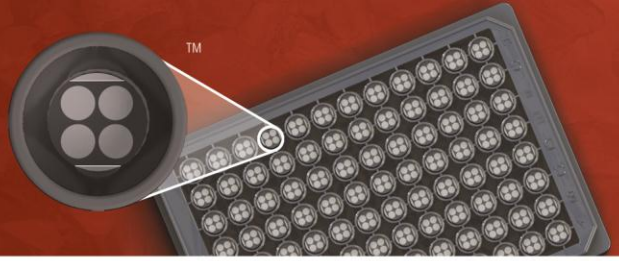
MSD® Human Aβ42 Kit



For quantitative determination in human cerebrospinal fluid

Alzheimer's Disease
BioProcess
Cardiac
Cell Signaling
Clinical Immunology
Cytokines
Hypoxia
Immunogenicity
Inflammation
Metabolic
Oncology
Toxicology
Vascular

Catalog Numbers

Human Aβ42 Kit	
Kit size	
1 plate	K151LBE-1
5 plates	K151LBE-2
25 plates	K151LBE-4

Ordering information

MSD Customer Service
Phone: 1-301-947-2085
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Company Address

MESO SCALE DISCOVERY®
A division of
Meso Scale Diagnostics, LLC.
9238 Gaither Road
Gaithersburg, MD 20877 USA

For a complete list of products, visit www.mesoscale.com®

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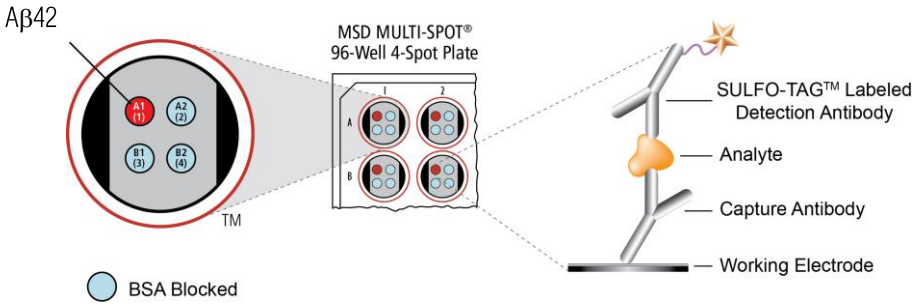


The Aβ42 peptide is a C-terminal cleavage product of the neuronal transmembrane protein amyloid precursor protein (APP). Under normal circumstances, Aβ42 may play a role in normal cellular homeostasis. In a variety of neurodegenerative diseases, Aβ42 accumulates and aggregates, resulting in significant physical and functional changes to the brain. Most notably, Aβ42 is the primary component of the neuritic plaques characteristic of Alzheimer's disease (AD), and together with tau has emerged as a core biomarker of the disease. Their levels in cerebrospinal fluid (CSF) reproducibly distinguished normal and Alzheimer's patients. CSF tau and Aβ42 levels are effective in discriminating incipient Alzheimer's disease from age-related memory impairment, depression, and some secondary dementias as well.[1-3] Studies aimed at evaluating the association between Alzheimer-type pathologic changes in the brain and antemortem CSF levels of Aβ42 and tau protein indicated that levels of both proteins correlated with the presence of neurofibrillary tangles and Aβ in the brain.[4]

The MSD Human Aβ42 Assay has been validated for the detection of Aβ42 in CSF. The performance of this kit is consistent with the principles outlined in "Fit-for-Purpose Method Development and Validation for Successful Biomarker Measurement" by J.W. Lee, et al.[5] Representative data from the assay validation are presented below. Lot-specific standard curve can be found in the certificate of analysis (C of A) supplied with the kit. A copy of the lot-specific C of A can be found at www.mesoscale.com by entering the kit model number into the search box.

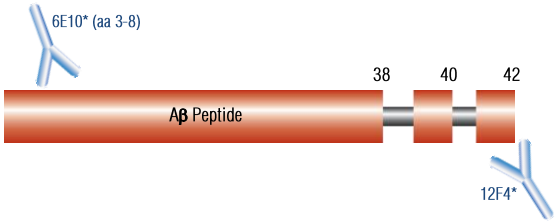
This datasheet outlines the performance of the assay. The assay is available on 96-well 4-spot plates.

Assay Sensitivity

	Aβ42 (pg/mL)
LLOD Range	0.070–0.96
LLOQ	3.0
ULOQ	2000

Testing of the kit involved a minimum of 12 runs conducted by three analysts across at least 3 days of testing (N=42 runs across three kit lots). In-well concentrations are reported.

The lower limit of detection (LLOD) is a calculated concentration based on a signal of 2.5 standard deviations above the background. The lower limit of quantification (LLOQ) is the lowest concentration where the %CV of the calculated concentration is less than 20% and the percent recovery of the standard is between 80% and 120%. The upper limit of quantification (ULOQ) is the highest concentration where the %CV of the calculated concentration is less than 20% and the percent recovery of the standard is between 80% and 120%.



