Statistical Analysis Plan

for

DCT216

Linus Health, Inc.

A Randomized Crossover Study to Assess the Reliability and Equivalence of Alternate Forms of the Digital Clock Drawing Test

DCT216

Version 1.0, 23JUL2021

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SIGNATURE PAGE

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Document History

Revision Date	Author	Version	Reason for Change
27MAY2021	Marisa Massaro	0.1	NA – Initial Version
02JUN2021	Marisa Massaro	0.2	Updated signature page and number of sites from 1-3 to 2
19JUL2021	Marisa Massaro	0.3	Updated based on sponsor initial round of comments
20JUL2021	Timothy Helbig	0.4	Added/modified primary effectiveness analyses, exploratory analyses and figure shells. Primary analysis population was changed from the Validation Population to the Evaluable Population given no initial training of a new tablet model will be done
19JUL2021	Marisa Massaro	1.0	Updating formatting

1 ABBREVIATIONS

Abbreviation	Definition
AE	Adverse Event
ANOVA	Analysis of Variance
CI	Confidence Intervals
CRF	Case Report Forms
CSR	Clinical Study Report
ICC	Intraclass Correlation Coefficient
ITT	Intent-To-Treat Population
LoA	Limits of Agreement
MMSE	Mini-Mental State Exam
RBANS	Repeatable Battery for the Assessment of Neuropsychological Status
RMSD	Root Mean Squared Difference
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
TEAE	Treatment Emergent Adverse Event

2 SUMMARY

TITLE	A Randomized Crossover Study to Assess the Reliability and Equivalence of Alternate Forms of the Digital Clock Drawing Test
PREFACE	This Statistical Analysis Plan (SAP) describes the planned analysis and reporting for Linus Health, Inc. protocol DCT216 (A Randomized Crossover Study to Assess the Reliability and Equivalence of Alternate Forms of the Digital Clock Drawing Test). This study is being completed to assess the safety and effectiveness of DCTclock in healthy adults aged 55-95. The following documents were reviewed in preparation of this SAP: ● Clinical Research Protocol DCT216 Version 3 issued 12OCT2020 ● Case report forms (CRFs) issued 18NOV2020 for Protocol DCT216
PURPOSE	The purpose of this SAP is to outline the planned analyses in support of the Clinical Study Report (CSR) for protocol DCT216. Exploratory analyses not necessarily identified in this SAP may be performed to support the clinical development program. Any post-hoc, or unplanned, analyses not identified in this SAP will be clearly identified in the respective CSR.
STUDY OBJECTIVES	The overall objectives of the study are to establish the equivalence of DCTclock-tablet to DCTclock-pen, to establish the safety of Linus Platform tests administered with a tablet or smartphone, and to collect data to enable the development and validation of Linus Platform tests. Aim 1: Validate equivalence between DCTclock-pen and DCTclock-tablet for subjects with diverse levels of cognitive impairment Aim 2: Characterize the safety profile of DCTclock-tablet and other Linus Platform tests Aim 3: Obtain data to develop and validate Linus Platform tests
STUDY DESIGN	Randomized crossover trial consisting of two test visits separated by a washout period of 3 to 5 weeks. Subjects are randomized into two equal groups. Group 1 receives the digital pen (DCTclock-pen) version of the test at the first visit, with the tablet version (DCTclock-tablet) given at the second visit; Group 2 receives DCTclock-tablet at the first visit, followed by DCTclock-pen at the second visit. At Visit 1 (Day 0), eligibility is assessed and a version of the DCTclock test is administered based on the group allocation. A battery of Linus Platform tests and reference standard tests are also administered. At Visit 2 (Day 21-35), eligibility is assessed and the alternate version of the DCTclock test is administered based on the group allocation. A battery of Linus Platform tests is also administered, together with reference standard tests. Equivalence of DCTclock-pen and DCTclock-tablet will be tested. Linus Platform test data will also be collected to develop novel measures of cognitive and motor function and assess their accuracy in detecting impairment, construct validity, and test-retest

	reliability. 200 subjects will be recruited to participate with the anticipation that 175 will be available for analysis.
ENDPOINTS AND ANALYSIS	The study's **primary effectiveness endpoint** analysis is assessing the equivalence of DCTclock-pen and DCTclock-tablet with respect to cognitive impairment specifically by comparing the DCTclock total score (created by the DCTclock analysis algorithm) from the DCTclock-pen to the DCTclock total score from the DCTclock-tablet. The study's **primary safety endpoint** analysis is the incidence of subjects with serious device-related adverse events from enrollment to completion of the study. **Secondary endpoints' analyses:** ● Agreement of DCTclock-pen and DCTclock-tablet in assessing cognitive impairment specifically by comparing each of the DCTclock composite scales (created by the DCTclock analysis algorithm) from the DCTclock-pen to the DCTclock composite scales from the DCTclock tablet. The composite scales are as follows ○ Drawing Efficiency ○ Information Processing ○ Simple and Complex Motor ○ Spatial Reasoning **Exploratory endpoints analyses:** ● Linus Platform individual tests will be compared to Mini-Mental State Exam (MMSE) and Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) to measure agreement in assessment of cognitive status in the evaluable dataset. The list of Linus platform individual tests are as follows: ○ Linus Platform drawing tests ▪ Pre-test ▪ Pathfinding test ▪ Symbol test ▪ Connect test ▪ Tracing test ○ Linus Platform decision making and reaction time tests ▪ Simple reaction time ▪ Procedural reaction time ▪ Go/No-go ▪ PHQ-9 ○ Linus Platform speech elicitation tasks ▪ Complex picture description ▪ Category naming ▪ Object recall ▪ Sentence reading

	▪ Sustained phonation ▪ Diadochokinetic rate ▪ Story recall ▪ List learning ○ Linus Platform eye tracking-based memory assessments ○ Linus Platform gait and balance assessment ○ Linus Platform lifestyle questionnaire ● Subjects will undergo cognitive testing with both the Linus Platform tests and the reference standard RBANS twice, where the second examination will be three to five weeks after the first examination. Linus Platform individual tests will be combined to obtain a Linus overall score (Linus score) to measure cognitive status and its agreement with MMSE and RBANS will be assessed. ● Test-retest reliability of both individual Linus Platform tests and the combined Linus score will be compared to the test-retest reliability of the RBANS.
INTERIM ANALYSES	No formal interim analyses are planned for this study.
FINAL ANALYSES	All final planned analyses identified in this SAP will be completed following the final visit (or discharge) of the last enrolled subject.

3 Study Objectives and Endpoints

3.1 Study Objectives

The objectives of the study are to establish the equivalence of DCTclock-tablet to DCTclock-pen, to establish the safety of DCTclock-tablet and Linus Platform tests administered with a tablet or smartphone, and to collect the data to enable the development and validation of Linus Platform tests

3.2 Study Endpoints

3.2.1 Primary Endpoints

The study's **primary effectiveness endpoint** analysis is the equivalence of DCTclock-pen and DCTclock-tablet in assessing cognitive impairment specifically by comparing the DCTclock total score (created by the DCTclock analysis algorithm) from the DCTclock-pen to the DCTclock total score from the DCTclock-tablet.

The study's **primary safety endpoint** analysis is the incidence of subjects with serious device-related adverse events from enrollment to completion of the study.

3.2.2 Secondary Endpoints

Agreement of DCTclock-pen and DCTclock-tablet in assessing cognitive impairment specifically by comparing each of the DCTclock composite scales (created by the DCTclock analysis algorithm) for the

DCTclock-pen to the DCTclock composite scales from the DCTclock tablet. The composite scales are as follows

- Drawing Efficiency
- Information Processing
- Simple and Complex Motor
- Spatial Reasoning

3.2.3 *Exploratory Endpoints*

Linus Platform individual tests will be compared to Mini-Mental State Exam (MMSE) and Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) to measure agreement in assessment of cognitive status in the evaluable dataset. The list of Linus platform individual tests are as follows:

- Linus Platform drawing tests
  - Pre-test
  - Pathfinding test
  - Symbol test
  - Connect test
  - Tracing test
- Linus Platform decision making and reaction time tests
  - Simple reaction time
  - Procedural reaction time
  - Go/No-go
  - PHQ-9
- Linus Platform speech elicitation tasks
  - Complex picture description
  - Category naming
  - Object recall
  - Sentence reading
  - Sustained phonation
  - Diadochokinetic rate
  - Story recall
  - List learning
- Linus Platform eye tracking-based memory assessments
- Linus Platform gait and balance assessment
- Linus Platform lifestyle questionnaire

Linus Platform individual tests will be combined to obtain a Linus overall score (Linus score) to measure cognitive status and its agreement with MMSE and RBANS will be assessed.

