August 19, 2026

Roche Diagnostics
Todd Davis
Regulatory Affairs Manager
9115 Hague Rd.
P.O. Box 50416
Indianapolis, Indiana 46250

Re: K261686
Trade/Device Name: Elecsys Phospho-Tau (217P) Plasma
Regulation Number: 21 CFR 866.5840
Regulation Name: Alzheimer's disease pathology assessment test
Regulatory Class: Class II
Product Code: SET
Dated: May 21, 2026
Received: May 21, 2026

Dear Todd Davis:

We have reviewed your section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (the Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality Management System Regulation (QMSR) (21 CFR Part 820), which includes, but is not limited to, ISO 13485 clause 7.3 (Design controls), ISO 13485 clause 8.3 (Nonconforming product), ISO 13485 clause 8.5.2 (Corrective action), and ISO 13485 clause 8.5.3 (Preventative action). Please note that regardless of whether a change requires premarket review, the QMSR requires device manufacturers to review and approve changes to device design and production (ISO 13485 clause 7.3 and ISO 13485 clause 7.5) and document changes and approvals in the Medical Device File (ISO 13485 clause 4.2.3).

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR Part 803) for devices or postmarketing safety reporting (21 CFR Part 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the Quality Management System Regulation (QMSR) (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

All medical devices, including Class I and unclassified devices and combination product device constituent parts are required to be in compliance with the final Unique Device Identification System rule ("UDI Rule"). The UDI Rule requires, among other things, that a device bear a unique device identifier (UDI) on its label and package (21 CFR 801.20(a)) unless an exception or alternative applies (21 CFR 801.20(b)) and that the dates on the device label be formatted in accordance with 21 CFR 801.18. The UDI Rule (21 CFR 830.300(a) and 830.320(b)) also requires that certain information be submitted to the Global Unique Device Identification Database (GUDID) (21 CFR Part 830 Subpart E). For additional information on these requirements, please see the UDI System webpage at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-system-udi-system.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-

assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Ying Mao -S

Ying Mao, Ph.D.
Branch Chief
Division of Immunology and
Hematology Devices
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

Indications for Use

Please type in the marketing application/submission number, if it is known. This textbox will be left blank for original applications/submissions.	K261686

Please provide the device trade name(s).

Elecsys Phospho-Tau (217P) Plasma

Please provide your Indications for Use below.

The Elecsys Phospho-Tau (217P) Plasma assay is an in vitro immunoassay for the determination of the phospho-tau (217P) (pTau217) protein in human plasma from individuals aged 55 years and older.

The assay is intended for use as an aid in identifying patients with amyloid pathology presenting with signs, symptoms, or complaints of cognitive decline associated with Alzheimer's disease. The Elecsys Phospho-Tau (217P) Plasma assay result must be used in the diagnostic pathway in conjunction with other clinical information.

The electrochemiluminescence immunoassay “ECLIA” is intended for use on cobas e immunoassay analyzers.

Please select the types of uses.	☒ Prescription Use (21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)
Please select the age group(s) for which the device(s) is to be used.	☐ Neonates/Newborns (Birth to < 29 days old) ☐ Infants (29 days old to < 2 years old) ☐ Children (2 years old to < 12 years old) ☐ Adolescents (12 years old to < 22 years old) ☒ Adults (22 years old and greater)

Elecsys Phospho-Tau (217P) Plasma
510(k) Summary

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of 21 CFR 807.92.

Submitter Name	Roche Diagnostics
Address	9115 Hague Rd., Indianapolis, IN 46250 United States
Contact	Todd Davis Phone: +1 317-313-7112 Email: todd.davis@roche.com
Date Prepared	June 12, 2026
Proprietary Name	Elecsys Phospho-Tau (217P) Plasma (09697870190)
Common Name	Elecsys Phospho-Tau (217P) Plasma
Classification Name	Immunoassay blood test for amyloid pathology assessment
Regulation Number	866.5840
Product Codes	SET
Predicate Devices	Lumipulse ***G*** pTau217/ß-Amyloid 1-42 Plasma Ratio
Submission Where 510(k) Clearance was Granted	K242706

1. DEVICE DESCRIPTION

In vitro electrochemiluminescence immunoassay (ECLIA) intended for the measurement of the phosphorylated Tau 217 protein in human plasma.

Elecsys Phospho-Tau (217P) Plasma utilizes a sandwich test principle and has a total duration time of 18 minutes.

- First incubation: 60 µL of sample, biotinylated monoclonal antibody specific for phosphorylation at threonine 217, and a monoclonal tau-specific antibody labeled with a ruthenium complex[a)] react to form a sandwich complex.
- Second incubation: After streptavidin-coated microparticles have been added, the complex becomes bound to the solid phase via interaction of biotin and streptavidin.
- The reaction mixture is aspirated into the measuring cell, where the microparticles are magnetically captured onto the surface of the electrode. Unbound substances are then removed with ProCell II M. Application of a voltage to the electrode then induces chemiluminescent emission, which is measured by a photomultiplier.
- Results are determined via a calibration curve that is instrument-specifically generated by 2-point calibration and a leading calibration curve provided via **cobas** link.

a. Tris(2,2'-bipyridyl)ruthenium(II)-complex ($Ru(bpy)_3^{2+}$)

2. INDICATIONS FOR USE

The Elecsys Phospho-Tau (217P) Plasma assay is an in vitro immunoassay for the determination of the phospho-tau (217P) (pTau217) protein in human plasma from individuals aged 55 years and older.

The assay is intended for use as an aid in identifying patients with amyloid pathology presenting with signs, symptoms, or complaints of cognitive decline associated with Alzheimer's disease.

The Elecsys Phospho-Tau (217P) Plasma assay result must be used in the diagnostic pathway in conjunction with other clinical information.

The electrochemiluminescence immunoassay “ECLIA” is intended for use on cobas e immunoassay analyzers.

3. TECHNOLOGICAL CHARACTERISTICS

The Roche Elecsys Phospho-Tau (217P) Plasma is substantially equivalent to the predicate device Lumipulse ***G*** pTau217/ß-Amyloid 1-42 Plasma Ratio. Both products measure the respective analytes in a very similar fashion utilizing monoclonal antibodies which bind with the analyte and are both measured using chemiluminescence technology.

4. INDICATIONS FOR USE COMPARISON

Elecsys Phospho-Tau (217P) Plasma is substantially equivalent to the G pTau 217/β-Amyloid 1-42 Plasma Ratio in analytical and clinical performance. Both test systems measure phospho-tau (217P) (pTau217) protein in human plasma in adult patients with signs and symptoms of cognitive decline.

5. NON-CLINICAL PERFORMANCE EVALUATION

5.1. Precision (Repeatability and Intermediate Precision)

Repeatability and Intermediate Precision were conducted according to CLSI guidance EP05-A3 using a **cobas** e 801 in **cobas pro** integrated solutions analyzer and one reagent lot. Sixteen human K2-EDTA plasma samples spanning the measuring range were tested in two replicates per run, two runs separated by two hours per day for 21 days at a single site.

Lot-to-lot Precision was conducted according to CLSI guidance EP05-A3 using a **cobas** e 801in **cobas pro** integrated solutions analyzer and three reagent lots. Sixteen human K2-EDTA plasma samples spanning the measuring range were tested in five replicates per run, one run per day for five days per lot at a single site. The three lots were evaluated on separate days.

