 15 mins. Immediately remove supinant in aliquots in new, low binding tubes. Label each tube using low-temperature resistant laboratory labels (e.g., Cryo-Babies by USA Scientific). Document number of aliquots and volume of each aliquot. Immediately place aliquots on dry ice or into -80^{0}C freezer for storage.
D. Additives or preservatives (e.g., protease and phosphatase inhibitors) may be combined with CSF depending on experimental objectives.
E. Store all CSF samples at or below -80^{0}C to minimize proteolytic breakdown (Wagner et al, 2007). Avoid repeated freeze and thawing cycles and storage at -20˚C (Carrette et al, 2005).

Tabel 1 MAXIMUM ALLOWABLE TOTAL BLOOD DRAW VOLUMES

Body Wt (Kg)	Body Wt (lbs)	Total blood volume (mL)	Maximum allowable volume (mL) in one blood draw (= 2.5% of total blood volume)	Maximum volume (clinical + research) (mL) in a 30-day period	Minimum Hgb required at time of blood draw	Minimum Hgb required at time of blood draw if subject has respiratory/CV compromise
1	2.2	100	2.5	5	7.0	9.0-10.0
2	4.4	200	5	10	7.0	9.0-10.0
3	6.3	240	6	12	7.0	9.0-10.0
4	8.8	320	8	16	7.0	9.0-10.0
5	11	400	10	20	7.0	9.0-10.0
6	13.2	480	12	24	7.0	9.0-10.0
7	15.4	560	14	28	7.0	9.0-10.0
8	17.6	640	16	32	7.0	9.0-10.0
9	19.8	720	18	36	7.0	9.0-10.0
10	22	800	20	40	7.0	9.0-10.0
11-15	24-33	880-1200	22-30	44-60	7.0	9.0-10.0
16-20	35-44	1280-1600	32-40	64-80	7.0	9.0-10.0
21-25	46-55	1680-2000	42-50	64-100	7.0	9.0-10.0
26-30	57-66	2080-2400	52-60	104-120	7.0	9.0-10.0
31-35	68-77	2480-2800	62-70	124-140	7.0	9.0-10.0
36-40	79-88	2880-3200	72-80	144-160	7.0	9.0-10.0
41-45	90-99	3280-3600	82-90	164-180	7.0	9.0-10.0
46-50	101-110	3680-4000	92-100	184-200	7.0	9.0-10.0

Body Wt (Kg)	Body Wt (lbs)	Total blood volume (mL)	Maximum allowable volume (mL) in one blood draw (= 2.5% of total blood volume)	Maximum volume (clinical + research) (mL) in a 30-day period	Minimum Hgb required at time of blood draw	Minimum Hgb required at time of blood draw if subject has respiratory/CV compromise
51-55	112-121	4080-4400	102-110	204-220	7.0	9.0-10.0
56-60	123-132	4480-4800	112-120	224-240	7.0	9.0-10.0
61-65	134-143	4880-5200	122-130	244-260	7.0	9.0-10.0
68-70	145-154	5280-5600	132-140	264-280	7.0	9.0-10.0
71-75	156-185	5680-6000	142-150	284-300	7.0	9.0-10.0
76-80	167-176	6080-6400	152-160	304-360	7.0	9.0-10.0
81-85	178-187	6480-6800	162-170	324-340	7.0	9.0-10.0
86-90	189-198	6880-7200	172-180	344-360	7.0	9.0-10.0
91-95	200-209	7280-7600	182-190	364-380	7.0	9.0-10.0
96-100	211-220	7680-8000	192-200	384-400	7.0	9.0-10.0

References:

Blennow K, Fredman P, Wallin A, Gottfries CG, Karlsson I, Långström G, Skoog I, Svennerholm L, Wikkelsö C. Protein analysis in cerebrospinal fluid. II. Reference values derived from healthy individuals 18-88 years of age. Eur Neurol. 1993;33(2):129–133.

Carrette O, Burkhard PR, Hughes S, Hochstrasser DF, Sanchez JC. Truncated cystatin C in cerebrospiral fluid: Technical [corrected] artefact or biological process? Proteomics. 2005;5(12):3060–3065. Erratum in: Proteomics. 2005;5(14):3822.

Hesse C, Larsson H, Fredman P, Minthon L, Andreasen N, Davidsson P, Blennow K. Measurement of apolipoprotein E (apoE) in cerebrospinal fluid. Neurochem Res. 2000;25(4):511–517.