Subjects will undergo cognitive testing with both the Linus Platform tests and the reference standard RBANS twice, where the second examination will be three to five weeks after the first examination. Test-retest reliability of both individual Linus Platform tests and the combined Linus score will be compared to the test-retest reliability of the RBANS.

4 Sample Size

The primary null and alternative hypotheses are:

H0: $LCI_{LLoA} \leq -\delta \; or \; UCI_{ULoA} \geq \delta$

H1: $-\delta < LCI_{LLoA} < UCI_{ULoA} < \delta$

where δ = 30 is the pre-specified maximum allowable difference, LCI_{LLoA} is the lower bound of the two-sided 95% confidence interval (CI) for the lower bound of the two-sided 95% limits of agreement (LoA), UCI_{ULoA} is the upper bound of the two-sided 95% CI for the upper bound of the two-sided 95% LoA.

The primary endpoint will be analyzed using Bland-Altman method. This study will produce LoA and associated CIs from the two measurements on each subject (further details are below). The conclusion that the two measurements are in agreement (i.e. equivalent) depends on whether the CIs constructed from the data are within the boundaries set from the maximum allowable difference. An evaluable sample size of 41 subjects achieves at least 90% power to detect agreement when the confidence level of the LoA is 95%, the confidence level of the CIs about the LoA is 95%, and the maximum allowable difference is 30 (δ = 30). The mean and standard deviation of the sample differences are anticipated to be 10 and 7, respectively.

Accordingly, approximately 175 subjects will be enrolled in order to obtain a DCTclock-tablet training dataset of at least 100 subjects and a DCTclock-tablet validation dataset of greater than 41 evaluable subjects.

5 Sequence of Planned Analyses

5.1 Interim Analyses

There are no planned Interim Analyses for this study.

5.2 Final Analyses and Reporting

All final, planned, analyses identified in the protocol and in this SAP will be performed after the last subject has completed their final visit and the database is locked. Key statistics and study results will be made available following database lock and statistical analysis on the locked database. Any post-hoc, exploratory analyses completed to support planned study analyses, which were not identified in this SAP, will be documented, and reported as necessary. Any results from these unplanned analyses will also be clearly identified as post-hoc analyses.

6 Analysis Populations

6.1 Intent to Treat Population (ITT)

The intent-to-treat (ITT) population for this study includes all enrolled subjects. Subjects are considered enrolled in the trial after they have signed the informed consent form and are not screening failures.

6.2 Evaluable Population

The evaluable population for this study includes all ITT subjects who undergo cognitive testing with both DCTclock-pen and DCT-clock table and the Linus Platform tests. Given that no initial tablet model needs to be trained, the evaluable population is the primary analysis population for effectiveness.

6.3 Validation Population

The validation population is a randomly selected subset of 50 subjects from the evaluable population. If there is a need to train a tablet specific model, this will become the primary population for evaluating effectiveness.

6.4 Training Population

The training population consists of subjects from the evaluable population that were not selected for the validation population.

6.5 Safety Population

The safety population includes all ITT subjects who undergo cognitive testing with DCTclock (DCTclock-pen and/or DCTclock-tablet) and/or the Linus Platform tests. The safety population is the primary analysis population for safety.

7 General Issues for Statistical Analysis

Descriptive statistics (mean, standard deviation, frequencies, etc.) for baseline subject characteristics, subject disposition and other relevant study parameters will be reported.

7.1 Analysis Software

Analysis data sets, statistical analyses and associated output generated by Linus Health will be generated using R version 4.1.

7.2 Disposition of Subjects and Withdrawals

All subjects who were screened will be accounted for. The number of subjects who were screened, eligible, in the ITT Population, in the Evaluable Population, in the Validation Population, in the Training Population, and in the Safety Population will be presented by randomized group (tablet-pen vs. pen-tablet) and overall (both randomized groups combined). The number and percent of ITT subjects who attended visit 1 and who attended visit 2 will be presented by randomized group and overall. This by-visit breakdown will be repeated for the Evaluable and Safety Populations.

The number and percent of ITT subjects prematurely withdrawing will be presented overall, by timing of withdrawal (during first visit, after first visit and before second visit, during second visit) and by reason for withdrawal (Subject did not want to complete this testing session; Subject did not want to return for a second testing session; Subject did not show up for scheduled testing session and could not be reached for rescheduling within the time window; PI felt that it was not in the best interest of the subject to continue in the study; Subject met exclusion criteria during visit 2; None given; Other) for each randomization group and overall.

7.3 Methods for Withdrawals and Missing Data

Subjects who withdraw or terminate from the study will not be pursued as the study has no follow-up or long-term safety and effectiveness endpoints. Subjects who withdraw or do not complete the second visit will not be replaced as the overall sample size will take into account potential withdrawals. There will be no imputation of missing data in the analyses.

7.4 Protocol Deviation

A listing of protocol deviations for the ITT Population will be created which will include randomization group, site, subject ID, whether or not the subject is in the Validation Population, protocol deviation #, type of deviation, date of deviation, time of occurrence, reason for deviation and the justification/corrective action.

7.5 Multiple Comparisons and Multiplicity

There is one primary effectiveness analysis. There are several secondary and exploratory effectiveness analyses; there will be no adjustment for multiple comparisons across these analyses.

7.6 Timing of Assessments and Events for Analysis

Per the protocol, Study Day 0 is the date the index procedure (a.k.a. Visit 1 which consists of screening and the first set of study assessments). Study days will be calculated as follows:

Pre-index procedure, Study Day = Assessment Date – Index Procedure Date

Post-index procedure, Study Day = Assessment Date – Index Procedure Date

Visit 2 will take place between Day 21 and Day 35.

All baseline values will be taken from the index procedure (Visit 1).

The last non-missing measurement prior to the index procedure/first treatment will be used as the baseline measurement. This definition of baseline will be used for all effectiveness and safety analyses.

The following conversion factors will be used to convert days into weeks or months or years, or vice versa:

- 1 week = 7 days
- 1 month = 30.4375 days
- 1 year = 365.25 days

8 Demographics and Other Baseline Characteristics

8.1 Demographics

Basic summary of demographics by randomization group and overall will be presented. These analyses will be conducted for the ITT Population and the Evaluable Population. The tables will display statistics on age, gender, race, ethnicity, handedness, and education.

8.2 Prior And Concurrent Medications

A listing will detail all the concurrent medications being taken at baseline along with the randomization group, site, subject ID and whether or not the subject is a member of the Validation Population, for all ITT subjects with a medication recorded in the CRF.

Tables will display the percent and number of subjects who are currently or were previously taking the dementia medication specified in the CRF at baseline by randomization group and overall. One table will be for the ITT Population while another table will be for the Evaluable Population.

8.3 Baseline and Screening Conditions

Descriptive statistics (N, mean, standard deviation, median, minimum and maxim) will be presented for baseline MMSE total scores and sub-scores by randomization group and overall. One table will be for the ITT Population while another table will be for the Evaluable Population.

The number and percent of ITT subjects who had MRI in past will be presented; the number and percent of these subjects with an MRI in the past will then be presented within each MRI result category. The number and percent of ITT subjects using a cane or other walking aid will be presented. The number and percent of ITT subjects with a lower extremity neurological exam will be presented; the number and percent of these exam subjects (a) with ability to perceive monofilament; and (b) with ability to perceive vibration will be presented by foot (left, right) and overall (both feet combined). These statistics will be presented by randomized group and overall (both randomized groups combined). The analyses will be repeated for the Evaluable Population.

Tables will also be created for the Hamilton-Vaele Contrast Sensitivity score and the Purdue Peg Board Score for both the ITT Population and the Evaluable Population. These tables will display statistics (N, mean, standard deviation, median, minimum, maximum) for the left, right and binocular scores by randomization group and overall.

8.4 Baseline Medical History

The number and percent of subjects with a previous medical history and with a current medical history will be presented for each medical history category (e.g., Parkinson's and related conditions, Sleep apnea, Stroke or TIA, etc.). Descriptive statistics (N, mean, standard deviation, median, minimum, maximum) will be presented for total number of traumatic brain injuries. These statistics will be presented by randomized group and overall (only subjects reporting previous traumatic brain injuries will be included). The analyses will be presented for the ITT and Evaluable Populations.

