FMS-OXYGEN
HEADSPACE ANALYZER

Operation Manual

LIGHTHOUSE

About This Manual

Intended Audience and Scope

The intent of this manual is to provide essential information on installation and operation of the FMS-Oxygen Headspace Analyzer. Following the instructions in this manual should assure problem free installation and operation. Read this manual in its entirety. Make sure that you understand all installation, operation, and maintenance information before using the instrument. Obey all the safety instructions.

Liability

Lighthouse Instruments assumes no responsibility whatsoever for accident or equipment trouble arising from the failure to observe handling instructions contained herein. Do not perform any operation or handle the equipment in any way or form that is not described in this manual. Careless usage may result in unexpected damage to the equipment.

Note: The instrument cover is to be removed and the instrument is to be serviced by qualified personnel only. Contact Lighthouse Instruments for service.

Service and Support

If you require service or technical support, please contact Lighthouse Instruments.

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Revision 4.1706

Table of Contents

General Information

Product Overview

The FMS Series is a family of nondestructive gas analyzers intended for monitoring headspace gas composition in optically transparent, sealed containers. The analyzers utilize high sensitivity, near infrared spectroscopy and are suitable for a number of research and production applications. The instruments are compact, robust, and allow for measurements to be made in the laboratory or on the production floor.

The FMS-Oxygen Headspace Analyzer is designed specifically for monitoring oxygen in sealed containers and is useful during stability testing or in-process monitoring of pharmaceutical products that are packaged using inert gas overlays. The analyzer is capable of measuring oxygen concentrations in the headspace of optically transparent packages that contain liquid, dry powder, or lyophilized products. Light from a near infrared laser is passed through a container in the region above the product and below the seal (headspace region). The laser frequency is tuned to match an internal absorption frequency of the oxygen molecule. The amount of light absorbed while passing through the container is measured and related to the oxygen concentration. For more information, refer to “Theory of Operation” in the Appendix.

Specifications

General System Specifications

Measurement Time:	5 seconds (default)
Initial warm-up period:	30 minutes
Dimensions (HxWxD):	292 x 305 x 305 mm (11.5" x 12.0" x 12.0")
Weight:	13.6 kg (30 lbs)

Power Requirements

Input Voltage:	100/115/230 VAC (noted on rear panel)
Input Frequency:	50/60 Hz
Power:	60 Watts
Fuse Rating:	2A (100–115 VAC) or 1A (230 VAC)
Fuse Type:	5x20mm, 250V

Purge Gas Requirements

Gas Type:	Nitrogen
Gas Purity:	less than 20ppm of oxygen
Maximum Inlet Pressure:	6 bar (90 PSI)

Environment

Storage Temperature:	-40 to 70°C (-40 to 158°F)
Optimum Operating Temperature:	15 to 30°C (59 to 86°F)

Safety

Caution: Laser power up to 3 mW at 760 nm could be accessible at the laser aperture.

Caution: Use of controls or adjustments or performance of procedures other than those specified herein may result in hazardous laser radiation exposure.

The system utilizes a laser sensor for headspace measurements. The system is classified as a **Class I laser product** and **complies with US CDRH 21 CFR 1040 and IEC/EN 60825-1:2014** when the system is operated as intended. Care should be taken to avoid direct exposure to the laser. Reflective surfaces (such as mirrors) should not be inserted into the laser beam path while the system power is on.

ID/Certification Label:

100 VAC

LIGHTHOUSE INSTRUMENTS
2020 AVON COURT
CHARLOTTESVILLE, VA 22902
CLASS 1 LASER PRODUCT PER
US CDRH 21 CFR 1040 AND
IEC/EN 60825-1:2014
MODEL: FMS-XXX
PART #: 10E-880-XXX
SERIAL #: XXX
MFG DATE: XX-XX-XXXX
FREQ: 50/60 Hz
AMPS: 0.5A
VOLTS: 100V
FUSE: 5mm X 20mm, 250V, 2A

115 VAC

LIGHTHOUSE INSTRUMENTS
2020 AVON COURT
CHARLOTTESVILLE, VA 22902
CLASS 1 LASER PRODUCT PER
US CDRH 21 CFR 1040 AND
IEC/EN 60825-1:2014
MODEL: FMS-XXX
PART #: 10E-880-XXX
SERIAL #: XXX
MFG DATE: XX-XX-XXXX
FREQ: 50/60 Hz
AMPS: 0.5A
VOLTS: 115V
FUSE: 5mm X 20mm, 250V, 2A

230 VAC

LIGHTHOUSE INSTRUMENTS
2020 AVON COURT
CHARLOTTESVILLE, VA 22902
CLASS 1 LASER PRODUCT PER
US CDRH 21 CFR 1040 AND
IEC/EN 60825-1:2014
MODEL: FMS-XXX
PART #: 10E-880-XXX
SERIAL #: XXX
MFG DATE: XX-XX-XXXX
FREQ: 50/60 Hz
AMPS: 0.25A
VOLTS: 230V
FUSE: 5mm X 20mm, 250V, 1A

Maintenance

Always turn off the instrument before performing maintenance work.

