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E3 AND PROFILE USER GUIDE

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I. Introduction

The Espion E3 and Profile is a full featured, modular electrophysiology system capable of generating visual stimuli of patterns and flash. It can perform all of the ISCEV clinical tests (see www.iscev.org) and also can be used for research purposes.

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Software Version

Covers Version 6+

Disclaimer

Information in this manual is subject to change without notice and does not represent a commitment on the part of Diagnosys LLC nor can it be held responsible for any errors or omissions herein.

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You may install and use one copy of the Espion software on a single console. You may not install it on any additional system consoles or computers. You may make one copy of the Espion software solely for backup purposes.

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Trademarks

All trademarks acknowledged.

See separate warranty document.

Diagnosys supplies certain non Diagnosys products on an "as is" basis. Non Diagnosys manufacturers or suppliers may provide their own warranty.

Technical Support, Software Support & Updates

For support, contact your local dealer or Diagnosys.

See system IFU (Doc #16519, #16520) for further information regarding service and maintenance.

Software updates are available from http://www.diagnosysllc.com

Cables

Caution. See IFU (Doc #16519, #16520) for information on cable lengths and external connections.

Power and software restart

If the system loses power, restart the system. If the system software closes, restart the software. Resume normal operations of the system.

Intended User Profile

Federal law in the USA and Canada restricts this device to sale by or on the order of a licensed medical practitioner.

Operator: Ophthalmologists, Optometrists (or equivalent), other medical doctor, nurse, certified medical technician, non-certified assistant.

Data Analyst: Ophthalmologists, Optometrists (or equivalent), or other medical doctor.

Job requirements (Operators)

Must be able to perform all of the following operations:

- Be fully trained in the aspects of this User Guide and the system IFU
- Power on the system
- Enter patient data
- Clean surfaces of the equipment
- Position patient with the device, including moving the patient, the device, and the patient's chair
- Setup electrodes on patient
- Select protocol and acquire electrophysiology data
- Review, quality check and save the test, or try again
- Generate reports using the available print report
- Review reports for completeness
- Turn off the system

Job requirements (Data Analyst)

- Training and certification are required by governing bodies to interpret the analysis in the treatment of ophthalmic diseases or other eye-related medical issues.
- The data created using this device is to be analyzed by clinicians with professional training in diagnostic interpretation of the electrophysiology waveforms generated.
    - Recommendations for additional electrophysiology data analysis training are provided in Appendix 4, conducted by other international, medical organizations.
- Accurately identify ocular anomalies
- Have a history of correct diagnoses of eye disease or work solely within a research environment
- Be fully trained in the use of electrophysiology equipment, and particularly, in the analysis of the electrophysiology waveforms

⚠ **Caution.** Example test results and other instructions given in this User Guide are not meant for data analysis, interpretation or interpretation training purposes. They are meant solely to provide examples of a high quality (that are ready to be further assessed by a qualified Data Analyst) vs low quality test (that has artifacts and should be repeated) across a range of patient types of test results.

⚠ **Caution.** All output of this system is subject to verification by a qualified clinical Operator and Analyst.

II. Electrodes (sold separately)

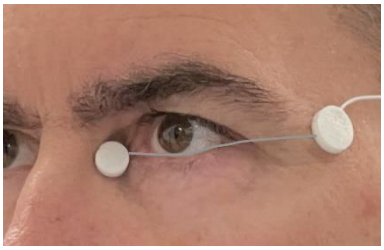
The E3 and Profile systems utilize three categories of electrodes: active, reference, and ground. Active electrodes (placed on or as close as possible to the eye or the occipital cortex) record the signal from the stimulated region. The reference electrode (usually placed on the temples or the forehead) acts as the control – it is placed somewhere that doesn't react to flashes or patterns of light and is there to help the equipment distinguish between the signal and biological 'noise'. The ground electrode (commonly placed on the forehead, wrist, or ear) helps to eliminate noise from other electrical equipment or power cables.

Electrode Types

Corneal Electrodes

Corneal Electrodes measure the electrical signal from the eye.

DTL Plus



The DTL Plus is an ultra-low impedance, medical grade silver/nylon electrode developed for use in ERG testing. The electrode comes in one size and can be easily inserted into the patient's eye. The DTL Plus is comfortable and can be worn for hours at a time.

Burian-Allen

The Burian-Allen is a reusable contact lens electrode that comes in eight different sizes. These electrodes hold the eye open to prevent blinking which results in higher amplitudes but can be uncomfortable for the patient.

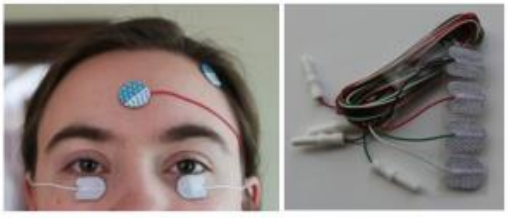
Skin Electrodes

Skin electrodes are generally used as the reference and ground but can be used as an active in certain cases.

Gold Cups

Gold Cups are reusable electrodes placed on the temples, forehead, or back of the head depending on test type. This electrode type requires the use of conductive electrode paste or gel.

Disposable Skin Electrodes



Disposable skin electrodes are placed in the same locations as Gold Cups and can be used as active electrodes placed below the eye. They are non-reusable and use a self-adhesive instead of conductive electrode paste.

Note. The electrical responses measured are very small signals and the choice of electrode type should be based on consideration of the signal to noise ratio, patient comfort and test type. ISCEV (www.iscev.org) has some very good recommendations in their procedures guide for choosing electrode types for its tests, and recommendations are also provided in this user guide. All electrode types that utilize a 1.5mm DIN connector are compatible with the E^3 and Profile System.

Caution. Follow the instructions for use (IFU) that come with the electrode type you choose. This user guide shows the general location for electrode placement for each type of test, but specific instructions from the electrode manufacturer should also be used.

Caution. Pediatric and infant testing. Before testing pediatric or infant patients read fully Appendix 3 of this user guide and also consult the ISCEV guidelines for tests (www.iscev.org) on their recommendations for which test type is most appropriate for different age groups of infants and pediatric patients. As noted by ISCEV, the electrodes used for adults are generally also the same electrodes used for pediatric and infant testing. In some cases the electrode manufacturer provides different size electrodes (e.g. Burian-Allen electrodes); follow the IFU guidance from the electrode manufacturer for which electrode option to choose for the age and physical size of your patient. Also, according to ISCEV guidelines, the electrode locations for pediatric testing are the same as those used for adults, proportionate to the smaller size face and head of a pediatric patient, regardless of age. Consult Appendix 3 of this user guide for additional recommendations on testing pediatric patients, in addition to following the electrode position guidance for each section of this manual for each test type.

III. System

E³

The E³ is a tabletop-based system that can run a wide range of electrophysiology tests in one compact platform. The E³ has a small footprint and can operate any of the five Diagnosys flash- and pattern-based stimulators. One stimulator can be used at a time.

Profile

The Profile is a cart-based system that can run a wide range of electrophysiology tests in one compact platform. The Profile has a small footprint and can operate any of the five Diagnosys flash- and pattern-based stimulators. One stimulator can be used at a time.

IV. Stimulators

ColorDome

The ColorDome is a binocular Ganzfeld flash stimulator that can be mounted on a tabletop, cart, or adjustable arm. It has a wide flash range and is suitable for scotopic threshold testing as well as tests that involve photobleaching or otherwise very bright flashes and an infrared camera that allows for monitoring the patient during testing. In addition, it has EOG testing capability. It can also run Diagnosys*FST*, Dark Adaptometry and pupillometry tests (add-on modules). Follow instruction popup messages during the protocol for patient position. Generally, the patient will be immediately in front of the ColorDome during test.

ColorBurst

The ColorBurst is a monocular Ganzfeld flash stimulator. It's ideal for situations requiring flexibility where a larger binocular stimulator may pose difficulties. Follow instruction popup messages during the protocol for patient position. Generally, the patient will be 1-2 cm in front of the ColorBurst during test.

ColorFlash

The ColorFlash is a monocular flash paddle stimulator. It is primarily intended for testing patients when a Ganzfeld flash stimulator is not appropriate or available. The ColorFlash is optimized for testing children who may not have a long attention span or be able to sit next to a stimulator during ERG or VEP testing. It can also run Diagnosys*FST* and Dark Adaptometry tests (add-on modules). Follow instruction popup messages during the protocol for patient position. Generally, the patient will be 30 cm in front of the ColorFlash during test.

Envoy Monitor

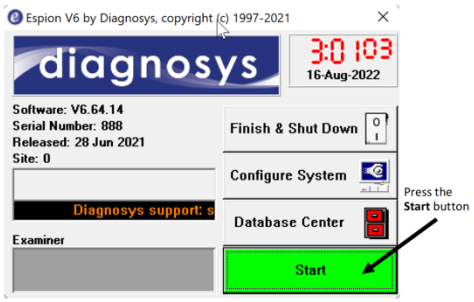
The Envoy is a small OLED monocular pattern stimulator that has no luminance artifact. This makes it suitable for all forms of pattern stimulation including pattern ERGs, pattern onset VEPs, and pattern reversal VEPs. It will also run mfERG protocols. Follow instruction popup messages during the protocol for patient position. Generally, the patient will be 1-2 cm in front of the Envoy during test.

LCD Monitor

The LCD Monitor is used to generate a variety of patterns such as hexagonal, dartboard, bar, grating, and square stimulus patterns. This stimulator can run tests such as multifocal ERGs, pattern VEPs, and pattern ERGs. Follow instruction popup messages during the protocol for patient position. Generally, the patient will be 30-100 cm in front of the LCD monitor during test.

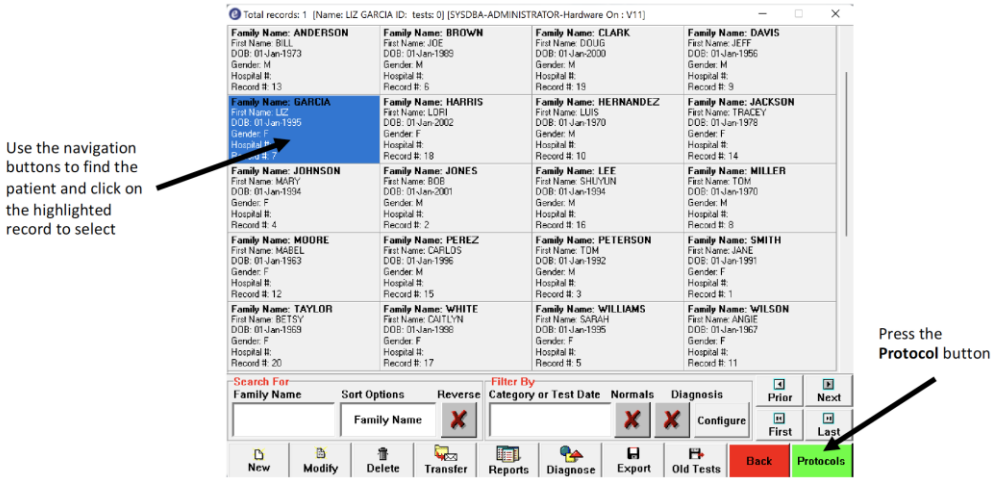
V. General Test Instructions

Open Espion Software and Press Start



Click on the Espion software icon to run the program and then press **Start** button

1. Select the Patient



Step 1: select a patient from the patient menu and press the **Protocol** button

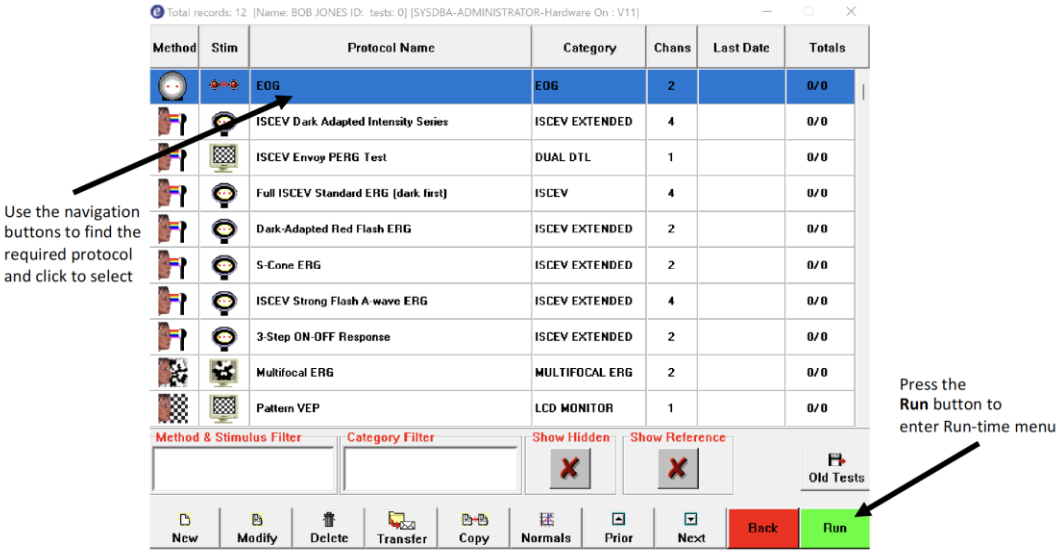
Click and highlight the patient's details to select the patient. The current patient's name and number of tests performed is displayed in the caption or title bar at the top of the menu. All tests subsequently performed are referenced to this current patient.

After a patient has been selected, press the **Protocols** button on the patient list menu to select a test protocol.

To enter a new patient, click **New** and fill in the patient information required by your institution. Then click **Close** and **Yes** to save.

2. Choose the Protocol

A protocol is a collection of parameters that define how a test is run, how the data is collected and



Step 2: Choose a protocol from the list in the Protocol menu and press **Run**

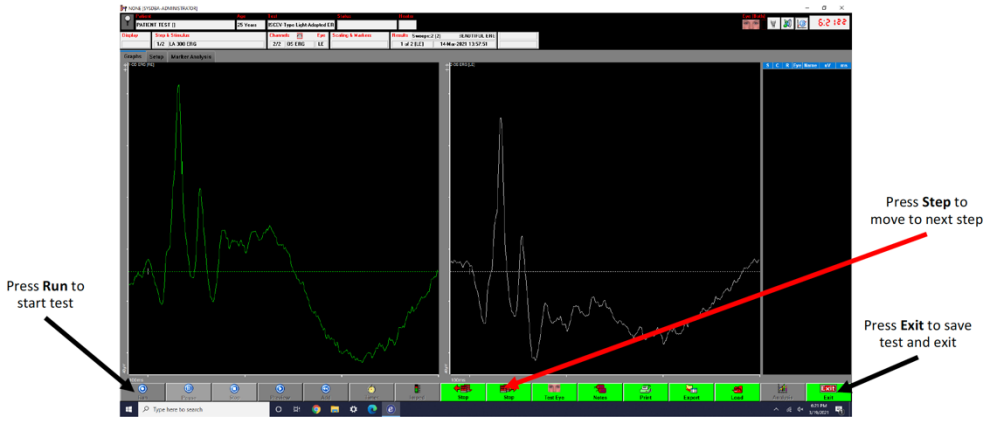
presented on the screen, and how it is printed and even exported. A protocol stored in the database does not contain any test results although stored test results are referenced to a protocol when they are saved.

Included in the system installation is a set of locked protocols that cover all the ISCEV tests as defined in the relevant ISCEV standard. See Appendix 2 for the current list of ISCEV protocols that are included with the system. See Section IX for information on how to receive a new protocol from Diagnosys.

⚠ **Caution**. Deletion or modification of a protocol is considered permanent. You will be asked twice by the software to confirm your choice. Diagnosys recommends NOT deleting any test from the database. If you need to recover a deleted test on your system contact Diagnosys support for assistance in restoring the test to your database.

⚠ **Caution**. Deletion of a test is considered permanent. You will be asked twice by the software to confirm your choice). Diagnosys recommends NOT deleting any test from the database. If you need to recover a deleted test on your system contact Diagnosys support for assistance in restoring the test to your database.

3. Run and Record Test



Step 3: Press the **Run** button to start the test and record data. Move through the protocol steps by pressing the **Step** button. Save and exit the test by pressing the **Exit** button.

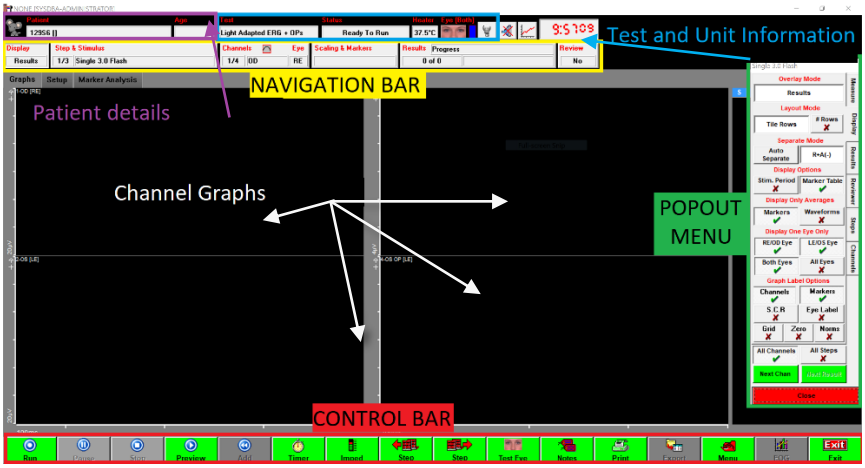
Having selected a test patient and protocol, the final stage is to run and record data. The main run-time display is similar for all the main standard tests including VEP, ERG and EOG.

Press the **Run** button to display the main run-time window.

NOTE: The appearance of the certain buttons may differ between steps and protocols.

Runtime Menu Controls

This is the runtime menu of the Diagnosys software for full-field/pattern ERG, VEP, EOG tests:



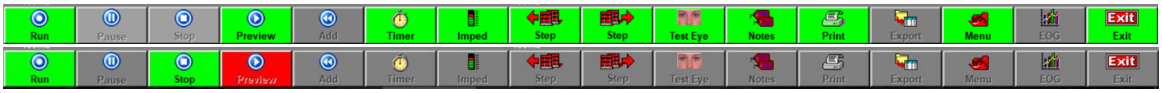
The **Patient Details Bar** includes the identifying information filled out in the subject record, such as patient name, patient ID number, date of birth, and age.

The **Test and Unit Information** includes the name of the test being performed and the test status (ready to run, paused, previewing, waiting for an adaptation timer to complete, or waiting for an interstimulus delay to end).

The **Navigation Bar** at the top controls the popout menu at the right. Pressing any of those buttons will cause the corresponding popout menu to appear; depressing the buttons will cause it to close. The popout menu can also be navigated using the tabs on the right edge of the menu.

The first button on the navigation bar is **Display**, which controls the display settings for the test. The **Step & Stimulus** menu reports current stimulus and acquisition parameters; these are primarily used during new protocol creation, not typical use. The **Channels & Eye** menu houses the 50/60 Hz line filter; it also reports the current filter and auto-rejection window settings. The **Scaling and Markers** button allows you to adjust marker placement or change channel scaling as necessary. The **Results** menu allows you to delete or toggle the visibility of recorded results, reject individual artifacts, change the color of responses, and create grand averages.

The **Control Bar** at the bottom of the page controls the test. By default, buttons that can be pressed are green or yellow; buttons that are active are red; buttons that cannot be used at the moment are greyed out. Below are images of a Control Bar in the ready state and in the Preview State – note that in the second image the array of available commands has changed now that the amplifiers are actively sampling and saving data. The color of the control bar buttons can be customized in the Local Configuration Settings.



The **Run** button will start the test. Manually sequenced protocols will require the operator to use the Step ➡ button to advance through the protocol. The **Pause** button will pause a running test, and **Stop** will stop the recording. **Preview** will begin recording data, but not saving it. The **Add** button will add a full complement of sweeps to the selected result.

The **Timer** button will allow you to see or control the timer in a protocol that has adaptation timers defined.

Imped will allow you to check the impedance (resistance; a measure of electrode connection quality) of the setup. Ideal impedances are between 5 and 15KΩ. Protocols will automatically launch the impedance checker when you start the test.

The **Step Forward** and **Step Back** buttons allow the operator in a manually-sequenced protocol to advance through a test. The step you are on (and how many steps there are in the test) are updated in the Step and Stimulus button in the navigation bar.

Test Eye will allow you to change the eye being tested from the default.

Notes allows you to write free-form notes (for example, “eyelids taped due to ptosis”) that will appear on printouts of the test.

The **Print** and **Export** buttons allow you to print results, either to hard copy or a PDF printer, and to Export graphic or ASCII data to third party software. To print, while in Runtime menu of a test (see Runtime image above) click the **Print** button, select the printer from the menu and click **Print** again. To

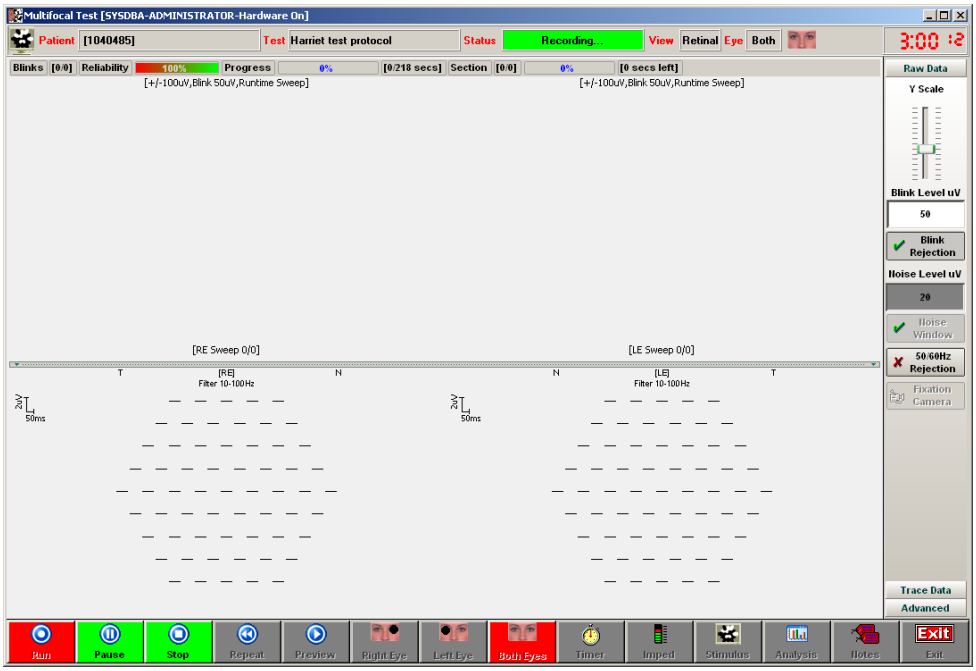
export, click the **Export** button (see Control bar image above), navigate to the location you would like to save the .TXT file, and click **Save**.

The **Menu** button launches the popout menu.

The **EOG** button performs EOG analysis following an EOG test. This button must be pressed in order to generate the Arden ratio.

The **Exit** button allows the operator to exit the test. When exiting the test, the operator will be prompted to save. A 'no' response will require confirmation. If a test is discarded in error, contact Diagnosys for help in retrieving the test data.

Runtime menu for mfERG tests:



The control buttons at the bottom of the screen are the same as described above in the general ERG section.

Additionally, the following controls are on the right side of the screen. **Y scale**, which is a slider bar that adjusts the Y-scaling of the runtime traces. **Blink Rejection**, and **Noise Level** which Diagnosys recommends to always leave on and the **50/60 Hz (line noise) Rejection** which may be turned on or off as required in the test.

Impedance

Impedance is the measure of electrical resistance to flow that provides a measure of patient connection quality. The Espion software allows users to measure impedance to ensure patient connection is acceptable. Values are directly influenced by patient setup. The electrode impedance is displayed as a bar graph and is not only calibrated in ohms, but also color coded to ISCEV suggestions.

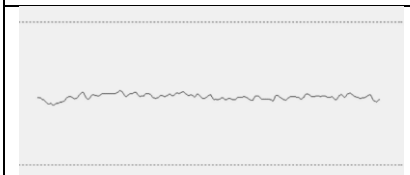
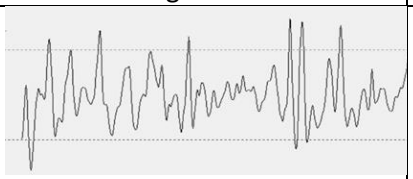
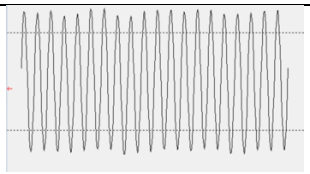
Impedance	Color	Action required
<5k Ohm	☺	None
>5k and <10k Ohm	😐	Try to improve connection if possible
>10k Ohm	☹	May require electrode replacement and/or skin re-preparation

Additionally, there are LED lights on the amplifier surrounding each electrode port. The lights will do the following, matching the cases in the table above:

1. **Bright, steady light on:** no action required
2. **Slow blinking light:** try to improve connection if possible
3. **Fast blinking light:** may require electrode replacement and/or skin repreparation

Preview and Artifacts

The **Preview** button allows you to view the incoming trace of the patient, but the data will not be saved. The software will not save data until you press **Run**. This provides insight into the quality of the patient setup and is a good predictor of test quality.

Ideal Baseline	Biological Noise	Electrical Noise
		
This trace has a very “quiet” baseline. The patient is calm, not moving or blinking, and fixated straight ahead. This is what an ideal signal looks like. Note that there is quite a lot of empty space between the trace and the dotted lines.	This has a lot of random, high-frequency noise superimposed on the trace. Note how the spikes are irregular, and frequently go outside the boundary of the dotted line. **What you can do to fix it:** Have the patient relax their shoulders and jaw. They should not be eating, talking, laughing, chewing gum, or even smiling. A drop of artificial tears may help. If the patient is uncomfortable, an additional drop of corneal anesthetic may help.	This has a lot of noise superimposed on the trace. Note how the spikes occur at regular periods – this indicates that the noise is coming from other electrical equipment, or power lines in the wall. **What you can do to fix it:** 1. Make sure that the electrodes are all well-connected to the patient and have low impedances, especially the ground electrode.

