AGE READER SU
Know their risk.

User Manual

DiagnOptics

CE 0344

Version 2.3
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Contents

1. Introduction

AGEs (Advanced Glycation End products) have a pivotal role in the development of chronic complications of diabetes, renal failure and
other common conditions, but are also a marker of oxidative stress. The amount of AGE in tissue can serve as a risk predictor of cardiovascular risk in such complications.

The AGE Reader™ is a proprietary device that can non-invasively assess the tissue accumulation of Advanced Glycation Endproducts (AGEs). This technological breakthrough enables clinicians and scientific researchers to non-invasively measure the AGEs level in 30 seconds. The AGE Reader may help in clinical intervention and scientific research on subjects related to AGEs.

The AGE Reader was developed and is being commercialized by DiagnOptics Technologies B.V., an innovative life science company based in the Netherlands.

This manual provides the setup and operating procedures for the AGE Reader.

DiagnOptics Technologies B.V.

2. Intended use

The AGE reader non-invasively gives, if used as intended, an estimate of (AGE) in tissue. Clinical evidence shows that AGE levels may assist the physician in clinical practice to assess the risk on cardiovascular disease.

The AGE Reader is intended to be used by medical personnel to assess the level of auto fluorescence in human skin. Users are expected to be familiar with all standard medical practices as required for patient monitoring.

AGE measurements should be performed directly on intact healthy skin on the lower forearm. The skin at the measuring area should be homogenous and without exposure to skin care creams or any substance that may have fluorescent properties.

All instructions, procedures and information in this user manual and on the labelling on the device is to be regarded as the "Intended Use" and will fully inform the user about the correct and safe use and installation of the AGE Reader.

2.1. Declarations

Pigmented skin

The device and its software have been validated in patients with skin reflection >6% (Fitzpatrick class 1-4). In patients with darker skin colour (Fitzpatrick class 5-6, dark brown or black), a correction is made to the AF value if the UV reflectance is between 6% and 10%. If the UV reflectance is below 6%, the AGE Reader will give a warning that the signal is too low for valid results.

UV-Radiation
Using the guidelines of the ICNIRP it is concluded that during AGE Reader measurements, as intended, even when repeated up to 100 times on the same skin site within an 8-hour period, the local radiation exposure on the skin of the patients, and to the eyes of patients and operators remains considerably below the maximally allowed values for that period. Radiation exposure to the eyes normally does not occur. Exposures of the eyes longer than 60 seconds per 8-hour period should be avoided.

3.   Warnings and precautions

The following warnings and precautions are essential for correct and safe functioning of the AGE Reader as is intended by DiagnOptics Technologies B.V., its manufacturer.

Table 1. Warnings & precautions

⚠	This device emits UV-A radiation**
⚠	Measurements are advised to be taken on the dominant arm on healthy undamaged skin without birthmarks or excessive hair growth. Self tanning agents must not be used for at least 2 days. Sun-blockers and other skin creams should be removed before measurement.
⚠	Protected against falls and mechanical shocks
⚠	Always use the accompanying external power supply (art.nr.: 214B51601)
⚠	Always use a computer or laptop approved for medical use. The USB-port should be a limited circuit with a maximum current of 8A.
⚠	Always make sure that with the use of an, for medical use approved computer or laptop, the system complies with IEC 60601-1-1 for medical systems.
⚠	The mains plug of the power supply is the separator which connects or disconnects the AGE Reader and its power supply from the mains.
⚠	This device meets all requirements for electromagnetic compatibility per International Electrotechnical Commission (IEC) 60601-1-2 and the Medical Device Directive and has been fully tested to such requirements. It is unlikely that the user will encounter problems with this device because of inadequate electromagnetic immunity. However, electromagnetic immunity is always relative and standards are based on anticipated environments of usage. If the user notes unusual device behaviour particularity if such behaviour is intermittent and associated with nearby usage of radio or TV transmitters, cell phones or electrosurgical equipment, this could be an indication of electromagnetic interference. If such behaviour occurs, the user should try moving the interfering equipment further from this device. Failure to do so could result in the equipment not functioning properly.
⚠	The measurement window should always be kept clean
⚠	The AGE Reader is intended for static use
⚠	Never place anything on top of the device other than intended
⚠	Maintenance and repairs can only be done by DiagnOptics or authorized representatives
⚠	CD-ROM containing software is unique and is not interchangeable, store well
⚠	Correct positioning of the arm over the window is essential and should be maintained steady during the measurement process
⚠	Do not let fluids ingress
⚠	AGE Reader Software requires 32-bit windows 2000 or newer.

** UV-Radiation
Using the guidelines of the ICNIRP it is concluded that during AGE Reader measurements, as intended, even when repeated up to 100 times on the same skin site within an 8-h period, the local radiation exposure on the skin of the patients, and to the eyes of patients and operators remains considerably below the maximally allowed values for that period. Radiation exposure to the eyes normally does not occur. Exposures to the eyes longer than 60 seconds per 8-h period should be avoided.

4. Description of the AGE Reader

4.1. General

The AGE Reader is a small, desktop unit, see figure 1, designed to non-invasively measure skin auto-fluorescence and thereby to assess skin AGE levels. The unit is operated from a medically approved personal computer or notebook with a Windows operating system using proprietary AGE Reader software. Results of the measurements are presented in numerical form on the computer screen and automatically stored in dedicated folders on the computer.

Contents of transport box:
- AGE Reader
- This user manual
- External power supply article number 214B51601, complying with IEC 60601-1
- Mains supply cable fitted with mains plug to comply for use in country of usage
- USB-cable
- CD with unique AGE Reader software

Figure 1. The AGE Reader
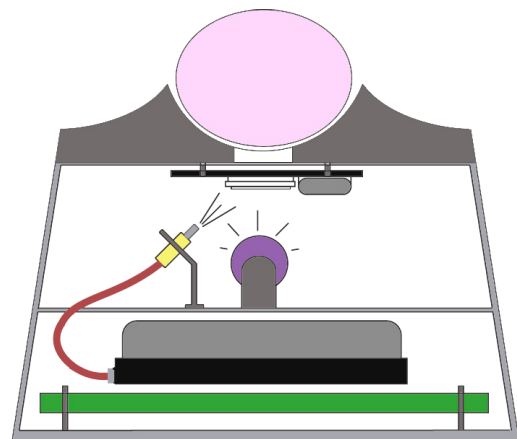
Figure 2. Schematic representation of AGE Reader

4.2. Description of the AGE Reader

The AGE Reader is a proprietary device to assist the doctor in assessing cardiovascular risk. This new way of non-invasive monitoring uses fluorescence of ultraviolet light in human tissue, the principle is presented in figure 2. The AGE Reader assesses the tissue accumulation of Advanced Glycation Endproducts (AGEs) in the patient. AGEs have a pivotal role in the development of chronic complications of diabetes and other common conditions, but are also a marker of oxidative stress. The amount of AGE in tissue can serve as a risk predictor of such complications.

The AGE Reader (as shown in figure 3) has the following external features:
- A detachable silicone mat.
- External power inlet which is installed in the device. We strongly advise to only use the medically approved power supply accompanying the device, with article number 214B51601.
- A USB port for connection to a computer (both connectors are located on the rear side).
- A measuring window made of special glass is located on the top of the AGE Reader.
- A front panel where all necessary information during use is presented visually for the user
- On the bottom of the unit, the serial number is located. It contains information about the spectrometer and lamp characteristics of the specific unit for the manufacturer.

The AGE Reader consists of a small table top housing with a detachable silicone-mat for the patient to rest his arm on for the measurement, shown in figure 3.

