ETNA™-MS App Instructions for Use (Patients)

ETNA™-MS App Version 1.0

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1   Introduction

1.1   About this Document

This document is intended to help MS patients and their caregivers understand and perform the **ETNA™-MS** test prescribed by a licensed physician/healthcare provider. It contains directions for use of the **ETNA™-MS App**, the patient-facing software component of the Eye-Tracking Neurological Assessment for Multiple Sclerosis (**ETNA™-MS**), a Software as a Medical Device. This document may be used together with the instructions provided by the software itself.

Directions for use of the **ETNA™-MS** software system are separately available for healthcare providers in document *ETNA™-MS Instructions for Use (Clinicians)*.

1.2   Intended Use of the Device

The Eye-Tracking Neurological Assessment for Multiple Sclerosis (ETNA™-MS) is a software as a medical device (SaMD) intended to administer a non-invasive test and provide an Expanded Disability Status Scale (EDSS) score in the range between 1.0 and 4.5 for use in tracking the disease progression in MS patients.

1.3   ETNA™-MS Device Overview

ETNA™-MS is a Software as a Medical Device (SaMD) comprising two components that operate as a software system in a client-server architecture:

- **ETNA™-MS App** is a visual stimulation, video recording and data collection App running on an off-the-shelf electronic tablet (iPad Pro). The App guides an MS patient to perform a test comprising distinct oculomotor (visual) tasks that require the patient to either follow, track, or respond to visual targets on the screen. Using the tablet's embedded front camera, the App captures facial images of the patient performing those tasks and analyzes the images to extract several gaze and eye-movement metrics. The test data and basic patient information are then uploaded for offline analysis to **ETNA™-Cloud**.

- **ETNA™-Cloud** is a software application running offline on a company-controlled server that is ISO/IEC 27001, PIPEDA and HIPAA compliant. It is intended for use by healthcare providers only. The software uses a clinically validated and locked AI Machine Learning Model (Classifier) to analyze the gaze and eye-movement metrics and patient information uploaded by the **ETNA™-MS App** at the end of a test session; it identifies relevant features that can best determine MS disease status and outputs an Expanded Disability Status Scale (EDSS) score for clinicians to consult.

1.4   ETNA™-MS App Overview

The **ETNA™-MS App** may be downloaded by healthcare providers or patients from the Apple Store and it is installed on an iPad Pro tablet. The healthcare provider assigns each MS patient a unique username and password needed by the App to log into the cloud-based server and connect with the **ETNA™-Cloud** software.

The App may be used to administer the prescribed test at a clinic/physician's office or at the patient's home. The first time the App is run, it installs on the tablet the video data and instructions associated with the oculomotor (visual) tasks of the test.

To perform the test, the patient must be positioned in front of the iPad, so that the screen is visible; the screen must be stable, straight, centered at eye level and positioned 45 cm from the patient's face. The App provides on-screen instructions to help ensure the patient is properly positioned and the patient's face and eyes are clearly seen by the camera.

Throughout the test session, the App guides the patient to perform 6 distinct oculomotor (visual) tasks (calibration, fixation, pro-saccade, anti-saccade, optokinetic nystagmus task, and smooth pursuit) and uses patent-pending machine learning technology to extract several gaze and eye-movement metrics.

At the end of the test session, the App uploads the test parameters, extracted metrics and basic patient information (Patient Identifier, Patient Age, and Timed 25-Foot Walk measure) to a secure cloud-based server for offline analysis by **ETNA™-Cloud**. The App does not provide any diagnostic information for patients or end users.

1.5   Terms Glossary

Term	Definition / Description
2FA	2-Factor Authentication
ETNA™	Eye-Tracking Neurological Assessment
MS	Multiple Sclerosis
ETNA™-MS	Eye-Tracking Neurological Assessment for Multiple Sclerosis
ETNA™-Cloud	Eye-Tracking Neurological Assessment Cloud (Server Application)
EDSS	Expanded Disability Status Scale (Clinical Measure)
HIPAA	Health Insurance Portability and Accountability Act (United States)
MS	Multiple Sclerosis
PIPEDA	Personal Information Protection and Electronic Documents Act (Canada)
SaMD	Software as a Medical Device
2FA	2-Factor Authentication
T25-FW	Timed 25-Foot Walk (Clinical Measure)

1.6   Symbols Glossary

Symbol	Title: Meaning	Standard (Reference)
RxOnly	Caution: US Federal law restricts this device to sale by or on the order of a physician.	21 CFR 801 (801.109)
	Consult instructions for use	ISO 15223-1 (5.4.3)
	Manufacturer	ISO 15223-1 (5.1.1)
	Date of Manufacture	ISO 15223-1 (5.1.3)
REF	Catalogue Number	ISO 15223-1 (5.1.6)
	Patient information website	ISO 15223-1 (5.7.4)
MD	Medical device	ISO 15223-1 (5.7.4)
ISO 15223-1:2021. Medical devices — Symbols to be used with information to be supplied by the manufacturer — Part 1: General requirements		
21 CFR 801. Code of Federal Regulations Title 21 – Chapter 1, Food and Drug Administration, Department of Health and Human Services – Subchapter H, Medical Devices – Part 801, Labeling		

2   Directions for Use

2.1   Requirements to Use the ETNA™-MS App

- Must have an iPad Pro 12.9" 5th or 6th generation with iPadOS 17 or later version
- Must have a tablet mount holder or stand
- Must have a Canadian Apple ID activated to access the Canadian App Store to "Get" and install the **ETNA™-MS App**
- Must have valid **ETNA™-MS App** login credentials (a user account will be assigned by your healthcare provider)
- Must have an email account that is accessible when ready to perform the test
- Must be familiar with the use of an iPad (if needed, your healthcare provider or caregiver may assist you to perform the test)

2.2   User Account Confirmation

Once your clinician has prescribed the **ETNA™-MS** test (to be performed at a predefined testing frequency), you will receive an email prompting you to create a password and download the **ETNA™-MS App** to begin testing (see example email content below).

Greeting Rosemberg Ramos,

Doctor Étienne de Villers-Sidani has prepared the way for your MS tests with ETNA-MS.

You have been asked to perform your test every **month**.

To use the ETNA-MS application, you will have to first install it from the Apple App Store.

You will need to choose a password first.

