



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
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January 13, 2017

Cambridge Cognition Ltd.,  
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Re: K161328

Trade/Device Name: Cantab Mobile  
Regulation Number: 21 CFR 882.1470  
Regulation Name: Computerized Cognitive Assessment Aid  
Regulatory Class: Class II  
Product Code: PKQ  
Dated: December 21, 2016  
Received: December 21, 2016

Dear Dr. Clementi:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

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

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in

510(k) Number (*if known*)  
K161328

Device Name  
CANTAB Mobile

**Indications for Use (Describe)**

The CANTAB Mobile is intended to be used as an adjunctive tool to assess memory by testing visuospatial associative learning in patients aged 50 to 90 years.

**Type of Use (Select one or both, as applicable)**

Prescription Use (Part 21 CFR 801 Subpart D)       Over-The-Counter Use (21 CFR 801 Subpart C)

**CONTINUE ON A SEPARATE PAGE IF NEEDED.**

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<sup>1</sup> Sections marked “N/A” are not applicable; an explanatory slip sheet is present for each N/A section in the electronic copy only. The paper copy only includes applicable section content.

<sup>2</sup> Sections are grouped under an “Administrative” tab in the paper copy of the submission.

<sup>3</sup> Sections are grouped under a “Statements” tab in the paper copy of the submission.

<sup>4</sup> For ease of review, cited literature is included in the electronic submission copy.

<sup>5</sup> Introductory signature pages are available upon request.

<sup>6</sup> References are available upon request.

<sup>7</sup> The majority of references present in the IFU are included electronically in either the Executive Summary (Section 10) or Device Description (Section 11). All other references are available upon request.

<sup>8</sup> Cited literature is available upon request in NMI-054. Rock et. al, 2014 is provided, however, as an appendix in the electronic submission copy.

## 1 BACKGROUND

### 1.1 Information on Dementia and Relevancy of Testing

It is estimated that dementia currently affects approximately 37 million people worldwide and, as the population ages, these prevalence rates can be expected to increase substantially. In addition to the devastating personal impact that a diagnosis of dementia may have upon the lives of patients and their caregivers, there is also a financial burden. The total monetary cost of dementia in 2010 was between \$157 billion and \$215 billion ([Hurd et al., 2013](#)).

Current criteria for the diagnosis of probable AD stipulates deterioration in two or more areas of cognition including memory of sufficient magnitude to interfere with work or social function. Critically however, substantial neuropathological change may have occurred before clinically significant symptoms ([Jack et al. 2010; Jansen et al. 2015](#)) appear. Thus, commencing treatment of AD at the time of clinical diagnosis (whether with cholinergic / glutamatergic drugs, anti-amyloid deposit agents or other putative disease modifying agents) may be sub-optimal or even ineffective because of the advanced stage of neurodegeneration at that time. The identification of cognitive tests that are sensitive to early pathological changes would facilitate the diagnosis of patients in a 'prodromal' state (i.e., those in whom the pathological process is present but whose symptoms are currently sub-clinical). Such early detection would serve to maximize the potential therapeutic benefit of treatment, enhance patient quality of life and, in so doing, reduce the burden on residential and nursing care services. Consequently, a very high therapeutic and economic premium is placed on the early detection and diagnosis of AD.

The CANTAB (Cambridge Neuropsychology Test Automated Battery) PAL (Paired Associates Learning) requires patients to learn and remember abstract visual patterns associated with various locations on a touch sensitive computer screen. See [Section 3](#) below for additional detail.

A series of independent studies have demonstrated that Cantab PAL measures of visuospatial associative learning and semantic memory are sensitive in detecting the earliest signs of prodromal Alzheimer's disease (up to 32 months prior to clinical diagnosis) both in memory clinic attendees ([Fowler et al., 1995; Fowler et al., 1997; Fowler et al., 2002; Swainson et al., 2001; Blackwell et al., 2004](#)) and in community dwelling cohorts of individuals classified as asymptomatic using current clinical measures ([De Jager et al., 2002; De Jager et al., 2005](#)).

Further studies using Cantab PAL have confirmed it to be of utility in early and differential diagnosis in AD on a case-by-case basis. The Cantab PAL performance of patients with mild AD was impaired relative to both demographically-matched healthy controls ([Sahakian et al., 1988](#)) and to individuals with Frontal Variant Fronto-Temporal Dementia ([Lee et al, 2003](#)). Of critical importance, Cantab PAL was also found to be relatively insensitive to major unipolar depression (only 7 percent of scores of patients with Depression and Alzheimer's disease fell within an overlapping range) ([Swainson et al., 2001](#)). This result suggests that Cantab PAL is of utility in the differential diagnosis of early AD and depression (unlike word recall tests – see [O'Carroll et al., 1997](#)). Unlike ADAS-COG, performance on Cantab PAL

was also found to correlate significantly with subsequent deterioration in global cognitive function. Furthermore, in a group of individuals with ‘questionable dementia’, baseline Cantab PAL results revealed an apparent subgroup of patients who performed like AD patients. In a follow up study, [Blackwell et al. \(2004\)](#) showed that by taking into account age and performance on one other neuropsychological test (The Graded Naming Test [[McKenna & Warrington, 1980](#)]), Cantab PAL gave a 100% distinction between patients with questionable dementia who either did or did not convert to probable AD (NINCDS-ADRDA criteria) 32 months after baseline testing (see also [De Jager et al., 2002](#)). These studies also revealed that the sensitivity (in detecting prodromal AD in a QD group) and specificity (in differentiating AD from depression) of Cantab PAL was considerably better than that of all other frequently-used tests included in the study (including ADAS-cog and Wechsler Logical Memory Delayed Passage Recall).

The accumulating evidence demonstrates the sensitivity and specificity of Cantab PAL as a tool for operationalizing the criteria for objective memory impairment in mild cognitive impairment (MCI).

## 2 INDICATION(S) AND INTENDED USE

The application is designed to detect episodic memory impairments in patients aged 50 to 90 years who may be experiencing MCI or dementia (Table 1). Along with the memory test there are optional mood and functional assessments which can help detect symptoms of depression (Geriatric Depression Screening Questionnaire [GDS]), and problems with performing regular activities of daily living (Activities of Daily Life Questionnaire [ADL]). Additional information on questionnaires is provided in the Device Description document, [Section 11](#) of this submission.

**Table 1. Indications for Use**

<b>Indications for Use</b>	The device is intended to be used to assess memory in patients aged 50 to 90 years.
<b>Contraindications</b>	Patients with severe visual impairment Patients outside the indicated age range

The application provides test results that are interpretive, however, Cantab Mobile is not a diagnostic test. The output provided by the device is not diagnostic. A diagnosis can only be made by a qualified physician using consensus diagnostic criteria. The option to test or not to test is a decision that rests with the medical professional.

### 2.1 Instructions for Use

The Instructions for Use (IFU) is included as a separate document in Section 13 of this submission. Please see [NMI-013](#) for the full Instructions for Use for Cantab Mobile.

### **3 DEVICE DESCRIPTION**

A full Device Description is included in a separate document in [Section 11](#) of this submission.

#### **3.1 Summary**

Cantab Mobile is software to be loaded and run on Apple iPad hardware and operating system. The software is intended to be administered by a healthcare professional to test the cognitive function of a patient. The Cantab Mobile memory test is based on the Cantab PAL test, which requires patients to learn and remember abstract visual patterns associated with various locations on a touch-sensitive computer screen. Two optional questionnaires are included to assess a patient's mood and ability to perform daily living activities. At the conclusion of the test, a 'thank you' screen is displayed with no information on test outcome. The healthcare professional will then be able to read or export a report, which summarizes the memory test results and also displays information on the patient's responses in the questionnaires, if these have been administered.

Cantab Mobile has been classified as a Class IIa Medical Device in accordance with:

- MEDDEV 2.1/6 – January 2012
- 93/42/EEC on Medical Devices, Classification Criteria, Annex IX, Rule 10.

## 5 SUBSTANTIAL EQUIVALENCE

### 5.1 Predicate Device

Cantab Mobile is substantially equivalent to DANA (manufactured by AnthroTronix; K141865). Cantab Mobile and DANA are both categorized as Attention Task Performance Recorders. The tests use different mobile devices; Cantab Mobile uses an Apple iPad and DANA uses a smartphone or tablet with the Android operating system. Cantab Mobile and DANA are both used by healthcare professionals to measure aspects of patients' cognition. Cantab Mobile and DANA differ in the areas of cognition measures in that Cantab Mobile assesses visuospatial episodic memory, whereas the DANA software measures reaction time (speed and accuracy). Cantab Mobile and DANA are similar in terms of technological characteristics as both electronically record objective performance measurements when the patient responds to stimuli presented on the screen by touching the screen. Differences in the design and performance of Cantab Mobile and DANA do not affect either the safety or effectiveness of Cantab Mobile for its intended use.

Table 3 presents a summary of each device for comparison. A complete comparison table is provided in [Appendix A](#).