Silicone mat (detachable)

Housing

Measurement window

Front panel
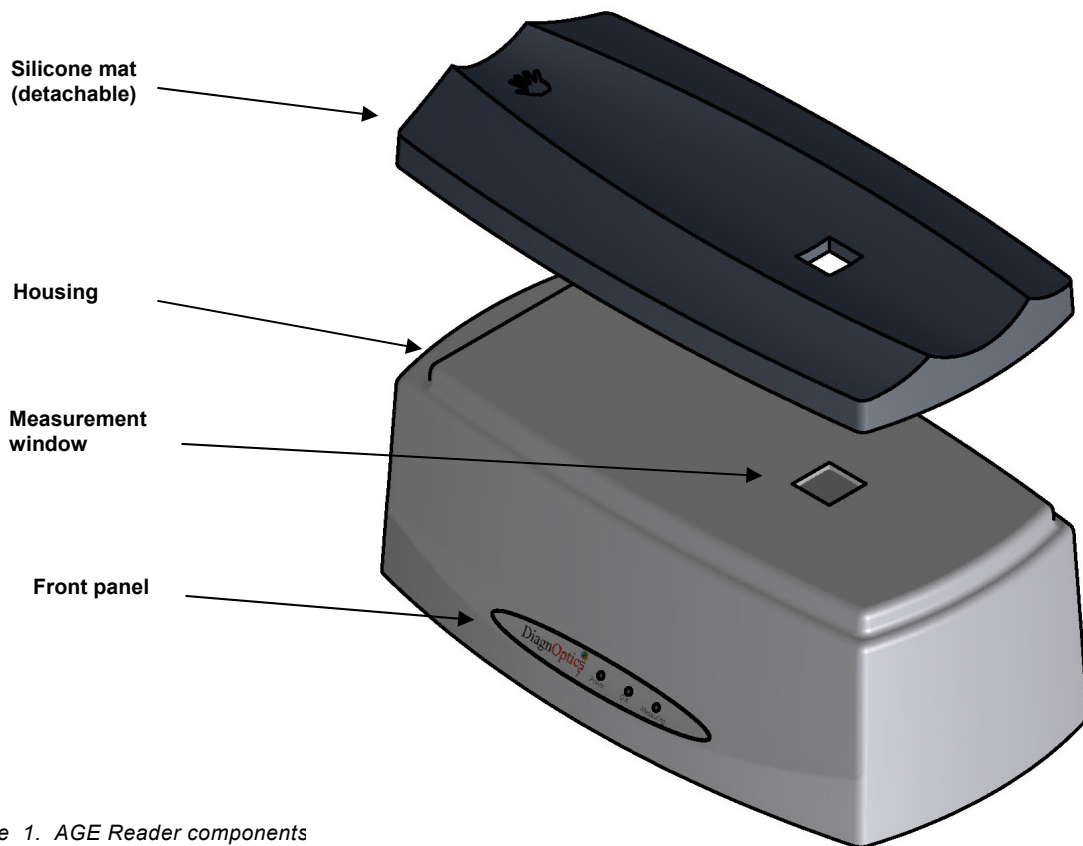
Figure 1. AGE Reader components

The AGE Reader is powered by a medically approved (IEC 60601-1) 12 VDC external power supply connected to the mains. The AGE Reader is connected by means of an USB port to a PC or notebook to control the device and through which the data of the internal spectrometer are relayed to your computer where the AGE Reader software shows and stores the auto fluorescence spectrum and calculates the AF value.

The fluorescence is excited by a 4 Watt UV-A fluorescent tube which is driven by an electronic starter. A shutter is mounted close to the measurement window, to be able to make a dark-reference measurement and a reflection reference on the white standard mounted underneath the shutter.

5.   Installing the AGE Reader

Before connecting the AGE Reader, the software needs to be installed!

5.1.   Installation of AGE Reader software

1. Check whether the CD has the same serial number as the AGE Reader.
    If you have multiple AGE Readers, always make sure that the serial number of the AGE Reader is the same as the serial number of the corresponding AGE Reader software as written on the CD and in the software.

2. For installation you need to have administrator rights. Insert the AGE Reader CD in the CD/DVD-drive of the computer. The installer should start automatically (autorun must be enabled). Otherwise run "Setup23.exe" from the CD. The computer should have a 32-bit Windows operating system (Windows 2000 or later editions) to be able to correctly install and use the AGE Reader software. 64-bit is not supported.

3. The AGE Reader program will now self-install the required drivers and software in a new folder "\AGE-Reader" in the "Program Files" folder (usually C:\Program Files\) of the computer. This can be changed if preferred.

5.2.   Installation of the AGE Reader

4. Place the AGE Reader on a horizontal, flat and stable surface.

5. Connect the mains supply cord with the DiagnOptics power supply with article number 214B51601 accompanying the device and connect it to the mains.

6. Insert the power plug in the power inlet which is located on the rear side of the AGE Reader and is labelled "Power in", see figure 4. A correct power connection will show a visual green "Power" signal on the front panel.

USB inlet   Power inlet   Power switch

Figure 2. AGE Reader connections & switch

7. Connect the USB-cable using the USB-port that is located on the rear side of the AGE Reader, labelled as "USB", see figure 4. Connect the other side of the USB cable to the USB port of a medical approved computer or notebook. The USB-port should be a limited circuit with a maximum current of 8A.

8. Turn the AGE Reader on by the power switch located on the left-rear side of the AGE Reader, see figure 4.

9. Windows should detect the hardware automatically and will display the "Found New Hardware" dialog, and starts searching for the driver.
    Under Windows XP, in answer to the question to connect to the internet, select "Not Now" and press continue. On the next screen select 'Install the Software Automatically', followed by "Next". The Wizard should now report that it has successfully completed installation for the device 'Ava-Spec-USB1'. During this process a window can be displayed that the spectrometer board "has not passed Windows Logo testing to verify compatibility with Windows XP, Vista or Windows 7": Select "Continue Anyway".
    For Windows 2000, the next dialog allows you to browse to the directory where the required USB driver is located. Browse to the dedicated Windows folder and go to folder: …\SYSTEM32\DRIVERS and select the *AvsUsb.sys* driver.

10. DiagnOptics software can be started from the desktop-shortcut "AGE Reader" that has been created during installation or from the Windows Start Menu where the group "AGE-Reader" has been added to the "programs" folder containing the "AGE Reader" shortcut.

11. Setup test: check the compatibility of the software and the AGE Reader unit by performing a test measurement.

12. For Vista and Windows 7 users: on first use, please create a new root data folder for data storage outside the 'Program Files' folder.

5.3. Uninstalling of AGE Reader Software

Remove the program by using:
"Start → Control Panel → Applications → AGE-Reader 2.3" "change/remove".

Do the same for "AGE READER USB Driver" to uninstall the USB driver for the AGE Reader.
This will remove all the program files.

6. Instructions for use

6.1. Starting the software

Once all the required connections to the AGE Reader have been made, the AGE Reader can be switched on. As described in paragraph 5.2 steps 4 to 8.

DiagnOptics software can now be started from the desktop-shortcut "AGE Reader" or from the Windows Start Menu by selecting "Start → programs → AGE-Reader → AGE Reader 2.3". The window in figure 5 will appear.
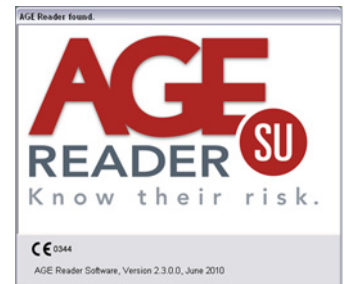
Figure 3. Start screen

If there is no AGE Reader connected during start-up, a message as in figure 6 will appear.
The AGE Reader can be connected at a later moment. In that case the user can establish the communication as described in section 6.3.4.
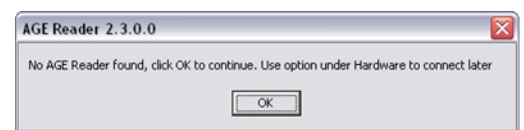
Figure 6. 'No-AGE Reader found' message

When the AGE Reader serial number and the corresponding number of the calibration file match, the communication with the AGE Reader will be established.

The blue "OK" LED on the front panel of the AGE Reader will switch on if the connection is successful and the Main Screen in figure 7 will appear.