Site-to-site Reproducibility was conducted according to CLSI guidance EP05-A3 at three sites with one **cobas** e 801 (8000) and two **cobas** e 801 in **cobas pro** integrated solutions analyzer using one reagent lot at each site. Ten human K2-EDTA plasma samples spanning the measuring range were tested in three replicates per run, two runs separated by two hours per day for five days.

Results for all plasma samples and the three controls (PC = PreciControl, PreciControl Phospho-Tau (217P) Plasma) tested in the precision and reproducibility studies met the predetermined acceptance criteria.

5.2. Limit of Blank (LoB)

The limit of Blank was determined according to CLSI EP17-A2. Experimental design included three reagent lots evaluated on **cobas** e 801 in **cobas pro** integrated solutions, six runs over three days with two replicates per run. Depleted plasma samples were used as the blank samples. The LoB claim in the labeling will be set to 0.0470 pg/mL.

5.3. Limit of Detection (LoD)

The limit of Detection was determined according to CLSI EP17-A2. Five human K2-EDTA plasma samples with low-analyte concentrations (i.e., > LoB) were measured with three lots in duplicate determination in six runs, distributed over three days, on **cobas** e 801 in **cobas pro** integrated solutions. The LoD claim in the labeling was set to 0.0560 pg/mL.

5.4. Limit of Quantitation (LoQ)

The limit of Quantitation was determined according to CLSI EP17-A2. Eight human K2-EDTA plasma samples with analyte concentrations close to the specified LoQ were measured within 5 days with one run per day and 5 replicates per run with three reagent lots on **cobas** e 801 in **cobas pro** integrated solutions. All lots met the predetermined acceptance criterion and the LoQ claim in the labeling was set to 0.0560 pg/mL.

5.5. Linearity

Linearity was performed according to CLSI EP06-Ed2. Linearity was assessed on the **cobas** e 801 in **cobas pro** integrated solutions utilizing dilutions of three high native K2-EDTA plasma samples spiked with Tau(207-227)[pThr217]amid and a native sample that covers at least 50% of the measuring range. Each sample dilution was measured in 4-fold determination within one run using one reagent lot. For each sample, the mean value of the measured values, predicted value and the deviation from linearity were calculated. Percent deviations from linearity (%DL) were calculated as differences between the observed values and the predicted values divided by the predicted values. The %DLs were within ± 10% for each dilution level in all four sample panels. The assay is linear over the measuring range of 0.0560 pg/mL to 2.40 pg/mL.

5.6. High Dose Hook Effect

To determine the hook concentration, two high concentration K2-EDTA plasma samples spiked with Tau(207-227)[pThr217]amid were used to prepare dilution series using native K2-EDTA plasma. Each sample level was measured in three replicates within one run on a **cobas** e 801 in **cobas pro** integrated solutions and the median measured counts were plotted against the expected sample concentrations. The data supports the claim that there is no hook effect up to 24 pg/mL.

5.7. Human Anti-Mouse Antibodies (HAMA)

The effect on quantitation of analyte in the presence of human anti-mouse (HAMA) antibodies or human anti-rabbit antibodies (HARA) and Streptavidin was determined on the **cobas** e 801 in **cobas pro** integrated solutions. HAMA and HARA interference was assessed in two K2-EDTA plasma sample pools (low and slightly above the cut-off). One aliquot of each sample was spiked with the interfering substance (HAMA pool at 1200 µg/mL or HARA pool at 100 µg/mL) (test samples) and another aliquot was spiked with the same volume of the base pool (control sample). Both pools were tested in the same run in duplicate determination. The % interference was calculated by comparing measurements of the test and control samples. The result fulfilled the specification for HAMA and HARA interference.

To determine the effect of Anti-Streptavidin Antibodies five samples with different concentrations were divided into different basis pools. One pool of each sample was spiked with Anti-Streptavidin Antibodies (interference pool) to a total concentration of 100 µg/mL. One pool of each sample is spiked with an unspecific antibody (spiked control pool) to a total concentration of 100 µg/mL to mask out matrix effect and the third pool of each sample remains native (non spiked control pool) to check for matrix effects of the unspecific antibody.
All samples were measured in replicates. The result fulfilled the specification for Anti-Streptavidin Antibodies interference.

5.8. Endogenous Interferences

The effect on the quantitation of Elecsys Phospho-Tau (217P) Plasma in the presence of nine interfering substances (Hemoglobin, Bilirubin (conjugated and unconjugated), Intralipid, Biotin, Rheumatoid Factor, Human Serum Albumin, IgG, IgM, IgA) was determined on the **cobas** e 801 in **cobas pro** integrated solutions. A total of six K2-EDTA plasma samples pools covering the measuring range, including the medical decision points (low, medium, high, and MDP) were prepared. For each interfering substance, one aliquot of each plasma sample was spiked with the potential interferent (test sample), and another aliquot was spiked with the same volume of solvent used to create the interfering substances panel (control sample). A dilution series was then prepared by proportionally mixing the test and control samples. Each level was tested in five-fold determination within one run using one reagent lot. The % interference was calculated by comparing measurements of the test and control samples. All compounds exhibited no significant interference and met the acceptance criteria.

5.9. Exogenous (drugs) Interferences

The effect on quantitation of the pTau217 analyte in the presence of exogenous interfering substances using the Elecsys Phospho-Tau (217P) Plasma was determined on the **cobas** e 801 in **cobas pro** integrated solutions. Seventeen common and twenty-six special pharmaceuticals were tested by spiking into six K2-EDTA human plasma sample pools covering the measuring range including the medical decision points (low, medium, high, and MDPs). All plasma sample pools were divided into two aliquots. One was spiked with the potential interferent (test sample) and the other without interferent was spiked with the respective amount of solvent only (control sample). Each sample was tested in five-fold determination within one run. The % interference was calculated by comparing measurements of the test and control samples. All compounds exhibited no significant interference and met the acceptance criteria.

5.10. Cross Reactivity / Analytical Specificity

Cross-reactivity to the non-phosphorylated Tau protein, pTau181, pTau205, pTau212 and pTau231 was assessed on a **cobas** e 801 in **cobas pro** integrated solutions. One K2-EDTA human plasma sample pool with a low analyte concentration was used. The sample pool was divided into aliquots. The test aliquots were spiked with the respective putative cross-reactants at concentrations of 60.0 pg/mL and 66.0 pg/mL. One unmodified aliquot served as the unspiked reference sample. Each sample was tested in five-fold determination within one run. The mean

value was used to compare the expected value with the measured value. All values are within specification.

5.11. Lot Calibration Stability

A set of fifteen K2-EDTA plasma samples covering the measuring range was generated for lot calibration stability testing on a **cobas** e 801 in **cobas pro** integrated solutions. A fresh reagent **cobas** e pack was placed on the analyzer and calibrated. Reference values for the samples tested were determined in two runs and in duplicates at day 0. After 10 weeks, 12 weeks and 14 weeks, a fresh kit (stored at 2-8°C) from the same lot was tested with the same samples, using the calibration established on day 0. Samples were tested in duplicates. Results of the samples at 10, 12, and 14 weeks were compared to the results of the samples at day 0, by calculating the percentage recovery. All samples met the acceptance criteria. The results support the lot calibration stability claim of 12 weeks when using a new Elecsys Phospho-Tau (217P) Plasma reagent kit of the same lot.