	Refer to Section VII, Troubleshooting, for additional guidance.	2. Make sure the patient, the electrode cables, and the amplifier cable are all situated far away from any power cables. 3. Refer to Section VII, Troubleshooting, for additional guidance.

Caution. During the test, the system has a number of features to help identify biological and electrical noise that may affect the test. These are described in this manual. Generally, the impedance checking features of the system are intended to help prevent low quality tests due to some forms of biological and electrical noise before any recording is done. For most tests the software also has settings that allow it to detect and reject recordings that have artifacts caused by blinking (by setting upper and lower bounds to an expected response) and have features that detect line noise during the test (by looking for excessive 50 or 60 Hz energy in the signal). However, the ERG, VEP and EOG signals being measured by the tests are small (micro-volts) and artifacts caused by noise can and will happen in practice. It is the responsibility of the trained medical professional to identify these artifacts. Suggestions for additional training resources are provided in Appendix 4.

Caution. It is the responsibility of the Operator and Data Analyst to identify large noise artifacts and to eliminate the artifacts and retest. This user guide has a number of example waveforms to help the Operator and Data Analyst identify the noise artifact (Section VI in each specific test section), troubleshoot and eliminate the cause (Section VII) and then retest. Thoroughly familiarize yourself with these potential artifacts and means to avoid them, before using the system.

Electrode Placement

Caution. Electrode placement and correct connection into the amplifier port is an important responsibility of the person conducting the test. The instructions below will specifically tell you each of these for every test. The system can detect and will give you feedback when no electrode cable is connected into a required port for a test. It is also possible in post analysis to determine if active and reference electrodes were inverted as they were put into the amplifier ports for a given eye (the waveform will be upside down) and this can be corrected in post-test operations. However, it is important to avoid this issue in setting up the patient. Importantly, the system cannot detect if the active/reference electrodes from one eye are placed in the amplifier ports for the other eye. This is an important responsibility for the Operator conducting the test to ensure the test is done correctly. Always double check the connections of electrode cables are correct from patient to amplifier ports, before running a test.

As described below, some monocular tests utilize a test strategy of using the fellow eye as the reference electrode, rather than a location on the skin (e.g. a temple location). The fellow eye has been shown to be an optimal reference location when it is available for a recording (generally only in a monocular stimulation/recording protocol) and also the test strategy uses fewer electrodes than alternatives strategies. The software automatically handles this operation for those protocols in utilizing the correct amplifier port for each test, right eye and left eye.

Other important information

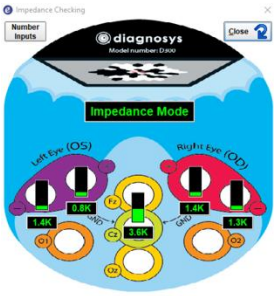
Refer to the system **Instructions for Use (IFU)** (Doc #16519, 16520) that was delivered with your Diagnosys system and forms an important aspect of labeling and instructions for the system.

Refer to the **Symbols Glossary** (Doc #15905) that was delivered with your Diagnosys system and forms an important aspect of labeling and instructions for the system.

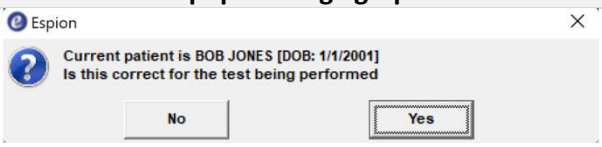
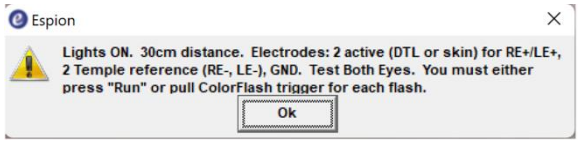
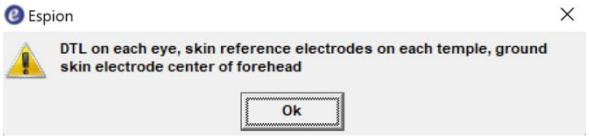
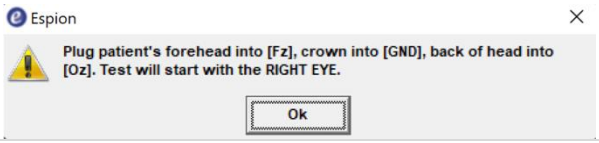
Refer to the **EMC Guidance and Manufacturer's Declaration** (Doc #16566) that was delivered with your Diagnosys system and forms an important aspect of labeling and instructions for the system.

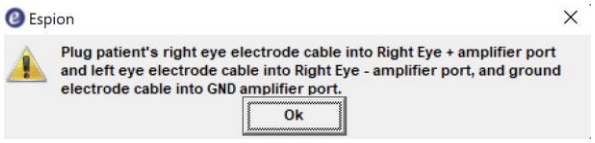
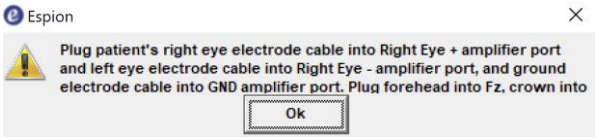
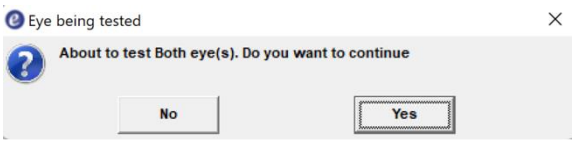
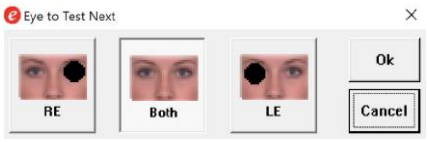
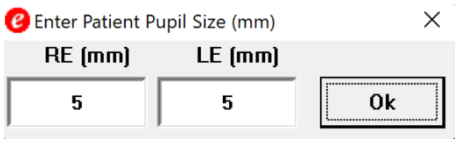
Popup messages that occur before and during the test

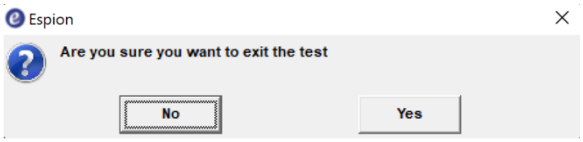
1) Impedance popup when **Imped** is pressed. Use this popup for two purposes. First, verify that an electrode connection required for a protocol has been made on the amplifier and the patient for each channel required for the test. Second, to verify good impedance between each electrode and the patient. Refer to the Troubleshooting section to improve impedance if necessary. As shown below the popup shows each connection required for the test (binocular ERG example shown below) and that connection's impedance.



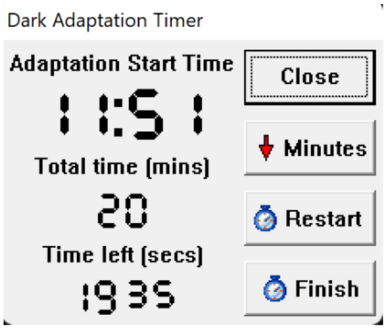
2) Protocol instructions popup messages. Will automatically occur when you open the protocol and at transition points during the protocol (e.g. transition from a dark to a light adapted step). Read and follow these instructions to verify patient setup for electrodes, room light conditions, and other important parameters for the test. Examples are shown below.

Description of popup message	Popup message graphic
Confirmation of patient before running protocol	
Confirmation of room conditions, electrode positions and operating instructions at the beginning of a protocol	
Confirmation of electrode position at the beginning of a protocol. Typical 5-electrode ERG setup.	
Confirmation of electrode position at the beginning of a protocol. Typical 1-channel VEP electrode setup.	

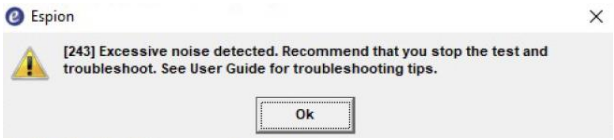
Confirmation of electrode position at the beginning of a protocol. Typical ERG 3-electrode monocular test setup using fellow eye as reference. **NOTE** the LE electrode is plugged into RE- port on amplifier.	
Confirmation of electrode position at the beginning of a protocol. Typical ERG 3-electrode plus 1-channel VEP electrode setup. **NOTE** the LE electrode is plugged into RE- port on amplifier.	
Confirmation of which eye to test at the beginning of, or during a protocol. Monocular test (eye patch over other eye).	
Confirmation of which eye to test at the beginning of, or during a protocol. Binocular test.	
Option to select RE, LE or both eyes to test in a protocol step. Click the option you want to run.	
Confirmation of room conditions, and stimulator position in front of patient (e.g. ColorFlash protocol).	
Protocols recommend reporting the pupil diameter. Click on box and input correct pupil diameter for each eye. This also serves as a reminder to dilate pupils, as applicable for certain tests.	
When you click **Stop** during a test you will be asked to confirm if you intend to stop running the test or not.	

When you click **Exit** before a test is recorded you will be asked to confirm that you do want to exit the test or not.	

3) Timer popup for Dark or Light adapting times. This will show the total time necessary for adapting. The timer counts down to zero and then you may begin the test by clicking **Run**.



4) Excessive noise popup. When this occurs, too much electrical line noise (50 or 60 Hz) has occurred and is detected by the system during the test. Refer to Preview section above and Troubleshooting guide in Section VII for recommendations on how to resolve the noise issue before continuing the test. **Please note that this functionality is not used in every protocol and only monitors for one type of noise (electrical line noise) and does so only when electrical line noise becomes very large. It should not be counted on as the first method to detect excessive noise. The Operator is responsible for detecting noise through Preview (described above) and post-test quality checks of the data (described in Section VI), as instructed throughout this user guide** and, even for line noise, should have made corrections based on instructions in this User Guide, before the popup occurred.



VI. Specific Test Instructions

Any equipment not connected via an isolated connection to the E3 or Profile system and not powered from the Base Unit must be outside the patient environment.

The instructions below describe for each test: 1) patient setup, 2) test procedure, 3) test quality check, and 4) test markers for analysis. See Troubleshooting Section VII for further information on troubleshooting during a test. See the test examples below for data markers used for each test (under the 'markers for analysis' section of each table with example tests). General analysis instructions are in Appendix 4.

ERG Tests

Full-Field ERG (ffERG) Tests

Purpose

The ffERG tests the full field global retinal response by illuminating the entire visual field with a flash or flicker of light. The standard ISCEV 5-step test includes a dark and light adapted section to separately measure rod from cone system function. Biomarker timing and amplitudes are used diagnostically for several Inherited Retinal Diseases. Full-field ERGs require one full-field stimulator: ColorDome, ColorBurst, or ColorFlash.

Patient types

According to ISCEV guidelines, full-field ERG tests may be conducted on adults, pediatric children and infants. Before conducting the test review the procedures below to ensure the patient will be able to comply with all aspects of the testing. For pediatric and infant testing, read Appendix 3 of this guide before conducting the tests. The ColorBurst and ColorFlash stimulators may be used for any age patient but are particularly well suited for young patients, as the stimulator is placed in front of the patient, and for the youngest patients they may sit in their parents lap during the test.

Items Needed (sold separately)

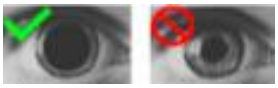
1) Eye drops
    a. Dilating drops (such as tropicamide or phenylephrine): used to allow the maximum amount of light in the eye
    b. Topical anesthetic drops (such as proparacaine or tetracaine): used to make the patient more comfortable with DTL or other corneal electrodes
    c. Artificial tears: used when patient has dry eyes/to improve impedance

2) Electrodes
    b. Two DTL Plus electrodes or other electrodes used as the active electrode
    c. One set of extender cables
    d. Three gold cup or disposable skin pad electrodes

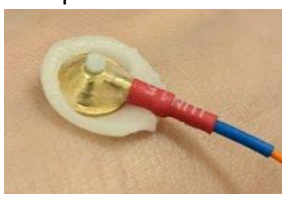
3) Alcohol pads
4) Skin Prep
    a. Either skin scrub pads or exfoliating scrub (such as Nu Prep)
5) Conductive electrode paste (such as Ten20)

6) 3 strips of medical tape (if using gold cups)

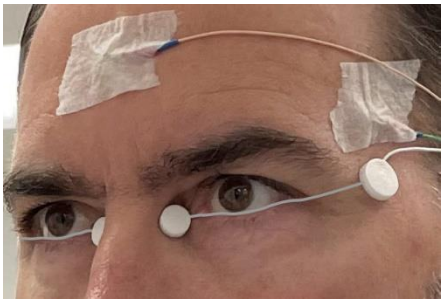
Patient Setup



1) Dilate the patient's eyes using the appropriate eye drops.
2) Scrub forehead and temples where electrodes will be placed with Skin Prep. Follow up with an alcohol pad scrub.

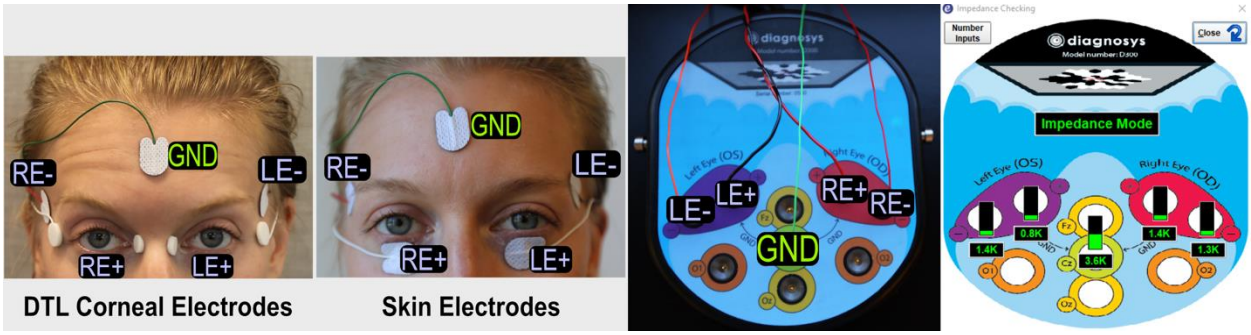


3) Place skin electrodes on forehead and temples. If using gold cups, over fill with conductive paste. Position the skin electrodes at each temple and on the forehead where skin has been prepared. Gold cups require tape to stay in place.
4) Place a drop of corneal anesthetic in each eye, then place the DTL electrodes. The DTL small sticky pad goes next to the nasal canthus; the larger pad next to the temporal canthus. The DTL fiber should drape across the lower lid & should NOT fall into the conjunctival sac.



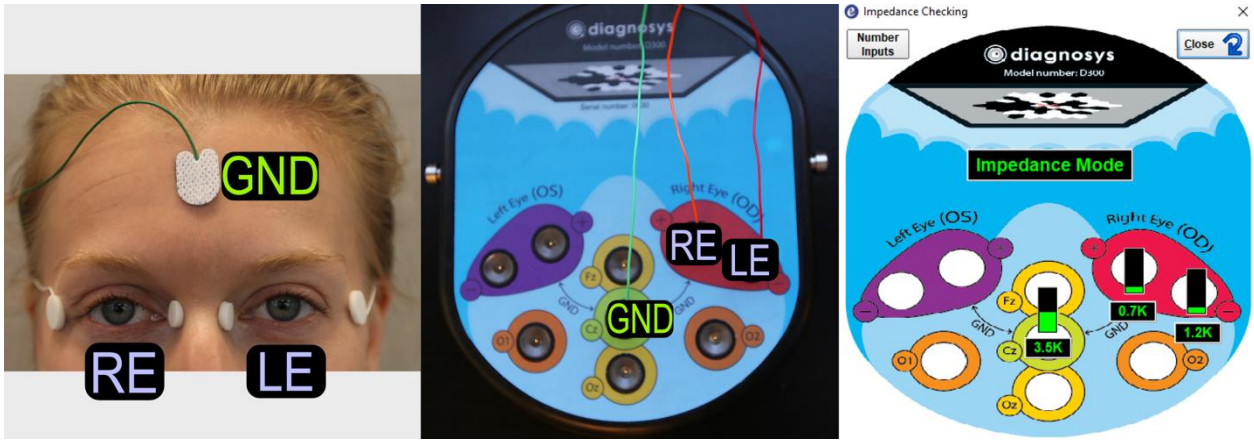
5) Plug the DTL electrode into the extender cables. Connect all patient inputs to the amplifier as shown below.

Electrode and Amplifier Setup (ColorDome)

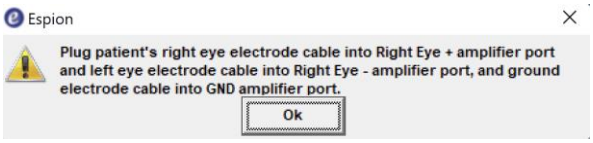


a. Left images: Correct position of electrodes, with two options shown using either a corneal electrode (e.g. DTL) or a skin electrode as the active electrode.
b. Middle image: Connections of each electrode cable into the amplifier.
c. Right image: Electrode position and impedance checking popup to confirm correct electrodes plugged in and good impedance.

Electrode and Amplifier Setup (ColorBurst)

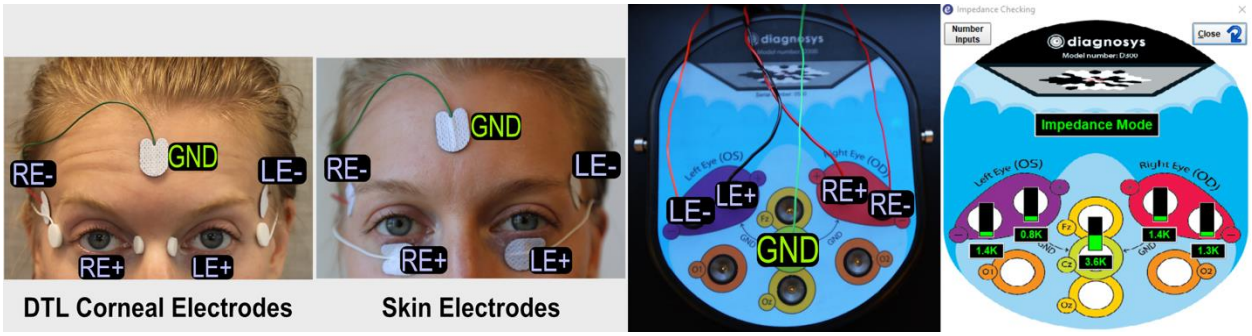


a. Left image: Correct position of electrodes, using a corneal electrode (e.g. DTL) as the active electrode.
b. Middle image: Connections of each electrode cable into the amplifier. **NOTE** the LE electrode is plugged into RE- port on amplifier to use the fellow eye as a reference in this test. This is done for monocular tests to take advantage of the low noise position of using fellow eye as a reference. You will be asked to confirm this electrode connection setup in a popup before beginning the test (see below).



c. Right image: Electrode position and impedance checking popup to confirm correct electrodes plugged in and good impedance.

Electrode and Amplifier Setup (ColorFlash)



a. Left images: Correct position of electrodes, with two options shown using either a corneal electrode (e.g. DTL) or a skin electrode as the active electrode.
b. Middle image: Connections of each electrode cable into the amplifier.
c. Right image: Electrode position and impedance checking popup to confirm correct electrodes plugged in and good impedance.

Test Procedure

1) Refer to Section V for general instructions to run a test.
2) Use the **Pause** button to pause the test as needed during the test.
3) Use artificial tears as necessary during the test to keep patient eyes relaxed.
4) Explain the test procedure to the patient:

'We will flash a series of lights during the test. During the flashes, hold your eyes open while looking at the fixation point in the center of the stimulator. It is important to keep your eyes and face relaxed. There will be pauses during the test where you can rest. Try to minimize blinking and eye movements.'

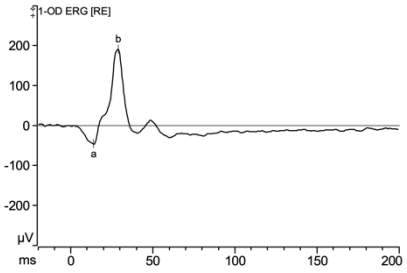
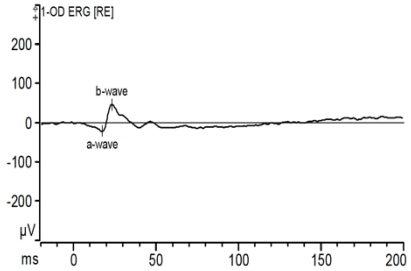
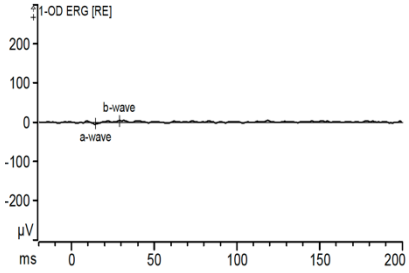
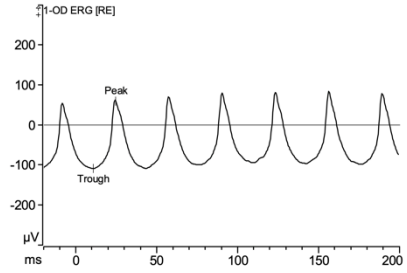
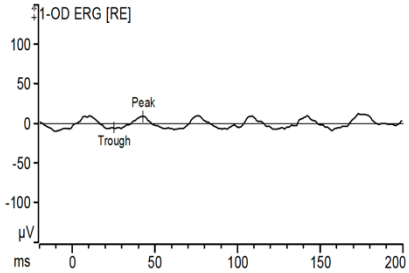
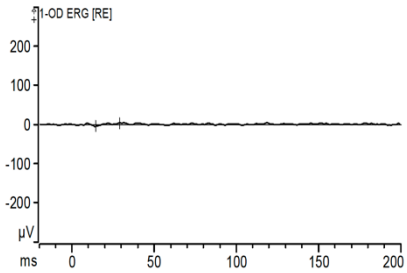
5) For dark adapted tests ensure the room is dark and then dark adapt the patient for 20 minutes, or as otherwise prescribed by your protocol (e.g. unique clinical trial requirements or as prescribed by popup menus in the protocol). For light adapted tests room lights are on and light adapt the patient for 10 minutes, or as otherwise prescribed by your protocol.
6) For binocular tests, test both eyes at the same time. For monocular tests, cover the eye not being tested with an eye patch.
7) Press the **Imped** button and ensure the impedance is green (optimal) or yellow (minimal). Press the **Preview** button and check signal quality.
8) Position the patient centered in front of the stimulator and press **Run** button to begin the test. Run each step of the test in the protocol. Press the **Exit** button once the test is complete.
9) Refer to the test decision guide below to determine if an acceptable quality test has been completed, or if a retest should be considered. Finally, check that the waveform is not inverted. In the case of retest or inverted waveforms refer to the troubleshooting Section VII for steps to improve test results.
10) Refer to Section VIII for instructions on saving, printing and analysis.

Test Quality Check and Markers for Analysis

Once data acquisition is complete, tests must be reviewed by the Operator for acceptance prior to being released for analysis. The test quality check can be done immediately after the test is complete in Runtime (before the test is saved) or by double clicking on the test to open and review it after it has been saved. If possible, this should be done before electrodes are removed from the patient, in case a repeat test is recommended. Below are examples of test examples with sufficient quality ('High Quality') to be accepted for analysis as well as tests with insufficient quality ('Low Quality') where troubleshooting and repeating the test is recommended or in the case of inverted electrodes where inverting the test result in software is required. Tests from a variety of patient types are included to show examples for Quality Check purposes, not for medical analysis/interpretation purposes.

High Quality

The tests below are High Quality and after review by the operator are ready to be released for analysis. Patient test examples below from the E[3] and Profile system.

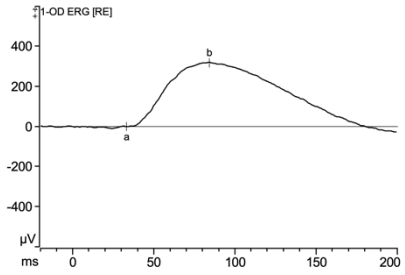
Test Type and Description	Example Waveforms
Light-adapted ERG (e.g. ISCEV LA 3.0 test) Waveform shape: the a-wave and b-wave peaks are well defined and marked by the software or the response is flat with no indications of excess noise. Peak amplitudes may be anywhere from about 150 uV to 0 uV. Quality check: waveforms start near 0 uV, but may end significantly different than 0 uV. Markers for analysis: a-wave, b-wave	 Typical waveform (eg. Normal patient)  Typical waveform (eg. Retinal disease patient)  Flat response (eg. Late stage RP patient)
Light-adapted Flicker ERG (e.g. ISCEV LA 30 Hz Flicker test) Waveform shape: the Trough and Peak peaks are well defined and marked by the software or the response is flat with no indications of excess noise. Peak amplitudes may be anywhere from about 200 uV to 0 uV. Quality check: waveforms generally are at the same amplitude from right to left. Markers for analysis: trough, peak	 Typical waveform (eg. Normal patient)  Typical waveform (eg. X-Linked RP patient)  Flat response (eg. Late stage RP patient)

Dark-adapted Rod ERG (e.g. ISCEV DA 0.01 ERG)

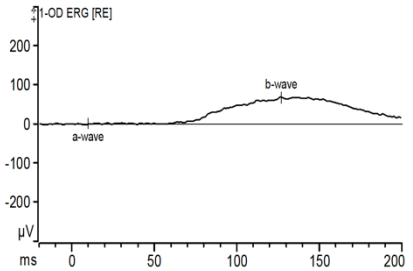
Waveform shape: no a-wave peak is present. The b-wave peak is well defined and marked by the software or the response is flat with no indications of excess noise. Peak amplitudes may be anywhere from about 500 uV to 0 uV.

Quality check: waveforms start near 0 uV, but may end significantly different than 0 uV.