9 EFFECTIVENESS ANALYSES

9.1 PRIMARY EFFECTIVENESS VARIABLE AND ANALYSES (CONSTANT VARIANCE)

Agreement of DCTclock-pen and DCTclock-tablet in assessing cognitive impairment will be assessed by using the Bland-Altman method on the DCTclock total score. The following hypothesis test will be carried out:

H0: $Lower_{LoA} \leq -\delta \; or \; Upper_{LoA} \geq \delta$

H1: $-\delta < Lower_{LoA} < Upper_{LoA} < \delta$

where δ = 30 is the pre-specified maximum allowable difference, $Lower_{LoA}$ is the lower bound of the two-sided 95% LoA, $Upper_{LoA}$ is the upper bound of the two-sided 95% LoA. The conclusion that the two measurements are in agreement (i.e. equivalent) depends on whether the two-sided 95% CIs of each (lower, upper) LoA are within the boundaries set from the maximum allowable difference.

Specifically, Bland-Altman analysis will consist of the following:

1. Calculate the paired difference in scores between the two tests (i.e., Discrepancy scores) for each subject.

2. Calculate the mean of these paired differences.

3. Calculate the average of the two test results for each subject.

4. Plot the paired differences (y-axis) vs. the average of the two test results (x-axis). This is commonly called the Bland-Altman plot.

5. Calculate a two-sided 95% LoA of the paired differences as: mean difference +/- 1.96*standard deviation (sd) of the differences.

6. Calculate two-sided 95% CI of each (lower, upper) LoA. The formulas for calculating these CIs are as follows:

$$Lower: mean\ difference\ -\ 1.96 * sd\ -(t0.975, N-1) * sd * sqrt(1/N\ +\ 1.96^2/(2*(N-1))).$$

$$Upper: mean\ difference\ +1.96 * sd\ +(t0.975, N-1) * sd * sqrt(1/N\ +\ 1.96^2/(2*(N-1))).$$

where $t0.975, N-1 * sd$ is the upper 0.025 critical value of the *t* distribution with *N-1* degrees of freedom and where *N* is the sample size.

7. The conclusion that the two measurements are in agreement (i.e. equivalent) depends on whether the CIs constructed from the data are within the boundaries set from the maximum allowable difference. Success is declared on the primary endpoint if the lower CI of the lower LoA is >-30, and the upper CI of the upper LoA is <+30.

The Evaluable Population will be used for these analyses.

A table will summarize the primary effectiveness endpoint. This table will include descriptive statistics for the DCTclock-pen total score, for the DCTclock-tablet total score, for the paired difference between the DCTclock-pen overall score and the DCTclock-tablet overall score (calculated as pen minus tablet), upper and lower LoA and their respective CIs, root mean squared differences (RMSD) as defined in the next section, and ANOVA p-value (for the assessment of homogeneity across randomized groups, as discussed previously). The descriptive statistics will be presented by randomization group and overall.

A figure will display the Bland-Altman plot described above.

9.2 Non-Constant Variance & Assessment of Site Homogeneity

A generative model will be fit of the following form:

Score Difference ~ N($\boldsymbol{\mu}$, $\boldsymbol{\sigma}$)
$\boldsymbol{\mu}$ = $\boldsymbol{\alpha\mu}$ + β1 * Location + β2 * Test Order
$\boldsymbol{\sigma}$ = k*exp($\boldsymbol{\alpha\sigma}$ + β3 * Average Score2 + β4 * Average Score)

- 'Location' and 'Test Order' will be one hot encoded indicator variables for the trial location site and order in which the test was given (ie. DCTclock pen assessment first or DCTclock tablet assessment first) respectively.
- Average Score will be calculated as: (DCTclock pen score + DCTclock tablet score) / 2
- Score Difference will be calculated as: (DCTclock tablet score - DCTclock pen score)
- The parameters k, $\boldsymbol{\alpha\mu}$, and $\boldsymbol{\alpha\sigma}$ are constants

This model will permit the disentangling of site specific impacts and the rate of learning improvement between the first and second assessments while also allowing the variance in score difference to vary as a function of the average score.

The Evaluable Population will be used for this analysis.

Two tables will summarize this model. The first will include the mean estimated coefficient values along with their 96% credible intervals. The second will breakdown the estimated differences in average Score Difference between the site locations and the order in which the assessments were completed. This table will include the mean differences as well as the max 96% prediction interval ranges for each combination of site and order.

A figure will display the 96% prediction intervals for Score Difference (y-axis) as a function Average Score (x-axis) over the range 0 - 100 generated from the fit model above. The Evaluable Population will be plotted over this interval for a visual assessment of the model fit. The max 96% prediction interval range will be added to the figure.

9.3 Secondary Effectiveness Variables and Analyses

In addition to the above primary analysis, the following additional agreement analyses between DCTclock-tablet and DCTclock-pen scores will be conducted on the DCTclock overall score as well as the scores from each of the Composite Scales (Drawing Efficiency, Information Processing, Simple and Complex Motor, and Spatial Reasoning) unless otherwise specified:

- Perform the Bland-Altman analysis on the scores from the composite scales; however, there will be no formal equivalence testing for the composite scales.

- DCTclock-tablet scores will be plotted against DCTclock-pen scores in a scatter plot, superimposed with a line of identity.

- An unweighted Deming regression (where the variance of the measurement error for each of DCTclock-pen and DCTclock-tablet is determined by the two measurements that were collected 3-5 weeks apart) will be carried out to determine the y-intercept, slope and their two-sided 95% CIs.

- The intraclass correlation coefficient (ICC) between DCTclock-table and DCTclock-pen will be calculated and will be placed on the above-mentioned plot of tablet vs. pen score scatter plot.

• Root mean squared differences (RMSD), the square root of the average squared discrepancy score, will be calculated to indicate the average amount by which scores differ. RMSD will be calculated using the following formula:

$$RMSD = \sqrt{\frac{\Sigma_{i=1}^{N}(x_{1,i} - x_{2,i})^2}{N}}$$

where $x_{1,i}$ is the DCTclock-pen score for subject *i*, $x_{2,i}$ is the DCTclock-tablet score for subject *i*, and where *N* is the sample size.

• Mean differences will be compared between pen and tablet using paired t-tests for equivalence, where lower and upper equivalence limits are -30 and 30, respectively. The following is the hypothesis test for equivalence. This hypothesis testing will be done only for the DCTclock Overall Score.

H0: μ_d <= -30 or μ_d >= 30

H1: -30 < μ_d < 30

where μ_d is the true average difference of the pen minus tablet total scores.

The Evaluable Population will be used for these analyses.

Tables will summarize the secondary effectiveness endpoints. These tables will include descriptive statistics for the DCTclock-pen score, for the DCTclock-tablet score, for the difference between the DCTclock-pen score and the DCTclock-tablet score (calculated as tablet minus pen), upper and lower LoA and their respective CIs, and RMSD. These statistics will be generated by randomization group and overall. One table will be created for each of the DCTclock composite scale scores.

Figures will display the plots described above.

10 Safety Analyses

All safety analyses will be performed on the Safety Population.

10.1 Primary Safety Variable

The study's primary safety endpoint is the incidence of subjects with serious device-related adverse events from enrollment to completion of the study. Safety will be analyzed on the Safety Population.

A table of treatment emergent adverse events (TEAEs), which are events that started or worsened during or after the first DCTclock or Linus Platform test, will be created. This table will present the number of TEAEs and the number and percent of subjects with at least one TEAE in each visit category (visit 1, between visits, visit 2, or at any time) with which the TEAE is associated.

TEAES will be categorized as follows at each visit, with the number of TEAEs and number and percent of subjects with at least one TEAE presented for each category at each visit:

- Any TEAE,
- TEAE by severity (mild/moderate/severe; if a subject has more than one TEAE, then only the events in the most severe category experienced will be tabulated, and the subject will be placed in the most severe category experienced),
- Relationship (not related or related, where related is further broken down by the categories of possible, probable, definite) to each of the following (if a subject has more than one TEAE, then only the events in the most related category experienced will be tabulated, and the subject will be placed in the most related category experienced):
    - DCTclock-pen (the denominator at Visit 1 and between visits will be those subjects who underwent testing with the pen at Visit 1; the denominator at Visit 2 will be those subjects who underwent testing with the pen at Visit 2)
    - DCTclock-tablet/drawing tests,
    - Decision making/reaction time,
    - Balance/walking,
    - PHQ-9/Lifestyle questionnaire (Visit 2 only),
    - Speech elicitation assessments,
    - Eye tracking assessments (Visit 2 only),
    - Other study assessments,
    - Concomitant medication,
    - Intercurrent intervention/procedure,
    - Pre-existing condition/underlying disease,
    - Intercurrent condition,
    - Incidental finding,
    - Unknown,
    - Other.
- Whether the TEAE led to study discontinuation or not,
- Whether the TEAE is a serious adverse event (SAE or not),
- Whether the TEAE led to death or not.