5.12. On-Board Calibration Stability

A set of seventeen K2-EDTA plasma samples covering the measuring range was generated for onboard calibration stability testing on a **cobas** e 801 in **cobas pro** integrated solutions. A fresh reagent **cobas** e pack was placed on the analyzer and calibrated. Reference values for the samples tested were determined in two runs and in duplicates at day 0. The same samples were tested in duplicates after 8, 16 and 31 days with the same reagents kept at 10°C +/- 2°C (on-board conditions) using the calibration established on day 0. The mean recovery compared to the mean reference value was determined for all plasma samples using the calibration curve established on day 0. All samples were within specification. The results support the on-board calibration stability claim of 28 days when using the same reagent kit kept in on-board condition.

5.13. Reagent On-Board Stability

Reagent on-board stability for the Elecsys Phospho-Tau (217P) Plasma assay was tested on **cobas** e 801 analyzer. A set of fifteen K2-EDTA plasma samples covering the measuring range was generated for reagent on-board stability testing. A freshly opened reagent **cobas** e pack was placed on the analyzer and calibrated. Reference values for the samples at time point t=0 were measured in two independent runs and with double determination. After 9, 16 and 18 weeks on the **cobas** e 801 in **cobas pro** integrated solutions analyzer (reagent kit kept at 10°C (± 2°C)), frozen aliquots of the same samples were measured again in duplicate with the stressed kit. At

each time point, the stressed kit was calibrated, and the sample concentrations were determined using the respective daily valid calibration curve. The mean recovery compared to the mean reference value (time point 0) was determined for all samples. All samples were within specification. The Elecsys Phospho-Tau (217P) Plasma reagent kits can be stored on-board of the analyzers for up to 16 weeks.

5.14. Reagent Shelf-life Stability

Reagent shelf-life stability of the Elecsys Phospho-Tau (217P) Plasma **cobas** e pack was determined with two reagent lots on a **cobas** e 801 (8000) analyzer and one reagent lot on **cobas** e 801 in **cobas pro** integrated solutions. A set of seven plasma samples covering the measuring range of the Elecsys Phospho-Tau (217P) Plasma assay was generated from native human plasma. To determine a robust reference value at time point t=0, the samples were measured in one or two independent runs and with double determination on a **cobas** e 801 (8000) or a **cobas** e 801 in **cobas pro** integrated solutions. The median value from each sample at t=0 was calculated and set as a reference value. For the subsequent time points a new calibration is established and the samples are determined in one run in duplicates. The kits are continuously stored at 2-8 °C and aliquots of the above-mentioned samples are deep-frozen until the next measurement point. At each timepoint, absolute and relative recovery of the test samples with respect to the initial measurement at t=0 is evaluated. All samples are within specification.

6. EXPECTED VALUES

The reference range was based on results from 167 individuals aged 55 to 80 who showed no signs of cognitive impairment using the Quick Dementia Rating System (QDRS), with a score of zero. For each K2-EDTA sample, the level of pT217p was determined on the cobas e 801 analyzer. The mean, median, 2.5th percentile, and 97.5th percentile of pT217p for the reference population are calculated and listed below.

Assay	Mean (SD) [pg/mL]	Median [pg/mL]	2.5th percentile (90 % CI)	97.5th percentile (90 % CI)
pT217p	0.222 (0.148)	0.176	0.0832 (< 0.056-0.104)	0.628 (0.544-1.21)

Note: *In this reference population, 68.3% of the Elecsys Phospho-Tau (217P) Plasma assay results were equal to or below the lower (rule-out) cutoff (0.223 pg/mL, see above), 8.98% were above the upper (rule-in) cutoff (0.378 pg/mL, see above), and 22.8% fell within the intermediate zone.*

Each laboratory is advised to investigate the transferability of the expected values to its own patient population and, if necessary, to determine its own reference ranges.

The following table reports the reference ranges partitioned by race:

Statistic	White	Black or African American	Asian	Others (including Not Reported)	Overall
N (%)	136 (81.4%)	16 (9.58%)	5 (2.99%)	10 (5.99%)	167 (100%)
Mean (SD) [pg/mL]	0.231 (0.156)	0.172 (0.0781)	0.187 (0.0826)	0.192 (0.129)	0.222 (0.148)
Median [pg/mL]	0.180	0.146	0.192	0.139	0.176
Range [pg/mL]	<0.056 –1.21	<0.056 –0.304	0.0590 –0.276	0.0870 –0.524	<0.056 –1.21
2.5th Percentile [pg/mL]	0.0989	N/A [a]	N/A [a]	N/A [a]	0.0832
97.5th Percentile [pg/mL]	0.642	N/A [a]	N/A [a]	N/A [a]	0.628
N (%) ≤ 0.223 pg/mL	92 (67.6%)	12 (75.0%)	3 (60.0%)	7 (70.0%)	114 (68.3%)
N (%) > 0.223 and ≤ 0.378 pg/mL	30 (22.1%)	4 (25.0%)	2 (40.0%)	2 (20.0%)	38 (22.8%)
N (%) > 0.378 pg/mL	14 (10.3%)	0 (0%)	0 (0%)	1 (10.0%)	15 (8.98%)

[a] Reported as not applicable (N/A) due to insufficient sample size for robust estimation.

The following table reports the reference ranges partitioned by sex:

Statistic	Female	Male	Overall
N (%)	75 (44.9%)	92 (55.1%)	167 (100%)
Mean (SD) [pg/mL]	0.198 (0.112)	0.241 (0.170)	0.222 (0.148)
Median [pg/mL]	0.168	0.197	0.176
Range [pg/mL]	<0.056 –0.595	<0.056 –1.21	<0.056 –1.21
2.5th Percentile [pg/mL]	0.0587	0.0934	0.0832
97.5th Percentile [pg/mL]	0.582	0.828	0.628
N (%) ≤ 0.223 pg/mL	56 (74.7%)	58 (63.0%)	114 (68.3%)
N (%) > 0.223 and ≤ 0.378 pg/mL	14 (18.7%)	24 (26.1%)	38 (22.8%)
N (%) > 0.378 pg/mL	5 (6.67%)	10 (10.9%)	15 (8.98%)

The following table reports the reference ranges partitioned by age groups:

Statistic	55-70 years	71-80 years	Overall
N (%)	123 (73.7%)	44 (26.3%)	167 (100%)
Mean (SD) [pg/mL]	0.198 (0.0956)	0.288 (0.229)	0.222 (0.148)
Median [pg/mL]	0.169	0.204	0.176
Range [pg/mL]	<0.056 –0.646	<0.056 –1.21	<0.056 –1.21
2.5th Percentile [pg/mL]	0.0875	0.0593	0.0832
97.5th Percentile [pg/mL]	0.543	1.17	0.628
N (%) ≤ 0.223 pg/mL	88 (71.5%)	26 (59.1%)	114 (68.3%)
N (%) > 0.223 and ≤ 0.378 pg/mL	29 (23.6%)	9 (20.5%)	38 (22.8%)
N (%) > 0.378 pg/mL	6 (4.88%)	9 (20.5%)	15 (8.98%)

7. CLINICAL PERFORMANCE EVALUATION

The clinical performance of the Elecsys Phospho-Tau (217P) Plasma assay was assessed in a retrospective study (RD007230) using amyloid PET visual read as the reference method. This study utilized samples from two multicenter clinical cohorts: the Roche study RD006263 (APPROACH cohort), and screening samples from the AACI study. The APPROACH cohort enrolled subjects from 16 clinical sites across the US and Europe, representative of primary and secondary/tertiary care settings. Enrolled individuals had cognitive complaints or objective memory impairment of unknown etiology. They were undergoing evaluation for Alzheimer's disease, for other causes of cognitive decline, or to fulfil a required referral for further cognitive

assessment. With the exception of active delirium or encephalopathy, participants with comorbidities were included unless the investigator deemed a condition likely to interfere with study procedures or long-term participation. Study AACI was a phase III clinical trial involving patients at a more advanced stage of disease (mild stages of cognitive impairment or dementia). A sub-set of screening samples from this study, collected at US clinical sites representative of secondary/tertiary care settings, were provided for study RD007230.

