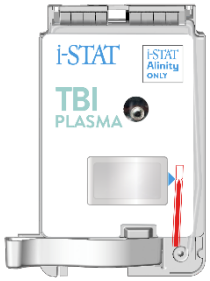
i-STAT TBI Plasma Cartridge



NAME

i-STAT TBI Plasma Cartridge REF 04X64-25

INTENDED USE

The i-STAT TBI Plasma test is a panel of *in vitro* diagnostic immunoassays for the quantitative measurements of glial fibrillary acidic protein (GFAP) and ubiquitin carboxyl-terminal hydrolase L1 (UCH-L1) in plasma and a semi-quantitative interpretation of test results derived from these measurements, using the i-STAT Alinity Instrument. The interpretation of test results is used, in conjunction with other clinical information, to aid in the evaluation of patients, 18 years of age or older, presenting with suspected mild traumatic brain injury (Glasgow Coma Scale score 13-15) within 12 hours of injury, to assist in determining the need for a CT (computed tomography) scan of the head. A 'Not Elevated' test interpretation is associated with the absence of acute traumatic intracranial lesions visualized on a head CT scan.

The test is to be used with plasma prepared from EDTA anticoagulated specimens in clinical laboratory settings by a healthcare professional. The i-STAT TBI Plasma test is not intended to be used in point of care settings.

SUMMARY AND EXPLANATION / CLINICAL SIGNIFICANCE

Test Principle

The i-STAT TBI Plasma cartridge is a multiplex immunoassay that contains assays for both ubiquitin carboxyl-terminal hydrolase L1 (UCH-L1) and glial fibrillary acidic protein (GFAP). The assays test for the presence of these biomarkers in a single plasma sample and yield a semi-quantitative test interpretation based on measurements of both UCH-L1 and GFAP in approximately 15 minutes. The i-STAT TBI Plasma cartridge is designed to be run only on the i-STAT Alinity instrument.

Both assays on the cartridge use the sandwich enzyme-linked immunosorbent assay (ELISA) method with electrochemical detection of the resulting enzyme signal. The capture antibodies specific for the antigens (GFAP and UCH-L1) are each immobilized to a separate electrochemical sensor fabricated on a silicon chip. Also deposited in another location on the sensor silicon chip are the detection antibodies conjugated to the alkaline phosphatase enzyme (detection antibody-AP conjugates) that are specific to a separate region or epitope of each antigen. The plasma sample is brought into contact with the sensors allowing the detection antibody-AP conjugates to dissolve into the sample. The antigens present in the sample interact with both the detection antibody-AP conjugates and the immobilized capture antibodies to form a sandwich (detection antibody-AP/antigen/capture antibody) on the surfaces of their respective electrochemical sensors during an incubation period of approximately twelve minutes. The sample and excess detection antibody-AP conjugates are then washed off the sensors. Within the wash fluid is a substrate for the AP enzyme. The AP enzyme within the sandwich cleaves the substrate, releasing an

electrochemically detectable product. The electrochemical (amperometric) sensor for each assay measures this enzyme product, which is proportional to the concentration of GFAP and UCH-L1 within the sample.

The i-STAT TBI Plasma cartridge is a single use test cartridge. The cartridge contains a biosensor chip and all reagents required to execute the test cycle. All fluid movements (test sample or reagent) are automatically controlled by the i-STAT Alinity instrument by electro-mechanical interaction with the cartridge. No additional reagents or steps are required to run the cartridge.

Clinical Significance

Traumatic brain injury (TBI) is the structural injury or physiologic disruption of brain function caused by the impact of an external mechanical force on the brain. The resulting injury can be ranked from mild to severe based on clinical symptoms, conscious level, and neuroimaging techniques. While severe TBI presents with more overt symptoms, patients presenting with mild TBI remain difficult to diagnose objectively. Computed tomography (CT), the most commonly used neuroimaging technique in the acute investigation of head injury patients, has advantages over Magnetic Resonance Imaging (MRI) due to its rapid acquisition and high spatial resolution for detailed anatomical structures in the head. An estimated 90% of head CT scans in patients suspected of having mild TBI have negative results for clinically important brain injuries [1]. A single non-contrast CT scan of the head exposes a patient to a dose of radiation comparable to eight months of background radiation [2]. Preventing unnecessary use of neuroimaging and associated radiation exposure is important in patient care, especially for preventing development of cataracts or malignant tumors on radiosensitive organs such as the salivary gland, thyroid gland, and retina. Measurement of glial fibrillary acid protein (GFAP) and ubiquitin carboxyl-terminal hydrolase L1 (UCH-L1) released from the brain into the blood has been proposed as a method of reducing unnecessary radiation exposure in patients suspected of having mild TBI and provide an opportunity to improve the care of this patient group [3,4].

Glial Fibrillary Acid Protein

Glial fibrillary acidic protein (GFAP) is an astrocyte structural protein. GFAP is found in brain parenchyma. Metting and colleagues demonstrated that serum GFAP was increased in TBI patients with an abnormal CT and also demonstrated that GFAP was elevated in patients with axonal injury on MRI three months post injury [5]. In a study by Papa and colleagues, GFAP was detectable in serum less than 1 hour after head injury and it was able to reliably distinguish between trauma patients with mild TBI and those without head injury [6]. In this same study, blood GFAP levels were elevated in patients with traumatic intracranial abnormalities on CT compared with those without lesions and could also be used to predict those patients who required neurosurgical intervention [6].

Ubiquitin Carboxyl-Terminal Hydrolase L1

Ubiquitin carboxyl-terminal hydrolase-L1 (UCH-L1) is a protein that is involved in the metabolism of ubiquitin within neurons [7]. Increases in blood UCH-L1 have been detected in the serum of mild and moderate TBI patients within an hour of injury [8]. Levels measured within 4 hours of injury were significantly higher in those with TBI lesions on CT than those with a normal intracranial appearance on CT. Blood levels of UCH-L1 have been demonstrated to be able to discriminate mild TBI patients from patients without head injuries and, similar to GFAP, UCH-L1 levels were much higher in patients who required neurosurgical intervention [8].

REAGENTS

Contents

Each i-STAT TBI Plasma cartridge contains all the necessary reagents needed to perform the test. The cartridge contains a buffer and preservatives. A list of reactive ingredients is provided below:

Reactive Ingredient	Biological Source	Minimum Quantity
Antibody / Alkaline Phosphatase Conjugate	Murine IgG / Bovine intestine	0.005 µg
IgG	Murine IgG	18.0 µg
IgG	Caprine IgG	12 µg
IgG	Leporine IgG	18.0 µg
IgM	Murine IgM	0.60 µg
Sodium Aminophenyl Phosphate	N/A	2.7 mg
Heparin	Porcine intestine	0.45 IU

Warnings and Precautions

IVD

- For *in vitro* diagnostic use.