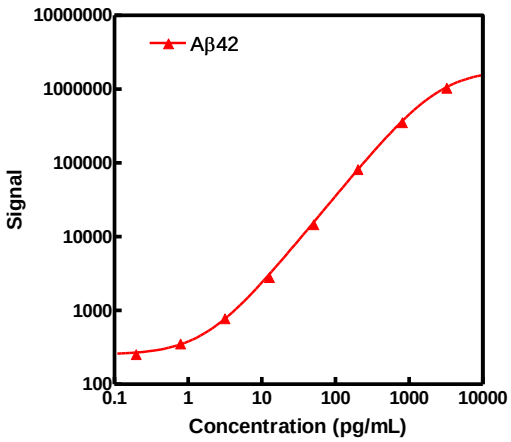
Aβ peptide Antibody Recognition Site

*The 6E10 and 12F4 antibodies used in MSD Human Ab 42 Kit are supplied by Covance Research Products, Inc.

Spot the Difference®

Typical Standard Curve

The following standard curve is an example of the dynamic range of the Human Aβ42 Assay.



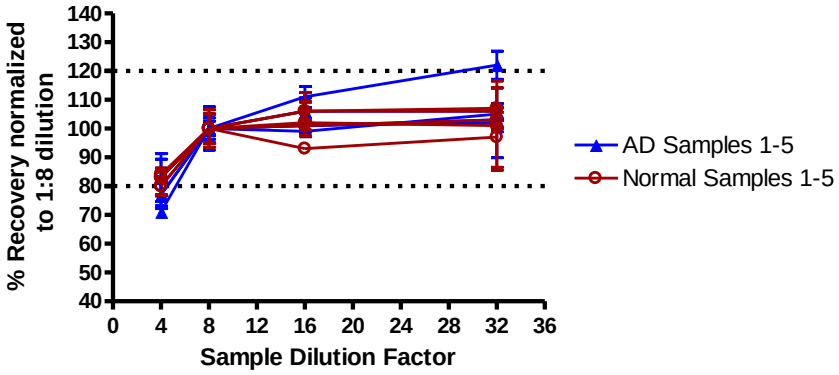
	Aβ42	
Conc. (pg/mL)	Average Signal	%CV
0	245	5.8
0.193	258	4.0
0.774	361	2.6
3.10	793	2.9
12.4	2870	4.3
49.5	14 931	4.1
198	83 291	3.2
793	359 727	3.3
3170	1 054 859	3.7

Linearity

To assess linearity, CSF from normal and Alzheimer's disease (AD) individuals were diluted 4-fold, 8-fold, 16-fold, and 32-fold with Diluent 35. The measured concentrations were corrected for dilution factor to determine the actual Aβ42 levels in the sample. Recovery at each dilution was calculated relative to the optimal sample dilution, 1:8.

Average percent recovery and range of recovery for normal and AD samples at each dilution are presented in the graph and table below. A minimum sample dilution of 8-fold is recommended.

% Recovery=(measured∗dilution factor)/(measured at 1:8 dilution∗8)∗100



		Aβ42	
Sample	Fold Dilution	Average %Recovery	%Recovery Range
Normal CSF (N=5)	4	82	80–84
	8	100	N/A
	16	102	93–106
	32	103	97–107
AD CSF (N=5)	4	78	71–83
	8	100	N/A
	16	104	99–111
	32	108	102–122

Spike Recovery

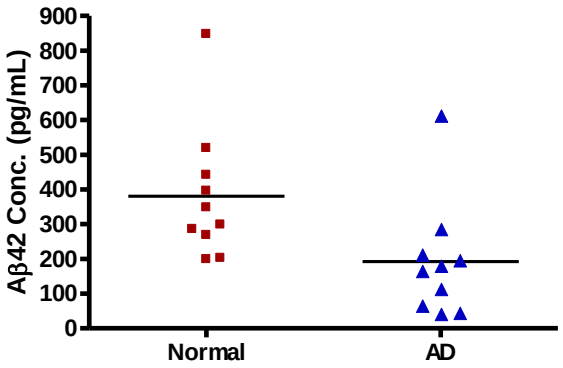
CSF from normal and Alzheimer's disease (AD) individuals was spiked with calibrator at multiple levels throughout the range of the assay. The samples were diluted 8-fold and tested for recovery.
% Recovery=measured/expected∗100

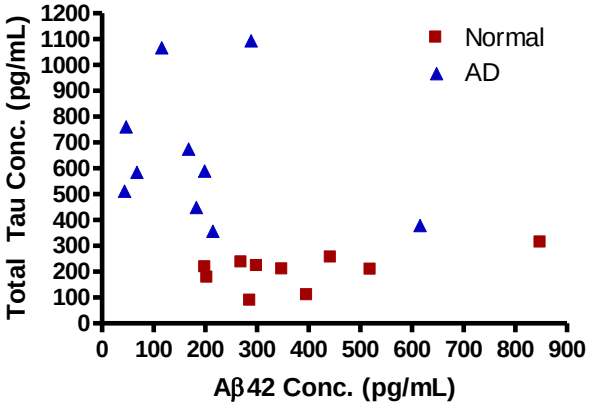
	Aβ42		
Sample	Spike Conc. (pg/mL)	Average %Recovery	%Recovery Range
Normal CSF (N=5)	4000	88	81–92
	1000	98	92–105
	250	95	87–104
AD CSF (N=5)	4000	89	84–94
	1000	95	93–99
	250	95	90–103

