MANUSCRIPT#49882 - RESPONSE LETTER

Editorial FILE requests

#	Item description	Authors' response
1	49882-Manuscript File	A revised manuscript has been uploaded.
2	49882-Answering Reviewers	A response letter has been uploaded.
3	49882-Audio Core Tip	An audio file has been uploaded.
4	49882-Biostatistics Review Certificate	The requested document has been uploaded.
5	49882-Conflict-of-Interest Disclosure Form	This was included with the original submission, however the file has also been included with the revised manuscript in the current upload. Please advise if there is a specific issue with this file.
6	49882-Copyright License Agreement	This was included with the original submission, however the file has also been included with the revised manuscript in the current upload. Please advise if there is a specific issue with this file.
7	49882-Approved Grant Application Form(s) or Funding Agency Copy of any Approval Document(s)	This file does not apply to the current manuscript. The added heading (*"Supported by…"*) has been deleted in the revised manuscript.
8	49882-Signed Informed Consent Form(s) or Document(s)	The requested documents have been uploaded.
9	49882-Institutional Review Board Approval Form or Document	This was included with the original submission, however the file has also been included with the revised manuscript in the current upload. Please advise if there is a specific issue with this file.
10	49882-Non-Native Speakers of English Editing Certificate	This file does not apply to the current manuscript.
11	49882-Video	This file does not apply to the current manuscript.
12	49882-Image File	The requested files have been uploaded.
13	49882-STROBE Statement	The checklist **as downloaded** from the BPG site has been uploaded; a STROBE statement was/is included on the title page of the manuscript, as requested. Please advise if there is a specific issue with the file and/or statement.
14	49882-Supplementary Material	The manuscript **does not** have supplementary material **to be published with the paper itself**. However, as requested, a pdf file for the references not indexed by PubMed with the 1st page of the reference as requested has been uploaded w/ the revised manuscript [Cognivue.WJP#49882.non-indexed.refs.pdf].

Editorial comments [from '49882-edited.docx', with original formatting]

Comment #	Comment/question	Authors' response
Title page		
1	**Answer to reviewers: Please provide point to point answer to all reviewers**. Authors should revise their article according to the reviewers' comments/suggestions and **provide point-by-point responses to each in a letter** that is to accompany their resubmission.	A copy of this response letter has been uploaded.
	CrossCheck report: Similar sentences with other articles (highlighted in the 49882-**CrossCheck Report**), please rephrase these sentences. Your manuscript has been checked by CrossCheck. Please read the attached CrossCheck report for details. **Our editorial policy states the overall similarity should be less than 30%, the overlapped section should be less than 5% in single papers, including author's own work.**	As is the case for most published studies which have presented their findings at a conference prior to publication of a full manuscript, there is necessary overlap between the two. The similarity noted in the CrossCheck report is primarily due to the posters pertaining to the current studies being made available to the public via the Cognivue website. **Both posters have been removed and are no longer available from the website**. The "overlapped section" should now be >5% as requested.
	Title: The title should be **no more than 12 words.** A succinct and impactful title will include minimal nonfunctional words, such as "a," "an," "the," "roles of," *etc*. and will avoid non-standard abbreviations. **Please don't include abbreviations in the title.**	The title has been modified.
2	A short running title of **no more than 6 words** should be provided. It should state the topic of the paper. e.g. Losurdo G *et al*. Two-year follow-up of duodenal lymphocytosis. A short running title should be **no more than 6 words**	A running title has been added.
3	**Designation of co-first authors and co-corresponding authors is not permitted.** Author names (unabbreviated) should be given as first name, middle name (acronym, with no period) and family (sur) name, and typed in bold with the first letter capitalized; **a hyphen should be included between the syllables of Chinese names.**	This comment does not appear to apply. Neither co-first authors nor co-corresponding authors are indicated and no authors are Chinese. **Please advise if there is further issue.**
4	ORCID provides a persistent digital identifier that distinguishes you from every other researcher and, through integration in key research workflows such as manuscript and grant submissions, supports automated linkages between you and your professional activities, thereby ensuring that your work is recognized. **Please visit the ORCID website at https://orcid.org/for more information. All authors must provide their personal ORCID registration number.** For example, Marcos Pasarín (0000-0002-4122-1235); Juan G Abraldes (0000-0002-4392-660X); Eleonora Liguori (0000-0002-0244-927X); Beverley Kok (0000-0002-1727-5030); Vincenzo La Mura (0000-0003-4685-7184).	ORCID numbers have been added to the title page.
5	Please provide the author contributions. Authors must indicate their specific contributions to the published work. This information will be published as a footnote to the paper. See the format in the attachment file-revision policies.	The requested paragraph has been added to the title page of the manuscript.