**Table 3. Device Comparison Summary (Proposed Device vs. Predicate Device)**

Comparison Items	CANTAB Mobile-Cambridge Cognition Ltd.	DANA – AnthroTronix (Submitted September 18, 2014)
510(k) Number	Not Yet Assigned	K141865
Trade Name	Cantab Mobile	DANA
Common Name:	Mobile Based Task Performance Recorder	
Classification Name:	Recorder, Attention Task Performance	
Regulatory Class:	Unclassified	
Indications for Use	Cantab Mobile is intended to be used to assess memory in patients aged 50 to 90 years. Along with the memory test there are optional mood and functional assessments which can help detect symptoms of depression, and problems with performing regular activities of daily living.	DANA provides clinicians with objective measurements of reaction time (speed and accuracy) to aid in the assessment of an individual's medical or psychological state. DANA also delivers and scores standardized psychological questionnaires.

## 7 RISKS TO HEALTH

### 7.1 Summary

Risk management for the device is handled under controlled procedures within a Quality Management System. These procedures are designed to meet applicable requirements of EN ISO 13485:2012 and EN ISO 14971:2012.

A tabular summary of the risk analysis and other document references are provided in [Section 11](#) of this submission.

### 7.2 Determination of Level of Concern

Cantab Mobile's level of concern is classified as minor based upon the parameters and recommendations outlined in FDA's *Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices* (2005), with negative responses to all questions in Tables 1 and 2. Regarding question 3 in Table 2, the app is a screening device for use by a learned intermediary in conjunction with other investigations; its operation does not lead directly to diagnosis or choice of appropriate medical care.

## 8 OVERALL CONCLUSIONS

Cantab Mobile is an app that runs on an iPad. It detects episodic memory impairments, in patients aged 50 to 90 years, and includes optional mood and functional assessments which can help detect symptoms of depression and problems with performing regular activities of daily living. The Cantab tests have a 30-year history of use in a range of clinical populations, supported by over 1500 published papers. Cantab Mobile includes the Cantab PAL test, which has been developed as a way of assessing episodic memory without language barriers. A series of independent studies have demonstrated that PAL is sensitive in detecting the earliest signs of prodromal Alzheimer's disease, up to 32 months prior to clinical diagnosis, and that it is relatively insensitive to major unipolar depression. The accumulating evidence demonstrates the sensitivity and specificity of PAL as a tool for operationalizing the criteria for objective memory impairment in mild cognitive impairment (MCI).

Cantab Mobile is not a diagnostic test. The results for a patient's PAL memory test are presented to the healthcare professional as one of three traffic-light coded categories. In conjunction with other investigations, these provide information to assist the professional in their assessment of the patient.

Cantab Mobile is substantially equivalent to AnthroTronix's DANA software in that they share the intended use of providing clinicians with objective measurements of cognition. Both are mobile applications that electronically record objective performance measurements as the patient responds to stimuli presented on the screen by touching the screen. Differences in the design and performance of Cantab Mobile from DANA, the predicate device, do not affect either the safety or effectiveness of Cantab Mobile for its intended use.

## 10 APPENDICES

### Appendix A. Predicate Device Comparison (Cantab Mobile and DANA)

Comparison Items	CANTAB Mobile-Cambridge Cognition Ltd.	DANA - AnthroTronix
510(k) Number	Not Yet Assigned	K141865
Device Information: Trade Name	Cantab Mobile	DANA
Device Information: Common Name:	Mobile Based Task Performance Recorder	Mobile Based Task Performance Recorder
Device Information: Classification Name:	Recorder, Attention Task Performance	Recorder, Attention Task Performance
Device Information: Device Class:	Unclassified  The device has the same intended use, indications for use, and relies on technology that does not raise new safety and effectiveness questions to DANA.	Unclassified  <a href="http://www.accessdata.fda.gov/cdrh_docs/pd/f14/k141814.pdf">http://www.accessdata.fda.gov/cdrh_docs/pd/f14/k141814.pdf</a>
Predicate Device:	DANA (K141865)	QbTest, Qbtech AB (K122149)
Type of Use	Prescription Use (Part 21 CFR 801 Subpart D)	Prescription Use (Part 21 CFR 801 Subpart D)
Submission Date:	TBD	September 18, 2014
Submitter Information: Company:	Cambridge Cognition Limited. Tunbridge Court, Tunbridge Lane Bottisham Cambridgeshire, CB25 9TU UK	AnthroTronix, Inc. 8737 Colesville Road, Suite L203 Silver Spring, MD 20910 USA
Design and Intended Use	<p>Cantab Mobile is a mobile application indicated to provide clinicians with objective measurements of visuospatial episodic memory and mood to aid in the assessment of an individual's medical or psychological state.</p> <p>Results should be interpreted only by qualified professionals.</p> <p>Cantab Mobile was developed on a mobile platform to improve the access and availability of assessments.</p>	<p>DANA is a mobile application indicated to provide clinicians with objective measurements of reaction time (speed and accuracy) and standardized health assessments to aid in the assessment of an individual's medical or psychological state.</p> <p>Results should be interpreted only by qualified professionals.</p> <p>DANA was developed on a mobile platform to improve the access and availability of assessments.</p>

<b>Comparison Items</b>	<b>CANTAB Mobile-Cambridge Cognition Ltd.</b>	<b>DANA - AnthroTronix</b>
Target population	Patients aged 50 to 90 years with concerns about their memory. Results are automatically adjusted for age, gender, education.	A wide age range from high school students to older patients with dementia.
Anatomical site	The brain: cognitive function	The brain: cognitive function
Test duration	The test takes approximately 10 minutes to complete.	Spectrum of tests: 5-Minute Rapid; 15-Minute Brief; 45-Minute Standard.
Scoring and reports	Automatic scoring and instant reports	Automatic scoring and instant reports
Where used	Cantab Mobile is software used on a tablet, therefore it can be administered in any suitable setting, e.g. a clinic or home.	DANA is software on a tablet or smartphone, therefore it can be administered anywhere.
Energy used	Cantab Mobile software runs on an Apple iPad, which has the following features: <ul style="list-style-type: none"> <li>▪ built-in 25-watt-hour rechargeable lithium-polymer battery;</li> <li>▪ charging via power adapter or USB to computer system;</li> <li>▪ up to 10 hours of use when charged.</li> </ul>	The DANA software runs on Android tablets and smartphones, containing a rechargeable battery, charged via power adapter or USB to computer system. The energy used is hardware-dependent.
Human factors	Any healthcare professional can administer the test. To ensure reliable results, the iPad should be placed on a stand and the assessment should be administered in a quiet room, without disturbance.  The voiceover and questionnaire texts are provided in a choice of languages.	DANA software can be self-administered by patients or administered by a health aide.
To whom is the product marketed /target audience?	Healthcare Rehabilitation	Healthcare Education Pharmaceutical Rehabilitation Government
Materials	N/A	N/A
Biocompatibility	N/A	N/A
Compatibility with the environment and other devices	N/A	N/A
Sterility	Sterility status is not needed for this software-only device	Sterility status is not needed for this software-only device
Safety: electrical; mechanical; chemical;	These safety issues are not applicable to this software-only device.	These safety issues are not applicable to this software-only device.

Comparison Items	CANTAB Mobile-Cambridge Cognition Ltd.	DANA - AnthroTronix
thermal; radiation.		
To whom is the product marketed /target audience?	Healthcare Rehabilitation	Healthcare Education Pharmaceutical Rehabilitation Government
How the device differs from Predicate device	Cantab Mobile is similar to DANA in terms of technological characteristics, as both electronically record objective performance accuracy as the patient responds to stimuli presented on the screen by touching the screen. Cantab Mobile differs from DANA in that it provides an assessment of episodic memory, compared to DANA which assesses attention. Cantab Mobile also presents assessments of depression and activities of daily living, which are not included in DANA.	

## 11. DEVICE DESCRIPTION

**Product Name:**

Cantab Mobile

**Indication:**

Assess Memory in Patients Aged 50 to 90 Years



### Sponsor

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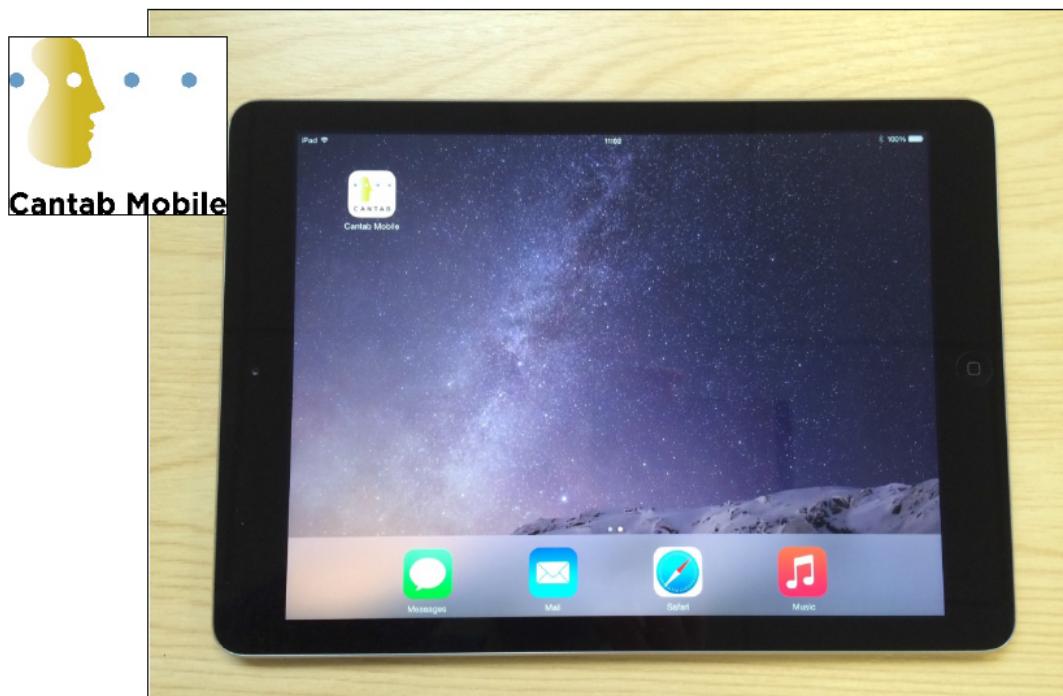
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## 1 DEVICE DESCRIPTION

Cantab Mobile is software to be loaded and run on Apple iPad hardware and operating system (Figure 1). Below is a list of possible device accessories:

- The iPad<sup>1</sup> is an essential accessory
- Disposable iPad Sleeve (see also **Instructions for Use [Section 13]**) for cleaning recommendations)
- iPad stand
- A iPad battery charger is also supplied with the iPad

**Figure 1. iPad with App Icon at Top Left**



Cantab Mobile does not have a restricted shelf-life. Ongoing support of the manufacturer is required, however, and is detailed below.