In a prior analysis (study RD007216), the Elecsys Phospho-Tau (217P) Plasma assay cutoffs had been established at 0.223 pg/mL and 0.378 pg/mL, with the following cutoff rule:

- If pT217p > 0.378 pg/mL, the test result is positive (high likelihood of amyloid pathology)
- If pT217p > 0.223 pg/mL and ≤ 0.378 pg/mL, the test result is intermediate (indeterminate likelihood of amyloid pathology)
- If pT217p ≤ 0.223 pg/mL, the test result is negative (low likelihood of amyloid pathology)

The cutoffs were validated in an analysis population derived from the current study, which consisted of 958 participants with available amyloid PET scan results (PET tracers: 18F-florbetapir, 18F-florbetaben, or 18F-flutemetamol). The average age in the study population was 71.1 years (range: 55-85 years, median: 72 years), 55 % of patients were females, 45 % of patients were males. In terms of race, 84.7 % were white, 11.5 % were black or African American, 1.57 % were Asian, and 2.19 % identified as other. Regarding ethnicity, 71.2 % of participants were not Hispanic or Latino, 19.6 % were Hispanic or Latino, and for 9.19 % of the participants', information on ethnicity was missing.

The demographic and clinical characteristics of the patients across 4 MMSE subgroups and according to PET scan results are presented in the table below:

	MMSE subgroups				Amyloid PET visual read		
	MMSE 28-30	**MMSE 25-27**	**MMSE 22-24**	**MMSE 20-21**	**Positive**	**Negative**	**All**
	(N = 295, 30.8 %)	**(N = 363, 37.9 %)**	**(N = 227, 23.7 %)**	**(N = 73, 7.62 %)**	**(N = 378, 39.5 %)**	**(N = 580, 60.5 %)**	**(N = 958, 100 %)**
Age [years]							
55 to 70	n = 149 (50.5 %)	n = 157 (43.3 %)	n = 98 (43.2 %)	n = 26 (35.6 %)	n = 108 (28.6 %)	n = 322 (55.5 %)	n = 430 (44.9 %)
71 to 85	n = 146 (49.5 %)	n = 206 (56.7 %)	n = 129 (56.8 %)	n = 47 (64.4 %)	n = 270 (71.4 %)	n = 258 (44.5 %)	n = 528 (55.1 %)
Mean (SD)	69.9 (6.64)	71.4 (6.66)	71.7 (6.61)	72.6 (6.55)	73.6 (5.91)	69.5 (6.65)	71.1 (6.67)
Median	70	72	72	73	74	69	72
Q1-Q3	65-75	67-76	66-77	68-78	70-78	64-75	66-76
Min-Max	55-84	55-85	55-85	56-84	55-85	55-85	55-85
Sex							
Male	n = 136 (46.1 %)	n = 178 (49.0 %)	n = 90 (39.6 %)	n = 27 (37.0 %)	n = 174 (46.0 %)	n = 257 (44.3 %)	n = 431 (45.0 %)
Female	n = 159 (53.9 %)	n = 185 (51.0 %)	n = 137 (60.4 %)	n = 46 (63.0 %)	n = 204 (54.0 %)	n = 323 (55.7 %)	n = 527 (55.0 %)
Race							
White	n = 264 (89.5 %)	n = 295 (81.3 %)	n = 183 (80.6 %)	n = 69 (94.5 %)	n = 363 (96.0 %)	n = 448 (77.2 %)	n = 811 (84.7 %)
Black or African American	n = 21 (7.12 %)	n = 48 (13.2 %)	n = 39 (17.2 %)	n = 2 (2.74 %)	n = 11 (2.91 %)	n = 99 (17.1 %)	n = 110 (11.5 %)
Asian	n = 3 (1.02 %)	n = 10 (2.75 %)	n = 0 (0 %)	n = 2 (2.74 %)	n = 2 (0.529 %)	n = 13 (2.24 %)	n = 15 (1.57 %)
Other	n = 7 (2.37 %)	n = 9 (2.48 %)	n = 5 (2.20 %)	n = 0 (0 %)	n = 1 (0.265 %)	n = 20 (3.45 %)	n = 21 (2.19 %)
Missing	n = 0 (0 %)	n = 1 (0.275 %)	n = 0 (0 %)	n = 0 (0 %)	n = 1 (0.265 %)	n =0 (0 %)	n = 1 (0.104 %)
Ethnicity							
Not Hispanic or Latino	n = 241 (81.7 %)	n = 258 (71.1 %)	n = 132 (58.1 %)	n = 51 (69.9 %)	n = 301 (79.6 %)	n = 381 (65.7 %)	n = 682 (71.2 %)
Hispanic or Latino	n = 20 (6.78 %)	n = 77 (21.2 %)	n = 78 (34.4 %)	n = 13 (17.8 %)	n = 36 (9.52 %)	n = 152 (26.2 %)	n = 188 (19.6 %)
Not reported	n = 1 (0.339 %)	n = 2 (0.551 %)	n = 1 (0.441 %)	n = 1 (1.37 %)	n = 4 (1.06 %)	n = 1 (0.172 %)	n = 5 (0.522 %)
Unknown	n = 0 (0 %)	n = 1 (0.275 %)	n = 0 (0 %)	n = 0 (0 %)	n = 0 (0 %)	n = 1 (0.172 %)	n = 1 (0.104 %)
Missing	n = 33 (11.2 %)	n = 25 (6.89 %)	n = 16 (7.05 %)	n = 8 (11.0 %)	n = 37 (9.79 %)	n = 45 (7.76 %)	n = 82 (8.56 %)