	The format of this section should be like this: **Author contributions:** XXX (family name should be put first in full, followed by middle names and first name in abbreviation with first letter in capital) designed research; XXX performed research; XXX contributed new reagents or analytic tools; XXX analyzed data; XXX wrote the paper. An author may list more than one contribution, and more than one author may have contributed to the same aspect.	
6	A copy of the full approved grant application form(s), consisting of the information section and body section, should be provided to the BPG in PDF format. You need to provide the grant application form(s) or certificate of funding agency for every grant, or we will delete the part of "**Supported by...**".	The header added by WJP ("Supported by….") has been deleted.
7	Any article describing a study (basic research and clinical research) involving human and/or animal subjects is required to have the institutional review board (IRB) name, whether institutional (part of the author(s)' academic/medical institution, such as the Oak Grove Children's Hospital Institutional Review Board) or commercial/independent/private (contracted for-profit organizations, such as the ClinicCare Coalition for Human Rights Institutional Review Board), stated explicitly on the title page. **Please provide the approval file of Institutional review board, and state it on the title page.** e.g. The study was reviewed and approved by the [Name of Institution or Organization] Institutional Review Board.	The originally uploaded IRB file has been re-uploaded with the revised manuscript and the requested statement has been added to the title page. **Please advise if there is a specific issue with this file.**
8	Any article describing a study (basic research) involving animal subjects is required to have the institutional animal care and use committee (IACUC)'s institution name (such as the Genovese Institute) and protocol number (such as 14-9347-39G or EN-21549) stated explicitly in the title page section. **Please provide the approval file of Institutional animal care and use committee, and state it on the title page.** e.g. All procedures involving animals were reviewed and approved by the Institutional Animal Care and Use Committee of the [Name of institution] (IACUC protocol number: [protocol number]).	This does not apply to our study.
9	**Please provide the primary version (PDF) of the Informed Consent Form that has been signed by all subjects and investigators of the study, prepared in the official language of the authors' country to the system**; for example, authors from China should upload the Chinese version of the document, authors from Italy should upload the Italian version of the document, authors from Germany should upload the Deutsch version of the document, and authors from the United States and the United Kingdom should upload the English version of the document, *etc*. **Sample wording:** All study participants or their legal guardian provided informed written consent about personal and medical data collection prior to study enrolment.	The requested file has been uploaded and the informed consent statement added to the title page.
10	Please download the Conflict of Interest (PDF), fill it in, and then upload the completed PDF version to the system. Note: The Corresponding Author is responsible for filling out	The originally uploaded COI files have been re-uploaded with the revised manuscript. The COI statement was

	a Conflict-of-Interest Form. Please add Conflict-of-interest statement. e.g. There is no conflict of interest associated with any of the senior author or other coauthors contributed their efforts in this manuscript. All the Authors have no conflict of interest related to the manuscript.	included on the title page of the original submission. **Please advise if there is a specific issue with the file and/or statement.**
11	Basic research and clinical research studies require a data sharing statement. The data sharing statement will be provided in the title page, and will be presented in the form as shown in the sample below. Please add Data sharing statement. **e.g.** Technical appendix, statistical code, and dataset available from the corresponding author at [email address or URL]. Participants gave informed consent for data sharing [or ...consent was not obtained but the presented data are anonymized and risk of identification is low... or consent was not obtained but the potential benefits of sharing these data outweigh the potential harms because...]". If no other data, please state: No additional data are available.	The requested paragraph has been added to the title page..
12	**Telephone:** **Fax:** Telephone and fax numbers should consist of +, country number, district number and telephone or fax number; for example, +86-10-85381892	The telephone # has been formatted as requested. The corresponding author does not have a fax # to provide. Please use the corresponding author's contact telephone # and email address.
Abstract		
13	(no more than 20 words) The purpose of the study should be stated clearly, with no or minimal background information, following the format of: "To investigate/study/determine…"	The abstract section has been modified as requested.
14	(no less than 80 words) This section should describe the materials and methods used for all of the data presented in the proceeding Results section of the abstract. This information should include the following details, as applicable: basic study design (*e.g.*, randomized controlled trial, cross sectional study, cohort study, case series, *etc.*)*;* setting, please specify study location (*e.g.*, primary or tertiary care setting, hospital, general community, *etc.*)*;* number of participants and how they were selected; intervention, the method of administration and the duration.	The abstract section has been modified as requested.
15	(no more than 30 words) This section should succinctly and cogently present the findings and implications that are within the scope of the data you have presented in the preceding Results section of the abstract. You should state only conclusions that are directly supported by the evidence presented and the implications of the findings presented. This section should be written in the present tense.	The abstract section has been modified as requested.
16 ("Core tip")	Please write a summary of no more than 100 words to present the core content of your manuscript, highlighting the most innovative and important findings and/or arguments. The purpose of the Core Tip is to attract readers' interest for reading the full version of your article and increasing the impact of your article in your field of study. **70~100 words, please supplement.**	We are uncertain as to what is specifically being requested since the "Core tip" as originally included was <100 words and provided a summary of the core content. However, the "Core tip" in the revised manuscript has been reformatted to a single