TEAEs will also be presented in a listing. This listing will include the randomization group, site, subject ID, visit number, date of visit, date of TEAE onset, study day number of onset, date TEAE resolved, number of study days from start to resolution of TEAE, whether it is an SAE or not (if so the reasons for the SAE will be listed after 'Y' in the SAE column), whether or not the study resulted in study discontinuation, outcome, severity, relationship to any study device/test component (any instance in which the TEAE is at least possibly related will be listed and in parentheses will be the exact noted relationship i.e. balance/walking (probable)) and action taken (in any instance in which

the action taken requires a specification, the specification will be written in parentheses i.e. medication (Ativan)).

A listing for device observations (observations associated with the Linus Platform devices) will be presented. This listing will display the randomization group, site, subject ID, description of the observation, observation #, date and study day of observation, whether or not the observation is related to an AE, whether or not the observation is related to Linus platform device components (and if so, which one(s)), time the observation occurred, type of observation, action taken to address the observation/outcome.

11 Other Planned Analyses

11.1 Agreement with MMSE and RBANS Analyses

Linus Platform individual tests will be compared to MMSE and RBANS to measure agreement in assessment of cognitive status in the Evaluable Population. Additionally, Linus Platform individual tests will be combined to obtain a Linus overall score (Linus score) to measure cognitive status: the training dataset will be used to create a Linus score based on the individual Linus Platform tests and the Evaluable Population will be used to validate the Linus score by assessing its agreement with MMSE and RBANS. I.e., all analyses below will be carried out on the Evaluable Population.

Since most of the Linus Platform tests are administered twice (once at visit 1 and once at visit 2), the RBANS is administered twice (at visit 1 and visit 2) and the MMSE is only administered once (at visit 1) the following sets of comparisons will be made:

1. MMSE at Visit 1 vs. Individual Linus Platform Score or Developed Linus Score at Visit 1
2. RBANS at Visit 1 vs. Individual Linus Platform Score or Developed Linus Score at Visit 1
3. RBANS at Visit 2 vs. Individual Linus Platform Score or Developed Linus Score at Visit 2

For each pairing of the individual Linus Platform scores or the developed Linus score and the reference standard MMSE and RBANS (Reference score), agreement analyses will be carried out as follows:

• Linus scores will be standardized by taking the subject's Linus score, subtracting by the overall Linus score mean and dividing by the overall Linus score standard deviation. This method will also be used to standardize the MMSE scores and RBANS scores. To better visualize the relationship between the two tests, the standardized Linus score and will be plotted separately against a standardized reference score (either MMSE or RBANS) in a scatter plot, superimposed with a line of identity.

• Linear and rank linear regression analyses will be conducted and p-values with 95% CI will be calculated for the y-intercept and slope of each model. Either the Pearson (linear regression) or the

Spearman (rank regression) correlation coefficients will be produced and superimposed onto the scatter plots for each regression method, along with 95% CIs and the estimated regression line. In these regressions, the dependent variables are either the individual Linus Platform score or the developed Linus scores and the independent variables are either the MMSE scores or the RBANS scores.

In addition to above, descriptive statistics (N, mean, standard deviation, median, minimum, maximum) for the MMSE score, RBANS score, Linus total score and the Linus Platform individual test scores will be presented by visit and overall.

Figures will display the above described plots.

11.2 Test-Retest Reliability Analyses

Subjects will undergo cognitive testing with both the Linus Platform tests and the reference standard RBANS twice, where the second examination will be three to five weeks after the first examination. Test-retest reliability of both individual Linus Platform tests and the combined Linus score will be compared to the test-retest reliability of the RBANS. For the analysis, subjects who no longer satisfy the inclusion/exclusion criteria prior to the second examination will be excluded.

For, the individual Linus Platform scores, the developed Linus score, and the reference standard RBANS, agreement analyses will be carried out as follows:

- Agreement between the first and second measurements will be measured. A scatter plot of measurement 2 vs. measurement 1 will be generated, superimposed with a line of identity. An unweighted Deming regression (where the variance of the measurement error is determined by the two measurements that were collected 3-5 weeks apart) will be carried out to determine the y-intercept, slope and their two-sided 95% CIs. The ICC will also be determined.

- A hypothesis test of the slope vs. 1 and of the y-intercept vs. 0 will be carried out. Specifically, the following hypothesis test will be carried out:' H0: $\beta 0 = 0$ vs. H1: $\beta 0 \neq 0$ and H0: $\beta 1 = 1$ vs. H0: $\beta 1 \neq 1$ where $\beta 0$ and $\beta 1$ are the y-intercept and slope, respectively, from the Deming unweighted regression. Each of these will be carried out at a two-sided 0.05 level of significance.

The Evaluable Population will be used for these analyses.

In addition to the above, descriptive statistics (N, mean, standard deviation, median, minimum and maximum) of the Visit 1, Visit 2 and the difference between Visit 1 and Visit 2 (calculated as Visit 1

minus Visit 2) will be presented for the RBANS score, for the Linus total score and for the Linus Platform individual test scores.

Figures will display the above described plots and the associated statistics (y-intercept and slope and their Cis, ICC, estimates of β0 and β1 from the Deming regression, and the p-values from the test of the Deming null hypotheses).

11.3 Expand Non-Constant Variance Model

The model developed in section 9.2 will be expanded to include relevant demographic and baseline characteristics as determined by exploratory data analysis on those features. The model will also be modified to try and include the Composite Scores so that the influence of each Composite Score's difference on the overall difference can be seen/fit simultaneously. Hierarchical modelling will be used here to pool information across relevant demographic/baseline/composite score groups. This model will be used to predict an individual's likelihood and uncertainty to be classified in the same Linus Score Categorization (In range, Indeterminate, Out of Range) as a function of the average score of the two assessments.

The Evaluable Population will be used for these analyses.

A table will summarize Score Differences (both credible and prediction interval differences) across relevant baseline/demographic groups.

A second table will summarize score differences (both credible and prediction interval differences) for the overall and Composite Scores based on the above model.
A figure will summarize the likelihood of a participant to be classified in the same Linus Score Categorization (y-axis) across a range (0 - 100) of score averages (x-axis). The mean line, 96% credible intervals around that mean line, and 96% prediction intervals around that mean line will all be plotted on the same figure.

12 Summary of Changes from the Protocol

The following table provides a list of changes from the protocol to the SAP, and the justification for each change.

Section	Description	Justification
7.1 Analysis Software	Added SAS® Software version 9.4 or later (the protocol only specifies R version 3.6 or later)	This will allow for programmers to use either SAS or R for analyses

13 Reporting Conventions

All reporting will meet the standards of SOP-68 AS Data Analysis Reporting and SOP-83 AS Programming Standards.

14 Appendix A: Table, Listing and Figure Shells

Table # Subject Accountability			
	Group 1 DCTclock-pen First	**Group 2 DCTclock-tablet First**	**Total**
Screened N			
Eligible N			
ITT N			
Visit 1 [% (n/ITT N)]			
Visit 2 [% (n/ITT N)]			
Evaluable N			
Visit 1 [% (n/Evaluable N)]			
Visit 2 [% (n/Evaluable N)]			
Validation N			
Visit 1 [% (n/Validation N)]			
Visit 2 [% (n/Validation N)]			
Training N			
Visit 1 [% (n/Training N)]			
Visit 2 [% (n/Training N)]			
Safety N			
Visit 1 [% (n/Safety N)]			
Visit 2 [% (n/Safety N)]			

Table # Withdrawals ITT Population			
	Group 1 DCT Clock-pen First N =	**Group 2 DCT clock-tablet First N =**	**Total N =**
All Withdrawals % (n/ITT N)			
Timing of withdrawal % (n/ITT N)			
During first visit			
After first visit but before second visit			
During second visit			
Reason for withdrawal % (n/ITT N)			
Subject did not want to complete this testing session			
Subject did not want to return for a second testing session			
Subject did not show up for scheduled testing session and could not be reached for rescheduling within the time window			
PI felt that it was not in the best interest of the subject to continue in the study			
Subject met exclusion criteria during visit 2			
None given			
Other			

Note: Percentages are based on the number of subjects in the ITT Population.