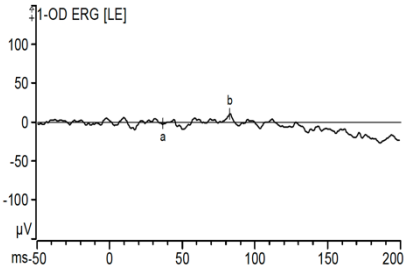
Markers for analysis: a-wave, b-wave



Typical waveform (eg. Normal patient)



Typical waveform (eg. Retinal disease patient)



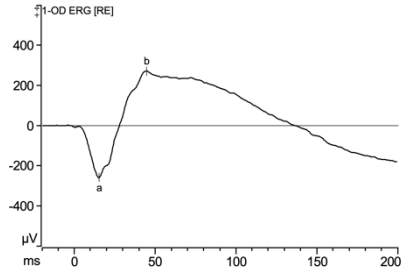
Flat response (eg. X-linked RP patient)

Dark-adapted Mixed Rod-Cone ERG (e.g. ISCEV DA 3.0 ERG)

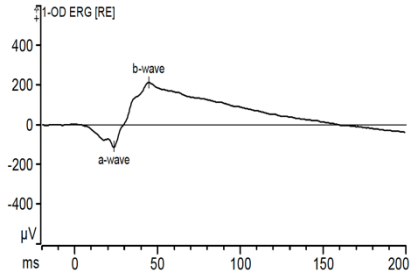
Waveform shape: the a-wave and b-wave peaks are well defined and marked by the software or the response is flat with no indications of excess noise. Peak amplitudes may be anywhere from 700 uV to 0 uV.

Quality check: waveforms start near 0 uV, but may end significantly different than 0 uV.

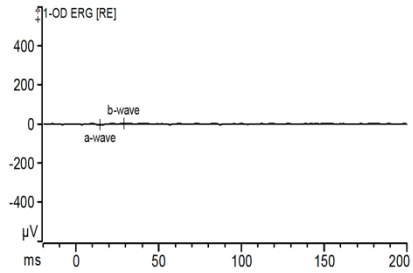
Markers for analysis: a-wave, b-wave



Typical waveform (eg. Normal patient)



Typical waveform (eg. Retinal disease patient)

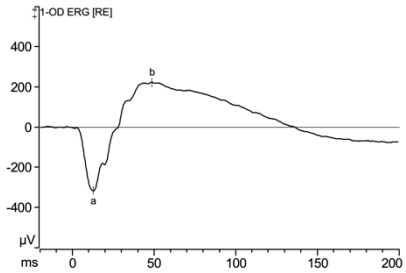


Flat response (eg. Late stage LCA patient)

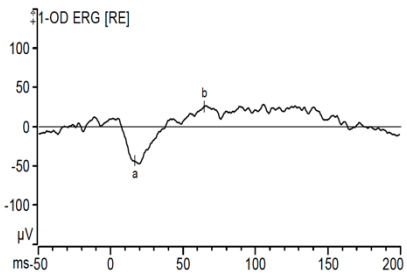
Dark-adapted Maximal ERG (e.g. ISCEV DA 10.0 ERG)

Waveform shape: the a-wave and b-wave peaks are well defined and marked by the software or the response is flat with no indications of excess noise. Peak amplitudes may be anywhere from 700 uV to 0 uV.

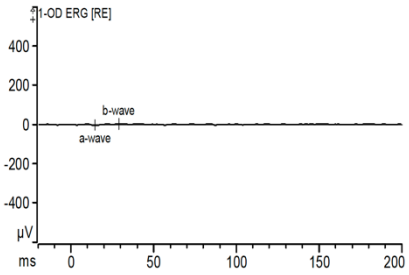
Quality check: waveforms start near 0 uV, but may end significantly different than 0 uV.



Typical waveform (eg. Normal patient)

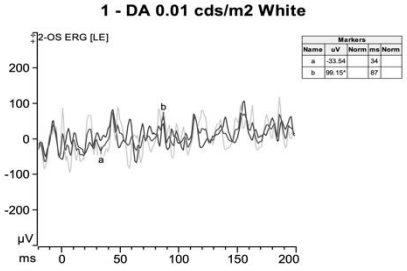
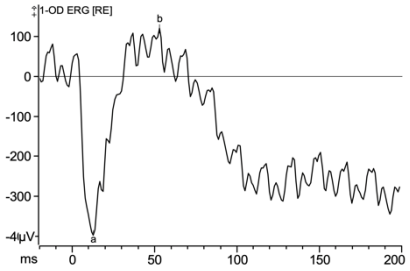
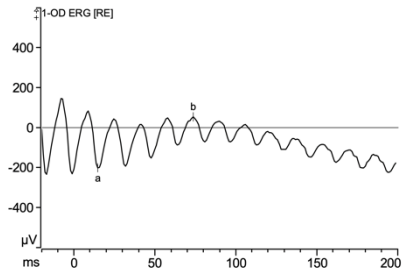
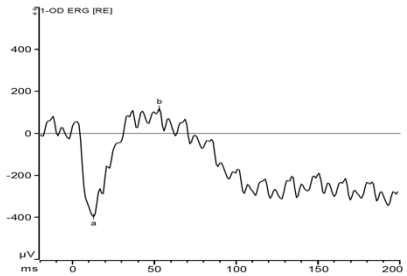


Typical waveform (eg. X-Linked RP patient)

Markers for analysis: a-wave, b-wave	 Typical waveform (eg. Late stage LCA)

Low Quality

The tests below are Low Quality and not ready to be released for analysis. See Troubleshooting Section VII for recommendations on how to resolve excess biological noise, excess electrical noise or inverted waveform issues. Repeat the test once the noise issue has been eliminated to minimized sufficiently to conduct a High Quality test. Inverted waveforms can be corrected in software without a retest. See Section VII. Patient test examples below from the E3 and Profile system.

Test Type and Description	Example Waveforms
Excess higher frequency biological noise Dark- and Light-adapted ERG test examples Generally, this is characterized by peaks that are >20 uV and spaced <10 ms apart. Case 1: the retinal signal may be small or non-existent but that is not possible to determine given random, higher frequency noise. Case 2: a strong retinal response (the a-wave and b-wave structure to the waveform) is present but higher frequency noise is as well.	 Case 1: DA or LA ERG.  Case 2: DA ERG
Excess electrical (line) noise Dark-adapted ERG test examples Case 1: a small waveform may exist, or it may be flat. That is not possible to determine given electrical line noise. Line noise is characterized by regular sinusoidal shaped peaks, that are about 17 ms apart (60 Hz line) or 20 ms apart (50 Hz line). Case 2: a larger DA waveform with a- and b-wave responses, but regular-spaced smaller waveforms from before time = 0 through the entire response is indicative of electrical line noise.	 Case 1: 0.01 DA ERG  Case 2: 10.0 DA ERG

Excess lower frequency biological noise

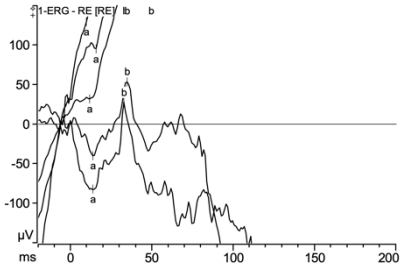
Dark- and Light-adapted ERG test examples

No good baseline before and near time 0 (before the flash happened) was established. In each case there is likely a good waveform possible, but both cases are not appropriate for analysis given the large upward and/or downward swings to the entire waveform that are likely caused by excess eye movements during the test.

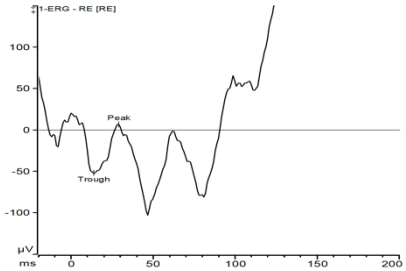
Case 1: complete lack of repeatability when comparing the individual results, along with a baseline trace before time 0 that is very irregular indicates the patient's eyes were moving too much during the test.

Case 2: in a Flicker ERG the peaks, regardless of amplitude, typically all are the same height. In this case there is excessive blinking or eye movements.

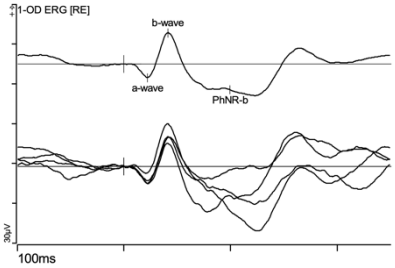
Case 3: lack of repeatability when comparing the individual results (lower curves) along with a baseline trace before time 0 that is very irregular indicates the patient's eyes were moving too much during the test.



Case 1: LA ERG



Case 2: Flicker ERG



Case 3: PhNR ERG

Inverted active and reference electrodes

Dark- and Light-adapted ERG test examples

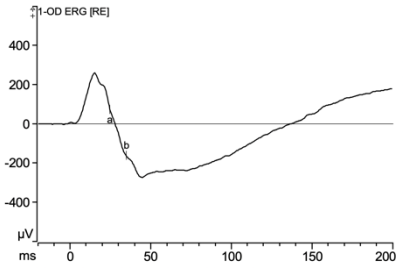
Compare the wave form to the expected waveform and it is seen that in each case the a-wave (expected to be negative or 0) and b-wave (expected to be positive or 0) are upside down in each case. Also notice than in most cases the markers are not placed at a peak or a trough (because the software is looking for the peak where it should be in a negative going wave, rather than a positive going wave (e.g. a-wave).

Case 1: Inverted dark adapted ERG.

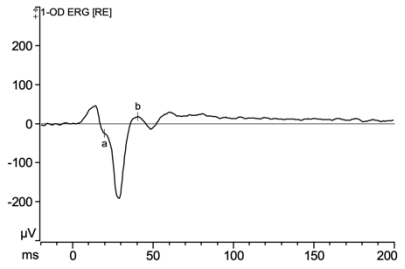
Case 2: Inverted light adapted ERG.

Case 3: Inverted On-Off ERG.

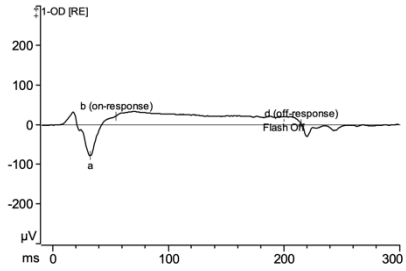
This is a good waveform (low noise), but the waveform is inverted. See Troubleshooting Section VII on how to invert the waveform in software, to be correct.



Case 1: Inverted dark adapted ERG



Case 2: Inverted light adapted ERG

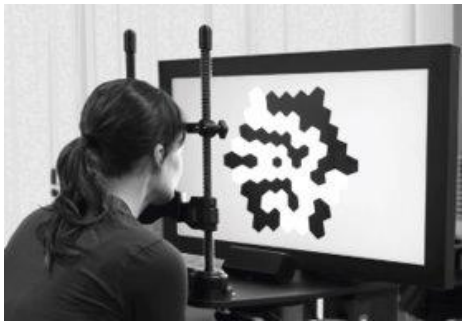


Case 3: Inverted On-Off ERG

Multi-focal ERG (mfERG) Tests

Purpose

The Multifocal ERG (mfERG) test shows visual function across the macula and central vision area. This test divides the stimulated region into multiple hexagonal sub-regions. The stimulus is a pseudo-random sequence of black and white hexagons that alternate many times per second.



mfERG responses are primarily derived from cone on- and off-bipolar cells, with additional contributions from cone photoreceptors. Multifocal ERGs can be readily utilized to distinguish between macular and generalized retinal dystrophies, as well as to localize retinal defects. The mfERG requires one display monitor stimulus: LCD monitor or Envoy monitor.

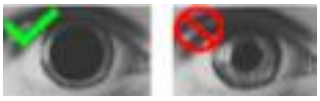
Patient types

According to ISCEV guidelines, multi-focal ERG tests may be conducted on adults and pediatric children who are able to sit for 5-10 minutes and fixate during the test. This will preclude many younger children from taking the test. Before conducting the test review the procedures below to ensure the patient will be able to comply with all aspects of the testing. For pediatric testing, consult Appendix 3 of this guide before conducting the tests.

Items Needed (sold separately)

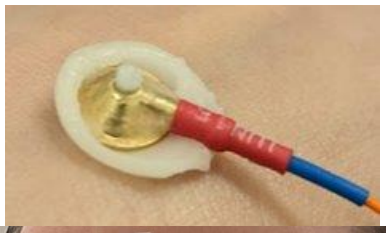
1) Eye drops
    a. Dilating drops (such as tropicamide or phenylephrine): used to allow the maximum amount of light in the eye
    b. Corneal anesthetic drops (such as proparacaine or tetracaine): used to make the patient more comfortable with a corneal electrode
    c. Artificial tears: used when patient has dry eyes/to improve impedance
2) Electrodes
    a. Two DTL Plus electrodes or other corneal electrodes used as the active electrode
    b. One set of extender cables
    c. Three gold cup or sticky pad electrodes (one if using Envoy)
3) Alcohol pads
4) Skin Prep
    a. Either skin scrub pads or exfoliating scrub (such as Nu Prep)
5) Conductive electrode paste (such as Ten 20)
6) 1 or 3 strips of medical tape depending on stimulator (if using gold cups)

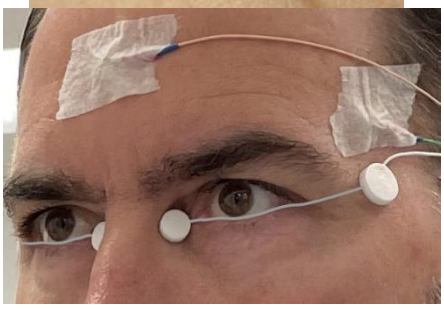
Patient Setup



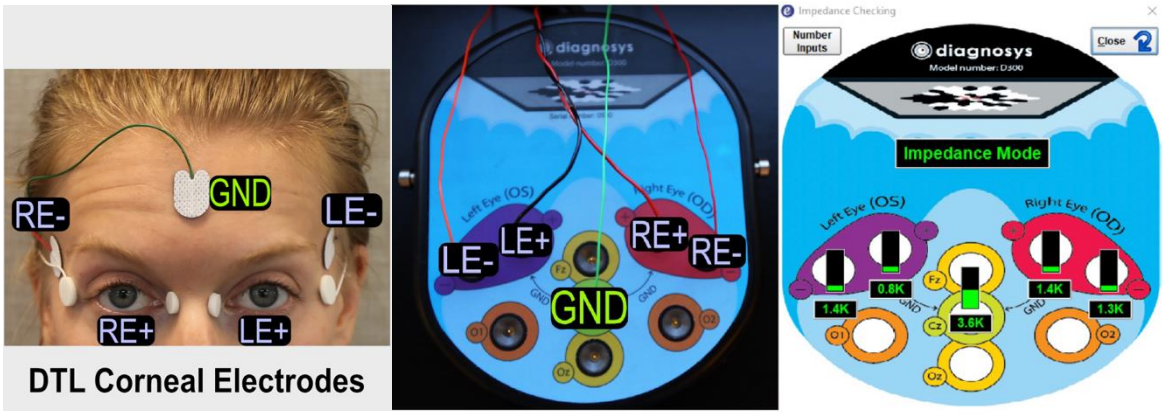
1) Dilate the patient's eyes using appropriate eye drops.

2) Scrub forehead and temples where electrodes will be placed with Skin Prep. Follow up with an alcohol pad scrub. (Envoy stimulators only require an electrode on the forehead).
3) Place skin electrodes on forehead and temples. If using gold cups, over fill with conductive paste. Position the skin electrodes at each temple and on the forehead where skin has been prepared. Gold cups require tape to stay in place.
4) Place a drop of corneal anesthetic in each eye, then place the DTL electrodes. The DTL small sticky pad goes next to the nasal canthus, the larger pad next to the temporal canthus. The DTL fiber should drape across the lower lid & should NOT fall into the conjunctival sac.
5) Patient should be vision corrected if applicable.
6) Eye not being stimulated should be patched if using the Envoy.



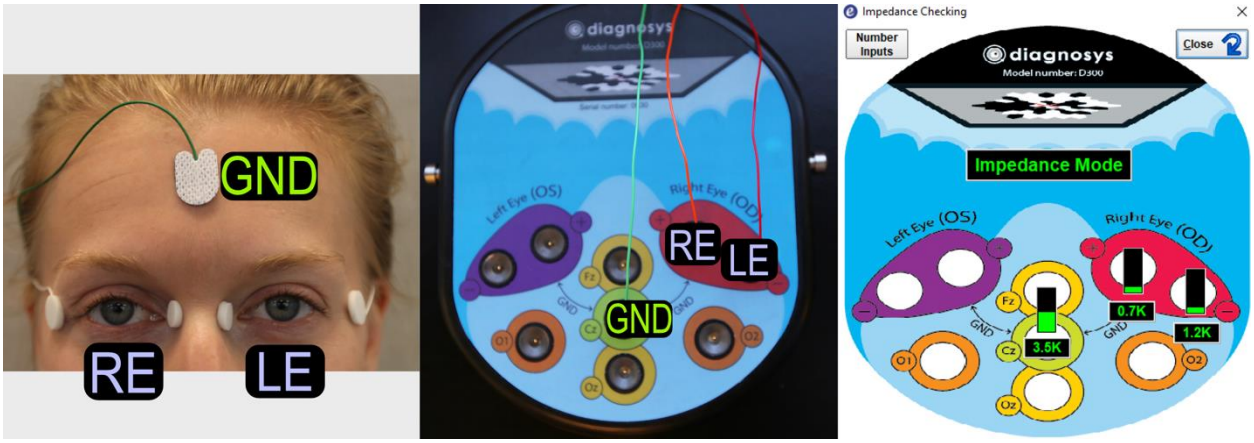


Electrode and Amplifier Setup (LCD monitor)

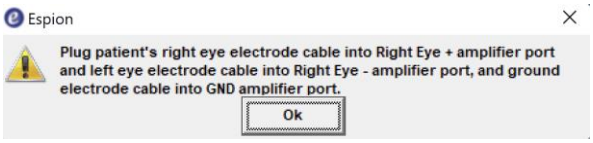


a. Left images: Correct position of electrodes, using a corneal electrode (e.g. DTL) as the active electrode.
b. Middle image: Connections of each electrode cable into the amplifier.
c. Right image: Electrode position and impedance checking popup to confirm correct electrodes plugged in and good impedance.

Electrode and Amplifier Setup (Envoy monitor)



a. Left image: Correct position of electrodes, using a corneal electrode (e.g. DTL) as the active electrode.
b. Middle image: Connections of each electrode cable into the amplifier. **NOTE** the LE electrode is plugged into RE- port on amplifier to use the fellow eye as a reference in this test. This is done for monocular tests to take advantage of the low noise position of using fellow eye as a reference. You will be asked to confirm this electrode connection setup in a popup before beginning the test (see below).



c. Right image: Electrode position and impedance checking popup to confirm correct electrodes plugged in and good impedance.

Test Procedure

1) Refer to Section V for general instructions to run a test.
2) Use the **Pause** button to pause the test as needed during the test.
3) Use artificial tears as necessary during the test to keep patient eyes relaxed.
4) Explain the test procedure to the patient:

'We are going to test each eye's response to patterns of light. The test will take about 4-7 minutes. You will have a break every 30 seconds to blink and relax. Try to minimize blinking during the test when the hexagons are flashing. All you need to do is relax, try not to blink, and fixate on the cross in the center of the screen."

5) Room lights are on.
6) For binocular tests, test both eyes at the same time. For monocular tests, cover the eye not being tested with an eye patch.
7) Press the **Imped** button and ensure the impedance is green (optimal) or yellow (minimal). Press the **Preview** button and check signal quality.
8) Position patient. First, adjust the height of the chinrest so that the patient is positioned in the center of the monitor, both up/down and left/right. The patient should be able to clearly see the

fixation X symbol in the center of the monitor. For patients with poor central vision, it may be necessary to enlarge the fixation X symbol. For these patients, press the Stimulator button and pull the Fix Size slider up to adjust size and width of the central red cross lines.

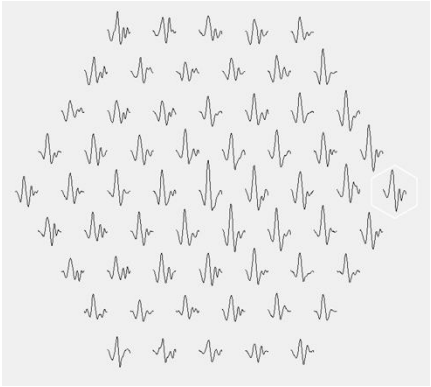
9) Once the patient is positioned and ready to take the test, press **Run** button to begin the test. Run each step of the test in the protocol. Press the **Exit** button once the test is complete. Place patient in front of monitor and on the chin rest.
10) Refer to the test decision guide below to determine if an acceptable quality test has been completed, or if a retest should be considered. Finally, check that the waveform is not inverted. In the case of retest or inverted waveforms refer to the troubleshooting Section VII for steps to improve test results.
11) Refer to Section VIII for instructions on saving, printing and analysis.

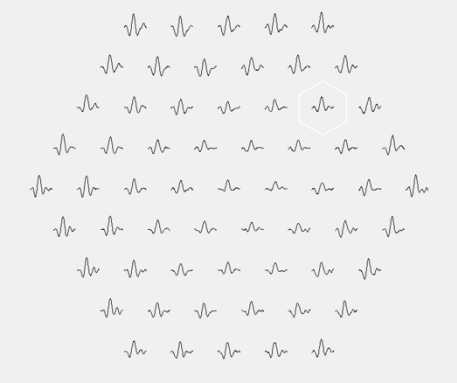
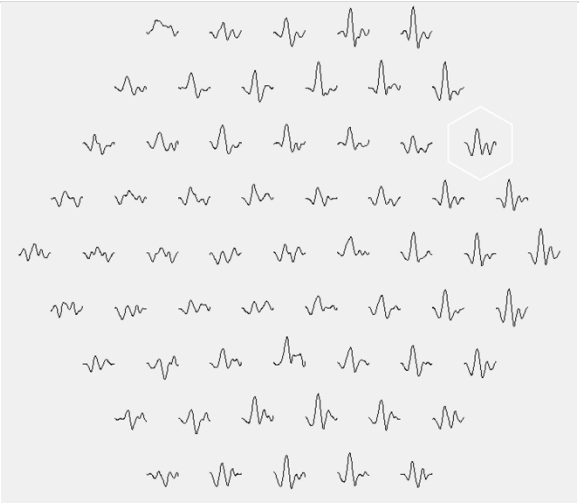
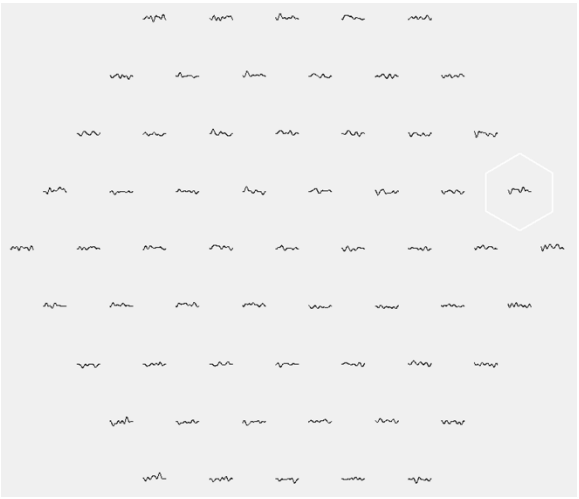
Test Quality Check and Markers for Analysis

Once data acquisition is complete, tests must be reviewed by the operator for acceptance prior to being released for analysis. The test quality check can be done immediately after the test is complete in Runtime (before the test is saved) or by double clicking on the test to open and review it after it has been saved. If possible, this should be done before electrodes are removed from the patient, in case a repeat test is recommended. Below are examples of test examples with sufficient quality ('High Quality') to be accepted for analysis as well as tests with insufficient quality ('Low Quality') where troubleshooting and repeating the test is recommended or in the case of inverted electrodes where inverting the test result in software is required. Tests from a variety of patient types are included to show examples for Quality Check purposes, not for medical analysis/interpretation purposes.

High Quality

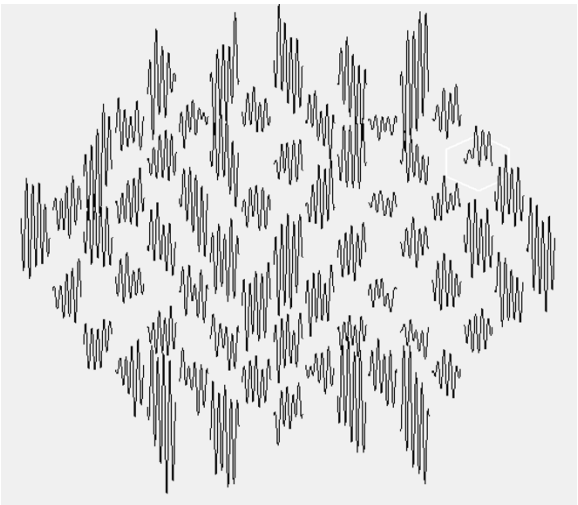
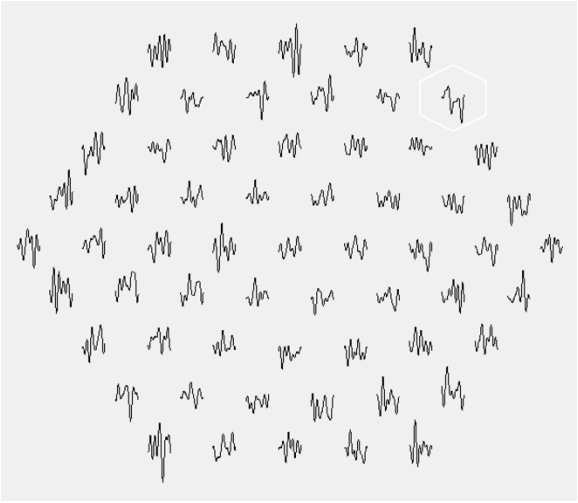
The tests below are High Quality and after review by the operator are ready to be released for analysis. Patient test examples below from the E3 and Profile system.

Test Type and Description	Example Waveforms
ISCEV 61-hexagon mfERG test Waveform shape: typically the mfERG trace array waveform, when little to no noise is present, will have a 'down-up-down' structure. There may be some smaller peaks late in the waveform, and that is acceptable. Quality check: typically high quality mfERG trace array waveforms have one prominent peak, regardless of the amplitude size. Markers for analysis: N1, P1	 Case: normal patient
ISCEV 61-hexagon mfERG test Waveform shape: typically the mfERG trace array waveform, when little to no noise is present, will have a 'down-up-down' structure. There may be some smaller peaks late in the waveform, and that is acceptable.	