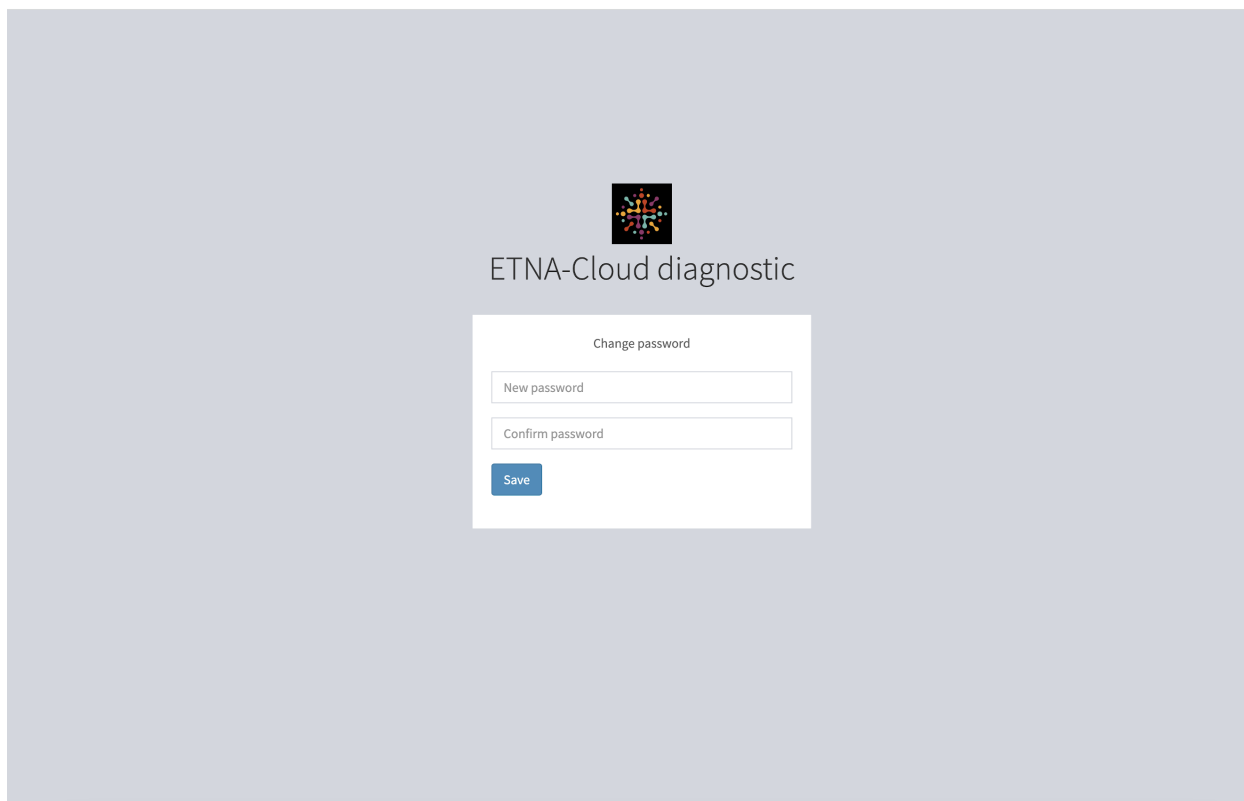**Choose My Password**

Once that is done, here are the credentials you need to do your tests:

User: **rosembergramos@hotmail.com**
Password: **The one you just created**

By clicking on the "Choose My Password" button, you will be directed to the following web page to create a unique password:

Upon entering and confirming your new password, click on "Save" to complete the process.

For data security purposes, 2-Factor Authentication via email onlyNote that users are required to periodically change passwords; the system will send an email message with instructions to all users at set time points.

2.3 ETNA™-MS App Installation

If the **ETNA™-MS App** is not pre-installed on the iPad, the App can be downloaded from the Canadian App Store.

- Log into the Canadian App Store
- Search for "ETNA-MS" to find the **ETNA™-MS App**
- "Get" (and install) the App

The App's user interface is available in English, French or Spanish and it will match the iPad language automatically if it is set to one of those three languages. It will default to English if the iPad is set to another language not supported by the **ETNA™-MS App**.

2.4   iPad Set-Up for Stable Internet Connection

- Before beginning the test, ensure that the iPad is connected to the Internet using a stable Wi-Fi or cellular data service (LTE or above; if applicable).

- Ensure the battery is charged to at least 50%.

  Note: *The iPad cannot be connected to the charging cable during the test as it may overheat and cause the test to be interrupted.*

2.5   Data Acquisition Guidelines

2.5.1 iPad Positioning

- Find a quiet area to test with no distractions, with a stable light (luminosity) source, and make sure the camera does not capture any movements other than yours.

- Position the iPad directly in front of you, approximately 45 cm (around 1.5 feet) from your eyes, using the tablet mount holder.

- Ensure the iPad is perpendicular to the table.

  Note: *This is a preliminary set up. If necessary, the App will prompt you to reposition the iPad once the test is started*.
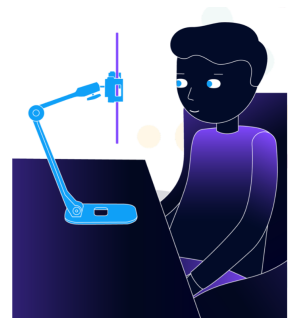
2.5.2 Pre-Test Procedure Checklist

- Make sure the lens of the iPad camera is clean and free of dirt and smudges (if necessary, clean it with a soft, slightly damp, lint-free cloth).

- Ensure only you are the only person visible by the iPad camera; no one else should be directly in the camera view.

- If you are wearing a mask, remove it.

- If you are wearing glasses, see if you can do the test without them. Rule of thumb: if you are able to read the instructions provided on-screen by the App without glasses, you will be able to do the test without glasses since the stimuli are much larger than the text.

- If you will do the test wearing glasses, ensure the frames or the glare in your glasses do not obstruct the iPad camera view of the eyes; push your glasses all the way up the nose. Try to eliminate any sources of glare.

- Remove any hat or headgear.

- Ensure your forehead and ears are clear of hair. Tie up the hair if needed.

- Make sure you are sitting comfortably (back against the wall if possible or sitting on a chair with mid to high backrest).

- Once sitting comfortably, begin adjusting the iPad/stand to accommodate the distance/ placement for optimal capture of your face.