The medical device software must be updated when new releases are made available. The iPad operating system should also be kept up to date. Both may be achieved automatically. The iPad battery should be charged as required. No calibration is necessary.

Ongoing support by the manufacturer is required. The app must be able to confirm periodically with the manufacturer that it is licensed, and be updated as required over time.

---

<sup>1</sup> Cantab Mobile is not authorized for use on the iPad mini or the iPad 1 (the first generation iPad). Do not install the app on these devices.

The test is not susceptible to environmental influences within the defined environment for its administration. We instruct that physicians must always administer the tests in a quiet, peaceful environment, with the iPad volume level set so that the patient can clearly hear instructions being given. For patients with impaired hearing, additional support may need to be provided to ensure they can correctly hear and understand the instructions during the test, e.g. use headphones.

A technical wireframe, or mobile app screen blueprint, of Cantab Mobile is a supportive document that presents the skeletal framework, interface elements, and navigational flow (See [Cantab Mobile Wireframes](#)).

## 1.1 Patient Data Entry

Prior to the PAL test itself, the healthcare professional administering the test enters patient data (patient ID, date of birth, gender, educational background etc.).<sup>2</sup> This is used in assessing the patient's performance against a set of normative data.

**Figure 2. Data Entry Screen**



## 1.2 Memory Test

Cantab Mobile provides an optional patient self assessment of memory (Self Assess - enabled on the data entry screen). If this assessment is enabled, the patient will rate his/her memory prior to taking Cantab PAL. The patient is presented a rating scale against which they rate their memory as above average (left of center), average (center), or below average (right of center) (See [Appendix A](#)). Comparing self-rated memory with the objective

- 2 Patient details must be entered correctly. Incorrect patient details can lead to incorrect reporting of patient impairment.

measure of memory, provided by Cantab PAL, can reveal any discrepancies between actual and perceived memory ability.

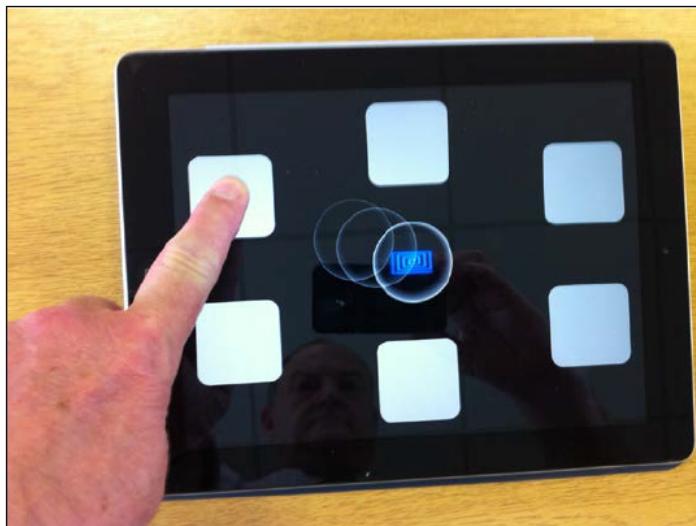
The Cantab Mobile memory test is based on the Cantab PAL test previously used on other hardware platforms. The Cantab PAL requires patients to learn and remember abstract visual patterns associated with various locations on a touch-sensitive computer screen. The patterns were all created to be bold, brightly colored, abstract and with no cultural context. See [Appendix B](#) for examples of patterns used.

Patterns are presented in six boxes around the edge of the screen (See Figure 3). The patterns disappear from the screen, leaving empty boxes and, after a brief delay, the same patterns are presented sequentially in the middle of the screen and the patient is required to touch the box in which they previously saw that pattern appear. ([Figure 4](#))

**Figure 3. Pattern Appears in Box**



**Figure 4. Patient Chooses Box**



If the patterns' locations are not recalled correctly, this is identified to the patient via audio prompts and pattern presentation and recall is repeated. This process continues until the task is completed successfully, at which point the next task is started, or repeated failures by the patient to recall the locations correctly cause the test to end. The whole test consists of a series of such tasks with increasing levels of difficulty.

The patient's responses are recorded by screen touches. The number of errors that they make are recorded and their performance is graded using algorithms derived from a normative database (b) (4)

### 1.3 Questionnaire(s)

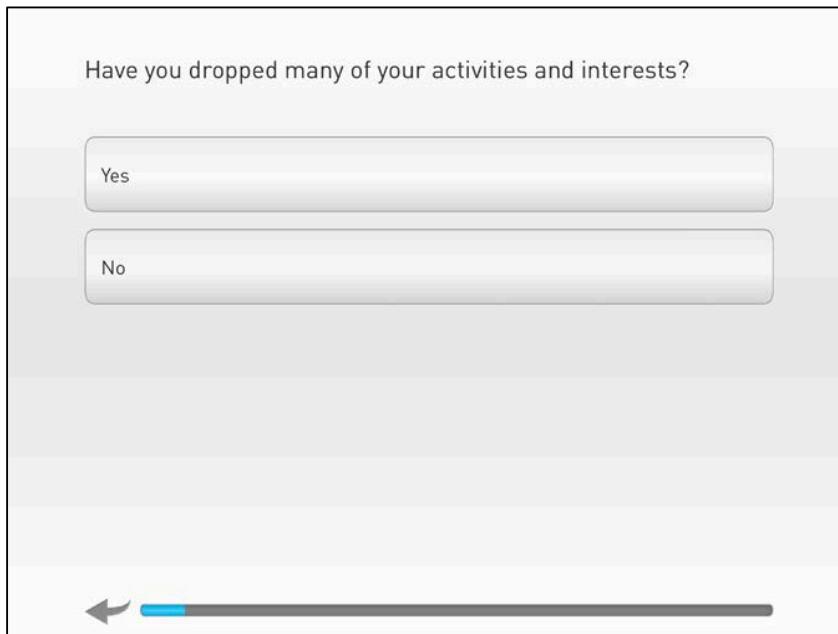
Cantab Mobile additionally includes optional questionnaires. Questionnaires operate by presenting a series of questions to the patient, with clearly labeled response boxes that the patient may touch in order to answer each question (Figure 5). Ratings scales administered (depending on patient performance, and if not disabled by the healthcare professional) comprise:

1. GDS – Geriatric Depression Screening Questionnaire (See [Appendix C](#))
2. ADL – Activities for Daily Living Questionnaire (See [Appendix D](#))

The GDS rating scale in the app is the shorter version of GDS including 15 questions, the GDS-15 ([Almeida and Almeida 1999](#)), which is based on the GDS described by Yesavage and colleagues ([Yesavage et al 1983](#)): The GDS rating scale comprises a series of questions, each presented in turn textually on the screen using the language in force, two buttons below to allow the patient to respond 'yes' and 'no' (or equivalent in the language in force). A progress bar gives an approximate indication of progress through the questions and

a button with a backward arrow allows the user to return to the preceding question (if any) and choose again. See Figure 5 below for an example of a GDS-15 rating scale question and its format, as it is presented in the app.

**Figure 5. GDS Rating Scale and Format**



Administration of the ADL rating scale comprises a series of questions, each presented in turn textually on the screen using the language in force<sup>3</sup>, with the introductory text given above the question and buttons below to allow the patient to choose from the responses permitted for the question. A progress bar gives an approximate indication of progress through the questions and a button with a backward arrow allows (except on questions 1 and 11) the user to return to the preceding question and choose again.

(b) (4)

- 3 The entire user interface respects the text direction (left-to-right or right-to-left) of the language in force including the backward arrow button and progress bar

## **2.2 Device Safety Characteristics and Risks**

Risk management for the device is handled under controlled procedures within a Quality Management System. These procedures are designed to meet applicable requirements of EN ISO 13485:2012 and EN ISO 14971:2012.