This table will be repeated for Evaluable Population

Table # Protocol Deviation ITT Population									
Randomization Group	**Site**	**Subject ID**	**Validation Population**	**Protocol Deviation #**	**Date Type**	**Date of Deviation**	**Time of Occurrence**	**Reason for Deviation**	**Justification/ Corrective Action**
Group X	XXX	XXX-XXX	Y/N	XXXXX	XX/XX/XXXX	XXXXX	XXXXXXXX	XXXXXXXX	XXXXXXXX
					XX/XX/XXXX	XXXXX	XXXXXXXX	XXXXXXXX	XXXXXXXX
					XX/XX/XXXX	XXXXX	XXXXXXXX	XXXXXXXX	XXXXXXXX
	XXX	XXX-XXX	Y/N	XXXXX	XX/XX/XXXX	XXXXX	XXXXXXXX	XXXXXXXX	XXXXXXXX
					XX/XX/XXXX	XXXXX	XXXXXXXX	XXXXXXXX	XXXXXXXX
									…

This listing will be ordered by randomization group, then site, then subject ID.

Table # Subject Demographics ITT Population			
	Group 1 **DCTclock-pen First** **N =**	**Group 2** **DCTclock-tablet First** **N =**	**Total** **N =**
Age (yrs)			
Mean ± SD (ITT N)			
Median (Min, Max)			
Gender % (n/ITT N)			
Male			
Female			
Other			
Unavailable			
Race % (n/ITT N)			
American Indian			
Alaskan Native			
Asian			
Black/African American			
Hispanic/Latino			
Native Hawaiian/Pacific Islander			
White/Caucasian			
Unavailable			
Ethnicity % (n/ITT N)			
Non-Hispanic/Latin			
Hispanic/Latin			
Unknown			
Unavailable			
Handedness % (n/ITT N)			
Right			
Left			
Ambi			
Ambi L>R			
Ambi R>L			
Unknown			
Unavailable			
Education % (n/ITT N)			
Mean ± SD (ITT N)			
Median (Min, Max)			

Note: Percentages are based on the number of subjects in the ITT Population.

This table will be repeated for Evaluable Population

Table # Medications at Baseline ITT Population				
Randomization Group	**Site**	**Subject ID**	**Validation Population**	**Medication Name**
Group X	XXXX	XXX-XXX	Y/N	XXXXXXXXXXX
			Y/N	XXXXXXXXXXX
			Y/N	XXXXXXXXXXX
			Y/N	XXXXXXXXXXX
			Y/N	XXXXXXXXXXX
			Y/N	XXXXXXXXXXX
Group X	XXXX	XXX-XXX	Y/N	XXXXXXXXXXX
				…

This listing will be ordered by randomization group, then site, then subject ID.

Table # Dementia Medications at Baseline ITT Population			
	Group 1 DCTclock-pen First N =	**Group 2 DCTclock-tablet First N =**	**Total N =**
Aricept (Donepezil) % (n/ITT N)			
Currently			
Previously			
Namenda (Mematine) % (n/ITT N)			
Currently			
Previously			
Axona % (n/ITT N)			
Currently			
Previously			
Exelon (Rivastigmine) % (n/ITT N)			
Currently			
Previously			
Razadyne (Galantamine) % (n/ITT N)			
Currently			
Previously			

This table will be repeated for Evaluable Population.

Table # MMSE Score at Baseline ITT Population			
	Group 1 DCTclock-pen First N =	**Group 2 DCTclock-tablet First N =**	**Total N =**
Orientation to time			
Mean ± SD (N)			
Median (Min, Max)			
Orientation to place			
Mean ± SD (N)			
Median (Min, Max)			
Registration			
Mean ± SD (N)			
Median (Min, Max)			
Attention and calculation (WORLD)			
Mean ± SD (N)			
Median (Min, Max)			
Recall			
Mean ± SD (N)			
Median (Min, Max)			
Naming			
Mean ± SD (N)			
Median (Min, Max)			
Repetition			
Mean ± SD (N)			
Median (Min, Max)			
Comprehension			
Mean ± SD (N)			
Median (Min, Max)			
Reading			
Mean ± SD (N)			
Median (Min, Max)			
Writing			
Mean ± SD (N)			
Median (Min, Max)			
Drawing			
Mean ± SD (N)			
Median (Min, Max)			
Total			
Mean ± SD (N)			
Median (Min, Max)			

This table will be repeated for Evaluable Population.

Table # Brief Neurological Exam at Baseline ITT Population			
	Group 1 DCTclock-pen First N =	**Group 2 DCTclock-tablet First N =**	**Total N =**
Had MRI in Past % (n/ITT N)			
Yes			
No			
MRI Results % (n/N with Past MRI)			
Stroke			
Large Bleed			
Punctate Bleed			
Atrophy			
Small Vessel Disease			
Mass/Tumor			
Amyloid Scan			
Amyloid CSF			
Uses Cane or Other Walking Aid % (n/ITT N)			
Yes			
No			
Lower Extremity Neurological Exam % (n/ITT N)			
Able to Perceive Monofilament % (n/N with Exam)			
Left foot % (n/N with Exam)			
Yes			
No			
Right foot % (n/N with Exam)			
Yes			
No			
Able to Perceive Vibration % (n/N with Exam)			
Left foot % (n/N with Exam)			
Yes			
No			
Right foot % (n/N with Exam)			
Yes			
No			

This table will be repeated for Evaluable Population.

Table # Hamilton-Veale Contrast Sensitivity Score at Baseline ITT Population			
	Group 1 DCTclock-pen First N =	**Group 2 DCTclock-tablet First N =**	**Total N =**
Left Score			
Mean ± SD (N)			
Median (Min, Max)			
Right Score			
Mean ± SD (N)			
Median (Min, Max)			
Binocular Score			
Mean ± SD (N)			
Median (Min, Max)			

This table will be repeated for Evaluable Population

Table # Purdue Peg Board Score at Baseline ITT Population			
	Group 1 DCTclock-pen First N =	**Group 2 DCTclock-tablet First N =**	**Total N =**
Left Score			
Mean ± SD (N)			
Median (Min, Max)			
Right Score			
Mean ± SD (N)			
Median (Min, Max)			
Binocular Score			
Mean ± SD (N)			
Median (Min, Max)			

This table will be repeated for Evaluable Population.

Table # Medical History ITT Population			
	Group 1 DCTclock-pen First N =	**Group 2 DCTclock-tablet First N =**	**Total N =**
Parkinson's and related conditions % (n/ITT N)			
Currently			
Previously			
Sleep Apnea % (n/ITT N)			
Currently			
Previously			
Stroke or TIA % (n/ITT N)			
Currently			
Previously			
Liver or kidney disease % (n/ITT N)			
Currently			
Previously			
Tremor % (n/ITT N)			
Currently			
Previously			
Brain tumor % (n/ITT N)			
Currently			
Previously			
Psychiatric disorder (including anxiety or depression) % (n/ITT N)			
Currently			
Previously			
Dementia (any type) % (n/ITT N)			
Currently			
Previously			
Diabetes % (n/ITT N)			
Currently			
Previously			
Epilepsy % (n/ITT N)			
Currently			
Previously			
Mild cognitive impairment (MCI) % (n/ITT N)			
Currently			
Previously			
Multiple sclerosis % (n/ITT N)			
Currently			
Previously			
Traumatic brain injury (with loss or consciousness) % (n/ITT N)			
Currently			
Previously			
Total number of traumatic brain injuries (among those who had indicated previous traumatic brain injury)			
Mean ± SD (N)			
Median (Min, Max)			

This table will be repeated for Evaluable Population.