- DO NOT REUSE—cartridges are intended for single-use only.

- Although the sample is contained within the cartridge, used cartridges should be disposed of as biohazardous waste according to local, state, and national regulatory guidelines.

Rx ONLY

- Caution: Federal law restricts this device to sale by or on the order of a physician

- The i-STAT System automatically runs a comprehensive set of quality checks of instrument and cartridge performance each time a sample is tested. This internal quality system will suppress results by generating a Quality Check Failure (QCF), if the instrument or cartridge does not meet certain specifications. To minimize the probability of delivering a result with medically significant error the internal specifications are very stringent. It is typical for the system to suppress a very small percentage of results in normal operation given the stringency of these specifications. If however the instrument or cartridges have been compromised, results may be persistently suppressed, and one or the other must be replaced to restore normal operating conditions. Where unavailability of results while awaiting replacement of instruments or cartridges is unacceptable, Abbott Point of Care Inc. recommends maintaining both a backup i-STAT Alinity instrument and cartridges from an alternate lot number.

- When a QCF occurs, a code number and the next step to be taken will be displayed on the i-STAT instrument. Refer to the i-STAT Alinity System Operations Manual for additional information on QCFs. The failure rate due to QCFs may be as high as 3.45% with an average of 2.33%. The rate of failure for two consecutive cartridges due to QCFs may be as high as 0.51%

For additional warnings and precautions about the i-STAT Alinity System refer to the i-STAT Alinity System Operations Manual located at www.globalpointofcare.abbott.

Storage Conditions

Note: For optimal performance, cartridge storage at 2 to 8 ºC (35 to 46 ºF) is recommended.

- The expiration date, expressed as YYYY-MM-DD on the packaging, indicates the last day the product may be used.
- Refrigeration at 2 to 8 ºC (35 to 46 ºF) until expiration date.
- Room Temperature at 18 to 30 ºC (64 to 86 ºF). While within the cartridge expiration dating, the cartridge may be kept at room temperature for up to 14 days.
- Allow refrigerated cartridges to equilibrate at room temperature for 5 minutes for a single cartridge and 1 hour for an entire box before use as described in Procedure for Patient Testing below. Cartridges must be at room temperature before removing from the portion pack.

INSTRUMENTS

The i-STAT TBI Plasma cartridge is intended for use with i-STAT Alinity instrument.

For a detailed description of the instrument and system procedures, refer to the i-STAT Alinity System Operations Manual located at www.globalpointofcare.abbott.

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

Specimen Type(s)

EDTA Plasma prepared from venous whole blood
Sample volume: Approximately 20 µL of plasma is required to fill the cartridge to the 'fill-to' mark.

Blood Collection Options

Assay	Evacuated Tubes
GFAP UCH-L1	• EDTA without plasma separator Fill tube according to manufacturer's recommendation

Sample Preparation and Sample Stability

1. Centrifuge sample within 30 minutes of collection.
2. Centrifuge the whole blood collection tube **for 10 minutes** at **2100 RCF to produce plasma.**

   A fixed-angle or swinging bucket centrifuge can be used to prepare the plasma

   - The recommended duration and spin-speed will result in the application of at least 21,000 'g-minutes' (the product of the Relative Centrifugal Field (RCF, or 'g') and the spin duration in minutes).
   - The minimum of 21,000 g-minutes may also be obtained using other combinations of RCF and duration, *e.g.*:

     1300 RCF for 17 minutes (**minimum** recommended RCF)

     3000 RCF for 7 minutes (**maximum** recommended RCF)

     1300 ≤ RCF ≤ 3000 with adapted duration to reach 21,000 g-minutes.
3. After centrifugation, immediately and carefully transfer a small amount of plasma into the i-STAT cartridge sample well using a transfer device (i.e. transfer pipette) without

anticoagulant. Take care not to disturb the buffy coat interface between the plasma and red blood cell layers.

4. If plasma testing is not planned for immediately after centrifugation, remove the top 1/3 of the separated plasma. Place in an aliquot tube, cover and store at room temperature for up to 2 hours.

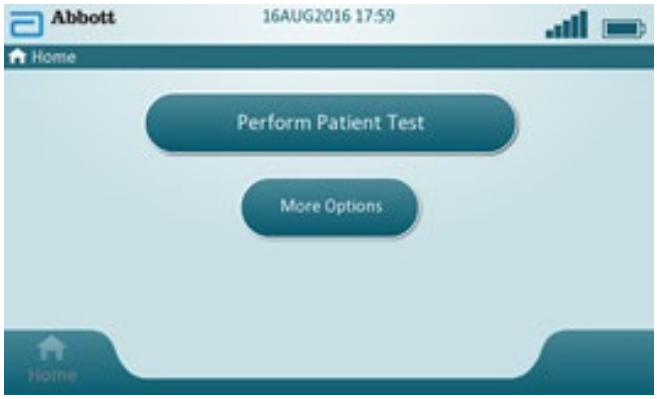
PROCEDURE FOR PATIENT TESTING

Each cartridge is sealed in a portion pack (individual cartridge package) for protection during storage--do not use if the portion pack has been damaged or punctured.

- A cartridge should not be removed from its protective portion pack until it is at room temperature (18-30 °C or 64-86 °F). For best results, the cartridge and instrument should be at room temperature.
- Since condensation on a cold cartridge may prevent proper contact with the instrument allow refrigerated cartridges to equilibrate at room temperature for 5 minutes for a single cartridge and 1 hour for an entire box before use.
- Use a cartridge immediately after removing it from its protective portion pack; prolonged exposure may cause a cartridge to fail a Quality Check.
- Do not return unopened, previously refrigerated cartridges to the refrigerator.
- Cartridges may be stored at room temperature for the time frame indicated on the cartridge box.

Performing Patient Analysis

1. Press the power button to turn instrument on.
2. From the Home screen, touch *Perform Patient Test.* This initiates the patient testing pathway.



3. Follow instructions on the screen to “Scan or Enter OPERATOR ID”.
4. Follow instructions on the screen to “Scan or Enter PATIENT ID”
5. Continue to follow prompts on the screen to proceed with patient testing. “Scan (CARTRIDGE POUCH) Barcode”, Scanning is required. Information cannot be entered manually.
6. Follow instructions on the screen to “Close and Insert Filled Cartridge”. The action buttons at the bottom of the screen allow forward, backward and pause functionality.