Hühmer AF, Biringer RG, Amato H, Fonteh AN, Harrington MG. Protein analysis in human cerebrospinal fluid: Physiological aspects, current progress and future challenges. Dis Markers. 2006;22(1-2):3-26.

Shore PM, Thomas NJ, Clark RS, Adelson PD, Wisniewski SR, Janesko KL, Bayir H, Jackson EK, Kochanek PM. Continuous versus intermittent cerebrospinal fluid drainage after severe traumatic brain injury in children: effect on biochemical markers. J Neurotrauma. 2004;21(9):1113–1122.

Wagner AK, Ren D, Conley YP, Ma X, Kerr ME, Zafonte RD, Puccio AM, Marion DW, Dixon CE. Sex and genetic associations with cerebrospinal fluid dopamine and metabolite production after severe traumatic brain injury. J Neurosurg. 2007;106(4):538–547.

Biospecimen Collection and Processing

[Study Name/ID pre-filled] Site Name:

Subject ID:

~~Participant/Subject Information~~

1. ~~Genetic Disorder?~~
   ~~☐ No known single gene disorder~~ ~~☐ Mendelian~~
   ~~☐ Mitochondrial~~ ~~☐ Other, specify:~~
2. ~~Pregnant or in postpartum state?~~
   ~~☐ Yes~~ ~~☐ No~~ ~~☐ Unknown~~
   ~~If YES, specify current state:~~
   ~~☐ Pre-partum 1st trimester~~ ~~☐ Pre-partum 2nd trimester~~
   ~~☐ Pre-partum 3rd trimester~~ ~~☐ Active labor~~
   ~~☐ Postpartum first 24 hrs~~ ~~☐ Postpartum first week~~
   ~~☐ Postpartum > 1 week~~
3. ~~Taking supplements?~~
   ~~☐ Yes~~ ~~☐ No~~ ~~☐ Unknown~~
   ~~If YES, type(s) of supplements (Choose all that apply):~~
   ~~☐ Beta Carotene~~ ~~☐ Calcium~~
   ~~☐ Dehydroepiandrosterone (DHEA)~~ ~~☐ Echinacea~~
   ~~☐ Flax Seed Oil~~ ~~☐ Folic Acid~~
   ~~☐ Gingko~~ ~~☐ Ginseng~~
   ~~☐ Saw Palmetto~~ ~~☐ Soy Protein Powder~~
   ~~☐ Soy Supplements~~ ~~☐ St. John's Wort~~
   ~~☐ Vitamin A~~ ~~☐ Vitamin C~~
   ~~☐ Vitamin E~~ ~~☐ Weight Loss Supplements~~
   ~~☐ Wheat Germ~~ ~~☐ Other, specify:~~

~~The remainder of t~~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):
2. Date last had an alcoholic drink:
   (MM/DD/YYYY):
   ☐ N/A – has not consumed an alcoholic drink within the past year
3. 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
4. Date and time last ate:

Biospecimen Collection and Processing

[Study Name/ID pre-filled] Site Name:

Subject ID:

(MM/DD/YYYY):
(HH:MM, 24 hr. clock):

5. Sample source:*
   - ☐ Biological tissue
   - ☐ Biological fluid
   - ☐ Unknown
6. Living or Deceased at time of collection:
   - ☐ Living
   - ☐ Deceased
7. Type of sample:

   Venous blood: (Further indicate venous type)
   - ☐ Whole
   - ☐ Serum
   - ☐ Buffy coat
   - ☐ Plasma
   - ☐ Platelets

   Arterial blood: (Further indicate arterial type)
   - ☐ Whole
   - ☐ Serum
   - ☐ Buffy coat
   - ☐ Plasma
   - ☐ Platelets

   Tissue (Further indicate type and specific area):
   - ☐ Clot
   - ☐ Blood vessel
   - ☐ Cardiac
   - ☐ Other, specify:
   - ☐ Saliva
   - ☐ Buccal swab
   - ☐ Cerebral Spinal Fluid
   - ☐ Newborn cord blood
   - ☐ Brain tissue
   - ☐ Placenta
   - ☐ Amniotic fluid
   - ☐ Other, specify:
   - ☐ Dura Tissue
8. Reason(s) sample excluded:*
   - ☐ Nervous system infection
   - ☐ ~~Target organ infection~~ Infection at site of sample
   - ☐ Nervous system neoplasm
   - ☐ Paraneoplastic conditions
   - ☐ Demyelinating conditions
   - ☐ Exclusionary medication being taken
   - ☐ Inflammatory conditions
   - ☐ Malignancy
   - ☐ Renal failure
   - ☐ Liver failure
   - ☐ Participant declined to provide specimen
9. Baseline specimen collected:*