Table # Primary Effectiveness Endpoint for DCTclock Overall Score Validation Population			
	Group 1 DCTclock-pen First N =	**Group 2 DCTclock-tablet First N =**	**Total N =**
DCTclock-pen			
Mean ± SD (N)			
Median (Min, Max)			
DCTclock-tablet			
Mean ± SD (N)			
Median (Min, Max)			
Difference (DCTclock-tablet – DCTclock-pen)			
Mean difference ± SD (CI)			
Median (Min, Max)			
p-value for Equivalence (Margins of +/- 30)			
Comparison			
Lower Limit of Agreement (CI)			
Upper Limit of Agreement (CI)			
RMSD			
ANOVA p-value			

Figure #
Primary Effectiveness Figure (Bland-Altman Plot)

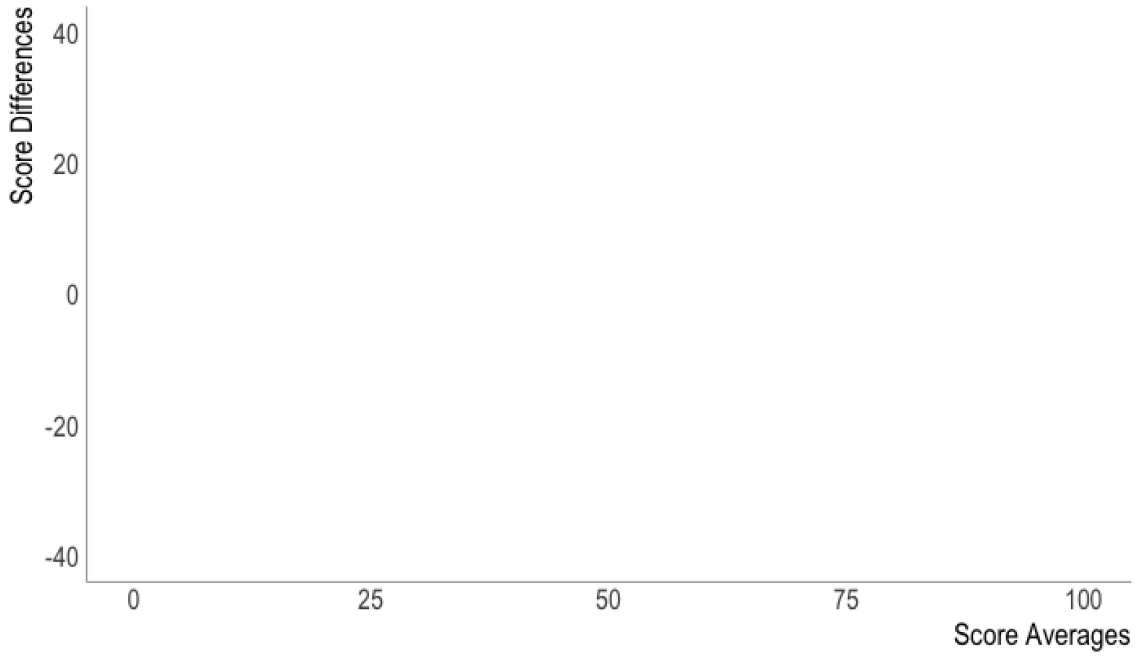


Table # Primary Effectiveness Non-Constant Variance Model Summary Evaluable Population	
	Coefficient Value (96% Credible Interval)
Constants	
$\alpha\mu$	
$\alpha\sigma$	
k	
Betas	
β1	
β2	
β3	
β4	

Table # Score Differences of Sites/Assessment Order w/ Non-Constant Variance Model Evaluable Population	
	Mean Score Difference (96% Credible Interval)
Site 1	
Tablet Assessment First (n = X)	
Pen Assessment First (n = X)	
Site 2	
Tablet Assessment First (n = X)	
Pen Assessment First (n = X)	

Table # Homogeneity by Site for DCTclock Overall Score Evaluable Population			
	Site 1 N =	Site 2 N =	Total N =
DCTclock-pen			
Mean ± SD (N)			
Median (Min, Max)			
DCTclock-tablet			
Mean ± SD (N)			
Median (Min, Max)			
Difference (DCTclock-pen – DCTclock-tablet)			
Mean difference ± SD (CI)			
Median (Min, Max)			
Comparison			
Lower Limit of Agreement (CI)			
Upper Limit of Agreement (CI)			

Figure #
Primary Effectiveness Figure for Non-Constant Variance Model

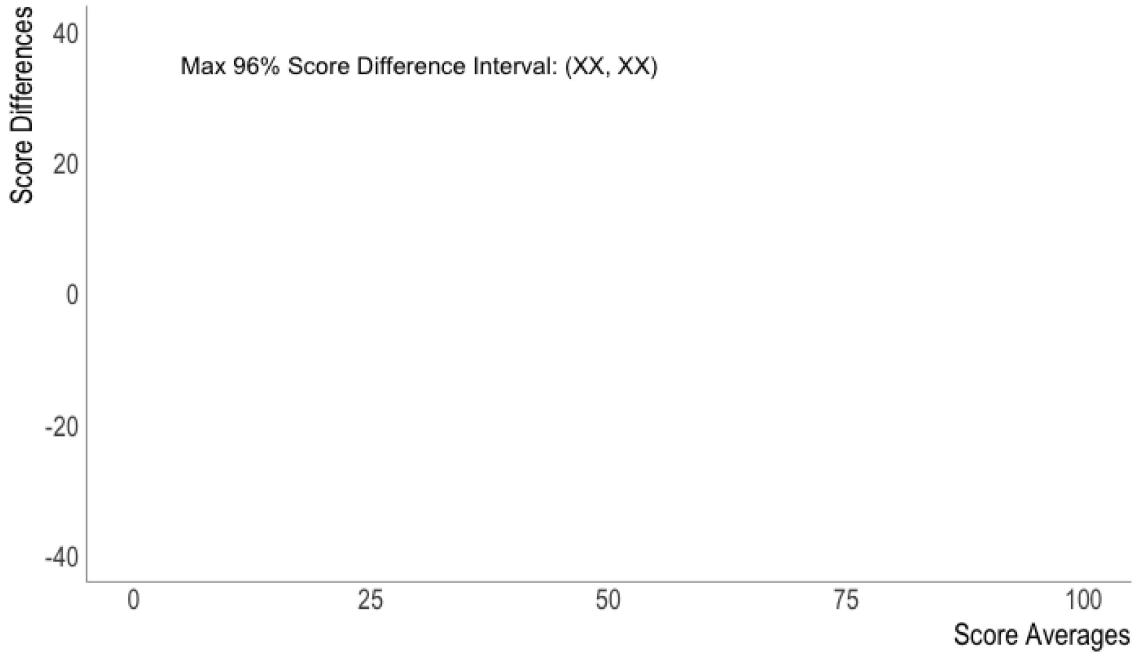
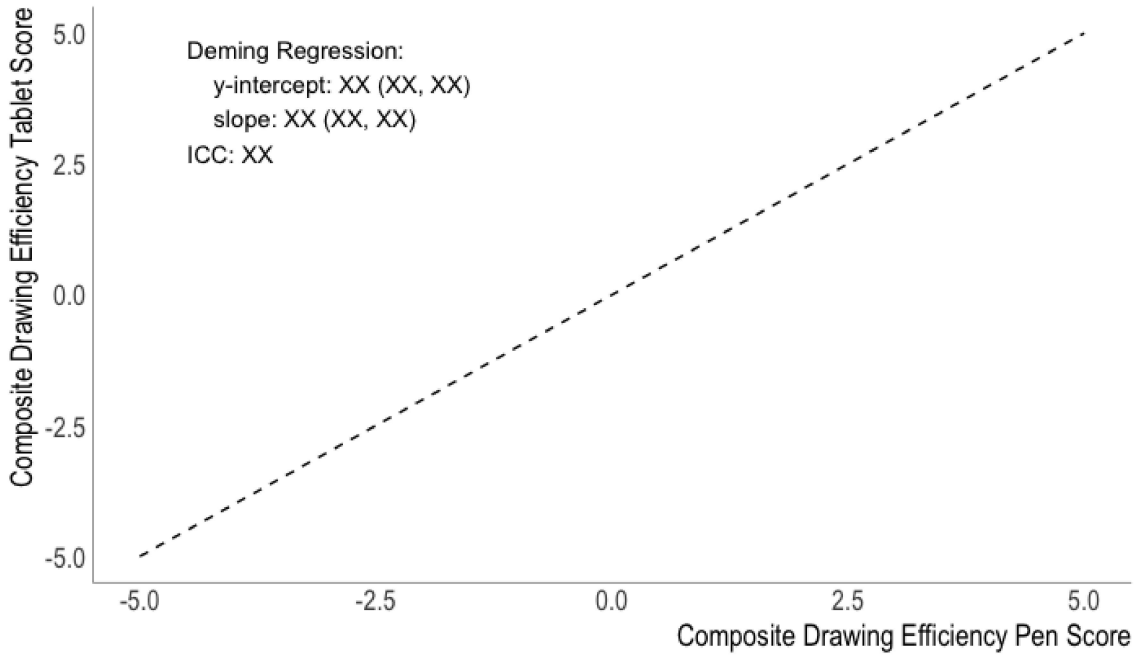


Table # Secondary Effectiveness Endpoints for DCT-clock Drawing Efficiency Evaluable Population			
	Group 1 DCTclock-pen First N =	**Group 2 DCTclock-tablet First N =**	**Total N =**
DCTclock-pen			
Mean ± SD (N)			
Median (Min, Max)			
DCTclock-tablet			
Mean ± SD (N)			
Median (Min, Max)			
Difference (DCTclock-pen – DCTclock-tablet)			
Mean difference ± SD (CI)			
Median (Min, Max)			
p-value for Equivalence (Margins of +/- 30)			
Comparison			
Lower Limit of Agreement (CI)			
Upper Limit of Agreement (CI)			
RMSD			