Filling and Sealing the Cartridge

7. Place the room temperature equilibrated cartridge on a flat surface.

8. Using a transfer device without anticoagulant, remove a small sample from the EDTA tube that has been spun down so that the plasma has separated from the cells. See Sample Preparation above.
9. Fill the cartridge by directing the tip of the transfer device into the sample well inlet port of the cartridge.
10. Slowly dispense sample until the sample reaches the 'fill to' mark indicated on the cartridge. Cartridge is properly filled when the sample reaches the 'fill to' mark and a small amount of sample is in the sample well. The sample should be continuous, no bubbles or breaks.
11. Slide the closure clip of the cartridge over the sample well.
12. **Immediately** insert the sealed cartridge into the cartridge port until it clicks into place. Once the cartridge is inserted, "Contacting Cartridge" will display followed by the countdown bar. The following alerts are also displayed: "Cartridge locked in instrument. Do not attempt to remove the Cartridge" and "Testing – Instrument Must Remain Level".
13. Wait for the test to complete. When the test is complete, the results are displayed.
14. Review the results.

Analysis Time

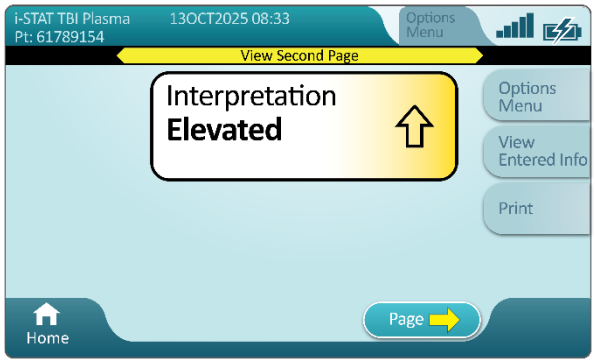
Approximately 15 minutes.

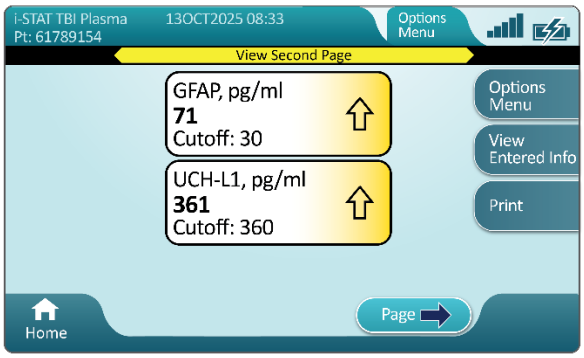
Results

The i-STAT TBI Plasma test is a semi-quantitative assay.

Interpretation of results

i-STAT TBI Plasma results are displayed on two pages on the i-STAT Alinity Instrument. The first page is the test interpretation (Elevated, Not Elevated, Repeat Test) (**Table 1**). The second page shows the quantitative results. In the case of a Repeat Test interpretation, the second page is not available. An example of the interpretation and results pages are below.





- In the example, the result bubbles are marked with yellow. On the interpretation page, yellow indicates an "elevated" interpretation. On the results page, yellow indicates quantitative results above cutoff. This is intended to draw the attention of the operator.
- The blinking page button at the bottom of the screen appears when there is more than one page of results. All action tabs are inactive until the second page of results has been viewed.
- An audible cue will be heard when results are ready. Touch **Silence** or remove cartridge to silence.

The table below outlines the test interpretation matrix based on the GFAP and UCH-L1 assay results relative to cutoffs. The assay cutoffs were established to be 30 pg/mL for GFAP and 360 pg/mL for UCH-L1.

Table 1: Test Interpretation Matrix

GFAP Assay Result (relative to cutoff of 30 pg/mL)	UCH-L1 Assay Result (relative to cutoff of 360 pg/mL)	Test Interpretation
Below	Below	Not Elevated
Below	Equal or Above	Elevated
Equal or Above	Below	Elevated
Equal or Above	Equal or Above	Elevated
Equal or Above	***†	Elevated
Below	Not reported	Repeat Test‡
***†	Equal or Above	Elevated
Not reported	Below	Repeat Test‡
Not reported	Not reported	Repeat Test‡

†Starout condition. "***" is displayed rather than a quantitative result. Instrument is unable to determine a quantitative result from a particular sensor on the cartridge due to detection of a signal from the sensor that is uncharacteristic. Because the other assay provides a result at or above cutoff, a test interpretation can be reported. Refer to the i-STAT Alinity System Operations Manual for addition information on starouts.

‡Results are not available for both assays, or for one assay and the other assay provides a result below cutoff. Repeat Test will appear as a Quality Check Failure (QCF) screen with error code 152-01. Repeat test with a freshly filled cartridge. If the same QCF displays, contact the system administrator for further instruction. Refer to the i-STAT Alinity System Operations Manual for additional information on QCFs.

'Not Elevated' test interpretation is associated with the absence of acute traumatic intracranial lesions visualized on a head CT scan.
'Elevated' test interpretation suggests further evaluation by head CT scan should be considered.

REPORTABLE RANGE

Assay	Lower Reportable Range (pg/mL)	Upper Reportable Range (pg/mL)
GFAP	30	10000*
UCH-L1	200	3200

Results may be preceded by the symbols for greater than (>) or less than (<) if the result is outside of the reportable range. GFAP with concentrations below 30 pg/mL and UCH-L1 with concentrations below 200 pg/mL can be reliably measured by each assay (refer to LoQ in Performance Characteristics section).

*Under a rare set of circumstances, the GFAP assay quantitative result may be reported as ">5574". When this result is shown, the GFAP assay range has been automatically truncated due to detection of signal response variability that could lead to an underestimate of the reported value. In these cases, another cartridge may be run to obtain a quantitative result.

PROCEDURE FOR QUALITY TESTING

Liquid Quality Control

For information on performing liquid quality control, refer to the i-STAT TBI Control Levels 1, 2 instructions for use located at www.globalpointofcare.abbott.

Calibration Verification

For information on performing calibration verification testing, refer to the i-STAT TBI Calibration Verification 1-3 instructions for use located at www.globalpointofcare.abbott.

METROLOGICAL TRACEABILITY

The i-STAT System test for glial fibrillary acidic protein (GFAP) or ubiquitin carboxyl-terminal hydrolase L1 (UCH-L1) measures GFAP and UCH-L1 amount-of-substance concentration in plasma (units of measure: pg/mL) for *in vitro* diagnostic use.

There are no internationally recognized standard reference materials available for either glial fibrillary acidic protein (GFAP) or ubiquitin carboxyl-terminal hydrolase L1 (UCH-L1). GFAP and UCH-L1 values assigned to i-STAT controls and calibration verification materials are traceable to Abbott Point of Care's working calibrators prepared using recombinant GFAP and UCH-L1 (expressed and purified from *E. coli*). The working calibrators are traceable to an in-house Reference Standard prepared from recombinant GFAP and UCH-L1 (expressed and purified from *E. coli*).

i-STAT System controls and calibration verification materials are validated for use only with the i-STAT System and assigned values may not be commutable with other methods. Further information regarding metrological traceability is available from Abbott Point of Care Inc.

