Quanterix™
The Science of Precision Health

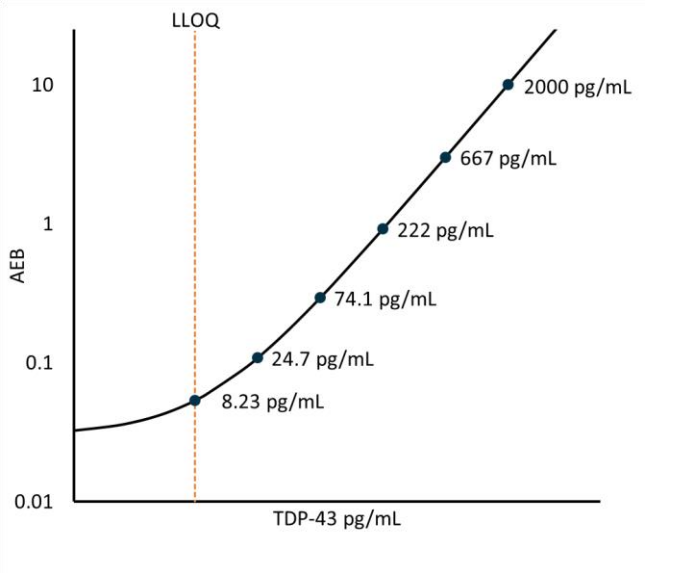
Simoa® TDP-43 Advantage Kit
HD-1/HD-X Data Sheet

Item 103293

Description

The TAR DNA binding protein of 43 kDa (TDP-43 or TARDBP) is a highly conserved and ubiquitously expressed nuclear protein with roles in transcription and splicing regulation. It is also the major component of ubiquitin-positive cytoplasmic inclusions found in the brains of patients with frontotemporal lobar degeneration (FTLD) and amyotrophic lateral sclerosis (ALS). In addition, TDP-43-containing aggregates are found in a significant number of patients with Alzheimer's Disease (AD) and other neuromuscular disorders. The majority of TDP-43 protein found in cytoplasmic inclusions is truncated, and it has been shown that the C-terminal domain is intrinsically prone to aggregation. Mutations in the C-terminal region of the TDP-43 gene have been associated with both ALS and FTLD, and are thought to facilitate ubiquitination and phosphorylation of the TDP-43 protein, leading to the formation of pathological inclusions and eventual neurodegeneration. Analysis of TDP-43 levels in plasma may allow the indexing of TDP-43 pathology within the brain to aid in the diagnosis of different forms of dementia and distinguish between TDP-43 proteinopathy and tauopathy. The Simoa TDP-43 assay has been developed with a full-length protein calibrator and antibodies against AA 203 – 209 and the C-terminal region; it is expected to detect both full-length and pathological, truncated forms of the protein.

Calibration Curve: Calibrator concentrations and Lower Limit of Quantification depicted.



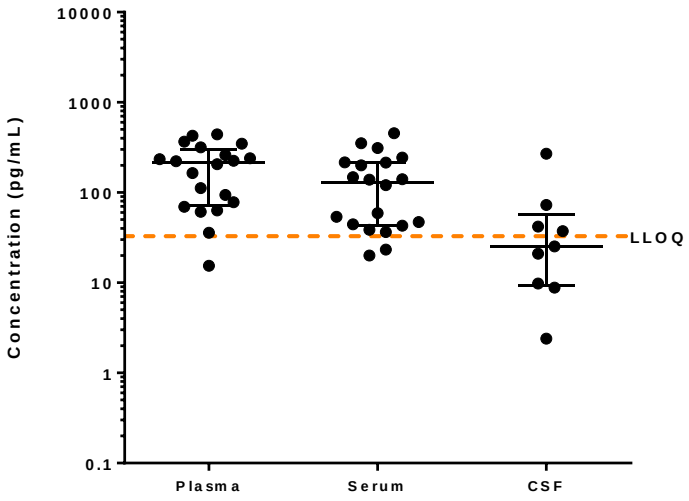
Lower Limit of Quantification (LLOQ): Triplicate measurements of serially diluted calibrator were read back on the calibration curve over 12 runs each for 2 reagent lot across 2 instruments (12 runs total).

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 each for 2 reagent lot across 2 instruments (12 runs total).

Analytical LLOQ	**8.23 pg/mL** pooled CV 13% mean recovery 113%
LOD	**2.48 pg/mL** range 0.234-5.08 pg/mL
Dynamic range (serum and plasma)	0–8000 pg/mL
Diluted Sample volume*	100 µL per measurement
Tests per kit	96

***See Kit Instruction for details**

Endogenous Sample Reading: Healthy donor matched EDTA plasma (n=20), and serum (n=20) were measured. Nine CSF samples were measured. Bars depict median with interquartile range. Orange line represents functional LLOQ.



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Sample Type	Mean TDP-43 pg/mL	Median TDP-43 pg/mL	% Above LOD
Serum	159	130	100%
Plasma	209	214	100%
CSF	127	25.3	69%

Precision: Measurements of 1 plasma-based panel, 3 serum-based panels and 2 calibrator-based controls. Triplicate measurements were made for 6 runs each for 2 reagent lots across 2 instruments (12 runs total, 36 measurements).

Sample	Mean (pg/mL)	Within run CV	Btwn run CV	Btwn inst CV	Btwn lot CV
Control 1	195	4.3%	4.0%	3.4%	1.8%
Control 2	1953	3.1%	4.5%	2.5%	2.5%
Panel 1	59.0	11.8%	11.3%	0.1%	1.1%
Panel 2	73.5	6.2%	14.1%	3.3%	1.3%
Panel 3	316	3.2%	11.1%	7.3%	3.4%
Panel 4	1771	4.0%	8.2%	5.7%	6.0%

Spike and Recovery: 2 serum, 2 EDTA plasma and 2 CSF samples were spiked at high and low concentrations within the range of the assay and analyzed on HD-1.

Observed recovery was consistently low in serum and plasma, but results from dilutional linearity and immuno-depletion experiments support specificity of the assay signal.

Dilution Linearity: 2 spiked EDTA plasma and 2 spiked serum samples were diluted 2x serially with Sample Diluent from MRD (4x) to 32x. 2 spiked CSF samples were diluted 2x serially with Sample Diluent from MRD (4x) to 64x. All dilutions were performed offline with Sample Diluent and run neat on the HD-1 analyzer. Offline dilution is recommended when assessing dilution linearity for this assay on HD-1/HD-X.

Spike and Recovery (Serum/Plasma)	**Mean = 32%** Range: 26-42%
Dilution Linearity (Serum/Plasma) (32x)	**Mean = 116%** Range: 101–135%
Spike and Recovery (CSF)	**Mean = 92%** Range: 87-100%
Dilution Linearity (CSF) (64x)	**Mean = 103%** Range: 98–109%

Immuno-depletion: 1 Serum and 2 plasma samples were separately incubated with TDP-43 beads and Antibody isotype control beads prior to analysis on HD-1. Mean depletion was 98%.

The Simoa TDP-43 Advantage assay kit is formulated for use on the SR-X®, HD-1, or HD-X® platform. Data in this document was obtained from runs on the HD-1 platform unless otherwise noted. Some differences in performance claims between SR-X and HD-1/HD-X may be observed when comparing datasheets for these platforms. This may be due to experiments run at different time-points with different reagent lots and different samples, or it may be due to minor differences in antibody and analyte behavior in the different assay formats.