NOTE: if no AGE Reader is connected; the blue LED will not turn on and no peak will be visible in the chart of the spectrum.
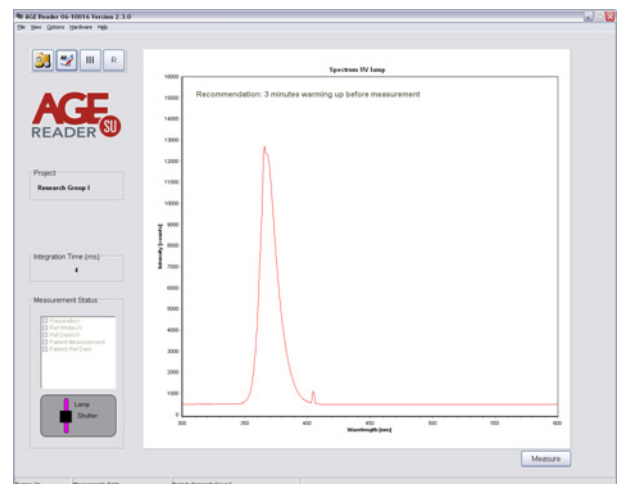
Figure 7. Main screen

6.2. Warming up

A graph is shown of the AGE Reader lamp spectrum as detected by the spectrometer. The wavelength in nm is on the horizontal axis and the light intensity in counts on the vertical axis. The spectrometer integration time is shown on the left. The red spectrum will appear and shows changes in lamp intensity after the first seconds of warming up in the spectrum of the AGE Reader lamp. Above this graph, in the same panel, the following recommendation appears: ***"Recommendation: 3 minutes warming up before measurement"***. This recommendation is given to allow the lamp output to stabilise. When consecutive measurements are performed on different patients during one session no further warming up time for the lamp is needed.
If no measurement is taken within 10 minutes, the AGE Reader Software will turn off the lamp to reduce lamp wear and to reduce system heating up. When a new measurement is started by pressing the 'measure' button, the lamp will turn on again. This will take about 15 seconds. If the AGE Reader isn't used for a long time, warming up as described above is required before measurements can be performed.

6.3. Change settings

The AGE Reader Software has several settings and options that can be changed by the user before the measurement, by choosing the options in the main menu or the optional tool bar at the top of the screen.

The AGE Reader settings are stored for the current project in the file "AFRdata.txt", located in the data folder for that project. Also, the name of the last measurement file is stored in this file.

Main Menu ⟶
Toolbar ⟶

6.3.1. File

- **Exit**
  This option will exit the AGE Reader Software. Alternatively the normal Windows exit-cross at the right-top of the screen can be selected.
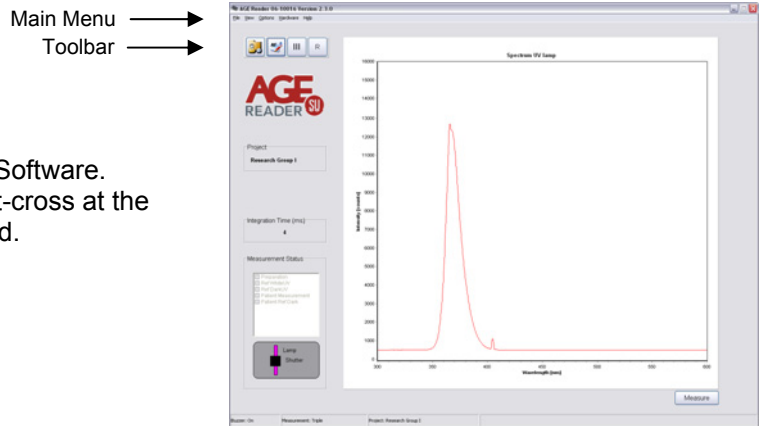
Figure 8. Main Screen & Toolbar

6.3.2. View

- **View Measurement Results**
  This will show the summary results which are stored in the file "info.out" located in the selected folder for Data Storage, see section 6.3.3. Double clicking on a result line will produce the corresponding patient report.

- **Toolbar**
  Toggle the optional toolbar:

⟶ Toggle patient report
⟶ Toggle single or triple measurement
⟶ Show measurement results
⟶ Open measurement file
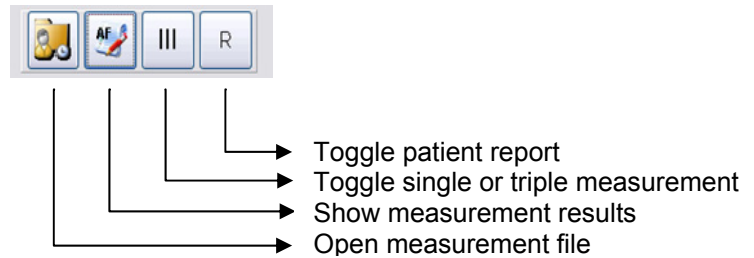
Figure 9. Toolbar

6.3.3. Options

General Settings:
- **Report**
  If enabled, a full patient report including a chart is produced, otherwise only patient data and a numerical AF value are shown.

- **Print Risk**
  If enabled, when printing a full patient report, a second page with information about the different risk classes is printed in addition to the full patient report.

- **Buzzer settings**
  When selected, a buzzer signal is produced at the beginning and end of the patient measurement.

- **Set Project**
  The current project can be changed to another existing project, or a new project can be created. Each project has its own data folder within the root data folder. For each project the project measurements and project settings are stored in the corresponding project folder. The current project is shown on the main screen. When a new project is created, a folder with the project name is created in the root data folder. Initially the project is assigned default user settings. (see also section 6.5.1). See figure 10.
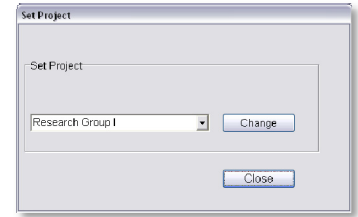
Figure 10. Set Project

- **Printer settings**
  This option opens the Windows Printer Settings Screen where the printer preferences can be changed. The settings affect the print option in the Show Results screen and the print option of the "Patient Report".

- **Report logo**
  This option opens a File Browser where your company logo can be selected to be placed in the head of the "Patient Report". The advised maximum size of this logo is 200x200 pixels. If no logo is selected the default AGE Reader logo will be used instead.

- **Root Data Folder**
  The user can set the root data folder. Data of all subsequent new projects will be stored in subfolders of the root data folder. It is recommended to only set the root folder once on first use. See figure 11.

Measurement settings:

Figure 11. Set root data folder

This option lets you choose whether you want to perform a single measurement or a triple measurement. The triple measurement has been included for increased accuracy. The measurement type selected is shown by the corresponding toolbar button, when enabled, and at the bottom of the main screen.

6.3.4. Hardware

- **Connect AGE Reader**
  If there is no AGE Reader connected and switched on during start-up, the AGE Reader can be connected by this option.

  As described in section 5.2 steps 4 to 8, first, all the required connections to the AGE Reader must have been made before the AGE Reader can be switched on. The user can establish the communication by selecting "Connect AGE Reader" under the Hardware Tab. When the connection is established successfully, the message in figure 12 is shown and the blue "OK" LED on the front panel of the AGE Reader will switch on. On the main screen, a peak will become visible in the chart of the spectrum. Warming up as described in section 6.2 is required before measurements can be taken.

*Figure 12.
AGE Reader found*

6.3.5. Help about

This option will open the About screen. This screen provides information regarding the software version and AGE Reader serial number and calibration file currently used. Also the contact information for DiagnOptics Technologies B.V. is presented here. From this screen the user can also display the "Declaration of Conformity" and the "CE Certificate".