		paragraph, if that is preferable.
17 ("Audio core tip")	**Please offer the audio core tip,** the requirement are as follows: In order to attract readers to read your full-text article, we request that the first author make an audio file describing your final core tip. This audio file will be published online, along with your article. Please submit audio files according to the following specifications: **Acceptable file formats:** .mp3, .wav, or .aiff **Maximum file size:** 10 MB To achieve the best quality, when saving audio files as an mp3, use a setting of 256 kbps or higher for stereo or 128 kbps or higher for mono. Sampling rate should be either 44.1 kHz or 48 kHz. Bit rate should be either 16 or 24 bit. To avoid audible clipping noise, please make sure that audio levels do not exceed 0 dBFS.	An audio file has been uploaded.
Main text		
18	The author should **number the references in Arabic numerals according to the citation order in the text.** The reference numbers will be **superscripted** in **square brackets** at the end of the sentence with the citation content or after the cited author's name, **with no spaces[1].** **e.g.** Tools for assessing cognitive function decline are often limited by issues of measurement efficacy[1-5], and excessive test length can make some tools impractical for routine use in clinical practice[6,9,10].	This comment does not appear to apply. The in-text references are formatted as requested.
Add'l section requested		
19	The guidelines for writing and formatting Article Highlights are as follows: (1) ***Research background*** The background, present status and significance of the study should be described in detail. (2) ***Research motivation*** The main topics, the key problems to be solved, and the significance of solving these problems for future research in this field should be described in detail. (3) ***Research objectives*** The main objectives, the objectives that were realized, and the significance of realizing these objectives for future research in this field should be described in detail. (4) ***Research methods*** The research methods (*e.g.*, experiments, data analysis, surveys, and clinical trials) that were adopted to realize the objectives, as well as the characteristics and novelty of these research methods, should be described in detail. (5) ***Research results*** The research findings, their contributions to the research in this field, and the problems that remain to be solved should be described in detail. (6) ***Research conclusions*** The following questions should be briefly answered: What are the new findings of this study? What are the new theories that this study proposes?	The requested section has been added to the revised manuscript.