Note: *You do not need to touch the iPad during the test aside from tapping the "Continue" button.*

2.5.3 Examples of Incorrect Camera Positioning

Glasses covering eyes   Glare obstructing eyes   Improper mask removal   Face not entirely visible/centered

2.6 Test Quality Safeguards

To maximize the quality of the test data, the App verifies the following parameters while displaying on-screen instructions before each visual task. Those parameters must meet built-in acceptance criteria in order to proceed with the visual task. The same parameters are also verified in real time during each task; the App will interrupt the task and request that it is restarted if any of those parameters no longer meets acceptance criteria (as reported in the interruption error message).

- iPad temperature
- Proper luminosity
- Single face is in the field of view
- Face distance to the iPad
- Face centered
- Head not tilted (3 axes)
- Eyes are open at least 80% of the time during task execution
- Same patient in front of the camera (visual reference taken at the first calibration task)
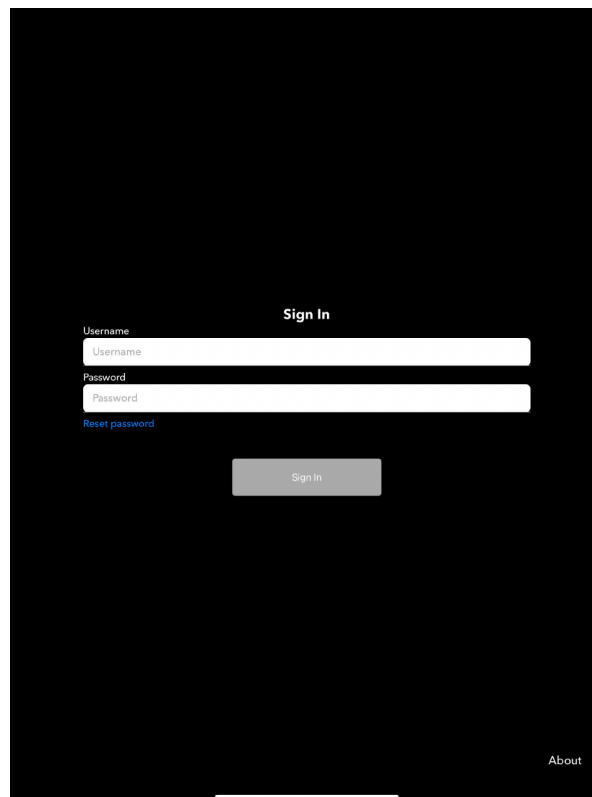
3   Test Execution

3.1   ETNA^{TM}-MS App Session Login Instructions

To begin a test session, start by opening the **ETNA™-MS App**.
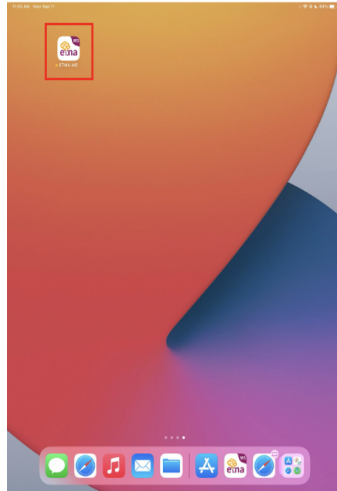
Once in the App, enter the username and password that have been created for your **ETNA™-MS** account as per Section 2.2 above, and tap "Sign in."

If the password is forgotten, click "Reset Password" to set up a new one. A prompt will appear asking "Do you wish to reset your password?"

After tapping "Yes", you will be asked to "Please check your email inbox to complete the process"; tap "OK". Check your email associated with the **ETNA™-MS** account for an email similar to the below example:

Hello,

We received a request to reset your password.

Please click on the button below to do that.

Reset My Password

If you did not request this, you don't have to do anything.

Your password will not be affected and you can still log in to your account.

Thank you

Clicking "Reset My Password" will redirect you to a web page to set your new password, as per Section 2.2 above. Use this new password to "Sign In" to the **ETNA™-MS App**.