Identification of characteristics of the device that could impact on safety are documented in [\*\*QRM-01-001\*\*](#). Risk analysis was conducted according to a risk analysis plan referencing controlled procedures, namely [\*\*QRM-02-002\*\*](#), and the conclusion of the risk analysis process is documented in report [\*\*QRM-02-003\*\*](#).

The summary of all points of the risk analysis is provided in [\*\*QRM-02-001\*\*](#).

## **Appendix C. Mood Assessment (GDS)**

The Mood Assessment (GDS) is automatically administered. Cantab PAL performance is not a conditional factor in administering the Mood Assessment.

**Are you basically satisfied with your life?**

- Yes
- No

**Have you dropped many of your activities and interests?**

- Yes
- No

**Do you feel that your life is empty?**

- Yes
- No

**Do you often get bored?**

- Yes
- No

**Are you in good spirits most of the time?**

- Yes
- No

**Are you afraid that something bad is going to happen to you?**

- Yes
- No

**Do you feel happy most of the time?**

- Yes
- No

**Do you often feel helpless?**

- Yes
- No

**Do you prefer to stay at home, rather than going out and doing new things?**

- Yes
- No

**Do you feel you have more problems with memory than most?**

- Yes
- No

**Do you think it is wonderful to be alive now?**

- Yes
- No

**Do you feel pretty worthless the way you are now?**

- Yes
- No

**Do you feel full of energy?**

- Yes
- No

**Do you feel that your situation is hopeless?**

- Yes
- No

**Do you think that most people are better off than you are?**

- Yes
- No

## **Appendix D. Functional Assessment (ADL)**

This test is automatically administered after Cantab PAL if the patient's Cantab PAL performance has indicated that they fall in the "Investigate" category

### **Part 1:**

**In the past 3 months, were you able to:**

**Do your own shopping?**

- Yes
- Yes, but I had some problems or needed some help
- No, I could not do it
- I did not try

**Prepare meals?**

- Yes
- Yes, but I had some problems or needed some help
- No, I could not do it
- I did not try

**Write checks, pay bills, or use an ATM cash machine?**

- Yes
- Yes, but I had some problems or needed some help
- No, I could not do it
- I did not try

**Travel by car or public transport?**

- Yes
- Yes, but I had some problems or needed some help
- No, I could not do it
- I did not try

**Carry out housework, laundry or home repairs?**

- Yes
- Yes, but I had some problems or needed some help
- No, I could not do it
- I did not try

**Do hobbies such as a card games or crosswords?**

- Yes
- Yes, but I had some problems or needed some help
- No, I could not do it
- I did not try

**Follow the story of a TV program, book or movie?**

- Yes
- Yes, but I had some problems or needed some help
- No, I could not do it
- I did not try

**Keep track of current events in the news or the media?**

- Yes
- Yes, but I had some problems or needed some help
- No, I could not do it
- I did not try

**Remember appointments or important dates such as birthdays?**

- Yes
- Yes, but I had some problems or needed some help
- No, I could not do it
- I did not try

**Remember to take your medication?**

- Yes
- Yes, but I had some problems or needed some help
- No, I could not do it
- I did not try

**Part 2:**

**Can you:**

**See well enough to recognize someone across the street (wearing glasses or contact lenses if necessary?)**

- Yes
- No

**Hear what people are saying when they are speaking at a normal volume?**

- Yes
- No

**Walk up and down a set of stairs without help?**

- Yes
- No

## **5 REFERENCED DOCUMENTS**

**Cantab Mobile Technical Wireframes**

**Cantab Mobile Managing Reports Quick Reference Guide**

**Demographic Adjustment of Scores (NMI-020)**

**Identification of Characteristics (QRM-01-001)**

**PALD Risk Management Plan (QRM-02-002)**

**Risk Summary Report (QRM-02-003)**

**Risk Analysis (QRM-02-001)**

Approval by the following personnel signifies agreement that the content, rationale and approach are consistent with requirements, that a review for clarity, accuracy, completeness and compliance has been completed, and the document is approved for use.

---

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---

Name:	Ian Cartland	Role:	Project Manager
Signature:		Date:	

---

---

*M a n a g e m e n t A p p r o v a l : A d d i t i o n a l*

---

Name:	Jenny Barnett	Role:	Requirements Representative (Science)
Signature:		Date:	

---

Approval by the Quality Manager (QA), indicates that a review has been completed for clarity, accuracy, completeness and compliance with company standards and regulatory requirements and that the document is approved for use.

---

*Q u a l i t y A s s u r a n c e A p p r o v a l*

---

Name:	Ricky Dolphin	Role:	Nominated Delegate Quality Manager
Signature:		Date:	

---

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*Document History*

Version	Date released for approval	Developer Initials	Reviewer Initials	Changes from Previous Version
4.0	29 May 2015	IC	JB	Revisions for multi-domain mode and from review. Updated document template.

## **1. Purpose**

The purpose of this document is to review the Risk Management Plan and the associated documents to determine their compliance with the requirements of EN ISO 14971:2012 Medical Devices – Application of Risk Management to Medical Devices.

## **2. Introduction**

The Risk Management Plan is divided into two phases:

- i) Description of the intended use of the device and identification of the characteristics that could affect the safety of the device to patients, carers and the environment. Annex C of EN ISO 14971:2012 will be used to identify the device characteristics that could impact on safety.
- ii) Identification of known or foreseeable hazards, using as a guide, Annex E of EN ISO 14971:2012. For each hazard identified, its risk potential will be estimated based on the severity and occurrence likelihood identified in the Risk Management Plan and **SOP QRM-02, Risk Management Process** and the actions taken to reduce the risk(s) identified.

On completion of the above analyses the Project Manager will review the actions to ensure that the risk control measures are appropriate for reducing the risk(s) to an acceptable level. If any residual risk has a 'high' level of concern, the Project Manager will ensure that the medical benefits of the device outweigh the residual risks.

## **3. Review of medical device characteristics that could impact on safety**

**QRM-01-001** v4.0 addresses the characteristics that could impact on safety identified in EN ISO 14971:2012, Annex C.

## **4. Review of hazards**

All hazards identified in **QRM-02-001** v6.0 have an acceptable level of concern hence no reports are required to demonstrate that medical benefits of the device outweigh the residual risks.

## **5. Conclusion**

This report confirms that the hazards associated with Cantab Mobile have been identified and the risks associated with each hazard estimated and evaluated. The methods for mitigating these risks have been identified. On completion of this Risk Management Process all residual risks have an acceptable level of concern.

This Risk Management Plan will be reviewed as a result of any negative post market feedback.



## Cantab Mobile

### 12. Substantial Equivalence Discussion

This section is not applicable. This material is covered in the Executive Summary of this submission ([Section 10](#)).

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## Cantab Mobile

### 14. Sterilization and Shelf Life

Sterilization and shelf-life regulations are not applicable to Cantab Mobile. Therefore, this section is not applicable.

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## Cantab Mobile

### 15. Biocompatibility

This section is not applicable.

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## Cantab Mobile

### 16. Software

This report outlines Cambridge Cognition's software development lifecycle and procedures relevant to medical device software development with respect to the requirements of *IEC 62304:2006 Medical device software – Software life cycle processes* for class A software systems. Documents referenced in the report are available upon request.

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**Cantab Mobile**

## **17. Electromagnetic Compatibility and Electrical Safety**

Cantab Mobile's device design does not include an electronic component in which an evaluation of its electromagnetic compatibility (EMC) is applicable. Therefore, this section is not applicable.

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## Cantab Mobile

### 18. Performance Testing - Bench

No bench tests were conducted as a part of this 510(k) submission. Therefore, this section is not applicable.

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## Cantab Mobile

### 19. Performance Testing - Animal

Animal performance testing is not applicable to Cantab Mobile's testing and development. Therefore, this section is not applicable.

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## **Appendix D: Cognitive impairment in depression: a systematic review and meta-analysis**

The referenced article is shown below

Rock, P. L., Roiser, J. P., Riedel, W. J., & Blackwell, A. D. (2013). Cognitive impairment in depression: a systematic review and meta-analysis. *Psychological medicine*, 1-12.

## Contents of Submission: 510(k) CANTAB Mobile<sup>1</sup>

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<sup>1</sup> Document signature pages are available upon request.

<sup>2</sup> Updated or amended document

<sup>3</sup> New Document

<sup>4</sup> Only newly submitted key references are included in the electronic submission. Please refer to the Original CANTAB Mobile 510(k) submission (10-May-2016) for other references listed.

<sup>5</sup> The majority of references present in the IFU are included electronically in either the Executive Summary (Section 10 of original submission) or Device Description (Section 11 of original submission). All other references are available upon request.

<sup>6</sup> References are available upon request.

<sup>7</sup> This document is available in the electronic version of the submission. It resides in the statistical data folder in its native.xml format (zipped). A PDF version is present in Volume 5 (Item 6 Response).



