2.7.1.4.17 ヒト血清中 NAb 測定法（BAV-0031-R v02）

Method reproducibility	NA	-
Study sample analysis/stability	All sample handling and analyses were conducted within the limits of sample stability for freeze/thaw, ambient temperature processing and 2-8 °C incubation established during method validation.	bas-0044-r; Section 6.0
Standard calibration curve performance during accuracy and precision runs	NA	

AD = Alzheimer's disease, ADA = anti-lecanemab antibodies, CV = coefficient of variation, ECL = electrochemiluminescence, HQC = high QC, IgG = immunoglobulin G, LLOQ = lower limit of quantitation, LQC = low QC, MRD = minimum required dilution, MSD = meso scale discovery, MSR = minimum significant ratio, NA = not applicable, NAb = neutralizing antibodies, NC = negative control, NQC = negative QC, PC = positive control, QC = quality control, TE = total error, ULOQ = upper limit of quantification.
a: The HQC samples generated an acceptable pooled repeatability %CV of 8.2%, but did not meet the intermediate precision acceptance criteria with a %CV of 27.6% (BAV-0031-R v02; Appendix H). Assay precision for the LQC was considered acceptable, and the validation plan was amended to repeat assay precision for a new HQC concentration. Results from the LQC and NQC analyses were used to establish system suitability.
b: Four samples were analyzed outside of the established long-term stability, these samples are identified with a * in Table 5 of the report bas-0052-r v00.
Source: bav-0031-r v02, bas-0052-r v00, bas-0044-r.

2.7.1.4.18 ヒト血清中 NAb 測定法（45-1808）

Bioanalytical method validation report name, amendments, and hyperlinks	The Validation of an ECL method for the Detection of Neutralizing Antibodies (NAb) Directed Against BAN2401 in Human Serum - 45-1808 ([redacted] 20[redacted])		
Method description	Assay Platform: ECL immunoassay A quasi-quantitative immunogenicity assay to detect the presence of anti-BAN2401 NAb in human serum was validated.		
Biological matrix	Human serum		
Sample pre-treatment	Acid dissociation: acetic acid		
PC Antibody	Anti-BAN2401 monoclonal antibody (clone 3G7G6)		
NC	Pooled human serum only		
Materials used for standard calibration curve and concentration	NA		
Validated assay range	NA		
Materials used for QCs and concentration	Anti-BAN2401 (Clone 3G7G6) 0.872 mg/mL in PBS with 0.02% sodium azide, pooled human serum. LPC: 1.385 µg/mL anti-BAN2401 monoclonal antibody HPC: 20.0 µg/mL anti-BAN2401 monoclonal antibody		
MRDs	1:10		
Source and lot of reagents	Monoclonal anti-BAN2401 clone 3G7G6 0.872 mg/mL (20[redacted]-0009 [redacted] 20[redacted]) from Eisai, Inc.; BAN2401 [redacted] mg/mL ([redacted] [redacted] 20[redacted]) from Eisai, Inc.; biotin-BAN2401 1000 µg/mL (DJB190712-01 or equivalent [redacted] 20[redacted]) labeled at [redacted]; Sulfo Tag-[redacted] 500 µg/mL (20[redacted]-0047 [redacted] 20[redacted]) from Eisai, Inc.; pooled human serum (HMN81175 [redacted] 20[redacted]) from [redacted]		
Regressing model and weighting	NA		
Validation parameters	**Method Validation Summary**		**Source Location**
Standard calibration curve performance during accuracy and precision runs	Number of standard calibrators from LLOQ to ULOQ	NA	NA
	Cumulative accuracy (%bias) from LLOQ to ULOQ Product A	NA	NA
	Cumulative precision (%CV) from LLOQ to ULOQ Product A	NA	NA
Performance of QCs during accuracy and precision runs	**Cumulative accuracy (%bias) in 5 QCs** QCs for product A:	NA	NA
	Inter-batch %CV QCs for Product A:	NA	NA
	TE QCs for Product A:	NA	NA
Screening, titration, and confirmation cut points	[redacted] individual normal human serum samples and [redacted] individual AD human serum samples with no prior exposure to the drug were tested for SCPF determination Two TCPF were determined from the data based on the 99.9% and 99% lower confidence intervals from the data. • SCPF: 0.832		45-1808; Section 4.0 45-1808; Table 2

2.7.1.4.18 ヒト血清中 NAb 測定法（45-1808）

<table>
<tr><td></td><td>• TCPF1: 0.770
• TCPF2: 0.832</td><td></td></tr>
<tr><td>Sensitivity</td><td>Assay sensitivity was evaluated by analyzing titer PC samples diluted 1:3 in pooled human serum for 7 tiers by two analysts over three days for a total of 18 titration curves.
The estimated assay sensitivity was 1385 ng/mL (1.385 µg/mL).</td><td>45-1808; Section 4.0
45-1808; Table 3</td></tr>
<tr><td>Matrix selectivity</td><td>The matrix selectivity test was performed by analyzing 10 normal, 10 AD, 5 hemolyzed and 5 lipemic individual lots of human serum and NC tested blank and spiked with 1.385 and 20.0 µg/mL anti-BAN2401 antibodies.
The response of at least 80% of the unspiked individual lots should be greater than the PSCP. The RLU of at least 80% of the individual lots of matrix spiked at each PC level should be ≤PSCP. The response of at least 80% of the individual lots of matrix spiked at each PC level should have a Recovery within 75 to 125%.
100% of lots spiked with LPC or HPC level screened positive. 100% LPC-spiked lots showed %Recovery within 75 to 125%. 96.7% of HPC spiked lots showed %Recovery within 75% to 125%. 100% of non-spiked lots screened negative.</td><td>45-1808; Section 4.0
45-1808; Table 6</td></tr>
<tr><td>Intra- and inter-assay precision of PC, NC and titer</td><td>The intra-assay precision was determined from HPC and LPC samples at N = 6 and NC samples at N=3 on one plate. The inter-assay precision of the assay was determined from all 6 accepted runs tested on three days by two analysts. The intra and inter-run precision of titers was evaluated from the 18 assay sensitivity curves.
Intra- and inter-assay precision met pre-specified acceptance criteria.
<table>
<tr><th></th><th>NC</th><th>LPC</th><th>HPC</th><th>Titer</th></tr>
<tr><td>Intra-assay Precision (%CV)</td><td>4.5%</td><td>8.2%</td><td>7.3%</td><td>0.2% to 7.0%</td></tr>
<tr><td>Inter-assay Precision (%CV)</td><td>14.1%</td><td>6.6%</td><td>6.6%</td><td>4.2%</td></tr>
</table></td><td>45-1808; Section 4.0
45-1808; Table 4
45-1808; Table 5
45-1808; Table 7
45-1808; Table 8</td></tr>
<tr><td>Drug tolerance</td><td>Positive controls (1.385, 5.0 and 20.0 µg/mL) were pre-incubated in the presence of elevating BAN2401 concentrations, i.e., 0, 1, 2.5, 5, 10, 25, 50, and 100 µg/mL and then frozen at - 70 °C for a minimum of twelve hours prior to analysis. Drug tolerance was determined as follows:
• 0.25 µg/mL BAN2401 for 1.385 µg/mL LPC
• 10.0 µg/mL BAN2401 for 5.0 µg/mL PC
• 50 µg/mL BAN2401 for 20 µg/mL HPC</td><td>45-1808; Section 4.0
45-1808; Table 10</td></tr>
<tr><td>Interference & specificity</td><td>NA</td><td>NA</td></tr>
<tr><td>Hemolysis effect</td><td>Selectivity for hemolytic serum was found to be within the criteria in 5 individual lots of hemolyzed serum.</td><td>45-1808; Table 6</td></tr>
</table>

2.7.1.4.18 ヒト血清中 NAb 測定法（45-1808）

<table>
<tr><td>Lipemic effect</td><td colspan="3">Selectivity for lipemic serum was found to be within the criteria in 5 individual lots of lipemic serum.</td><td>45-1808; Table 6</td></tr>
<tr><td>Dilution linearity & hook effect</td><td colspan="3">NA</td><td>NA</td></tr>
<tr><td>Bench-top/process stability</td><td colspan="3">6 hours for the LPC and HPC in pooled human serum. %CV: LPC, 7.0%; HPC, 5.7%</td><td>45-1808; Section 4.0
45-1808; Table 11</td></tr>
<tr><td>Freeze-Thaw stability</td><td colspan="3">5 cycles at -20 °C and -70 °C for the LPC and HPC in pooled human serum.
%CV for -20 °C: LPC, 1.8%; HPC, 3.6%
%CV for -70 °C: LPC, 5.6%; HPC, 2.4%</td><td>45-1808; Section 4.0
45-1808; Table 12
45-1808; Table 13</td></tr>
<tr><td>Long-term storage</td><td colspan="3">NA</td><td>NA</td></tr>
<tr><td>Parallelism</td><td colspan="3">NA</td><td>NA</td></tr>
<tr><td>Carry over</td><td colspan="3">NA</td><td>NA</td></tr>
<tr><td colspan="5">Method performance in study: Detection of Neutralizing Anti-BAN2401 Antibodies in Human Serum Samples by ECL from Clinical Study BAN2401-G000-201 (45-1810)</td></tr>
<tr><td>Assay passing rate</td><td colspan="3">No samples were reassayed during the interim analysis.</td><td>45-1810; Section 13.2</td></tr>
<tr><td>Assay Performance</td><td colspan="3">Of the 1380 primary samples received, 25 ADA positive samples from [redacted] study 45-1809 were analyzed in two analytical runs. Both runs met the assay acceptance criteria. Neutralizing anti-BAN2401 antibodies were detected in one sample.</td><td>45-1810; Section 5
45-1810; Table 4</td></tr>
<tr><td>Standard curve performance</td><td colspan="3">NA</td><td>NA</td></tr>
<tr><td>QC performance</td><td colspan="3">The %CV of the NC was 8.8% while the PCs ranged from 6.0% to 6.1%.
<table><tr><th></th><th>NC</th><th>LPC</th><th>HPC</th></tr><tr><td>Mean RLU</td><td>4061</td><td>2947</td><td>359.3</td></tr><tr><td>%CV</td><td>8.8%</td><td>6.0%</td><td>6.1%</td></tr></table></td><td>45-1810; Section 13.1
45-1810; Table 3</td></tr>
<tr><td>Method reproducibility</td><td colspan="3">NA</td><td>NA</td></tr>
<tr><td>Study sample analysis/stability</td><td colspan="3">Samples were received on dry ice and upon arrival, and they were stored at -70 °C. The storage period between sample collection and analysis for all the samples was 933 days.</td><td>45-1810; Section 10.5</td></tr>
<tr><td>Standard calibration curve performance during accuracy and precision runs</td><td colspan="4">NA</td></tr>
</table>

AD = Alzheimer's disease, ADA = anti-lecanemab antibodies, CV = coefficient of variation, ECL = electrochemiluminescence, HPC = high PC, LPC = low PC, MRD = minimum required dilution, NA = not applicable, NC = negative control, PBS = phosphate-buffered saline, PC = positive control, PSCP = plate specific cut point, QC = quality control, RLU = relative light unit, SCPF = screening assay cut point factor, TCPF = titration cut point factor, TE = total error.
Source: 45-1808, 45-1810.

2.7.1.4.19 ヒト血漿中 Aβ(1-40)測定法要約

	Method Validation #1	Method Validation #2	Clinical Study #1	Clinical Study #2
Analyte	Aβ(1-40)	NA	NA	NA
Validation type	Partial validation	NA	NA	NA
eCTD reference number	NA	NA	NA	NA
Method ID	NA	NA	NA	NA
Duration of time method is in use	Dec 20[redacted]-NA	NA	NA	NA
Bioanalytical site	[redacted]	NA	NA	NA
Matrix	Plasma			
Platform	Enzyme-linked immunosorbent assay (ELISA)			
Format	A validated sandwich format using anti-human beta (35-40) mouse IgG monoclonal antibody as capture and HRP conjugated anti-human amyloid Beta (N, 82E1) mouse IgG monoclonal antibody as detection			
Stock reference, lot number, expiration date	Human Aβ (1-40) peptide Lot: NA, expiration date: NA	NA	NA	NA
Calibration range from the lower limit of quantitation (LLOQ) to the upper limit of quantitation (ULOQ)	[redacted]pg/mL	NA	NA	NA
Matrix study population	Normal and diseased (AD)	NA	NA	NA
Link to reports and applicable amendments	aβ40_plasma_20[redacted]	NA	NA	NA
Synopsis of amendment history	NA	NA	NA	NA

AD = Alzheimer's disease, eCTD = electronic Common Technical Document, HRP = horseradish peroxidase, ID = identification, IgG = immunoglobulin G, NA = not applicable.

2.7.1.4.20 ヒト血漿中 Aβ(1-42)測定法要約

	Method Validation #1	Method Validation #2	Clinical Study #1	Clinical Study #2
Analyte	Aβ(1-42)	NA	NA	NA
Validation type	Partial validation	NA	NA	NA
eCTD reference number	NA	NA	NA	NA
Method ID	NA	NA	NA	NA
Duration of time method is in use	Aug 20[redacted] -NA	NA	NA	NA
Bioanalytical site	[redacted]	NA	NA	NA
Matrix	Plasma			
Platform	Enzyme-linked immunosorbent assay (ELISA)			
Format	A validated sandwich format using anti-human beta (38-42) Mouse IgG Monoclonal Antibody as capture and HRP conjugated anti-Human amyloid Beta (N, 82E1) mouse IgG monoclonal antibody as detection			
Stock reference, lot number, expiration date	Human Aβ (1-42) Lot: NA, expiration date: NA	NA	NA	NA
Calibration range from the lower limit of quantitation (LLOQ) to the upper limit of quantitation (ULOQ)	[redacted]pg/mL	NA	NA	NA
Matrix study population	Normal and diseased (AD)	NA	NA	NA
Link to reports and applicable amendments	aβ42_plasma_20[redacted]	NA	NA	NA
Synopsis of amendment history	NA	NA	NA	NA

AD = Alzheimer's disease, eCTD = electronic Common Technical Document, ELISA = enzyme-linked immunosorbent assay, ID = identification, IgG = immunoglobulin G, LLOQ = lower limit of quantitation, NA = not applicable, ULOQ = upper limit of quantitation,

2.7.1.4.21 ヒト血漿中 Aβ(1-x)測定法要約

	Method Validation #1	Method Validation #2	Clinical Study #1 BAN2401-A001-101	Clinical Study #2
Analyte	Aβ(1-x)	NA	Aβ(1-x)	NA
Validation type	Full validation	NA	In-study	NA
eCTD reference number	5.3.1.4	NA	NA	NA
Method ID	TCAM-018.01	NA	TCAM-047	NA
Duration of time method is in use	11/20[redacted] - present	NA	04/20[redacted]-03/20[redacted]	NA
Bioanalytical site	[redacted]	NA	[redacted]	NA
Matrix	Plasma			
Platform	Enzyme-linked immunosorbent assay (ELISA)			
Format	A validated sandwich format using anti-human Amyloid Beta (N) (82E1) mouse IgG MoAb affinity purified antibody as capture and HRP-conjugated anti-human Amyloid Beta (11-28) mouse IgG affinity purified antibody as detection			
Stock reference, lot number, expiration date	Lyophilised Aβ1-40, Lot X12013T1, expiration date: 01/27/20[redacted]	NA	Amyloid Beta (1-X), Lot Y09035T1, expiration date: 09/17/20[redacted]	NA
Calibration range from the lower limit of quantitation (LLOQ) to the upper limit of quantitation (ULOQ)	[redacted] pg/mL	NA	[redacted] pg/mL	NA
Matrix study population	Normal	NA	Diseased (Mild to Moderate Alzheimer's disease)	NA
Link to reports and applicable amendments	tcar10-001	NA	tcar10-056	NA
Synopsis of amendment history	NA	NA	NA	NA

AD = Alzheimer's disease, eCTD = electronic Common Technical Document, ELISA = enzyme-linked immunosorbent assay, ID = identification, IgG = immunoglobulin G, LLOQ = lower limit of quantitation, NA = not applicable, ULOQ = upper limit of quantitation,.