	What are the appropriate summarizations of the current knowledge that this study provided? What are the original insights into the current knowledge that this study offered? What are the new hypotheses that this study proposed? What are the new methods that this study proposed? What are the new phenomena that were found through experiments in this study? What are the hypotheses that were confirmed through experiments in this study? What are the implications of this study for clinical practice in the future? (7) ***Research perspectives*** What experiences and lessons can be learnt from this study? What is the direction of the future research? What is/are the best method/s for the future research? Please write this section.	
References		
20	Please check and confirm that there are no repeated references! Please add PubMed citation numbers (**PMID** NOT PMCID) and DOI citation to the reference list and **list all authors.** Please revise throughout. The author should provide the first page of the paper without PMID and DOI. PMID (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed) (Please begin with PMID:) DOI (http://www.crossref.org/SimpleTextQuery/) (Please begin with DOI: 10.**) **e.g.** 1 **Frezza EE**, Fung JJ, van Thiel DH. Non-lymphoid cancer after liver transplantation. *Hepatogastroenterology* 1997; **44**: 1172-1181 [PMID: 9261620]	It is unclear as to how the 1st comment applies to our manuscript as there are no repeated references. PMIDs and DOIs have been provided and formatted as requested, where available, for the references cited in the manuscript. For the references not indexed by PubMed, a pdf file [Cognivue.WJP#49882.non-indexed.refs.pdf] with the 1st page of the reference as requested has been uploaded w/ the revised manuscript.
Figures/tables		
21 (Fig 1)	**Please provide the decomposable figure of figures, whose parts are all movable and editable, organize them into a PowerPoint file, and submit as "Manuscript No. - Figures.ppt" on the system, we need to edit the words in the figures. All submitted figures, including the text contained within the figures, must be editable. Please provide the text in your figure(s) in text boxes.**	The requested file has been uploaded.
22-23 (Fig 2)	Please don't include abbreviations in the title of the figure/table.	The title has been modified as requested
	Please provide the decomposable figure of figures, whose parts are all movable and editable, organize them into a PowerPoint file, and submit as "Manuscript No. - Figures.ppt" on the system, we need to edit the words in the figures. All submitted figures, including the text contained within the figures, must be editable. Please provide the text in your figure(s) in text boxes.	The requested file has been uploaded.
24-25 (Fig 3)	Please don't include abbreviations in the title of the figure/table.	The title has been modified and abbreviations have been expanded as

	Please explain all the abbreviations of each figure/table under each piece of figure/table legends.	requested.
	Please provide the decomposable figure of figures, whose parts are all movable and editable, organize them into a PowerPoint file, and submit as "Manuscript No. - Figures.ppt" on the system, we need to edit the words in the figures. All submitted figures, including the text contained within the figures, must be editable. Please provide the text in your figure(s) in text boxes.	The requested file has been uploaded.
26-27 (Fig 4)	Please don't include abbreviations in the title of the figure/table. Please explain all the abbreviations of each figure/table under each piece of figure/table legends.	The title has been modified and abbreviations have been expanded as requested.
	Please provide the decomposable figure of figures, whose parts are all movable and editable, organize them into a PowerPoint file, and submit as "Manuscript No. - Figures.ppt" on the system, we need to edit the words in the figures. All submitted figures, including the text contained within the figures, must be editable. Please provide the text in your figure(s) in text boxes.	The requested file has been uploaded.
28-29 (Table 2)	Please explain all the abbreviations of each figure/table under each piece of figure/table legends. Please don't include abbreviations in the title of the figure/table.	The title has been modified as requested.
30 (Table 5)	According to the rules of BPG, we do not allow color labels in the table, please revise it.	The table has been modified as requested.

Reviewer #1 (code 02445242)

#	Comment/question	Authors' response
1	**Clarify that the 2 studies referred to on p7 of the FDA de novo request, the 2 posters presented at AAGP, and the current paper are all referring to the same 2 studies** "Cognivue® was cleared by the FDA in 2015. This was done based on two studies (reference 31 of manuscript). Page 7 of this reference states that: "The sponsor conducted two separate studies. The first study was conducted to determine the cut-off values for Cognivue (eg, impaired, intermediate, and unimpaired cognitive function) by comparing the performance of Cognivue against a reference standard, the St. Louis University Mental Status (SLUMS) Examination. The second study was a clinical validation study which examined the agreement between the Cognivue classifications and the SLUMS classifications. The clinical validation study also examined the test – retest reliability study of Cognivue, and the determination of the construct validity of Cognivue via comparison with traditional paper and pencil neuropsychological tests." The "Cut-off" study had 92 participants and the "Clinical validation" study had 401 participants. More recently the same authors appeared to have presented their results as posters at the AAGP Annual Meeting 2019. One of these posters is about the "Cut-off study" with 92 participants (American journal of Geriatric Psychiatry - March 2019 Volume 27, Issue 3, Supplement, Page S211), while the other is regarding the results of the "Clinical validation" study with 401 participants (March 2019 Volume 27, Issue 3, Supplement, Page S212). Now in this manuscript the authors again present the results of "Cut-off" and "Clinical validation" studies. It is not at all clear if these 3 sources of data leading to the 3 pairs of studies are the same. I think the authors need to clarify this."	The last paragraph of the introduction section has been rephrased for clarity.
2a	**Preference for a more independent group of authors** "Secondly, the authors have clearly disclosed their conflicts of interest and source of funding. One of them has acted as a consultant and speaker for Cognivue Inc. while the other two are employees of Cognivue Inc. Though this is not clearly stated the study appeared to be funded by the same company. Although the full disclosure is helpful, personally I would have been happier to read a paper on the usefulness of the Cognivue® by an independent set of authors. This would have done away with lingering suspicion of bias that will always exist when the authors have such a close connection with the company marketing the device."	We appreciate the reviewer's comment and would like to clarify that the data presented in this manuscript are the original data from the US FDA clearance study for Cognivue. All methods and analyses were discussed in detail with the FDA which provided full product clearance based on their independent review of the validity and significance of our data.
2b	**Request for information pertaining to additional**	As mentioned in the previous response, this