## Tabular Listing of Deficiency Letter Item and Corresponding Sponsor Response

**Product Name:** Cantab Mobile (K161328)  
**Indication:** Assess Memory by Testing Visuospatial Associative Learning in Patients Aged 50 to 90 Years

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Item #	FDA Deficiency Description and Sponsor Response
<b>Substantial Equivalence Discussion #1</b>	<p><b>FDA Comment:</b> “You have identified the AnthroTronix – DANA (K141865) as the primary predicate device for comparison to the Cantab Mobile for the purposes of establishing substantial equivalence. The DANA indications for use state that it “provides clinicians with objective measurements of reaction time (speed and accuracy) to aid in the assessment of an individual's medical or psychological state. DANA also delivers and scores standardized psychological questionnaires”). In comparison, the Cantab Mobile seeks to be indicated “for the assessment of memory in adult individuals aged 50 to 90 years of age.” The device also specific in that it is “indicated to provide clinicians with objective measurements of visuospatial episodic memory and mood.”</p> <p>Reaction Time and Memory are two distinct cognitive processes which are used to assess different aspects of cognition. Therefore, the predicate device you have chosen is not appropriate. Please select a predicate device whose intended use is similar to the Cantab Mobile and revise your application accordingly. We believe it is appropriate for you to consider using DEN130033 (Cerebral Assessment Systems, Inc. – Cognivue) or K150154 (Vista Lifesciences – ANAM Test System) as potential predicate devices as these devices are indicated as computerized adjunctive assessments of memory. However, please note that you will need to provide a detailed comparison to the new predicate device, and where differences exist, information to support how Cantab Mobile can be considered equivalent. For example, while considering these predicates please keep in mind that these testing systems use multiple tests to produce an outcome; you would need to support the use of the PAL as a single test used to assess memory in comparison to these predicates which test memory in multiple domains. Additionally, it is important to provide evidence that the PAL may be used without an assessment of baseline function in the proposed use and that decrements cited as severe are outside the range that could be attributed to normal aging.”</p> <p><b>Sponsor Response:</b> Per the Division's recommendation above, the Sponsor has updated the predicate device for comparison to Cognivue. The <b>Executive Summary (Section 5.1 and Appendix A)</b> as well as <b>CDRH Premarket Review Submission Cover Sheet, FDA Form 3514</b> have been updated to reflect this change and are submitted herein.</p>

<b>Indications for Use #2</b>	<p><i>"Your Indications for Use Statement states that the Cantab Mobile will be used to assess memory in patients aged 50 to 90 years. The assessment of memory is a broad term and your Indications for Use should specify the type of memory that is being assessed in order to provide the user with an accurate description of the purpose of the device. Since the Cantab Mobile will use the PAL test to make its assessment of visuospatial learning, please revise your Indications for Use Statement to "assess visuospatial associative learning in patients aged 50 to 90 years."</i></p> <p><b>Sponsor Response:</b> The <a href="#">Indications for Use statement (FDA Form 3881)</a> has been revised in accordance with the Division's recommendations. All documents containing this statement have been updated and are resubmitted in this amendment.</p>
<b>Device Description #3</b>	<p><b>FDA Comment:</b> <i>"Within your Executive Summary and Device Labeling, you make multiple references to specific conditions such as Mild Cognitive Impairment and Dementia and state that the Cantab Mobile can detect memory impairment in such individuals. Please note that indicating your device for "assessment of memory in adult individuals aged 50 to 90 years of age" is different from making claims related to specific disease states; test scores resulting in this outcome may be attributed to other causes and patients should be referred for clinical evaluation. Indicating your device for MCI or Dementia would constitute a new intended use which would need to be reviewed via the DeNovo pathway due to lack of a suitable predicate. Therefore, please revise your Executive Summary, Device Results, and labeling by removing the reference to MCI or Dementia. In addition, please include a statement that the results of the Cantab Mobile should only be interpreted by a qualified professional."</i></p> <p><b>Sponsor Response:</b> The Sponsor has ensured that any references to Mild Cognitive Impairment and Dementia are contained only in reference to peer-reviewed publications where PAL has been used to assess these conditions in a research context. It is not claimed that Cantab Mobile can detect memory impairments in specific disease states.</p> <p>The Sponsor includes a statement in the <a href="#">Executive Summary (Section 2)</a> and (b) (4) "CANTAB Mobile is not a diagnostic test. A diagnosis can only be made by a qualified physician using consensus diagnostic criteria."</p>

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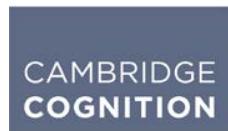
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## 10. Executive Summary

**Product Name:** Cantab Mobile (K161328)  
**Indication:** Assess Memory by Testing Visuospatial Associative Learning in Patients Aged 50 to 90 Years



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## LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

AD	Alzheimer's disease
ADAS-cog	Alzheimer's Disease Assessment Scale – Cognition
ADHD	Attention deficit hyperactivity disorder
ADL	Activities for Daily Living Questionnaire
CANTAB	Cambridge Neuropsychology Test Automated Battery
CAPA	Corrective and Preventative Action
DLB	Dementia with Lewy Bodies
FDS	Functional Design Specification
GDS	Geriatric Depression Screening Questionnaire
HD	Huntington's disease
ID	Identification
IFU	Instructions for Use
MCI	Mild Cognitive Impairment
MEDDEV	Medical Device guidance document
NINCDS-	National Institute of Neurological and Communicative Disorders
ADRDA	and Stroke - Alzheimer's Disease and Related Disorders Association
PAL	Paired Associates Learning
PIN	Personal Identification Number
RS	Requirements Specification
SCM	Software Configuration Management
SDLC	Software Development Life Cycle
SDS	Software Design Specification
SOP	Standard Operating Procedure
SOUP	Software Of Unknown Provenance
QD	Questionable dementia
QMS	Quality Management System
VMP	Validation Master Plan

## 1 BACKGROUND

### 1.1 Information on Dementia and Relevancy of Testing

It is estimated that dementia currently affects approximately 37 million people worldwide and, as the population ages, these prevalence rates can be expected to increase substantially. In addition to the devastating personal impact that a diagnosis of dementia may have upon the lives of patients and their caregivers, there is also a financial burden. The total monetary cost of dementia in 2010 was between \$157 billion and \$215 billion ([Hurd et al., 2013](#)).

Current criteria for the diagnosis of probable AD stipulates deterioration in two or more areas of cognition including memory of sufficient magnitude to interfere with work or social function. Critically however, substantial neuropathological change may have occurred before clinically significant symptoms ([Jack et al. 2010; Jansen et al. 2015](#)) appear. Thus, commencing treatment of AD at the time of clinical diagnosis (whether with cholinergic / glutamatergic drugs, anti-amyloid deposit agents or other putative disease modifying agents) may be sub-optimal or even ineffective because of the advanced stage of neurodegeneration at that time. The identification of cognitive tests that are sensitive to early pathological changes would facilitate the diagnosis of patients in a 'prodromal' state (i.e., those in whom the pathological process is present but whose symptoms are currently sub-clinical). Such early detection would serve to maximize the potential therapeutic benefit of treatment, enhance patient quality of life and, in so doing, reduce the burden on residential and nursing care services. Consequently, a very high therapeutic and economic premium is placed on the early detection and diagnosis of AD.

The CANTAB (Cambridge Neuropsychology Test Automated Battery) PAL (Paired Associates Learning) requires patients to learn and remember abstract visual patterns associated with various locations on a touch sensitive computer screen. See [Device Description Section 1.2](#) for additional detail.

A series of independent studies have demonstrated that Cantab PAL measures of visuospatial associative learning and semantic memory are sensitive in detecting the earliest signs of prodromal Alzheimer's disease (up to 32 months prior to clinical diagnosis) both in memory clinic attendees ([Fowler et al., 1995; Fowler et al., 1997; Fowler et al., 2002; Swainson et al., 2001; Blackwell et al., 2004](#)) and in community dwelling cohorts of individuals classified as asymptomatic using current clinical measures ([De Jager et al., 2002; De Jager et al., 2005](#)).

Further studies using Cantab PAL have confirmed it to be of utility in early and differential diagnosis in AD on a case-by-case basis. The Cantab PAL performance of patients with mild AD was impaired relative to both demographically-matched healthy controls ([Sahakian et al., 1988](#)) and to individuals with Frontal Variant Fronto-Temporal Dementia ([Lee et al., 2003](#)). Of critical importance, Cantab PAL was also found to be relatively insensitive to major unipolar depression (only 7 percent of scores of patients with Depression and Alzheimer's disease fell within an overlapping range) ([Swainson et al., 2001](#)). This result suggests that Cantab PAL is of utility in the differential diagnosis of early AD and depression (unlike word recall tests – see [O'Carroll et al., 1997](#)). Unlike ADAS-COG, performance on Cantab PAL

was also found to correlate significantly with subsequent deterioration in global cognitive function. Furthermore, in a group of individuals with ‘questionable dementia’, baseline Cantab PAL results revealed an apparent subgroup of patients who performed like AD patients. In a follow up study, [Blackwell et al. \(2004\)](#) showed that by taking into account age and performance on one other neuropsychological test (The Graded Naming Test [[McKenna & Warrington, 1980](#)]), Cantab PAL gave a 100% distinction between patients with questionable dementia who either did or did not convert to probable AD (NINCDS-ADRDA criteria) 32 months after baseline testing (see also [De Jager et al., 2002](#)). These studies also revealed that the sensitivity (in detecting prodromal AD in a QD group) and specificity (in differentiating AD from depression) of Cantab PAL was considerably better than that of all other frequently-used tests included in the study (including ADAS-cog and Wechsler Logical Memory Delayed Passage Recall).

