Simoa® pTau-181 Advantage V2.1 Kit

SR-X Data Sheet

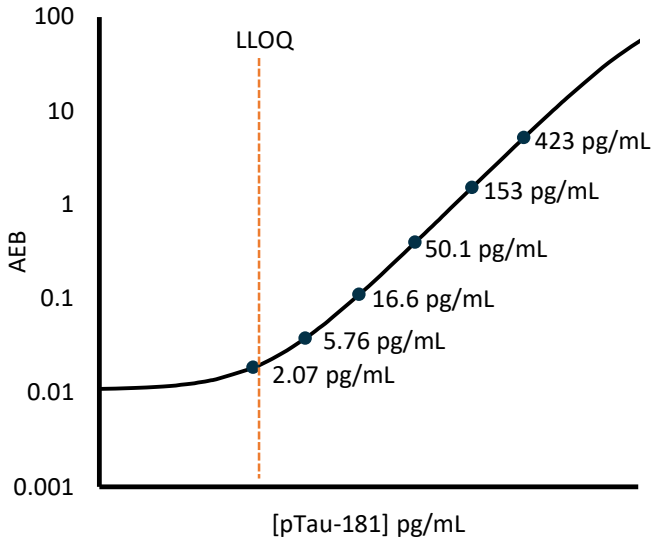
Item 104111

Description

This datasheet summarizes data from analytical validation performed at Quanterix to characterize performance of the pTau-181 Advantage V2.1 kit on the SR-X platform.

Threonine 181 is one of the phosphorylation sites of human tau protein (pTau-181). Tau is a microtubule-stabilizing protein primarily localized in neurons of the central nervous system but also expressed at low levels in astrocytes and oligodendrocytes. Tau consists of six isoforms in the human brain with molecular weights of 48,000 to 67,000 Daltons, depending on isoform. The Simoa pTau-181 assay targets the proline rich region of the Tau protein which is highly conserved amongst these isoforms. Tau elevation is observed in the cerebrospinal fluid (CSF) of patients with neurodegenerative disease and severe head injuries, suggesting its extracellular release during neuronal damage and a role as a biomarker with specificity for brain injury. In Alzheimer's disease (AD) and related neurodegenerative diseases, including chronic traumatic encephalopathy, tau is abnormally phosphorylated and aggregated into bundles of filaments. pTau-181 has been found to be more strongly associated with markers of AD than total tau.

Calibration Curve: Representative calibrator concentrations and Lower Limit of Quantification (LLOQ) depicted. Concentrations of Reference Calibrators provided with individual kit lots will vary, as they are value assigned to maintain consistent calibration and sample readings across lots. For pTau-181 V2.1 Reference Calibrator sets, the minimum allowable concentration for Cal G is 320 pg/mL and the maximum allowable concentration for Cal B is 3.09 pg/mL.



Minimum Required Dilution (MRD)

Diluted Sample Volume	100 µL per replicate
Human Serum, Plasma & Control Dilution	1:4
Human CSF Dilution	1:10
Tests per kit	96

See Kit Instruction for details.

Lower Limit of Quantification (LLOQ): Triplicate measurements of serially diluted calibrator were read back on the calibration curve over 12 runs across 2 reagent lots and 2 instruments (3 runs per lot, per instrument). The analytical LLOQ was set at the lowest concentration that read back within 80 – 120% of the expected value with a CV < 20%. The functional LLOQ values represent the analytical LLOQ multiplied by the dilution factor used for the samples. The functional LLOQ for plasma/serum and CSF are 4x and 10x the analytical LLOQ, respectively.

Kit Release Lower Limit of Quantification (LLOQ): The Kit Release LLOQ is a criterion applied during QC testing of each kit lot; it specifies the highest acceptable value for LLOQ. For QC testing, LLOQ is determined from HD-X or HD-1 data using the CV Profiling method described in the Technical Note, ***Lower Limit of Quantification*** (TECH-0034), available on the Quanterix Customer Portal. This is an analytical LLOQ and must be multiplied by the sample dilution factor to convert to functional LLOQ.

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DS-0544 01

DOC TEMPLATE-0061 07

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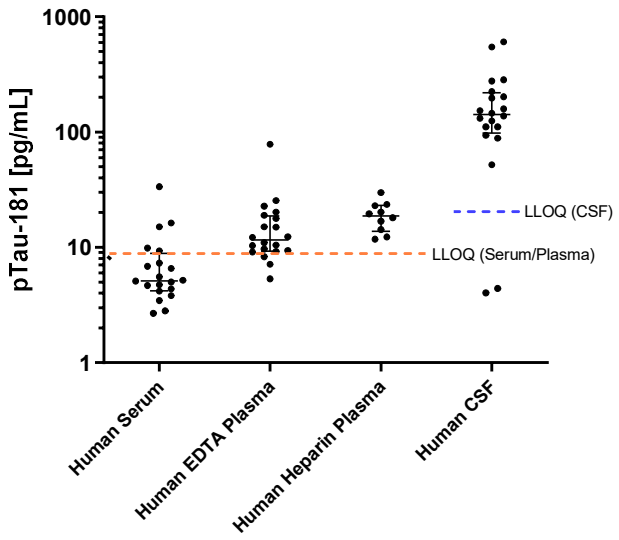
Limit of Detection (LOD): Calculated as 2.5 standard deviations from the mean of background signal read back on each calibration curve over 12 runs across 2 reagent lot and 2 instruments (3 runs per lot, per instrument).