Quality check: typically high quality mfERG trace array waveforms have one prominent peak, regardless of the amplitude size. Markers for analysis: N1, P1	 Case: AMD patient
ISCEV 61-hexagon mfERG test Waveform shape: typically the mfERG trace array waveform, when little to no noise is present, will have a 'down-up-down' structure. There may be some smaller peaks late in the waveform, and that is acceptable. This case shows where retinal function may be degraded, waveforms will be smaller and look a little noisier, but that is acceptable for smaller waveforms, compared to the larger well formed waveforms. Quality check: typically high quality mfERG trace array waveforms have one prominent peak, regardless of the amplitude size. Markers for analysis: N1, P1	 Case: Diabetic Retinopathy patient
ISCEV 61-hexagon mfERG test Waveform shape: typically the mfERG trace array waveform, when little to no noise is present, will have a 'down-up-down' structure. There may be some smaller peaks late in the waveform, and that is acceptable. This case shows a flat response, with relatively low noise. Quality check: typically high quality mfERG trace array waveforms have one prominent peak, regardless of the amplitude size. Markers for analysis: N1, P1	 Case: RP patient

Low Quality

The tests below are Low Quality and not ready to be released for analysis. See Troubleshooting Section VII for recommendations on how to resolve excess biological noise, excess electrical noise or inverted waveform issues. Repeat the test once the noise issue has been eliminated to minimized sufficiently to conduct a High Quality test. Inverted waveforms can be corrected in software without a retest. See Section VII. Patient test examples below from the E3 and Profile system.

Test Type and Description	Example Waveforms
Excess electrical (line) noise 61-hexagon mfERG test example Generally, this is characterized by peaks that are regular spaced and typically 5-10 positive peaks, rather than 1 prominent central peak that occurs in a high-quality test.	 Case: excess electrical (line) noise
Excess biological noise 61-hexagon mfERG test example Generally, this is characterized by multiple peaks (rather than 1 prominent central peak) that are not small and they are irregular. This is often caused by excessive eye movement and/or flinches during the test.	 Case: excess biological noise

Pattern ERG (PERG) Tests

Purpose

The Pattern ERG (PERG) produces a macular retinal ganglion cell response. When done as a follow-up to an abnormal pattern VEP, the pERG can elucidate whether the abnormality is caused by retinal or optic nerve dysfunction. This test may also assist in diagnosing glaucoma, optic neuropathies, and primary ganglion cell diseases. Pattern ERG tests require one pattern stimulator: LCD monitor or Envoy monitor.

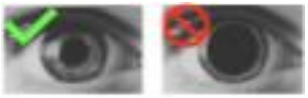
Patient types

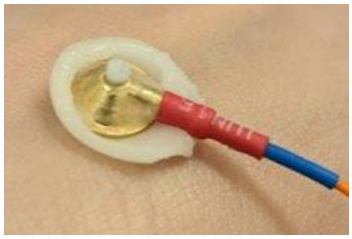
According to ISCEV guidelines, PERG tests may be conducted on adults and pediatric children who are able to sit for 5-10 minutes and fixate during the test. This will preclude many younger children from taking the test. Before conducting the test review the procedures below to ensure the patient will be able to comply with all aspects of the testing. For pediatric testing, consult Appendix 3 of this guide before conducting the tests.

Items Needed (sold separately)

1) Eye Drops
    a. Corneal anesthetic drops (such as proparacaine or tetracaine): used to make the patient more comfortable with DTL electrodes
    b. Artificial tears: used when patient has dry eyes/to improve impedance
2) Electrodes
    a. Two DTL Plus electrodes or other electrodes used as the active electrode
    b. One set of extender cables
    c. Three gold cup or sticky pad electrodes (one if using Envoy)
3) Alcohol Pads
4) Skin Prep (such as Nu Prep)
5) Conductive Paste (such as Ten 20)
6) 1 or 3 strips of medical tape depending on stimulator (if using gold cups)

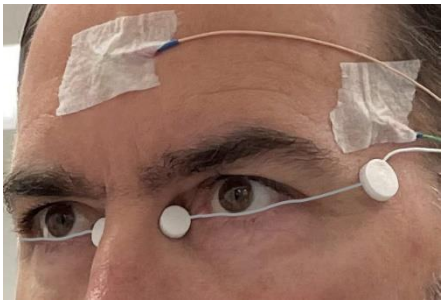
Patient Setup



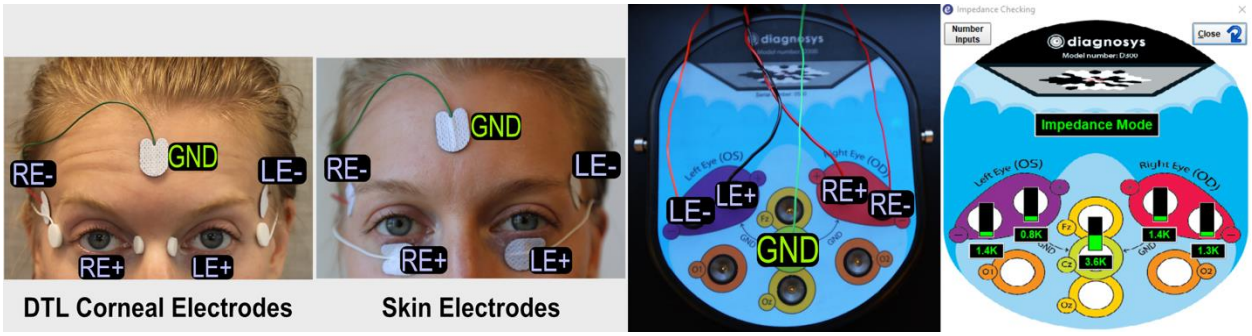


1) Patient Eyes should NOT be dilated.
2) Scrub forehead and temples where electrodes will be placed with Skin Prep. Follow up with an alcohol pad scrub. (Envoy stimulators only require an electrode on the forehead).
3) Place skin electrodes on forehead and temples. If using gold cups, over fill with conductive paste. Position the skin electrodes at each temple and on the forehead where skin has been prepared. Gold cups require tape to stay in place.

4) Place a drop of corneal anesthetic in each eye, then place the DTL electrodes. The DTL small sticky pad goes next to the nasal canthus; the larger pad next to the temporal canthus. The DTL fiber should drape across the lower lid & should NOT fall into the conjunctival sac.
5) Patient should be vision corrected to 20/30 or better.
6) Eye not being stimulated should be patched if using the Envoy.

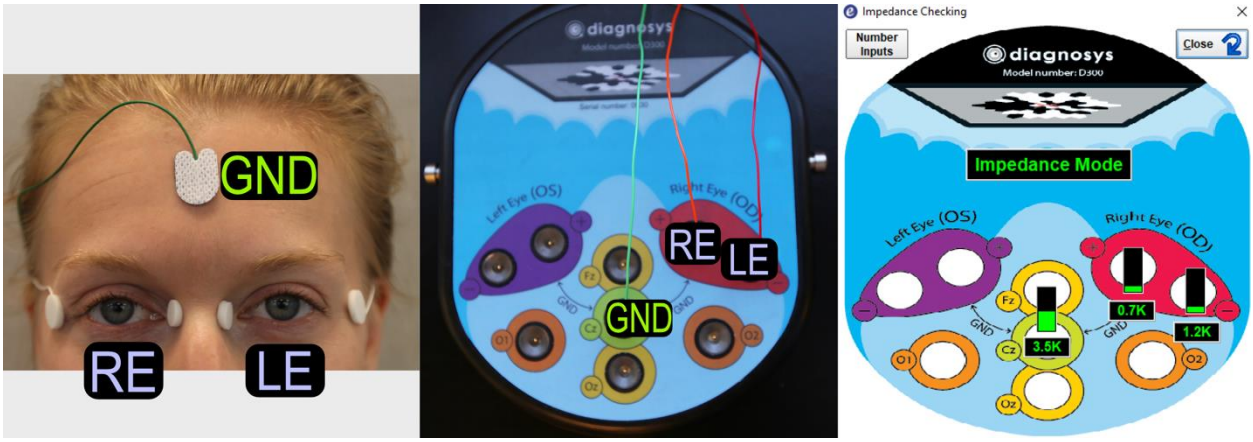


Electrode and Amplifier Setup (LCD monitor)



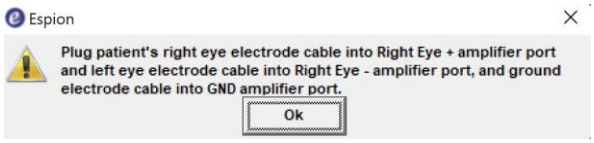
a. Left images: Correct position of electrodes, with two options shown using either a corneal electrode (e.g. DTL) or a skin electrode as the active electrode.
b. Middle image: Connections of each electrode cable into the amplifier.
c. Right image: Electrode position and impedance checking popup to confirm correct electrodes plugged in and good impedance.

Electrode and Amplifier Setup (Envoy monitor)



a. Left image: Correct position of electrodes, using a corneal electrode (e.g. DTL) as the active electrode.
b. Middle image: Connections of each electrode cable into the amplifier. **NOTE** the LE electrode is plugged into RE- port on amplifier to use the fellow eye as a reference in this test. This is done for

monocular tests to take advantage of the low noise position of using fellow eye as a reference. You will be asked to confirm this electrode connection setup in a popup before beginning the test (see below).



c. Right image: Electrode position and impedance checking popup to confirm correct electrodes plugged in and good impedance.

Test procedure

1) Refer to Section V for general instructions to run a test.
2) Use the **Pause** button to pause the test as needed during the test.
3) Use artificial tears as necessary during the test to keep patient eyes relaxed.
4) Explain the test procedure to the patient:

"Pattern rotations will occur during the test. During the test, hold your eyes open while looking at the fixation cross in the center of the stimulator. It is important that you keep your eyes and face relaxed during the test. There will be pauses during the test where you can rest. Try to minimize blinking and eye movements."

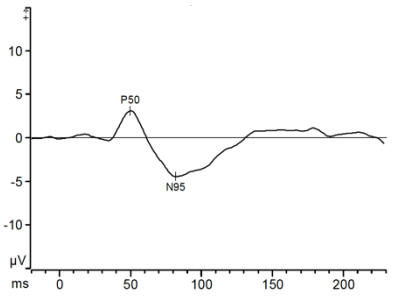
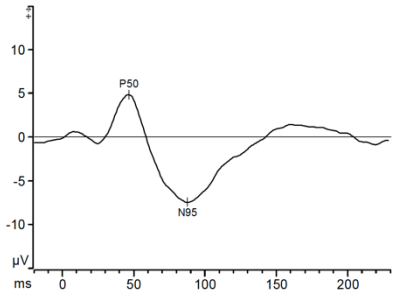
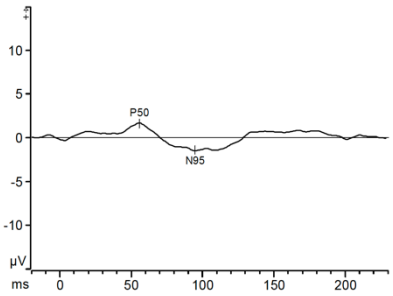
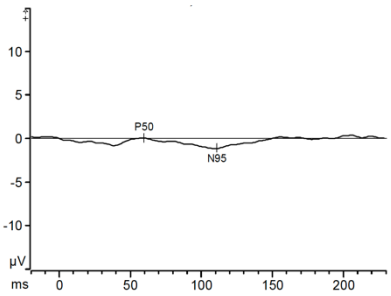
5) Room lights can be on, or dimmed.
6) For binocular tests, test both eyes at the same time. For monocular tests, cover the eye not being tested with an eye patch.
7) Press the **Imped** button and ensure the impedance is green (optimal) or yellow (minimal). Press the **Preview** button and check signal quality.
8) Position the patient centered in front of the stimulator and press **Run** button to begin the test. Run each step of the test in the protocol. Press the **Exit** button once the test is complete.
9) Refer to the test decision guide below to determine if an acceptable quality test has been completed, or if a retest should be considered. Finally, check that the waveform is not inverted. In the case of retest or inverted waveforms refer to the troubleshooting Section VII for steps to improve test results.
10) Refer to Section VIII for instructions on saving, printing and analysis.

Test Quality Check and Markers for Analysis

Once data acquisition is complete, tests must be reviewed by the operator for acceptance prior to being released for analysis. The test quality check can be done immediately after the test is complete in Runtime (before the test is saved) or by double clicking on the test to open and review it after it has been saved. If possible, this should be done before electrodes are removed from the patient, in case a repeat test is recommended. Below are examples of test examples with sufficient quality ('High Quality') to be accepted for analysis as well as tests with insufficient quality ('Low Quality') where troubleshooting and repeating the test is recommended or in the case of inverted electrodes where inverting the test result in software is required. Tests from a variety of patient types are included to show examples for Quality Check purposes, not for medical analysis/interpretation purposes.

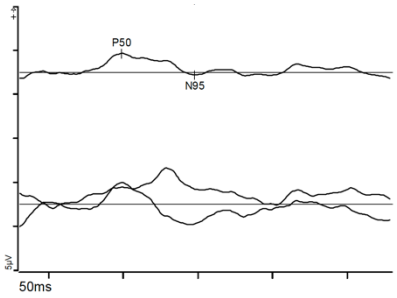
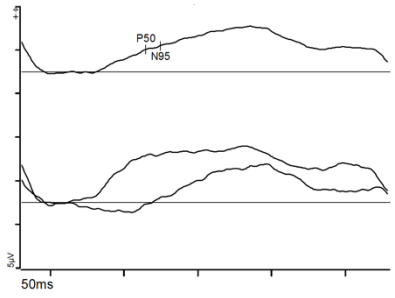
High Quality

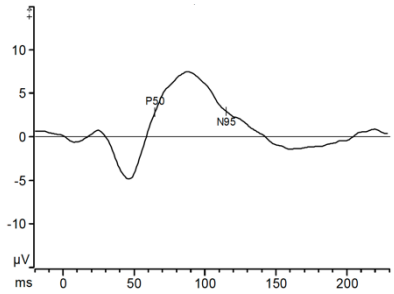
The tests below are High Quality and after review by the operator are ready to be released for analysis. Patient test examples below from the E3 and Profile system.

Test Type and Description	Example Waveforms
PERG test Waveform shape: the PERG waveform has a P50 positive peak at about 50 ms and an N95 negative peak at about 85-100 ms. Quality check: typically, high quality PERG waveforms have a defined P50 peak and the waveform at time = 0 is at about 0 uV. Markers for analysis: P50, N95	 Case: normal patient  Case: normal patient  Case: glaucoma patient  Case: glaucoma patient

Low Quality

The tests below are Low Quality and not ready to be released for analysis. See Troubleshooting Section VII for recommendations on how to resolve excess biological noise, excess electrical noise or inverted waveform issues. Repeat the test once the noise issue has been eliminated to minimized sufficiently to conduct a High Quality test. Inverted waveforms can be corrected in software without a retest. See Section VII. Patient test examples below from the E3 and Profile system.

Test Type and Description	Example Waveforms
Excess biological noise PERG test In reviewing the individual test results (the lower two waveforms) they are dissimilar in shape in comparison to each other (e.g. they did not repeat), both have non-zero pre-time = 0 noize. Finally the average waveform (the top waveform) does not have a well formed P50 nor N95 waves. Additionally, Case 2 markers are not in good locations (e.g. P50 is not in the range of 50 ms). Both tests are likely affected by too much eye movement during the test.	 Case 1: excess biological noise  Case 2: excess biological noise

Inverted test PERG test Notice there is not a positive P50 waveform. In fact, there is a strong negative wave at about 50 ms. Similarly, the waveform at about 95 ms is positive, not negative. There is no known patient condition that will cause these inversions. Finally, the markers are not in good locations (e.g. P50 is not in the range of 50 ms). This is a good waveform (low noise), but the waveform is inverted. See Troubleshooting Section VII on how to invert the waveform in software, to be correct.	

Visual Evoked Potential (VEP) Tests

VEP tests are used to investigate conduction along the visual pathway. They may be used to quantify and follow progression of nerve pathology, localize lesions and measure slow–downs for multiple reasons such as: compression, inflammation, demyelination, or trauma.

There are two types of VEP tests: Pattern VEP and Flash VEP.

Pattern VEP Tests

Purpose

Pattern VEP tests are commonly used for patients who have good central vision and an ability to fixate. This test primarily utilizes the central 15 degrees of visual field. This is a monocular test that presents a black/white checkerboard pattern.

Amongst VEP tests, pattern VEPs have the least degree of inter-subject variability, both in timing and in waveform morphology, making it the most performed VEP test. Since it is primarily driven by the contrast between the black and white checks, patients with very low visual acuity may require alternate methods of testing, such as Flash VEPs. Pattern VEPs require one display monitor: LCD monitor or Envoy monitor.

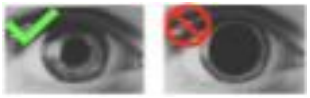
Patient types

According to ISCEV guidelines, pattern VEP tests may be conducted on adults and pediatric children who are able to sit for 5-10 minutes and fixate during the test. This will preclude many younger children from taking the test (see Flash VEP below for another option). Before conducting the test review the procedures below to ensure the patient will be able to comply with all aspects of the testing. For pediatric testing, consult Appendix 3 of this guide before conducting the tests.

Items Needed (sold separately)

1) Eye Drops
    a. Artificial tears, as needed
2) Electrodes
    a. 3 Gold Cup or Sticky Pad Electrodes
3) Alcohol Pads
4) Skin Prep (such as Nu Prep)
5) Conductive Electrode Paste (such as Ten 20)
6) 3 strips of medical tape (if using gold cups)
7) Felt tip pen
8) Eye Patch

Patient Setup

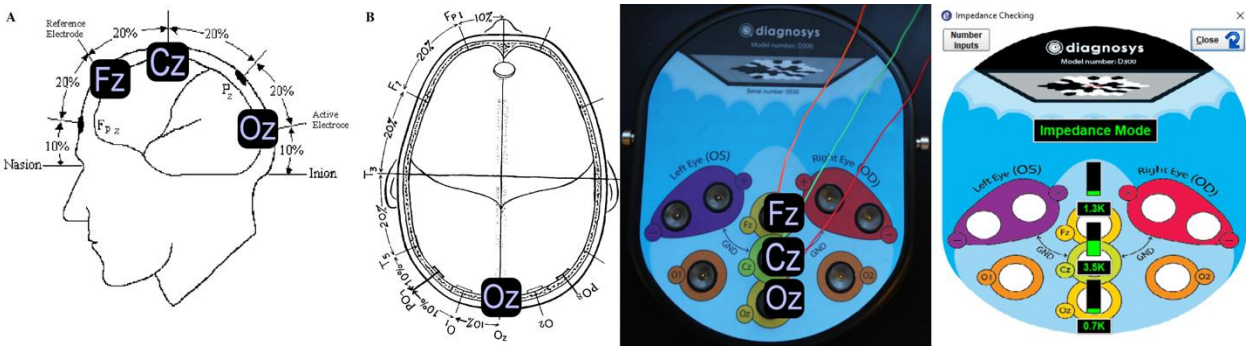


1) Patient's eyes should NOT be dilated.
2) Have patient's vision corrected to 20/30 or better.
3) Locate the areas electrodes will be placed. It may be helpful to mark the areas to be scrubbed with a skin marker or felt tip pen. The active electrode will be placed on the midline at location

Oz according to the International 10-20 system. 3-channel VEPs will place additional electrodes at O1 and O2. There will also be reference electrodes placed at Fz, and a ground electrode placed on top of the head. See diagrams below in the Electrode and Amplifier Setup sections.

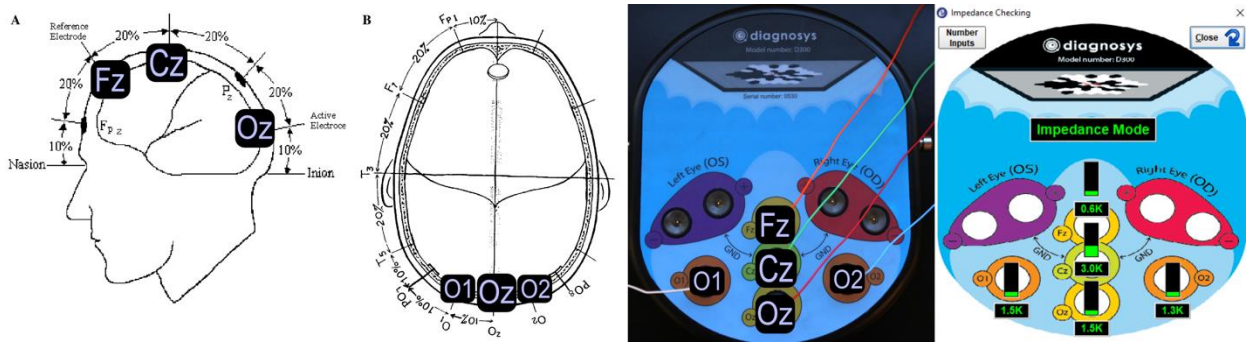
4) Scrub where electrodes will be placed with Skin Prep. Follow up with an alcohol pad scrub. Note: it may be easiest to prepare and place each electrode, one at a time, to ensure that each electrode is placed accurately in the prepared spot.
5) Overfill gold cups with electrode paste and place electrodes in their respective areas. Gold cups require tape to stay in place.

Electrode and Amplifier Setup, 1-channel VEP (LCD or Envoy monitor)



a. Left images: Correct position of 3 electrodes for a 1-channel VEP test. *(Note: images reproduced with permission from 'Odom, J, et al, 2016. ISCEV standard for clinical visual evoked potentials: (2016 update). Documenta Ophthalmologica, 133 (1), pp 1-9.)*
b. Middle image: Connections of each electrode cable into the amplifier.
c. Right image: Electrode position and impedance checking popup to confirm correct electrodes plugged in and good impedance.

Electrode and Amplifier Setup, 3-channel VEP (LCD or Envoy monitor)



a. Left images: Correct position of 5 electrodes for a 3-channel VEP test. *Note: images reproduced with permission from 'Odom, J, et al, 2016. ISCEV standard for clinical visual evoked potentials: (2016 update). Documenta Ophthalmologica, 133 (1), pp 1-9.)*
b. Middle image: Connections of each electrode cable into the amplifier.
c. Right image: Electrode position and impedance checking popup to confirm correct electrodes plugged in and good impedance.

Test procedure

1) Refer to Section V for general instructions to run a test.
2) Use the **Pause** button to pause the test as needed during the test.
3) Use artificial tears as necessary during the test to keep patient eyes relaxed.
4) Explain the test procedure to the patient:

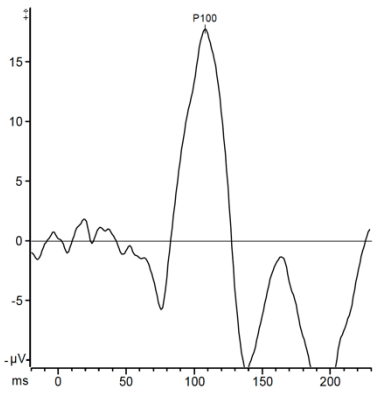
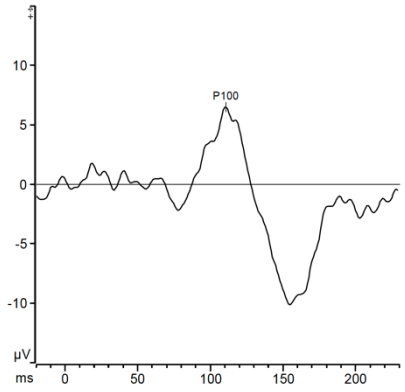
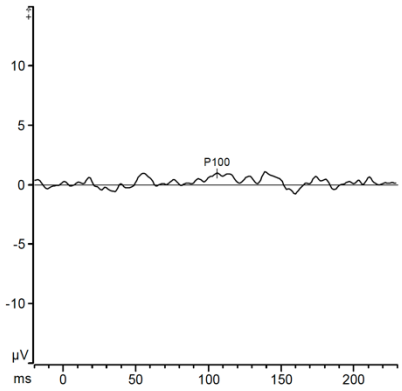
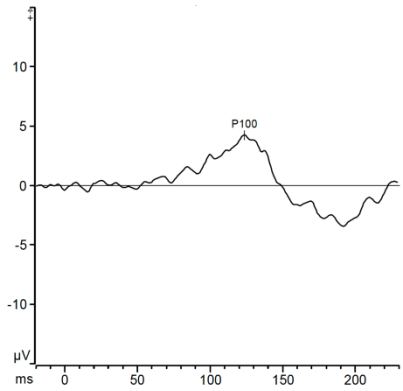
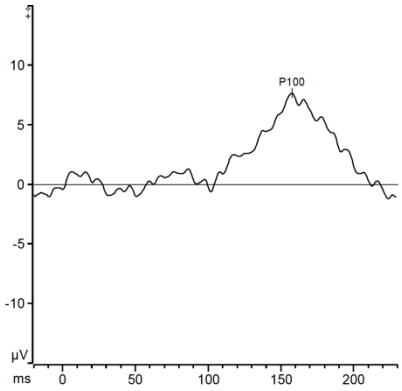
   "Pattern rotations will occur during the test. During the test, hold your eyes open while looking at the fixation cross in the center of the stimulator. It is important that you keep your eyes and face relaxed during the test. There will be pauses during the test where you can rest. Try to minimize blinking and eye movements."

5) Room lights can be on, or dimmed.
6) For binocular tests, test both eyes at the same time. For monocular tests, cover the eye not being tested with an eye patch.
7) Press the **Imped** button and ensure the impedance is green (optimal) or yellow (minimal). Press the **Preview** button and check signal quality.
8) Position the patient centered in front of the stimulator and press **Run** button to begin the test. Run each step of the test in the protocol. Press the **Exit** button once the test is complete.
9) Refer to the test decision guide below to determine if an acceptable quality test has been completed, or if a retest should be considered. Finally, check that the waveform is not inverted. In the case of retest or inverted waveforms refer to the troubleshooting Section VII for steps to improve test results.
10) Refer to Section VIII for instructions on saving, printing and analysis.