To complete the login process, you must also enter the 2FA code that will be sent to the email associated with the ETNA™-MS account.
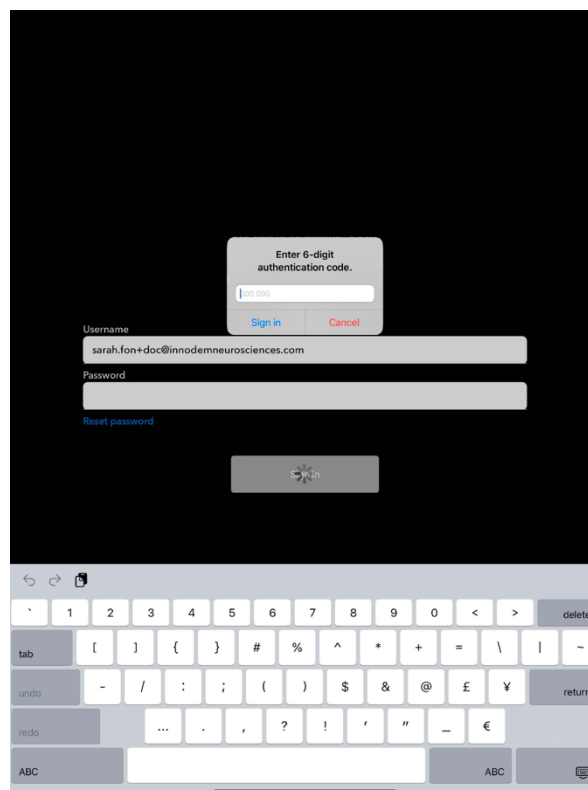
Upon successful login, the following screen will appear, indicating that the **ETNA™-MS App** is downloading from the **ETNA™-Cloud** server the video data and instructions associated with the visual tasks of the test.
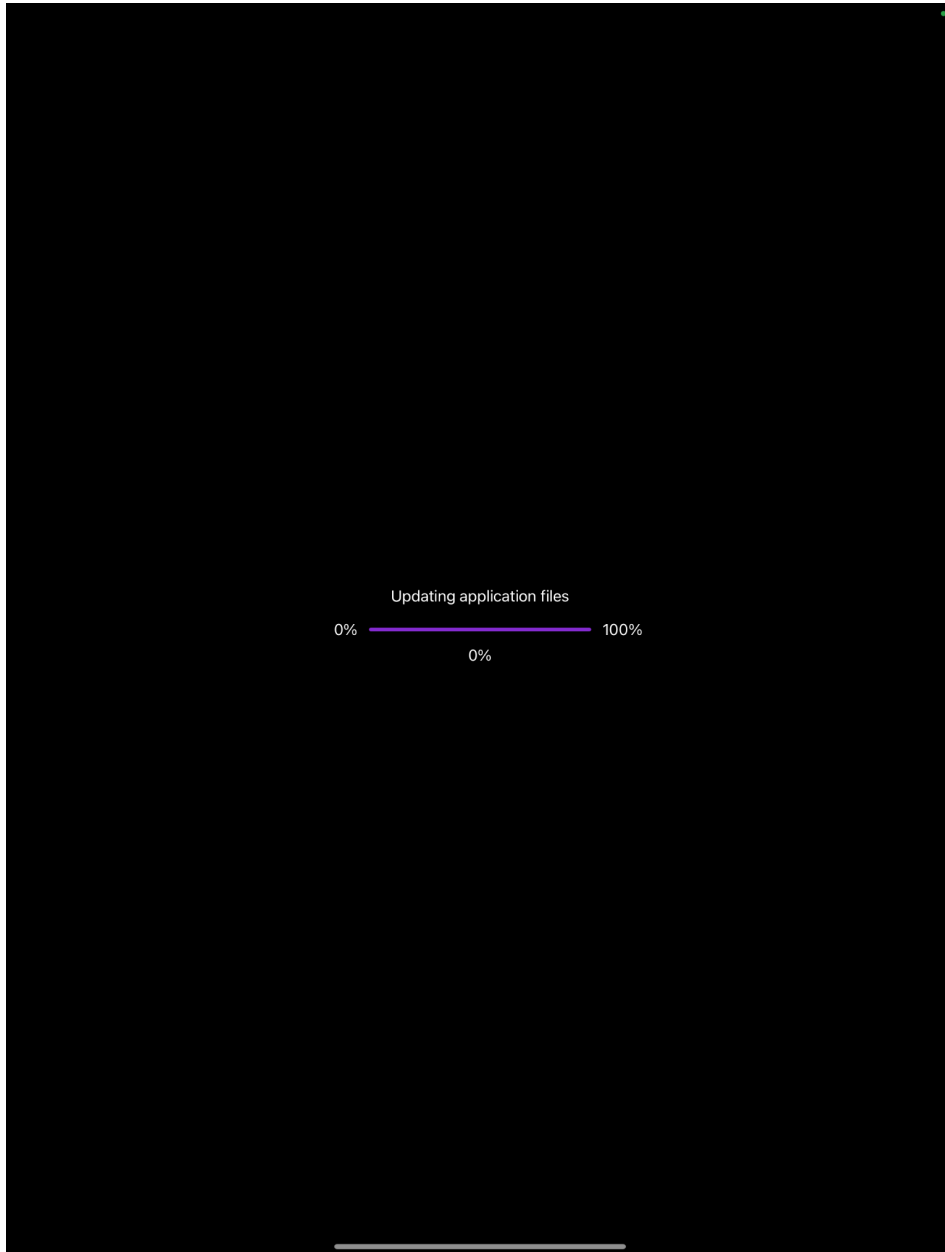
The first time the **ETNA™-MS App** opens, it will download the required data files in the iPad memory and it may therefore take some time (a few minutes) to complete, depending on the internet connection speed. Subsequent execution of the App will be significantly faster. It will also ask you to agree to the "Privacy Policy" and "Terms and Conditions".

Welcome to ETNA-MS

Please read the Privacy Policy and Terms and Condition before getting started

☑ I agree to the Privacy Policy and Terms and Conditions
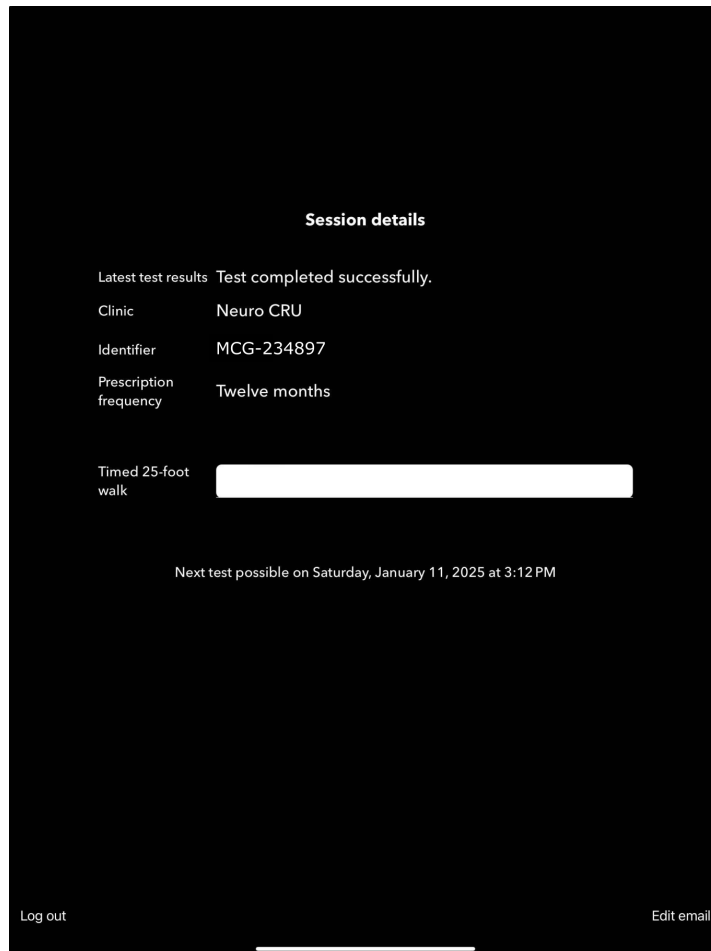
[Get started]
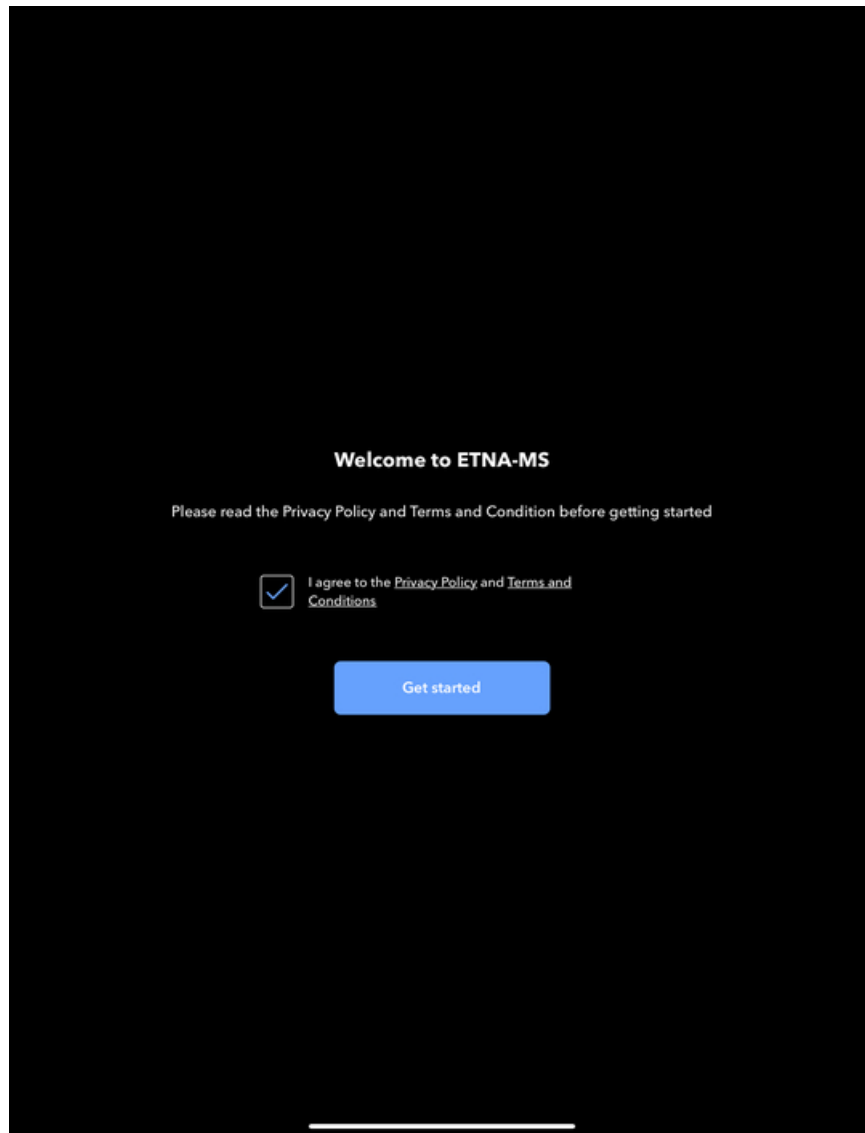
*Note: Each time the **ETNA™-MS App** opens, it will check for updated information on the **ETNA™-Cloud** server and it will download the latest compatible data files.*