- The cabinet exterior may be wiped with a towel moistened with alcohol.
- Debris may be removed from the interior of the sample chamber by blowing into the chamber with an inert duster of the type used to clean electronics (e.g. RX1100-10 manufactured by NTE Electronics). Do not invert the can, as liquid propellant may be emitted. Wear eye protection to guard against flying debris.

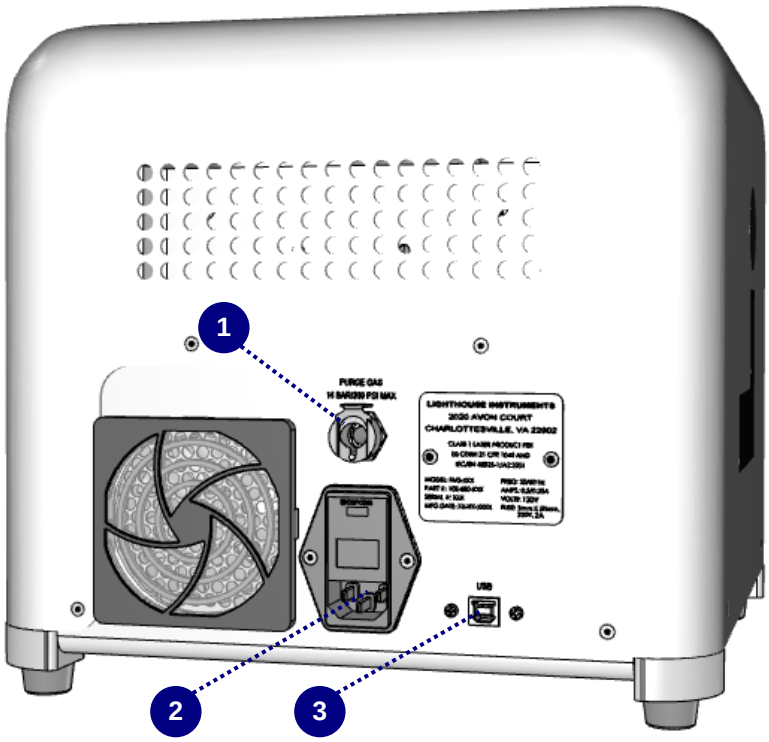
Service

The instrument cover is to be removed and the instrument is to be serviced by qualified personnel only. Contact Lighthouse Instruments for service.

Installation and Setup

Rear Panel Connections

The image below shows the FMS-Oxygen Headspace Analyzer rear panel. The instrument installation and setup involves making three connections to the instrument rear panel. The required connections are the purge gas, power supply, and USB cable.



1. Purge Gas Connection
2. Power Entry Module
3. USB Connection

Purge Gas Connection

The purge gas connects to the instrument on the rear panel. Tubing is supplied with the instrument and connects to a female 0.25-inch quick-connect coupler labeled *Purge Gas*. Press the male connector of the tubing into the coupler until it snaps into place. To release the connector, press the metal tab on the top of the coupler.

The requirements for the purge gas are listed under “Specifications” on page 4.

Power Entry Module

The power entry module consists of a power line connection and two fuses. The input voltage is noted on the rear panel. Power is supplied to the instrument through a standard IEC-60320-C13 power cable, which is supplied with the instrument.

USB Connection

The instrument connects to the computer with a standard USB A-to-B (male/male) cable. A USB cable is supplied with the instrument.

Computer Setup

Please refer to the computer manufacturer's manuals supplied with the instrument for computer setup, operation, and troubleshooting.

Software Installation

The FMS control software and associated hardware drivers are provided by Lighthouse. Follow the instructions in the readme.txt file located on the installation disk.

Instrument-Computer Connection

Connect the A Type end of the USB cable to the computer and the B Type end to the rear of the instrument. This connection should not be made until all software has been installed.

Recommended Setup for GxP Compliance

When collecting data that must be compliant with data integrity regulations, measurements should be performed using the GxP mode of the software. (See "Open and GxP Software Modes" on page 9 for a description of the software modes.) In order to protect data from modification, it is recommended that the computer be configured to restrict user access to the software and file system. Refer to the procedures "GxP Setup for FMS Software Using Network File Storage" and "GxP Setup for FMS Software Using Printed Reports" in the Appendix for instructions on the recommended computer setup.

For systems with the GxP Database software package installed, the GxP data is already protected and additional computer setup is not required.