2.7.1.4.22 ヒト血漿中 p-tau181 測定法要約

	Method Validation #1	Method Validation #2	Clinical Study #1 BAN2401-G000-201 Core and OLE Phase	Clinical Study #2 BAN2401-G000-301 Core and OLE Phase
Analyte	ptau 181	NA	ptau 181	ptau 181
Validation type	Full validation	NA	In-study	In-study
eCTD reference number	5.3.1.4	NA	NA	NA
Method ID	BTM-3467-R0	NA	BTM-3467-R0	BTM-3467-R1
Duration of time method is in use	08/20[redacted]- Present	NA	08/20[redacted]-09/20[redacted]	07/20[redacted]-08/20[redacted]
Bioanalytical site	[redacted]	NA	[redacted]	[redacted]
Matrix	Plasma			
Platform	Quanterix Simoa (Single Molecule Array)			
Format	A validated sandwich format using anti-pTau 181 antibody-coated paramagnetic beads as capture and biotinylated anti-pTau 181 antibody as detection			
Stock reference, lot number, expiration date	Calibration standard lot 107004, expiration date 03/11/20[redacted]	NA	Calibration standard lot 107004, expiration date 03/11/20[redacted]	Calibration standard lot Lot#503356, expiration date 02/15/20[redacted]
Calibration range from the lower limit of quantitation (LLOQ) to the upper limit of quantitation (ULOQ)	[redacted]pg/mL	NA	[redacted]pg/mL	[redacted]pg/mL
Matrix study population	Normal	NA	Diseased (Early Alzheimer's disease)	Diseased (Early Alzheimer's disease)
Link to reports and applicable amendments	110-r11817-r1 110-r11817a1 110-r11817a2 110-r11817a3	NA	110-r12068	110-r12754
Synopsis of amendment history	[redacted]months stability Interference assessment (Drug, Limpic and Hemolysis) and additional QC validation [redacted] stability	NA	NA	NA

eCTD = electronic Common Technical Document, ID = identification, LLOQ = lower limit of quantitation, NA = not applicable, OLE = open-label extension, QC = quality control, ULOQ = upper limit of quantitation.

2.7.1.4.23 ヒト血漿中 NfL 測定法要約

	Method Validation #1	Method Validation #2	Clinical Study #1 BAN2401-G000-201 Core only	Clinical Study #2
Analyte	NfL	NA	NfL	NA
Validation type	Partial validation	NA	In-study	NA
eCTD reference number	5.3.1.4	NA	NA	NA
Method ID	NA	NA	NA	NA
Duration of time method is in use	11/20[redacted]-present	NA	08/20[redacted]-12/20[redacted]	NA
Bioanalytical site	[redacted]	NA	[redacted]	NA
Matrix	Plasma			
Platform	Quanterix Simoa (Single Molecule Array)			
Format	In a 2-step immunoassay, target antibody coated paramagnetic beads are combined with sample and biotinylated detector antibody in the same incubation. Target molecules present in the sample are captured by the antibody coated beads and bind with the biotinylated antibody detector simultaneously			
Stock reference, lot number, expiration date	Reference Calibrators provided by Simoa NfL kit, Lot #500957 Expiration date 06/22/20[redacted]	NA	Calibrators provided by Simoa NfL kit, Lot# 501279, Expiration date 02/02/20[redacted] and Lot# 501484, Expiration date 29/08/20[redacted]	NA
Calibration range from the lower limit of quantitation (LLOQ) to the upper limit of quantitation (ULOQ)	[redacted] pg/mL	NA	[redacted] pg/mL (Lot# 501279) [redacted] pg/mL (Lot# 501484)	NA
Matrix study population	Surplus diagnostic plasma samples of AD subjects at [redacted]	NA	Diseased (Early Alzheimer's disease)	NA
Link to reports and applicable amendments	nfl_plasma_20[redacted] nfl-plasma-20[redacted]r1 Package insert of Simoa NfL kit	NA	sar-[redacted]-nflp/nrgn/ykl-40/cntn-2	NA
Synopsis of amendment history	NA	NA	NA	NA

AD = Alzheimer's disease, eCTD = electronic Common Technical Document, ID = identification , LLOQ = lower limit of quantitation, NA = not applicable, NfL = neurofilament light chain, ULOQ = upper limit of quantitation.

2.7.1.4.24 ヒト血漿中 NfL 測定法要約

	Method Validation #1	Method Validation #2	Clinical Study #1 BAN2401-G000-301 Core and OLE Phase	Clinical Study #2
Analyte	NfL	NA	NfL	NA
Validation type	Full validation	NA	In-study	NA
eCTD reference number	5.3.1.4	NA	NA	NA
Method ID	BTM-3218-R0	NA	BTM-3218-R0	NA
Duration of time method is in use	11/20[redacted]- Present	NA	07/20[redacted]-09/20[redacted]	NA
Bioanalytical site	[redacted]	NA	[redacted]	NA
Matrix	Plasma			
Platform	Quanterix Simoa (Single Molecule Array)			
Format	A validated sandwich format using anti-NfL antibody-coated paramagnetic beads as capture and biotinylated anti-NfL antibody as detection			
Stock reference, lot number, expiration date	Calibration standard lot 018301, expiration date 07/01/20[redacted]	NA	Calibration standard lot 203104, expiration date 01/21/20[redacted]	NA
Calibration range from the lower limit of quantitation (LLOQ) to the upper limit of quantitation (ULOQ)	[redacted] pg/mL		[redacted] pg/mL	NA
Matrix study population	Normal	NA	Diseased (Early Alzheimer's disease)	NA
Link to reports and applicable amendments	1629-r11293	NA	110-r12755	NA
Synopsis of amendment history	NA	NA	NA	NA

eCTD = electronic Common Technical Document, ID = identification, LLOQ = lower limit of quantitation, NA = not applicable, ULOQ = upper limit of quantitation.

2.7.1.4.25 ヒト血漿中 GFAP 測定法要約

	Method Validation #1	Method Validation #2	Clinical Study #1 BAN2401-G000-301 Core and OLE Phase	Clinical Study #2
Analyte	GFAP	NA	GFAP	NA
Validation type	Full validation	NA	In-study	NA
eCTD reference number	5.3.1.4	NA	NA	NA
Method ID	BTM-3750-R0	NA	BTM-3750-R0	NA
Duration of time method is in use	06/20[redacted]- Present	NA	07/20[redacted]-09/20[redacted]	NA
Bioanalytical site	[redacted]	NA	[redacted]	NA
Matrix	Plasma			
Platform	Quanterix Simoa (Single Molecule Array)			
Format	A validated sandwich format using anti-GFAP antibody-coated paramagnetic beads as capture and biotinylated anti-GFAP antibody as detection			
Stock reference, lot number, expiration date	Calibration standard lot 136102, expiration date 12/27/20[redacted]	NA	Calibration standard lot 203112, expiration date 02/15/20[redacted]	NA
Calibration range from the lower limit of quantitation (LLOQ) to the upper limit of quantitation (ULOQ)	[redacted]pg/mL	NA	[redacted]pg/mL	NA
Matrix study population	Normal	NA	Diseased (Early Alzheimer's disease)	NA
Link to reports and applicable amendments	1679-r12607	NA	110-r12753	NA
Synopsis of amendment history	NA	NA	NA	NA

eCTD = electronic Common Technical Document, GFAP = glial fibrillary acidic protein, ID = identification, LLOQ = lower limit of quantitation, NA = not applicable, OLE = open-label extension, ULOQ = upper limit of quantitation.

2.7.1.4.26 ヒト CSF 中 Aβ(1-42)測定法要約

	Method Validation #1	Method Validation #2	Clinical Study #1 BAN2401-J081-104	Clinical Study #2 BAN2401-J081-104	Clinical Study #3 BAN2401-G000-201 Core
Analyte	Aβ(1-42)	Aβ(1-42)	Aβ(1-42)	Aβ(1-42)	Aβ(1-42)
Validation type	Partial validation	Partial validation	In study	In study	In study
eCTD reference number	5.3.1.4	5.3.1.4	5.3.1.4	5.3.1.4	5.3.1.4
Method ID	mos-cmf-103.v1	mos-cmf-103. v2	mos-cmf-103.v1	mos-cmf-103. v2	mos-cmf-103. v2
Duration of time method is in use	Jun 20[redacted]-Nov 20[redacted]	Nov 20[redacted]-Feb 20[redacted]	Jun 20[redacted]- Mar 20[redacted]	Jun 20[redacted]- Mar 20[redacted]	Dec 20[redacted]- Jun 20[redacted]
Bioanalytical site	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Matrix	CSF				
Platform	Enzyme-linked immunosorbent assay (ELISA)				
Format	A partially validated sandwich format using monoclonal antibody 21F12 (IgG2a) as capture and one biotinylated antibody 3D6 (IgG2b) as detection				
Stock reference, lot number, expiration date	Calibration standard lot 204108, (20[redacted]-01) lot 207210, (20[redacted]-07) Lot 206189, (20[redacted]-03)	Calibration standard lot 239855 (20[redacted]-12) lot 400087, (20[redacted]-05) lot 400227 (20[redacted]-07)	Calibration standard lot 239957 (20[redacted]-01)	Calibration standard lot 400227, (20[redacted]-06) lot 400770 (20[redacted]-01)	Calibration standard lot 400499, (20[redacted]-09) lot 400770, (20[redacted]-01) lot 401023(20[redacted]-05) lot 401991(20[redacted]-01) lot 402364 (20[redacted]-04) lot 402864 (20[redacted]-09) lot 404606, (20[redacted]-)01 lot 404791, (20[redacted]-03)
Calibration range from the lower limit of quantitation (LLOQ) to the upper limit of quantitation (ULOQ)	[redacted] pg/mL	[redacted] pg/mL	[redacted] pg/mL	[redacted] pg/mL	[redacted] pg/mL
Matrix study population	NA	NA	Mild cognitive impairment and mild Alzheimer's disease	Mild cognitive impairment and mild Alzheimer's disease	Early Alzheimer's disease
Link to reports and applicable amendments	pt181, aβ42 and htauag_csf-20[redacted] Package Insert (PI) 25685 v11 [80324]	dv-cmf-103-02 Package Insert (PI) 28910 v0 [81576]	bar79/e97	bar79/e97	mse6q-bar86
Synopsis of amendment history	NA	NA	NA	NA	NA

CSF = cerebrospinal fluid, eCTD = electronic Common Technical Document, ELISA = enzyme-linked immunosorbent assay, ID = identification, IgG = immunoglobulin G, LLOQ = lower limit of quantitation, NA = not applicable, ULOQ = upper limit of quantitation.
a: [redacted].

2.7.1.4.27 ヒト CSF 中 p-tau181 測定法要約

	Method Validation #1	Method Validation #2	Clinical Study #1 BAN2401-J081-104	Clinical Study #2 BAN2401-J081-104	Clinical Study #3 BAN2401-G000-201Core
Analyte	PHOSPHO-TAU(181p)	PHOSPHO-TAU(181p)	PHOSPHO-TAU(181p)	PHOSPHO-TAU(181p)	PHOSPHO-TAU(181p)
Validation type	Partial validation	Partial validation	In study	In study	In study
eCTD reference number	5.3.1.4	5.3.1.4	5.3.1.4	5.3.1.4	5.3.1.4
Method ID	mos-cmf-102.v1	mos-cmf-102. v2[a]	mos-cmf-102.v1	mos-cmf-102. v2	mos-cmf-102. v2
Duration of time method is in use	Jul 20[redacted]-Nov 20[redacted]	Nov 20[redacted]- Feb 20[redacted]	Jun 20[redacted]- Mar 20[redacted]	Jun 20[redacted]- Mar 20[redacted]	Dec 20[redacted]- Jun 20[redacted]
Bioanalytical site	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Matrix	CSF				
Platform	Enzyme-linked immunosorbent assay (ELISA)				
Format	A partially validated sandwich format using a monoclonal antibody HT7(IgG1) as capture and a biotinylated antibody AT270 (IgG1) as detection				
Stock reference, lot number, expiration date	Calibration standard lot 201219, (20[redacted]-02) lot 206656 (20[redacted]-06)	Calibration standard lot 239851, (20[redacted]-01) lot 400074, (20[redacted]-03) lot 400232, (20[redacted]-09)	Calibration standard lot 239851, (20[redacted]-01)	Calibration standard lot 400232, (20[redacted]-09)	Calibration standard lot 400232, (20[redacted]-09) lot 401020, (20[redacted]-03) lot 401699, (20[redacted]-10) lot 400942, (20[redacted]-10) lot 40254, (20[redacted]-06) lot 402888, (20[redacted]-09) lot 404389, (20[redacted]-02) lot 404835, (20[redacted]-05)
Calibration range from the lower limit of quantitation (LLOQ) to the upper limit of quantitation (ULOQ)	[redacted] pg/mL	[redacted] pg/mL	[redacted] pg/mL	[redacted] pg/mL	[redacted] pg/mL
Matrix study population	NA	NA	Mild cognitive impairment and mild Alzheimer's disease	Mild cognitive impairment and mild Alzheimer's disease	Early Alzheimer's disease
Link to reports and applicable amendments	pt181, aβ42 and htauag_csf_20[redacted] Package Insert (PI): 24898 v12 [80317]	dv-cmf-102-02[a] Package Insert (PI): 28906 v0 [81574]	bar79/e97	bar79/e97	mse6q-bar86
Synopsis of amendment history	NA	NA	NA	NA	NA

CSF = cerebrospinal fluid, eCTD = electronic Common Technical Document, ELISA = enzyme-linked immunosorbent assay, ID = identification, IgG = immunoglobulin G, LLOQ = lower limit of quantitation, NA = not applicable, ULOQ = upper limit of quantitation.

a: LLOQ and ULOQ are based on mos-cmf-102.v2 because dv-cmf-102-02 needs to be revised.

b: [redacted].