Biospecimen Collection and Processing

[Study Name/ID pre-filled] Site Name:

Subject ID:

☐ Yes ☐ No ☐ Unknown

Blood Sample Collection Information

1. Normal/Control samples collected:
   ☐ Yes ☐ No ☐ Unknown

2. Patient position during sample collection:
   ☐ Seated ☐ Lying

   ☐ Standing

3. ~~Site of sample acquisition:*~~
   ~~☐ Arterial blood source ☐ Venous blood source~~

   ~~☐ Peripheral venipuncture ☐ Vascular access~~

   ~~☐ Unknown~~

4. 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

5. Was sample hemolyzed (Gross hemolysis, microscope not required)?
   ☐ Yes ☐ No ☐ Unknown

6. Needle gauge size:
   ☐ 16 gauge ☐ 18 gauge

   ☐ 20 gauge ☐ Unknown

   ☐ Other, specify:

7. Type and volume/number of collection tubes used:*
   ☐ Blood cultures- SPS ☐ Citrate Tube

   ☐ Serum Tube ☐ ~~BD~~ Vacutainer
   SST/ Gel Separator Tube

Biospecimen Collection and Processing

[Study Name/ID pre-filled] Site Name:

Subject ID:

☐ ~~BD~~ Vacutainer PST ☐ Heparin Tube

☐ Gel Separator Tube with Heparin ☐ EDTA tube

☐ Fluoride (glucose) Tube ☐ Polypropylene

☐ Other, specify:

Cerebral Spinal Fluid (CSF) Sample Collection Information

8. Normal/Control samples collected:
   ☐ Yes ☐ No ☐ Unknown
9. Method of CSF acquisition:*
   ☐ ~~Sample collected directly from~~Collection catheter ☐ Sample collected from bag/reservoir
   ☐ Lumbar puncture ☐ Other, specify:
10. Site~~Location~~ of CSF ~~collection~~acquisition:*
    ☐ Ventricular cistern ☐ Lumbar cistern
    ☐ Other, specify:
11. Type and volume/number of collection tubes used:*
    ☐ Coated with EDTA ☐ Polystyrene tubes
    ☐ Coated with heparin tubes ☐ Polypropylene
    ☐ Coated with citrate ☐ No coating
    ☐ Other, specify:
12. CSF and serum collected simultaneously?
    ☐ Yes ☐ No
    ☐ Unknown

    If Yes, laboratory test(s) conducted:
    ☐ Glucose ☐ Oligoclonal bands
    ☐ IgG ☐ Other, specify:
13. CSF and plasma collected simultaneously?
    ☐ Yes ☐ No
    ☐ Unknown

    If Yes, laboratory test(s) conducted:
    ☐ Glucose ☐ Oligoclonal bands
    ☐ IgG ☐ Other, specify:
14. Collection grossly bloody?
    ☐ Yes ☐ No ☐ Unknown

Sample Shipping Information

1. Sample shipped?
   ☐ Yes ☐ No (Skip Q2) ☐ Unknown (Skip Q2)
2. Shipping conditions (choose all that apply):

Biospecimen Collection and Processing

[Study Name/ID pre-filled] Site Name:

Subject ID:

☐ Dry ice ☐ Overnight
☐ Other, specify:

Sample Processing

1. Sample protected from ambient light?:
   ☐ Yes ☐ No ☐ Unknown
2. Sample kept cooler than room temperature?:
   ☐ Yes ☐ No ☐ Unknown
3. Sample centrifuged?:
   ☐ Yes ☐ No (Skip to Q6) ☐ Unknown (Skip to Q6)
4. Time sample centrifuged*
   (MM/DD/YYYY):

   (HH:MM, 24 hr clock):
5. Centrifugation methods:*
   RPM:

   Temperature:

   Duration:
6. Date and time of sample freezing:
   (MM/DD/YYYY):

