Lumbar Puncture & Cerebrospinal Fluid Sampling

Cerebrospinal fluid (CSF) is an ultra-filtrate of plasma that surrounds and protects the brain and spinal cord. Like plasma, CSF contains nutrients, such as minerals, glucose and proteins, as well as immunoglobulins and drugs, but often at a lower concentration than those attained systemically.

In drug development, CSF sampling and analysis can be applied to confirm an investigational product reaches the brain for targeted pharmacological activity or to evaluate changes in CNS biomarkers.

CSF Collection at a Glance

- Lumbar punctures are performed on-site, at our Clinical Pharmacology Units, allowing for sample collections from multiple subjects a day
- Subjects are screened for lumbar puncture contraindications such as intracranial hypertension, bleeding disorders, and abnormalities at the puncture site
- Experienced specialists use an atraumatic spinal needle during lumbar puncture procedure to collect CSF
- Post-procedure monitoring identifies procedure-related complications such as postdural puncture headache (PDPH; often referred to as a “spinal headache”), as well as backache, bleeding, infection, or neurological symptoms
- These risks are minimized by collecting only the minimum sample volume required for analysis and by optimally limiting the sampling frequency

Global Experience

- We have the expertise to conduct lumbar punctures at all 3 of our Clinical Pharmacology Units
  - Belfast, UK
  - Lincoln, NE
  - Phoenix, AZ
- We partner with local experts
  - Highly trained specialists with over 2,000 punctures in clinical and research settings
- Completed over a dozen studies with CSF sampling in the past 5 years
- Excellent success rate using atraumatic spinal needles
  - Well tolerated procedure, <2% of subjects reported PDPH
- Can deliver time-matched pharmacokinetic (PK) blood sampling
- Ability to perform procedure on up to 12 subjects per day

Bioanalytical Considerations for CSF Samples

Bioanalysis of CSF samples can often present challenges due to the low analyte concentration and high degree of non-specific binding to collection and storage containers. Our expert team of scientists have optimized CSF collection procedures and developed and validated several bioanalytical methods for CSF analytes to overcome these hurdles.

- In most cases, the same chromatographic assay conditions can be used for CSF as for plasma – ***this can save time and expedite method development.***
- The assay must achieve lower limits of quantification – ***typically 10-20% lower than the plasma assay.***
- Due to low total protein concentrations in the CSF matrix (in comparison to plasma), there is the potential for greater non-specific binding to the collection device and storage containers – ***absorption testing and use of an additive is a critical mitigation step.***
- All calibration standards and quality control samples contain the additive for accurate matrix concentration results – ***other labs often apply a correction factor, which can result in inaccurate concentrations.***

Case Study

NEED: A pharmaceutical company developing an oral small molecule to treat CNS diseases aimed to confirm drug distribution to the brain and explore biomarker changes.

APPROACH: Eight healthy adults were enrolled in the study to evaluate drug concentration and key biomarkers in CSF at baseline and following multiple doses.

– Specific Inclusion/Exclusion criteria relevant to CSF collection were incorporated in the study design to mitigate procedure risks.
– ~3-6 mL of CSF was collected in a single lumbar puncture and processed for analysis of drug concentration and biomarkers at baseline and steady state.

BENEFIT: Celerion has the capacity and experience to perform the lumbar puncture procedure on all 8 subjects in a single day.

– The ability to collect CSF samples on multiple subjects in 1 day maintains critical study timelines.
– Subjects remained confined at the clinic for the duration of the study and were closely monitored post-procedure.
– Overall, the CSF collection procedure was well tolerated, only 1 subject reported adverse events of erythema and tenderness at lumbar puncture site.

RESOURCES:

Celerion Bioanalytical Science

Global Early Phase Services