	MMSE subgroups				Amyloid PET visual read		
	MMSE 28-30	**MMSE 25-27**	**MMSE 22-24**	**MMSE 20-21**	**Positive**	**Negative**	**All**
	(N = 295, 30.8 %)	**(N = 363, 37.9 %)**	**(N = 227, 23.7 %)**	**(N = 73, 7.62 %)**	**(N = 378, 39.5 %)**	**(N = 580, 60.5 %)**	**(N = 958, 100 %)**
Body Mass Index (BMI) [kg/m^2]							
Mean (SD)	28.4 (5.75)	27.9 (5.30)	27.9 (5.69)	25.8 (4.94)	26.4 (4.97)	29.0 (5.69)	27.9 (5.55)
Median	27.3	27.1	26.8	25.5	25.6	28.4	27.0
Q1-Q3	24.6-31.3	24.3-30.4	24.3-30.9	22.3-28.7	23.2-28.5	25.0-31.9	24.2-30.6
Min-Max	16.0-48.8	18.5-49.6	16.7-61.4	17.2-45.8	16.0-49.6	17.2-61.4	16.0-61.4
Missing (n, %)	n = 14 (4.75 %)	n = 39 (10.7 %)	n = 13 (5.73 %)	n = 6 (8.22 %)	n = 10 (2.65 %)	n = 62 (10.7 %)	n = 72 (7.52 %)
Mini-Mental State Examination (MMSE)							
Mean (SD)	28.7 (0.794)	26.1 (0.837)	23.1 (0.796)	20.7 (0.478)	24.9 (2.73)	26.3 (2.43)	25.8 (2.63)
Median	28	26	23	21	25	27	26
Q1-Q3	28.0-29.0	25.0-27.0	22.0-24.0	20.0-21.0	23.0-27.0	25.0-28.0	24.0-28.0
Min-Max	28.0-30.0	25.0-27.0	22.0-24.0	20.0-21.0	20.0-30.0	20.0-30.0	20.0-30.0
Education [years]							
Mean (SD)	15.8 (3.47)	15.3 (5.66)	13.9 (4.92)	15.4 (10.2)	15.4 (5.76)	15.0 (5.26)	15.2 (5.46)
Median	16	15	14	14	16	14	15
Q1-Q3	13.0-18.0	12.0-17.0	12.0-16.0	12.0-16.0	12.0-18.0	12.0-17.0	12.0-17.0
Min-Max	7.00-32.0	6.00-76.0	4.00-63.0	0-76.0	0-76.0	4.00-69.0	0-76.0
ApoE4 status [A)]							
Carrier	n = 105 (35.6 %)	n = 138 (38.0 %)	n = 86 (37.9 %)	n = 41 (56.2 %)	n = 253 (66.9 %)	n =117 (20.2 %)	n = 370 (38.6 %)
Non carrier	n = 184 (62.4 %)	n = 218 (60.1 %)	n = 140 (61.7 %)	n = 31 (42.5 %)	n = 119 (31.5 %)	n = 454 (78.3 %)	n = 573 (59.8 %)
Missing (n, %)	n = 6 (2.03 %)	n = 7 (1.93 %)	n = 1 (0.441 %)	n = 1 (1.37 %)	n = 6 (1.59 %)	n = 9 (1.55 %)	n = 15 (1.57 %)
Collection site location							
U.S	n = 262 (88.8 %)	n = 338 (93.1 %)	n = 211 (93.0 %)	n = 65 (89.0 %)	n = 341 (90.2 %)	n = 535 (92.2 %)	n = 876 (91.4 %)
non-U.S.	n = 33 (11.2 %)	n = 25 (6.89 %)	n = 16 (7.05 %)	n = 8 (11.0 %)	n = 37 (9.79 %)	n = 45 (7.76 %)	n = 82 (8.56 %)
Care Setting							
Primary	n = 79 (26.8 %)	n = 101 (27.8 %)	n = 55 (24.2 %)	n = 3 (4.11 %)	n = 51 (13.5 %)	n = 187 (32.2 %)	n = 238 (24.8 %)
Secondary/Tertiary	n = 216 (73.2 %)	n = 262 (72.2 %)	n = 172 (75.8 %)	n = 70 (95.9 %)	n = 327 (86.5 %)	n = 393 (67.8 %)	n = 720 (75.2 %)

A. Based on Elecsys Apolipoprotein E4 (protein) or genotyping

A total of 958 subjects underwent amyloid PET scans using an FDA approved amyloid tracers (18F-Florbetapir, 18F-Florbetaben, or 18F-Flutemetamol). The amyloid PET scans were read independently by 6 trained readers. The readers stem from two different vendors and each image was read by 3 experts from each vendor. Images that were rated positive by at least four readers had a positive majority vote, images that were rated positive by at most 2 readers had a negative majority vote. In cases of a 3-3 split vote (3 positive and 3 negative ratings), a tie-breaking method was established based on reader performance relative to CSF results: in the event of a tie, the reader with the lowest agreement with CSF results (the greatest outlier) was excluded, and the final assessment was determined by the majority vote of the remaining five readers. Final majority voting resulted in 378 (39.5 %) positive and 580 (60.5 %) negative amyloid PET reads. The independent readers were blinded to all clinical information, including the patient's clinical status, diagnosis, and plasma and/or cerebrospinal fluid (CSF) biomarker measurements. Amyloid PET reads were conducted according to the approved instructions for use of the amyloid tracers. Across the full cohort, 20.7 % (n = 198) of images received 6 positive votes, and 50.7 % (n = 486) received 0 positive votes; 6.26 % (n = 60) received 5 positive votes, and 6.47 % (n = 62) received 1 positive vote; 3.86 % (n = 37) received 4 positive votes, and 3.24 % (n = 31) received 2 positive votes; 8.77 % (n = 84) of images received a 3-3 split vote.

The positive percent agreement (PPA) between readers was 83.6 % on average (range: 44.3 % - 100 %), the negative percent agreement (NPA) was 91.3% on average (range: 68.1 % - 100 %), and the Overall Percentage Agreement (OPA) was 87.3 % on average (range: 74.4 % - 96.6 %). The time difference between blood collection and PET imaging exhibited a mean of 37.7 days (SD = 28.9), a median of 30 days, and ranged from -32 to 179 days. Timing was consistent between PET positive (mean = 32.0 days; SD = 24.0; median = 27 days; range: -32 to 139 days) and PET negative (mean = 41.5 days; SD = 31.2; median = 34 days; range: -15 to 179 days) participants.

The predictive values and agreement rates for the Elecsys Phospho-Tau (217P) Plasma assay with amyloid PET visual read in the pivotal clinical trial cohort (prevalence of amyloid pathology at 39.5 %) were as follows:

pT217p Results	Amyloid PET[A)]		Total (n)	Frequency (%)	Positive (%)	Negative (%)	PV[B)]% (95 % CI)	LR[C)] (95 % CI)
	Pos (n)	Neg (n)						
Positive (pT217p > 0.378 pg/mL)	285	37	322	33.6%	75.4%	6.4%	88.5% (84.9% - 91.4%)	11.82 (8.65 - 16.25)
Intermediate (0.223 pg/mL < pT217p ≤ 0.378 pg/mL)	72	119	191	19.9%	19.0%	20.5%	37.7% (31.7% - 44.0%)	0.93 (0.71 - 1.20)
Negative (pT217p ≤ 0.223 pg/mL)	21	424	445	46.5%	5.6%	73.1%	4.7% (3.2% - 6.9%)	0.08 (0.05 - 0.11)
Sum	378	580	958	100%	/	/	/	/

A. PET = positron emission tomography

B. PV = predictive value, 95 % CIs are calculated based on 95 % CI of corresponding likelihood ratio

C. LR = likelihood ratio, 95 % CIs are calculated using an asymptotic method for ratios of two independent binomial proportions

The predictive values and agreement rates for the Elecsys Phospho-Tau (217P) Plasma assay with amyloid PET visual read in the primary (prevalence of amyloid pathology at 21.4 %) and secondary/tertiary (prevalence of amyloid pathology at 45.4 %) care setting subgroups were as follows:

Setting	pT217p Results	Amyloid PET[A)]		Total (n)	Frequency (%)	Positive (%)	Negative (%)	PV[B)]% (95 % CI)	LR[C)] (95 % CI)
		Pos (n)	Neg (n)						
Primary care	Positive (pT217p > 0.378 pg/mL)	36	10	46	19.3%	70.6%	5.3%	78.3% (66.1% - 87.0%)	13.20 (7.16 - 24.62)
	Intermediate (0.223 pg/mL < pT217p ≤ 0.378 pg/mL)	13	34	47	19.7%	25.5%	18.2%	27.7% (17.7% - 39.4%)	1.40 (0.79 - 2.38)
	Negative (pT217p ≤ 0.223 pg/mL)	2	143	145	60.9%	3.9%	76.5%	1.4% (0.4% - 4.5%)	0.05 (0.01 - 0.17)
	Sum	51	187	238	100%	/	/	/	/
Secondary/ tertiary care	Positive (pT217p > 0.378 pg/mL)	249	27	276	38.3%	76.1%	6.9%	90.2% (86.5% - 93.0%)	11.08 (7.72 - 16.06)
	Intermediate (0.223 pg/mL < pT217p ≤ 0.378 pg/mL)	59	85	144	20.0%	18.0%	21.6%	41.0% (34.0% - 48.3%)	0.83 (0.62 - 1.12)
	Negative (pT217p ≤ 0.223 pg/mL)	19	281	300	41.7%	5.8%	71.5%	6.3% (4.2% - 9.4%)	0.08 (0.05 - 0.13)
	Sum	327	393	720	100%	/	/	/	/

A. PET = positron emission tomography

B. PV = predictive value, 95 % CIs are calculated based on 95 % CI of corresponding likelihood ratio

C. LR = likelihood ratio, 95 % CIs are calculated using an asymptotic method for ratios of two independent binomial proportions

The predictive values and agreement rates provided in the table above, in primary care settings, translate into a Positive Predictive Value (PPV) of 78.3% and a Negative Percent Agreement (NPA) of 94.7% for the upper cutoff; as well as a Negative Predictive Value (NPV) of 98.6% and a Positive Percent Agreement (PPA) of 96.1% for the lower cutoff. 19.7% of the results fell into the intermediate range between the two cutoffs. In secondary/tertiary care settings, the values translate into a PPV of 90.2% and a NPA of 93.1% for the upper cutoff; as well as a NPV of 93.7% and a PPA of 94.2% for the lower cutoff. 20.0% of the results fell into the intermediate range between the two cutoffs.

The following table details the clinical performance of the Elecsys Phospho-Tau (217) Plasma assay across different clinical stages, as categorized by Mini- Mental State Examination (MMSE):

MMSE groups	pT217p Results	Amyloid PET[A)]		Total (n)	Frequency (%)	Positive (%)	Negative (%)	PV%[B)]% (95 % CI)	LR[C)] (95 % CI)
		Pos (n)	Neg (n)						
28-30	Positive (pT217p > 0.378 pg/mL)	51	15	66	22.4%	65.4%	6.9%	77.3% (67.3% - 85.0%)	9.46 (5.72 - 15.80)
	Intermediate (0.223 pg/mL < pT217p ≤ 0.378 pg/mL)	21	57	78	26.4%	26.9%	26.3%	26.9% (19.2% - 35.7%)	1.02 (0.66 - 1.54)
	Negative (pT217p ≤ 0.223 pg/mL)	6	145	151	51.2%	7.7%	66.8%	4.0% (1.9% - 7.9%)	0.12 (0.05 - 0.24)
	Sum	78	217	295	100%	/	/	/	/
	Prevalence	26.4%							
25-27	Positive (pT217p > 0.378 pg/mL)	103	11	114	31.4%	73.0%	5.0%	90.4% (84.2% - 94.4%)	14.74 (8.36 - 26.40)
	Intermediate (0.223 pg/mL < pT217p ≤ 0.378 pg/mL)	31	45	76	20.9%	22.0%	20.3%	40.8% (31.4% - 50.7%)	1.08 (0.72 - 1.62)
	Negative (pT217p ≤ 0.223 pg/mL)	7	166	173	47.7%	5.0%	74.8%	4.0% (2.0% - 7.8%)	0.07 (0.03 - 0.13)
	Sum	141	222	363	100%	/	/	/	/
	Prevalence	38.8%							
22-24	Positive (pT217p > 0.378 pg/mL)	84	7	91	40.1%	79.2%	5.8%	92.3% (85.7% - 96.1%)	13.70 (6.86 - 28.16)
	Intermediate (0.223 pg/mL < pT217p ≤ 0.378 pg/mL)	15	15	30	13.2%	14.2%	12.4%	50.0% (34.2% - 65.8%)	1.14 (0.59 - 2.20)
	Negative (pT217p ≤ 0.223 pg/mL)	7	99	106	46.7%	6.6%	81.8%	6.6% (3.3% - 12.3%)	0.08 (0.04 - 0.16)
	Sum	106	121	227	100%	/	/	/	/
	Prevalence	46.7%							

MMSE groups	pT217p Results	Amyloid PET[A)]		Total (n)	Frequency (%)	Positive (%)	Negative (%)	PV%[B)]% (95 % CI)	LR[C)] (95 % CI)
		Pos (n)	Neg (n)						
<22	Positive (pT217p > 0.378 pg/mL)	47	4	51	69.9%	88.7%	20.0%	92.2% (84.8% - 96.7%)	4.43 (2.11 - 11.04)
	Intermediate (0.223 pg/mL < pT217p ≤ 0.378 pg/mL)	5	2	7	9.6%	9.4%	10.0%	71.4% (38.4% - 91.5%)	0.94 (0.24 - 4.07)
	Negative (pT217p ≤ 0.223 pg/mL)	1	14	15	20.5%	1.9%	70.0%	6.7% (1.2% - 27.9%)	0.03 (0.00 - 0.15)
	Sum	53	20	73	100%	/	/	/	/
	Prevalence	72.6%							

A. PET = positron emission tomography

B. PV = predictive value, 95 % CIs are calculated based on 95 % CI of corresponding likelihood ratio

C. LR = likelihood ratio, 95 % CIs are calculated using an asymptotic method for ratios of two independent binomial proportions

The Elecsys Phospho-Tau (217P) Plasma clinical performance stratified by sex is summarized in the table below:

Sex	pT217p Results	Amyloid PET[A)]		Total (n)	Frequency (%)	Positive (%)	Negative (%)	PV[B)]% (95 % CI)	LR[C)] (95 % CI)
		Pos (n)	Neg (n)						
Male	Positive (pT217p > 0.378 pg/mL)	122	22	144	33.4%	70.1%	8.6%	84.7% (78.8% - 89.3%)	8.19 (5.48 - 12.39)
	Intermediate (0.223 pg/mL < pT217p ≤ 0.378 pg/mL)	40	64	104	24.1%	23.0%	24.9%	38.5% (30.6% - 46.7%)	0.92 (0.65 - 1.30)
	Negative (pT217p ≤ 0.223 pg/mL)	12	171	183	42.5%	6.9%	66.5%	6.6% (3.9% - 10.7%)	0.10 (0.06 – 0.18)
	Sum	174	257	431	100%	/	/	/	/
	Prevalence	40.3%							
Female	Positive (pT217p > 0.378 pg/mL)	163	15	178	33.8%	79.9%	4.6%	91.6% (87.0% - 94.7%)	17.21 (10.57 - 28.32)
	Intermediate (0.223 pg/mL < pT217p ≤ 0.378 pg/mL)	32	55	87	16.5%	15.7%	17.0%	36.8% (28.1% - 46.3%)	0.92 (0.62 - 1.36)
	Negative (pT217p ≤ 0.223 pg/mL)	9	253	262	49.7%	4.4%	78.3%	3.4% (1.8% - 6.2%)	0.06 (0.03 - 0.10)
	Sum	204	323	527	100%	/	/	/	/
	Prevalence	38.7%							