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6.4. Measurements

To start a measurement, press the "Measure" button on the lower right side of the panel.
The 'Patient Data' screen will appear.
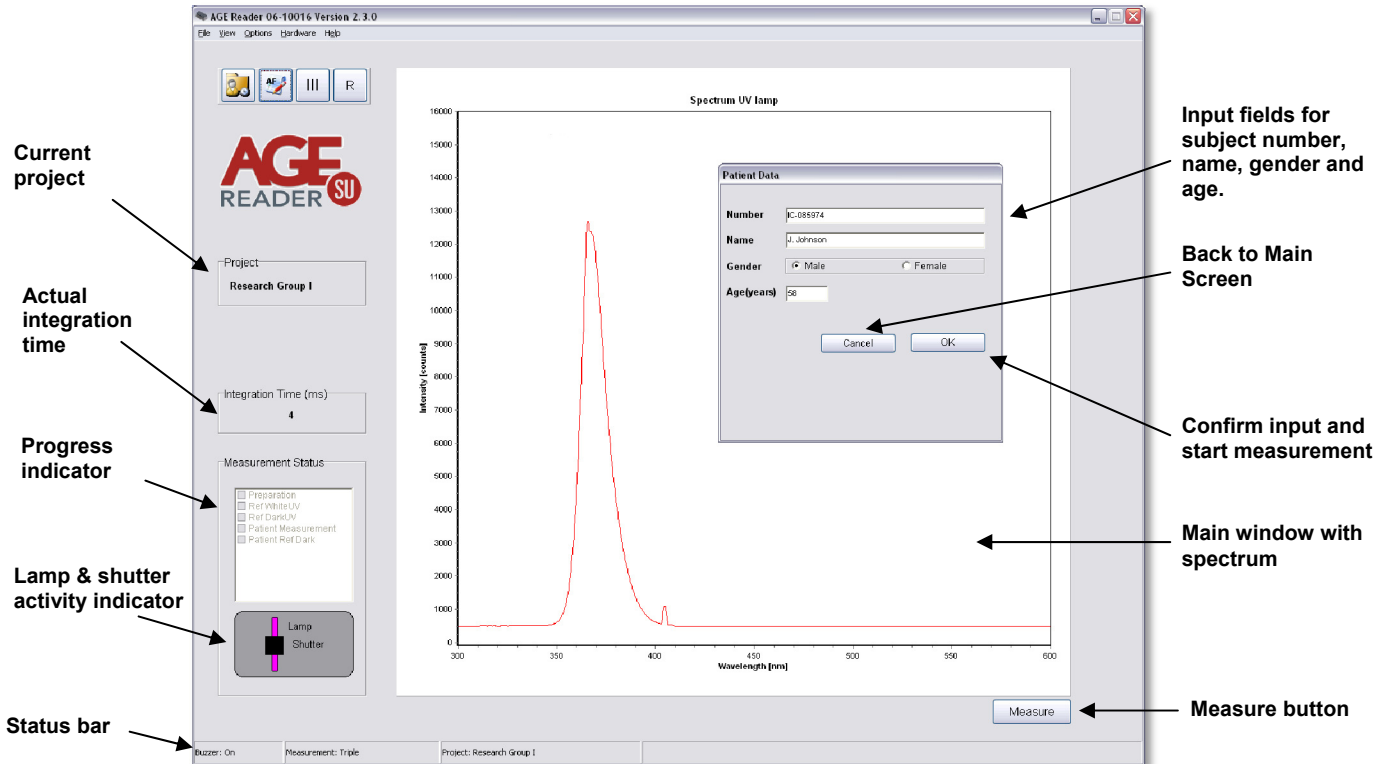
Figure 13. Main screen Layout & Subject Data input screen

The "Patient Data" window as shown in figure 13, allows entering patient number, name, gender and age. (It is also possible to use the first two lines differently, as long as two lines with alpha-numerical characters are used.) If no value, or an invalid value for number name or age are given, a message is produced. Measurements will only start when these fields are valid. If desired, the gender field may be left blank. The lower part of this window shows the folder where the subject data and measurement spectra are stored.

After filling in the patient data, select OK.

The software now starts the automatic measurement procedure of the AGE Reader.

The progress of this procedure is indicated in the progress panel on the left of the main screen. In the left lower panel of the window a symbolic representation informs the user of the activity of the lamp, LED and shutter. The violet colour shows that the lamp is on; if the lamp is off, the colour is black. The black rectangle shows that the shutter is closed. If the shutter is open, the rectangle will be transparent. A white disk indicates that the white LED is on.

During measurement the actual integration time may vary during the measurement steps: it is the time that the spectrometer needs to perform a single scan of the spectrum. It depends on the light source (UV lamp or White LED) and for the subject measurement on the reflectivity of the arm.

The measurement can be cancelled during the measurement process by pressing the Cancel button at the right left bottom of the main screen. In that case after completion of the current measurement step the program reverts back to the ain screen, and no measurement data is stored.

Before the AGE Reader asks for the lower arm to be put on the measurement window of the AGE Reader in step 4, for the actual fluorescence measurement on the patient, the first three steps are done automatically by the AGE Reader Software:

1. **Preparation**

2. **Reference white UV measurement**
   The AGE Reader now detects the UV light intensity reflected from the reference white reflecting sheet within the device. This provides the standard to calculate the reflectance of the skin in the subsequent steps. The lamp will be switched on in this phase.

3. **Reference dark UV measurement**
   The reference dark measurement is performed to allow for corrections to be made for "dark-current" of the spectrometer and possible light leakage. The lamp will be switched off in this phase.

   These first 3 phases should take no more than app. 15 seconds.

4. **Patient measurement**
   During the patient measurement the actual measurement with UV-A light is performed. Before the start of the measurement, optionally a buzzer will be audible to warn the patient that the arm measurement will begin and a window appears asking to put the lower arm on the measurement window, see figure 14.
   Measurements are preferably performed on the dominant arm on healthy undamaged skin without birthmarks or excessive hair growth. Self tanning agents must not have been used for at least 2 days. Sun blockers and other skin creams, when used at the site of the measurement, can also influence the results and should for that reason be removed before the measurement.
   After the patient has put his/her arm on the window as in figure 15 and thereby fully covering it; select "OK". The shutter will open after the OK button is pressed. The yellow "Measuring" LED will switch on. If the window is not covered by an arm, a violet-blue light can be observed through the measurement window.

Figure 14. Notification panel for subject measurement start

Figure 15. Positioning of arm on the AGE Reader

5. **Patient dark measurement**
   The patient dark measurement is the next step in the measurement procedure. The UV lamp is turned off and the shutter remains open. This step is taken to be able to correct for possible leakage of surrounding light between the skin and the upper surface of the AGE Reader during the UV-A measurement. The result will be subtracted from the results of the measurement with the lamp on. Therefore, it is important that the patient keeps the arm in the same position during this part of the measurement. As soon as the last checkbox is filled, the procedure is ended, which is marked by an optional second signal (double beep) from the buzzer. From that moment the "Measuring" LED will turn off.

After the patient has put his/her arm on the window as in figure 15 and thereby fully covering it, the measurement usually takes 20-30 seconds. For increased accuracy, the user may use the "Triple Measurement". This option can be selected on the taskbar (under settings) or on the toolbar see sections 6.3.2 and 6.3.3. In case of a "Triple Measurement", it is advised that the patient covers the window with the arm each time at a slightly different position. For a Triple measurement steps 4-5 are repeated 3 times.

If the UV reflectance of the arm is less than 12%, steps 2-5 are repeated with a white LED light source, to enable corrections for low reflectance. This is indicated by the appearance of a further 4 check boxes. In the case of a triple measurement and low reflectance the LED measurement is only performed once.

If the reflectance is less than 6%, a warning message is given and no result is produced.

After successful completion of the measurement, within a few seconds the "Patient Report" is shown. If "Report" is selected, the full report shown in figure 16 will appear. Pressing "Next Page" on this report displays a second page with information about the Risk Classes as shown in section 6.8. This report can be printed. If in addition "Print Risk" is selected, the second page with risk information is also printed. When "Report" is not selected, a brief summary is given as shown in figure 17.