Assay Range: The upper end of the dynamic range, or functional Upper Limit of Quantification (ULOQ) is equal to the minimum top calibrator concentration multiplied by MRD. Note that the concentration of the highest calibrator will vary between kit lots, as Reference Calibrators are value assigned to maintain consistency of results across lots.

Analytical LLOQ	**2.23 pg/mL** pooled CV 19.0% mean recovery 97.0%
Functional LLOQ (serum and plasma)	**8.92 pg/mL**
Functional ULOQ (serum and plasma)	**1280 pg/mL**
Functional LLOQ (CSF)	**22.3 pg/mL**
Functional ULOQ (CSF)	**12,800 pg/mL**
LOD	**1.04 pg/mL** range 0.146-1.750 pg/mL
Kit Release LLOQ	**2.87 pg/mL**

Endogenous Sample Reading: Presumably healthy donor matched human serum and EDTA plasma (n=20), and unmatched normal human heparin plasma (n=10) and CSF (n=20) were measured. Bars depict median with interquartile range. Orange line represents functional LLOQ for serum/plasma samples and blue line represents functional LLOQ for CSF samples.



Sample Type	Mean* pTau-181 pg/mL	Median pTau-181 pg/mL	% Above LOD	% Above LLOQ
Human Serum	16.9	5.15	80%	25%
Human Plasma	18.1	11.6	100%	85%
Human CSF	203	142	90%	90%
Human Heparin Plasma**	19.0	18.8	100%	100%

*** Values below LLOQ are not included in the mean.**
****For information only, not a fully validated matrix.**

Precision: Measurements were obtained with 1 serum-based panel, 2 EDTA plasma-based panels, 1 CSF-based panel and 2 calibrator-based controls. Triplicate measurements were made for 12 runs (36 measurements in total) across 2 reagent lots and 2 instruments (3 runs per lot, per instrument). All samples were diluted at the appropriate MRD for the sample matrix.

Sample	Mean (pg/mL)	Within run CV	Between run CV	Between inst CV	Between Lot CV
Control 1	50.5	5.0%	7.8%	0.6%	1.4%
Control 2	530	4.5%	11.2%	5.6%	6.0%
Panel 1	22.3	8.4%	6.7%	1.5%	3.1%
Panel 2	22.5	10.1%	8.1%	4.0%	4.5%
Panel 3	636	5.9%	10.8%	0.3%	0.7%
Panel 4	212	6.4%	9.4%	4.4%	6.4%

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Spike and Recovery: Spike recovery was measured with human serum, EDTA plasma and CSF samples in the feasibility phase of assay development. Results indicate that matrix effects are observed with this assay, as a limited dilution was chosen to maximize the detectability / quantifiability of the analyte in serum and EDTA plasma samples from healthy donors.

Dilution Linearity: Dilution linearity was measured with human serum, EDTA plasma and CSF samples in the feasibility phase of assay development. Likely due to matrix effects, pTau-181 readings do not exhibit linearity upon dilution of the matrix with sample diluent. For valid comparison between results, it is recommended to run all samples at a consistent dilution.

Admixture Linearity: Samples with high concentrations of analyte were created by spiking with calibrators. One EDTA plasma and 1 serum sample were mixed with low-analyte samples of the same matrix at 12 different ratios. The dilution series was run on the SR-X with the MRD (4x) dilution applied. Data was generated with two different lots of kits.

Admix Linearity Plasma **low matrix 7.30 pg/mL** **high matrix 223 pg/mL**	**Mean 90%** range 76–98% Slope = 1.0221, R^2 = 0.9946
Admix Linearity Plasma **low matrix 10.5 pg/mL** **high matrix 340 pg/mL**	**Mean 97%** range 88–107% Slope = 0.9815, R^2 = 0.9977
Admix Linearity Serum **low matrix 7.44 pg/mL** **high matrix 232 pg/mL**	**Mean 97%** range 86–108% Slope = 0.9968, R^2 = 0.9925
Admix Linearity Serum **low matrix 8.22 pg/mL** **high matrix 318 pg/mL**	**Mean 84%** range 69–97% Slope = 1.0001, R^2 = 0.9871

The Simoa pTau-181 Advantage V2.1 assay kit is formulated for use on the SR-X, HD-1, or HD-X platform. Some differences in performance claims between the HD and SR-X platforms may be observed when comparing data sheets for these platforms. This may be due to experiments run at different time-points with different reagent lots and different samples or may be due to minor differences in antibody and analyte behavior in the different assay formats.

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DS-0544 01