	validation studies "In this regard, something I found surprising was the lack of validation studies apart from the ones cited above. Since the Cognivue® has been around for 3-4 years I would have expected many more studies examining its properties in detecting cognitive impairment. However, I could find only one more study on multiple sclerosis (reference 30 of the manuscript). Perhaps the authors could let us know if there have been other studies."	manuscript contains the original US FDA clearance data for Cognivue. We understand the reviewer's point regarding a lack of additional studies in the 3 to 4 years after clearance, and this is due to the fact that the company has been focused on presenting/publishing existing data and pursuing additional data-generation opportunities. With that, at present we are not aware of any other published studies using Cognivue other than the MS paper referred to in the reviewer's question.
3	**Clarification of similarities and differences between sensitivity/specificity and the results as presented in terms of NPA and PPA** "The authors present the results of cross-validation with the SLUMS in terms of negative percent agreement (NPA) and positive percent agreement (PPA). These are somewhat different the sensitivity, specificity, PPV and NPV values, which are the indices generally used to evaluate screening instruments including those for cognitive impairment (for example - Mitchell & Malladi, Am J Geriatr Psychiatry 2010; 18:759–782). It would be helpful if the authors could clarify the similarities and differences between the NPA/PPA and these more traditional indices of screening."	This manuscript contains original data used for the US FDA Cognivue clearance. The statistical methods were discussed with, and agreed upon, by the FDA, which wanted to confirm that Cognivue would not cause any false-positive or false-negative results when testing for cognitive impairment. Additionally, the FDA wanted us to compare conservatively with the SLUMS, which is a validated cognitive testing method used in most US government facilities. The FDA agreed that NPA and PPA analyses were appropriate for the purpose of clinical validation.
4	**Further comment regarding: the issue of utility of Cognivue vs. paper and pencil tests (MMSE, Mini-Cog, MoCA), relative higher cost in an uninsured context, and/or "nature of sub-tests"** "The final question that needs to be answered is about the usefulness of the Cognivue® versus paper and pencil tests particularly the ones such as the MMSE, Mini-Cog and the MOCA which have been found useful earlier (Mitchell & Malladi, 2010; Tsoi et al. JAMA Intern Med. 2015;175(9):1450-1458). The authors do address this issue on pages 10 and 11 but it is quite apparent that without further testing on larger samples it would not be possible to comment on the usefulness of the Cognivue® versus other screening instruments. Moreover, some of its utility may be offset by the high costs of the test in settings where insurance is not available. In this regard, a recent systematic review of the diagnostic accuracy of automated tests for cognitive impairment concluded that: "Some tests have shown promising results for identifying MCI and early dementia. However, concerns over small sample sizes, lack of replicability of studies, and lack of evidence available make it difficult to make recommendations on the clinical use of the computerised tests for diagnosing, monitoring progression, and treatment response for MCI and early dementia. Research is required to establish stable cut-off points for automated computerised tests used to	We thank the reviewer for their comment. Cognivue is distinct from other computerized tests mentioned due to the unique science behind it—adaptive psychophysics—which is described in the manuscript. We believe computerized cognitive testing rooted in adaptive psychophysics is an evolution in the optimization of cognitive impairment detection and test-retest reliability, in addition to other advantages mentioned in the discussion section of this manuscript. The data analyses and results presented in this first manuscript are based on the original US FDA clearance study. We agree that additional data generation and dissemination are needed to solidify the benefits of Cognivue as compared to other traditional methods such as the MMSE and MoCA, and we are working on the initial stages of such trials and additional long-term longitudinal studies. We do think it is important to publish our first manuscript based on these relevant FDA clearance data so that it might be included in future independent meta-analyses, as mentioned in the reviewer's comment. We fully agree with the reviewer's comment pertaining to the importance of specific cognitive domains (eg, memory, executive function) in helping with the evaluation of the cognitive health