This table will be repeated for the other DCTclock composite scales (Information Processing, Simple and Complex motor, Spatial Reasoning)

Figure #
Secondary Effectiveness Figure for DCT-clock Drawing Efficiency Composite Scale



This figure will be repeated for the other DCTclock composite scales (information processing, simple and complex motor, spatial reasoning)

Table # Treatment-Emergent Adverse Events Safety Population								
	Visit 1		Between Visits		Visit 2		Total	
	Number of Events	Number of Subjects with Event [% (n/N)]	Number of Events	Number of Subjects with Event [% (n/N)]	Number of Events	Number of Subjects with Event [% (n/N)]	Number of Events	Number of Subjects with Event [% (n/N)]
Any TEAE								
Severity*								
Mild								
Moderate								
Severe								
Resulted in Study Discontinuation								
Yes								
No								
SAE								
Yes								
No								
Led to Death								
Yes								
No								
Relationship**								
DCTclock-pen								
Not Related								
Related								
Possible								
Probable								
Definite								
DCTclock-tablet/drawing tests								
Not Related								
Related								
Possible								
Probable								
Definite								
Decision making/ reaction time								
Not Related								
Related								
Possible								
Probable								
Definite								
Balance/walking								
Not Related								
Related								
Possible								
Probable								
Definite								
PHQ-9/Lifestyle questionnaire								
Not Related								
Related								
Possible								
Probable								
Definite								
Speech elicitation assessments								
Not Related								
Related								
Possible								
Probable								
Definite								

Eye tracking assessments								
Not Related								
Related								
Possible								
Probable								
Definite								
Other study assessments								
Not Related								
Related								
Possible								
Probable								
Definite								
Concomitant medication								
Intercurrent intervention/procedure								
Pre-existing condition/Underlying disease								
Intercurrent condition								
Incidental finding								
Unknown								
Other								

*If a subject has more than one TEAE the events/subject are placed in the most severe category experienced.
**If subject has more than one TEAE, the events/subject are placed into the most related category experienced.

Table # Treatment Emergent Adverse Events Safety Population												
Random-ization Group	**Site**	**Subject ID**	**Description**	**Visit Number / Date of Visit**	**Date of AE Onset/ Study Day Number**	**Date Resolved / Number of Study Days from Start of AE**	**SAE**	**Resulted in Study Dis-continuation**	**Outcome**	**Severity**	**Related To**	**Action Taken**
Group XX	XX	XXX-XXX	XXXXX	XXXXX XX/XX/XXXX	XX/XX/XXXX	XX/XX/XXXX XX	Y/N	Y/N	XXXXX	XXXXX	XXXXX	XXXX
		XXX-XXX	XXXXX	XXXXX XX/XX/XXXX	XX/XX/XXXX	XX/XX/XXXX XX	Y/N	Y/N	XXXXX	XXXXX	XXXXX	XXXX
		XXX-XXX	XXXXX	XXXXX XX/XX/XXXX	XX/XX/XXXX	XX/XX/XXXX XX	Y/N	Y/N	XXXXX	XXXXX	XXXXX	XXXX
Group XX	XX	XXX-XXX	XXXXX	XXXXX XX/XX/XXXX	XX/XX/XXXX	XX/XX/XXXX XX	Y/N	Y/N	XXXXX	XXXXX	XXXXX	XXXX
		XXX-XXX	XXXXX	XX/XX/XXXX	XX/XX/XXXX	XX/XX/XXXX XX	Y/N	Y/N	XXXXX	XXXXX	XXXXX	XXXX
												…

*Only AEs that have the onset time of "during assessments" or "between assessment visits" are included in this listing

Any specified reasons for SAEs will be listing in the SAE column after 'Y'
Any instance in which the AE is at least possibly related will be listed and in parentheses will be the exact noted relationship i.e. balance/walking (probable)
In any instance in which the action taken requires a specification, the specification will be written in parentheses i.e. medication (Ativan)
This listing will be ordered by randomization group, then site, then subject ID.

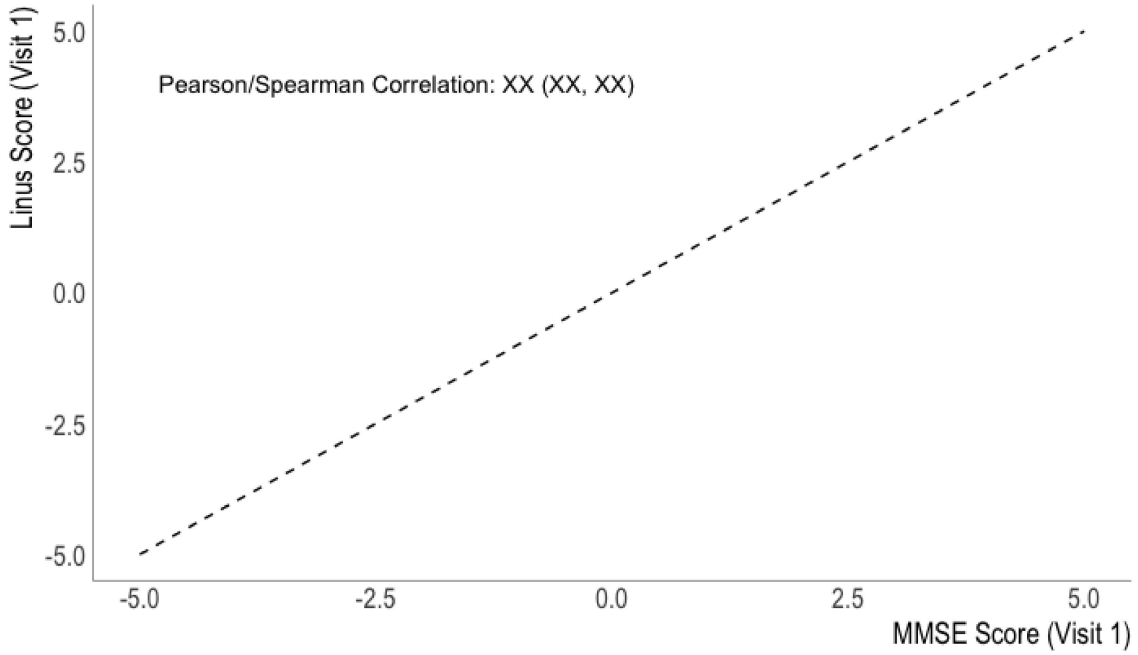
Table # Device Observations Safety Population										
Randomization Group	**Site**	**Subject ID**	**Description**	**Observation #**	**Date of Observation (Study Day of Observation)**	**Related to AE**	**Related to Linus Platform Device Components**	**Time Observation Occurred**	**Type of Observation**	**Action Taken to Address Observation/ Outcome**
Group X	XXX	XXX-XXX	XXXXX	XXXXX	XX/XX/XXXX (XX)	Y/N	XXXXXX	XXXXX: XXXXX	XXXXX	XXXXX
		XXX-XXX	XXXXX	XXXXX	XX/XX/XXXX (XX)	Y/N	XXXXXX	XXXXX: XXXXX	XXXXX	XXXXX
		XXX-XXX	XXXXX	XXXXX	XX/XX/XXXX (XX)	Y/N	XXXXXX	XXXXX: XXXXX	XXXXX	XXXXX
Group X	XXX	XXX-XXX	XXXXX	XXXXX	XX/XX/XXXX (XX)	Y/N	XXXXXX	XXXXX: XXXXX	XXXXX	XXXXX
		XXX-XXX	XXXXX	XXXXX	XX/XX/XXXX (XX)	Y/N	XXXXXX	XXXXX: XXXXX	XXXXX	XXXXX

This listing will be ordered by randomization group, then site, then subject ID.