EXPECTED VALUES

A reference interval study was conducted with a US-based general population. Plasma specimens from 225 self-declared subjects between the ages of 18 and 79 years reporting no history of neurological disease within 1 year were tested with the i-STAT TBI Plasma Cartridge with the i-STAT Alinity System to determine GFAP and UCH-L1 levels. Based on the test results, a 95% reference interval of an apparently healthy population of each biomarker was determined to be as follows:

Table 2: Reference Interval

Biomarker	N	Mean (pg/mL)	SD (pg/mL)	Median (pg/mL)	Reference Interval (2.5^{th} to 97.5^{th} Percentile) (pg/mL)
GFAP	225	19	16.2	15	2 – 51
UCH-L1	225	81	42.4	71	21 – 204

In Section 12.2.1 of CLSI EP28-A3c[9], the CLSI working group encourages laboratories to report decision limits or reference intervals. For the i-STAT TBI Plasma Cartridge, as shown under "Interpretation of Results", the decision limits (assay cutoffs) are reported on the screen.

CLINICAL PERFORMANCE

A pivotal study using prospectively collected and archived (frozen) plasma specimens was conducted to establish the clinical performance of the i-STAT TBI Plasma test. The testing of the archived plasma specimens was conducted at three clinical sites in the United States.

The specimens were originally collected in a prospective, multi-center clinical study[3] that enrolled consenting men and women 18 years of age or older who presented to emergency departments (ED) with suspected traumatic brain injury with initial Glasgow Coma Scale (GCS) scores of 13-15 and who had a computed tomography (CT) scan performed per the clinical site's standard of care. Subjects were enrolled at 22 clinical sites in three countries: United States, Germany and Hungary.

CT scans were performed in accordance with the clinical site's standard of care. Images were transmitted to a central neuroimaging processing center. Images were interpreted by at least two neuroradiologists who were masked to other clinical and laboratory data; procedures for scoring images were established before conducting image review. The clinical outcome was based on the consensus interpretation between two neuroradiologists with adjudication by a third neuroradiologist if necessary. Outcomes were positive or negative as defined by the presence or absence of acute traumatic intracranial lesions, respectively. Acute intracranial lesion was defined as any trauma induced or related finding visualized upon head CT scan.

Whole blood was collected into K2EDTA blood collection tubes from each subject using venipuncture and centrifuged to obtain plasma. Specimens were collected within 12 hours of head injury. The plasma specimens were divided into aliquots and frozen in cryovials before being provided to testing sites.

Of the 1994 subjects with GCS scores of 13 to 15 enrolled in the original study, specimens from 93 subjects were not included in the performance analysis due to subject discontinuation, lack of consent for specimen archiving for future testing, inconclusive or unreadable CT scan results, and/or unknown time from injury to blood collection. Specimens from 1901 subjects were included in the analysis.

The demographic characteristics of the subjects represented in the performance analysis are summarized in **Table 3** below.

Table 3: Demographic Characteristics

Characteristic	Head CT Scan Result		Total
	Positive	Negative	
N	120	1781	1901
Age[1] (Years)			
Mean	58.8	48.5	49.1
Median	58.5	48.0	49.0
Standard Deviation	18.29	21.01	20.99
Range	(20, 95)	(18, 98)	(18, 98)
Gender, N (%)			
Male	70 (58.3%)	1005 (56.4%)	1075 (56.6%)
Female	50 (41.7%)	776 (43.6%)	826 (43.5%)
Race[2], N (%)			
White	98 (81.7%)	1245 (69.9%)	1343 (70.6%)
Black or African American	16 (13.3%)	483 (27.1%)	499 (26.2%)
Asian	5 (4.2%)	24 (1.3%)	29 (1.5%)
Native Hawaiian/Pacific Islander	1 (0.8%)	2 (0.1%)	3 (0.2%)
American Indian or Alaska Native	1 (0.8%)	9 (0.5%)	10 (0.5%)
Unknown	1 (0.8%)	27 (1.5%)	28 (1.5%)
Ethnicity, N (%)			
Hispanic or Latino	1 (0.8%)	89 (5.0%)	90 (4.7%)
Not Hispanic or Latino	118 (98.3%)	1691 (94.9%)	1809 (95.2%)
Not Reported	1 (0.8%)	1 (0.1%)	2 (0.1%)

[1] Age was calculated relative to the date of informed consent.
[2] Subjects could have indicated more than one race.

The head injury characteristics of the subjects represented by the 1901 specimens included in the performance analysis were tabulated. Information regarding time from head injury to exam, head injury to CT scan, and head injury to blood draw, as well as GCS, neurological assessment and physical evidence of trauma, categorized by head CT scan results, are shown in **Table 4**.

Table 4: Head Injury Characteristics

Characteristic	Head CT Scan Result		Total
	Positive	Negative	
N	120	1781	1901
Time from head injury to exam (hours)[1]			
Mean	1.9	1.6	1.6
Median	1.2	1.0	1.1
Standard Deviation	1.73	1.71	1.71
Range	(0.3, 7.8)	(0.1, 10.7)	(0.1, 10.7)
Time from head injury to CT scan (hours)[1]			
Mean	2.8	2.7	2.7
Median	2.1	2.2	2.1
Standard Deviation	1.95	1.93	1.93
Range	(0.5, 8.9)	(0.2, 13.3)	(0.2, 13.3)
Time from head injury to blood draw (hours)[1]			
Mean	3.8	3.5	3.5
Median	3.3	3.1	3.2
Standard Deviation	1.91	1.88	1.89
Range	(0.3, 9.3)	(0.3, 11.9)	(0.3, 11.9)
Glasgow Coma Score – N (%)			
13	7 (5.8%)	15 (0.8%)	22 (1.2%)
14	19 (15.8%)	71 (4.0%)	90 (4.7%)
15	94 (78.3%)	1695 (95.2%)	1789 (94.1%)
Neurological assessment - N (%) of subjects experiencing:			
Loss of Consciousness (LOC)	82 (68.3%)	721 (40.5%)	803 (42.2%)
Alteration of Consciousness (AOC)	92 (76.7%)	978 (54.9%)	1070 (56.3%)
Confusion	44 (36.7%)	313 (17.6%)	357 (18.8%)
Vomiting	14 (11.7%)	128 (7.2%)	142 (7.5%)
Post Traumatic Amnesia (PTA)	81 (67.5%)	546 (30.7%)	627 (33.0%)
Post Traumatic Seizures	2 (1.7%)	11 (0.6%)	13 (0.7%)
Subjects With Drug or Alcohol Intoxication at the Time of Presentation to Facility	33 (27.5%)	369 (20.7%)	402 (21.1%)
Dangerous Mechanism of Injury[2]	27 (22.5%)	369 (20.7%)	396 (20.8%)
Physical Evidence[3]			
Visible Trauma Above the Clavicle	101 (84.2%)	1102 (61.9%)	1203 (63.3%)
Suspected Open or Depressed Skull Fracture	14 (11.7%)	46 (2.6%)	60 (3.2%)
Signs of Basal Skull Fracture	10 (8.3%)	26 (1.5%)	36 (1.9%)