Test Quality Check

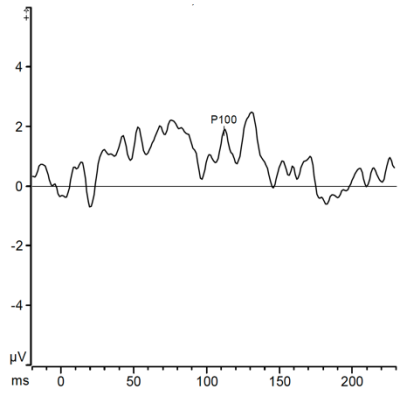
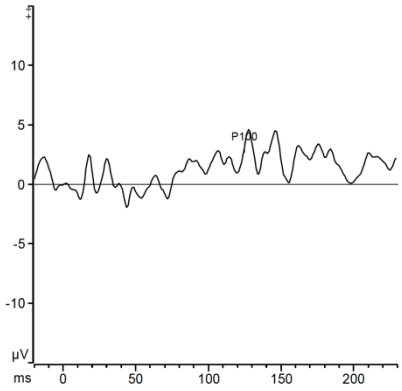
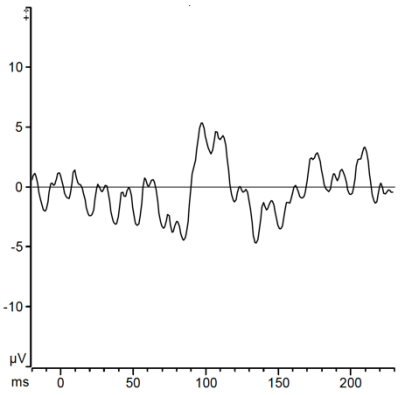
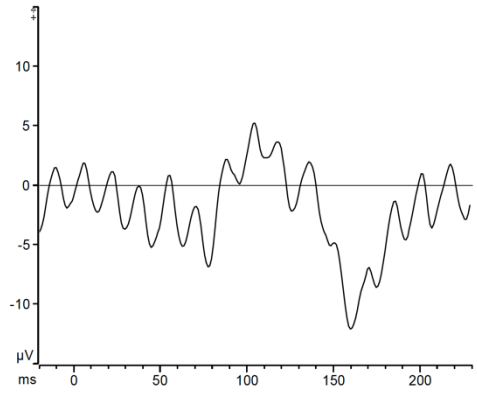
Once data acquisition is complete, tests must be reviewed by the operator for acceptance prior to being released for analysis. The test quality check can be done immediately after the test is complete in Runtime (before the test is saved) or by double clicking on the test to open and review it after it has been saved. If possible, this should be done before electrodes are removed from the patient, in case a repeat test is recommended. Below are examples of test examples with sufficient quality ('High Quality') to be accepted for analysis as well as tests with insufficient quality ('Low Quality') where troubleshooting and repeating the test is recommended or in the case of inverted electrodes where inverting the test result in software is required. Tests from a variety of patient types are included to show examples for Quality Check purposes, not for medical analysis/interpretation purposes.

High Quality
The tests below are High Quality and after review by the operator are ready to be released for analysis. Patient test examples below from the E3 and Profile system.

Test Type and Description	Example Waveforms
pVEP test Waveform shape: the pVEP waveform has a prominent P100 positive peak. As shown in the cases, the peak amplitude can be in the range of about 20 uV down to non-existent/flat. Quality check: typically, a good quality pVEP test has one prominent positive peak (P100). If no peak exists, and waveform in full has peaks <2 uV then it is likely a quality test with no P100 response. Markers for analysis: P100	 Case 1: normal patient  Case 2: lower P100 (optic neuritis patient)  Case 3: flat pVEP (optic neuropathy patient)
pVEP test Delayed P100 response. Waveform shape: the pVEP waveform has a prominent positive peak. These cases show a P100 peak that is delayed. Quality check: typically, a good quality pVEP test has one prominent positive peak (P100). If no peak exists, and waveform in full has peaks <2 uV then it is likely a quality test with no P100 response. Markers for analysis: P100	 Case 1: Delayed P100 peak (MS patient).  Case 2: Delayed P100 peak (optic neuritis patient)

Low Quality

The tests below are Low Quality and not ready to be released for analysis. See Troubleshooting Section VII for recommendations on how to resolve excess biological noise, excess electrical noise or inverted waveform issues. Repeat the test once the noise issue has been eliminated to minimized sufficiently to conduct a High Quality test. Inverted waveforms can be corrected in software without a retest. See Section VII. Patient test examples below from the E3 and Profile system.

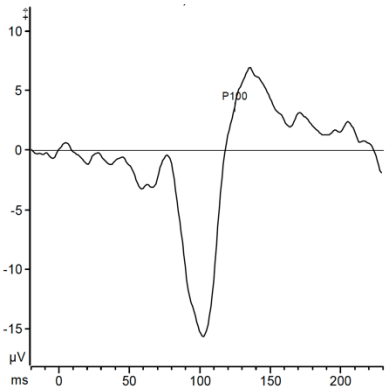
Test Type and Description	Example Waveforms
pVEP test Excess biological noise Waveform shape: Case 1 and 2: there is no prominent P100 peak; all 'peaks' in the test result are of similar height and greater than 2 uV, which is indicate of excess biological noise. Case 3: while there is a prominent P100 peak, it has sub-peaks to it (which is not typical) and those peaks look similar to other smaller peaks in the waveform. This is indicative of excess biological noise.	 Case 1  Case 2  Case 3
pVEP test Excess electrical line noise Waveform shape: while there is a prominent P100 peak, it has sub-peaks to it (which is not typical) and those peaks look similar to other smaller peaks in the waveform. Further the smaller peaks are of similar amplitude and equally spaced at about 17 ms. This is indicative of excess electrical line noise.	 Case: waveform with excess electrical line noise

Inverted test

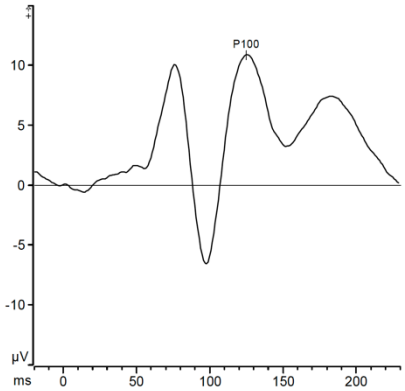
pVEP test

Notice that there is a well defined peak at about 100 ms. However it is a negative peak, rather than positive. There is no known patient condition that will cause this inversion.

This is a good waveform (low noise), but the waveform is inverted. See Troubleshooting Section VII on how to invert the waveform in software, to be correct.



Case 1: inverted waveform



Case 2: inverted waveform

Flash VEP Tests

Purpose

The flash VEP is primarily useful when poor optical quality, poor cooperation or poor visual acuity makes the use of pattern VEP testing inappropriate. The stimulus is a series of flashes of white light whose responses are averaged to form a final waveform. Flash VEPs require one full-field stimulator: ColorDome, ColorBurst, or ColorFlash.

Patient types

According to ISCEV guidelines, flash VEP tests may be conducted on adults and pediatric children who are able to sit for at least 1-2 minutes and look at the stimulus. Fixation is not required during the test. Before conducting the test review the procedures below to ensure the patient will be able to comply with all aspects of the testing. For pediatric and infant testing, consult Appendix 3 of this guide before conducting the tests.

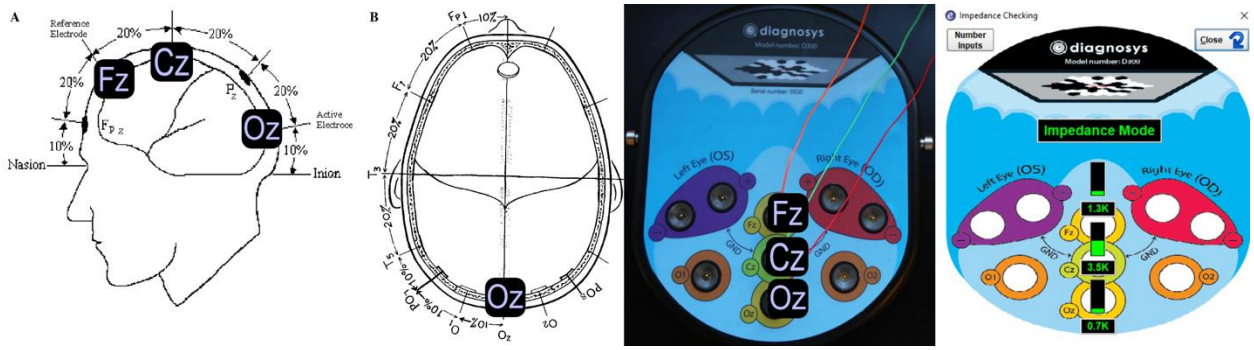
Items Needed (sold separately)

1) Eye Drops
    a. Artificial tears, as needed
2) Electrodes
    a. 3 Gold Cup or Sticky Pad Electrodes
3) Alcohol Pads
4) Skin Prep (such as Nu Prep)
5) Conductive Electrode Paste (such as Ten 20)
6) 3 strips of medical tape (if using gold cups)
7) Felt tip pen
8) Eye Patch

Patient Setup

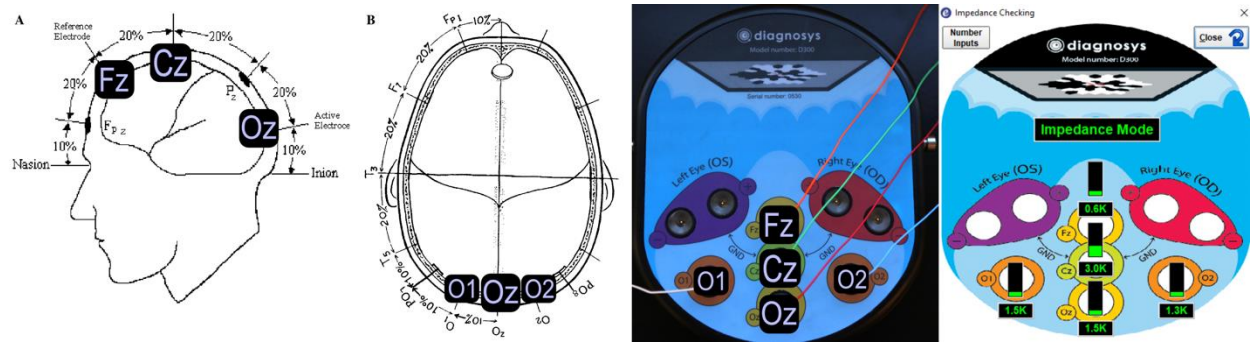
1) Dilation is not required nor prohibited; if the patient is already dilated, a flash VEP may be performed, but it is not required for the test.
2) Locate the areas electrodes will be placed. It may be helpful to mark the areas to be scrubbed with a skin marker or felt tip pen. The active electrode will be placed on the midline at location Oz according to the International 10-20 system (see diagram, right). 3-channel VEPs will place additional electrodes at O1 and O2. There will also be reference electrodes placed at Fz, and a ground electrode placed elsewhere on the forehead. See diagrams below in the Electrode and Amplifier setup section.
3) Scrub where electrodes will be placed with Skin Prep. Follow up with an alcohol pad scrub. Note: it may be easiest to prepare and place each electrode, one at a time, to ensure that each electrode is placed accurately in the prepared spot.
4) Overfill gold cups with electrode paste and place electrodes in their respective areas. Gold cups require tape to stay in place.

Electrode and Amplifier Setup, 1-channel VEP (ColorDome, ColorBurst, or ColorFlash)



a. Left images: Correct position of 3 electrodes for a 1-channel VEP test. *(Note: images reproduced with permission from 'Odom, J, et al, 2016. ISCEV standard for clinical visual evoked potentials: (2016 update). Documenta Ophthalmologica, 133 (1), pp 1-9.)*
b. Middle image: Connections of each electrode cable into the amplifier.
c. Right image: Electrode position and impedance checking popup to confirm correct electrodes plugged in and good impedance.

Electrode and Amplifier Setup, 3-channel VEP (ColorDome, ColorBurst, or ColorFlash)



a. Left images: Correct position of 5 electrodes for a 3-channel VEP test. *Note: images reproduced with permission from 'Odom, J, et al, 2016. ISCEV standard for clinical visual evoked potentials: (2016 update). Documenta Ophthalmologica, 133 (1), pp 1-9.)*
b. Middle image: Connections of each electrode cable into the amplifier.
c. Right image: Electrode position and impedance checking popup to confirm correct electrodes plugged in and good impedance.

Test procedure

1) Refer to Section V for general instructions to run a test.
2) Use the **Pause** button to pause the test as needed during the test.
3) Use artificial tears as necessary during the test to keep patient eyes relaxed.
4) Explain the test procedure to the patient:

   'We will flash a series of lights during the test. During the flashes, hold your eyes open while looking at the fixation point in the center of the stimulator. It is important to keep your eyes and

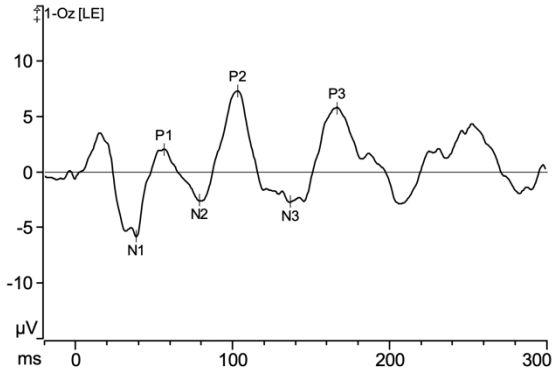
face relaxed. There will be pauses during the test where you can rest. Try to minimize blinking and eye movements.'

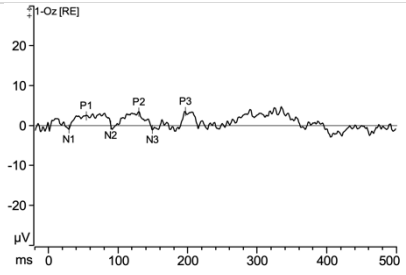
5) Room lights can be on, or dimmed.
6) For binocular tests, test both eyes at the same time. For monocular tests, cover the eye not being tested with an eye patch.
7) Press the **Imped** button and ensure the impedance is green (optimal) or yellow (minimal). Press the **Preview** button and check signal quality.
8) Position the patient centered in front of the stimulator and press **Run** button to begin the test. Run each step of the test in the protocol. Press the **Exit** button once the test is complete.
9) Refer to the test decision guide below to determine if an acceptable quality test has been completed, or if a retest should be considered. Finally, check that the waveform is not inverted. In the case of retest or inverted waveforms refer to the troubleshooting Section VII for steps to improve test results.
10) Refer to Section VIII for instructions on saving, printing and analysis.

Test Quality Check and Markers for Analysis

Once data acquisition is complete, tests must be reviewed by the operator for acceptance prior to being released for analysis. The test quality check can be done immediately after the test is complete in Runtime (before the test is saved) or by double clicking on the test to open and review it after it has been saved. If possible, this should be done before electrodes are removed from the patient, in case a repeat test is recommended. Below are examples of test examples with sufficient quality ('High Quality') to be accepted for analysis as well as tests with insufficient quality ('Low Quality') where troubleshooting and repeating the test is recommended or in the case of inverted electrodes where inverting the test result in software is required. Tests from a variety of patient types are included to show examples for Quality Check purposes, not for medical analysis/interpretation purposes.

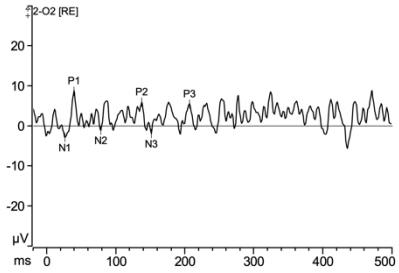
High Quality
The tests below are High Quality and after review by the operator are ready to be released for analysis. Patient test examples below from the E3 and Profile system.

Test Type and Description	Example Waveforms
Flash VEP test Waveform shape: the Flash VEP waveform typically has a prominent P2 positive peak around 100 ms and oftentimes also a P1 and P3 peak. As shown in the cases, the peak amplitude can be in the range of about 15 uV down to non-existent/flat. Quality check: typically, a good quality flash VEP test has a prominent positive peak (P2). If no peak exists, and waveform in full has peaks <2 uV then it is likely a quality test with no P2 response. The waveform should start and end near 0 uV amplitude. Markers for analysis: N1/P1, N2/P2, N3/P3	 Case 1: larger normal waveforms

	 Case 2: smaller waveforms (optic neuritis patient)

Low Quality

The tests below are Low Quality and not ready to be released for analysis. See Troubleshooting Section VII for recommendations on how to resolve excess biological noise, excess electrical noise or inverted waveform issues. Repeat the test once the noise issue has been eliminated to minimized sufficiently to conduct a High Quality test. Inverted waveforms can be corrected in software without a retest. See Section VII. Patient test examples below from the E3 and Profile system.

Test Type and Description	Example Waveforms
Flash VEP test Excess biological noise Waveform shape: while the P1, P2, P3 peaks are marked there is no prominent peak; all 'peaks' in the test result are of similar height and greater than 2 uV, which is indicate of excess biological noise.	

Simultaneous PERG and pVEP Tests

Purpose

Because the stimulus requirements for a PERG and pVEP are the same, and the E3 and Profile amplifier has 5 channels, it is possible to simultaneously record a PERG and pVEP. Each test purpose is the same as when they are done individually. All PERG and pVEP electrodes are placed on the patient at the same time, for one combined recording session.

Combined PERG and pVEP tests require one display monitor: Envoy monitor.

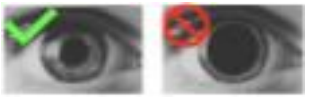
Patient types

According to ISCEV guidelines, PERG and pattern VEP tests may be conducted on adults and pediatric children who are able to sit for 5-10 minutes and fixate during the test. This will preclude many younger children from taking the test. Before conducting the test review the procedures below to ensure the patient will be able to comply with all aspects of the testing. For pediatric testing, consult Appendix 3 of this guide before conducting the tests.

Items Needed (sold separately)

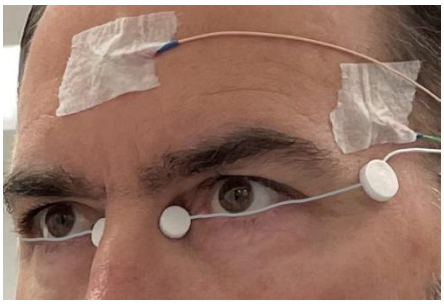
1) Eye Drops
    a. Corneal anesthetic drops (such as proparacaine or tetracaine): used to make the patient more comfortable with DTL electrodes
    b. Artificial tears: used when patient has dry eyes/to improve impedance
2) Electrodes
    a. Two DTL Plus electrodes
    b. One set of extender cables
    c. 3 Gold Cup or Sticky Pad Electrodes
3) Alcohol Pads
4) Skin Prep (such as Nu Prep)
5) Conductive Electrode Paste (such as Ten 20)
6) 3 strips of medical tape (if using gold cups)
7) Felt tip pen
8) Eye Patch

Patient Setup

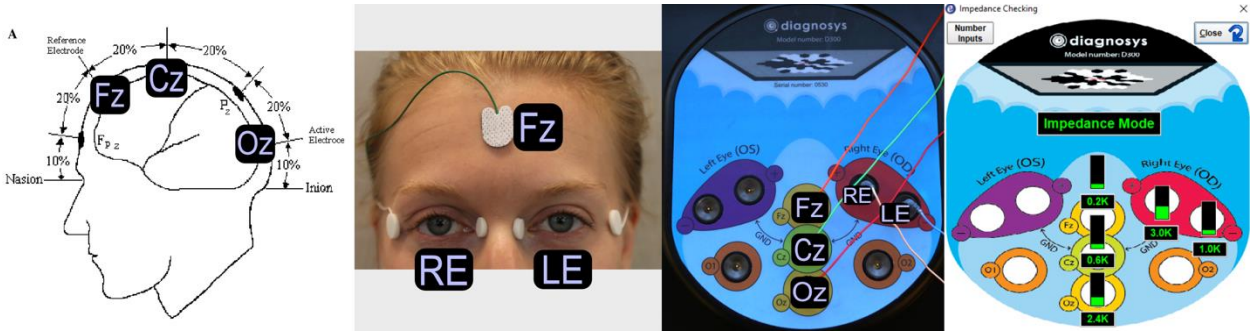


1) Patient's eyes should NOT be dilated.
2) Have patient's vision corrected to 20/30 or better.
3) Locate the areas electrodes will be placed. It may be helpful to mark the areas to be scrubbed with a skin marker or felt tip pen. The active electrode will be placed on the midline at location Oz according to the International 10-20 system. 3-channel VEPs will place additional electrodes at O1 and O2. There will also be reference electrodes placed at Fz, and a ground electrode placed on top of the head. See diagrams below in the Electrode and Amplifier Setup sections.
4) Scrub where electrodes will be placed with Skin Prep. Follow up with an alcohol pad scrub. Note: it may be easiest to prepare and place each electrode, one at a time, to ensure that each electrode is placed accurately in the prepared spot.

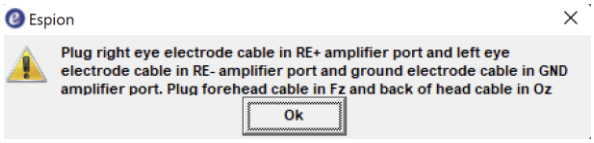
5) Overfill gold cups with electrode paste and place electrodes in their respective areas. Gold cups require tape to stay in place.
6) Place a drop of corneal anesthetic in each eye, then place the DTL electrodes. The DTL small sticky pad goes next to the nasal canthus; the larger pad next to the temporal canthus. The DTL fiber should drape across the lower lid & should NOT fall into the conjunctival sac.



Electrode and Amplifier Setup, PERG and 1-channel VEP (Envoy monitor)

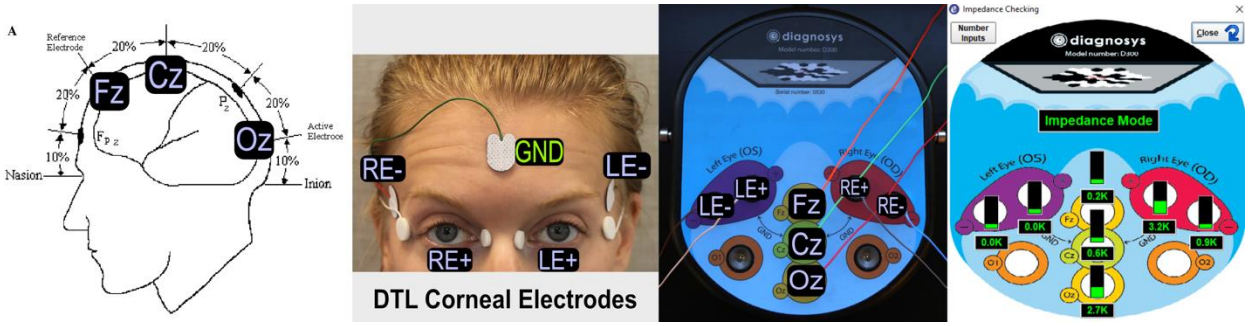


a. Left images: Correct position of electrodes for a 1-channel VEP and PERG test *(Note: images reproduced with permission from 'Odom, J, et al, 2016. ISCEV standard for clinical visual evoked potentials: (2016 update). Documenta Ophthalmologica, 133 (1), pp 1-9.)*.
b. Middle image: Connections of each electrode cable into the amplifier. **NOTE** the LE electrode is plugged into RE- port on amplifier to use the fellow eye as a reference in this test. This is done for monocular tests to take advantage of the low noise position of using fellow eye as a reference. You will be asked to confirm this electrode connection setup in a popup before beginning the test (see below).



c. Right image: Electrode position and impedance checking popup to confirm correct electrodes plugged in and good impedance.

Electrode and Amplifier Setup, PERG and 1-channel VEP (LCD monitor)



a. Left images: Correct position of electrodes for a 1-channel VEP and PERG test (*Note: images reproduced with permission from 'Odom, J, et al, 2016. ISCEV standard for clinical visual evoked potentials: (2016 update). Documenta Ophthalmologica, 133 (1), pp 1-9.)*.
b. Middle image: Connections of each electrode cable into the amplifier.
c. Right image: Electrode position and impedance checking popup to confirm correct electrodes plugged in and good impedance.

Test procedure

1) Refer to Section V for general instructions to run a test.
2) Use the **Pause** button to pause the test as needed during the test.
3) Use artificial tears as necessary during the test to keep patient eyes relaxed.
4) Explain the test procedure to the patient:

   "Pattern rotations will occur during the test. During the test, hold your eyes open while looking at the fixation cross in the center of the stimulator. It is important that you keep your eyes and face relaxed during the test. There will be pauses during the test where you can rest. Try to minimize blinking and eye movements."

5) Room lights can be on, or dimmed.
6) For binocular tests, test both eyes at the same time. For monocular tests, cover the eye not being tested with an eye patch.
7) Press the **Imped** button and ensure the impedance is green (optimal) or yellow (minimal). Press the **Preview** button and check signal quality.
8) Position the patient centered in front of the stimulator and press **Run** button to begin the test. Run each step of the test in the protocol. Press the **Exit** button once the test is complete.
9) Refer to the test decision guide below to determine if an acceptable quality test has been completed, or if a retest should be considered. Finally, check that the waveform is not inverted. In the case of retest or inverted waveforms refer to the troubleshooting Section VII for steps to improve test results.
10) Refer to Section VIII for instructions on saving, printing and analysis.

Test Quality Check

Refer to the individual PERG and pVEP High Quality vs Low Quality Test Results sections above.

EOG Tests

Purpose

An electrooculogram (EOG) measures the resting potential of the retinal pigmented epithelium (RPE) in response to dark and light conditions. The EOG measures the resting potential by placing electrodes on the nasal and temporal canthi to measure the voltage swing as the patient moves their eyes left to right following a single LED stimulus. The EOG can only be performed on a ColorDome.

Patient types

According to ISCEV guidelines, EOG tests may be conducted on adults and pediatric children who are able to sit for 30 minutes and fixate during the test. This will preclude many younger children from taking the test.