2.7.1.4.28 ヒト CSF 中 t-tau 測定法要約

	Method Validation #1	Method Validation #2	Clinical Study #1 BAN2401-J081-104	Clinical Study #2 BAN2401-J081-104	Clinical Study #3 BAN2401-G000-201Core
Analyte	hTAU Ag	hTAU Ag	hTAU Ag	hTAU Ag	hTAU Ag
Validation type	Partial validation	Partial validation	In study	In study	In study
eCTD reference number	5.3.1.4	5.3.1.4	5.3.1.4	5.3.1.4	5.3.1.4
Method ID	mos-cmf-101.v1	mos-cmf-101.v2	mos-cmf-101.v1	mos-cmf-101.v2	mos-cmf-101.v2
Duration of time method is in use	Jul 20[redacted]- Nov 20[redacted]	Nov 20[redacted]- Feb 20[redacted]	Jun 20[redacted]- Mar 20[redacted]	Jun 20[redacted]- Mar 20[redacted]	Dec 20[redacted]- Jun 20[redacted]
Bioanalytical site	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Matrix	CSF				
Platform	Enzyme-linked immunosorbent assay (ELISA)				
Format	A partially validated sandwich format using a monoclonal antibody AT120 (IgGl) as capture and two biotinylated antibodies HT7 (IgG 1) and BT2(IgG 1) as detection				
Stock reference, lot number, expiration date	Calibration standard lot 199790, (20[redacted]-12) lot 202823, (20[redacted]-02)	Calibration standard lot 233818, (20[redacted]-02) lot 400062, (20[redacted]-03) lot 400219, (20[redacted]-08)	Calibration standard lot 239860, (20[redacted]-05) lot 243354, (20[redacted]-08)	Calibration standard lot 400599, (20[redacted]-12)	Calibration standard lot 400599, (20[redacted]-12) lot 401018, (20[redacted]-03) lot 401605, (20[redacted]-07) lot 401798, (20[redacted]-12) lot 4002493(20[redacted]-05) lot 402688, (20[redacted]-08) lot 404371, (20[redacted]-08) lot 404810, (20[redacted]-06)
Calibration range from the lower limit of quantitation (LLOQ) to the upper limit of quantitation (ULOQ)	[redacted] pg/mL	[redacted] pg/mL	[redacted] pg/mL	[redacted] pg/mL	[redacted] pg/mL
Matrix study population	NA	NA	Mild cognitive impairment and mild Alzheimer's disease	Mild cognitive impairment and mild Alzheimer's disease	Early Alzheimer's disease
Link to reports and applicable amendments	pt181, aβ42 and htauag_csf_20[redacted] PI 25684 v12 [80323]	dv-cmf-101-02 PI: 28902 v0 [81572]	bar79/e97	bar79/e97	mse6q-bar86

2.7.1.4.28 ヒト CSF 中 t-tau 測定法要約

Synopsis of amendment history	NA	NA	NA	NA	NA

CSF = cerebrospinal fluid, eCTD = electronic Common Technical Document, ELISA = enzyme-linked immunosorbent assay, ID = identification, IgG = immunoglobulin G, LLOQ = lower limit of quantitation, NA = not applicable, ULOQ = upper limit of quantitation.
a: [redacted].

2.7.1.4.29 ヒト CSF 中 Aβ(1-40)測定法要約

	Method Validation #1	Method Validation #2	Clinical Study #1 BAN2401-G000-301 Core and OLE Phase	Clinical Study #2
Analyte	Aβ(1-40)	NA	Aβ(1-40)	NA
Validation type	Full (CAP/CLIA)	NA	In-study (CAP/CLIA)	NA
eCTD reference number	5.3.1.4	NA	NA	NA
Method ID	TrackWise QR# 906209	NA	TrackWise QR# 906209 ([redacted]) TrackWise QR# 1062707 [redacted]	NA
Duration of time method is in use	02/20[redacted]-Present	NA	02/20[redacted]-09/20[redacted]	NA
Bioanalytical site	[redacted]	NA	[redacted]	NA
Matrix	Cerebrospinal Fluid (CSF)			
Platform	Chemiluminescence enzyme immunoassay (CLEIA)			
Format	A validated sandwich format using anti-β-amyloid1-40 mouse monoclonal antibody as capture and alkaline phosphatase (ALP)-labeled anti-β-amyloid monoclonal antibody as detection			
Stock reference, lot number, expiration date	Lumipulse® G β-amyloid$_{1-40}$ Calibrators set /Fujirebio, Inc., lot number 4ZX9031E, expiration date 03/31/20[redacted]	NA	Lumipulse® G β-Amyloid$_{1-40}$ Calibrator set / Fujirebio, Inc., product number: 231692 or 231531, Lot number and expiration date NA (CLIA)	NA
Calibration range from the lower limit of quantitation (LLOQ) to the upper limit of quantitation (ULOQ)	[redacted] pg/mL	NA	[redacted] pg/mL	NA
Matrix study population	NA	NA	Early Phase Alzheimer's Disease	NA
Link to reports and applicable amendments	aβ40-csf-lumipulse-20[redacted]	NA	aβ40-csf-lumipulse-sar-20[redacted]	NA
Synopsis of amendment history	NA	NA	NA	NA

CAP = College of American Pathologists, CLIA = Clinical Laboratory Improvement Amendments, CSF = cerebrospinal fluid, eCTD = electronic Common Technical Document, ID = identification, LLOQ = lower limit of quantitation, NA = not applicable, ULOQ = upper limit of quantitation.

2.7.1.4.30 ヒト CSF 中 Aβ(1-42)測定法要約

	Method Validation #1	Method Validation #2	Clinical Study #1 BAN2401-G000-301 Core and OLE Phase	Clinical Study #2
Analyte	Aβ(1-42)	NA	Aβ(1-42)	NA
Validation type	Full (CAP/CLIA)	NA	In-study (CAP/CLIA)	NA
eCTD reference number	NA	NA	NA	NA
Method ID	TrackWise QR# 753055 and 945155	NA	TrackWise QR# 753055 and 945155 [redacted] TrackWise QR# 898220 and 1062704 [redacted]	NA
Duration of time method is in use	11/20[redacted]-Present	NA	05/20[redacted]-09/20[redacted]	NA
Bioanalytical site	[redacted]	NA	[redacted]	NA
Matrix	Cerebrospinal Fluid (CSF)			
Platform	Chemiluminescence enzyme immunoassay (CLEIA)			
Format	A validated sandwich format using anti-β-amyloid1-42 mouse monoclonal antibody as capture and biotinylated anti-β-amyloid mouse monoclonal antibody as detection			
Stock reference, lot number, expiration date	Lumipulse® G β-amyloid1-42 Calibrators set /Fujirebio, Inc., lot number 5JX7122U, expiration date 12/31/20[redacted], lot number 5JX9042U, expiration date 04/30/20[redacted]; lot number 5JX9093U, expiration date 09/30/20[redacted]	NA	Lumipulse® G β-amyloid1-42 Calibrators set /Fujirebio, Inc., product number: 231487 or 230343 expiration date and lot number NA (CLIA)	NA
Calibration range from the lower limit of quantitation (LLOQ) to the upper limit of quantitation (ULOQ)	[redacted] pg/mL	NA	[redacted] pg/mL	NA
Matrix study population	NA	NA	Early Alzheimer's Disease	NA
Link to reports and applicable amendments	aβ42-csf-lumipulse-20[redacted]	NA	aβ42-csf-lumipulse-sar-20[redacted]	NA
Synopsis of amendment history	NA	NA	NA	NA

CAP = College of American Pathologists, CLIA = Clinical Laboratory Improvement Amendments, eCTD = electronic Common Technical Document, ID = identification, NA = not applicable.

2.7.1.4.31 ヒト CSF 中 p-tau181 測定法要約

	Method Validation #1	Method Validation #2	Clinical Study #1 BAN2401-G000-301 Core and OLE Phase	Clinical Study #2
Analyte	pTau181	NA	pTau181	NA
Validation type	Full (CAP/CLIA)	NA	In-study (CAP/CLIA)	NA
eCTD reference number	5.3.1.4	NA	5.3.1.4	NA
Method ID	TrackWise QR# 906183	NA	TrackWise QR# 906183 ([redacted]) TrackWise QR #1062711 ([redacted])	NA
Duration of time method is in use	02/20[redacted]-Present	NA	05/20[redacted]-09/20[redacted]	NA
Bioanalytical site	[redacted]	NA	[redacted]	NA
Matrix	Cerebrospinal Fluid (CSF)			
Platform	Chemiluminescence enzyme immunoassay (CLEIA)			
Format	A validated sandwich format using mouse anti-phosphorylated Tau (181) monoclonal antibody as capture and alkaline phosphatase (ALP)-labeled mouse anti-Tau monoclonal antibody as detection			
Stock reference, lot number, expiration date	Lumipulse® G pTau181 Calibrators set/Fujirebio, Inc., lot number 5EX9011E, expiration date 01/31/20[redacted]	NA	Lumipulse® G pTau181 Calibrators set/Fujirebio, Inc., product number: 231661 or 230367, lot number and expiration date NA (CLIA)	NA
Calibration range from the lower limit of quantitation (LLOQ) to the upper limit of quantitation (ULOQ)	[redacted] pg/mL	NA	[redacted] pg/mL	NA
Matrix study population	NA	NA	Early Alzheimer's Disease	NA
Link to reports and applicable amendments	pt181-csf-lumipulse-20[redacted]	NA	pt181-csf-lumipulse-sar-20[redacted]	NA
Synopsis of amendment history	NA	NA	NA	NA

CAP = College of American Pathologists, CLIA = Clinical Laboratory Improvement Amendments, CSF = cerebrospinal fluid, eCTD = electronic Common Technical Document, ID = identification, LLOQ = lower limit of quantitation, NA = not applicable, ULOQ = upper limit of quantitation.

2.7.1.4.32 ヒト CSF 中 t-tau 測定法要約

	Method Validation #1	Method Validation #2	Clinical Study #1 BAN2401-G000-301 Core and OLE Phase	Clinical Study #2
Analyte	tTau	NA	tTau	NA
Validation type	Full (CAP/CLIA)	NA	In-study (CAP/CLIA)	NA
eCTD reference number	5.3.1.4	NA	5.3.1.4	NA
Method ID	TrackWise QR# 753051	NA	TrackWise QR# 753051 TrackWise #1062722 ( )	NA
Duration of time method is in use	11/20 -Present	NA	05/20 -09/20	NA
Bioanalytical site		NA		NA
Matrix	Cerebrospinal Fluid (CSF)			
Platform	Chemiluminescence enzyme immunoassay (CLEIA)			
Format	A validated sandwich format using mouse anti-total Tau monoclonal antibody as capture and mouse biotinylated anti-Tau monoclonal antibody as detection, and binding to biotinylated immune-complexes by alkaline phosphatase-labeled streptavidin			
Stock reference, lot number, expiration date	Lumipulse® G Total Tau Calibrators set/Fujirebio, Inc., lot number 6CX7121U, expiration date 12/31/20	NA	Lumipulse® G Total Tau Calibrators set/Fujirebio, Inc., Product number 231326 or 230329, lot number and expiration date NA (CLIA)	NA
Calibration range from the lower limit of quantitation (LLOQ) to the upper limit of quantitation (ULOQ)	pg/mL	NA	pg/mL	NA
Matrix study population	NA	NA	Early Alzheimer's Disease	NA
Link to reports and applicable amendments	ttau-csf-lumipulse-20	NA	ttau-csf-lumipulse-sar-20	NA
Synopsis of amendment history	NA	NA	NA	NA

CAP = College of American Pathologists, CLIA = Clinical Laboratory Improvement Amendments, CSF = cerebrospinal fluid, eCTD = electronic Common Technical Document, ID = identification, LLOQ = lower limit of quantitation, NA = not applicable, ULOQ = upper limit of quantitation.

2.7.1.4.33 ヒト CSF 中 NfL 測定法要約

	Method Validation #1	Method Validation #2	Clinical Study #1 BAN2401-G000-201 Core Only	Clinical Study #2
Analyte	NfL	NA	NfL	NA
Validation type	Partial validation	NA	In-Study	NA
eCTD reference number	NA	NA	NA	NA
Method ID	NA	NA	NA	NA
Duration of time method is in use	09/20[redacted]-present	NA	08/20[redacted]-12/20[redacted]	NA
Bioanalytical site	[redacted]	NA	[redacted]	NA
Matrix	CSF			
Platform	Enzyme-linked immunosorbent assay (ELISA)			
Format	A partially validated sandwich format using two highly specific non-competing monoclonal antibodies. One is immobilized on a solid phase and catches the neurofilament light (NF-L) in solution. The other antibody acts as detector which interacts with the bound protein and gives rise to a signal through biotin – horseradish peroxidase avidin binding. The signal obtained from the calibrator curve corresponds to the amount of NF-L.			
Stock reference, lot number, expiration date	Calibration standard Lot 70583, expiration date 07/31/20[redacted]	NA	Calibration standard Lot 70583 expiration date 07/31/20[redacted]	NA
Calibration range from the lower limit of quantitation (LLOQ) to the upper limit of quantitation (ULOQ)	[redacted] pg/mL	NA	[redacted] pg/mL	NA
Matrix study population	Surplus diagnostic CSF samples of AD subjects at [redacted]	NA	Diseased (Early Alzheimer's disease)	NA
Link to reports and applicable amendments	nfl_csf-20[redacted] nfl-csf-20[redacted]r1	NA	sar-[redacted]-nflp/nrgn/ykl-40/cntn-2	NA
Synopsis of amendment history	NA	NA	NA	NA

AD = Alzheimer's disease, CSF = cerebrospinal fluid, eCTD = electronic Common Technical Document, ELISA = enzyme-linked immunosorbent assay, ID = identification, IgG = immunoglobulin G, LLOQ = lower limit of quantitation, NA = not applicable, NfL = neurofilament light chain, ULOQ = upper limit of quantitation.

2.7.1.4.34 ヒト CSF 中 NfL 測定法要約

	Method Validation #1	Method Validation #2	Clinical Study #1 BAN2401-G000-301 Core and OLE Phase	Clinical Study #2
Analyte	NfL	NA	NfL	NA
Validation type	Partial validation	NA	In-study	NA
eCTD reference number	5.3.1.4	NA	NA	NA
Method ID	Simoa™ NfL® Kit	NA	Simoa™ NfL® Kit	NA
Duration of time method is in use	03/20[redacted] - Present	NA	01/20[redacted]-08/20[redacted]	NA
Bioanalytical site	[redacted]	NA	[redacted]	NA
Matrix	CSF			
Platform	Quanterix Simoa (Single Molecule Array)			
Format	A validated sandwich format using anti-NfL antibody-coated paramagnetic beads as capture and biotinylated anti-NfL antibody as detection			
Stock reference, lot number, expiration date	Calibration standard lot 830302, expiration date 08/29/20[redacted]	NA	Calibration standard lot 106801, expiration date 03/08/20[redacted]	NA
Calibration range from the lower limit of quantitation (LLOQ) to the upper limit of quantitation (ULOQ)	[redacted] pg/mL		[redacted] pg/mL	NA
Matrix study population	Normal	NA	Diseased (Early Alzheimer's disease)	NA
Link to reports and applicable amendments	nfl-csf-20[redacted]	NA	sar-[redacted]-nfl-nrgn-csf[redacted]	NA
Synopsis of amendment history	NA	NA	NA	NA

CSF = cerebrospinal fluid, eCTD = electronic Common Technical Document, ID = identification, LLOQ = lower limit of quantitation, NA = not applicable, NfL = neurofilament light chain, OLE = open-label extension, ULOQ = upper limit of quantitation.