After the App files have been downloaded, the "Session details" screen will appear.

The Patient Identifier will already be prefilled if your doctor prescribed you a test.

In the App, scroll and select the value that corresponds to the closest, rounded average of the two T25-FW trials that was last completed in the clinic (provided by the clinician). This will be written on your At-Home Testing 1-pager provided by your clinician.

Session details

Latest test results	Test completed successfully.
Clinic	Neuro CRU
Identifier	MCG-234897
Prescription frequency	Twelve months
Timed 25-foot walk	

Next test possible on Saturday, January 11, 2025 at 3:12 PM

Log out   Edit email

3.2   Positioning Stage

Before starting the test, make sure you are following the Data Acquisition Guidelines in Section 2.5 above and you are positioned comfortably in a chair, with the tablet held in place by a tablet mount holder or stand.
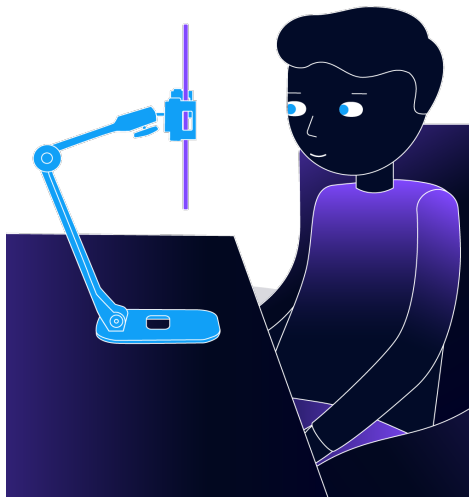
