ADNI Alzheimer's Disease Neuroimaging Initiative

# ADNI3 second BATCH CSF analyses of $A\beta_{1-42}$, $A\beta_{1-40}$, t-tau and p-$tau_{181}$ using the automated Roche Elecsys and cobas e 601 immunoassay analyzer system

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## Introduction

The second batch analysis of ADNI3 CSF samples included a total of 228 aliquot samples from ADNI3 and ADNI DOD participants.

## Summary

A total of 228 pristine aliquots of CSF, collected from ADNI3 and DOD (n=12) participants, were analyzed by the electrochemiluminescence immunoassays (ECLIA) Elecsys β-Amyloid(1-42) CSF, β-Amyloid(1-40) CSF, Phospho-Tau(181P) CSF, and Total-Tau CSF on a fully automated Elecsys **cobas e** 601 instrument and a single lot of reagents for each of the 4 measured biomarkers (provided in "UPENNBIOMK12_2020" .CSV file). These immunoassays are for investigational use only in the USA. They are currently under development by Roche Diagnostics and not commercially available yet. Included in this report are summaries for precision performance and lot-to-lot performance for these analytes (Figure 1 and Figure 2).

## Method

The Roche Elecsys β-Amyloid(1-42) CSF, Elecsys β-Amyloid(1-40) CSF, Elecsys Total-Tau CSF, and Elecsys Phospho-Tau(181P) CSF immunoassays were used following a Roche Study Protocol at the UPenn/ADNI Biomarker Laboratory, according to the preliminary kit manufacturer's instructions and as described in previous studies (1-3). Analyses were performed in a series of 3 runs, each sample run one time (in singlicate) for each of the 4 biomarker tests, over the time period of August 20, 2020 through August 25, 2020 following a standard new lot rollover protocol from the manufacturer over a 10 working day timeline that involved repeated analyses of quality control samples. Acceptance criteria as documented according to the Roche Protocol in the UPenn/ADNI Biomarker Laboratory were followed for these analyses.

In each of the 3 days of performing analyses, quality control results were within stated limits to meet acceptance criteria for precision and accuracy.

The analyte measuring ranges were, lower technical limit to upper technical limit for each biomarker: 200 to 1700 pg/mL for the Elecsys β-Amyloid (1-42) CSF immunoassay, 11 to 40,300 pg/mL for the Elecsys β-Amyloid (1-40) CSF immunoassay, 80 to 1300 pg/mL for the Elecsys Total-Tau CSF immunoassay and 8 to 120 pg/mL for the Elecsys Phospho-Tau (181P) CSF immunoassay. For results that are above the upper technical limit, the result is stated as ">" the respective upper technical limit values or if below the lower technical limit, the result is stated as "<" the respective lower technical limit value in the .CSV file "UPENNBIOMK12_2020".

The following is a brief description of the analytical performance results (Figure1 and Figure 2): %CVs based on a normal and an abnormal CSF pool run throughout the 3 analytical runs ranged from 0.47 to 0.76% for t-tau, 0.39 to 0.48% for p-tau181, from 0.85 to 4.14% for Aβ42 and from 1.83 to 2.26% for Aβ40 (Figure 1). These precision results are consistent with our expectation using this highly automated system. We evaluated lot-to-lot performances for Aβ42, t-tau and p-tau181 and determined acceptable results for each of these 4 analytes, with linear regression slopes within 10% of 1.0 for between-lot variance (Figure 2). The linear regression analyses in the form of equations {Y(2020 results) = m*X(prior results on pristine replicate aliquots) + Y intercept}(see Figure 1) were: Y=1.014X + 29.25 and $R^2$=0.882 for Aβ42; Y=0.907X + 1964 and $R^2$=0.981 for Aβ40; Y=0.963X + 5.767 and $R^2$=0.993 for t-tau; Y=0.961X-0.694 and $R^2$=0.996 for p-tau181.
Exploratory Elecsys β-Amyloid(1-42) CSF immunoassay measurement results above the technical limit of 1700 pg/mL have been provided by Roche Diagnostics based on an extrapolation of the calibration curve. Thus all results above 1700 pg/mL for Aβ42 in the .CSV file "UPENNBIOMK12_2020" were obtained by extrapolation.

Please note:

The Elecsys β-Amyloid(1-42) CSF immunoassay in use is not a commercially available IVD assay. It is an assay that is currently under development and for investigational use only. The measuring range of the assay is 200 (lower technical limit) – 1700 pg/mL (upper technical limit). The performance of the assay beyond the upper technical limit has not been formally established. Therefore use of values above the upper technical limit, which are provided based on an extrapolation of the calibration curve, is restricted to exploratory research purposes and is excluded for clinical decision making or for the derivation of medical decision points.