[1] Based on time subject was initially examined at the medical facility
[2] Dangerous mechanism of injury was pedestrian struck by a motor vehicle, an occupant ejected from a motor vehicle, or a fall from an elevation of 3 or more feet or 5 stairs
[3] Prior to head CT

The i-STAT TBI Plasma test clinical performance estimates are shown in **Table 5**. Of the 1901 specimens, 120 were associated with positive CT scan results. Of these 120 specimens, 115 had an 'elevated' i-STAT TBI Plasma test interpretation (115/120, clinical sensitivity = 95.8%). Five specimens associated with CT scan positive results had an i-STAT TBI Plasma test interpretation that was 'not elevated'. The rate of false negative (FN) results was 4.2% (5/120). Five subjects in the study were identified with lesion requiring surgical intervention; none of these five subjects had a FN result, suggesting that the i-STAT TBI Plasma test correctly classified all these five CT-positive subjects with a test interpretation of 'elevated.' Of the 1781 specimens associated with negative CT scan results, 720 had an i-STAT TBI Plasma test interpretation that was 'not elevated' (720/1781, clinical specificity =

40.4%). The rate of False Positive (FP) results was 59.6% (1061/1781).

Overall, there were 725 specimens with i-STAT TBI Plasma test interpretations of 'not elevated'. Of these, 720 specimens were associated with negative CT scan results. The Negative Predictive Value (NPV) of the assay was 99.3% (720/725).

Table 5: Clinical Performance

i-STAT TBI Plasma Test Interpretation	Adjudicated CT Scan Result Positive	Negative	Total
Elevated	115	1061	1176
Not Elevated	5	720	725
Total	120	1781	1901

Clinical Performance Parameters	N=1901	95% Confidence Interval
Clinical Sensitivity	95.8%	90.6%, 98.2%
Clinical Specificity	40.4%	38.2%, 42.7%
Negative Predictive Value (NPV)	99.3%	98.5%, 99.7%
Positive Predictive Value (PPV)	9.8%	9.2%, 10.2%
Likelihood Ratio Negative (LRN)	0.10	0.04, 0.23
Likelihood Ratio Positive (LRP)	1.61	1.51, 1.69

To supplement the results of the pivotal study (N=1901) described above, a study was conducted using freshly collected plasma specimens from consenting men and women 18 years of age or older who presented to Level 1 trauma center emergency departments (ED) with suspected traumatic brain injury, with initial Glasgow Coma Scale(GCS) scores of 13-15, and who had a computed tomography (CT) scan of the head performed per the clinical site's standard of care. A total of 88 subjects were enrolled across 4 clinical sites of the Transforming Research and Clinical Knowledge in Traumatic Brain Injury (TRACK-TBI) study in the United States.

Similar to the pivotal study, CT scans were performed in accordance with the clinical site's standard of care. Images were interpreted by at least two neuroradiologists who were masked to other clinical and laboratory data; procedures for scoring images were established before conducting image review. The clinical outcome was based on the consensus interpretation between two neuroradiologists, with adjudication by a third neuroradiologist if necessary. Outcomes were positive or negative as defined by the presence or absence of acute traumatic intracranial lesions, respectively. Acute intracranial lesion was defined as any trauma induced or related finding visualized upon head CT scan.

Whole blood was collected into K3EDTA blood collection tubes from each subject using venipuncture and centrifuged to obtain plasma. Specimens were collected within 12 hours of head injury. The demographic characteristics of the subjects represented in the performance analysis are summarized in **Table 6** below:

Table 6: Demographic Characteristics - Supplemental Fresh Specimen Study

Characteristic	Head CT Scan Result		Total
	Positive	Negative	
N	29	59	88
Age (Years)			
Mean	49.2	39.3	42.5
Median	47	36	41
Standard Deviation	16.92	15.43	16.52
Range	(24, 85)	(18, 76)	(18, 85)
Gender			
Male	23	40	63
Female	6	19	25

The head injury characteristics of the subjects in the supplemental plasma fresh specimen study including information regarding time from head injury to exam, head injury to CT scan, and head injury to blood draw, as well as GCS, neurological assessment and physical evidence of trauma, categorized by head CT scan results, are shown in **Table 7**.

Table 7: Head Injury Characteristics – Supplemental Fresh Specimen Study

Characteristic	Head CT Scan Result		Total
	Positive	Negative	
N	29	59	88
Time from head injury to CT scan (hours)			
Mean	2.5	2.2	2.3
Median	2.0	1.9	1.9
Standard Deviation	1.76	1.39	1.51
Range	(0.7, 8.7)	(0.7, 7.5)	(0.7, 8.7)
Time from head injury to blood draw (hours)			
Mean	6.6	4.4	5.1
Median	6.0	3.9	4.3
Standard Deviation	2.93	1.96	2.54
Range	(2.3, 11.8)	(2.0, 9.9)	(2.0, 11.8)
Glasgow Coma Score – N (%)[1]			
13	1 (1.1%)	0 (0.0%)	1 (1.1%)
14	6 (6.8%)	9 (10.2%)	15 (17.0%)
15	22 (25.0%)	50 (56.8%)	72 (81.8%)
Neurological assessment - N (%) of subjects experiencing:			
Loss of Consciousness (LOC)	23 (79.3%)	37 (62.7%)	60 (68.2%)
Presence of Confusion	19 (65.5%)	40 (67.8%)	59 (67.0%)
Vomiting[2]	-	-	-
Post-traumatic Amnesia (PTA)	22 (75.9%)	38 (64.4%)	60 (68.2%)
Post-traumatic Seizures	0 (0%)	0 (0%)	0 (0%)

Characteristic	Head CT Scan Result		Total
	Positive	Negative	
Subjects with Drug Intoxication at the Time of Presentation to Site	3 (10.3%)	2 (3.4%)	5 (5.7%)
Subjects with Alcohol Intoxication at the Time of Presentation to Site	6 (20.7%)	4 (6.8%)	10 (11.4%)
Physical Evidence - N (%)			
Signs of Skull Fracture	9 (31.0%)	1 (1.7%)	10 (11.4%)
Mechanism of Injury - N (%)			
Acceleration/ Deceleration	24 (82.8%)	41 (69.5%)	65 (73.9%)
Blow to Head	4 (13.8%)	8 (13.6%)	12 (13.6%)
Head Against Object	24 (82.8%)	42 (71.2%)	66 (75.0%)
Fall	19 (65.5%)	21 (35.6%)	40 (45.5%)

[1] Percent based on total subjects

[2] Information not collected

The i-STAT TBI Plasma test clinical performance estimates from the supplemental fresh plasma specimen study are shown in **Table 8**. Of the 88 subjects tested, 29 were associated with positive head CT scan results. Of these 29 subjects, 29 had an 'elevated' i-STAT TBI Plasma test interpretation (29/29, clinical sensitivity = 100.0%). The rate of False Negatives (FN) was 0% (0/29). Of the 59 subjects associated with negative CT scan results, 14 had an i-STAT TBI Plasma test interpretation that was 'not elevated' (14/59, clinical specificity = 23.7%). The rate of False Positive (FP) results was 76.3% (45/59).