2.7.1.4.35 ヒト CSF 中 Neurogranin 測定法要約

	Method validation #1	Method validation #2	Clinical study #1 BAN2401-G000-201 Core Only	Clinical study #2 BAN2401-G000-301 Core and OLE Phase
Analyte	Neurogranin	NA	Neurogranin	Neurogranin
Validation type	Partial validation	NA	In-study	In-study
eCTD reference number	5.3.1.4	NA	5.3.1.4	5.3.1.4
Method ID	NA	NA	NA	NA
Duration of time method is in use	02/20[redacted]- Present	NA	08/20[redacted]-12/20[redacted]	01/20[redacted]-08/20[redacted]
Bioanalytical site	[redacted]	NA	[redacted]	[redacted]
Matrix	CSF			
Platform	Enzyme-linked immunosorbent assay (ELISA)			
Format	A validated sandwich format using anti-neurogranin antibody specific for human neurogranin truncated at P75 as capture and biotinylated monoclonal anti-neurogranin antibody as detection			
Stock reference, lot number, expiration date	Calibrator provided by Euroimmun: Neurogranin ELISA kit, lot #160616AW, expiration date :06/15/20[redacted]	NA	Calibrator provided by Euroimmun : Neurogranin ELISA kit, lot # E180222AU, expiration date 02/21/20[redacted]	Calibrator provided by Euroimmun : Neurogranin ELISA kit, lot # E211029CX, expiration date 10/28/20[redacted]
Calibration range from the lower limit of quantitation (LLOQ) to the upper limit of quantitation (ULOQ)	[redacted] pg/mL	NA	[redacted] pg/mL	[redacted] pg/mL
Matrix study population	Surplus diagnostic CSF samples of AD subjects at [redacted]	NA	Diseased (Early Alzheimer's disease)	Diseased (Early Alzheimer's disease)
Link to reports and applicable amendments	neurogranin_csf_20[redacted] nrgn-csf-20[redacted]r1	NA	sar-[redacted]-nflp/nrgn/ykl-40/cntn-2	sar-[redacted]-nfl-nrgn-csf20[redacted]
Synopsis of amendment history	NA	NA	NA	NA

AD = Alzheimer's disease, CSF = cerebrospinal fluid, eCTD = electronic Common Technical Document, ELISA = enzyme-linked immunosorbent assay, ID = identification, LLOQ = lower limit of quantitation, NA = not applicable, ULOQ = upper limit of quantitation.

2.7.1.4.36 ヒト CSF 中 Contactin-2 測定法要約

	Method Validation #1	Method Validation #2	Clinical Study #1 BAN2401-G000-201 Core only	Clinical Study #2
Analyte	Contactin-2	NA	Contactin-2	NA
Validation type	Partial validation	NA	In-study	NA
eCTD reference number	NA	NA	NA	NA
Method ID	NA	NA	NA	NA
Duration of time method is in use	04/20[redacted]-present	NA	08/20[redacted]-12/20[redacted]	NA
Bioanalytical site	[redacted]	NA	[redacted]	NA
Matrix	CSF			
Platform	Enzyme-linked immunosorbent assay (ELISA)			
Format	A validated sandwich format using a mouse anti-human contactin-2 antibody as capture and a biotinylated mouse anti-human contactin-2 antibody as detection			
Stock reference, lot number, expiration date	Recombinant Human Contactin-2 Standard, lot # P109345, expiration date: 09/09/20[redacted]	NA	Recombinant Human Contactin-2 Standard, lot 1327633, expiration date 11/10/20[redacted]	NA
Calibration range from the lower limit of quantitation (LLOQ) to the upper limit of quantitation (ULOQ)	[redacted] pg/mL	NA	[redacted] pg/mL	NA
Matrix study population	Surplus diagnostic CSF samples of AD subjects at [redacted]	NA	Diseased (Early Alzheimer's disease)	NA
Link to reports and applicable amendments	contactin-2_csf_20[redacted] contactin-2-csf-20[redacted]r1 Package insert of Human contactin-2/TAG1 DuoSet ELISA kit (R&D)	NA	sar-[redacted]-nflp/nrgn/ykl-40/cntn-2	NA
Synopsis of amendment history	NA	NA	NA	NA

AD = Alzheimer's disease, CSF = cerebrospinal fluid, eCTD = electronic Common Technical Document, ELISA = enzyme-linked immunosorbent assay, ID = identification, LLOQ = lower limit of quantitation, NA = not applicable, ULOQ = upper limit of quantitation.

2.7.1.4.37 ヒト CSF 中 YKL-40 測定法要約

	Method validation #1	Method validation #2	Clinical study #1 BAN2401-G000-201 Core	Clinical study #2
Analyte	YKL-40	NA	YKL-40	NA
Validation type	Partial validation	NA	In-study	NA
eCTD reference number	5.3.1.4	NA	NA	NA
Method ID	NA	NA	NA	NA
Duration of time method is in use	06/20[redacted] - Present	NA	08/20[redacted]-12/20[redacted]	NA
Bioanalytical site	[redacted]	NA	[redacted]	NA
Matrix	CSF			
Platform	Enzyme-linked immunosorbent assay (ELISA)			
Format	A validated sandwich format using a biotinylated murine monoclonal antibody to human YKL-40 as capture and an ALP-conjugated rabbit polyclonal antibody to YKL-40 as detection			
Stock reference, lot number, expiration date	YKL-40 calibrator purified from osteosarcoma MG-63 cells in a buffered solution with stabilizer and sodium azide (0.1%) as a preservative and provided by MicroVue YKL-40 Elisa kit, Ref: 8020, Lot# 908565, expiration date:02/20[redacted]	NA	YKL-40 calibrator purified from osteosarcoma MG-63 cells in a buffered solution with stabilizer and sodium azide (0.1%) as a preservative and provided by MicroVue YKL-40 Elisa kit, Lot 088337, expiration date 01/20[redacted]	NA
Calibration range from the lower limit of quantitation (LLOQ) to the upper limit of quantitation (ULOQ)	[redacted] ng/mL	NA	[redacted] ng/mL	NA
Matrix study population	Surplus diagnostic CSF samples of FTD subjects at [redacted]	NA	Diseased (Early Alzheimer's disease)	NA
Link to reports and applicable amendments	ykl-40_csf_20[redacted] ykl-40-csf-20[redacted]r1 Package insert of MicroVue YKL-40 EIA Kit	NA	sar-[redacted]-nflp/nrgn/ykl-40/cntn-2	NA
Synopsis of amendment history	NA	NA	NA	NA

ALP = alkaline phosphatase, CSF = cerebrospinal fluid, eCTD = electronic Common Technical Document, ELISA = enzyme-linked immunosorbent assay, FTD = frontotemporal dementia, ID = identification, LLOQ = lower limit of quantitation, NA = not applicable, ULOQ = upper limit of quantitation.

2.7.1.4.38 *APOE4* 遺伝子型決定法要約

	Method Validation #1	Method Validation #2	Clinical Study #1 BAN2401-G000-301	Clinical Study #2
Analyte	*APOE*	NA	*APOE*	NA
Validation type	CLIA (Full Validation)	NA	In-study	NA
eCTD reference number	NA	NA	NA	NA
Method ID	NA	NA	NA	NA
Duration of time method is in use	09/20[redacted]- Present	NA	05/20[redacted]-09/20[redacted]	NA
Bioanalytical site	[redacted]	NA	[redacted]	NA
Matrix	Whole blood			
Platform	Quantitative polymerase chain reaction (qPCR)			
Format	Two Allelic Discrimination (AD) assays, which are commercially available from Thermo-Fisher Scientific as TaqMan SNP Genotyping assay for SNPs rs429358 and rs7412, on 18 HapMap controls and 100 random whole blood samples			
Stock reference, lot number, expiration date	NA	NA	NA	NA
Calibration range from the lower limit of quantitation (LLOQ) to the upper limit of quantitation (ULOQ)	NA	NA	NA	NA
Matrix study population	NA	NA	Subjects With Early Alzheimer's Disease	NA
Link to reports and applicable amendments	apoe_whole blood_20[redacted]	NA	apoe-[redacted]-20[redacted]	NA
Synopsis of amendment history	NA	NA	NA	NA

APOE = apolipoprotein E, CLIA = Clinical Laboratory Improvements Act, eCTD = electronic Common Technical Document, ID = identification, LLOQ = lower limit of quantitation, NA = not applicable, ULOQ = upper limit of quantitation.

2.7.1.4.39 ヒト血漿中 Aβ(1-40)測定性能

Bioanalytical method validation report name, amendments, and hyperlinks	Validation of IBL ELISA kit for the determination of full length amyloid beta 1-40 in human EDTA plasma (aβ40_plasma_2[redacted])
Method Description	Full length amyloid beta 1-40 present in EDTA plasma sample will bind to anti-human beta (35-40) mouse IgG monoclonal antibody precoated on the plate. After overnight incubation at 4 °C, and washing step, HRP conjugated anti-Human amyloid Beta (N, 82E1) mouse IgG monoclonal antibody is added. Next, after incubation and wash step, TMB substrate is added, and absorbance is measured at a wavelength of 450 nm and the measured absorbance is proportional to the amount of bound amyloid beta 1-40.
Materials used for standard calibration curve and concentration	[redacted]
Validated assay range	
Materials used for quality controls (QCs) and concentration	
Minimum required dilutions (MRDs)	
Source and lot of reagents	
Regressing model and weighting	
Validation parameters	
Standard calibration curve performance during accuracy and precision runs	
Performance of QCs during accuracy and precision runs	

2.7.1.4.39 ヒト血漿中 Aβ(1-40)測定性能

Selectivity & matrix effect	[redacted]
Interference & specificity	
Hemolysis effect	
Lipemic effect	
Dilution linearity & hook effect	
Bench-top/process stability	
Freeze-Thaw stability	
Long-term storage	
Parallelism	
Carry over	
Method performance: NA	
Assay passing rate	
Standard curve performance	
QC performance	
Method reproducibility	
Study sample analysis/stability	
Standard calibration curve performance during accuracy and precision runs	

2.7.1.4.39 ヒト血漿中 Aβ(1-40)測定性能

AD = Alzheimer's disease, CSF = cerebrospinal fluid, CV = coefficient of variation, ELISA = enzyme-linked immunosorbent assay, IgG = immunoglobulin G, LBA = ligand binding assay, LLOQ = lower limit of quantitation, NA = not applicable, QC = quality control, TE = total error, ULOQ = upper limit of quantitation.

2.7.1.4.40 ヒト血漿中 Aβ(1-42)測定性能

Bioanalytical method validation report name, amendments, and hyperlinks	Validation of IBL ELISA kit for the determination of full length amyloid beta 1-42 in human EDTA plasma (aβ42_plasma_20[redacted])
Method Description	The ELISA kit is a sandwich ELISA, using high specific antibodies. Full length amyloid beta 1-42 present in EDTA plasma sample will bind to anti-human beta (38-42) Mouse IgG Monoclonal Antibody precoated on the plate. After overnight incubation at 4 °C, and washing step, HRP conjugated anti-Human amyloid Beta (N, 82E1) mouse IgG monoclonal is added. Next, after incubation and wash step, TMB substrate is added, and absorbance is measured at a wavelength of 450 nm and the measured absorbance is proportional to the amount of bound amyloid beta 1-42.
Materials used for standard calibration curve and concentration	[redacted]
Validated assay range	
Materials used for quality controls (QCs) and concentration	
Minimum required dilutions (MRDs)	
Source and lot of reagents	
Regressing model and weighting	
Validation parameters	
Standard calibration curve performance during accuracy and precision runs	
Performance of QCs during accuracy and precision runs	
Selectivity & matrix effect	
Interference & specificity	
Hemolysis effect	
Lipemic effect	
Dilution linearity & hook effect	

2.7.1.4.40 ヒト血漿中 Aβ(1-42)測定性能

Bench-top/process stability	[redacted]
Freeze-Thaw stability	
Long-term storage	
Parallelism	
Carry over	
Method performance: NA	
Assay passing rate	
Standard curve performance	
QC performance	
Method reproducibility	
Study sample analysis/stability	
Standard calibration curve performance during accuracy and precision runs	

CSF = cerebrospinal fluid, CV = coefficient of variation, ELISA = enzyme-linked immunosorbent assay, IgG = immunoglobulin G, LBA = ligand binding assay, LLOQ = lower limit of quantitation, NA = not applicable, OD = optical density, PI = package insert, QC = quality control, TE = total error, ULOQ = upper limit of quantitation.

2.7.1.4.41 ヒト血漿中 Aβ(1-x)測定性能

Bioanalytical method validation report name, amendments, and hyperlinks	Biomarker Validation of an Enzyme Immunoassay for the Measurement of Amyloid Beta 1-X in Human Plasma (tcar10-001)
Method Description	In this method, the amount of Amyloid Beta 1-X in human K2EDTA plasma is measured by a sandwich enzyme immunoassay. The ELISA plates are coated with anti-human Amyloid Beta (N) (82E1) mouse IgG MoAb affinity purified antibody. Plasma samples containing Amyloid Beta are added to the plate. Following an overnight incubation, HRP-conjugated anti-human Amyloid Beta (11-28) mouse IgG affinity purified antibody solution is added to form antibody antigen-antibody HRP complex. After incubation, unbound materials are removed by washing and TMB (3, 3', 5, 5' -tetramethyl benzidine dihydrochloride) is allowed to react with the bound HRP complex. The color intensity that develops is proportional to the amount of Amyloid Beta 1-X bound to the antibody. A regression of the absorbance of the standard curve against the concentration is performed and the concentrations of Amyloid Beta (1-X) in the samples are determined.
Materials used for standard calibration curve and concentration	[redacted]
Validated assay range	
Materials used for quality controls (QCs) and concentration	
Minimum required dilutions (MRDs)	
Source and lot of reagents	
Regressing model and weighting	
Validation parameters	
Standard calibration curve performance during accuracy and precision runs	

2.7.1.4.41 ヒト血漿中 Aβ(1-x)測定性能

Performance of QCs during accuracy and precision runs	[redacted]
Selectivity & matrix effect	
Interference & specificity	
Hemolysis effect	
Lipemic effect	
Dilution linearity & hook effect	

2.7.1.4.41 ヒト血漿中 Aβ(1-x)測定性能

	[redacted]
Bench-top/process stability	
Freeze-Thaw stability	
Long-term storage	
Parallelism	
Carry over	
Method performance in study BAN2401-A001-101 **Report # tcar10-056: Quantification of Samples for Measurement of Amyloid Beta 1-X in Human Plasma in Support of Eisai Protocol BAN2401-A001-101**	
Assay passing rate	[redacted]
Standard curve performance	
QC performance	
Method reproducibility	
Study sample analysis/stability	
Standard calibration curve performance during accuracy and precision runs	

CSF = cerebrospinal fluid, CV = coefficient of variation, ELISA = enzyme-linked immunosorbent assay, IgG = immunoglobulin G, LBA = ligand binding assay, LLOQ = lower limit of quantitation, NA = not applicable, OD = optical density, PI = package insert, QC = quality control, TE = total error, ULOQ = upper limit of quantitation.