The first test screen will provide feedback and instructions to help you with positioning. To ensure that the face is centered in the field of view of the iPad camera, please position yourself such that your face is within the displayed rectangle.
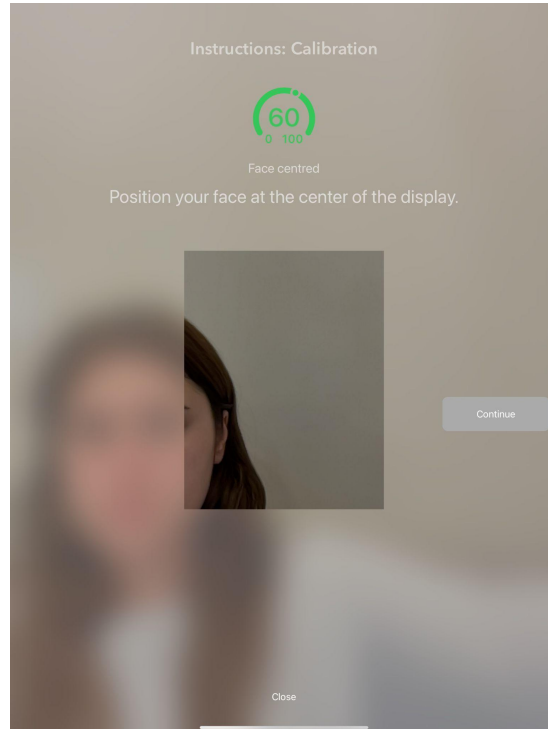
Adjust the position of the tablet or chair if the "Too close" or "Too far" prompt appears.
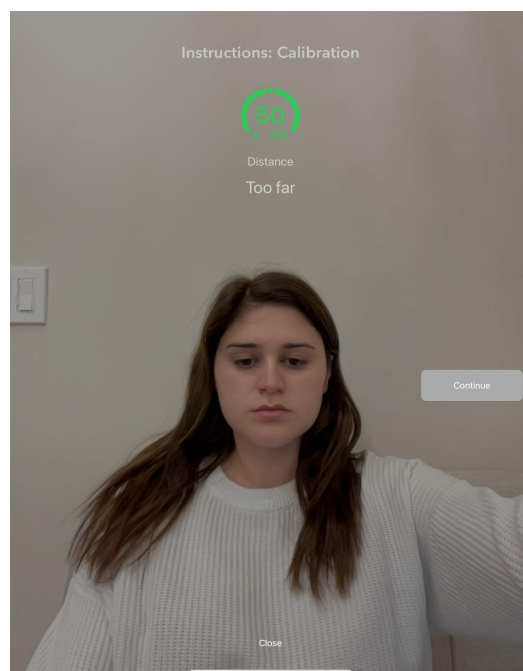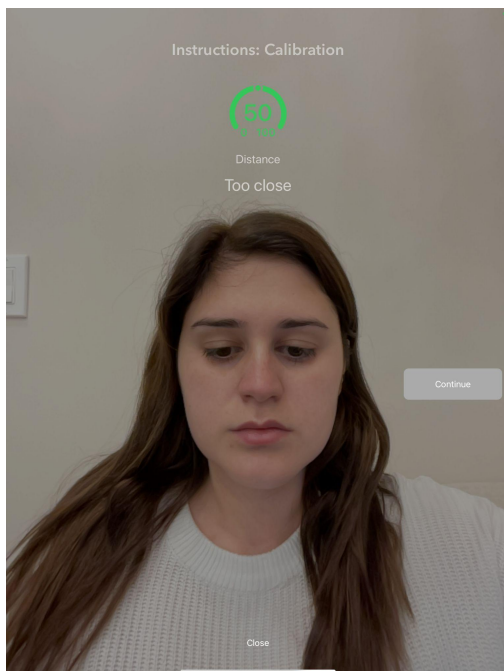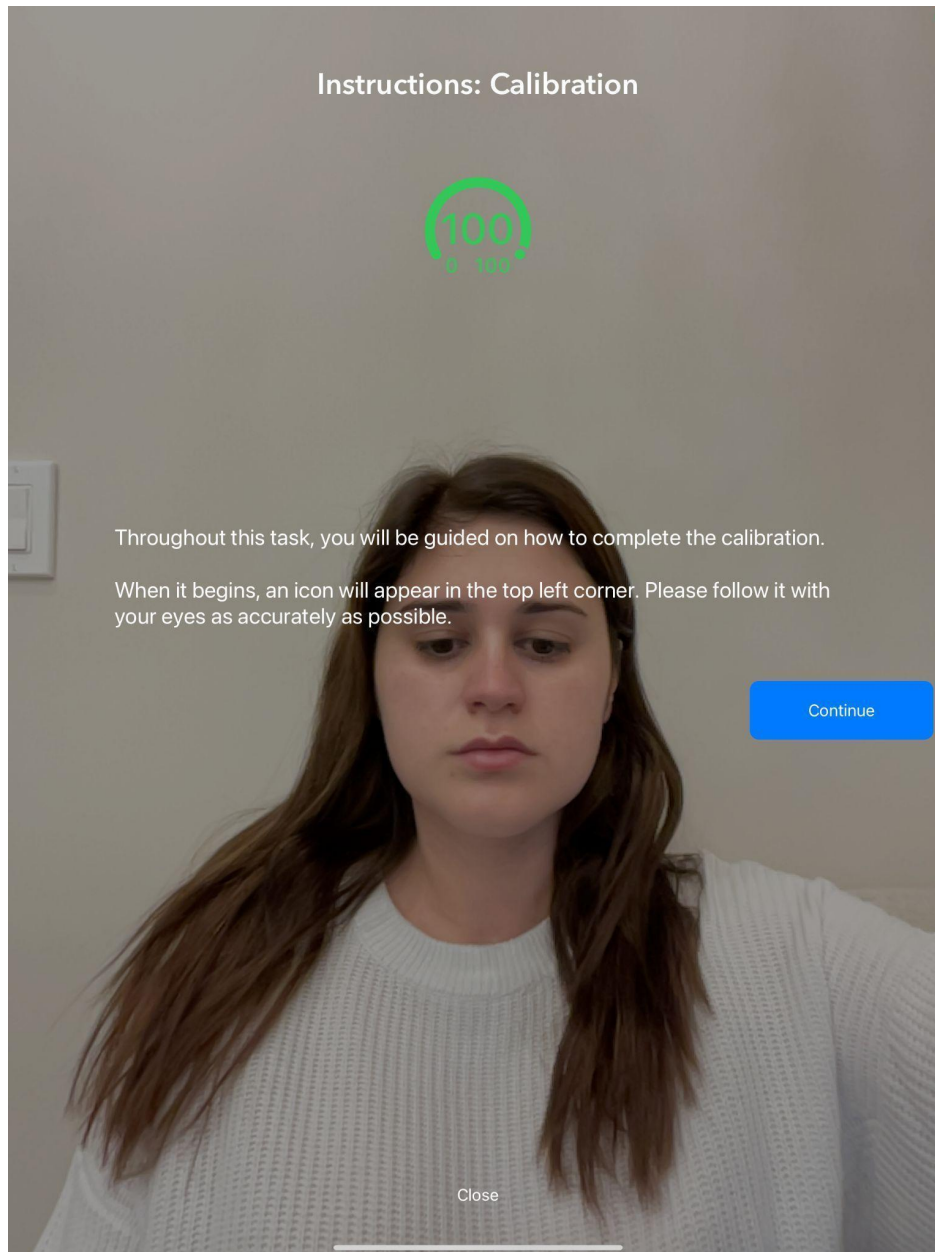
Arrows might appear to prompt you to turn your face or tilt your head. The arrows will disappear when you are in the correct position.
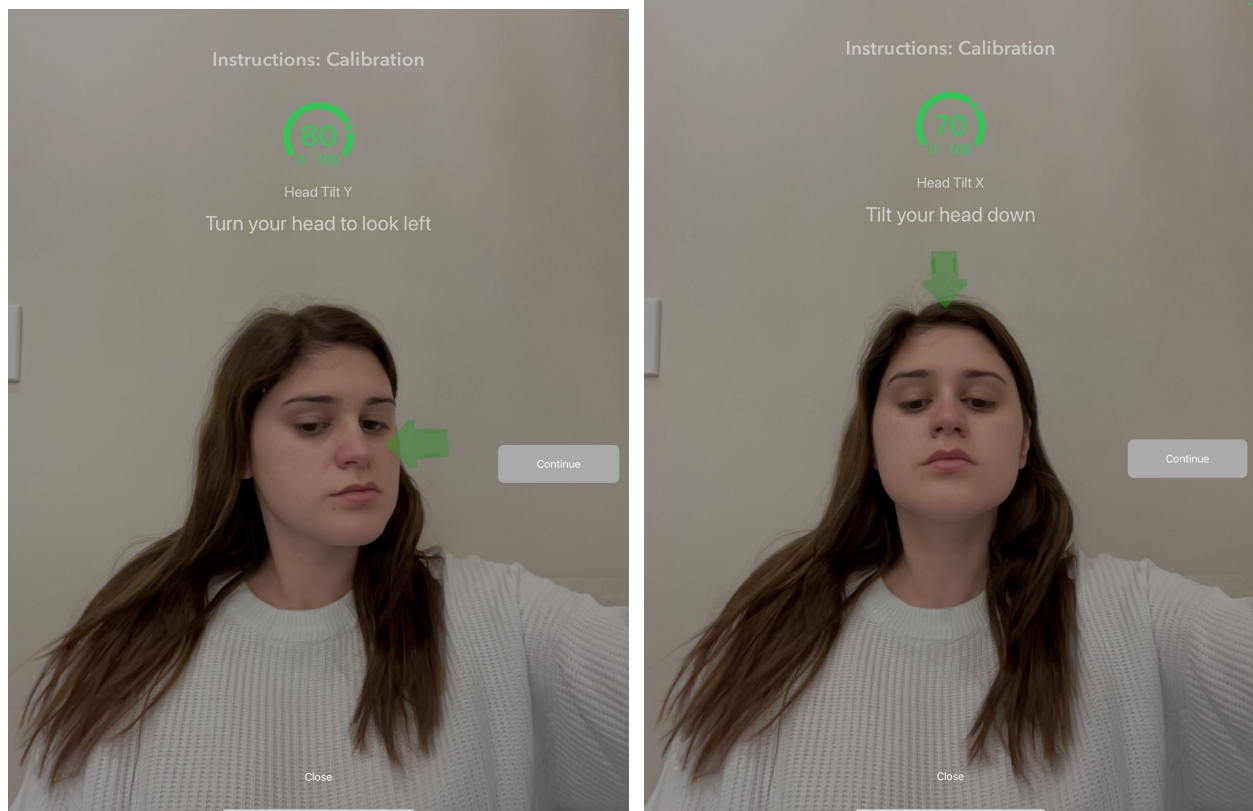
At any time during the test, a prompt will appear if you are too far, too close, moving too much, or if your face cannot be detected. The relevant information will be displayed on the screen (i.e., Image is too far, too close, or moving). Arrows will also appear if the face/head needs to be adjusted if you have moved.