Overall, there were 14 specimens with i-STAT TBI Plasma test interpretations of 'not elevated'. All 14 specimens were associated with negative head CT scan results. The Negative Predictive Value (NPV) of the assay was 100% (14/14).

Table 8: Clinical Performance – Supplemental Fresh Specimen Study

i-STAT TBI Plasma Test Interpretation	Adjudicated CT Scan Result		Total
	Positive	Negative	
Elevated	29	45	74
Not Elevated	0	14	14
Total	29	59	88

Clinical Performance Parameters	N=88	95% Confidence Interval
Clinical Sensitivity	100.0%	88.3%, 100.0%
Clinical Specificity	23.7%	14.7%, 36.0%
Negative Predictive Value (NPV)*	100.0%	80.2%, 100.0%
Positive Predictive Value (PPV)*	39.2%	35.9%, 43.4%
Likelihood Ratio Negative (LRN)	0.00	0.00, 0.50
Likelihood Ratio Positive (LRP)	1.31	1.14, 1.56

*NPV and PPV estimated at 33.0% prevalence of CT scan positive rate for suspected mild TBI subjects. Adjusted NPV and PPV at 6% prevalence (to be comparable to the pivotal study) are 100.0% (95% CI: 96.9%, 100.0%) and 7.7% (95% CI: 6.8%, 9.1%), respectively.

PERFORMANCE CHARACTERISTICS

The typical performance of GFAP and UCH-L1 assays within the i-STAT TBI Plasma cartridge with i-STAT Alinity System are summarized below.

Precision

Plasma samples representing nine (9) levels of GFAP and seven (7) levels of UCH-L1 spanning the reportable range as well as the i-STAT TBI Controls (L1 and L2) were used to assess assay precision. A single-site study was conducted based on CLSI guidance EP05-A3 [10]. Each sample was tested for at least 20 days with two (2) runs per day and two (2) results per run for a total of 80 measurements per sample per cartridge lot. Runs were separated by a minimum of 2 hours.

Table 9 and **Table 10** estimate the components of variability in the GFAP and UCH-L1 assays, respectively. Precision performance observed with the i-STAT TBI Controls across 3 cartridge lots are tabulated in **Table 11.**

Table 9: Estimate of GFAP Assay Precision

Sample	N	Mean (pg/mL)	Repeatability		Between-Run		Between-Day		Between-Lot		Within-Laboratory	
			SD (pg/mL)	CV (%)	SD (pg/mL)	CV (%)	SD (pg/mL)	CV (%)	SD (pg/mL)	CV (%)	SD (pg/mL)	CV (%)
1	238‡	17.0	1.76	10.4%	0.91	5.4%	0.61	3.6%	1.31	7.7%	2.46	14.5%
2	238‡	30.8	2.49	8.1%	0.00	0.0%	0.00	0.0%	0.52	1.7%	2.55	8.3%
3	238‡	65.6	3.21	4.9%	0.87	1.3%	1.03	1.6%	0.62	0.9%	3.54	5.4%
4	238*§	104.9	3.37	3.2%	2.08	2.0%	0.00	0.0%	1.50	1.4%	4.24	4.0%
5	238‡	962.9	22.42	2.3%	13.61	1.4%	17.33	1.8%	21.17	2.2%	37.90	3.9%
6	160	2029.5	39.18	1.9%	26.30	1.3%	19.10	0.9%	94.89	4.7%	107.69	5.3%
7	240	3139.5	75.98	2.4%	35.92	1.1%	49.34	1.6%	97.09	3.1%	137.57	4.4%
8	160*†	5713.3	143.96	2.5%	42.68	0.7%	65.72	1.2%	170.29	3.0%	236.36	4.1%
9	159†	7537.2	129.57	1.7%	133.30	1.8%	35.89	0.5%	187.57	2.5%	266.51	3.5%

* Additional GFAP result was obtained due to cartridge re-run due to a UCH-L1 star-out
†one (1) outlier removed from analysis
‡two (2) outliers removed from analysis
§three (3) outliers removed from analysis

Table 10: Estimate of UCH-L1 Assay Precision

Sample	N	Mean (pg/mL)	Repeatability		Between-Run		Between-Day		Between-Lot		Within-Laboratory	
			SD (pg/mL)	CV (%)	SD (pg/mL)	CV (%)	SD (pg/mL)	CV (%)	SD (pg/mL)	CV (%)	SD (pg/mL)	CV (%)
1	238‡	72.5	4.88	6.7%	1.73	2.4%	0.00	0.0%	3.93	5.4%	6.50	9.0%
2	239†	300.1	15.12	5.0%	5.94	2.0%	0.00	0.0%	15.54	5.2%	22.48	7.5%
3	240	519.9	29.56	5.7%	1.54	0.3%	13.38	2.6%	8.21	1.6%	33.51	6.4%
4	238‡	1058.9	56.88	5.4%	22.59	2.1%	15.13	1.4%	33.60	3.2%	71.44	6.7%
5	159*	1639.6	91.57	5.6%	8.72	0.5%	15.74	1.0%	28.46	1.7%	97.56	6.0%
6	240	2067.4	111.09	5.4%	54.99	2.7%	46.01	2.2%	15.00	0.7%	133.06	6.4%
7	239†	2849.7	145.40	5.1%	100.56	3.5%	0.00	0.0%	15.16	0.5%	177.44	6.2%

*one (1) result was unavailable due to star-out
†one (1) outlier removed from analysis
‡two (2) outliers removed from analysis

Table 11: Estimate of GFAP and UCH-L1 assay Precision with i-STAT TBI Controls

Sample	N	Mean (pg/mL)	Repeatability		Between-Run		Between-Day		Between-Lot**		Within-Laboratory	
			SD (pg/mL)	CV (%)	SD (pg/mL)	CV (%)	SD (pg/mL)	CV (%)	SD (pg/mL)	CV (%)	SD (pg/mL)	CV (%)
GFAP Assay												
L1	238*§	196.7	9.94	5.1%	2.69	1.4%	2.25	1.1%	5.70	2.9%	11.98	6.1%
L2	242*	5153.8	236.89	4.6%	94.93	1.8%	28.10	0.5%	183.00	3.6%	315.29	6.1%
UCH-L1 Assay												
L1	239†	562.6	29.79	5.3%	9.57	1.7%	11.92	2.1%	13.21	2.3%	36.00	6.4%
L2	240	1624.7	90.14	5.5%	53.68	3.3%	0.00	0.0%	32.25	2.0%	109.76	6.8%

* Additional GFAP result was obtained due to cartridge re-run due to a UCH-L1 star-out

†one (1) outlier removed from analysis

‡two (2) outliers removed from analysis

§three (3) outliers removed from analysis

**This refers to precision estimates calculated between cartridge lots. A single lot of i-STAT TBI controls was used for this study.