Further, quoting from the ISCEV EOG standard: 'Patients will have difficulty performing saccadic eye movements if they cannot fixate reliably because of poor central vision, diplopia or ocular motility problems (including nystagmus). Patients with diplopia may be advised to look between the pair of images, or one eye can be patched if the suspected retinal disorder is binocular. Patients who are very young or those with a physical or learning disability may not be able to perform the EOG. In young children with suspected Best disease, it may be useful to test their parents, since a carrier of Best disease will have an abnormal light-rise, irrespective of whether the fundus is normal.'

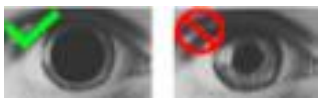
Before conducting the test review the procedures below to ensure the patient will be able to comply with all aspects of the testing. For pediatric testing, consult Appendix 3 of this guide before conducting the tests.

Items Needed (sold separately)

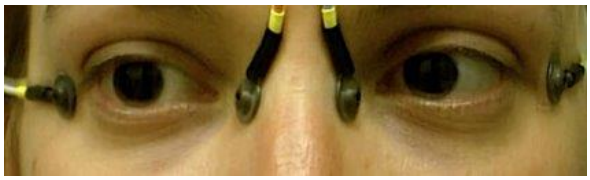
1) Eye Drops
    a. Dilating drops (such as tropicamide or phenylephrine): used to allow the maximum amount of light in the eye
    b. Artificial tears: optional for patient comfort
2) Electrodes
    a. Five gold cup or disposable skin electrodes
3) Alcohol Pads
4) Skin Prep
    a. Either skin scrub pads or exfoliating scrub (such as Nu Prep)
5) Conductive electrode paste (if using gold cups)
6) Five strips of medical tape (if using gold cups)

Patient Setup

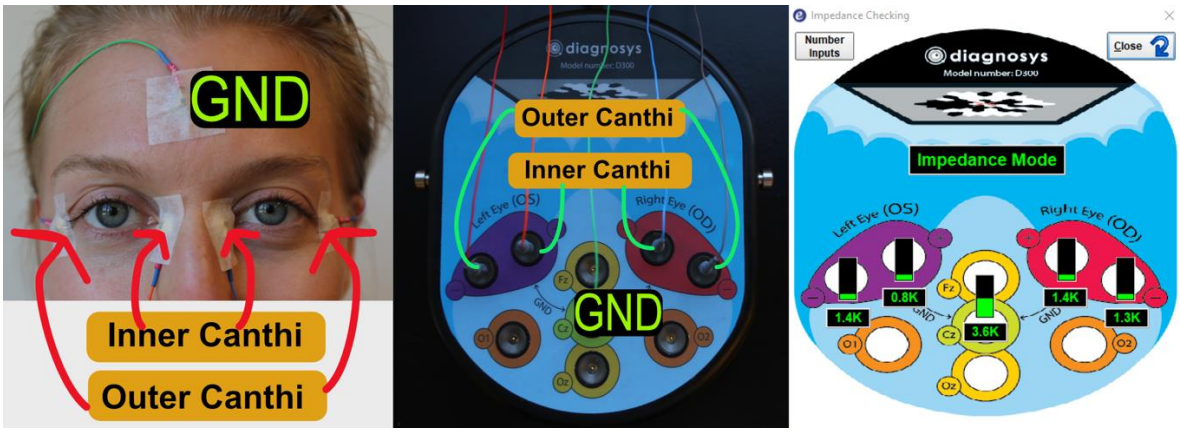
1) Dilate the patient's eyes using appropriate eye drops.
2) Scrub forehead, temples, and nasal canthi where electrodes will be placed with Skin Prep. Follow up with an alcohol pad scrub.



3) Place skin electrodes on forehead, temples, and nasal canthi. If using gold cups, over fill with conductive paste. Position the skin electrodes nest to the inner and outer canthi of each eye. Gold cups require tape to stay in place.



Electrode and Amplifier Setup



a. Left image: Correct position of electrodes, on either side of each eye and on forehead.
b. Middle image: Connections of each electrode cable into the amplifier.
c. Right image: Electrode position and impedance checking popup to confirm correct electrodes plugged in and good impedance.

Test procedure

1) Refer to Section V for general instructions to run a test.
2) Use the **Pause** button to pause the test as needed during the test.
3) Use artificial tears as necessary during the test to keep patient eyes relaxed.
4) Explain the test procedure to the patient:

   "You will see a single red light inside the ColorDome. When you hear a countdown chimer (a series of four beeps), the red light will begin to move from side to side. Follow this light with your gaze as smoothly as possible. Do not anticipate the light movement; only move your eyes to follow the red light after it has changed from one side to the other."

5) Test both eyes at the same time.
6) Press the **Imped** button and ensure the impedance is green (optimal) or yellow (minimal). Press the **Preview** button and check signal quality.
7) Position the patient centered in front of the stimulator.
8) Phase 1 of the test is a 2-minute practice session. Press **Run** button to begin
9) Phase 2 of the test: performed in the dark. Turn off the room lists and press the **Run** button to begin. It will run for 15 minutes.
10) Phase 3 of the test: performed in the light. Turn on the room lists and press the **Run** button to begin. It will run for 15 minutes.
11) Press the **Exit** button once the test is complete.

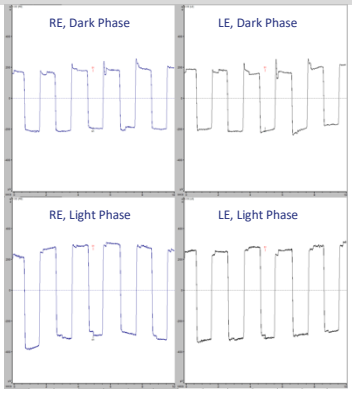
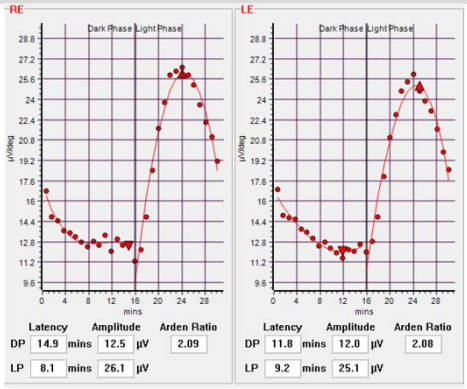
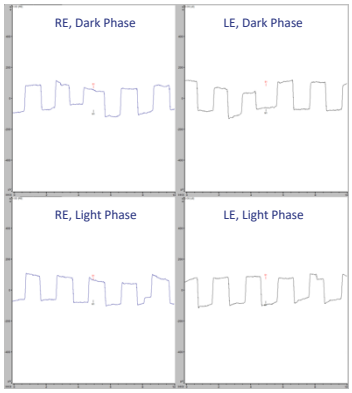
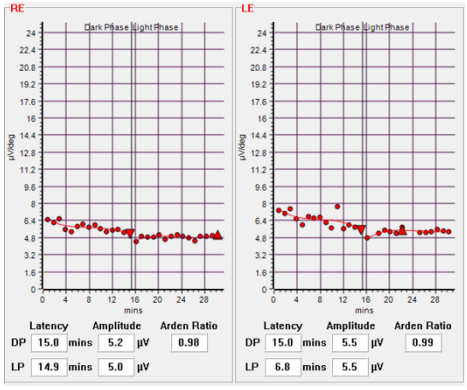
12) Refer to the test decision guide below to determine if an acceptable quality test has been completed, or if a retest should be considered. In the case of retest refer to the troubleshooting Section VII for steps to improve test results.
13) Refer to Section V for directions to save and print the test.

Test Quality Check

Once data acquisition is complete, tests must be reviewed by the operator for acceptance prior to being released for analysis. The test quality check can be done immediately after the test is complete in Runtime (before the test is saved) or by double clicking on the test to open and review it after it has been saved. If possible, this should be done before electrodes are removed from the patient, in case a repeat test is recommended. Below are examples of test examples with sufficient quality ('High Quality') to be accepted for analysis as well as tests with insufficient quality ('Low Quality') where troubleshooting and repeating the test is recommended or in the case of inverted electrodes where inverting the test result in software is required. Tests from a variety of patient types are included to show examples for Quality Check purposes, not for medical analysis/interpretation purposes.

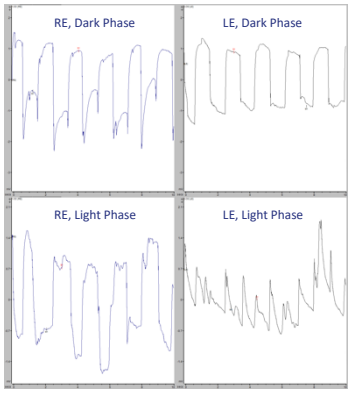
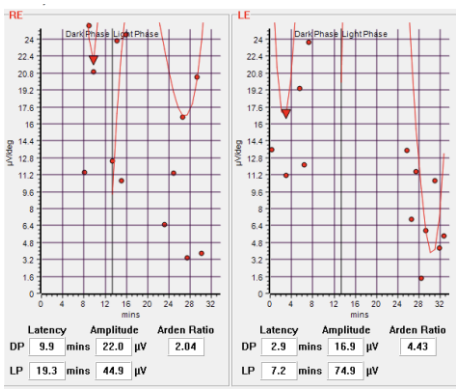
High Quality

The tests below are High Quality and after review by the operator are ready to be released for analysis. Patient test examples below from the E3 and Profile system.

Test Type and Description	Example Waveforms
EOG test Waveform shape (left graph): in good quality tests the EOG waveform is essentially a square wave shape with similar amplitudes from left-to-right. Amplitudes of the square wave can vary from about 100 to 1,000 uV. EOG plot (right graph): The 'dark phase' of the plot is typically either a gently sloping downward shape or flat. The 'light phase' of the plot is typically parabolic with a peak of various heights, down to flat. Quality check: The waveforms are generally square; the EOG plot line matches most of the data (red circles).	 Typical waveform (normal patient)  Typical resulting EOG plot (normal patient)  Typical waveform (Best disease patient)  Typical resulting EOG plot (Best disease patient)

Low Quality

The tests below are Low Quality and not ready to be released for analysis. See Troubleshooting Section VII for recommendations on how to resolve excess biological noise, excess electrical noise or inverted waveform issues. Repeat the test once the noise issue has been eliminated to minimized sufficiently to conduct a High Quality test. Inverted waveforms can be corrected in software without a retest. See Section VII. Patient test examples below from the E3 and Profile system.

Test Type and Description	Example Waveforms
Low quality EOG test Waveform shape (left graph): the waveforms are not square and they are not at the same height from left to right. EOG plot (right graph): The 'dark phase' of the plot is neither a gently sloping downward shape or flat. The 'light phase' of the plot is neither parabolic with a peak of various heights, or flat. The EOG plot line does not match most of the data (red circles). This is indicative of a patient who was not consistently able to follow the alternating fixation points. Ensure they understand the test instructions, try a practice test again to evaluate their performance and consider re-running a higher quality test.	 Example waveform  Example resulting EOG plot

VII. Troubleshooting

Biological Noise

In practice, biological noise is the most common artifact which can affect recordings. It is caused by the patient themselves (eye or body movements). As shown in the patient examples of this manual, normal recording should be relatively calm and quiet with distinct waveform morphologies and marked peaks (regardless of amplitude). If the signal becomes sporadic and random, biological noise is interfering. This type of noise is caused by various types of patient movement(s).

Higher frequency types of biological noise.

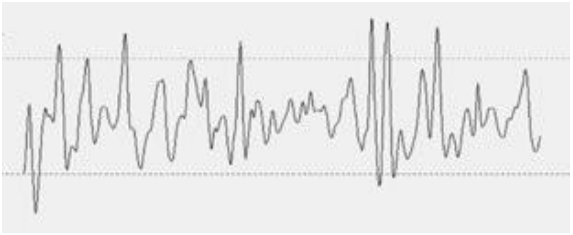
Causes:

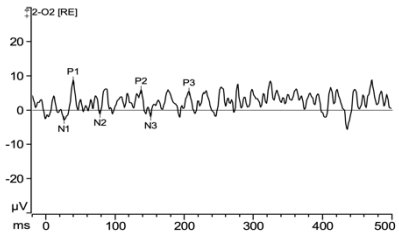
Excessive blinking, jaw movements such as talking and smiling, and other body movements can cause this type of noise. Irritated and dry eyes can cause increased blinking. A poor electrical connection between a corneal electrode and the eye all can cause higher frequency biological noise. Worn out electrode cables may also cause this type of noise. See examples below.

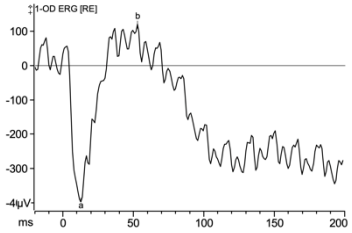
Solutions:

1. Apply additional artificial tears to the patient's eye(s).
2. If impedances are moderate-to-high, take electrodes off and rescrub respective areas, being sure to replace electrodes on top of the prepared area.
3. Ensure the patient has the ability to relax their eyes and understands they should minimize eye movements during the test.
4. Ensure patient is comfortable (room temperature/noise level, chair, stimulator height) and understands they should not talk and should minimize mouth/jaw movements during the test.
5. Discuss with the patient any other issues that may be preventing them from completely relaxing their eyes, and help resolve that issue if possible.
6. Inspect the electrode cables. If any appear worn/broken, then try a different cable and check **Preview** and **Imped**. If that solves the problem, discard the worn cable which should not be used.

Examples of higher frequency biological noise (shown above in this manual):







Lower frequency types of biological noise.

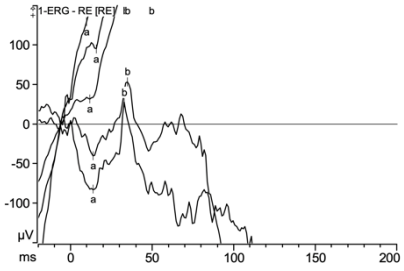
Causes:

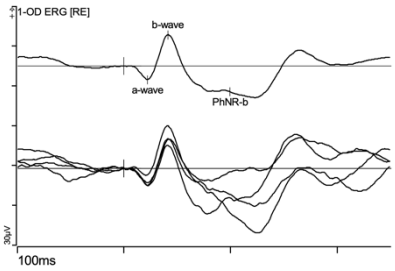
Eye or eyelid movement, both slow or fast, are the primary causes of lower frequency biological noise. See examples below.

Solutions:

1. Most tests utilize a fixation point or cross. Discuss with the patient the importance of relaxing their eyes and body while focusing on the fixation target. Some patients will have difficulty seeing the target, and in those cases coach the patient to relax and look straight ahead at the stimulator during the test.
2. Apply artificial tears to the patient's eye(s).
3. Ensure the patient has the ability to relax their eyes and understands they should minimize eye movements during the test.
4. Ensure patient is comfortable (room temperature/noise level, chair, stimulator height) and understands they should not talk and should minimize mouth/jaw movements during the test.
5. Discuss with the patient any other issues that may be preventing them from completely relaxing their eyes, and help resolve that issue if possible.

Examples of higher frequency biological noise (shown above in this manual):





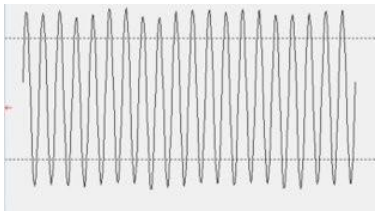
Note: the example on the left should not generally occur to the magnitude of artifact shown, due to the blink rejection function in the system (which sets a max and min limit to a sweep (e.g. 300 uV) to eliminate sweeps that are clearly blink artifacts, per ISCEV recommendations), but is shown to clearly illustrate what can happen when a patient's eyes are moving too much during the test.

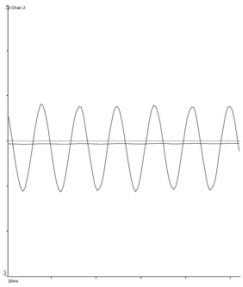
Contact Diagnosys support (support@diagnosysllc.com) for additional help, if necessary.

Electrical Noise

Line noise artifacts

By far the most common type of electrical noise artifact is line noise, which is identified by its sinusoidal, regular shape as shown in the images below (with no ERG, VEP signal present) and as shown in the ERG, VEP test examples above.



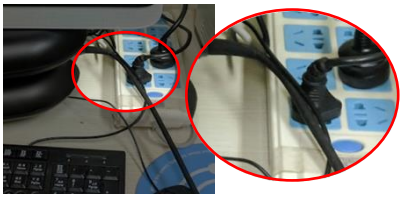


Electrical line noise in a signal is displayed as 50 or 60 Hz sinusoidal waves, whose peak-to-peak timing is 20 ms or 16.7 ms, respectively.

Causes:

If line noise is present, there is a problem with cable management and/or patient preparation. See above example and examples of tests affected by electrical line noise throughout this manual.

Examples of issues to avoid:



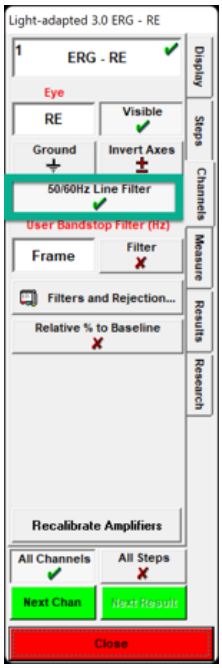
Solutions:

The first step should be to check and make sure there are no power cables nearby. Power cables should be kept as far from the patient, electrode wires, and amplifier cable as possible. Ensure that the E3 and Profile system is plugged directly into a grounded outlet and not into a power strip. If necessary, turn off any other electrical equipment in the room to determine if they interfere with the electrophysiology signal.

If electrical noise is still present, check the electrode impedance. If impedances are moderate-to-high, follow the guidance for improving impedance in the Biological Noise section above. As shown in the test sections of this manual the goal is to have all electrode impedances be in the green region, and no worse than yellow.

The Espion software is equipped with a 50/60 Hz line noise filter that can be enabled under the *Channels* popout in the run time menu. This filter can only be applied before a test is run and will not work post acquisition. Usage of this filter should only be used as a last resort. Proper cable management and patient preparation should be enough to prevent electrical noise.

Refer to the **EMC Guidance and Manufacturer's Declaration** (Doc #16566) for further technical information on location of electrical equipment near the E³ and Profile.

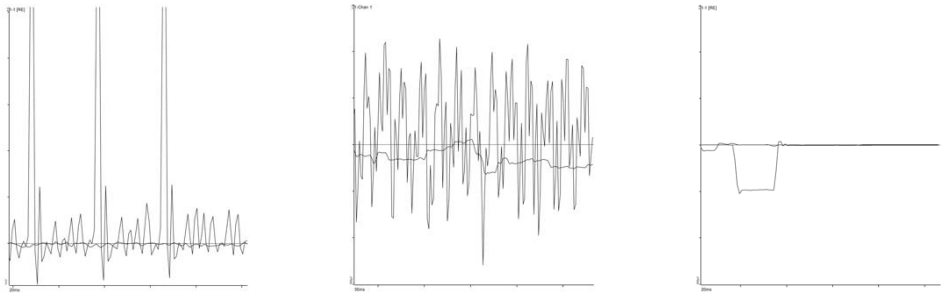


Other types of electrical noise artifacts (less common)

As described in Doc #16566, the E³ and Profile system has been tested to 60601-1-2 EMC tests. During those tests, the E³ and Profile system was exposed to a wide variety of other types of electrical noise. The E³ and Profile system is a system designed to measure very small retinal and cortical electrical signals (as small as a micro-volt) amidst an environment of other electrical equipment generating signals that are 1,000 or even a million times larger. The E³ and Profile system, including its stimulators and amplifiers, was operated through all of the EMC tests (over 200 hours of recordings) and shown to be robust. There are, however, some electrical noise events which in practice are quite uncommon, but if they do occur have the potential to create an artifact in the recording. Many of the other electrical sources which are near an electrophysiology system operate at relatively high frequencies and a subset of those can generate artifacts which are measured in the electrophysiology pass band (typically about 0.1 to 300 Hz, because most of the biological retinal and cortical signal of interest is in the 10 to 100 Hz range). These were characterized during the EMC tests, and below are examples of artifact recordings on E³ and Profile during the EMC test, source, and troubleshooting suggestions. Each of these artifacts are significantly different in shape than any known electrophysiology signal (normal or disease patient) and with operator care, can be identified in the recordings. See the 4 categories below.

1. 'Conducted RF' artifact

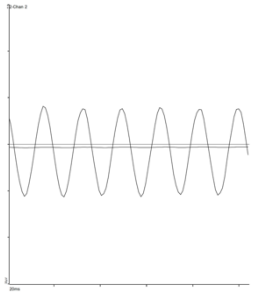
Example waveforms of the artifacts:



Possible cause and troubleshooting: The most likely cause of this artifact is other electrical equipment (or its cables) are in contact with the E3 and Profile system's line cord, amplifier cord or the electrode cables. Check that each of these cables are clear of other devices and their cables. Note the timing of the third example (10s of milliseconds) is much different than any EOG recording (seconds). Consult **EMC Guidance and Manufacturer's Declaration** (Doc #16566) for further guidance on minimum distances.

2. 'Magnetic interference' artifact

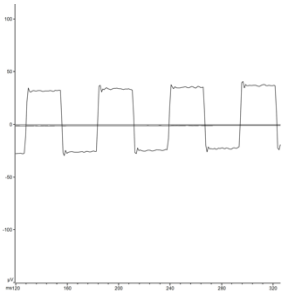
Example waveform of the artifact:



Possible cause and troubleshooting: the most likely cause is a system with a large magnet that is too close to the E3 and Profile. Consult **EMC Guidance and Manufacturer's Declaration** (Doc #16566) for further guidance on minimum separation distances.

3. 'RF interference' artifact

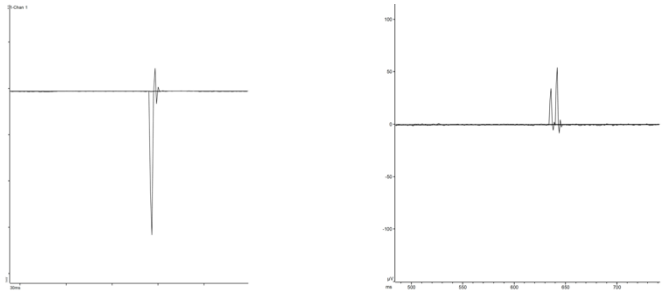
Example of the artifact (note the timing is different (100 ms) than any EOG recording (seconds)):



Possible cause and troubleshooting: the most likely cause is a system with a large RF broadcast transmitter is too close to the E3 and Profile. Consult **EMC Guidance and Manufacturer's Declaration** (Doc #16566) for further guidance on minimum separation distances.

4. Fast transient, Electrostatic discharge or Electrical surge artifact

Example waveform of the artifact (note: more than one spike may occur in your recording):



Possible cause and troubleshooting: the most likely cause is a system (likely in the same building as the E3 and Profile, and likely large: an elevator or MRI system) that is not isolated from other equipment on the electrical grid and causes electrical surges and/or transients in the building. Work with your facility management team to discuss solutions.

If you notice this artifact only once or twice, it may be an electrostatic discharge. Refer to the EMC declaration and guidance that came with the system for improvement solutions to the room setup.

Contact Diagnosys support (support@diagnosysllc.com) for additional help, if necessary.

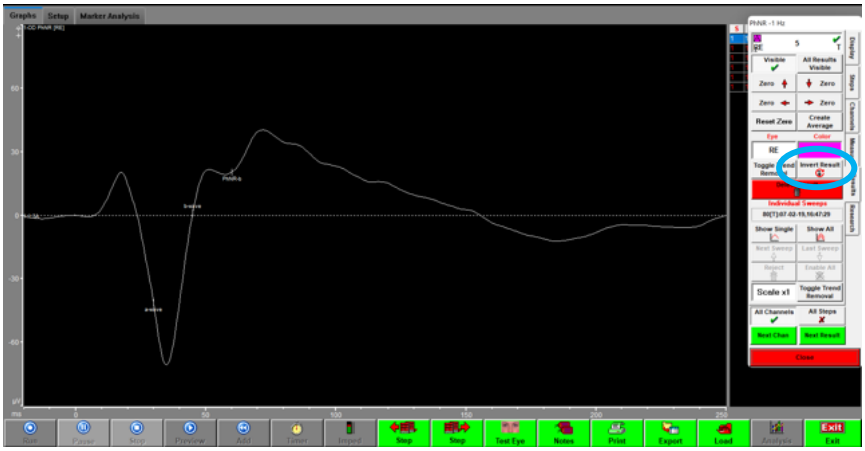
Inverted Waveform

As shown in the patient examples of this manual, waveforms can be inverted. Once identified, this is easy to correct in the system's software.

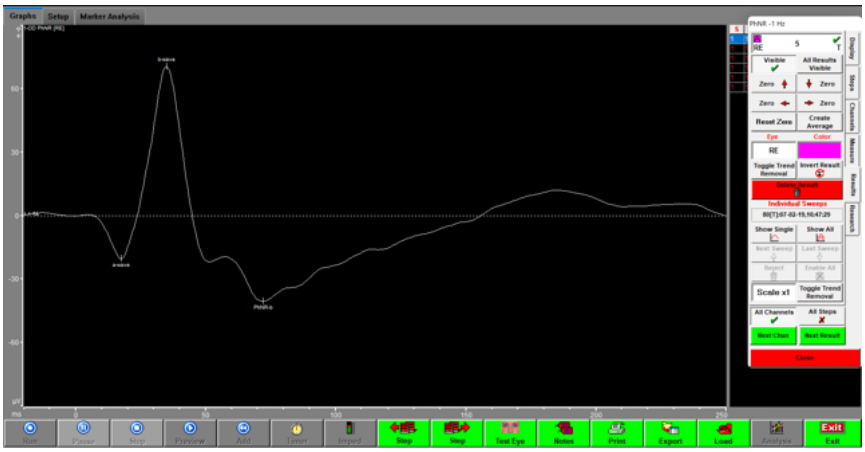
Cause: the active and reference electrode leads were reversed in the amplifier input ports by the operator.

Solution:

Step 1: Open the popout menu on the step in the test where the waveform is inverted. Select the waveform to be inverted by clicking on it (it will change color). See example inverted PhNR test below.