The measurement result is automatically stored in the current project folder.
Remark: in patients with darker skin colour (Fitzpatrick class 5-6, dark brown or black) a correction is made to the AF value when the reflectance is between 6 and 10%. If the UV reflectance is below 6%, the AGE Reader SU will give a warning that the signal is too low for valid results.
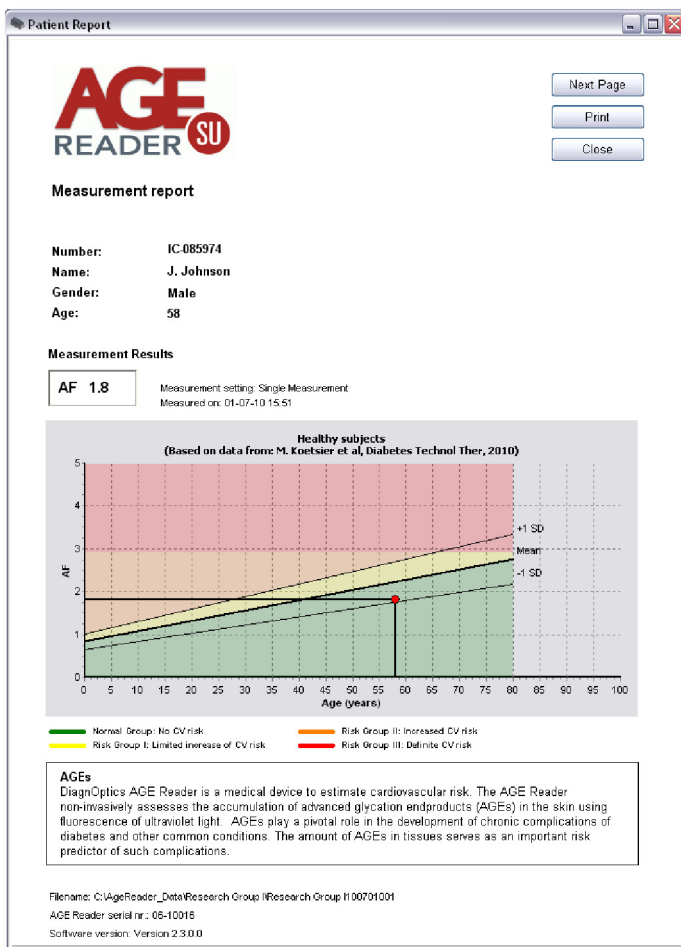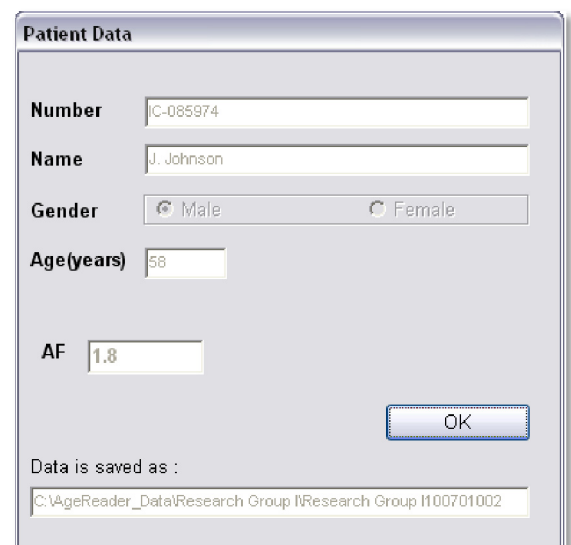

Figure 16. Patient Report

Figure 17. Brief summary

The measurement is now completed and the program can do another measurement or be closed.
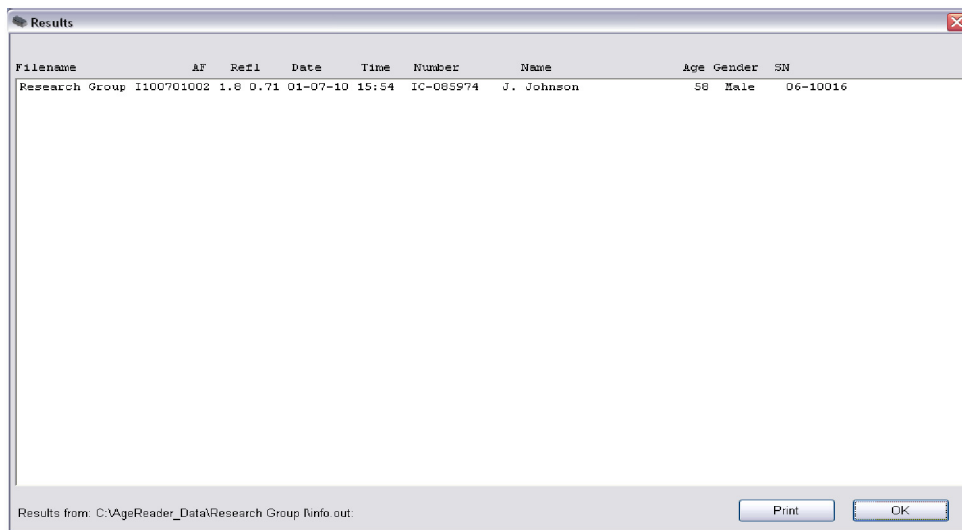
6.5. Data storage and additional information

This section explains and illustrates the type and location of the files of the saved measurements. It also shows the summarising info file which gives the AF and Reflectance results for each measurement. This section also gives background information on the calculation of AF.

Results are stored in the current project folder. Each time a successful measurement is made with the AGE Reader the AF result, Reflectance, and the patient data are added to the "info.out" summary file for the current project. This file is located in the project folder, which has the name of the project, situated in the Root Data Folder selected by the user under "Settings" (see section 6.3.3). At the same time the essential results of each measurement are also stored in a "DCF" File in the same folder, for backup and future use.

6.5.1. Summary results

The summary results are stored in the file "info-out" for the current project. The summary results can be accessed by the "view" tab in the taskbar or by the toolbar, see section 6.3.2. An example of this window is given in figure 18. By double-clicking on a line in this window, the corresponding patient report will be shown. The summary results presented in the info file are sufficient for normal use of the AGE Reader.

Figure 18. Summary results, Info.out

The file "info.out" contains the AF and reflectance results and the information supplied at the beginning of the measurement, stored as patient number, name, age and gender.

The file fields are, from left to right:
- File name: Designated by the AGE Reader, see section 6.5.2
- AF: The autofluorescence value as calculated
- Reflectance: The skin reflectance value as calculated
- Date   Date of measurement
- Time   Time of measurement
- Number: Subject number as given before measurement
- Name   Subject name as given before measurement
- Age: Subject age as given before measurement
- Gender :   Subject gender as given before measurement
- Serial number: Serial number of the AGE Reader used.

The data are stored in a text format, and can be exported to other file formats like Excel or Word in a conventional manner.

6.5.2. DCF Files

All the data from a measurement is stored in a DCF-file containing the raw spectra per measurement. This file is in a proprietary format and can only be read by DiagnOptics software.

The DCF filenames are constructed from the project name that has been given by the user in the File Storage window under Settings (see section 6.3.3), as well as by year, month and date of measurement and a consecutive number of the measurement made during this calendar day. When a new day has started, the numbering of files starts again with 001. In this way, all filenames remain unique.

The files are stored in a compact DCF file format, and also contain time and date of the measurement, spectrometer information and the patient data that was given by the user at the start of the measurement.

The DCF files are intended for back-up of the measurements for future use. When problems with the instrument are detected, the user may send the corresponding files to DiagnOptics for support. Future developments on the software of the AGE Reader may lead to further improvements of algorithms that can then be applied to recalculation of AF values on stored results. If you would be interested in this option, it is important to store the measured files for future use!

6.5.3. Storage of settings

For each project, the settings and preferences concerning the AGE Reader are stored in the file "AFRdata.txt", located in the current project folder. For a new project, the settings are given default values obtained from the file "DefaultAFRData.txt".
For Windows XP and older versions of Windows the DefaultAFRData.txt file is located in the Folder "Documents and Settings\All Users\Application Data\Age-Reader". For Windows Vista and Windows 7 this is stored in "ProgramData\Age-Reader".