A. PET = positron emission tomography

B. PV = predictive value, 95 % CIs are calculated based on 95 % CI of corresponding likelihood ratio

C. LR = likelihood ratio, 95 % CIs are calculated using an asymptotic method for ratios of two independent binomial proportions

The Elecsys Phospho-Tau (217P) Plasma clinical performance stratified by age group is summarized in the table below:

Age	pT217p Results	Amyloid PET[A)]		Total (n)	Frequency (%)	Positive (%)	Negative (%)	PV[B)]% (95 % CI)	LR[C)] (95 % CI)
		Pos (n)	Neg (n)						
55 to 70 years	Positive (pT217p > 0.378 pg/mL)	76	12	88	20.5%	70.4%	3.7%	86.4% (78.4% - 91.8%)	18.88 (10.84 - 33.21)
	Intermediate (0.223 pg/mL < pT217p ≤ 0.378 pg/mL)	25	59	84	19.5%	23.1%	18.3%	29.8% (21.8% - 38.8%)	1.26 (0.83 - 1.89)
	Negative (pT217p ≤ 0.223 pg/mL)	7	251	258	60.0%	6.5%	78.0%	(1.3% - 5.2%)	0.08 (0.04 - 0.16)
	Sum	108	322	430	100%	/	/	/	/
	Prevalence	25.1%							
71 to 85 years	Positive (pT217p > 0.378 pg/mL)	209	25	234	44.3%	77.4%	9.7%	89.3% (85.3% - 92.4%)	7.99 (5.53 - 11.70)
	Intermediate (0.223 pg/mL < pT217p ≤ 0.378 pg/mL)	47	60	107	20.3%	17.4%	23.3%	43.9% (35.8% - 52.4%)	0.75 (0.53 - 1.05)
	Negative (pT217p ≤ 0.223 pg/mL)	14	173	187	35.4%	5.2%	67.1%	7.5% (4.6% - 11.8%)	0.08 (0.05 - 0.13)
	Sum	270	258	528	100%	/	/	/	/
	Prevalence	51.1%							

A. PET = positron emission tomography

B. PV = predictive value, 95 % CIs are calculated based on 95 % CI of corresponding likelihood ratio

C. LR = likelihood ratio, 95 % CIs are calculated using an asymptotic method for ratios of two independent binomial proportions

The Elecsys Phospho-Tau (1217P) Plasma clinical performance stratified by race is summarized in the table below:

Race	pT217p Results	Amyloid PET[A)]		Total Frequency (n)	Frequency (%)	Positive (%)	Negative (%)	PV[B)]% (95 % CI)	LR[C)] (95 % CI)
		Pos (n)	Neg (n)						
White	Positive (pT217p > 0.378 pg/mL)	276	31	307	37.9%	76.0%	6.9%	89.9% (86.4% - 92.6%)	10.99 (7.83 - 15.53)
	Intermediate (0.223 pg/mL < pT217p ≤ 0.378 pg/mL)	69	97	166	20.5%	19.0%	21.7%	41.6% (35.0% - 48.3%)	0.88 (0.67 - 1.15)
	Negative (pT217p ≤ 0.223 pg/mL)	18	320	338	41.7%	5.0%	71.4%	5.3% (3.4% - 8.1%)	0.07 (0.04 - 0.11)
	Sum	363	448	811	100%	/	/	/	/
	Prevalence	44.8%							
Asian	Positive (pT217p > 0.378 pg/mL)	1	0	1	6.7%	50.0%	0.0%	100.0% (21.7% - 100.0%)	Inf (1.81 - inf)
	Intermediate (0.223 pg/mL < pT217p ≤ 0.378 pg/mL)	1	3	4	26.7%	50.0%	23.1%	25.0% (5.1% - 56.3%)	2.17 (0.35 – 8.37)
	Negative (pT217p ≤ 0.223 pg/mL)	0	10	10	66.7%	0.0%	76.9%	0.0% (0.0% - 12.4%)	0.00 (0.00 - 0.92)
	Sum	2	13	15	100%	/	/	/	/
	Prevalence	13.3%							

Race	pT217p Results	Amyloid PET[A)]		Total Frequency (n)	Frequency (%)	Positive (%)	Negative (%)	PV[B)]% (95 % CI)	LR[C)] (95 % CI)
		Pos (n)	Neg (n)						
Black or African - American	Positive (pT217p > 0.378 pg/mL)	6	5	11	10.0%	54.5%	5.1%	54.5% (30.2% - 75.7%)	10.80 (3.89 - 28.05)
	Intermediate (0.223 pg/mL < pT217p ≤ 0.378 pg/mL)	2	17	19	17.3%	18.2%	17.2%	10.5% (3.1% - 25.9%)	1.06 (0.28 - 3.15)
	Negative (pT217p ≤ 0.223 pg/mL)	3	77	80	72.7%	27.3%	77.8%	3.8% (1.4% - 7.6%)	0.35 (0.12 - 0.74)
	Sum	11	99	110	100%	/	/	/	/
	Prevalence	10.0%							
Other	Positive (pT217p > 0.378 pg/mL)	1	1	2	9.5%	100.0%	5.0%	50.0% (10.7% - 84.9%)	20 (2.40 - 112.59)
	Intermediate (0.223 pg/mL < pT217p ≤ 0.378 pg/mL)	0	2	2	9.5%	0.0%	10.0%	0.0% (0.0% - 45.0%)	0 (0.00 - 16.37)
	Negative (pT217p ≤ 0.223 pg/mL)	0	17	17	81.0%	0.0%	85.0%	0.0% (0.0% - 4.6%)	0 (0.00 - 0.96)
	Sum	1	20	21	100%	/	/	/	/
	Prevalence	4.8%							

A. PET = positron emission tomography

B. PV = predictive value, 95 % CIs are calculated based on 95 % CI of corresponding likelihood ratio

C. LR = likelihood ratio, 95 % CIs are calculated using an asymptotic method for ratios of two independent binomial proportions

The Elecsys Phospho-Tau (217P) Plasma clinical performance stratified by selected comorbidities (from most to least common) is summarized in the table below.