   (HH:MM, 24 hr clock):
7. Method of freezing~~before analysis~~:
   ☐ Snap- frozen ☐ Dry ice-ethanol
   ☐ Slowly cooled ☐ Storage at -20°C
   ☐ Storage at -80°C ☐ Other, specify:
8. 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, specify

Biospecimen Collection and Processing

[Study Name/ID pre-filled] Site Name:

Subject ID:

☐ Saliva ☐ Cerebral Spinal Fluid
☐ Buccal swab ☐ Newborn cord blood
☐ Brain tissue ☐ Placenta

☐ Amniotic fluid ☐ Other, specify:
☐ Dura tissue

~~9. Material used to store sample:~~
~~☐ Glass ☐ Plastic, specify type:~~

10. Additives used to store sample (Choose all that apply):
☐ EDTA ☐ Heparin
☐ Citrate ☐ None
☐ Other, specify:

11. Sample storage temperature: (C°)*

12. Number of Aliquots:

13. Volume of Aliquots (µL):

14. Date of sample expiration (MM/DD/YYYY):
☐ N/A – no expiration

15. Date and time of analysis
(MM/DD/YYYY):
(HH:MM, 24 hr clock):

Supplemental Data Element Recommendations

15. Convalescent samples collected:
☐ Yes ☐ No ☐ Unknown

16. Serial specimens collected (over time):
☐ Yes ☐ No ☐ Unknown

17. Sample storage bar-code system (automated date/time) method used:
☐ Yes ☐ No ☐ Unknown

18. Number of freeze/thaw cycles the sample went through prior to biomarker assay:

19. Selective inhibitors used (depending on target analyte):
☐ Yes ☐ No

If YES,

☐ Protease inhibitor ☐ RNAase inhibitor ☐ Unknown

20. Condition of shipping (if samples shipped prior to biomarker assay):

Biospecimen Collection and Processing

[Study Name/ID pre-filled] Site Name:

Subject ID:

a. Potentially hazardous biological materials are triple packaged to withstand leakage, shocks, temperature and pressure changes that occur during handling and transportation:
   ☐ Yes ☐ No

b. Samples surrounded by dry ice to maintain temperature -80C or below throughout shipment:
   ☐ Yes ☐ No

c. Use insulated bio-shipment box:
   ☐ Yes ☐ No

21. For cerebral microdialysis specimens:
    a. Location of probe placement:
    b. Number of probes:
    c. Probe molecular weight cut-off:
    d. Membrane length:
    e. Manufacturer:
    f. Model #:
    g. Time from ictus to monitoring:
    h. Composition and source of the microdialysate:
    i. Analyte values (mmol/l):
       a. Glucose:
       b. Pyruvate:
       c. Lactate:
       d. L/P ratio:
    j. Any novel target analytes?
       ☐ Yes ☐ No

22. For multiplex platforms (proteomics, metabolomics, luminex assays): ***
    a. Normalization techniques:
    b. Presence of batch-effect?
       ☐ Yes ☐ No

    c. Statistical methodology used to address multiple hypothesis testing:

Biospecimen Collection and Processing

[Study Name/ID pre-filled] Site Name:

Subject ID:

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~~ 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 -80^{0}C 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.

Biospecimen Collection and Processing

[Study Name/ID pre-filled] Site Name:

Subject ID:

  - 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 C° 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.

Laboratory Tests

[Study Name/ID pre-filled] Site Name:

Subject ID:

Lab Panel Table

Lab Panel: (check one)	Date Collected	Accession Number:
☐ CHEMISTRY ☐ HEMATOLOGY ☐ URINALYSIS ☐ Other, specify:	(M M/D D/Y Y Y Y): ~~Time Collected (HH:MM):~~ ~~☐ AM~~ ~~☐ PM~~ ~~☐ 24-hr clock~~	Accession Number:

Indicate the appropriate result for each test.