The "AFRdata.txt" file for the current project is automatically updated when changes to settings are made in the program and should not be edited by the user.
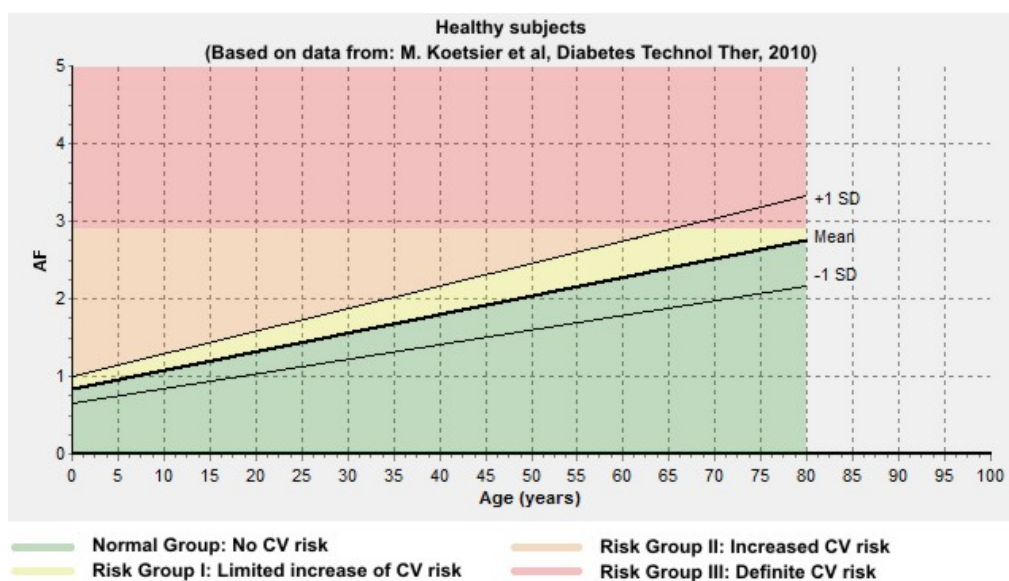
6.6. Background on AF

Age is usually the most important factor determining AGE content in different organs. Skin AF as measured by the AGE Reader is also influenced by age. The reference values for skin AF have been based on 456 measurements in Caucasian subjects without cardiovascular disease (smokers and non-smokers) [Lutgers et al., Diabetes Care 2006, and Koetsier et al, Diabetes Technology & Therapeutics, 2010; 12(5):399-403].
Table 2 shows the mean values of the AF for several age decades. Values of skin AF are in arbitrary units ± 1 standard deviation. N represents the number of subjects in the respective age groups.

Table 2. Mean skin autofluorescence per age decades

age group (years)	AF	N	p
0-10	0.97 ± 0.17	45	< 0.01
10-20	1.11 ± 0.20	50	< 0.01
20-30	1.53 ± 0.30	62	< 0.01
30-40	1.73 ± 0.42	86	0.21
40-50	1.81 ± 0.36	72	< 0.01
50-60	2.09 ± 0.36	64	< 0.01
60-70	2.46 ± 0.57	45	0.12
70-80	2.73 ± 0.55	27	0.51
80+	2.71 ± 0.44	5	

Graph 1 Mean values of skin AF as a function of age, together with the lines representing mean +/- 1 standard deviation. The coloured areas indicate the risk classes corresponding to skin AF combined with age value.

6.7. Background on calculation of skin AF

Skin AF is calculated as the ratio of the light intensity reflected by the skin in the 420-600 nm wavelength range, and the light intensity in the 300-420 nm wavelength range. By using calibrated spectrometers, the results obtained by different AGE Reader CUs are comparable.
When skin reflectance R < 12%, an additional measurement is performed with a white LED to allow for more reliable skin AF values.
Each AGE Reader CU has a unique calibration file that is stored on the internal flash-drive. In this an individual correction factor for each wavelength, corrections for reflectance and several other parameters are stored.

No reliable skin AF results are possible with the current AGE Reader SU software (version 2.3) if the reflectance is below 6 %. In that case no value is given for the skin AF.

6.8. Cardiovascular risk interpretation
for Type 2 diabetes patients based on the measured AF value

The AF value provided by the AGE Reader increases considerably with age, both in healthy persons and in those with diabetes or renal disease. Calendar age is in fact the strongest determinant of AF values. Keep in mind that calendar age itself is also by far the strongest risk indicator in terms of cardiovascular risk (CV risk), as is evident from all known risk scores. Thus, a healthy elderly person may have a higher AF value than a much younger patient with diabetes. Therefore, age-dependent AF values within levels up to 1 standard deviation (1 SD) above the age-corrected mean may serve as reference values for a certain age, but can be considered normal only for the corresponding age group.

AF values provided by the AGE Reader should be considered as complementary to, and not a replacement for assessment of conventional cardiovascular risk factors and risk scores. When other risk factors such as blood pressure or cholesterol levels are clearly increased, a low AF level is not a reason to withhold treatment. This especially holds for younger people with extreme values of conventional risk factors.

Always keep in mind that in case of markedly abnormal AF values (high or low) one should make sure that the AF measurement has been properly performed and that the measured person has not used skin creams, sun blockers or tanning agents.

Normal group*: No CV risk*
If the AF value is below or equal to the age-related mean, the subject has no calendar age-corrected increase in risk of diabetes or cardiovascular disease. However if the subject is an elderly person and the AF value is above 2.5 (even though it is at the age-related mean), the subject may still have increased cardiovascular risk due to his/her calendar age.

Risk Group I: Limited Increase of CV risk
If the AF measurement value is above the average but within 1 SD of the age-related mean, the subject has a limited increase, corrected for calendar age, in his/her risk of diabetes or cardiovascular disease.

Risk Group II: Increased CV risk
If the AF measurement value is above 1 SD of the age related mean, the subject has increased risk in comparison to his/her age group. In such a case, the advice is to check the levels of other cardiovascular risk factors such as blood pressure and lipid levels. Depending on overall CV risk, lifestyle or even pharmaceutical treatment should be considered.

Risk Group III: Definite CV risk
If the AF measurement value is 2.9 or above, the subject definitely has a high risk of cardiovascular disease or diabetes. It is recommended that other cardiovascular risk factors should be assessed and treated, with low threshold and target values for starting or intensifying treatment.

Used in combination with conventional risk scores (UKPDS, SCORE) the following advice applies:
- **Normal Group**: no risk reclassification to be considered
- **Risk Group I**:   no risk reclassification to be considered
- **Risk Group II**: consider reclassification to a higher CV risk class
- **Risk Group III:** classification as high or very high CV risk class suggested

For further information please contact DiagnOpticsTechnologies B.V. at info@diagnoptics.com.

7. Cleaning & maintenance

7.1. Cleaning instructions

- **The measurement window**
  The measurement window should always be kept clean!
  In the design of the AGE Reader, special attention is given to make cleaning of the window easy by removing the silicone-mat, which is designed with an integrated grip for easy removal, see figures 3 and 4. Hold the housing down on a stable surface and carefully remove the mat. Clean the window with a slightly humidified soft non-fluorescent cleaning wipe (for example the soft reusable cleaning wipes used for spectacles) using a standard 70% alcohol solution. Avoid scratches on the window and take care that no parts of textile or paper are remaining on the window, as textiles and paper show fluorescence and so may affect the autofluorescence measurement!

- **The silicone patient mat**
  The silicone patient mat can be cleaned with standard cleaning agents by removing the silicone mat by its integrated grip for easy removal.
  If desired, the silicone mat can be disinfected with alcohol or chlorhexidine.

- **The housing**
  The housing can be wiped with standard cleaning agents; for example a slightly humidified cloth or alcohol tissues. Make sure no fluids enter the housing at the connector inlets.

7.2. Maintenance instructions

This system does not contain parts that can be serviced by the user!
The AGE Reader is a very sensitive instrument which has been carefully calibrated before use. Small differences exist in the characteristics of the internal optics of the individual spectrometers used. The same holds for differences in lamp spectrum characteristics. Albeit small, such differences may affect the measurement results of the AGE Reader, and may impede comparisons of results between individual instruments. The software takes these differences into account and makes comparisons of AGE Reader autofluorescence and reflectance results possible for different AGE Readers. Therefore, unique calibration files of each individual system are used in the AGE Reader software. The software will detect which spectrometer is contained in the AGE Reader, and will only function after recognition of the correct spectrometer. **So, never make changes in the system on your own!**
If damage is done only to the silicone mat, the USB cable or the power supply, a replacement can be ordered, see chapter 11.

Frequency of maintenance:
Replacement of lamp by DiagnOptics after +/- 2000 measurements.

Contact:
Contact the DiagnOptics Technologies B.V. head office in Groningen (The Netherlands) preferably by e-mail or fax, if necessary by telephone. Always have the serial number of the AGE Reader at your disposal.

Our address for support is as follows:

> DiagnOptics Technologies B.V.
> E-mail: support@diagnoptics.com
> Fax: +31 50 5890613
> Tel.: +31 50 5890612

8.   Problems & solutions

If a malfunctioning of the AGE Reader or the AGE Reader software occurs, always make sure that:
- The external power supply (art. nr.: 214B51601) accompanying the AGE Reader is used.
- A computer approved for medical use is used, running 32-bit Windows 2000 or newer versions.
- The power supply and USB-cable are correctly connected.