You will know you are in the correct position when the pie chart at the top center of the screen shows "100" and the "Continue" button has turned blue.

To begin each visual task, tap "Continue."

Instructions: Calibration

100
0 100

Throughout this task, you will be guided on how to complete the calibration.

When it begins, an icon will appear in the top left corner. Please follow it with your eyes as accurately as possible.

Continue

Close

3.3 Oculomotor Tasks

Throughout the test session, the App will guide you to perform 6 distinct oculomotor (visual) tasks (calibration, fixation, pro-saccade, anti-saccade, optokinetic nystagmus task, and smooth pursuit). Each visual task will be preceded by a positioning check with on-screen feedback (as described in Section 3.2 above), a brief description of the task, and on-screen instructions for performing the task.

You can begin a task when you are ready and in the correct position (when the pie chart at the top center of the screen shows "100" and the "Continue" button has turned blue.)

To begin each visual task, tap "Continue."

3.3.1 Task 1 - Calibration

● The calibration task begins with a moving target starting in the top left corner of the screen. You must simply follow the target with your eyes as it moves around the screen.

3.3.2 Task 2 - Fixation

● This task will have a white cross on a black screen positioned at 5 different positions

● The white cross will be displayed in each position for 7 seconds

● You need to fixate your eyes on the cross at each position until it disappears
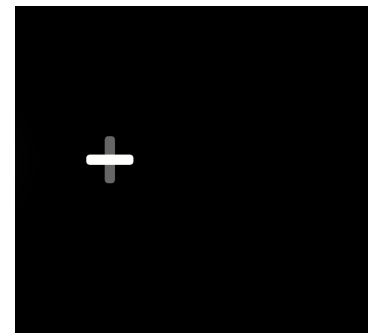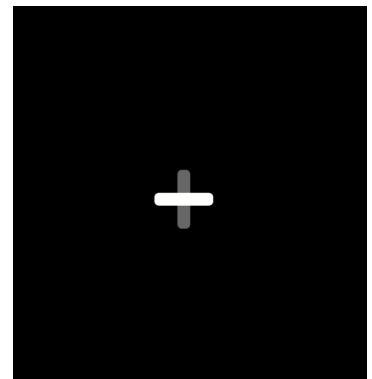
3.3.3 Task 3 - Pro-Saccades

- This task will have a white cross on a black screen positioned in the center of the screen

    ○ You will need to fixate on the cross until it disappears

- Each time the cross disappears, a target will appear in a random location on the screen

    ○ You will need to fixate your eyes on the target as quickly as possible

- The target will disappear and the white cross will be displayed again

    ○ You will need to fixate back on the cross again until it disappears

- This sequence of looking at the cross and then at the target will repeat several times
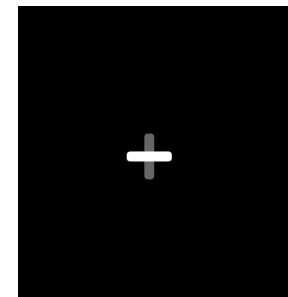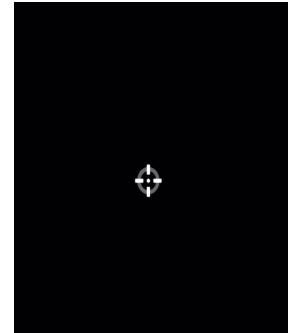
3.3.4 Task 4 - Antisaccades

- This task is completed three times during the test to let you rest in between tests. To help you understand how this task should be executed, a demonstration video is available at the instructions screen (It is recommended that you watch it prior to starting the task).