Investigators should include the above disclaimer in any publication using Elecsys b-Amyloid(1-42) CSF immunoassay values above the upper technical limit.
It should also be noted that values above the measuring range for a particular sample may differ from concentration values measured by any potential future Elecsys b-Amyloid (1-42) CSF immunoassay assay.
As part of the validation process for the Ab1-42 test method, Roche conducted collaborative studies of comparisons between the Elecsys b-Amyloid (1-42) CSF immunoassay and two reference methods (4,5) certified by the Joint Committee for Traceability in Laboratory Medicine (JCTLM) (1-5).

Figure 1. Precision performance for Roche Elecsys immunoassays for A42, A40, t-tau and p-tau181.

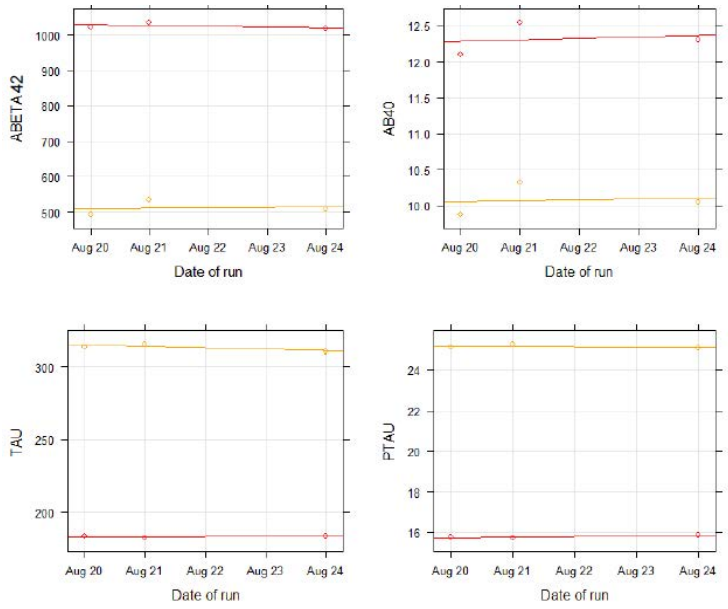
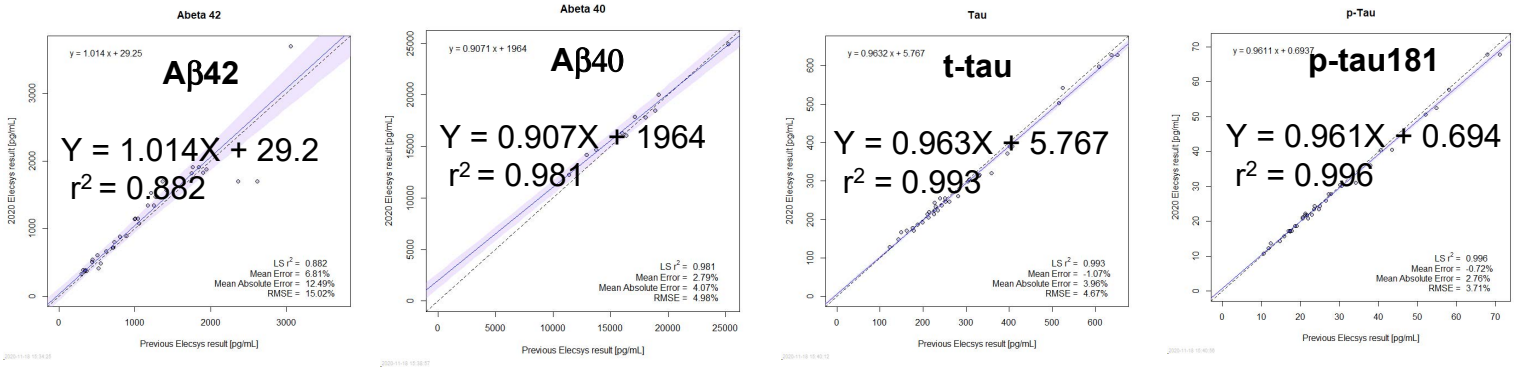



Figure2. Lot-to-lot performance for Roche Elecsys immunoassays for Aβ42, Aβ40, t-tau and p-tau181 (see text for more details).



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