2.7.1.4.42 ヒト血漿中 p-tau181 測定性能

Bioanalytical method validation report name, amendments, and hyperlinks	Quantitation of pTau-181 in Human Plasma (K2EDTA) on the Quanterix Simoa Platform (110-r11817-r1), 110-r11817a1, 110-r11817a2, 110-r11817a3
Method Description	In the first step, anti-pTau-181 antibody-coated paramagnetic capture beads and an anti-pTau-181 antibody conjugated with Biotin are incubated with samples diluted in Sample Diluent. pTau-181 molecules present in the samples are captured by the anti-pTau-181 antibody-coated capture beads and bind with the biotinylated antibody detector simultaneously. The beads are washed, and a streptavidin-ß-galactosidase (SBG) conjugate is mixed with the beads. SBG binds to the biotinylated detection antibody, resulting in the enzymatic labeling. Following a final wash, the beads are re-suspended in a resorufin ß-D-galactopyranoside (RGP) substrate solution and transferred to the Simoa Disc. Individual beads are then sealed within microwells in the array. If pTau-181 is captured and labeled, the ß-galactosidase hydrolyzes the RGP substrate is converted into a fluorescent product that yields a signal for measurement. A single labeled pTau-181 molecule results in sufficient fluorescent signal in 30 seconds to be detected and counted by the Simoa optical system. At a low pTau-181 concentration, the percentage of bead-containing wells in the array with a positive signal is proportional to the amount of pTau-181 present in the sample, thus yielding a “digital” signal. At a high pTau-181 concentration, when most of the bead-containing wells have one or more labeled pTau-181 molecules, the total fluorescence signal is proportional to the amount of pTau-181 present in the sample, thus yielding an “analog” signal.
Materials used for standard calibration curve and concentration	[redacted]
Validated assay range	
Materials used for quality controls (QCs) and concentration	
Minimum required dilutions (MRDs)	
Source and lot of reagents	
Regressing model and weighting	
Validation parameters	

2.7.1.4.42 ヒト血漿中 p-tau181 測定性能

Standard calibration curve performance during accuracy and precision runs	[redacted]
Performance of QCs during accuracy and precision runs	
Selectivity & matrix effect	
Interference & specificity	
Hemolysis effect	

2.7.1.4.42 ヒト血漿中 p-tau181 測定性能

	[redacted]
Lipemic effect	
Dilution linearity & hook effect	
Bench-top/process stability	
Freeze-Thaw stability	
Long-term storage	
Parallelism	
Carry over	
Method performance in study BAN2401-G000-201 **Report # 110-r12068: Sample analysis report: Quantitation of pTau-181 in Human Plasma (K2EDTA) on the Quanterix Simoa Platform**	
Assay passing rate	[redacted]
Standard curve performance	
QC performance	
Method reproducibility	

2.7.1.4.42 ヒト血漿中 p-tau181 測定性能

Study sample analysis/stability	[redacted]
Standard calibration curve performance during accuracy and precision runs	
Method performance in study BAN2401-G000-301 Report # 110-r12754: Sample analysis report: Quantitation of pTau-181 in Human Plasma (K2EDTA) on the Quanterix Simoa Platform	
Assay passing rate	[redacted]
Standard curve performance	
QC performance	
Method reproducibility	
Study sample analysis/stability	
Standard calibration curve performance during accuracy and precision runs	

CSF = cerebrospinal fluid, CV = coefficient of variation, ELISA = enzyme-linked immunosorbent assay, IgG = immunoglobulin G, LBA = ligand binding assay, LLOQ = lower limit of quantitation, NA = not applicable, OD = optical density, PI = package insert, QC = quality control, TE = total error, ULOQ = upper limit of quantitation.

2.7.1.4.43 ヒト血漿中 NfL 測定性能

Bioanalytical method validation report name, amendments, and hyperlinks	BAN2401-G000-201 – NfL validation in Plasma (nfl_plasma_20[redacted], nfl-plasma-20[redacted]r1)
Method Description	2 step digital immunoassay: target antibody coated paramagnetic beads are combined with sample and biotinylated detector antibody in the same incubation. Target molecules present in the sample are captured by the antibody coated beads and bind with the biotinylated antibody detector simultaneously.
Materials used for standard calibration curve and concentration	Reference calibrator (lot 830302) provided by Simoa NfL Kit (Lot 501484) and concentration NA Reference calibrator (lot 81570) provided by Simoa NfL Kit (Lot 501279) and concentration NA
Validated assay range	[redacted]
Materials used for quality controls (QCs) and concentration	
Minimum required dilutions (MRDs)	
Source and lot of reagents	
Regressing model and weighting	
Validation parameters	
Standard calibration curve performance during accuracy and precision runs	
Performance of QCs during accuracy and precision runs	

2.7.1.4.43 ヒト血漿中 NfL 測定性能

Selectivity & matrix effect	[redacted]
Interference & specificity	
Hemolysis effect	
Lipemic effect	
Dilution linearity & hook effect	
Bench-top/process stability	
Freeze-Thaw stability	
Long-term storage	
Parallelism	
Carry over	
Method performance in study BAN2401-G000-201 **Report # sar-[redacted]-nflp/nrgn/ykl-40/cntn-2: sample analysis report: Determination of Neurofilament light protein (NFLP), Neurogranin (NRGN), YKL-40, Contactin-2 (CNTN-2) in human CSF samples and NFLP in plasma using ELISA and SIMOA for Eisai Study BAN2401-G000-201**	
Assay passing rate	[redacted]

2.7.1.4.43 ヒト血漿中 NfL 測定性能

Standard curve performance	[redacted]
QC performance	
Method reproducibility	
Study sample analysis/stability	
Standard calibration curve performance during accuracy and precision runs	

CSF = cerebrospinal fluid, CNTN = contactin, CV = coefficient of variation, ELISA = enzyme-linked immunosorbent assay, HQC = high quality control, LQC = low quality control, LLOD = lower limit of detection, LLOQ = lower limit of quantitation, MQC = mid quality control, MRD = minimum required dilution, NA = not applicable, NfL = neurofilament light chain, NRGN = neurogranin, QC = quality control, TE = total error, ULOQ = upper limit of quantitation, YKL = chitinase-3-like protein 1.

2.7.1.4.44 ヒト血漿中 NfL 測定性能

Bioanalytical method validation report name, amendments, and hyperlinks	Quantitation of NF-Light in Human Plasma, Serum and CSF on the Quanterix Simoa Platform (1629-r11293)
Method Description	This assay uses a commercial Simoa NF-Light (NfL) Assay Kit provided by Quanterix Corp. In the first step, anti-NfL antibody-coated paramagnetic capture beads and an anti-NfL antibody conjugated with Biotin are incubated with samples diluted in Sample Diluent. NfL molecules present in the samples are captured by the anti-NfL antibody-coated capture beads. The detection antibody will then bind to the captured NfL molecules. The beads are washed and a streptavidin-ß-galactosidase (SßG) conjugate is mixed with the capture beads. SßG binds to the biotinylated detection antibody, resulting in the enzymatic labeling of the captured NfL. Following a second wash, the capture beads are re-suspended in a resorufin ß-D-galactopyranoside (RGP) substrate solution and transferred to the Simoa Disc. Individual capture beads are then sealed within microwells in the array. If NfL is captured and labeled, the ß-galactosidase hydrolyzes the RGP substrate into a fluorescent product that yields a signal for measurement. A single labeled NfL molecule results in sufficient fluorescent signal in 30 seconds to be detected and counted by the Simoa optical system. At a low NfL concentration, the percentage of bead-containing wells in the array with a positive signal is proportional to the amount of NfL present in the sample, thus yielding a “digital” signal. At a high NfL concentration, when most of the bead-containing wells have one or more labeled NfL molecules, the total fluorescence signal is proportional to the amount of NfL present in the sample, thus yielding an “analog” signal. The concentration of NfL in an unknown sample is interpolated from a standard curve.
Materials used for standard calibration curve and concentration	[redacted]
Validated assay range	
Materials used for quality controls (QCs) and concentration	
Minimum required dilutions (MRDs)	
Source and lot of reagents	

2.7.1.4.44 ヒト血漿中 NfL 測定性能

	[redacted]
Regressing model and weighting	
Validation parameters	
Standard calibration curve performance during accuracy and precision runs	
Performance of QCs during accuracy and precision runs	

2.7.1.4.44 ヒト血漿中 NfL 測定性能

	[redacted]
Selectivity & matrix effect	
Interference & specificity	
Hemolysis effect	
Lipemic effect	
Dilution linearity & hook effect	
Bench-top/process stability	
Freeze-Thaw stability	
Long-term storage	
Parallelism	

2.7.1.4.44 ヒト血漿中 NfL 測定性能

	[redacted]
Carry over	
Method performance in study BAN2401-G000-301 **Report # 110-r12755: Sample analysis report: Quantitation of NFL in Human Plasma (K_2EDTA) on the Quanterix Simoa Platform**	
Assay passing rate	[redacted]
Standard curve performance	
QC performance	
Method reproducibility	
Study sample analysis/stability	
Standard calibration curve performance during accuracy and precision runs	

CSF = cerebrospinal fluid, CV = coefficient of variation, ELISA = enzyme-linked immunosorbent assay, IgG = immunoglobulin G, LBA = ligand binding assay, LLOQ = lower limit of quantitation, NA = not applicable, OD = optical density, PI = package insert, QC = quality control, TE = total error, ULOQ = upper limit of quantitation.

2.7.1.4.45 ヒト血漿中 GFAP 測定性能

Bioanalytical method validation report name, amendments, and hyperlinks	Quantitation of GFAP in Human Plasma and Cerebrospinal Fluid (CSF) using Quanterix Simoa Platform (1679-r12607)
Method Description	This assay uses a commercial Simoa GFAP Discovery Kit provided by Quanterix Corp. In a 2-step immunoassay, target antibody coated paramagnetic beads are combined with sample and biotinylated detector antibody in the same incubation. Target molecules present in the sample are captured by the antibody coated beads and bind with the biotinylated antibody detector simultaneously. Following a wash, a conjugate of streptavidin-ß-galactosidase (SBG) is mixed with the beads. SBG binds to the biotinylated detector antibodies, resulting in enzyme labeling of captured target. Following a final wash, the beads are resuspended in a resorufin ß-D-galactopyranoside (RGP) substrate solution and transferred to the Simoa Disc. Individual beads are then sealed within microwells in the array. (The beads are loaded into arrays of 216,000 femtoliter-sized wells, each of which hold no more than one bead. Beads are added in the presence of substrate, and wells are subsequently sealed with oil and imaged) If the target has been captured and labeled on the bead, ß-galactosidase hydrolyzes the RGP substrate in the microwell into a fluorescent product that provides the signal for measurement. A single-labeled target molecule results in sufficient fluorescent signal in 30 seconds to be detected and counted by the Simoa optical system (HD-X analyzer). At low target concentration, the percentage of bead-containing wells in the array that have a positive signal is proportional to the amount of target present in the sample. At higher target concentration, when most of the bead-containing wells have one or more labeled target molecules, the total fluorescence signal is proportional to the amount of target present in the sample. The concentration of target in unknown samples is interpolated from the calibration curve.
Materials used for standard calibration curve and concentration	[redacted]
Validated assay range	
Materials used for quality controls (QCs) and concentration	
Minimum required dilutions (MRDs)	
Source and lot of reagents	

2.7.1.4.45 ヒト血漿中 GFAP 測定性能

	[redacted]
Regressing model and weighting	
Validation parameters	
Standard calibration curve performance during accuracy and precision runs	
Performance of QCs during accuracy and precision runs	

2.7.1.4.45 ヒト血漿中 GFAP 測定性能

Selectivity & matrix effect	[redacted]
Interference & specificity	
Hemolysis effect	
Lipemic effect	
Dilution linearity & hook effect	
Bench-top/process stability	
Freeze-Thaw stability	
Long-term storage	
Parallelism	
Carry over	
Method performance in study BAN2401-G000-301	

2.7.1.4.45 ヒト血漿中 GFAP 測定性能

Method performance in study BAN2401-G000-301 Report # 110-r12753: Sample analysis report: Quantitation of GFAP in Human Plasma (K2EDTA) on the Quanterix Simoa Platform	
Assay passing rate	[redacted]
Standard curve performance	
QC performance	
Method reproducibility	
Study sample analysis/stability	
Standard calibration curve performance during accuracy and precision runs	

CSF = cerebrospinal fluid, CV = coefficient of variation, EQC = electronic quality control, GFAP = glial fibrillary acidic protein, HQC = high quality control, K2EDTA = dipotassium ethylene diamine tetraacetic acid, LLOQ = lower limit of quantitation, LQC = low quality control, MQC = mid quality control, MRD = minimum required dilution, NA = not applicable, QC = quality control, RGP = resorufin β-D-galactopyranoside, SBG = streptavidin-β-galactosidase, TBD = to be determined, TE = total error, ULOQ = upper limit of quantitation.

2.7.1.4.46 ヒト CSF 中 Aβ(1-42)測定性能 (バージョン 1)

Bioanalytical method validation report name, amendments, and hyperlinks	Validation of phospho-tau(181P), β-Amyloid (1-42) and hTauAg ELISA method with Innotest kits from Innogenetics in CSF (pt181, aβ42 and htauag_csf_20[redacted])
Method Description	Amyloid peptide is captured by a first monoclonal antibody, 21F12 (IgG2a). CSF samples are added and incubated with a biotinylated antibody, 3D6 (IgG2b). The Ag-Ab complex is then detected by a peroxidase-labeled streptavidin. After addition of substrate working solution, color intensity measures the concentration of human Aβ(1-42) protein in the sample.
Materials used for standard calibration curve and concentration	[redacted]
Validated assay range	
Materials used for quality controls (QCs) and concentration	
Minimum required dilutions (MRDs)	
Source and lot of reagents	
Regressing model and weighting	
Validation parameters	
Standard calibration curve performance during accuracy and precision runs	
Performance of QCs during accuracy and precision runs	
Selectivity & matrix effect	
Interference & specificity	
Hemolysis effect	
Lipemic effect	
Dilution linearity & hook effect	
Bench-top/process stability	
Freeze-Thaw stability	

2.7.1.4.46 ヒト CSF 中 Aβ(1-42)測定性能 (バージョン 1)

Long-term storage	[redacted]
Parallelism	
Carry over	
Method performance in study BAN2401-J081-104 **Report # bar79/e97: Determination of Aβ1-42, Tau and PTau proteins in CSF for EISAI study BAN2401-J081-104**	
Assay passing rate	[redacted]
Standard curve performance	
QC performance	
Method reproducibility	
Study sample analysis/stability	
Standard calibration curve performance during accuracy and precision runs	

CSF = cerebrospinal fluid, CV = coefficient of variation, ELISA = enzyme-linked immunosorbent assay, IgG = immunoglobulin G, LLOQ = lower limit of quantitation, MRD = minimum required dilution, NA = not applicable, OD = optical density, PI = package insert, QC = quality control, TE = total error, ULOQ = upper limit of quantitation.