The accumulating evidence demonstrates the sensitivity and specificity of Cantab PAL as a tool for operationalizing the criteria for objective memory impairment in mild cognitive impairment (MCI).

## 2 INDICATION(S) AND INTENDED USE

The application is designed to detect episodic memory impairments in patients aged 50 to 90 years by testing visuospatial associative learning (Table 1). Along with the memory test there are optional mood and functional assessments which can help detect symptoms of depression ([Geriatric Depression Screening Questionnaire \[GDS\]](#)), and problems with performing regular activities of daily living ([Activities of Daily Life Questionnaire \[ADL\]](#)). Additional information on questionnaires is provided in the amended Device Description (Vol. 3).

**Table 1. Indications for Use**

<b>Indications for Use</b>	The device is intended to be used to assess memory by testing visuospatial associative learning in patients aged 50 to 90 years.
<b>Contraindications</b>	Patients with severe visual impairment Patients outside the indicated age range

The results of Cantab Mobile should be interpreted only by qualified professionals. The application provides test results that are interpretive, however, Cantab Mobile is not a diagnostic test. The output provided by the device is not diagnostic. A diagnosis can only be made by a qualified physician using consensus diagnostic criteria. The option to test or not to test is a decision that rests with the medical professional.

### 2.1 Instructions for Use

The Instructions for Use (IFU) is included as a separate document in this submission. Please see [NMI-013](#) for the full Instructions for Use for Cantab Mobile.

### 3 DEVICE DESCRIPTION

A full **Device Description** is included as a separate document in this submission

#### 3.1 Summary

Cantab Mobile is software to be loaded and run on Apple iPad hardware and operating system. The software is intended to be administered by a healthcare professional to test the cognitive function of a patient. The Cantab Mobile memory test is based on the Cantab PAL test, which requires patients to learn and remember abstract visual patterns associated with various locations on a touch-sensitive computer screen. Two optional questionnaires are included to assess a patient's mood and ability to perform daily living activities. At the conclusion of the test, a 'thank you' screen is displayed with no information on test outcome. The healthcare professional will then be able to read or export a report, which summarizes the memory test results and also displays information on the patient's responses in the questionnaires, if these have been administered.

Cantab Mobile has been classified as a Class I Medical Device in accordance with:

- MEDDEV 2.1/6 – July 2016
- 93/42/EEC on Medical Devices, Classification Criteria, Annex IX, Rule 12.

The proposed regulatory classification, made under this 510(k) submission, is Class I. It is a Computerized Cognitive Assessment Aid (Product Code PKQ) and the classification regulation number is CFR 882.1470. [Appendix A](#) presents supportive information for this classification designation.

## 4 VERIFICATION, VALIDATION AND TRACEABILITY

Software development is carried out under a controlled Software Development Life Cycle within a Quality Management System. A summary of the current version of these procedures in relation to IEC 62304:2006 for Class A software systems is provided in

**QA-IEC62304Analysis.** **The Software Section** of this submission provides additional supportive information.

Version 1.4 is the current version of the application. The history of prior application changes and verification is reflected in the **Summary Table in the Software Section**.

In addition to the traceability of verification records and risk control activities provided in the above documents, traceability between requirements, functional design and software testing specifications is summarized in **NMI-018**.

Functional testing is conducted against controlled software versions using a defined test specification, which documents the criteria required for each test case to pass; the pass/fail outcome for each case is recorded in records of testing for the software version.

A revision history log of external software releases with version identification is maintained under the control of the software configuration management system.

## 5 SUBSTANTIAL EQUIVALENCE

### 5.1 Predicate Device

Cantab Mobile is substantially equivalent to Cognivue (manufactured by Cerebral Assessment Systems; DEN130033). Cantab Mobile and Cognivue are both categorized as Computerized Cognitive Assessment Aids. The tests use different devices; Cantab Mobile uses an Apple iPad and Cognivue uses a personal computer on a cart. Cantab Mobile and Cognivue are both used by healthcare professionals to measure aspects of patients' cognition. Cantab Mobile and Cognivue differ in the areas of cognition measured in that Cantab Mobile specifically assesses memory using a test of visuospatial associative learning (PAL) that is known to be correlated with hippocampal function, whereas the Cognivue software gives an overview of brain health, including memory, using ten short tests.

The results of the PAL test in Cantab Mobile are automatically compared to the results in the built-in normative dataset, accounting for age, gender and level of education, to indicate when a patient's memory is outside the range that could be attributed to normal aging. This is designed to be a triage test for people with concerns about their memory, to determine whether a patient should be tested further or their memory is normal for their age. Along with the memory test there are optional mood and functional assessments which can help detect symptoms of depression, and problems with performing regular activities of daily living. Cognivue is designed to be used to regularly monitor a patient's broad cognitive health, using 10 short tests to indicate decline, and potentially dementia, through comparison to baseline test performance of other age-normal adults.

Cantab Mobile and Cognivue are similar in terms of technological characteristics as both electronically record objective performance measurements when the patient responds to stimuli presented on the screen. Differences in the design and performance of Cantab Mobile and Cognivue do not affect either the safety or effectiveness of Cantab Mobile for its intended use.

Table 2 presents a summary of each device for comparison. A complete comparison table is provided in [Appendix A](#).

**Table 2. Device Comparison Summary (Proposed Device vs. Predicate Device)**

<b>Comparison Items</b>	<b>CANTAB Mobile-Cambridge Cognition Ltd.</b>	<b>Cognivue – Cerebral Assessment Systems, Inc. (Submitted June 26, 2013)</b>
510(k) Number	K161328	DEN130033
Trade Name	Cantab Mobile	Cognivue
Regulation Name:	Computerized Cognitive Assessment Aid	
Intended Use	<p>Cantab Mobile is intended to be used to assess memory by testing visuospatial associative learning in patients aged 50 to 90 years. Along with the memory test there are optional mood and functional assessments which can help detect symptoms of depression, and problems with performing regular activities of daily living.</p> <p>Results should be interpreted only by qualified professionals. The device is not intended to be used as a stand-alone diagnostic device. The device is not intended to identify the presence or absence of clinical diagnoses.</p>	<p>Cognivue testing is indicated as an adjunctive tool for evaluating perceptual and memory function in individuals aged 55 to 95 years old.</p> <p>Results should be interpreted only by qualified professionals. The device is not intended to be used as a stand-alone diagnostic device. The device is not intended to identify the presence or absence of clinical diagnoses.</p>

## 7 RISKS TO HEALTH

### 7.1 Summary

Risk management for the device is handled under controlled procedures within a Quality Management System. These procedures are designed to meet applicable requirements of EN ISO 13485:2012 and EN ISO 14971:2012.

A summary of the risk analysis and other document references are provided in the [Device Description \(Section 2.2\)](#).

### 7.2 Determination of Level of Concern

Cantab Mobile's level of concern is classified as minor based upon the parameters and recommendations outlined in FDA's *Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices* (2005), with negative responses to all questions in Tables 1 and 2. Regarding question 3 in Table 2, the app is a screening device for use by a learned intermediary in conjunction with other investigations; its operation does not lead directly to diagnosis or choice of appropriate medical care.

## 8 OVERALL CONCLUSIONS

Cantab Mobile is an app that runs on an iPad. It detects memory impairments by testing visuospatial associative learning, in patients aged 50 to 90 years, and includes optional mood and functional assessments which can help detect symptoms of depression and problems with performing regular activities of daily living. The Cantab tests have a 30-year history of use in a range of clinical populations, supported by over 1500 published papers. Cantab Mobile includes the Cantab PAL test, which has been developed as a way of assessing episodic memory without language barriers. A series of independent studies have demonstrated that PAL is sensitive in detecting the earliest signs of prodromal Alzheimer's disease, up to 32 months prior to clinical diagnosis, and that it is relatively insensitive to major unipolar depression. The accumulating evidence demonstrates the sensitivity and specificity of PAL as a tool for operationalizing the criteria for objective memory impairment in mild cognitive impairment (MCI).

Cantab Mobile is not a diagnostic test. The results for a patient's PAL memory test are presented to the healthcare professional as one of three traffic-light coded categories. In conjunction with other investigations, these provide information to assist the professional in their assessment of the patient.

Cantab Mobile is substantially equivalent to Cerebral Assessment Systems' Cognivue software in that they share the intended use of providing clinicians with objective measurements of cognition. Both are applications that electronically record objective performance measurements as the patient responds to stimuli presented on the screen. Differences in the design and performance of Cantab Mobile from Cognivue, the predicate device, do not affect either the safety or effectiveness of Cantab Mobile for its intended use.