Step 2: Click the **Invert Result** button.



Step 3: Repeat for each step with an inverted waveform, and then **Exit** and save the test.

Contact Diagnosys support (support@diagnosysllc.com) for additional help, if necessary.

Other Troubleshooting

Error messages

Contact Diagnosys support (support@diagnosysllc.com) for additional help if necessary.

Error Message or Condition	Cause(s)	Solution
DSP-USB Hardware failed to open or be detected	USB cable disconnected or broken; USB driver stopped or disabled; USB port broken or disabled; Espion/Profile DSP card malfunctioning	Exit the software. Ensure that the USB cable is securely plugged into the computer. Re-launch the software. If the error continues, contact Diagnosys.
AMP-USB Hardware failed to open or be detected	Espion/Profile DSP card malfunctioning; Amplifier malfunctioning; Amplifier requires reseating	Exit the software. Unplug the amplifier, wait 5 seconds, then firmly plug the amplifier back in. Re-launch the software. If the error continues, contact Diagnosys.
Amplifiers have new firmware version available. Contact Diagnosys for instructions of how to upgrade	Amplifier firmware has been updated.	Contact Diagnosys for assistance in updating amplifier firmware.
You must set the system Serial Number using the Global parameters in the Configure system menu	Local configuration settings missing.	Contact Diagnosys for assistance in restoring local configuration settings.
Error: Record being read has wrong signature, stream/file may be corrupted or not be of the correct type	Test file is corrupt	Contact Diagnosys for assistance in restoring test.
Stimulator 1 (L) has not been detected, try plugging it in	Stimulator unplugged Stimulator malfunction Local configuration settings incorrect	Exit the software. Ensure the stimulator is securely plugged in to the stimulator port by unplugging, waiting 5 seconds, then re-plugging it in. Re-launch the software. If the error persists, contact Diagnosys to ensure local configuration settings are correct and troubleshoot stimulator.
Stimulator [serial number] calibration has expired. Last calibrated [date]! Please contact Diagnosys for re-calibration	It has been more than 1 year since the stimulator has been recalibrated.	Contact Diagnosys to schedule recalibration.
ISC Error: Unavailable Database	Firebird is not installed or running	Contact Diagnosys for assistance in troubleshooting Firebird

[Red/Green/Blue] LEDs are out of calibration (check power is on)	Self calibration check determined that one or more; LED colors are out of calibration	Contact Diagnosys to schedule calibration
Background luminance of stimulator 1 is too high. Is the stimulator face covered	The stimulator face needs to be covered and	Click Ok to acknowledge the message, then exit the test. Place the dust cover over the face of the stimulator and turn off the room lights. Re-enter the protocol and re-run the self-calibration routine.
Timing file is incorrect for XXX board [filename] it must NOT be in the form XXX_xxx.CAL	USB hardware not detected when generating protocol Local configuration settings incorrect	Contact Diagnosys for troubleshooting assistance
Autobackup drive [location] not found	Autobackup set to external drive that is not plugged in Local configuration settings require updating	Ensure that drive is plugged in and unlocked Contact Diagnosys for assistance in updating configuration settings
Stimulator error: Color matrix for stimulator 1 serial number XXX cannot be found. Possible fault with stimulator.	Calibration file not loaded Possible communications fault with stimulator	Contact Diagnosys for assistance in loading calibration file.

VIII. Data after Testing

Print

Your data saves to the hard drive during testing. To save data to the database, press the **Exit** button at the bottom right at the end of the test.

When exiting the test, you will be asked if you wish to save the test to the database. Click **Yes** to save the data. A **No** answer will require confirmation. If you discard the test in error, contact Diagnosys support for instructions to retrieve the test.

To print the test, press the **Print** button on the Control bar. The print options tab on the side of the preview window will allow you to select the printer (e.g. hard copy printer, PDF, etc) before printing.

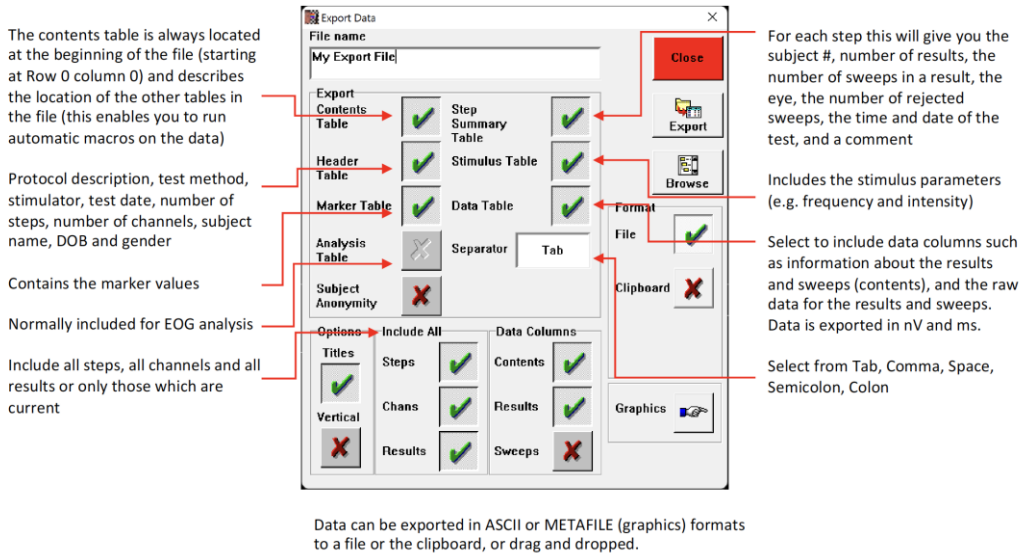
Caution. Adding peripheral equipment may result in noncompliance with the safety requirements of IEC 60601-1.

Caution. Placing peripheral devices closer than 1.5 meters (4.9 feet), or powering peripherals directly through a wall socket from the patient could result in electrical shock to the patient and/or operator.

Caution. Use of the acquisition device, a printer, or the power table with an extension cord or a power strip (multiple portable socket outlet) could cause electrical shock to the patient or operator.

Export

To export data, press the **Export** button. You can export ASCII data to either a .CSV or .TXT file or copy the data directly to the clipboard. Graphics (such as graphs, or images of marker tables) can also be copied directly to the clipboard.



Data can be exported in ASCII or METAFILE (graphics) formats to a file or the clipboard, or drag and dropped.

Transfer

The transfer button has different functions based on which screen it is used on. If pressed on the patient selected screen, it will allow one to transfer out tests. If pressed on the protocols page, protocol information will be transferred.

Data can also be transferred out of the E3 and Profile software in the form of .EXP files. This allows one to easily transfer batches of tests in one file between computers.

To transfer out tests, press the **Old Tests** button on the patient selection screen and then press **Transfer**. For instructions to **Transfer** in a protocol, see Appendix 2.

Analysis

If you wish to use reference ranges, ISCEV recommends collecting normal reference data using your test methods and subjects at your clinic. ISCEV has additional recommendations on normal reference ranges on their website, www.iscev.org. To load your reference ranges into your Diagnosys system, contact Diagnosys (support@diagnosysllc.com).

ERG, VEP tests

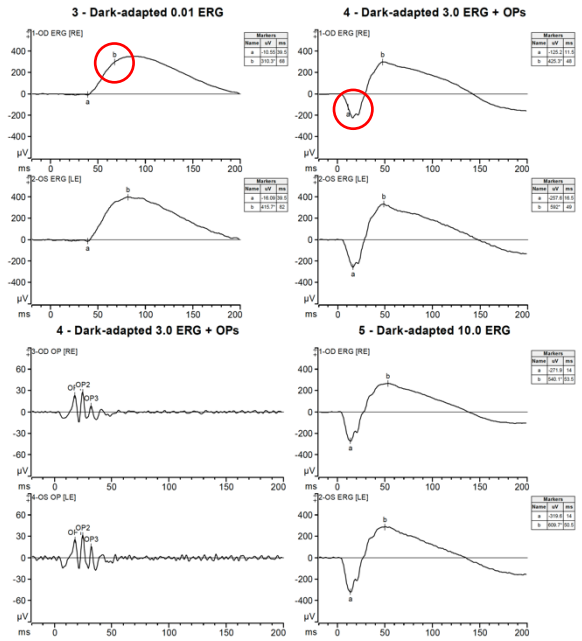
The analysis of marker data on any of the electrophysiology tests involves reviewing the test report and the marked data of the test. For all of the ISCEV tests on your system, there are standard markers recommended by ISCEV that are included in the Diagnosys test protocol, and are listed with each of the test types in Section VI of this guide. The software will automatically mark each of these waveform attributes (e.g. a-wave, b-wave) and show the marker on the waveform graph and its amplitude and timing (as applicable) in the data table. Usually the markers are positioned correctly, automatically by the software. But in some cases (usually a patient with a severe eye disease) the marker may not have

been placed at the peak of a waveform. This should be analyzed for each test, and corrected before the test is considered complete for medical analysis and interpretation. Follow ISCEV guidelines for correct marker positions for the test (www.iscev.org); the general guideline for each type of marker is that it should be positioned at the local maximum (e.g. b-wave marker) or minimum (e.g. a-wave, PhNR markers) of the waveform.

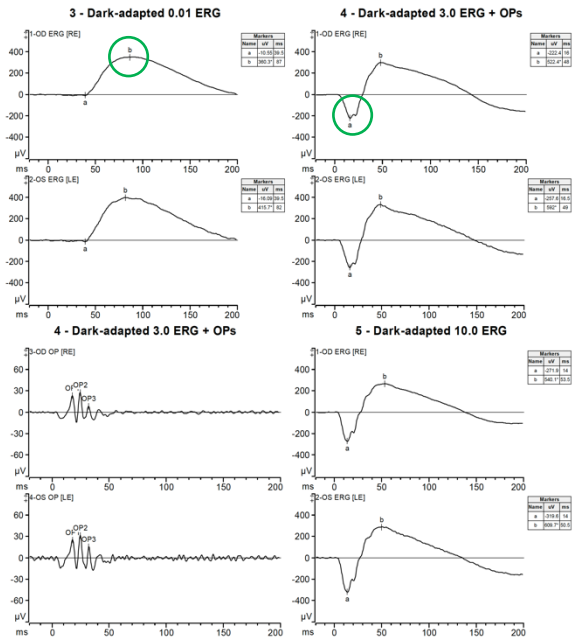
An example is shown below to demonstrate an incorrectly positioned marker and instructions on how to move the marker to its correct position. This is shown for the three dark-adapted steps of an ISCEV full-field ERG test. This adjustment method is the same for adjusting any of the ERG or VEP markers in any of the ISCEV tests.

Example test with 2 markers that were not automatically correctly positioned. In the left test report below, it is seen that the b-wave marker on the RE DA 0.01 ERG step is not at the positive peak of the b-waveform, and also that the a-wave markers on the RE 3.0 ERG step is not at the negative peak of the a-waveform. These are circled in red. On the right test report below the markers have been moved to their correct positions at the peaks. These are circled in green.

2 markers incorrectly positioned



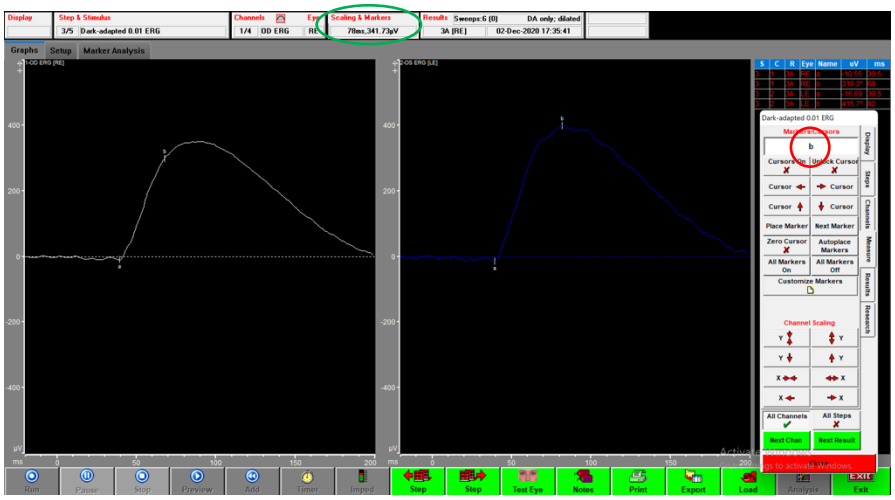
2 markers correctly positioned



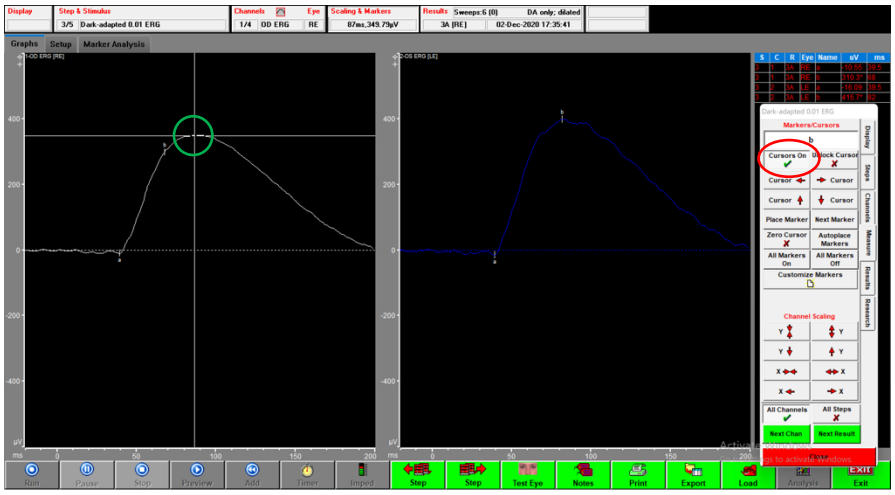
The markers can easily be adjusted to achieve the positions shown in the right graph above, by following the steps below.

1. In the test page for the subject select and double click on the test to open it up (the line will turn blue as you select the test).

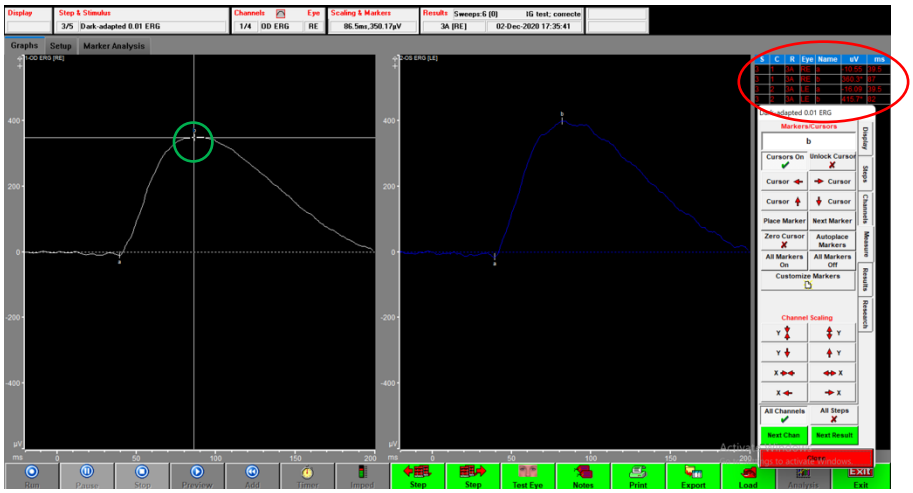
2. With the test open, click on the waveform whose marker needs to be adjusted (the waveform will turn white). Open the popout menu by clicking on the Scaling and Markers (green circle below) box near the top-center of the screen. Select 'b' from the Markers/Cursors selection box for the b-wave marker (red circle below).



3. Move the marker. Select Cursors On (red circle below) and then double click on the waveform where the marker should be placed. The cross hairs will move to that position (green circle below).



4. The marker will now be correctly positioned. The b-wave markers on the graph's waveform will be moved (green circle below) and the marked data (amplitude (uV) and timing (ms)) will also be changed automatically in the marker table data (red circle below)



5. **Step** forward to any other steps in the protocol that need to have marker positions adjusted and follow the instructions above to adjust those markers as well.
6. When all markers are correctly positioned, click **Exit** (green circle below) and **Yes** (red circle below) to save the test. You may want to type a comment that markers have been adjusted in the **Test Comment** box before saving.

7. The new marker locations will now be saved in the test record. If needed, markers can be further adjusted following the instructions above. When ready for final analysis of the test, the test may be printed.

EOG tests

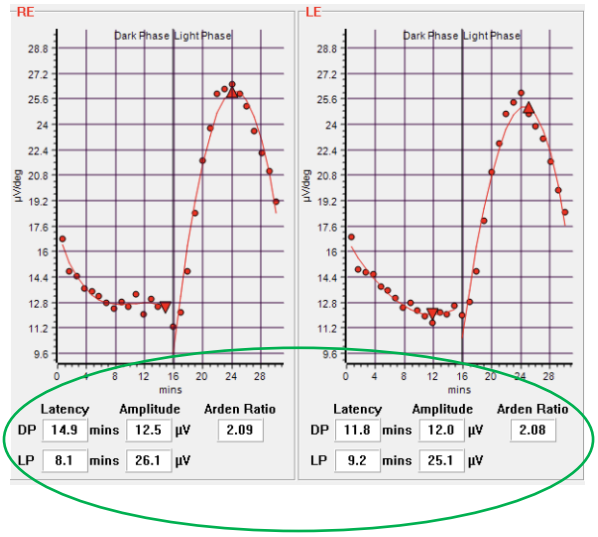
Analysis of EOG test results is done in reference to ISCEV guidelines for EOG tests (ISCEV Standard for clinical electro-oculography (2017 update); DOI 10.1007/s10633-017-9573-2).

The guideline provides for analyzing the following data:

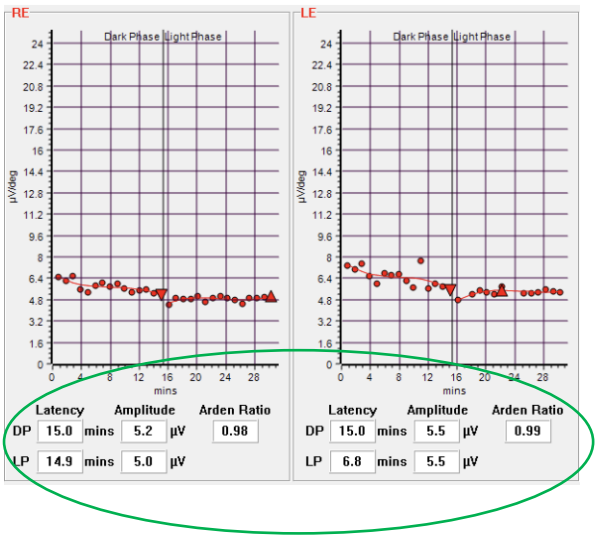
i. Dark Phase Trough (DP) timing (Latency) and Amplitude.
ii. Light Phase Peak (LP) timing (Latency) and Amplitude.
iii. Arden Ratio: the ratio of light peak to dark phase trough amplitudes

As shown in the examples below all of these measures are reported in the EOG test report, circled in green below. The graphs plot the electrophysiology measurements taken during the tests at every minute of the test. These are plotted in micro-volts per degree. The Dark Phase (DP) trough is marked at the lowest value measured during the dark phase of the test. The Light Phase (LP) peak is marked at the highest value measured during the light phase of the test. The data table presents DP and LP marked amplitudes in micro-volts and latency in minutes (from start of that phase).

Normal patient example



Best disease patient example



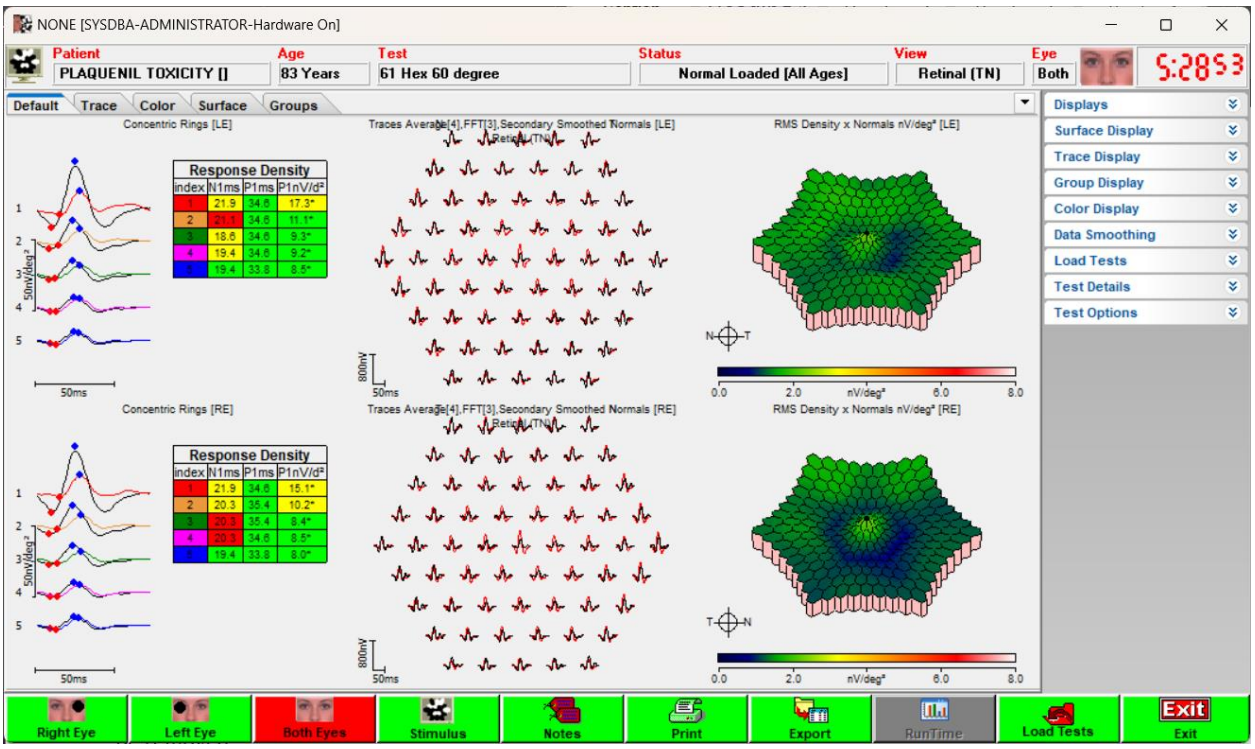
mfERG tests

Analysis of mfERG test results is done in reference to ISCEV guidelines for mfERG tests (ISCEV Standard for clinical multifocal electroretinography (mfERG) (2021 update); https://doi.org/10.1007/s10633-020-09812-w) where further definitions and background related to mfERG tests can be found.

Below is the mfERG test result as shown in the Diagnosys software, where a customer has loaded their reference normative data. There are three sections to the report:

1. Left side of graph: Group averages, both waveform and table summary of marker data
2. Middle of graph: Trace array, where responses from each of the hexagon stimuli are shown
3. Right side of graph: 3D plot of the individual response amplitudes

After reviewing the data, click the **Print** button to print the test.



Notes:

1. Choose **Right Eye**, **Left Eye** or **Both Eyes** to view those test results.
2. Click **Stimulus** to review the stimulus parameters that were used in the test.
3. Click **Notes** to add a note to the test report
4. Click **Export** to export the test (see further information above on exporting data)
5. Click **Load Tests** to load a different test

IX. System Maintenance and General Information

Calibration

Following ISCEV guidelines, all equipment that can be calibrated should be calibrated with a frequency of no less than once per year. Where possible, the E3 and Profile system has built in calibration systems which help to keep values stable over time to reduce this requirement to a minimum. When calibration must be performed, the system should be returned to an authorized dealer or to Diagnosys directly as this procedure requires specialized equipment calibrated to a national standard. An automatic 'stimulator calibration warning' popup will notify you when calibration is recommended. For more information about calibrating your equipment, contact Diagnosys directly.

For checking light calibration, we recommend the IL1700 photometer from International Light which may also be employed for some user re-calibration of the system.

E3 and Profile system amplifiers can be checked using a known input amplitude reference signal fed into the electrode inputs and measuring the resultant waveform from the screen. Like all analog components, the amplifiers will drift slightly with temperature and time, but in our experience, this drift is not significant over the usual lifetime of the equipment.

Software Updates

Diagnosys periodically releases software updates. Patch files are posted to a password-protected section of the Diagnosys website. Users will be notified via email as updates are released. Contact support (support@diagnosysllc.com) for access to the update page.

Protocol Updates

Diagnosys periodically releases new protocols and protocol updates. Diagnosys also has replacement ISCEV protocols available. Files are posted to a password-protected section of the Diagnosys website. Users will be notified via email as updates are released. Contact support (support@diagnosysllc.com) for access to the page.

Cybersecurity

Third-party purchased computers are provided with Diagnosys systems and are capable of connecting (wirelessly or hard-wired) to another device, to the Internet or other network, or to portable media (e.g. USB) which can make the system more vulnerable to cybersecurity threats than devices that are not connected.

- Internet connectivity enables third-party software, software drivers and updates to be downloaded to your system, either automatically or intentionally.
- When connected to the Internet, the instrument may be vulnerable to serious security risks, including viruses and worms that could disable your system or adversely affect its performance.

E3 and Profile systems include touchscreen Windows computers with Windows Defender installed on the machine. Definitions are updated during production and a full scan is performed prior to shipment.

It is the responsibility of the user to maintain definition updates or install alternative antivirus/firewall software.

Caution. Third party software or unapproved drivers could degrade the performance of the of the computer and/or lead to corrupted diagnostic or therapeutic information and may void the instrument warranty.

Caution. Do not perform a virus scan while acquiring exam data. The user is responsible for system performance degradation or any other change or defect resulting from unsupported network activities.

Device features have been implemented that protect critical functionality, even when the device's cybersecurity has been compromised. Diagnosys Software is configured to periodically perform backups of test records, calibration files and local configuration settings. Backing up to a network location is recommended in institutions that have network storage available. It is the responsibility of the user to ensure that these backups are performed and saved in a secure location external to the device. If your network does not allow you to access local network infrastructure, contact your institution's IT representative to request that an administrator establish access for you.