Linearity

The linearity of GFAP and UCH-L1 assays was established using plasma samples of varying antigen levels that range from below the lower limit of the reportable range to above the upper reportable range for both GFAP and UCH-L1. The study was based on CLSI guidance EP06-A [11]. The linearity for both GFAP and UCH-L1 was demonstrated over the reportable range for each assay in the i-STAT TBI Plasma cartridge using the i-STAT Alinity instrument. The regression equation for the linear range of the GFAP assay is y=1.02x-6.7. The regression equation for the linear range of the UCH-L1 assay is y=1.04x-17.7.

Table 12: Linearity Across Reportable Range

Assay	Slope	Intercept	r^2
GFAP	1.02	-6.7	0.9985
UCH-L1	1.04	-17.7	0.9869

Limit of Quantitation

The limit of quantitation (LoQ) is defined as the lowest amount of a measurand in a sample that can be measured with imprecision %CV ≤ 20%. A study to determine LoQ was performed based on CLSI guidance EP17-A2 [12]. Testing was conducted on five (5) days using four (4) cartridge lots and plasma from normal donors containing six (6) low levels of GFAP and UCH-L1. The estimated LoQ for the i-STAT TBI Plasma test from this study was 23 pg/mL for the GFAP assay and 70 pg/mL for the UCH-L1 assay.

High Dose Hook Effect

The GFAP and UCH-L1 assays in the i-STAT TBI Plasma cartridge on the i-STAT Alinity System were evaluated for high dose hook effect. The testing was conducted using plasma samples spiked to a high antigen level for each assay (>100,000 pg/mL). Each sample was tested to verify that the measured signal is greater than that of a nominal GFAP target of 10,000 pg/mL and a nominal UCH-L1 target of 4,000 pg/mL. Hook effect was not observed for the GFAP and UCH-L1 assays as the signal responses of high dose samples were significantly greater than 10,000 pg/mL for the GFAP assay and 4,000 pg/mL for the UCH-L1 assay.

Elevated Temperature Operating Performance

The performance of the GFAP and UCH-L1 assays at an elevated temperature operating condition was compared to performance at a room temperature. Plasma samples spiked with a GFAP and UCH-L1 antigens to concentrations around the respective assay cutoffs were tested on i-STAT TBI Plasma cartridges. 116 of the cartridges were run in a temperature chamber at 30.8°C / 87.4°F and 118 cartridges were run in a laboratory at 24.4°C / 75.9°F. The bias and percent bias are shown in **Table 13** below.

Table 13: Elevated Temperature Operating Performance

N	GFAP				UCHL-1			
	Mean (pg/mL)	%CV	Bias (pg/mL)	%Bias	Mean (pg/mL)	%CV	Bias (pg/mL)	%Bias
116	33.4	7.5	-3.1	-8.6%	404.0	5.9	-21.8	-5.1%

LIMITATIONS OF THE PROCEDURE

- The i-STAT TBI Plasma test is not intended to be used as a stand-alone device but as an adjunct to other clinical information to aid in the evaluation of patients who are being considered for standard of care neuroimaging.
- A 'Not Elevated' result is generally associated with the absence of acute intracranial lesions. An appropriate neuroimaging method is required for diagnosis of acute intracranial lesions.
- This device is for use by healthcare professionals in a clinical laboratory setting. The i-STAT TBI Plasma test is not intended to be used in point of care settings.
- The frequency of suppressed results is affected by atmospheric pressure. Suppressed result rates may increase with higher elevations (decreased barometric pressure) and may become persistent if testing is performed at more than 7500 feet (2286 meters) above sea level. Where unavailability of results is unacceptable, Abbott Point of Care recommends having an alternate method available for evaluating patients with potential traumatic brain injury.
- Samples from patients who have been exposed to animals or who have received therapeutic or diagnostic procedures employing immunoglobulins or reagents derived from immunoglobulins may contain antibodies, e.g., HAMA or other heterophile antibodies, which may interfere with immunoassays and produce erroneous results[13-19]. The generation of potentially interfering antibodies in response to bacterial infections has been reported[15]. While this product contains reagents that minimize the effect of these interferents and QC algorithms designed to detect their effects, the possibility of interference causing erroneous results should be evaluated carefully in cases where there are inconsistencies in the clinical information.
- The instrument must remain on a flat surface with the display facing up during testing. Motion of the instrument during testing can increase the frequency of suppressed results or quality check failures. A level surface includes running the instrument in the base station.
- The test results should be assessed in conjunction with the patient's symptoms, clinical examination, and other findings. If results appear inconsistent with the clinical assessment, the patient sample should be retested using another cartridge.

Factors Affecting Results

Factor	Assay	Effect
Hemolysis	GFAP UCH-L1	Grossly hemolyzed samples can cause a decreased alkaline phosphatase activity, increased assay background signal, and/or quality check failures. Increases in UCH-L1 concentration have been observed in hemolyzed samples.
Sample Handling	GFAP UCH-L1	Prior to processing blood samples to plasma, vortexing and mechanical rotating of the blood sample should be avoided. This type of agitation has been observed to lead to decreases in GFAP concentration and increases in UCH-L1 concentration. Post-processing, sample plasma should be removed carefully from the separated red blood cells, extracting from the top 1/3 of the separated plasma. Take care not to disturb the buffy coat interface between the plasma and red blood cell layers. Increased UCH-L1 results have been observed when sampling from the buffy coat layer.
Altitude	GFAP UCH-L1	The i-STAT TBI Plasma test has not been evaluated at altitudes >7,500 feet. No impact on performance was found up to 7,500 feet of altitude.

Interference Testing

Interference studies were based on CLSI guideline EP07 3rd edition [20]. The substances listed were evaluated in plasma for each assay. For those identified as an interferant the interference is described.

