Appendix 1: Biomarkers Targets in SAH

1. **Core Data Element Recommendations**:

None. To date, no molecular biomarker has been validated in SAH using large prospective studies and across different populations.

2. **Supplemental Data Element Recommendations**:

i. Biomarkers of Cell Death

- Serum S100b elevation in SAH is associated with initial clinical severity (Hunt and Hess grade) and may be associated with worse outcome. S100b elevation may be confounded by the presence of hydrocephalus.

ii. Biomarkers of Inflammation

- Elevation of serum von Willebrand fractor (vWf) and TNFa and decrease in serum plasma-type gelsolin may be associated with poor SAH outcome after adjustment for clinical predictors. However, there is little information about the sensitivity, specificity, PPV and NPV of these markers and their optimal cutoff value.

iii. CSF biomarkers

- Cytokines, metalloproteases, epinephrine and plasma-type gelsolin have been measured in SAH CSF and associated with outcome. These findings still require replication and validation

iv. Genetic biomarkers

- Carriers of apolipoprotein E4 genotype may be associated with worse outcome but it is unknown if genotype adds to prognostic accuracy of clinical prediction rules.

v. Non-CNS Biomarkers

- Elevation of peak serum cardiac troponin-I and serum BNP (brain naturitic peptide) on SAH presentation may be associated with increased risk of death after SAH.
- Trials should include careful measurement of cardiac injury and pulmonary edema as potential confounders of these biomarker measurements.

3. **Emerging Data Element Recommendations**:
The following markers have shown association with SAH outcome or delayed cerebral ischemia in prior studies:

- Serum and CSF S100β

- CSF CKBB
- Plasma and CSF plasma-type gelsolin (pGSN)
- Serum von Willebrand's factor
- Serum sICAM-1
- Serum TNFα
- Serum CRP
- Blood leukocyte and neutrophil counts
- CSF MMP-9
- CSF IL-1β
- CSF IL-6
- CSF IL-1Rα
- ApoE4 genotype
- Serum BNP
- Serum troponin-I