8.1.   Software errors

The following software errors and their corresponding error message can occur. The possible solution for each error is stated. If the problem is persistent, contact DiagnOptics.

Table 3. Software errors

ERROR MESSAGE	POSSIBLE SOLUTIONS
No AGE Reader found	Check USB cable and power supply connection to AGE Reader
Hardware error, switch AGE Reader off and on. Program will halt.	
USB connection lost. Switch AGE Reader off and on and restart software.	
Incompatible Calibration Data File	Contact your AGE Reader dealer
Error in reading Calibration data file. Contact DiagnOptics Technologies	Re-install AGE Reader<serial number>.dcf file or contact your AGE Reader dealer
Please install the file "AGEreader….DCF"; Program will be terminated.	
Error in reading Reflectance data file	
Correction File (AGEreader*.DCF) for this AGE Reader was not found. Program will be terminated.	
You exceeded 999 files on this day.	Start new File Project Name under Settings / File Storage
"Folder for DataStorage" not found, and set to C:\. May be changed under Settings'	You may have renamed the Folder for Data Storage. Choose new Folder under Options – General Settings - File Storage
AFRdata.txt not found in Folder of Program File: program HALTED	This file contains the name of the last saved file! Therefore: <u>Do not</u> copy from CD-ROM as loss of files of the current date may occur. Ask advice at DiagnOptics.
More than 5 correction files (AGEReader *.DCF) installed. Program will be terminated.	No more than 5 AGE Readers can be installed in the same folder, remove the excess files.
Filename already exists. Please change Project Name of the Files in the Project/Filestorage menu.	Choose new Project Name under Options – General Settings - File Storage
Screen adaptation necessary: PPI= …; Contact DiagnOptics Technologies	Change screen resolution to 96 or 120 dpi, Contact DiagnOptics Technologies
Minimum screensize for this version of the AGE Reader software is 800x600 pixels. Please contact DiagnOptics Technologies	Change screen size to at least 800x600 pixels, Contact DiagnOptics Technologies
******.DCF is a calibration file. Please select a measurement file.	Please select a measurement file.
This measurement file was not created with AGE Reader software version 2.1 or higher, please select another file.	Please select a measurement file created with Software version 2.1 or higher.
Info.out not found. Hint: Change Directory	Change Directory under Options – General Settings - File Storage
Shutter defect	Contact DiagnOptics

8.2. Hardware errors

Correct functioning of the software and the USB connection are conditions that are checked by the hardware. In case of failure lamp and shutter are turned off after one minute. In this way it is prevented that e.g. the lamp will remain on when the USB connection is disrupted and the power connection is not disrupted, or that the AGE Reader can persist in a condition with the shutter open with the lamp 'on' even when no measurement takes place.

A separate hardware condition to prevent too high temperatures is given by a thermal switch, checking that the temperature of the AGE Reader will not be too high, such as under the exceptional conditions that the lamp and/or shutter are ON during an exceptionally long period. In those situations the 12 V power is disconnected. It resets itself when the temperature is safe again.

In case the hardware of the AGE Reader stops functioning due to an error, the following warning signals will be given:

- Green "Power" LED   on
  Blue "OK" LED   off
  Long audible signal   yes

  Solutions:
  - Software does not function: Close the program and try to start it again.
  - Connection problem: Check USB connection. In this case, the software probably has already reported problems earlier.
  - AGE Reader is too hot: Wait until the green LED is turned on again.

- Green "Power" LED   off
  Blue "OK" LED   off
  Long audible signal   no

  Solutions:
  - Check power switch, power cable and supply connection.
  - If not corrected, contact DiagnOptics.

Contact:
Contact the DiagnOptics Technologies B.V. head office in Groningen (The Netherlands) preferably by e-mail or fax, if necessary by telephone. Always have the serial number of the AGE Reader at your disposal.

Our address for support is:

> DiagnOptics Technologies B.V.
> E-mail: support@diagnoptics.com
> Fax: +31 50 5890613
> Tel.:   +31 50 5890612

9. Product specifications

9.1. Technical specifications

AGE Reader:
- Operation   Continuous operation
- Power   12 VDC from external power supply (art. nr.: 214B51601) in compliance with IEC 60601-1 for general safety and IEC 60601-1-2 for EMC requirements, connected to mains.
- Output   UV-A light $\Delta\lambda$ = 345nm – 410nm
  Peak wavelength λ = 365nm
  Irradiance E = 123 W m^{-2}
- Physical   Width: 280 mm
  Depth: 150 mm
  Height: 115 mm
- Material (ext.)   Housing: ABS/PMMA
  Patient-mat: black Silicone
- Weight: 3 kg
- Operating Conditions:
  o temperature range: Lower limit + 10ºC
     Upper limit + 40°C
  o Relative humidity: 30% to 75%
- Storage & Transport Conditions:
  o temperature range: Lower limit - 40ºC
     Upper limit + 70°C
  o Relative humidity: 10% to 100%

Power Supply (214B51601):
- Input   100 - 240 VAC
  0,6 A
  47 - 63 Hz
- Output   12 VDC
  1,7A

9.2. Classifications

AGE Reader:
- Classification to 93/42/EEC   Class IIa
- Classification to IEC 60601-1   Class II
- Protection against elec.shock   Type B
- Protect. against ingress water IPX1
- Directive(s):   Council Directive 93/42/EEC
- Standard(s):   Safety: International Standard IEC 60601-1
  EMC: International Standard IEC 60601-1-2
  Risk Analysis   International Standard ISO 14971
  Quality   European Standard NEN-EN-ISO 13485

Power Supply (214B51601):
- Classification to IEC 60601-1   Class I
- Standard(s):   Safety: International Standard IEC 60601-1
  EMC: International Standard IEC 60601-1-2

10. Marking on AGE Reader

As far as practical and appropriate, the information needed to install the device safely is set out on the labelling on the device itself and/or on the packaging for each unit. Where possible, this information is presented in the form of symbols in conformance with the harmonized standards.

The labelling on the device itself consists of:

1.	Rear label	All necessary information for product identification, product specification, installation, use and warnings.
2.	Serial label	Serial number and contact information of manufacturer
3.	Front label	Information during use.
4.	On / off switch	Information regarding position of switch relative to its function.
5.	Symbol in applied part	Informs the patient the desired direction of the arm
6.	Power supply	Information on identification

10.1. The rear label

The rear label as shown in figure 20, is located at the back of the AGE Reader, see figure 19. All necessary information for identification of the manufacturer, product identification, installation, use and applicable warnings are presented visually for the user.
The rear label incorporates two connector inlets (see figure 20), one inlet for the accompanying power supply and one connector inlet for the USB connection and identifies them as such.
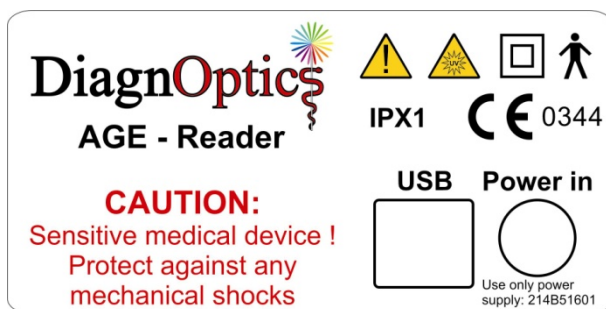

Figure 19. AGE Reader back view

Figure 20. Rear label (scale 1:1)

Table 4. Used symbols on rear label

DiagnOptics	Name / Logo of the manufacturer
AGE Reader	Identification of device, device name
⚠️	Attention, consult accompanying documents
▣	Class II symbol, double isolated
🧍	Type B symbol for protection against electric shock
IPX1	Symbol for degree of protection against dripping water
CE 0344	CE-Mark & Notified body number
⚠️ (UV)	Warning for UV emissions
CAUTION: Sensitive medical device! Protect against any mechanical shocks	Warning for mechanical shocks.
USB	Identifies the USB connector
Power in	Identifies the power-in connector
Use only power supply: 214B51601	Instruction to use only the certified power supply accompanying the device.