2.7.1.4.47 ヒト CSF 中 Aβ(1-42)測定性能 (バージョン 2)

Bioanalytical method validation report name, amendments, and hyperlinks	dv-cmf-103-02
Method Description	Amyloid peptide is captured by a first monoclonal antibody, 21F12 (IgG2a). CSF samples are added and incubated with a biotinylated antibody, 3D6 (IgG2b). The Ag-Ab complex is then detected by a peroxidase-labeled streptavidin. After addition of substrate working solution, color intensity measures the concentration of human Aβ(l-42) protein in the sample.
Materials used for standard calibration curve and concentration	[redacted]
Validated assay range	
Materials used for quality controls (QCs) and concentration	
Minimum required dilutions (MRDs)	
Source and lot of reagents	
Regressing model and weighting	
Validation parameters	
Standard calibration curve performance during accuracy and precision runs	
Performance of QCs during accuracy and precision runs	
Selectivity & matrix effect	

2.7.1.4.47 ヒト CSF 中 Aβ(1-42)測定性能 (バージョン 2)

Interference & specificity	[redacted]
Hemolysis effect	
Lipemic effect	
Dilution linearity & hook effect	
Bench-top/process stability	
Freeze-Thaw stability	
Long-term storage	
Parallelism	
Carry over	
Method performance in study BAN2401-J081-104 **Report # bar79/e97: Determination of Aβl-42, Tau and PTau proteins in CSF for EISAI study BAN2401-J081-104**	
Assay passing rate	[redacted]
Standard curve performance	
QC performance	
Method reproducibility	
Study sample analysis/stability	
Standard calibration curve performance during accuracy and precision runs	
Method performance in study BAN2401-G000-201 **Report # mse6q-bar86: Determination of Aβl-42, Tau and PTau proteins in human CSF samples for EISAI study BAN2401-G000-201**	

2.7.1.4.47 ヒト CSF 中 Aβ(1-42)測定性能 (バージョン 2)

Assay passing rate	[redacted]
Standard curve performance	
QC performance	
Method reproducibility	
Study sample analysis/stability	
Standard calibration curve performance during accuracy and precision runs	

CAL = calibrator, CSF = cerebrospinal fluid, CV = coefficient of variation, ELISA = enzyme-linked immunosorbent assay, IgG = immunoglobulin G, LLOQ = lower limit of quantitation, MRD = minimum required dilution, NA = not applicable, OD = optical density, PI = package insert, QC = quality control, RVC = run validation control, TE = total error, ULOQ = upper limit of quantitation.

2.7.1.4.48 ヒト CSF 中 p-tau181 測定性能(バージョン 1)

Bioanalytical method validation report name, amendments, and hyperlinks	Validation of phospho-tau(181P), B-Amyloid (1-42) and hTauAg ELISA method with Innotest kits from Innogenetics in CSF (pt181, aβ42 and htauag_csf_20[redacted])
Method Description	Phosphorylated tau protein or fragments are captured by a first monoclonal antibody, HT7 (IgG1). Human CSF samples are added and incubated with biotinylated antibodies AT270 (IgG1) monoclonal. The Ag-Ab complex is then detected by peroxidase-labeled streptavidin. After addition of substrate working solution, color intensity measures the concentration of human total phosphorylated tau protein in the sample.
Materials used for standard calibration curve and concentration	[redacted]
Validated assay range	
Materials used for quality controls (QCs) and concentration	
Minimum required dilutions (MRDs)	
Source and lot of reagents	
Regressing model and weighting	
Validation parameters	
Standard calibration curve performance during accuracy and precision runs	
Performance of QCs during accuracy and precision runs	
Selectivity & matrix effect	
Interference & specificity	
Hemolysis effect	
Lipemic effect	
Dilution linearity & hook effect	
Bench-top/process stability	
Freeze-Thaw stability	
Long-term storage	
Parallelism	
Carry over	

2.7.1.4.48 ヒト CSF 中 p-tau181 測定性能(バージョン 1)

Method performance in study BAN2401-J081-104 Report # bar79/e97: Determination of Aβl-42, Tau and PTau proteins in CSF for EISAI study BAN2401-J081-104	
Assay passing rate	[redacted]
Standard curve performance	
QC performance	
Method reproducibility	
Study sample analysis/stability	
Standard calibration curve performance during accuracy and precision runs	

CSF = cerebrospinal fluid, CV = coefficient of variation, ELISA = enzyme-linked immunosorbent assay, IgG = immunoglobulin G, LLOQ = lower limit of quantitation, MRD = minimum required dilution, NA = not applicable, OD = optical density, PI = package insert, QC = quality control, TE = total error, ULOQ = upper limit of quantitation.

2.7.1.4.49 ヒト CSF 中 p-tau181 測定性能(バージョン 2)

Bioanalytical method validation report name, amendments, and hyperlinks	dv-cmf-102-02
Method Description	Phosphorylated tau protein or fragments are captured by a first monoclonal antibody, HT7 (IgG1). Human CSF samples are added and incubated with biotinylated antibodies AT270 (IgG1) monoclonal. The Ag-Ab complex is then detected by peroxidase-labeled streptavidin. After addition of substrate working solution, color intensity measures the concentration of human total phosphorylated Tau protein in the sample.
Materials used for standard calibration curve and concentration	[redacted]
Validated assay range	
Materials used for quality controls (QCs) and concentration	
Minimum required dilutions (MRDs)	
Source and lot of reagents	
Regressing model and weighting	
Validation parameters	
Standard calibration curve performance during accuracy and precision runs	
Performance of QCs during accuracy and precision runs	
Selectivity & matrix effect	
Interference & specificity	
Hemolysis effect	
Lipemic effect	
Dilution linearity & hook effect	
Bench-top/process stability	
Freeze-Thaw stability	

2.7.1.4.49 ヒト CSF 中 p-tau181 測定性能(バージョン 2)

Long-term storage	[redacted]
Parallelism	
Carry over	
Method performance in study BAN2401-J081-104 **Report # bar79/e97: Determination of Aβl-42, Tau and PTau proteins in CSF for EISAI study BAN2401-J081-104**	
Assay passing rate	
Standard curve performance	
QC performance	
Method reproducibility	
Study sample analysis/stability	
Standard calibration curve performance during accuracy and precision runs	
Method performance in study BAN2401-G000-201 **Report # mse6q-bar86: Determination of Aβl-42, Tau and PTau proteins in human CSF samples for EISAI study BAN2401-G000-201**	
Assay passing rate	
Standard curve performance	
QC performance	
Method reproducibility	
Study sample analysis/stability	
Standard calibration curve performance during accuracy and precision runs	

C1 = control 1, C2 = control 2, CAL = calibrator, CSF = cerebrospinal fluid, CV = coefficient of variation, IgG = immunoglobulin G, LLOQ = lower limit of quantitation, MRD = minimum required dilution, NA = not applicable, OD = optical density, PI = package insert, RVC = run validation controls, QC = quality control, TE = total error, ULOQ = upper limit of quantitation.

2.7.1.4.50 ヒト CSF 中 t-tau 測定性能(バージョン 1)

Bioanalytical method validation report name, amendments, and hyperlinks	[redacted]
Method Description	
Materials used for standard calibration curve and concentration	
Validated assay range	
Materials used for quality controls (QCs) and concentration	
Minimum required dilutions (MRDs)	
Source and lot of reagents	
Regressing model and weighting	
Validation parameters	
Standard calibration curve performance during accuracy and precision runs	
Performance of QCs during accuracy and precision runs	
Selectivity & matrix effect	
Interference & specificity	
Hemolysis effect	
Lipemic effect	
Dilution linearity & hook effect	
Bench-top/process stability	
Freeze-Thaw stability	

2.7.1.4.50 ヒト CSF 中 t-tau 測定性能(バージョン 1)

Long-term storage	[redacted]
Parallelism	
Carry over	
Method performance in study BAN2401-J081-104 **Report # bar79/e97: Determination of Aβ1-42, Tau and PTau proteins in CSF for EISAI study BAN2401-J081-104**	
Assay passing rate	[redacted]
Standard curve performance	
QC performance	
Method reproducibility	
Study sample analysis/stability	
Standard calibration curve performance during accuracy and precision runs	

CSF = cerebrospinal fluid, CV = coefficient of variation, ELISA = enzyme-linked immunosorbent assay, IgG = immunoglobulin G, LBA = ligand binding assay, LLOQ = lower limit of quantitation, MRD = minimum required dilution, NA = not applicable, OD = optical density, PI = package insert, QC = quality control, TE = total error, ULOQ = upper limit of quantitation.

2.7.1.4.51 ヒト CSF 中 t-tau 測定性能(バージョン 2)

Bioanalytical method validation report name, amendments, and hyperlinks	dv-cmf-101-02
Method Description	Tau protein or fragments are captured by a first monoclonal antibody, AT120 (IgGl). Human CSF samples are added and incubated with two biotinylated antibodies, HT7 (lgG 1) and BT2(IgG 1). The Ag-Ab complex is then detected by a peroxidase-labeled streptavidin. After addition of substrate working solution, color intensity measures the concentration of human total Tau protein in the sample.
Materials used for standard calibration curve and concentration	[redacted]
Validated assay range	
Materials used for quality controls (QCs) and concentration	
Minimum required dilutions (MRDs)	
Source and lot of reagents	
Regressing model and weighting	
Validation parameters	
Standard calibration curve performance during accuracy and precision runs	
Performance of QCs during accuracy and precision runs	
Selectivity & matrix effect	
Interference & specificity	
Hemolysis effect	
Lipemic effect	
Dilution linearity & hook effect	
Bench-top/process stability	
Freeze-Thaw stability	
Long-term storage	

2.7.1.4.51 ヒト CSF 中 t-tau 測定性能(バージョン 2)

Parallelism	[redacted]
Carry over	
Method performance in study BAN2401-J081-104 **Report # bar79/e97: Determination of Aβl-42, Tau and PTau proteins in CSF for EISAI study BAN2401-J081-104**	
Assay passing rate	[redacted]
Standard curve performance	
QC performance	
Method reproducibility	
Study sample analysis/stability	
Standard calibration curve performance during accuracy and precision runs	
Method performance in study BAN2401-G000-201 **Report # mse6q-bar86: Determination of Aβl-42, Tau and PTau proteins in human CSF samples for EISAI study BAN2401-G000-201**	
Assay passing rate	[redacted]
Standard curve performance	
QC performance	
Method reproducibility	
Study sample analysis/stability	
Standard calibration curve performance during accuracy and precision runs	

C1 = control 1, C2 = control 2, CAL = calibrator, CSF = cerebrospinal fluid, CV = coefficient of variation, IgG = immunoglobulin G, LBA = ligand binding assay, LLOQ = lower limit of quantitation, MRD = minimum required dilution, NA = not applicable, OD = optical density, RVC = run validation control, PI = package insert, QC = quality control, RVC = run validation control, TE = total error, ULOQ =upper limit of quantitation.

2.7.1.4.52 ヒト CSF 中 Aβ(1-40)測定性能

Bioanalytical method validation report name, amendments, and hyperlinks	Quantitative Determination of β-Amyloid$_{1-40}$ in Cerebrospinal Fluid (CSF) Samples by Chemiluminescence Enzyme Immunoassay (CLEIA) using Fujirebio, Inc. Lumipulse® G1200 (aβ40-csf-lumipulse-2([redacted]))
Method Description	The Fujirebio, Inc. Lumipulse® G β-amyloid1-40 CSF assay is a two-step chemiluminescence enzyme immunoassay (CLEIA) method. The first reaction includes 40 µL of sample (specimen or calibrator) and an anti-β-amyloid1-40 monoclonal antibody (mouse) in particle solution, which reacts to form an antigen-antibody immuno-complex. The particles are then washed and rinsed to remove unbound materials. The second reaction utilizes alkaline phosphatase (ALP)-labeled anti-β-amyloid monoclonal antibody which specifically binds to the antigen-antibody immunocomplexes on the particles. The particles are then washed and rinsed to remove unbound materials. A substrate solution containing AMPPD, a 3-(2'-spiroadamantane)-4-methoxy-4-(3"-phosphoryloxy) phenyl-1, 2-dioxetane, disodium salt is added and mixed with the particles. AMPPD is dephosphorylated by the catalysis of ALP indirectly conjugated to the particles. Luminescence (at a maximum wavelength of 477 nm) is generated by the cleavage reaction of dephosphorylated AMPPD, and the luminescent signal reflects the amount of β-amyloid1-40 present in the sample
Materials used for standard calibration curve and concentration	[redacted]
Validated assay range	
Materials used for quality controls (QCs) and concentration	
Minimum required dilutions (MRDs)	
Source and lot of reagents	
Regressing model and weighting	

2.7.1.4.52 ヒト CSF 中 Aβ(1-40)測定性能

Validation parameters	Method Validation Summary	Source Location
Standard calibration curve performance during accuracy and precision runs	[redacted]	[redacted]
Performance of QCs during accuracy and precision runs		
Selectivity & matrix effect		
Interference & specificity		
Hemolysis effect		
Lipemic effect		

2.7.1.4.52 ヒト CSF 中 Aβ(1-40)測定性能

Dilution linearity & hook effect	[redacted]
Bench-top/process stability	
Freeze-Thaw stability	
Long-term storage	

2.7.1.4.52 ヒト CSF 中 Aβ(1-40)測定性能

	[redacted]
Parallelism	
Carry over	
Method performance in study BAN2401-G000-301 **Report # aβ40-csf-lumipulse-sar-20[redacted]: Sample analysis report: Quantitative Determination of β-Amyloid$_{1-40}$ in Cerebrospinal Fluid (CSF) Samples by Chemiluminescence Enzyme Immunoassay (CLEIA) Using Fujirebio, Inc. Lumipulse® G1200 Analyzer**	
Assay passing rate	[redacted]
Standard curve performance	
QC performance	
Method reproducibility	
Study sample analysis/stability	
Standard calibration curve performance during accuracy and precision runs	

ALP = alkaline phosphatase, AMPPD = 3-(2'-spiroadamantane)-4-methoxy-4-(3"-phosphoryloxy) phenyl-1, 2-dioxetane, ASE = allowable systematic error, ATE = allowable total error, CAL = calibrator, CLEIA = chemiluminescence enzyme immunoassay, CLSI = Clinical and Laboratory Standards Institute, CSF = cerebrospinal fluid, CV = coefficient of variation, EQV = equivalent, LLOQ = lower limit of quantitation, MRD = minimum required dilution, NA = not applicable, QC = quality control, TE = total error, ULOQ = upper limit of quantitation.