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## 10 APPENDICES

### Appendix A. Predicate Device Comparison (Cantab Mobile and Cognivue)

Comparison Items	CANTAB Mobile-Cambridge Cognition Ltd.	Cognivue – Cerebral Assessment Systems, Inc.
510(k) Number	K161328	DEN130033
Device Information: Trade Name	Cantab Mobile	Cognivue
Regulation Name:	Computerized Cognitive Assessment Aid Classification Regulation # CFR 882.1470	Computerized Cognitive Assessment Aid Classification Regulation # CFR 882.1470
Product Code	PKQ	PKQ
Device Information: Device Class:	Unclassified or Proposed Class I  The device has the same intended use, and relies on technology that does not raise new safety and effectiveness questions to Cognivue.	Class II
Predicate Device:	Cognivue (DEN130033)	<i>De novo</i> submission
Type of Use	Prescription Use (Part 21 CFR 801.109)	Prescription Use (Part 21 CFR 801.109)
Submission Date:	May 12, 2016	June 26, 2013
Submitter Information: Company:	Cambridge Cognition Limited. Tunbridge Court, Tunbridge Lane Bottisham Cambridgeshire, CB25 9TU UK	Cerebral Assessment Systems, Inc. 2850 Clover Street Pittsford, NY 14534 USA
Design and Intended Use	Cantab Mobile is intended to be used to assess memory by testing visuospatial associative learning in patients aged 50 to 90 years. Along with the memory test there are optional mood and functional assessments which can help detect symptoms of depression, and problems with performing regular activities of daily living.  Results should be interpreted only by qualified professionals. The device is not intended to be used as a stand-alone diagnostic device. The device is not intended to identify the presence or absence of clinical diagnoses.	Cognivue testing is indicated as an adjunctive tool for evaluating perceptual and memory function in individuals aged 55 to 95 years old.  Results should be interpreted only by qualified professionals. The device is not intended to be used as a stand-alone diagnostic device. The device is not intended to identify the presence or absence of clinical diagnoses.

<b>Comparison Items</b>	<b>CANTAB Mobile-Cambridge Cognition Ltd.</b>	<b>Cognivue – Cerebral Assessment Systems, Inc.</b>
Target population	Patients aged 50 to 90 years with concerns about their memory. Results are automatically adjusted for age, gender, education.	Patients aged 55 to 95 years for the purpose of identifying a potential decline in cognitive function relative to baseline test performance of other age-normal adults.
Anatomical site	The brain: cognitive function	The brain: cognitive function
Test duration	The test takes approximately 10 minutes to complete.	The test takes approximately 10 minutes to complete.
Scoring and reports	Automatic scoring and instant reports	Automatic scoring and instant reports
Where used	Cantab Mobile is software used on a tablet, therefore it can be administered in any suitable setting, e.g. a clinic or home.	The Cognivue software is used on a personal computer, situated on a cart to provide mobility within the healthcare setting.
Energy used	Cantab Mobile software runs on an Apple iPad, which has the following features: <ul style="list-style-type: none"> <li>▪ built-in 25-watt-hour rechargeable lithium-polymer battery;</li> <li>▪ charging via power adapter or USB to computer system;</li> <li>▪ up to 10 hours of use when charged.</li> </ul>	The Cognivue software runs on a personal computer – the energy used is hardware-dependent.
Human factors	Any healthcare professional can administer the test. To ensure reliable results, the iPad should be placed on a stand and the assessment should be administered in a quiet room, without disturbance.  The voiceover and questionnaire texts are provided in a choice of languages.	Any healthcare professional can administer the test. The battery is organized into three sub-batteries, with each sub-test preceded by transitional guidance that facilitates the test subject's engagement with minimal supervision.
To whom is the product marketed /target audience?	Healthcare Rehabilitation	Healthcare
Materials	N/A	N/A
Biocompatibility	N/A	N/A
Compatibility with the environment and other devices	N/A	N/A
Sterility	Based on the device function there is no sterilization testing required for this device.	Based on the device function there is no sterilization testing required for this device.

Comparison Items	CANTAB Mobile-Cambridge Cognition Ltd.	Cognivue – Cerebral Assessment Systems, Inc.
Safety: electrical; mechanical; chemical; thermal; radiation.	These safety issues are not applicable to this software-only device.	Electrical safety testing was performed by Canadian Standards Association. The sponsor provides a letter of attestation stating the device passed IEC 60601-1:2005. Electromagnetic compatibility was not tested.
How the device differs from Predicate device	<p>Cantab Mobile is similar to Cognivue in terms of technological characteristics, as both electronically record objective performance as the patient responds to stimuli presented on the screen. Both tests take about 10 minutes.</p> <p>Cantab Mobile differs from Cognivue in that it provides an assessment of memory using one staged cognitive assessment – the Paired Associates Learning task - compared to Cognivue which includes ten short brain function tests, measuring: adaptive motor control; dynamic visual contrast sensitivity; letter, word, shape, and motion processing ability; and memory.</p> <p>Cantab Mobile also presents assessments of depression and activities of daily living, which are not included in Cognivue.</p>	

## 11 REFERENCED DOCUMENTS

**Traceability Matrix (NMI-018)<sup>1</sup>**

**Change Control and Validation Report (CR-NMI-004)**

(b) (4)



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## 11. DEVICE DESCRIPTION

**Product Name:**

Cantab Mobile (K161328))

**Indication:**

Assess Memory by Testing Visuospatial Associative Learning in Patients Aged 50 to 90 Years



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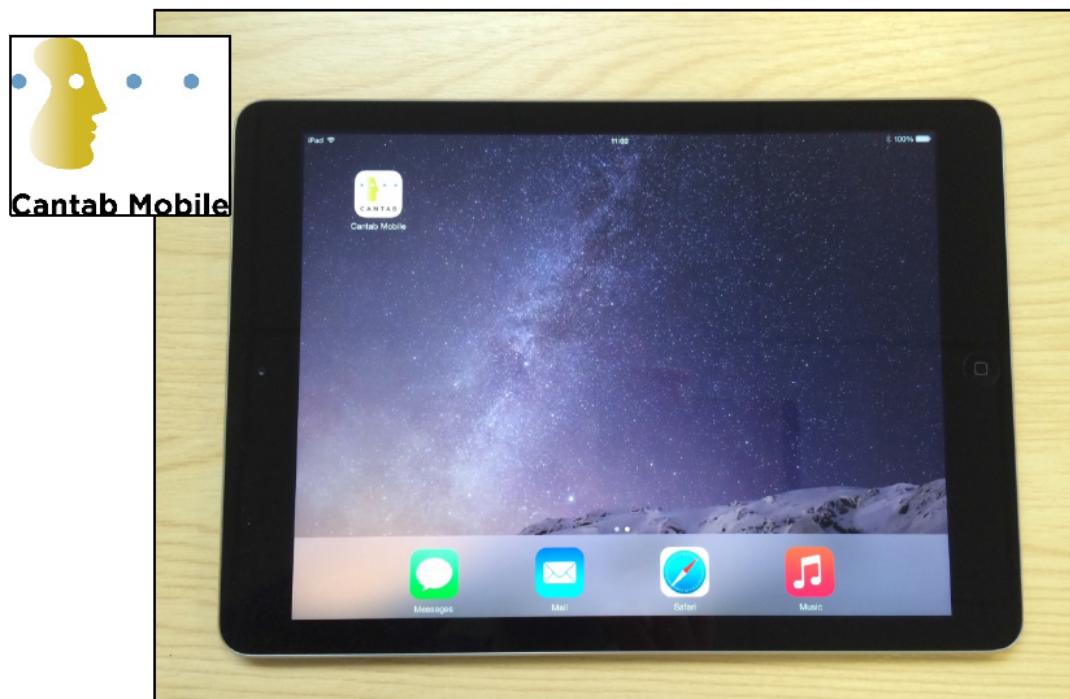
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## 1 DEVICE DESCRIPTION

Cantab Mobile is software to be loaded and run on Apple iPad hardware and operating system (Figure 1). Below is a list of possible device accessories:

- The iPad<sup>1</sup> is an essential accessory
- Disposable iPad Sleeve (see also [Instructions for Use](#)) for cleaning recommendations
- iPad stand
- A iPad battery charger is also supplied with the iPad

**Figure 1. iPad with App Icon at Top Left**



Cantab Mobile does not have a restricted shelf-life. Ongoing support of the manufacturer is required, however, and is detailed below.

The medical device software must be updated when new releases are made available. The iPad operating system should also be kept up to date. Both may be achieved automatically. The iPad battery should be charged as required. No calibration is necessary.

Ongoing support by the manufacturer is required. The app must be able to confirm periodically with the manufacturer that it is licensed, and be updated as required over time.

1 Cantab Mobile is not authorized for use on the iPad mini or the iPad 1 (the first generation iPad). Do not install the app on these devices.

The test is not susceptible to environmental influences within the defined environment for its administration. We instruct that physicians must always administer the tests in a quiet, peaceful environment, with the iPad volume level set so that the patient can clearly hear instructions being given. For patients with impaired hearing, additional support may need to be provided to ensure they can correctly hear and understand the instructions during the test, e.g. use headphones.

A technical wireframe, or mobile app screen blueprint, of Cantab Mobile is a supportive document that presents the skeletal framework, interface elements, and navigational flow (See [Cantab Mobile Wireframes](#)).

## 1.1 Patient Data Entry

Prior to the PAL test itself, the healthcare professional administering the test enters patient data (patient ID, date of birth, gender, educational background etc.).<sup>2</sup> This is used in assessing the patient's performance against a set of normative data.