	diagnose patients with MCI or early dementia." (Aslam et al. Int J Geriatr Psychiatry. 2018;33:561–575) Incidentally, this review of 11 studies did not mention the Cognivue® studies. A second review systematic review & meta-analysis on neuropsychological measures that predict progression from mild cognitive impairment to Alzheimer's type dementia in older adults found that: "Verbal memory measures and many language tests yielded very high predictive accuracy. Other domains (eg, executive functions, visual memory) showed better specificity than sensitivity. Predictive accuracy was highest when combining memory measures with a small set of other domains or when relying on broad cognitive batteries." (Belleville et al Neuropsychol Rev 2017 27:328–353) Thus, the nature of sub-tests included in the Cognivue® (page 4 of the manuscript) will probably be crucial in determining the ultimate utility of the test. I think it would be useful if the authors could comment on this issue."	of patients. With that, Cognivue was compared with the SLUMS and with a battery of other neuropsychological tests (RAVL, trail making A & B, etc; results described in Table 5), as needed for the FDA clearance. Subsequently, a factor analysis was used to describe the correlation between Cognivue scores/variables and each neuropsychological test. This is further described in Table 5 which shows significant correlations with memory (RAVL correlations) and executive function tests (Trail making A & B). The current Cognivue report provides an overall score based on the clinical validation and cut-off values from the comparison with SLUMS and an additional breakdown into cognitive domains.

Reviewer #2 (code 02726248)

#	Comment/question	Authors' response
1	**Repetition of introduction part in methods section** "There is substantial repetition of a part from introduction in methods section."	The methods section has been modified slightly to address the reviewer's concern.
2	**Addition of figure depicting Cognivue sub-tests w/ score range and corresponding SLUMS questions** "In methods there is a need to plot the 10 tests of Cognivue in a more illustrative [way] to illustrate the minimum and maximum score for each item and for each one of the 3 sub battery in order to make a more clear relation between each item with its relevant question in the gold standard test (SLUMS); this needs also to plot each question from SLUMS against its related test in Cognivue."	We thank the reviewer for their comment. The minimum and maximum value for each of the 10 sub-tests are 0 (zero) and 100 (one hundred), respectively. We did not explicitly show this because each sub-test alone does not account for the overall score comparing with SLUMS in the 3 categories (the cut-off explanation is in the methods section of the manuscript) or for the correlations with the other neuropsychological tests (factor analysis in Table 5). In addition, we do not have individual plotting for each SLUMS question, as the main point of correlation with cognitive domains was answered with the factor analysis we performed and is described in Table 5. Please note that the design, methodology, and statistical analyses described in this manuscript were discussed/determined by the US FDA as these are the study data used for the FDA clearance study.
3	**Addition of scatterplots showing data for Cognivue sub-tests and corresponding SLUMS questions** "Authors present well the factor analysis table with the data reduced to 5 factors but it will be more illustrative to plot all the Cognivue tests against the SLUMS questions also."	We appreciate the reviewer's comment, however we do not have individual plotting for each SLUMS question. The comparison with SLUMS was to conservatively determine Cognivue cut-off scores and main cognitive impairment ranges (described in the methods section of the manuscript). As it relates to an analysis broken down by cognitive domain, we performed factor analysis among Cognivue scores/variables and other neuropsychological tests performed during this study as well (Table 5). Please note that the design, methodology, and statistical analyses described in this manuscript were discussed/determined by the US FDA as these are the study data used for the FDA clearance study.
4	**Clarification re: rationale for not using standard ROC to estimate the cut-off values** "Why was the standard Receiver operator Curve (ROC) not used to estimate the cutoff values? please elaborate on this point."	This manuscript contains original data used for the US FDA Cognivue clearance. The statistical methods were discussed/directed by the FDA, which wanted to confirm that Cognivue would not cause any false-positive or false-negative results when testing for cognitive impairment. Additionally, the FDA wanted us to compare conservatively with the SLUMS, which is a validated cognitive testing method used in most US government facilities. The FDA agreed that NPA and PPA analyses were appropriate for the purpose of clinical validation.