2.7.1.4.53 ヒト CSF 中 Aβ(1-42)測定性能

Bioanalytical method validation report name, amendments, and hyperlinks	Quantitative Determination of β-Amyloid$_{1-42}$ (IFCC Standardized) in Cerebrospinal Fluid (CSF) Samples by Chemiluminescence Enzyme Immunoassay (CLEIA) Using Fujirebio, Inc. Lumipulse® G1200 (aβ42-csf-lumipulse-20[redacted])
Method Description	The Lumipulse® G β-amyloid1-42 assay kit includes a set of immunoassay reagents for the quantitative measurement of β-amyloid1-42 in CSF specimens based on CLEIA technology using a specific two-step immunoassay method on the Lumipulse® G1200. The first reaction includes 50 µL of sample (specimen or calibrator), an anti-β-amyloid1-42 monoclonal antibody (mouse) in particle solution, and a biotinylated antibody (mouse), which reacts to form a biotinylated antibody-antigen immuno-complex. The particles are then washed and rinsed to remove unbound materials. The second reaction utilizes alkaline phosphatase (ALP)-labeled streptavidin which specifically binds to the biotinylated immune-complexes on the particles. The particles are then washed and rinsed to remove unbound materials. A substrate solution containing AMPPD, a 3-(2'-spiroadamantane)-4-methoxy-4-(3"-phosphoryloxy) phenyl-1, 2-dioxetane, disodium salt is added and mixed with the particles. AMPPD is dephosphorylated by the catalysis of ALP indirectly conjugated to the particles. Luminescence (at a maximum wavelength of 477 nm) is generated by the cleavage reaction of dephosphorylated AMPPD, and the luminescent signal reflects the amount of β-amyloid1-42 present in the sample
Materials used for standard calibration curve and concentration	[redacted]
Validated assay range	
Materials used for quality controls (QCs) and concentration	
Minimum required dilutions (MRDs)	
Source and lot of reagents	

2.7.1.4.53 ヒト CSF 中 Aβ(1-42)測定性能

	[redacted]
Regressing model and weighting	
Validation parameters	
Standard calibration curve performance during accuracy and precision runs	
Performance of QCs during accuracy and precision runs	

2.7.1.4.53 ヒト CSF 中 Aβ(1-42)測定性能

	[redacted]
Selectivity & matrix effect	
Interference & specificity	
Hemolysis effect	
Lipemic effect	
Dilution linearity & hook effect	
Bench-top/process stability	
Freeze-Thaw stability	

2.7.1.4.53 ヒト CSF 中 Aβ(1-42)測定性能

Long-term storage	[redacted]
Parallelism	
Carry over	
Method performance in study BAN2401-G000-301 **Report # aβ42-csf-lumipulse-sar-20[redacted]: Sample analysis report: Quantitative Determination of β-Amyloid$_{1-42}$ (International Federation of Clinical Chemistry (IFCC) Standardized) in Cerebrospinal Fluid (CSF) Samples by Chemiluminescence Enzyme Immunoassay (CLEIA) Using Fujirebio, Inc. Lumipulse® G1200 and Lumipulse® G600II Analyzers**	
Assay passing rate	[redacted]
Standard curve performance	
QC performance	
Method reproducibility	
Study sample analysis/stability	
Standard calibration curve performance during accuracy and precision runs	

ALP = alkaline phosphatase, AMPPD = 3-(2'-spiroadamantane)-4-methoxy-4-(3"-phosphoryloxy) phenyl-1, 2-dioxetane, ASE = allowable systematic error, ATE = allowable total error, CAL = calibrator, CLEIA = chemiluminescence enzyme immunoassay, CLSI = Clinical and Laboratory Standards Institute, CSF = cerebrospinal fluid, CV =

2.7.1.4.53 ヒト CSF 中 Aβ(1-42)測定性能

coefficient of variation, EQV = equivalent, IFCC = International Federation of Clinical Chemistry, LLOQ = lower limit of quantitation, MRD = minimum required dilution, NA = not applicable, QC = quality control, TE = total error, ULOQ = upper limit of quantitation.

2.7.1.4.54 ヒト CSF 中 Aβ(1-42)測定法の製剤処方変更の検証

Bioanalytical method validation report name and hyperlink	Quantitative Determination of β-Amyloid$_{1-42}$ (IFCC Standardized) in Cerebrospinal Fluid (CSF) Samples by Chemiluminescence Enzyme Immunoassay (CLEIA) Using Fujirebio, Inc. Lumipulse® G1200 (aβ42-csf-lumipulse-20[redacted])
Changes in method	Correlation Factor Verified to Convert IFCC Standardization Results to Old Standardization Results (New IFCC Standardization*1.46)
New validated assay range if any	[redacted]
Validation parameters	
Standard calibration curve performance during accuracy and precision runs	
Performance of QCs during accuracy and precision runs	
Cross-validation	
List other parameters	

CLEIA = chemiluminescence enzyme immunoassay, CSF = cerebrospinal fluid, CV = coefficient of variation, IFCC = International Federation of Clinical Chemistry, LLOQ = lower limit of quantitation, NA = not applicable, QC = quality control, TE = total error, ULOQ = upper limit of quantitation.

2.7.1.4.55 ヒト CSF 中 p-tau181 測定性能

Bioanalytical method validation report name, amendments, and hyperlinks	Quantitative Determination of Phospho Tau (pTau) 181 in Cerebrospinal Fluid (CSF) Samples by Chemiluminescence Enzyme Immunoassay (CLEIA) Using Fujirebio, Inc. Lumipulse® G1200 (pt181-csf-lumipulse-20[redacted])
Method Description	The Lumipulse® G pTau181 assay kit includes a set of immunoassay reagents for the quantitative measurement of pTau181 in CSF specimens based on CLEIA technology using a specific two−step immunoassay method on the Lumipulse® G1200. The first reaction includes 40 µL of sample (specimen or calibrator), an anti-phosphorylated Tau (181) monoclonal antibody (mouse) in particle solution and the pTau181 present in the specimen (CSF), which reacts to form an antibody-antigen immuno-complex. The particles are then washed and rinsed to remove unbound materials. The second reaction utilizes alkaline phosphatase (ALP)-labeled anti-Tau monoclonal antibodies (mouse) which specifically binds to the prior formed immuno-complex on the particles and form additional immuno-complexes. The particles are then washed and rinsed to remove unbound materials. A substrate solution containing AMPPD, a 3-(2'-spiroadamantane)-4-methoxy-4-(3"- phosphoryloxy) phenyl-1, 2-dioxetane, disodium salt is added and mixed with the particles. AMPPD is dephosphorylated by the catalysis of ALP indirectly conjugated to particles. Luminescence (at a maximum wavelength of 477 nm) is generated by the cleavage reaction of dephosphorylated AMPPD, and the luminescent signal reflects the amount of pTau181 present in the sample
Materials used for standard calibration curve and concentration	[redacted]
Validated assay range	
Materials used for quality controls (QCs) and concentration	
Minimum required dilutions (MRDs)	
Source and lot of reagents	

2.7.1.4.55 ヒト CSF 中 p-tau181 測定性能

	[redacted]	
Regressing model and weighting		
Validation parameters	Method Validation Summary	Source Location
Standard calibration curve performance during accuracy and precision runs	[redacted]	
Performance of QCs during accuracy and precision runs		
Selectivity & matrix effect		

2.7.1.4.55 ヒト CSF 中 p-tau181 測定性能

Interference & specificity	[redacted]
Hemolysis effect	
Lipemic effect	
Dilution linearity & hook effect	
Bench-top/process stability	

2.7.1.4.55 ヒト CSF 中 p-tau181 測定性能

Freeze-Thaw stability	[redacted]
Long-term storage	
Parallelism	
Carry over	
Method performance in study BAN2401-G000-301 **Report # pt181-csf-lumipulse-sar-20[redacted]: Sample analysis report: Quantitative Determination of Phospho Tau (pTau) 181 in Cerebrospinal Fluid (CSF) Samples by Chemiluminescence Enzyme Immunoassay (CLEIA) Using Fujirebio, Inc. Lumipulse® G1200 Analyzer**	
Assay passing rate	
Standard curve performance	
QC performance	
Method reproducibility	

2.7.1.4.55 ヒト CSF 中 p-tau181 測定性能

Study sample analysis/stability	[redacted]
Standard calibration curve performance during accuracy and precision runs	

ALP = alkaline phosphatase, AMPPD = 3-(2'-spiroadamantane)-4-methoxy-4-(3"-phosphoryloxy) phenyl-1, 2-dioxetane, ASE = allowable systematic error, ATE = allowable total error, CAL = calibrator, CLEIA = chemiluminescence enzyme immunoassay, CLSI = Clinical and Laboratory Standards Institute, CSF = cerebrospinal fluid, CV = coefficient of variation, EQV = equivalent, LLOQ = lower limit of quantitation, MRD = minimum required dilution, NA = not applicable, PI = package insert, QC = quality control, p-tau = phosphorylated tau, SD = standard deviation, TE = total error, ULOQ = upper limit of quantitation.

2.7.1.4.56 ヒト CSF 中 t-tau 測定性能

Bioanalytical method validation report name, amendments, and hyperlinks	Quantitative Determination of Total Tau (tTau) in Human Cerebrospinal Fluid (CSF) Samples by Chemiluminescence Enzyme Immunoassay (CLEIA) Using the Fujirebio, Inc. Lumipulse® G1200 (ttau-csf-lumipulse-20[redacted])
Method Description	The Lumipulse® G Total Tau assay kit includes a set of immunoassay reagents for the quantitative measurement of tTau in CSF specimens based on CLEIA technology using a specific two-step immunoassay method on the Lumipulse® G1200. The first reaction includes 75 µL of sample (specimen or calibrator), an anti-total Tau monoclonal antibody (mouse) in particle solution, and a biotinylated monoclonal Tau specific antibody (mouse), which reacts to form a biotinylated antibody-antigen immuno-complex. The particles are then washed and rinsed to remove unbound materials. The second reaction utilizes alkaline phosphatase (ALP)-labeled streptavidin which specifically binds to the biotinylated immune-complexes on the particles. The particles are then washed and rinsed to remove unbound materials. A substrate solution containing AMPPD, a 3-(2'-spiroadamantane)-4-methoxy-4-(3"- phosphoryloxy) phenyl-1, 2-dioxetane, disodium salt is added and mixed with the particles. AMPPD is dephosphorylated by the catalysis of ALP indirectly conjugated to the particles. Luminescence (at a maximum wavelength of 477 nm) is generated by the cleavage reaction of dephosphorylated AMPPD, and the luminescent signal reflects the amount of total Tau present in the sample
Materials used for standard calibration curve and concentration	[redacted]
Validated assay range	
Materials used for quality controls (QCs) and concentration	
Minimum required dilutions (MRDs)	
Source and lot of reagents	

2.7.1.4.56 ヒト CSF 中 t-tau 測定性能

Regressing model and weighting	[redacted]
Validation parameters	
Standard calibration curve performance during accuracy and precision runs	
Performance of QCs during accuracy and precision runs	
Selectivity & matrix effect	
Interference & specificity	
Hemolysis effect	
Lipemic effect	

2.7.1.4.56 ヒト CSF 中 t-tau 測定性能

Dilution linearity & hook effect	[redacted]
Bench-top/process stability	
Freeze-Thaw stability	
Long-term storage	
Parallelism	

2.7.1.4.56 ヒト CSF 中 t-tau 測定性能

Carry over	[redacted]
Method performance in study BAN2401-G000-301 **Report # ttau-csf-lumipulse-sar-20[redacted]: Sample analysis report: Quantitative Determination of Total Tau (tTau) in Cerebrospinal Fluid (CSF) Samples by Chemiluminescence Enzyme Immunoassay (CLEIA) Using Fujirebio, Inc. Lumipulse® G1200 and Lumipulse® G600II Analyzers**	
Assay passing rate	[redacted]
Standard curve performance	
QC performance	
Method reproducibility	
Study sample analysis/stability	
Standard calibration curve performance during accuracy and precision runs	

ALP = alkaline phosphatase, AMPPD = 3-(2'-spiroadamantane)-4-methoxy-4-(3"-phosphoryloxy) phenyl-1, 2-dioxetane, ASE = allowable systematic error, ATE = allowable total error, CAL = calibrator, CLEIA = chemiluminescence enzyme immunoassay, CLSI = Clinical and Laboratory Standards Institute, CSF = cerebrospinal fluid, CV = coefficient of variation, LLOQ = lower limit of quantitation, MRD = minimum required dilution, NA = not applicable, QC = quality control, SD = standard deviation, TE = total error, t-tau = total tau, ULOQ = upper limit of quantitation.

2.7.1.4.57 ヒト CSF 中 NfL 測定性能(バージョン 1)

Bioanalytical method validation report name, amendments, and hyperlinks	BAN2401-G000-201 – NfL validation in CSF (nfl_csf-20[redacted], nfl-csf-20[redacted]r1)
Method Description	The assay is a 2-site solid phase sandwich ELISA. One specific monoclonal antibody is coated on a solid surface and binds Neurofilament light. Detection is performed by use of another specific conjugated monoclonal antibody. Quantitative determinations are performed by enzymatic turn-over of a colorless substrate to a colored product, which corresponds to the amount of Neurofilament light in the sample.
Materials used for standard calibration curve and concentration	[redacted]
Validated assay range	
Materials used for quality controls (QCs) and concentration	
Minimum required dilutions (MRDs)	
Source and lot of reagents	
Regressing model and weighting	
Validation parameters	
Standard calibration curve performance during accuracy and precision runs	
Performance of QCs during accuracy and precision runs	
Selectivity & matrix effect	
Interference & specificity	
Hemolysis effect	
Lipemic effect	

2.7.1.4.57 ヒト CSF 中 NfL 測定性能(バージョン 1)

Dilution linearity & hook effect	[redacted]
Bench-top/process stability	
Freeze-Thaw stability	
Long-term storage	
Parallelism	
Carry over	
Method performance in study BAN2401-G000-201 **Report # sar-[redacted]-nflp/nrgn/ykl-40/cntn-2: Determination of Neurofilament light protein (NFLP), Neurogranin (NRGN), YKL-40, Contactin-2 (CNTN-2) in human CSF samples and NFLP in plasma using ELISA and SIMOA for Eisai Study BAN2401-G000-201**	
Assay passing rate	[redacted]
Standard curve performance	
QC performance	
Method reproducibility	
Study sample analysis/stability	
Standard calibration curve performance during accuracy and precision runs	

CNTN-2 = contactin-2, CSF = cerebrospinal fluid, CV = coefficient of variation, ELISA = enzyme-linked immunosorbent assay, HQC = high quality control, LBA = ligand binding assay, LLOD = lower limit of detection, LLOQ = lower limit of quantitation, LQC = low quality control, NA = not applicable, NfL = neurofilament light chain, NFLP = neurofilament light protein, NRGN = neurogranin, QC = quality control, SAR = sample analysis report, SIMOA = single molecule array, TE = total error, ULOQ = upper limit of quantitation, [redacted], YKL-40 = chitinase-3-like protein 1.

2.7.1.4.58 ヒト CSF 中 NfL 測定性能(バージョン 2)

Bioanalytical method validation report name, amendments, and hyperlinks	Quantitation of NF-Light in Human CSF on the Quanterix Simoa Platform (nfl-csf-20[redacted])
Method Description	This assay uses a commercial Simoa NF-Light(NF-L) Assay Kit provided by Quanterix Corp. In the first step, anti-NF-L antibody-coated paramagnetic capture beads and an anti-NF-L antibody conjugated with Biotin are incubated with samples diluted in Sample Diluent. NF-L molecules present in the samples are captured by the anti-NF-L antibody-coated capture beads. The detection antibody will then bind to the captured NF-L molecules. The beads are washed and a streptavidin-ß-galactosidase (SßG) conjugate is mixed with the capture beads. SßG binds to the biotinylated detection antibody, resulting in the enzymatic labeling of the captured NF-L. Following a second wash, the capture beads are re-suspended in a resorufin ß-D-galactopyranoside (RGP) substrate solution and transferred to the Simoa Disc. Individual capture beads are then sealed within microwells in the array. If NF-L is captured and labeled, the ß-galactosidase hydrolyzes the RGP substrate into a fluorescent product that yields a signal for measurement. A single labeled NF-L molecule results in sufficient fluorescent signal in 30 seconds to be detected and counted by the Simoa optical system. At a low NF-L concentration, the percentage of bead-containing wells in the array with a positive signal is proportional to the amount of NF-L present in the sample, thus yielding a “digital” signal. At a high NF-L concentration, when most of the bead-containing wells have one or more labeled NF-L molecules, the total fluorescence signal is proportional to the amount of NF-L present in the sample, thus yielding an “analog” signal. The concentration of NF-L in an unknown sample is interpolated from a standard curve.
Materials used for standard calibration curve and concentration	[redacted]
Validated assay range	
Materials used for quality controls (QCs) and concentration	
Minimum required dilutions (MRDs)	
Source and lot of reagents	
Regressing model and weighting	

2.7.1.4.58 ヒト CSF 中 NfL 測定性能(バージョン 2)

Validation parameters	Method Validation Summary	Source Location
Standard calibration curve performance during accuracy and precision runs	[redacted]	[redacted]
Performance of QCs during accuracy and precision runs		
Selectivity & matrix effect		
Interference & specificity		
Hemolysis effect		
Lipemic effect		
Dilution linearity & hook effect		
Bench-top/process stability		

2.7.1.4.58 ヒト CSF 中 NfL 測定性能(バージョン 2)

Freeze-Thaw stability	[redacted]
Long-term storage	
Parallelism	
Carry over	
Method performance in study BAN2401-G000-301 **Report # sar-[redacted]-nfl-nrgn-csf20[redacted]: Sample analysis report: Determination of Neurofilament light protein (NfL) and Neurogranin (NRGN) in CSF samples using ELISA and SIMOA for Eisai Study BAN2401-G000-301**	
Assay passing rate	[redacted]
Standard curve performance	
QC performance	
Method reproducibility	
Study sample analysis/stability	
Standard calibration curve performance during accuracy and precision runs	

CSF = cerebrospinal fluid, CV = coefficient of variation, DF = dilution factor, ELISA = enzyme-linked immunosorbent assay, LLOD = lower limit of detection, LLOQ = lower limit of quantitation, MRD = minimum required dilution, NA = not applicable, NfL = neurofilament light chain, NfLP = neurofilament light protein, NRGN = neurogranin, QC = quality control, RGP = resorufin β-D-galactopyranoside, SBG = streptavidin-β-galactosidase, SIMOA = single molecule array, TE = total error, ULOQ = upper limit of quantitation.