- The task begins with a white cross appearing in the center. The cross will disappear, and a target will appear.
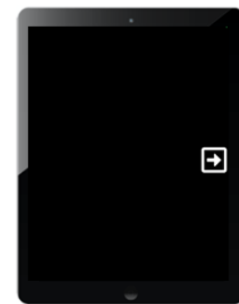
Figure 4a   Figure 4b   Figure 4c   Figure 4d

    ○ After the target disappears, you will need to look in the opposite direction of the target on the screen (i.e., if the target is on the left side, you will need to look on the right side)

- A few seconds later, an arrow pointing in 1 of 4 directions (up, down, left, right) will appear

    ○ You will need to remember the direction of the arrow

- After the arrow disappears, you will be shown all 4 directions of the arrows at once and you need to look at the same arrow they were just shown

- This series of fixation and stimulus periods will repeat 8 times in each of the three trials of this task, with each trial increasing in speed

3.3.5 Task 5 - Optokinetic Nystagmus

- This task will start with a cross in the center of the screen

    - You will need to fixate on the cross

- After 3 seconds, the cross will disappear

    - You will need to continue to fixate on the location where the cross was

- A horizontally moving grating (moving left to right) will appear

    - You will need to continue to fixate on the location where the cross was while the grating moves

- This will repeat with the horizontally grating moving right to left
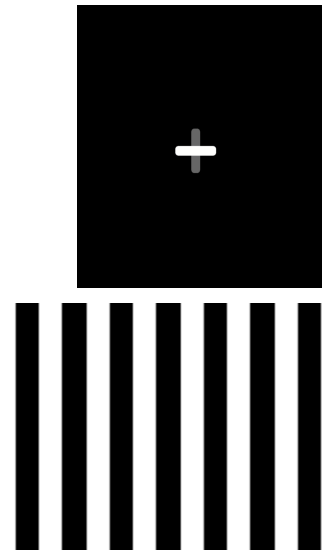
3.3.6 Task 6 - Smooth Pursuit

This task will start with a cross in the center of the screen

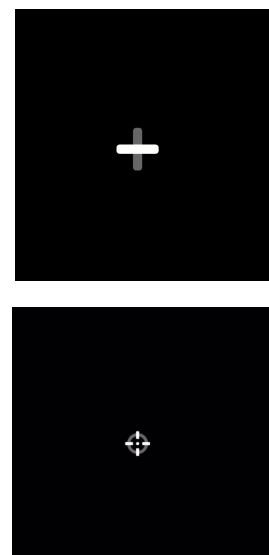The cross will disappear and a target will appear

The target will move in 1 of 4 directions (up, down, left right)

　　　You must follow the target as it moves until it disappears
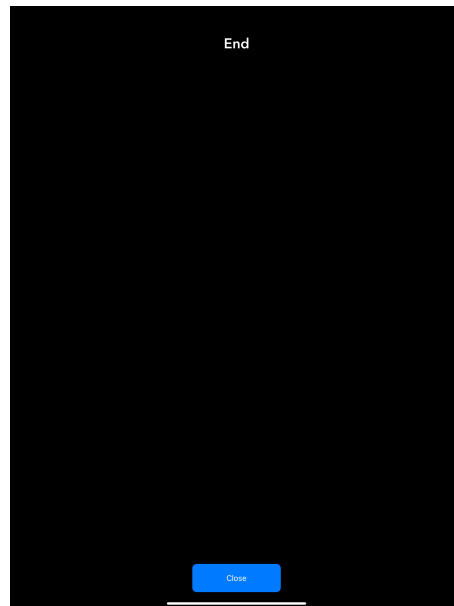
The cross will reappear

　　　You must fixate on the cross again

This will repeat 12 times and the target will move at 3 possible velocities (slow, fast, medium)
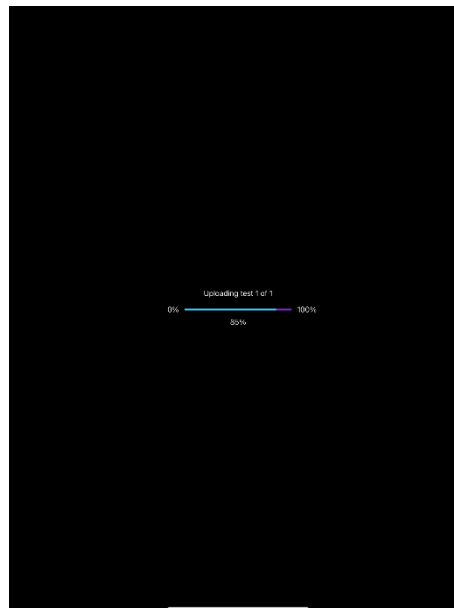
3.4 Completion of the Test

This page will appear when the test is complete. Press "Close" when finished.

The following screen will appear automatically after closing the test. The test data will upload on its own.

DO NOT EXIT THE APP OR LOCK YOUR IPAD WHILE THE TEST DATA IS UPLOADING.

The progress of your upload will appear on the screen. Once all the test data is uploaded, the App will return to the "Session Details" screen (see Section 3.1 above).

The test session is now complete. You can close the App.

4   Tech Support and Troubleshooting

4.1   Tech Support Contact Information

For technical support, please contact: support@innodemneurosciences.com

4.2   Troubleshooting Guide

The following error messages might appear before/during/after a test:

Error Message	Recommended Action
"Failed to download multimedia"	Contact Technical Support
"Sorry, your test session could not be saved, please run the test again at your earliest convenience"	Please restart the test
"Battery level must be 30% or more to run test"	Please make sure the iPad is charged before running a test
"No Face ID. Please contact your clinic to correct this"	Contact Technical Support
"Not enough credit available to start the test. Please contact your clinic to correct this"	Contact Technical Support
"There are results saved on the device which cannot be processed until they are uploaded. Are you sure you want to log out?"	Contact Technical Support
"Test interrupted because unexpected error"	This is most likely caused by the iPad overheating. Please wait a few minutes for the iPad to cool down before restarting the task. If the error persists, contact Technical Support.
"Lost too much data. Please start again"	This error is most likely caused by the iPad overheating. Please wait a few minutes to allow it to cool before restarting the task. If the error persists, contact Technical Support.
"Ambient light changed too much"	This is caused when the lighting in the room has changed during a task (i.e., lights got dimmer, lighting through a window was

	brighter/darker). Please make sure to be in a well lit and stable environment before beginning the test.
"Your eyes must stay opened at least 80% of the time during the test"	Restart the task keeping your eyes open/wide as much as possible.
"Detected too many invalid segments. Please redo the test"	This can be the result of two things: 1. The patient blinked too much throughout the task. Repeat the test with as little as possible blinking. 2. The patient's gaze is not detected near the target, meaning the visual task is not performed correctly. Please make sure you understand the visual task by reading the instructions before the beginning of the task.
"Device is too hot. Please wait a few minutes for the thermal state to return to nominal to resume the test"	Please wait a few minutes to allow the iPad to cool before restarting the task.
"Failed to connect to the server"	Contact Technical Support