Table # Exploratory Analysis: MMSE, RBANS and Linus Individual Tests and Overall Score Descriptives Validation Population			
	Visit 1	**Visit 2**	**Total**
MMSE			
Mean ± SD (N)		N/A	
Median (Min, Max)		N/A	
RBANS			
Mean ± SD (N)			
Median (Min, Max)			
Linus Total Score			
Mean ± SD (N)			
Median (Min, Max)			
Linus Platform Drawing Test: Pre-test			
Mean ± SD (N)			
Median (Min, Max)			
Linus Platform Drawing Test: Pathfinding			
Mean ± SD (N)			
Median (Min, Max)			
Linus Platform Drawing Test: Symbol			
Mean ± SD (N)			
Median (Min, Max)			
Linus Platform Drawing Test: Connect			
Mean ± SD (N)			
Median (Min, Max)			
Linus Platform Drawing Test: Tracing			
Mean ± SD (N)			
Median (Min, Max)			
Linus Platform Decision Making and Rection Time Test: Simple Reaction Time			
Mean ± SD (N)			
Median (Min, Max)			
Linus Platform Decision Making and Rection Time Test: Procedural Reaction Time			
Mean ± SD (N)			
Median (Min, Max)			
Linus Platform Decision Making and Rection Time Test: Go/No-Go			
Mean ± SD (N)			
Median (Min, Max)			
Linus Platform Decision Making and Rection Time Test: PHQ-9			
Mean ± SD (N)			
Median (Min, Max)			
Linus Platform Speech Elicitation Tasks: Complex Picture Description			
Mean ± SD (N)			
Median (Min, Max)			
Linus Platform Speech Elicitation Tasks: Category Naming			
Mean ± SD (N)			
Median (Min, Max)			
Linus Platform Speech Elicitation Tasks: Object Recall			
Mean ± SD (N)			
Median (Min, Max)			
Linus Platform Speech Elicitation Tasks: Sentence Reading			
Mean ± SD (N)			
Median (Min, Max)			
Linus Platform Speech Elicitation Tasks: Sustained Phonation			
Mean ± SD (N)			
Median (Min, Max)			

Linus Platform Speech Elicitation Tasks: Diadochokinetic Rate			
Mean ± SD (N)			
Median (Min, Max)			
Linus Platform Speech Elicitation Tasks: Story Recall			
Mean ± SD (N)			
Median (Min, Max)			
Linus Platform Speech Elicitation Tasks: List Learning			
Mean ± SD (N)			
Median (Min, Max)			
Linus Platform Eye Tracking-Based Memory Assessments			
Mean ± SD (N)	N/A		
Median (Min, Max)	N/A		
Linus Platform Gait and Balance Assessment			
Mean ± SD (N)			
Median (Min, Max)			
Linus Platform Lifestyle Questionnaire			
Mean ± SD (N)	N/A		
Median (Min, Max)	N/A		

Figure #
MMSE vs. Linus Score at Visit 1



This figure will be repeated for all other individual Linus platform test scores, as well as for RBANS at Visit 1 vs. Linus (Individual Platform Test or Overall Linus Score) at Visit 1 and RBANS at Visit 2 vs. Linus (Individual Platform Test or Overall Linus Score) at Visit 2

Table # Exploratory Analysis: Test-Retest Reliability Evaluable Population			
	Visit 1	**Visit 2**	**Difference between Visit 1 and 2 (Visit 1 – Visit 2)**
RBANS			
Mean ± SD (N)			
Median (Min, Max)			
Overall Linus Score			
Mean ± SD (N)			
Median (Min, Max)			
Linus Platform Drawing Test: Pre-test			
Mean ± SD (N)			
Median (Min, Max)			
Linus Platform Drawing Test: Pathfinding			
Mean ± SD (N)			
Median (Min, Max)			
Linus Platform Drawing Test: Symbol			
Mean ± SD (N)			
Median (Min, Max)			
Linus Platform Drawing Test: Connect			
Mean ± SD (N)			
Median (Min, Max)			
Linus Platform Drawing Test: Tracing			
Mean ± SD (N)			
Median (Min, Max)			
Linus Platform Decision Making and Rection Time Test: Simple Reaction Time			
Mean ± SD (N)			
Median (Min, Max)			
Linus Platform Decision Making and Rection Time Test: Procedural Reaction Time			
Mean ± SD (N)			
Median (Min, Max)			
Linus Platform Decision Making and Rection Time Test: Go/No-Go			
Mean ± SD (N)			
Median (Min, Max)			
Linus Platform Decision Making and Rection Time Test: PHQ-9			
Mean ± SD (N)			
Median (Min, Max)			
Linus Platform Speech Elicitation Tasks: Complex Picture Description			
Mean ± SD (N)			
Median (Min, Max)			
Linus Platform Speech Elicitation Tasks: Category Naming			
Mean ± SD (N)			
Median (Min, Max)			
Linus Platform Speech Elicitation Tasks: Object Recall			
Mean ± SD (N)			
Median (Min, Max)			
Linus Platform Speech Elicitation Tasks: Sentence Reading			
Mean ± SD (N)			
Median (Min, Max)			
Linus Platform Speech Elicitation Tasks: Sustained Phonation			
Mean ± SD (N)			
Median (Min, Max)			
Linus Platform Speech Elicitation Tasks: Diadochokinetic Rate			

Mean ± SD (N)			
Median (Min, Max)			
Linus Platform Speech Elicitation Tasks: Story Recall			
Mean ± SD (N)			
Median (Min, Max)			
Linus Platform Speech Elicitation Tasks: List Learning			
Mean ± SD (N)			
Median (Min, Max)			
Linus Platform Gait and Balance Assessment			
Mean ± SD (N)			
Median (Min, Max)			

*Does not include subjects who did not meet inclusion/exclusion criteria at Visit 2

This table will be repeated for all other individual Linus platform test scores, as well as for RBANS

Figure #
Test-Retest Reliability for Linus Score

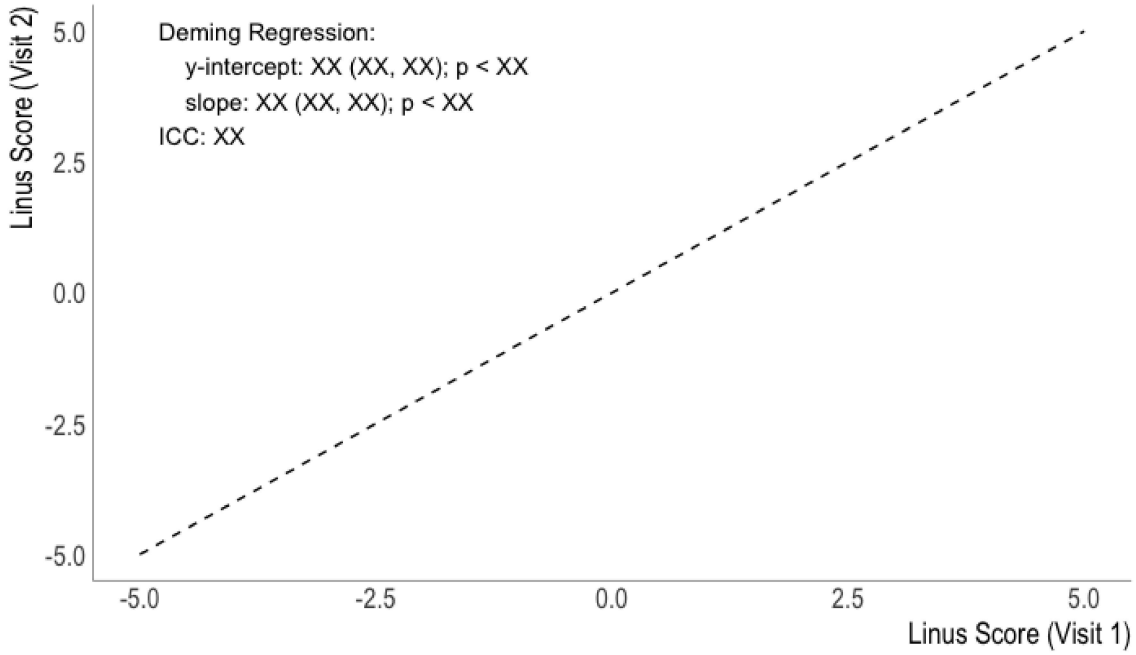


Table # Mean Score Differences of Relevant Demographic/Baseline Groups Evaluable Population	
	Mean Score Difference (96% Credible Interval)
Demographic/Baseline Group 1	
Category 1	
Category 2	
...	

The rows in this table will be repeated for all relevant baseline/demographic groups

Table # Mean/Max Prediction Interval Score Differences for Difference Composite Scores Evaluable Population		
	Mean Score Difference (96% Credible Interval)	**Max 96% Prediction Interval for Score Differences**
Overall Linus Score	,	
Drawing Efficiency Composite Score		
Simple and Complex Motor Composite Score		
Information Processing Composite Score		
Spatial Reasoning Composite Score		

Figure #
Extension of Non-Constant Variance Model; Linus Category Consistency