2.7.1.4.59 ヒト CSF 中 Nerurograinin 測定性能

Bioanalytical method validation report name, amendments, and hyperlinks	BAN2401-G000-201 – Neurogranin (NRGN) validation in CSF (neurogranin_csf_20[redacted], nrgn-csf-20[redacted]r1)
Method Description	The calibrators and patient samples are diluted with biotinylated monoclonal anti-neurogranin antibody and added to microplate wells coated with monoclonal antibodies specific for human neurogranin truncated at P75. In this process truncated (P75) neurogranin is bound in a complex. In a second incubation, biotin binds to streptavidin peroxidase conjugate (SV-HPR). Incubation of the complex with substrate and chromogen promotes a color reaction. The color intensity is proportional to the truncated (P75) neurogranin concentration in the sample.
Materials used for standard calibration curve and concentration	[redacted]
Validated assay range	
Materials used for quality controls (QCs) and concentration	
Minimum required dilutions (MRDs)	
Source and lot of reagents	
Regressing model and weighting	
Validation parameters	
Standard calibration curve performance during accuracy and precision runs	
Performance of QCs during accuracy and precision runs	

2.7.1.4.59 ヒト CSF 中 Nerurograinin 測定性能

Selectivity & matrix effect	[redacted]
Interference & specificity	
Hemolysis effect	
Lipemic effect	
Dilution linearity & hook effect	
Bench-top/process stability	
Freeze-Thaw stability	
Long-term storage	
Parallelism	
Carry over	
Method performance in study BAN2401-G000-201 **Report # sar-[redacted]-nflp/nrgn/ykl-40/cntn-2: Determination of Neurofilament light protein (NFLP), Neurogranin (NRGN), YKL-40, Contactin-2 (CNTN-2) in human CSF samples and NFLP in plasma using ELISA and SIMOA for Eisai Study BAN2401-G000-201**	
Assay passing rate	[redacted]
Standard curve performance	
QC performance	

2.7.1.4.59 ヒト CSF 中 Nerurograinin 測定性能

Method reproducibility	[redacted]
Study sample analysis/stability	
Standard calibration curve performance during accuracy and precision runs	
Method performance in study BAN2401-G000-301 **Report # sar-[redacted]-nfl-nrgn-csf20[redacted]: Sample analysis report: Determination of Neurofilament light protein (NfL) and Neurogranin (NRGN) in CSF samples using ELISA and SIMOA for Eisai Study BAN2401-G000-301**	
Assay passing rate	[redacted]
Standard curve performance	
QC performance	
Method reproducibility	
Study sample analysis/stability	

2.7.1.4.59 ヒト CSF 中 Nerurograinin 測定性能

Standard calibration curve performance during accuracy and precision runs	[redacted]

CSF = cerebrospinal fluid, CV = coefficient of variation, ELISA = enzyme-linked immunosorbent assay, LBA = ligand binding assay, LLOQ = lower limit of quantitation, NA = not applicable, QC = quality control, TE = total error, ULOQ = upper limit of quantitation.

2.7.1.4.60 ヒト CSF 中 Contactin-2 測定性能

Bioanalytical method validation report name, amendments, and hyperlinks	BAN2401-G000-201 – Contactin-2 (CNTN2) validation in CSF (contactin-2_csf_20[redacted], contactin-2-csf-20[redacted]r1)
Method Description	Dilute the Capture Antibody to the working concentration in PBS without carrier protein. Immediately coat a 96-well microplate with 100 µL per well of the diluted Capture Antibody. Seal the plate and incubate overnight at room temperature. Aspirate each well and wash with Wash Buffer, repeating the process two times for a total of three washes. Wash by filling each well with Wash Buffer (400 µL) using a squirt bottle, manifold dispenser, or autowasher. Complete removal of liquid at each step is essential for good performance. After the last wash, remove any remaining Wash Buffer by aspirating or by inverting the plate and blotting it against clean paper towels. Block plates by adding 300 µL of Reagent Diluent to each well. Incubate at room temperature for a minimum of 1 hour.Repeat the aspiration/wash as in step 2. The plates are now ready for sample addition. Add 100 µL of sample or standards in Reagent Diluent, or an appropriate diluent, per well. Cover with an adhesive strip and incubate 2 hours at room temperature. Repeat the aspiration/wash as in step 2 of Plate Preparation. Add 100 µL of the Detection Antibody, diluted in Reagent Diluent, to each well. Cover with a new adhesive strip and incubate 2 hours at room temperature. Repeat the aspiration/wash as in step 2 of Plate Preparation. Add 100 µL of the working dilution of Streptavidin-HRP to each well. Cover the plate and incubate for 20 minutes at room temperature. Avoid placing the plate in direct light. Repeat the aspiration/wash as in step 2. Add 100 µL of Substrate Solution to each well. Incubate for 20 minutes at room temperature. Avoid placing the plate in direct light. Add 50 µL of Stop Solution to each well. Gently tap the plate to ensure thorough mixing. Determine the optical density of each well immediately, using a microplate reader set to 450 nm. If wavelength correction is available, set to 540 nm or 570 nm. If wavelength correction is not available, subtract readings at 540 nm or 570 nm from the readings at 450 nm. This subtraction will correct for optical imperfections in the plate. Readings made directly at 450 nm without correction may be higher and less accurate
Materials used for standard calibration curve and concentration	[redacted]
Validated assay range	
Materials used for quality controls (QCs) and concentration	
Minimum required dilutions (MRDs)	
Source and lot of reagents	
Regressing model and weighting	
Validation parameters	
Standard calibration curve performance during accuracy and precision runs	

2.7.1.4.60 ヒト CSF 中 Contactin-2 測定性能

Performance of QCs during accuracy and precision runs	[redacted]
Selectivity & matrix effect	
Interference & specificity	
Hemolysis effect	
Lipemic effect	
Dilution linearity & hook effect	
Bench-top/process stability	
Freeze-Thaw stability	
Long-term storage	
Parallelism	
Carry over	
Method performance in study BAN2401-G000-201 **Report # sar-[redacted]-nflp/nrgn/ykl-40/cntn-2: sample analysis report: Determination of Neurofilament light protein (NFLP), Neurogranin (NRGN), YKL-40, Contactin-2 (CNTN-2) in human CSF samples and NFLP in plasma using ELISA and SIMOA for Eisai Study BAN2401-G000-201**	
Assay passing rate	[redacted]

2.7.1.4.60 ヒト CSF 中 Contactin-2 測定性能

Standard curve performance	[redacted]
QC performance	
Method reproducibility	
Study sample analysis/stability	
Standard calibration curve performance during accuracy and precision runs	

CNTN2 = contactin-2, CSF = cerebrospinal fluid, CV = coefficient of variation, ELISA = enzyme-linked immunosorbent assay, HQC = high quality control, HRP = horseradish peroxidase, LBA = ligand binding assay, LLOQ = lower limit of quantitation, LQC = low quality control, MRD = minimum required dilution, NA = not applicable, NFLP = neurofilament light protein , NRGN = neurogranin, PBS = phosphate-buffered saline, QC = quality control, SIMOA = single molecule array, TE = total error, ULOQ = upper limit of quantitation, YKL-40 = chitinase-3-like protein 1.

2.7.1.4.61 ヒト CSF 中 YKL-40 測定性能

Bioanalytical method validation report name, amendments, and hyperlinks	BAN2401-G000-201 – YKL-40 validation in CSF (ykl-40_csf_20[redacted], ykl-40-csf-20[redacted]r1)
Method Description	The MicroVue YKL-40 enzyme immunoassay kit for the detection of YKL-40 in experimental samples is a three step procedure utilizing (1) a microassay plate coated with streptavidin and a biotinylated murine monoclonal antibody to human YKL-40, (2) an AP-conjugated rabbit polyclonal antibody to YKL-40, and (3) a chromogenic substrate. In the first step, Standards, Controls, and test specimens are added to the avidin coated assay wells along with the capture solution containing a biotinylated F(ab) fragment of a murine monoclonal antibody to YKL-40. The monoclonal antibody binds to YKL-40 in the Standards, Controls, or specimens, and the biotin binds to the avidin on the microwell plate, immobilizing the antibody. After an incubation period, a wash cycle removes any unbound material. In the second step, alkaline phosphatase (AP) conjugated rabbit anti-YKL-40 is added to each assay well. The enzyme conjugated anti-YKL-40 binds to the immobilized YKL-40 captured in the first step. After an incubation period, a wash cycle removes any unbound conjugate. In the third step, p-nitrophenyl phosphate (pNPP), a chromogenic substrate solution, is added to the assay wells. The bound AP reacts with the substrate, forming a yellow color. After an incubation period, the reaction is stopped chemically, and the color intensity is measured spectrophotometically at A405. The color intensity of the reaction mixture is proportional to the concentration of YKL-40 present in the test specimens, Standards and Controls. Results are calculated from the generated standard curve using linear regression analysis.
Materials used for standard calibration curve and concentration	[redacted]
Validated assay range	
Materials used for quality controls (QCs) and concentration	
Minimum required dilutions (MRDs)	
Source and lot of reagents	
Regressing model and weighting	
Validation parameters	
Standard calibration curve performance during accuracy and precision runs	

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Performance of QCs during accuracy and precision runs	[redacted]
Selectivity & matrix effect	
Interference & specificity	
Hemolysis effect	
Lipemic effect	
Dilution linearity & hook effect	
Bench-top/process stability	
Freeze-Thaw stability	
Long-term storage	

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Parallelism	[redacted]
Carry over	
Method performance in study BAN2401-G000-201 **Report # sar-[redacted]-nflp/nrgn/ykl-40/cntn-2: sample analysis report: Determination of Neurofilament light protein (NFLP), Neurogranin (NRGN), YKL-40, Contactin-2 (CNTN-2) in human CSF samples and NFLP in plasma using ELISA and SIMOA for Eisai Study BAN2401-G000-201**	
Assay passing rate	[redacted]
Standard curve performance	
QC performance	
Method reproducibility	
Study sample analysis/stability	
Standard calibration curve performance during accuracy and precision runs	

AP = alkaline phosphatase, CNTN2 = contactin-2, CSF = cerebrospinal fluid, CV = coefficient of variation, ELISA = enzyme-linked immunosorbent assay, HQC = high quality control, LBA = ligand binding assay, LLOQ = lower limit of quantitation, LQC = low quality control, NA = not applicable, MRD = minimum required dilution, NFLP = neurofilament light protein, NRGN = neurogranin, pNPP = p-nitrophenyl phosphate, QC = quality control, SIMOA = single molecule array, TE = total error, ULOQ = upper limit of quantitation, YKL-40 = chitinase-3-like protein 1.

2.7.1.4.62 *APOE4* 遺伝子型決定法

Bioanalytical method validation report name, amendments, and hyperlinks	Genotyping of ApoE SNPs rs429358 and rs7412 (apoe_whole blood_20[redacted])
Method Description	Blood samples containing 5mL-9mL of blood are extracted using the Chemagic STAR DNA Blood 10k Kit (PerkinElmer Cat. No. CMG-1710-A) and blood samples containing 2mL-5mL of blood are extracted using the Chemagic STAR DNA Blood 5k Kit (PerkinElmer Cat. No. CMG-1705-B) on Chemagic 360 instrumentation. At the end of the run, the instrument aliquots the eluted DNA into the target plate (1mL or 500µL for the 10k or 5k kit, respectively), and an output file is produced. The DNA aliquots are created in LIMS, and the DNA samples are sent for Analytical QC (AQC)/Functional QC (FQC) processing. AQC quantifies samples using the Unchained Lunatic. This is a multichannel spectrophotometer which may be used for quick and precise UV/VIS spectral analysis of DNA, RNA, protein, PCR amplicons and other small compounds. It is a 96 well plate reader which uses specific DropPlates and 2-3µL of sample. AQC also involves volume estimation using a contact-independent ultrasound technology using our VolumeCheck instrument. FQC is a panel of 96 SNPs on which an aliquot of each parent DNA is analyzed. The DNA fingerprint generated is useful not only to predict downstream performance in other assays (eg, SNP genotyping by TaqMan AD assay), but also provides information about sample identity. An AD assay is a multiplexed end-point quantitative polymerase chain reaction (qPCR) assay which detects variants of a single nucleic acid sequence. The presence of two primer/probe pairs in each reaction allows genotyping of the two possible alleles at the single-nucleic polymorphism (SNP) site in a target template sequence. For each sample in an AD assay, a unique pair of fluorescent dye detectors is used, for example, two TaqMan MGB probes that target a SNP site. One fluorescent dye detector is a perfect match to the wild type (allele 1) and the other fluorescent dye detector is a perfect match to the variant (allele 2). The AD assay classifies unknown samples as: homozygotes (samples having only allele1 or allele2) and heterozygotes (samples having both allele1 and allele2). The AD assay measures the change in fluorescence of the dyes associated with the probes as a function of PCR cycle number. By using different reporter dyes, cleavage of allele-specific probes can be detected in a single PCR reaction. All assays are performed using a single reaction buffer and single thermocycling protocol. AD assays have been successfully used to discriminate alleles that differ by a single base substitution. In this study, BLS-NJ validated two AD assays, which are commercially available from Thermo-Fisher Scientific as TaqMan SNP Genotyping assay for SNPs rs429358 and rs7412, on 18 HapMap controls and 100 random whole blood samples. All samples were clearly called to be wild type homozygous, variant homozygous or heterozygous, for rs429358 and rs7412. No atypical results in the allelic discrimination plot for any samples were observed.
Materials used for standard calibration curve and concentration	[redacted]
Validated assay range	
Materials used for quality controls (QCs) and concentration	
Minimum required dilutions (MRDs)	
Source and lot of reagents	
Regressing model and weighting	
Validation parameters	