10.2. The serial label

The serial label as shown in figure 22 is located at the bottom of the AGE Reader, see figure 21.
All necessary information for product identification, product specification and the name and address of the manufacturer are presented visually for the user.

Figure 21. AGE Reader bottom

Type	**214B00102**
SN	**06-10001**
�	**2006-02**

DiagnOptics
L.J. Zielstraweg 1
9713 GX Groningen
The Netherlands
www.diagnoptics.com

No serviceable parts inside.
Servicing to any component of this device is to be performed by DiagnOptics only. Unauthorized repairs or modifications will void the warranty and may violate the conformity of the AGE-Reader with the requirements of the Medical Device Directive 93/42/EEG.

Figure 22. Serial label (scale 1:1)

Table 5. Used symbols on serial label

Type 214B00102	Type identification
SN 06-10001	Serial number
	Date of manufacture; YYYY-MM
No serviceable parts inside. Servicing to any component of this device is to be performed by DiagnOptics only. Unauthorized repairs or modifications will void the warranty and may violate the conformity of the AGE Reader with the requirements of the Medical Device Directive 93/42/EEG.	Warning not to service the device by the user
DiagnOptics L.J. Zielstraweg 1 9713 GX Groningen The Netherlands www.diagnoptics.com	Manufacturers name / logo and contact information

10.3. The front label

The front label, see figure 23, is located at the front of the AGE Reader as seen in figure 24.
All necessary information during use is presented visually for the user. The information presented will inform the user of the state of the device.
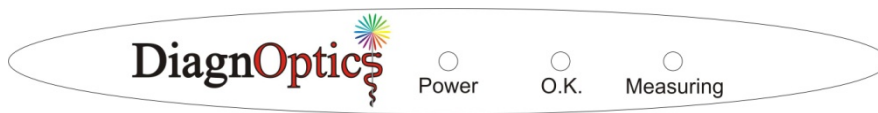

Figure 23. Front label (scale 1:1)

Figure 24. AGE Reader front side

Table 6. Symbols used on front label

DiagnOptics	Manufacturers name / logo
Power	Reference for green LED; on is "power connected"
O.K.	Reference for blue LED; on is "system O.K."
Measuring	Reference for yellow LED; on is "patient measurement"

10.4. On / off switch

The on / off switch is located at the back of the left side of the AGE Reader as shown in figure 25.
The different positions of the "power on / off switch" shall be indicated by visual means, as listed in table 7.

Figure 25. On / off switch

Table 7. Symbols used on On / Off switch

O	"Power off" symbol. If pressed, unit is turned off
I	"Power on" symbol. If pressed, unit is turned on
O I	Order of marking

10.5. Symbol in applied part

In the design of the silicone mat an ergonomically shaped armrest is moulded for the patient to rest the underarm in. The direction of the arm is shown by a figure of a hand that is moulded in the silicone mat as shown in figure 26.
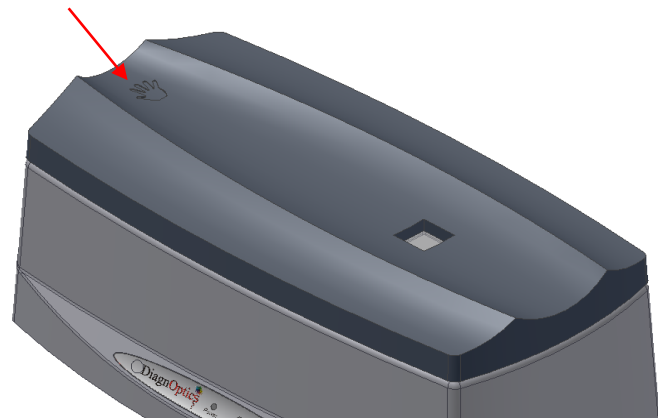

Figure 26. Applied part with symbol

10.6. Power supply label

The medical approved power supply accompanying the AGE Reader is labelled as in figure 27. The label is placed on the bottom of the power supply.
The label shows the DiagnOptics identification number of the power supply as is referred to on the rear label. This will identify this power supply as the only correct part in order to obtain a safe combination.

Power supply: 214B51601

Figure 27. Power supply lab

10.7. CD label

The AGE Reader is accompanied by a CD-ROM containing the necessary software to operate the AGE Reader. The CD-ROM is provided with a "DiagnOptics CD label" as shown in figure 28, the information presented on the CD-ROM is listed in table 8.

Each CD-ROM is unique for each device due to a unique calibration file and is not interchangeable. The serial number of the AGE Reader corresponds with the SN number in hand writing on the CD label. A note of this uniqueness for the user is stated under this number.
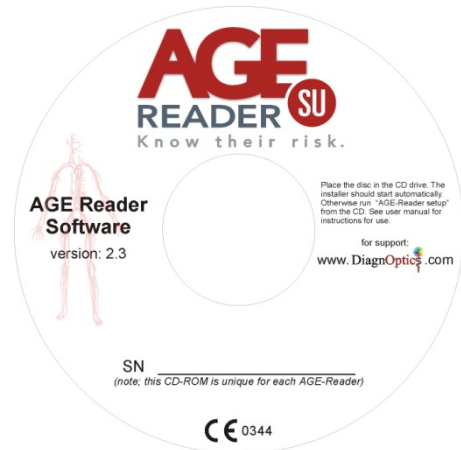
Figure 28. CD label (scale 1:2)

Table 8. Symbols used on CD label

AGE READER SU Know their risk.	Identification of device it belongs to
AGE Reader software version 2.3	Identification of software and software version.
SN _____ *(note; this CD-ROM is unique for each AGE Reader)*	Serial number & note to its uniqueness
Place the disc in the CD drive. The installer should start automatically. Otherwise run "AGE Reader setup" from the CD. See user manual for instructions for use.	Installation instructions & reference to the user manual.
For support: **www.DiagnOptics.com**	Name / Logo of the manufacturer with reference to the support and contact information on the website of the manufacturer.
CE 0344	CE-Mark & Notified body number (6 mm high)

10.8. Packaging

Each AGE Reader, together with its user manual, CD with software and its power supply will be packed in protective packaging right after production for storage and shipment. All packaging materials can be recycled if disposed of separately.

All following information will be placed on each package by the label as in figure 29:

- DiagnOptics logo & address,
- Serial number,
- Content,
- Weight,

Figure 29. DiagnOptics packaging label (scale 1:1)

11. Spare parts

If damage occurs to the silicone mat or the power supply, a replacement can be ordered at our head office in Groningen, The Netherlands.

Be sure that the damage is limited only to the silicone mat or the power supply. If any doubt should exist that damage has been done to the AGE Reader itself, please contact DiagnOptics.

Send your request by e-mail or fax and clearly state the serial number(s) of the AGE Reader(s) concerning. Also include the article number(s) of the spare parts you would like to order. The article numbers for the spare parts of this device are listed in table 9:

Table 9. Spare parts

Spare part	Article number
Silicone patient mat	214B13002
External power supply	214B51601
USB cable	214B51901

Our address for support is as follows:

DiagnOptics Technologies B.V.
E-mail: support@diagnoptics.com
Fax: +31 50 5890613
Tel.:   +31 50 5890612

12. Liability & warranty

12.1. Liability

DiagnOptics Technologies B.V. and its respective directors, officers, employees and agents and their respective successors, heirs and assigns, are not liable for any damages, losses, obligations, costs and expenses, including attorney's fees that may incur by third parties in connection with a claim for damage to or loss of tangible personal property, breach of warranty, or for bodily injury, sickness and/or death sustained by any customer (collectively "Damage") if or where the Damage is caused by or arises in connection with (a) improper use of the AGE Reader, (b) unauthorized modification of the AGE Reader, (c) fault or negligence by the user, (d) breach of any warranty or other obligation by the user or (e) invalid or wrong conclusions, and any consequences thereof, drawn by third parties from the measurement results provided by the AGE Reader.

12.2. Warranty

The warranty supplied with this AGE Reader System is provided separately.

12.3. Declaration of Conformity

The Declaration of Conformity is provided separately.