**Figure 2. Data Entry Screen**



## 1.2 Memory Test

Cantab Mobile provides an optional patient self assessment of memory (Self Assess - enabled on the data entry screen). If this assessment is enabled, the patient will rate his/her memory prior to taking Cantab PAL. The patient is presented a rating scale against which they rate their memory as above average (left of center), average (center), or below average (right of center) (See [Appendix A](#)). Comparing self-rated memory with the objective

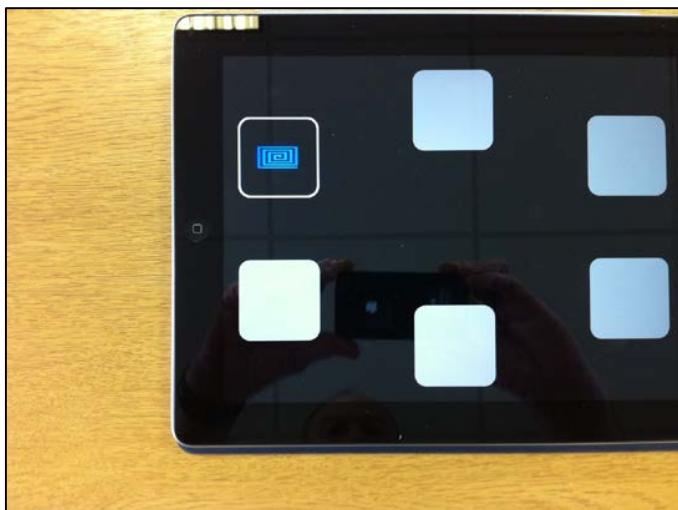
2 Patient details must be entered correctly. Incorrect patient details can lead to incorrect reporting of patient impairment.

measure of memory, provided by Cantab PAL, can reveal any discrepancies between actual and perceived memory ability.

The Cantab Mobile memory test is based on the Cantab PAL test previously used on other hardware platforms. The Cantab PAL requires patients to learn and remember abstract visual patterns associated with various locations on a touch-sensitive computer screen. The patterns were all created to be bold, brightly colored, abstract and with no cultural context. See [Appendix B](#) for examples of patterns used.

Patterns are presented in six boxes around the edge of the screen (See Figure 3). The patterns disappear from the screen, leaving empty boxes and, after a brief delay, the same patterns are presented sequentially in the middle of the screen and the patient is required to touch the box in which they previously saw that pattern appear. ([Figure 4](#))

**Figure 3. Pattern Appears in Box**



**Figure 4. Patient Chooses Box**



If the patterns' locations are not recalled correctly, this is identified to the patient via audio prompts and pattern presentation and recall is repeated. This process continues until the task is completed successfully, at which point the next task is started, or repeated failures by the patient to recall the locations correctly cause the test to end. The whole test consists of a series of such tasks with increasing levels of difficulty.

The patient's responses are recorded by screen touches. The number of errors that they make are recorded and their performance is graded using algorithms derived from a normative database(b) (4)

### 1.3 Questionnaire(s)

Cantab Mobile additionally includes optional questionnaires. Questionnaires operate by presenting a series of questions to the patient, with clearly labeled response boxes that the patient may touch in order to answer each question ([Figure 5](#)). Ratings scales administered (depending on patient performance – see [Appendix D](#) – and if not disabled by the healthcare professional) comprise:

1. GDS – Geriatric Depression Screening Questionnaire (See [Appendix C](#))
2. ADL – Activities for Daily Living Questionnaire (See [Appendix D](#))

The GDS rating scale in the app is the shorter version of GDS including 15 questions, the GDS-15 (validated by [Almeida and Almeida 1999](#)), which is based on the GDS described by Yesavage and colleagues ([Yesavage et al 1983](#)): The GDS rating scale comprises a series of questions, each presented in turn textually on the screen using the language in force, two buttons below to allow the patient to respond 'yes' and 'no' (or equivalent in the language in force). A progress bar gives an approximate indication of progress through the questions and

a button with a backward arrow allows the user to return to the preceding question (if any) and choose again. See Figure 5 below for an example of a GDS-15 rating scale question and its format, as it is presented in the app.

**Figure 5. GDS Rating Scale and Format**

The screenshot shows a mobile application interface for a rating scale. At the top, a header reads "Choose the best answer for how you felt over the past week." Below this is a question: "Have you dropped many of your activities and interests?". Two large, rounded rectangular buttons are present: "Yes" on the left and "No" on the right. At the bottom of the screen is a horizontal progress bar with a blue segment indicating progress. To the left of the progress bar is a small gray arrow pointing to the left, which serves as a back button.

The ADL rating scale in the app was developed and validated by Galasko and colleagues ([Galasko et al 2006](#)) with the goal of simplifying the assessment of this domain for primary prevention trials of Alzheimer's disease. The 15 items they selected for the questionnaire cover a broad range of activities, which are performed regularly by elderly individuals. Administration of the ADL rating scale comprises a series of questions, each presented in turn textually on the screen using the language in force<sup>3</sup>, with the introductory text given above the question and buttons below to allow the patient to choose from the responses permitted for the question. A progress bar gives an approximate indication of progress through the questions and a button with a backward arrow allows (except on questions 1 and 11) the user to return to the preceding question and choose again.

3 The entire user interface respects the text direction (left-to-right or right-to-left) of the language in force including the backward arrow button and progress bar

## 2.2 Device Safety Characteristics and Risks<sup>4</sup>

Risk management for the device is handled under controlled procedures within a Quality Management System. These procedures are designed to meet applicable requirements of EN ISO 13485:2012 and EN ISO 14971:2012.

Identification of characteristics of the device that could impact on safety are documented in **QRM-01-001**. Risk analysis was conducted according to a risk analysis plan referencing controlled procedures, namely **QRM-02-002**, and the conclusion of the risk analysis process is documented in report **QRM-02-003**.

The summary of all points of the risk analysis is provided in **QRM-02-001**.

<sup>4</sup> Risk Analysis documentation, cross referenced here, was previously submitted in the original 510(k) submission (dated May 11, 2016).

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Galasko D, Bennett DA, Sano M, Marson D, Kaye J, Edland SD for the Alzheimer's Disease Cooperative Study. ADCS Prevention Instrument Project: Assessment of Instrumental Activities of Daily Living for Community-dwelling Elderly Individuals in Dementia Prevention Clinical Trials. Alzheimer Dis Assoc Disord. 2006;20(Supp3):S152-69.<sup>5</sup>

<sup>5</sup> This reference was added to support the Sponsor's Response to the Division's Request for Additional Information.

## **Appendix C. Mood Assessment (GDS)**

The Mood Assessment (GDS) is automatically administered. Cantab PAL performance is not a conditional factor in administering the Mood Assessment.

**Choose the best answer for how you felt over the past week.<sup>6</sup>**

**Are you basically satisfied with your life?**

- Yes
- No

**Have you dropped many of your activities and interests?**

- Yes
- No

**Do you feel that your life is empty?**

- Yes
- No

**Do you often get bored?**

- Yes
- No

**Are you in good spirits most of the time?**

- Yes
- No

**Are you afraid that something bad is going to happen to you?**

- Yes
- No

**Do you feel happy most of the time?**

- Yes
- No

**Do you often feel helpless?**

- Yes
- No

<sup>6</sup> The GDS introductory statement precedes each GDS question listed in Appendix C.

**Do you prefer to stay at home, rather than going out and doing new things?**

- Yes
- No

**Do you feel you have more problems with memory than most?**

- Yes
- No

**Do you think it is wonderful to be alive now?**

- Yes
- No

**Do you feel pretty worthless the way you are now?**

- Yes
- No

**Do you feel full of energy?**

- Yes
- No

**Do you feel that your situation is hopeless?**

- Yes
- No

**Do you think that most people are better off than you are?**

- Yes
- No

## **Appendix D. Functional Assessment (ADL)**

This test is automatically administered after Cantab PAL if the patient's Cantab PAL performance has indicated that they fall in the "Investigate" category

### **Part 1:**

**In the past 3 months, were you able to:**

**Do your own shopping?**

- Yes
- Yes, but I had some problems or needed some help
- No, I could not do it
- I did not try

**Prepare meals?**

- Yes
- Yes, but I had some problems or needed some help
- No, I could not do it
- I did not try

**Write checks, pay bills, or use an ATM cash machine?**

- Yes
- Yes, but I had some problems or needed some help
- No, I could not do it
- I did not try

**Travel by car or public transport?**

- Yes
- Yes, but I had some problems or needed some help
- No, I could not do it
- I did not try

**Carry out housework, laundry or home repairs?**

- Yes
- Yes, but I had some problems or needed some help
- No, I could not do it
- I did not try

**Do hobbies such as a card games or crosswords?**

- Yes
- Yes, but I had some problems or needed some help
- No, I could not do it
- I did not try

**Follow the story of a TV program, book or movie?**

- Yes
- Yes, but I had some problems or needed some help
- No, I could not do it
- I did not try

**Keep track of current events in the news or the media?**

- Yes
- Yes, but I had some problems or needed some help
- No, I could not do it
- I did not try

**Remember appointments or important dates such as birthdays?**

- Yes
- Yes, but I had some problems or needed some help
- No, I could not do it
- I did not try

**Remember to take your medication?**

- Yes
- Yes, but I had some problems or needed some help
- No, I could not do it
- I did not try

**Part 2:**

**Can you:**

**See well enough to recognize someone across the street (wearing glasses or contact lenses if necessary?)**

- Yes
- No

**Hear what people are saying when they are speaking at a normal volume?**

- Yes
- No

**Walk up and down a set of stairs without help?**

- Yes
- No