Lipid Laboratory Tests

Lipid Laboratory Tests Table

Test	Result	Units for Result	Unit Type	Was test result abnormal?
Total Cholesterol (TCHOL)	Data to be entered by site	mg/dL~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Low Density Lipoprotein (LDL)	Data to be entered by site	mg/dL~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
High Density Lipoprotein (HDL)	Data to be entered by site	mg/dL~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Triglycerides (TGs)	Data to be entered by site	mg/dL~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Very Low Density Lipoprotein (VLDL)	Data to be entered by site	mg/dL~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Lipoprotein(a) [Lp(a)]	Data to be entered by site	mg/dL~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Apolipoprotein A-I (apo A1)	Data to be entered by site	mg/dL~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Apolipoprotein B (apo B)	Data to be entered by site	mg/dL~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Apolipoprotein E (apo E)	Data to be entered by site	☐ APOE ε2 (rare) ☐ APOE ε3 (most common) ☐ APOE ε4 (high risk) ~~Data to be entered by site~~	N/A	☐ Normal ☐ Abnormal ☐ Unknown

Laboratory Tests

[Study Name/ID pre-filled] Site Name:

Subject ID:

Complete Blood Count (CBC) Laboratory Tests

Complete Blood Count (CBC) Laboratory Tests Table

Test	Result	Units for Result	Unit Type	Was test result abnormal?
White Blood Cell Count (WBC)	Data to be entered by site	~~Data to be entered by site~~x10^3	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Lymphocyte Count	Data to be entered by site	thousand/microL~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Neutrophil Count (PMNs)	Data to be entered by site	thousand/microL~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Monocyte Count	Data to be entered by site	thousand/microLData to be entered by site	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Eosinophil Count	Data to be entered by site	thousand/microL~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Hematocrit (HCT)	Data to be entered by site	~~Data to be entered by site~~%	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Hemoglobin (HB)	Data to be entered by site	g/dL~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Platelet Count	Data to be entered by site	x10^3~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown

Laboratory Tests

[Study Name/ID pre-filled] Site Name:

Subject ID:

Test	Result	Units for Result	Unit Type	Was test result abnormal?
Hemoglobin Electrophoresis	Data to be entered by site	☐ Hemoglobin F (fetal hemoglobin) (HbF) ☐ Hemoglobin A (HbA) ☐ Hemoglobin A2 (HbA2) ☐ Hemoglobin S (HbS) ☐ Hemoglobin C (HbC) ☐ Hemoglobin E (HbE) ☐ Hemoglobin D (HbD) ☐ Hemoglobin H (heavy hemoglobin) (HbH)~~Data to be entered by site~~	N/A	☐ Normal ☐ Abnormal ☐ Unknown

Electrolyte Laboratory Tests

Electrolyte Laboratory Tests Table

Test	Result	Units for Result	Unit Type	Was test result abnormal?
Sodium (Na+)	Data to be entered by site	mEq/L OR mg/dL~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Potassium (K+)	Data to be entered by site	mEq/L OR mg/dL~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Chloride (Cl-)	Data to be entered by site	mEq/L OR mg/dL~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Carbon Dioxide (CO2)	Data to be entered by site	mEq/L~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Anion Gap	Data to be entered by site	mEq/L~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Blood Urea Nitrogen (BUN)	Data to be entered by site	mg/dL~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown

Laboratory Tests

[Study Name/ID pre-filled] Site Name:

Subject ID:

Test	Result	Units for Result	Unit Type	Was test result abnormal?
Creatinine	Data to be entered by site	mg/dL~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Glucose	Data to be entered by site	mg/dL~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Fasting Insulin	Data to be entered by site	µIU/mL	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Magnesium (Mg2+)	Data to be entered by site	mg/dL~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Phosphate (PO4)	Data to be entered by site	mg/dL~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Calcium (Ca2+)	Data to be entered by site	mg/dL~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Ionized Calcium (iCa2+)	Data to be entered by site	mmol/L~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Bicarbonate (HCO3)	Data to be entered by site	Meq/L~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown

Arterial Blood Gas Laboratory Tests

Arterial Blood Gas Laboratory Tests Table

Test	Result	Units for Result	Unit Type	Was test result abnormal?
Partial Pressure of Oxygen (PaO2)	Data to be entered by site	mmHg~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Partial Pressure of Carbon Dioxide (PaCO2)	Data to be entered by site	mmHgData to be entered by site	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Acidity/ pH	Data to be entered by site	~~Data to be entered by site~~Numeric value	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown

Liver Function Laboratory Tests

Laboratory Tests

[Study Name/ID pre-filled] Site Name:

Subject ID:

Liver Function Laboratory Tests Table

Test	Result	Units for Result	Unit Type	Was test result abnormal?
Albumin	Data to be entered by site	g/dL~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Total Protein	Data to be entered by site	g/dL~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Aspartate aminotransferase (AST)	Data to be entered by site	units/L~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Alanine Aminotransferase (ALT)	Data to be entered by site	units/L~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Total Bilirubin	Data to be entered by site	mg/dL~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Direct Bilirubin	Data to be entered by site	mg/dL~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Alkaline Phosphatase	Data to be entered by site	units/L~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Gamma-glutamyl transpeptidase (GGT)	Data to be entered by site	units/L	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown

Miscellaneous Chemistry Laboratory Tests

Miscellaneous Chemistry Laboratory Tests Table

Test	Result	Units for Result	Unit Type	Was test result abnormal?
Lactate Dehydrogenase (LDH)	Data to be entered by site	units/L~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Lactate	Data to be entered by site	mg/dL~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Iron	Data to be entered by site	µg/dL~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Total Iron Binding Capacity (TIBC)	Data to be entered by site	µg/dL~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown

Laboratory Tests

[Study Name/ID pre-filled] Site Name:

Subject ID:

Test	Result	Units for Result	Unit Type	Was test result abnormal?
Ferritin	Data to be entered by site	ng/mL~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown

Autoimmune Laboratory Tests

Autoimmune Laboratory Tests Table

Test	Result	Units for Result	Unit Type	Was test result abnormal?
Antinuclear Antibodies (ANA)	Data to be entered by site	☐ Negative ☐ Positive (with numeric value, if positive)~~Data to be entered by site~~	N/A	☐ Normal ☐ Abnormal ☐ Unknown
Classical AntiNeutrophil Cytoplasmic Antibodies (C-ANCA)	Data to be entered by site	☐ Negative ☐ Positive (with numeric value, if positive)~~Data to be entered by site~~	N/A	☐ Normal ☐ Abnormal ☐ Unknown
Protoplasmic-staining AntiNeutrophil Cytoplasmic Antibodies (P-ANCA)	Data to be entered by site	☐ Negative ☐ Positive (with numeric value, if positive)~~Data to be entered by site~~	N/A	☐ Normal ☐ Abnormal ☐ Unknown
Rheumatoid Factor	Data to be entered by site	☐ Negative ☐ Positive (with numeric value, if positive)~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Anticardiolipin Antibody IgM (ACA Igm)	Data to be entered by site	MPL units/mL~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Anticardiolipin Antibody IgG (ACA IgG)	Data to be entered by site	GPL units/mL~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
β 2- glycoprotein Antibody IgM	Data to be entered by site	~~Data to be entered by site~~Numeric value	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
β 2- glycoprotein Antibody IgG	Data to be entered by site	Numeric value~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown

Clotting Laboratory Tests

Laboratory Tests

[Study Name/ID pre-filled] Site Name:

Subject ID:

Clotting Laboratory Tests Table

Test	Result	Units for Result	Unit Type	Was test result abnormal?
Factor V Leiden Mutation (FVL)	Data to be entered by site	☐ Absent ☐ Heterozygous (1 allele) ☐ Homozygous (2 alleles)~~Data to be entered by site~~	N/A	☐ Normal ☐ Abnormal ☐ Unknown
Prothrombin Gene Mutation (Factor II/ G20210A)	Data to be entered by site	☐ Absent ☐ Heterozygous (1 allele) ☐ Homozygous (2 alleles)~~Data to be entered by site~~	N/A	☐ Normal ☐ Abnormal ☐ Unknown
Protein C Activity	Data to be entered by site	~~Data to be entered by site~~%	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Protein S Activity	Data to be entered by site	~~Data to be entered by site~~%	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Protein S Antigen, Free	Data to be entered by site	%	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Activated Protein C Resistance (APCR)	Data to be entered by site	~~Data to be entered by site~~ratio	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
~~5,10 Methylene Tetra Hydrofolate Reductase (MTHFR)~~	~~Data to be entered by site~~	~~Data to be entered by site~~	~~☐ Normal~~ ~~☐ Abnormal~~ ~~☐ Unknown~~	
Prothrombin Time (PT)	Data to be entered by site	~~Data to be entered by site~~seconds	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Activated Partial Thromboplastin Time (aPTT)	Data to be entered by site	seconds~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Antithrombin Activity (AT-III)	Data to be entered by site	~~Data to be entered by site~~%	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
International Normalized Ratio (INR)	Data to be entered by site	~~Data to be entered by site~~Numeric value	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown

Laboratory Tests

[Study Name/ID pre-filled] Site Name:

Subject ID:

Test	Result	Units for Result	Unit Type	Was test result abnormal?
Dilute Russell Viper Venom Time (DRVVT)	Data to be entered by site	~~Data to be entered by site~~seconds	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Confirmatory Testing for Lupus Anticoagulant	Data to be entered by site	~~Data to be entered by site~~ratio	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Fibrinogen	Data to be entered by site	mg/dL~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Plasmin	Data to be entered by site	Numeric value~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
D-dimer	Data to be entered by site	ng/mL~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Thrombin Time	Data to be entered by site	~~Data to be entered by site~~seconds	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown

Inflammatory Laboratory Tests

Inflammatory Laboratory Tests Table

Test	Result	Units for Result	Unit Type	Was test result abnormal?
High Sensitivity C Reactive Protein (hsCRP)	Data to be entered by site	mg/L~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Erythrocyte Sedimentation Rate (ESR)	Data to be entered by site	mm/hr~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown

Nutrition Laboratory Tests

Nutrition Laboratory Tests Table

Test	Result	Units for Result	Unit Type	Was test result abnormal?
Vitamin B12	Data to be entered by site	pg/ml~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Homocysteine	Data to be entered by site	u/mol/L~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Folate	Data to be entered by site	ng/mL~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown

Laboratory Tests

[Study Name/ID pre-filled] Site Name:

Subject ID:

Infectious Disease Laboratory Tests

Infectious Disease Laboratory Tests Table

Test	Result	Units for Result	Unit Type	Was test result abnormal?
Rapid Plasma Reagin (RPR)	Data to be entered by site	☐ Negative ☐ Positive ~~Data to be entered by site~~	N/A	☐ Normal ☐ Abnormal ☐ Unknown
HIV Antibodies	Data to be entered by site	☐ Negative ☐ Positive ~~Data to be entered by site~~	N/A	☐ Normal ☐ Abnormal ☐ Unknown

Cardiac Laboratory Tests

Cardiac Laboratory Tests Table

Test	Result	Units for Result	Unit Type	Was test result abnormal?
Troponin I	Data to be entered by site	ng/mL~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Troponin T	Data to be entered by site	ng/mL~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Creatine Kinase	Data to be entered by site	units/L~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Creatine Kinase - Myocardial Bands (CK-MB)	Data to be entered by site	U/L~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown

Cerebral Spinal Fluid (CSF) Laboratory Tests

Cerebral Spinal Fluid (CSF) Laboratory Tests Table

Test	Result	Units for Result	Unit Type	Was test result abnormal?
CSF Protein	Data to be entered by site	mg/dL~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
CSF Glucose	Data to be entered by site	ng/dL~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
CSF White Blood Cell Count (WBC)	Data to be entered by site	uL~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
CSF Red Blood Cell Count (RBC)	Data to be entered by site	uL~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown

Laboratory Tests

[Study Name/ID pre-filled] Site Name:

Subject ID:

Test	Result	Units for Result	Unit Type	Was test result abnormal?
Venereal Disease Research Laboratory (VDRL) Slide Test	Data to be entered by site	☐ Nonreactive ☐ Weakly reactive ☐ Reactive (with quantitation)~~Data to be entered by site~~	N/A	☐ Normal ☐ Abnormal ☐ Unknown
Immunoglobulin G (IgG)	Data to be entered by site	mg/dL	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Oligoclonal Bands	Data to be entered by site	☐ Negative ☐ Positive	N/A	☐ Normal ☐ Abnormal ☐ Unknown
Varicella-Zoster Virus (VZV) Antibodies	Data to be entered by site	☐ Negative ☐ Equivocal ☐ Positive	N/A	☐ Normal ☐ Abnormal ☐ Unknown
Varicella-Zoster Virus (VZV) PCR	Data to be entered by site	☐ Negative ☐ Positive	N/A	☐ Normal ☐ Abnormal ☐ Unknown