Caution. It is the responsibility of the user to configure physical access to the equipment, as well as software access control to the operating system. Some institutions only allow local IT administrators to perform networking activities. If your network does not allow you to access local network infrastructure, contact your institution's IT representative to request that an administrator establish access for you.

Diagnosys does not reserve remote access privileges to shipped machines.

Diagnosys has carefully considered the balance between cybersecurity safeguards and the usability of the device in its intended environment of use, the presence and intent of its electronic data interfaces, the type of cybersecurity vulnerabilities present, the likelihood the vulnerability will be exploited (either intentionally or unintentionally) to ensure that the security controls are appropriate for the intended users. Diagnosys software and cybersecurity controls cannot, under any circumstances, harm a patient and are never used during an emergency situation.

For added security:

1. Access is limited to trusted users only by automatic timed methods to terminate sessions within the system where appropriate for the use environment.
2. Layered authorization model is employed by differentiating privileges based on the user role
3. Limited access to trusted users only by the authentication of users via windows password or other appropriate controls before permitting software or firmware updates, including those affecting the operating system, applications, and anti-malware.
4. When choosing a password, avoid "hardcoded" passwords or common words (i.e., passwords which are the same for each device, difficult to change, and vulnerable to public disclosure) and limit public access to passwords used for privileged device access
5. It is strongly recommended that you allow a knowledgeable IT professional to assist you with network configuration and software installation; Diagnosys does not provide technical support for the use of third party hardware or software.
6. Use systematic procedures for authorized users to download version-identifiable software and firmware. Notices will be sent from Diagnosys, and Diagnosys Authorized Representatives, to

users when new versions and patches are available with instructions for password protected access. Contact support@diagnosysllc.com for details.

7. Ensure secure data transfer to and from the device, and when appropriate use methods for encryption for data transfer
8. Upon detection of a cybersecurity event Contact your network administrator.

Caution. Attempting to carry out activities not specifically endorsed by Diagnosys may void your warranty and could result in damage to the instrument.

For more information contact support@diagnosysllc.com.

Cleaning

The exterior of the E3 and Profile console and the exteriors of the amplifier and stimulators may be cleaned using a damp soft cloth or alcohol wipe.

Caution. Neglecting to disinfect the device could lead to cross infection between patients. Always wipe the chin and forehead rest with an alcohol wipe between patients.

The ColorDome and ColorBurst interiors may be cleaned using a slightly damp cloth. Do not scrub the interior lining, as this will degrade the reflective paint layer. Instead, use a gentle dabbing motion.

For components not manufactured by Diagnosys, such as laptop or all-in-one desktop computers or fixation cameras, please refer to the instruction book supplied by the original manufacturer.

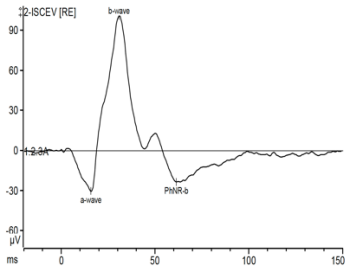
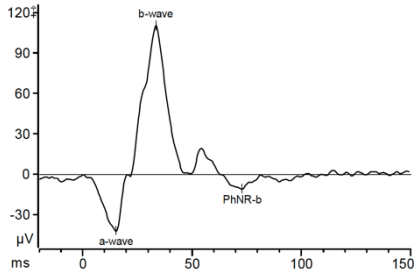
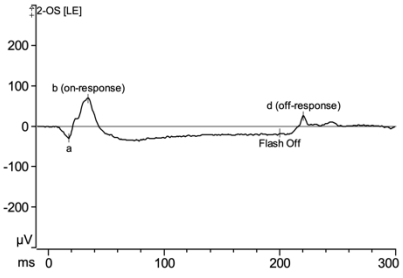
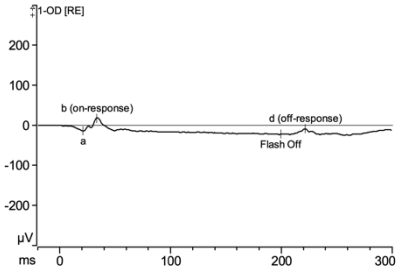
X. Appendices

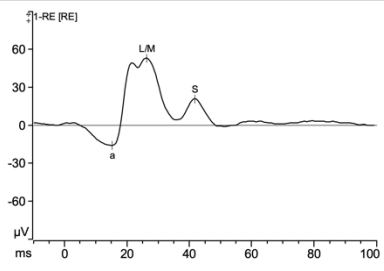
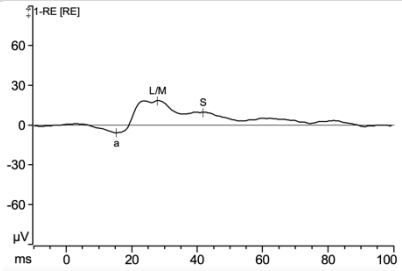
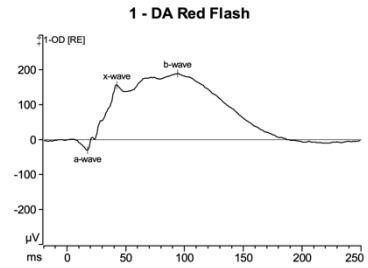
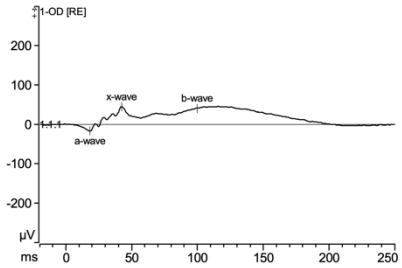
Appendix 1 - Test Quality Check (ISCEV Extended ERG Protocols Analysis)

Once data acquisition is complete, tests must be reviewed by the operator for acceptance prior to being released for analysis. The test quality check can be done immediately after the test is complete in Runtime (before the test is saved) or by double clicking on the test to open and review it after it has been saved. If possible, this should be done before electrodes are removed from the patient, in case a repeat test is recommended. Below are examples of test examples with sufficient quality ('High Quality') to be accepted for analysis as well as tests with insufficient quality ('Low Quality') where troubleshooting and repeating the test is recommended or in the case of inverted electrodes where inverting the test result in software is required.

High Quality

The tests below are High Quality and after review by the operator are ready to be released for analysis. Patient test examples below from the E³ and Profile system.

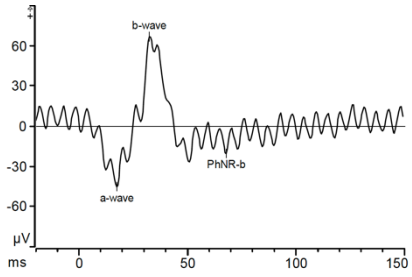
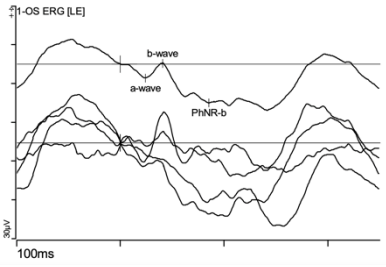
Test Type and Description	Example Waveforms
PhNR ERG The a-wave, b-wave and PhNR peaks are well defined and marked by the software or the response is flat with no indications of excess noise. PhNR amplitudes may be anywhere from -40 uV to 0 uV. Waveforms start near 0 uV, but may end significantly different than 0 uV. Markers for analysis: a-wave, b-wave, PhNR	 Typical normal waveform  Typical Glaucoma waveform (smaller PhNR)
On-Off ERG The a-wave, b-wave and d-wave peaks are well defined and marked by the software or the response is flat with no indications of excess noise. Peak amplitudes may be anywhere from 100 uV to 0 uV. Waveforms start near 0 uV, but may end significantly different than 0 uV. Markers for analysis: a-wave, b-wave, d-wave	 Typical normal waveform  Typical disease waveform (e.g. CSNB)
S-Cone ERG The a-wave, L/M-wave and S-wave peaks are well defined and marked by the software or the response is flat with no indications of excess noise. Peak amplitudes may be anywhere from 40 uV to 0 uV. Waveforms start near 0 uV, but may end significantly different than 0 uV. Markers for analysis: a-wave, L/M-wave, S-wave	

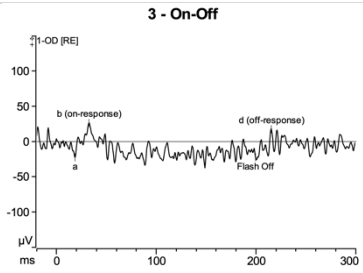
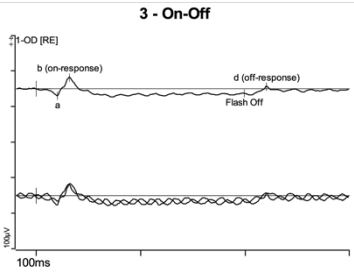
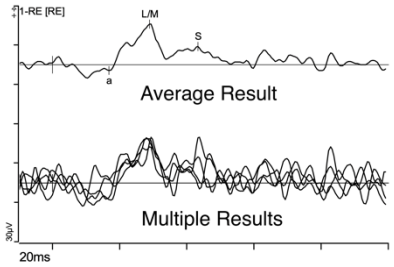
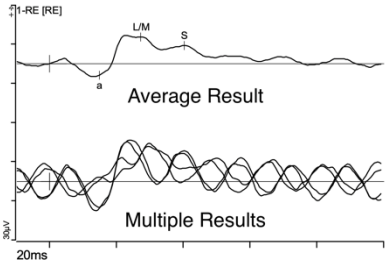
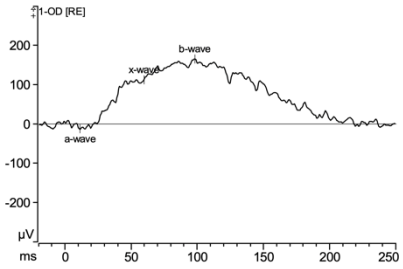
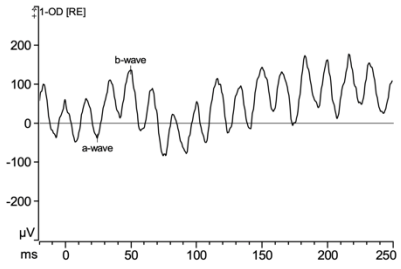
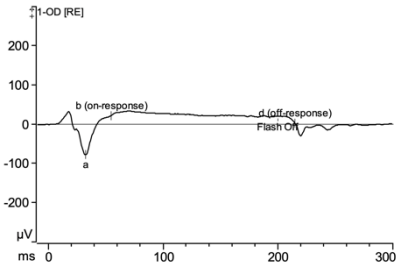
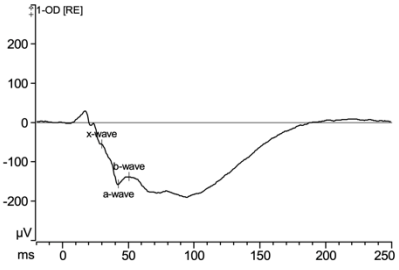
	 Typical normal S-cone response	 Smaller S-cone response (e.g. S-cone syndrome)
DA Red ERG The a-wave, x-wave and b-wave peaks are well defined and marked by the software or the response is flat with no indications of excess noise. Peak amplitudes may be anywhere from 100 uV to 0 uV. Waveforms start near 0 uV, but may end significantly different than 0 uV. Markers for analysis: a-wave, b-wave, x-wave	 Typical normal waveform	 Typical smaller waveform

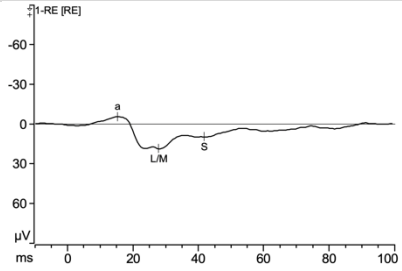
Note: for the ISCEV extended protocols Light-adapted intensity series, Dark-adapted intensity series and Rod isolated ERG protocols, the waveforms and markers are the same as the ISCEV full-field ERG protocol (see Section VI, full-field ERG tests).

Low Quality

The tests below are Low Quality and not ready to be released for analysis. See Troubleshooting Section VII for recommendations on how to resolve excess biological noise, excess electrical noise or inverted waveform issues. Repeat the test once the noise issue has been eliminated to minimized sufficiently to conduct a High Quality test. Inverted waveforms can be corrected in software without a retest. See Section VII. Patient test examples below from the E3 and Profile system.

Test Type and Description	Example Waveforms	
PhNR ERG Excess noise Waveform shape: excess electrical line noise with regular, repeating peaks as is typical of line noise. Excess low frequency noise shows no stable recording before flash and in multiple tests this issue continued and test repeatability is low.	 Excess electrical line noise	 Excess low frequency biological noise (multiple tests shown to demonstrate the noise)
On-Off ERG Excess noise		

Waveform shape: Excess high frequency noise shows noise amplitudes that are greater than 15 uV and similar to the waveforms measured. Excess electrical line noise with regular, repeating peaks as is typical of line noise.	 Excess high frequency biological noise	 Excess electrical line noise (multiple tests shown to demonstrate the noise)
S-Cone ERG Excess noise Waveform shape: Excess high frequency noise shows noise amplitudes that are greater than 15 uV and similar to the waveforms measured. Excess electrical line noise with regular, repeating peaks as is typical of line noise.	 Excess high frequency biological noise	 Excess electrical (line) noise
DA Red ERG Excess noise Waveform shape: Excess high frequency noise shows noise amplitudes that are greater than 15 uV and similar to the waveforms measured. Excess electrical line noise with regular, repeating peaks as is typical of line noise.	 Excess high frequency biological noise	 Excess electrical (line) noise
Inverted test On/off ERG, dark adapted red and S-cone test examples Notice that the peaks in the waveform are well defined. However, in each case they are upside down from their normal position and the markers are not in the correct position. There is no known patient condition that will cause this inversion.		

This is a good waveform (low noise), but the waveform is inverted. See Troubleshooting Section VII on how to invert the waveform in software, to be correct.	

For additional test examples obtained from literature, contact Diagnosys at support@diagnosysllc.com.

Appendix 2 – ISCEV Protocols included with system and 'transfer in' instructions

ISCEV protocols included with the system (based on stimulator type you have with your system):

A. ColorDome
   a. Flash ERG
   b. Red flash ERG
   c. PhNR ERG
   d. On-Off ERG
   e. Light-adapted intensity series
   f. Dark-adapted intensity series
   g. Rod isolated ERG
   h. S-cone ERG
   i. Flash VEP
   j. EOG

B. ColorFlash
   a. Flash ERG
   b. Red flash ERG
   c. PhNR ERG
   d. On-Off ERG
   e. Light-adapted intensity series
   f. Dark-adapted intensity series
   g. Rod isolated ERG
   h. Flash VEP

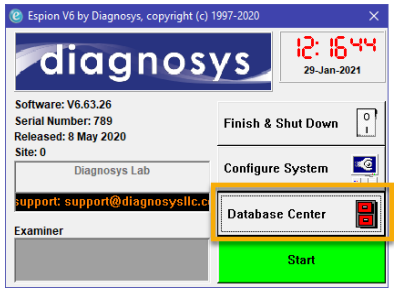
C. ColorBurst
   a. Flash ERG
   b. Red flash ERG
   c. PhNR ERG
   d. On-Off ERG
   e. Light-adapted intensity series
   f. Dark-adapted intensity series
   g. Rod isolated ERG
   h. Flash VEP

D. LCD monitor
   a. mfERG
   b. Pattern VEP
   c. Pattern ERG

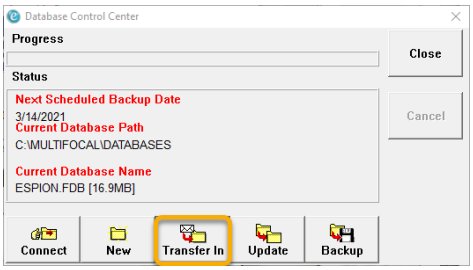
E. Envoy monitor
   a. mfERG
   b. Pattern VEP
   c. Pattern ERG

Contact Diagnosys if you wish to receive an updated or replacement protocol. Follow the instructions below to Transfer files into your database and other database functions.

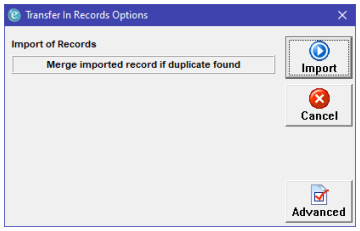
1. Open the software and click on Database Center



2. Click on Transfer In



3. Select the file(s) you'd like to import
4. Select Import to bring this file into the database



5. When the Progress Bar turns 100% Blue the transfer is complete.
6. You may close the window, transfer in another file or use other operations in the Database Center.
7. Other operations in the Database Center:
    a. **New**. Setup a new database
    b. **Connect**. Connect to a different database
    c. **Backup**. Manually backup a database

Appendix 3 – Pediatric and Infant Information for Testing

The guidance provided in this section is an overview of guidelines for pediatric and infant testing. For additional information consult the ISCEV guidelines for tests (www.iscev.org) on their recommendations for which test type is most appropriate for different age groups of infants and pediatric patients.

As ISCEV notes throughout its guidance documents, the use of electrophysiology testing has a very long history of clinical use with pediatric patients and infants, providing clinical diagnostic benefits in a wide range of patients. Diagnosys recommends you conduct a literature search, for example in PubMed (https://pubmed.ncbi.nlm.nih.gov) for additional information on the use of electrophysiology tests with pediatric patients and infants. There are many 100's of papers available from a wide range of clinicians and research organizations located in the US, Europe and many other countries.

Information from this section is taken from the references listed below.

Introduction (summarized from ISCEV, Procedures Guide)

Accurate diagnosis may be difficult in young children who are unable to describe their visual symptoms or who are difficult to examine. The objective data provided by electrophysiological testing are fundamental to the management of the child with suspected visual pathway dysfunction, but there are important considerations relating to maturation of responses, ability to comply with testing and causes of visual pathway dysfunction more specific to the pediatric population. Both ERG and VEP responses show profound developmental changes during infancy and childhood, and although all visual electrophysiological values are considered in relation to age, it is even more important in young patients. Infants up to the age of about 2 years can frequently undergo successful ERG testing without general anesthesia, while being held in a parent's lap, either by using only topical anesthetic eye drops and corneal electrodes or by using surface electrodes on the lower eyelids. It may be appropriate to shorten the standard ERG protocol, and many practitioners start with light-adapted ERGs and perform limited dark adaptation, dependent upon the compliance and comfort of the child. VEP testing in infants is equally feasible, but may require simple flash stimulation, if steady fixation on the center of the VEP pattern stimulus cannot be induced with a moving toy, jangling keys or similar to encourage central fixation. The use of skin electrodes limits sensitivity since the signal amplitude is lower, but in this age group there is rarely a need to detect subtle abnormalities and most clinically appropriate questions may be easily addressed. For example, is there a detectable ERG, is there a functioning cone system, is there a response after dark adaptation and is there an electronegative ERG waveform?

Pediatric ERG recording (summarized from ISCEV full-field ERG guidelines; this applies for all types of ERG, VEP, EOG tests)

ERGs can be recorded from infants and young children, but interpretation of results must take into account any variations in recording methods, compliance and age-appropriate reference data.

ERGs mature during infancy, and signals from very young infants must be interpreted with caution. Later in infancy and childhood, ERGs approach adult waveforms and amplitudes. Specifically, somewhat lower ERG amplitudes and longer peak times generally apply below 6–12 months of age under dark-adapted conditions, and below 2–3 months of age under light adapted conditions. Before 6 months of age, the

DA 0.01 ERG may be poorly defined in healthy infants; DA 3 and DA 10 ERGs are usually well defined at all ages in infants without retinal disease.

Most pediatric patients can be studied without sedation or general anesthesia.

If contact lens electrodes are used, pediatric sizes will be required for infants and young children. Other types of corneal and skin electrodes vary in their applicability to children; greater comfort may be offset by greater electrode movement or smaller ERG amplitudes. To minimize artifacts, special care is required with children to monitor electrode position and compliance. Limited compliance can make pediatric records variable, and several repetitions of each ERG should be recorded to recognize reproducible waveforms. Shortened protocols may be appropriate to obtain the ERGs most critical to the diagnostic question under investigation. Reports should note the methods used, degree of cooperation and any relevant medications.

Electrode Choice and Electrode Placement

As with adult patients, follow the electrode manufacturer's IFUs for patient type and specific electrode choice considerations for pediatric and infant patients. As noted by ISCEV the electrodes used for adults are generally also the same electrodes used for pediatric and infant testing. In some cases the electrode manufacturer provides different size electrodes (e.g. Burian-Allen electrodes); follow the IFU guidance from the electrode manufacturer for which electrode option to choose for the age and physical size of your patient. In its guidelines ISCEV generally recommends a corneal electrode for electrophysiology tests to optimize the signal-to-noise ratio of the recording However, they also note that for patients who are unable to sit very still or take directions to do so (e.g. adults with a learning disorder, infants and other small children) that skin electrodes placed just below the lower eyelide should be used at the active electrode.

Also, according to ISCEV guidelines, the electrode locations for pediatric testing are the same as those used for adults, proportionate to the smaller size face and head of a pediatric patient, regardless of age. Specifically:

1. For ERG tests (full-field, pattern, multi-focal):
    a. Active electrodes. If used, corneal electrodes are placed on the eye according to the manufacturers IFU. If used, skin electrodes are placed just below the lower eye lid.
    b. Reference skin electrodes are placed on the temple.
    c. Ground electrode is placed in the center of the forehead.
2. For VEP tests (flash, pattern)
    a. The active, reference and ground electrodes are placed in the same locations as with adults, proportionate to the patients head size. Consult the diagrams and descriptions in the VEP sections of this guide, which describe how to measure a patient's head and locate VEP electrodes.
3. For EOG tests
    a. As with adults the recording electrodes are placed on either side of each eye. Ground electrode is placed in the center of the forehead.
4. For all tests additional medical tape may also be used to further secure the electrodes, as needed.

Setting up and conducting the test

1. Use only skin preparation gels and electrode pastes that are indicated for pediatric and infant skin according to their manufacturer.
2. Active participation in the test description and testing process of the young patient's parent is often quite helpful.
3. Pediatric tests should be recorded when the infant or child is alert and attentive. Direct interaction with the child can help maintain attention and fixation, and two testers are beneficial; one to work with the child and the other to control data acquisition.
4. So long as the young patient is able to be positioned correctly in front of the stimulator during the test, sitting on their parent's lap during the test can be helpful, for infants in particular.
5. While the larger stimulators (ColorDome, LCD monitor) may be used for young patients as described above, the smaller stimulators (ColorFlash, ColorBurst, Envoy) are oftentimes easier to use for young patients because they are smaller/less intimidating, are positioned further away from the patient and do not require chin rests. For infant testing they also more easily enable the patient to sit in their parent's lap during the test.
6. Try a practice recording. This can always be done with adults, but with young pediatric children it is especially helpful to verify a high-quality recording and give the patient (and/or their parents) confidence that the test can be completed.
7. For tests such as VEP, per the ISCEV VEP test guidance:
    a. 'A smaller number of sweeps per test may sometimes produce a clearer response because the longer recording time required to increase sample size may introduce increased variability due to loss of attention and/or increased movement. This is especially true for infants and young children.'
    b. 'The order of stimulus presentation should be flexible and selected to ensure that responses most critical to the diagnostic question are obtained within an individual child's attention span.'
    c. 'It is particularly important to replicate VEPs in children to assure that the response measured is a reliable signal and not an artifact. Reports should note the degree of cooperation and arousal of the child.'

Test Quality Check

The quality check of an ERG, VEP, EOG test is the same for pediatric/infants as it is for adults. Artifacts will appear the same on waveforms as they do for adults. Follow the guidelines shown above for each test type to identify high quality vs low quality tests. Careful observation of the patient during the test and how stable they were able to keep themselves and their eyes is recommended as another input to help judge the quality of the test result.

Data Analysis

From the ISCEV Full-field ERG guidelines (this applies for all types of ERG, VEP and EOG tests): Reference ranges (previously termed 'normative' data) for standard ERGs are specific to the type of electrode, and each laboratory should use suitable reference data to interpret patient ERGs. Establishing reference values involves recruiting and testing sufficient reference subjects per clinically relevant partition (e.g. sex). Subjects should be matched to the patient population in demographic factors. Reference limits should be constructed to enclose the central 95% of values, i.e. the 2.5th and 97.5th percentile.

Nonparametric or robust techniques are likely to be more appropriate than parametric techniques. ERG parameters mature rapidly during infancy and there are age-associated changes throughout life: robust curve fitting may be a useful aid to interpretation, avoiding partitioning of a continuous variable.

Establishing laboratory-specific reference values is the optimal process. If external reference data are used, for example, published data, they must be verified as appropriate for local use with an understanding of possible limitations and how reference limits were defined. Legacy reference data may be transferred and validated, for example in response to a change of instruments, but the methods should be stated.

For each of the ERG, VEP and EOG tests the markers are the same (e.g. a-wave, b-wave, P100, etc) as those used for adults.

Data analysis methods are the same as for adults subject to the ISCEV guidance above on reference ranges, ability of patient compliance to instructions during the test and quality checking for artifacts (e.g. biological noise due to eye and/or body movement) after the test.

References:

1. The ISCEV clinical test guidelines which can be obtained at www.iscev.org
2. Brodie, SE; 'Tips and tricks for successful electroretinography in children'; Curr Opin Ophthalmol 2014, 25:366–373
   Sokol, S; 'Pattern visual evoked potentials: their use in pediatric ophthalmology;' 1980; 0020-8167/80/010251.

Appendix 4 – Additional Resources

Information on clinical analysis of electrophysiology tests may be obtained from the following sources:

1. International Society for Clinical Electrophysiology of Vision (ISCEV). ISCEV and many of its national organizations around the world conduct training sessions for clinical and research data analysis and interpretation each year. www.iscev.org.
2. Moorfields Eye Hospital. Moorfields typically conducts training session for clinical and research data analysis interpretation each year. https://checkout.moorfields.nhs.uk
3. Another suggestion is to contact the ophthalmology department of your local university. Numerous universities around the world conduct training sessions.