Samples

Normal and Alzheimer's disease (AD) individual patient CSF samples and pooled human CSF samples were purchased from commercial vendors. Sample collection methods and pre-analytical variables may cause variability in the measured range of normal and diseased samples. The individual patient samples were well-curated; handling was consistent with accepted protocols. The commercial vendors that supplied the pooled CSF samples were not able to adhere to stringent collection and handling procedures. Samples were diluted 8-fold prior to measuring with the Human Aβ42 Kit. The table below displays median and range of concentrations for each sample set. Concentrations have been corrected for sample dilution. A graphical representation is also provided for the individual normal and AD patient samples.

			Aβ42 (pg/mL)
Well-curated, Individual, Human CSF Samples	Normal	Median (pg/mL)	324
		Range (pg/mL)	199–848
		# of Samples	10
		% of Samples in Quantitative Range	100%
	AD	Median (pg/mL)	174
		Range (pg/mL)	42–614
		# of Samples	10
		% of Samples in Quantitative Range	100%
Pooled Human CSF		Median (pg/mL)	92
		Range (pg/mL)	20–247
		# of Samples	10
		% of Samples in Quantitative Range	80%





Precision

Control samples using pooled human CSF with or without spiked Aβ42 calibrator were built. Two sets of control samples were independently prepared and tested in the Human Aβ42 Assay. Each set contained three controls with Aβ42 levels spanning the expected range of Aβ42 in human CSF samples. Controls were diluted 8-fold. Concentrations for all controls were measured using three independent Human Aβ42 Kit lots. Representative data from one set of controls is presented in the tables below. For this study, three analysts ran tests over 11 days (N=29 runs across three kit lots). The control data for each kit lot and an inter-kit lot summary are presented in the upper table. Concentrations presented in the table have been dilution-adjusted. Avg. Intra-plate Calc. Conc. %CV is the average concentration %CV of the control replicates on an individual plate. Inter-plate Calc. Conc. %CV is the variability of measured control concentration across plates, with replicate information as indicated in the table. Total error was calculated as the (Inter-plate Calc. Conc. %CV)+(absolute value of % Conc. Recovery Relative to Final Expected Concentration-100%). The concentrations presented in the inter-lot summary represent the expected concentrations for each control. Measured concentrations for each kit relative to the final expected concentration are presented in the lower table.

The controls had low variability (CVs <20%), and the control concentrations measured on each kit lot were within 10% of the expected value (lower table).

	Sample ID	Calc. Conc. (pg/mL)	Inter-plate Calc. Conc. %CV	Avg. Intra-plate Calc. Conc. %CV	% Total Error
Kit Lot 1 N=2	Control 1	2586	9.7	5.1	13
	Control 2	683	10.1	7.0	19
	Control 3	210	8.5	8.0	9
Kit Lot 2 N=4	Control 1	2719	9.7	8.5	18
	Control 2	675	9.6	7.8	18
	Control 3	228	9.4	5.4	19
Kit Lot 3 N=23	Control 1	2453	12.4	6.8	14
	Control 2	611	16.6	10.0	19
	Control 3	205	10.9	6.6	13
Inter-Lot Summary N=29	Control 1	2499	12.1	7.0	
	Control 2	625	15.8	9.5	
	Control 3	208	11.1	6.5	

	% Conc. Recovery Relative to Final Expected Concentration		
	Kit Lot 1	Kit Lot 2	Kit Lot 3
Control 1	103	109	98
Control 2	109	108	98
Control 3	101	110	98

References

1. Shaw LM et al. Cerebrospinal fluid biomarker signature in Alzheimer's disease neuroimaging initiative subjects. Ann Neurol. 2009; 65:403-413.
2. Blennow K, Hampel H, Weiner M, Zetterberg H. Cerebrospinal fluid and plasma biomarkers in Alzheimer disease. Nat Rev Neurol. 2010 Mar;6(3):131-44.
3. Buchhave P, Minthon L, Zetterberg H, Wallin AK, Blennow K, Hansson O. Cerebrospinal fluid levels of β-Amyloid 1-42, but not of tau, are fully changed already 5 to 10 years before the onset of Alzheimer dementia. Arch Gen Psychiatry. 2012 Jan;69(1):98-106.
4. Tapiola T, Alafuzoff I, Herukka SK, Parkkinen L, Hartikainen P, Soininen H, Pirttilä T. Cerebrospinal fluid β-Amyloid 42 and tau proteins as biomarkers of Alzheimer-type pathologic changes in the brain. Arch Neurol. 2009 Mar;66(3):382-9.
5. Lee JW, Devanarayan V, Barrett YC, Weiner R, Allinson J, Fountain S, Keller S, Weinryb I, Green M, Duan L, Rogers JA, Millham R, O'Brien PJ, Sailstad J, Khan M, Ray C, Wagner JA. Fit-for-purpose method development and validation for successful biomarker measurement. Pharm Res. 2006 Feb;23(2):312-28.