Miscellaneous Laboratory Tests

Miscellaneous Laboratory Tests Table

Test	Result	Units for Result	Unit Type	Was test result abnormal?
Glycosylated Hemoglobin (HgbA1C)	Data to be entered by site	~~Data to be entered by site~~%	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Creatinine Clearance	Data to be entered by site	mL/minute~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Glomerular Filtration Rate (GFR)	Data to be entered by site	mL/min/1.73m2~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Stool Guaiac	Data to be entered by site	☐ Negative ☐ Positive ~~Data to be entered by site~~	N/A	☐ Normal ☐ Abnormal ☐ Unknown
~~Toxicology Screen~~	~~Data to be entered by site~~	~~Data to be entered by site~~	~~☐ Normal~~ ~~☐ Abnormal~~ ~~☐ Unknown~~	
Ammonia (NH3)	Data to be entered by site	ug of nitrogen/dL~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown

Laboratory Tests

[Study Name/ID pre-filled] Site Name:

Subject ID:

Test	Result	Units for Result	Unit Type	Was test result abnormal?
Amylase	Data to be entered by site	units/L~~Data to be entered by site~~	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown
Other, specify:	Data to be entered by site	Data to be entered by site	☐ Standard ☐ SI	☐ Normal ☐ Abnormal ☐ Unknown

Toxicology Screen Results

Toxicology Screen Results Table

Drug	Result	Units for Result	Unit Type	Was test result abnormal?
Analgesics	Data to be entered by site	☐ Negative ☐ Positive	N/A	☐ Normal ☐ Abnormal ☐ Unknown
Anticonvulsants	Data to be entered by site	☐ Negative ☐ Positive	N/A	☐ Normal ☐ Abnormal ☐ Unknown
Barbiturates	Data to be entered by site	☐ Negative ☐ Positive	N/A	☐ Normal ☐ Abnormal ☐ Unknown
Psychotropics	Data to be entered by site	☐ Negative ☐ Positive	N/A	☐ Normal ☐ Abnormal ☐ Unknown
Sedatives	Data to be entered by site	☐ Negative ☐ Positive	N/A	☐ Normal ☐ Abnormal ☐ Unknown
Stimulants	Data to be entered by site	☐ Negative ☐ Positive	N/A	☐ Normal ☐ Abnormal ☐ Unknown
Sympathomimetics	Data to be entered by site	☐ Negative ☐ Positive	N/A	☐ Normal ☐ Abnormal ☐ Unknown

Pregnancy Test

Was a pregnancy test performed?

☐ Yes ☐ Not applicable

☐ No (STOP)

Reason Test N/A:

☐ Post-Menopausal ☐ Non-surgically sterile

☐ Surgically sterile ☐ Male

Laboratory Tests

[Study Name/ID pre-filled]

Site Name:

Subject ID:

Date Performed (m m/d d/y y y y):

Test Type:

☐ Blood ☐ Urine

Result:

☐ Positive ☐ Negative

GENERAL INSTRUCTIONS

Laboratory tests are routinely administered in clinical trials of pharmacological interventions to assess subject safety. Laboratory tests may also be used to determine an individual's eligibility for a study.

Laboratory results may be received via electronic files directly from central study laboratories or recorded manually on case report forms if the study is using a local lab. In either scenario, it is recommended that the Laboratory Test form be used to record when samples were collected (date and time) so that the laboratory tests results can be matched with the samples collected for each subject.

SPECIFIC INSTRUCTIONS

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

- Lab Panel – Choose the lab panel that was performed.
- Date and Time Collected –Record the date (and time) the specimen was collected. 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.) and in the format acceptable to the study database.
- Accession Number – Provide the accession number or bar code number that is assigned to the specimen.
- Test – Indicate the name of each laboratory test that is run on the specimen. See the data dictionary for additional information on coding the test name using Logical Observation Identifiers Names and Codes (LOINC).
- Test Performed – Choose one. Indicate whether or not the test was performed on the specimen. 5,10 Methylene Tetra Hydrofolate Reductase (MTHFR) is no longer recommended as a first line test. Homocysteine is preferred.
- Result – Record the numeric or alpha-numeric results for each laboratory test.
- Unit for Result – ~~Record the~~The recommended units for the numeric results for each laboratory test ~~are measured in~~. For some laboratory tests, result option are included. See the data dictionary for additional information on coding the unit of measure using Unified Code for Units of Measure (UCUM).
- Unit Type – Choose one. Indicate if SI or Standard Units were used.
- Abnormal Result – Choose one. Indicate if the laboratory test result is abnormal. Abnormal means the test result falls outside the normal range.
- ~~Clinical Significance – Choose one. If the laboratory test result is abnormal, indicate if the physician considers the result clinically significant.~~