pT217p	**Types of Comorbidities** N (%Total)					
	Cardiovascular disease [C] N=500 (52.2%)	Hypertension N=475 (49.6%)	Vision loss N=312 (32.6%)	Depression N=258 (26.9%)	Obesity [D] N=258 (26.9%)	Metabolic conditions [E] N=228 (23.8%)
Positive PV [A] [n/N] (95% CI)	88.2% [157/178] (83.2%, 91.9%)	87.6% [149/170] (82.5%, 91.5%)	80.2% [65/81] (71.6%, 86.9%)	92.5% [99/107] (86.6%, 96.0%)	84.1% [37/44] (71.8%, 91.7%)	88.5% [69/78] (80.6%, 93.6%)
Intermediate PV [A] [n/N] (95% CI)	36.2% [34/94] (27.9%, 45.2%)	36.0% [32/89] (27.5%, 45.2%)	21.5% [14/65] (13.7%, 31.4%)	36.4% [16/44] (24.6%, 49.8%)	30.2% [16/53] (20.4%, 41.3%)	41.0% [16/39] (28.1%, 55.1%)
Negative PV [A] [n/N] (95% CI)	4.8% [11/228] (2.8%, 8.1%)	5.1% [11/216] (2.9% - 8.6%)	3.6% [6/166] (1.7%, 7.2%)	4.7% [5/107] (2.1%, 10.0%)	3.7% [6/161] (1.8%, 7.3%)	3.6% [4/111] (1.4%, 8.4%)
LR+ [B] (95% CI)	11.03 (7.33, 16.80)	10.46 (6.95, 15.93)	10.85 (6.75, 17.67)	14.23 (7.44, 27.94)	17.83 (8.60, 37.43)	11.97 (6.47, 22.71)
LR- [B] (95% CI)	0.07 (0.04, 0.13)	0.08 (0.04, 0.14)	0.10 (0.05 - 0.21)	0.06 (0.02 - 0.13)	0.13 (0.06, 0.26)	0.06 (0.02, 0.14)
Prevalence [n/N]	40.4% [202/500]	40.4% [192/475]	27.2% [85/312]	46.5% [120/258]	22.9% [59/258]	39.0% [89/228]
Frequency of Intermediate [n/N]	18.8% [94/500]	18.7% [89/475]	20.8% [65/312]	17.1% [44/258]	20.5% [53/258]	17.1% [39/228]

A) PV = predictive value, 95 % CIs are calculated based on 95 % CI of corresponding likelihood ratio

B) LR+ = positive likelihood ratio, LR- = negative likelihood ratio. 95 % CIs are calculated using an asymptotic method for ratios of two independent binomial proportions

C) Cardiovascular disease was classified as present when at least one of the following conditions were present: Atrial fibrillation, hypertension, cardiac failure, coronary artery disease.

D) Classification based on Body Mass Index (BMI): BMI ≥ 30 is considered obese.

E) Excluding diabetes

Stratification by selected comorbidities continued

pT217p	Types of Comorbidities N (%Total)				
	Hearing loss N=180 (18.8%)	Diabetes N=171 (17.8%)	Sleep apnea syndrome N=139 (14.5%)	Cancer N=97 (10.1%)	Kidney disease N=24 (2.5%)
Positive PV [A] [n/N] (95% CI)	84.1% [53/63] (74.8%, 90.7%)	81.6% [31/38] (68.4%, 90.2%)	83.8% [31/37] (70.7%, 92.0%)	80.0% [20/25] (63.4%, 90.5%)	100.0% [3/3] (46.5%, 100.0%)
Intermediate PV [A] [n/N] (95% CI)	41.7% [20/48] (30.3%, 53.6%)	23.8% [10/42] (14.2%, 35.9%)	50.0% [16/32] (35.4%, 64.3%)	36.0% [9/25] (21.7%, 52.2%)	0.0% [0/7] (0.0%, 24.6%)
Negative PV [A] [n/N] (95% CI)	4.3% [3/69] (1.5%, 11.3%)	2.2% [2/91] (0.6%, 7.0%)	5.7% [4/70] (2.3%, 12.6%)	6.4% [3/47] (2.3%, 15.2%)	7.1% [1/14] (1.4%, 19.5%)
LR+ [B] (95% CI)	7.25 (4.06, 13.35)	13.18 (6.45, 27.51)	8.92 (4.16, 19.73)	8.13 (3.53, 19.42)	Inf (4.34, Inf)
LR- [B] (95% CI)	0.06 (0.02 - 0.17)	0.07 (0.02, 0.22)	0.10 (0.04 - 0.25)	0.14 (0.05, 0.36)	0.38 (0.07, 1.21)
Prevalence [n/N]	42.2% [76/180]	25.1% [43/171]	36.7% [51/139]	33.0% [32/97]	16.7% [4/24]
Frequency of Intermediate [n/N]	26.7% [48/180]	24.6% [42/171]	23.0% [32/139]	25.8% [25/97]	29.2% [7/24]

A) PV = predictive value, 95 % CIs are calculated based on 95 % CI of corresponding likelihood ratio

B) LR+ = positive likelihood ratio, LR- = negative likelihood ratio. 95 % CIs are calculated using an asymptotic method for ratios of two independent binomial proportions

Stratification by number of comorbidities

pT217p	Number of Comorbidities N (%Total)		
	One N=76 (7.9%)	Two N=118 (12.3%)	Three or More N=628 (65.6%)
Positive PV [A] [n/N] (95% CI)	94.4% [17/18] (76.0%, 99.0%)	88.6% [31/35] (75.8%, 95.2%)	90.2% [220/244] (86.2%, 93.1%)
Intermediate PV [A] [n/N] (95% CI)	63.6% [7/11] (37.2%, 83.9%)	36.0% [9/25] (21.4%, 52.9%)	37.4% [46/123] (30.0%, 45.3%)
Negative PV [A] [n/N] (95% CI)	8.5% [4/47] (3.6%, 17.1%)	1.7% [1/58] (0.3%, 8.3%)	5.7% [15/261] (3.6%, 9.0%)
LR+ [B] (95% CI)	29.14 (5.42, 167.26)	14.55 (5.88, 37.58)	11.32 (7.72, 16.76)
LR- [B] (95% CI)	0.16 (0.06, 0.35)	0.03 (0.01, 0.17)	0.08 (0.05, 0.12)
Prevalence [n/N]	36.8% [28/76]	34.7% [41/118]	44.7% [281/628]
Frequency of Intermediate [n/N]	14.5% [11/76]	21.2% [25/118]	19.6% [123/628]

A) PV = predictive value, 95 % CIs are calculated based on 95 % CI of corresponding likelihood ratio

B) LR+ = positive likelihood ratio, LR- = negative likelihood ratio. 95 % CIs are calculated using an asymptotic method for ratios of two independent binomial proportions

8. SUBSTANTIAL EQUIVALENCE SUMMARY

The in vitro electrochemiluminescence immunoassay, Elecsys Phospho-Tau (217P) Plasma, is substantially equivalent to the Chemiluminescent Enzyme Immunoassay, Lumipulse ***G*** pTau217/ß-Amyloid 1-42 Plasma Ratio. Both test systems measure pTau 217 in plasma specimens and are intended as an aid in identifying adult subjects with amyloid pathology presenting with signs, symptoms, or complaints of cognitive decline associated with Alzheimer's disease. The data for Elecsys Phospho-Tau (217P) Plasma immunoassay demonstrate substantially equivalent rule in and rule out performance compared to Lumipulse ***G*** pTau217/ß-Amyloid 1-42 Plasma Ratio.

The Elecsys Phospho-Tau (217P) Plasma immunoassay is as safe and effective as Lumipulse ***G*** pTau217/ß-Amyloid 1-42 Plasma Ratio.

9. CONCLUSIONS

A comparison of the device regulation designations, the intended use, the technological characteristics, and the clinical performance demonstrates that the Elecsys Phospho-Tau (217P) Plasma is substantially equivalent (SE) to the predicate device. The candidate device is as safe and effective as the predicate device.