Table 14: Interfering Substance Testing

Substance	Test Concentration µmol/L	Test Concentration mg/dL	Assay	Interference (Yes/No)	Comment
Albumin	150 g/L	15 g/dL	GFAP	No	
			UCH-L1	No	
Bilirubin	684	40	GFAP	No	
			UCH-L1	No	
Bilirubin (conjugated)	475	40	GFAP	No	
			UCH-L1	No	
Hemoglobin	10 g/L	1000	GFAP	No	
			UCH-L1	No	
Human anti-mouse antibody (HAMA) [a]	>160x [b]	N/A	GFAP	No	
			UCH-L1	Yes	Highest concentration tested where no interference observed: 40x Testing above this level showed decreased results [c]
Intralipid (Intralipid 20%)	N/A	4747	GFAP	No	
			UCH-L1	No	
Rheumatoid Factor (RF) [a]	1000 IU/mL	N/A	GFAP	No	
			UCH-L1	Yes	Highest concentration tested where no interference observed: 500 IU/mL Testing above this level showed decreased results [c]
Triglycerides [a]	33.88 mmol/L	3000	GFAP	No	
			UCH-L1	No	
Acetaminophen [a]	1.324 mmol/L	20.01	GFAP	No	
			UCH-L1	No	
Sodium Ascorbate	298	5.90	GFAP	No	

Substance	Test Concentration µmol/L	mg/dL	Assay	Interference (Yes/No)	Comment
			UCH-L1	No	
Caffeine	556	10.8	GFAP	No	
			UCH-L1	No	
Clopidogrel [a]	21.4	9 µg/mL	GFAP	No	
			UCH-L1	No	
Dopamine	4.06	0.077	GFAP	No	
			UCH-L1	No	
Ethanol	130 mmol/L	600	GFAP	No	
			UCH-L1	Yes	Highest concentration tested where no interference observed: 65 mmol/L [d] Testing above this level showed decreased results
Erythromycin	188	13.80	GFAP	No	
			UCH-L1	No	
Nicotine	5.97	0.097	GFAP	No	
			UCH-L1	No	
Metoprolol Tartrate [a]	7.3	0.50	GFAP	No	
			UCH-L1	No	
Acetylsalicylic acid [a]	3.62 mmol/L	65.22	GFAP	No	
			UCH-L1	No	
Chloramphenicol	241	7.8	GFAP	No	
			UCH-L1	No	
Diclofenac	81	2.58	GFAP	No	
			UCH-L1	No	
Ibuprofen [a]	2.425 mmol/L	50.0	GFAP	No	
			UCH-L1	No	
Phenytoin	238	6	GFAP	No	
			UCH-L1	No	
Amphetamine [a]	2.39	0.032	GFAP	No	
			UCH-L1	No	
Benzoylecgonine [a]	8.64	2.5 µg/mL	GFAP	No	
			UCH-L1	No	
Nicardipine hydrochloride	0.97	0.050	GFAP	No	
			UCH-L1	No	
EDDP† perchlorate [a]	0.3308	125 ng/mL	GFAP	No	
			UCH-L1	No	
Methadone	10.3	0.318	GFAP	No	
			UCH-L1	No	
Methaqualone [a]	32.36	8.1 µg/mL	GFAP	No	
			UCH-L1	No	
d-Methamphetamine [a]	1.865	278.4 ng/mL	GFAP	No	
			UCH-L1	No	
Morphine	27.3	0.78	GFAP	No	
			UCH-L1	No	
Oxazepam	15.1	0.432	GFAP	No	
			UCH-L1	No	
Phencyclidine [a]	0.0357	8.7 ng/mL	GFAP	No	
			UCH-L1	No	
Secobarbital	66.8	1.59	GFAP	No	
			UCH-L1	No	
Cocaine [a]	11.406	3.46 µg/mL	GFAP	No	
			UCH-L1	No	
Propoxyphene [a]	9.46	0.32	GFAP	No	
			UCH-L1	No	

Substance	Test Concentration µmol/L	mg/dL	Assay	Interference (Yes/No)	Comment
Warfarin	243	7.5	GFAP	No	
			UCH-L1	No	
Diazepam	105	3.00	GFAP	No	
			UCH-L1	No	

†2-Ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine
[a] The test concentration used for this substance is not from CLSI guideline EP37 1st edition [21]
[b] The 'x' factor listed indicates the number of times more activity than a known negative sample for its ability to crosslink antibodies in a mouse system assay.
[c] One out of the five samples enriched for the presence of HAMA and two out of the five samples enriched for presence of RF exhibited an interference effect. See note regarding HAMA or other heterophile antibodies in Limitations of the Procedure section above.
[d] Note that the ethanol level is well above the CLSI highest therapeutic level of 43.4 mmol/L (200 mg/dL)

This is representative data and results may vary from study to study due to matrix effects. Viscosity, surface tension, turbidity, ionic strength and pH are common causes of matrix effects. It is possible that interfering substances other than those tested may be encountered. The degree of interference at concentrations other than those listed has not been tested.

Analytical Specificity

The i-STAT TBI Plasma cartridge is specific to the measurement of glial fibrillary acid protein (GFAP) and ubiquitin carboxyl-terminal hydrolase L1 (UCH-L1). The following proteins in **Table 15** with significant homology to GFAP or UCH-L1 were tested at highest known physiological levels and none were found to have significant impact on the measured GFAP or UCH-L1 levels.

Table 15: Cross-Reactivity Testing

Substance	Test Concentration pg/mL	Assay	Cross-reactivity (Yes/No)
Keratin type II	10 000	GFAP	No
Internexin	77 000	GFAP	No
Neurofilament medium	8600	GFAP	No
Neurofilament heavy	77 000	GFAP	No
Neurofilament light	68	GFAP	No
Peripherin	5000	GFAP	No
Desmin	127 000	GFAP	No
Vimentin	354 000	GFAP	No
Ubiquitin Carboxyl-Terminal Hydrolase L3 (UCH-L3)	354 000	UCH-L1	No

KEY TO SYMBOLS

Symbol	Definition/Use
14	14 days room temperature storage at 18–30 ºC.
	Use by or expiration date. The expiration date, expressed as YYYY-MM-DD, indicates the last day the product may be used.
LOT	Manufacturer's lot number or batch code. The lot number or batch code appears adjacent to this symbol.
Σ	Sufficient for <n> tests.
EC REP	Authorized representative in the European Community.
	Temperature limitations. The upper and lower limits for storage are adjacent to upper and lower arms.
REF	Catalog number, list number, or reference.
	Do not reuse.
	Manufacturer.
	Consult instructions for use or see System Manual for instructions.
IVD	*in vitro* diagnostic medical device.
CE	Conformity to the applicable requirements of the European Union Directive on *in vitro* diagnostic devices (98/79/EC).
Rx ONLY	For prescription use only.
i-STAT Alinity ONLY	For use with i-STAT Alinity System only.

Additional Information: to obtain additional product information and technical support, refer to the Abbott company website at www.globalpointofcare.abbott.

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