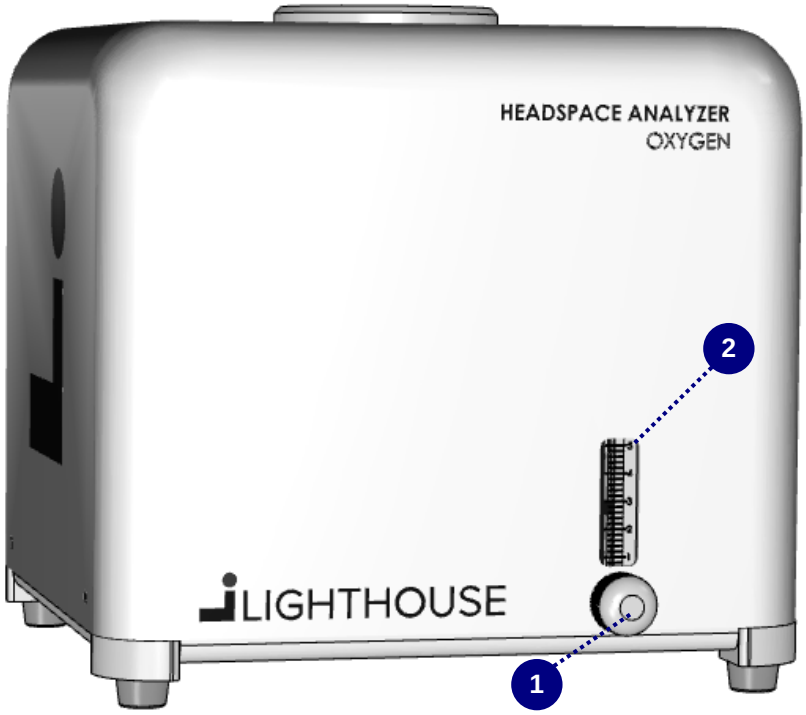
System Controls

The FMS-Oxygen Headspace Analyzer is a portable, benchtop instrument that requires no sample preparation or special configuration. The sample chamber (accessible from the top of the instrument) is purged with nitrogen gas to eliminate ambient oxygen from the measurement region. The nitrogen gas is input through a back panel connection and the flow rate is controlled from the front panel flowmeter. Containers are inserted into the sample chamber and the signal is output to the computer. The signal is analyzed and measurements are recorded through the use of the software interface

Power Up/Warm Up

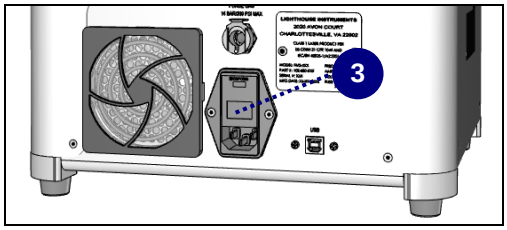
Once the software is installed and rear panel connections are made, the system may be turned on. The instrument should warm up for at least 30 minutes before making measurements.

Instrument Layout



1. Flowmeter control knob
2. Flowmeter gauge / Power Indicator
3. Power Switch (on rear panel)

Rear Panel



Flowmeter

The flowmeter controls the amount of purge gas flowing into the sample chamber. Turn the knob in the counter-clockwise direction to open the flow, and in the clockwise direction to close the flow. The flow rate in SLPM (standard liters per minute) is indicated by the vertical position of the black ‘float’ relative to the scale displayed on the face of the flowmeter. The purge should be set to at least 3.0 SLPM when the instrument is in use.

Power Switch

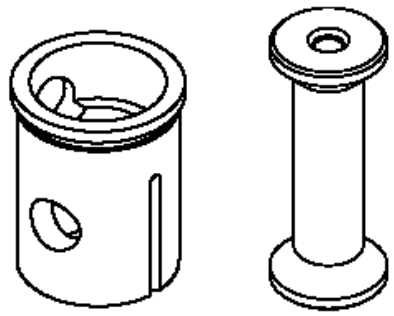
The power switch is located on the rear of the instrument above the power connection. When the instrument is turned on, the flowmeter gauge will illuminate.

Sample Chamber and Sample Holders

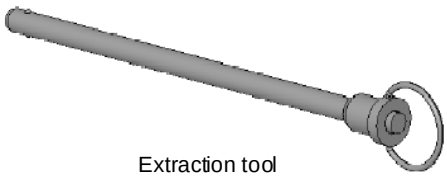
Headspace measurements are performed on samples placed in the sample chamber. The sample chamber is accessed from the top of the instrument and contains the laser source and detector. Containers of different sizes are accommodated through the use of custom sample holders.

The sample holders are comprised of two parts — the platter and the insert — and are customized for a specific container size. The sample platter positions the container at the proper height and allows the sample to be rotated during measurement. The sample inserts have a common outer diameter to fit the sample chamber and a custom inner diameter to accommodate a specific container size. The sample insert has two opposing holes to allow laser light to pass through the container headspace.

To install the sample holder, first depress the button on the extraction tool and push the tool into the top of the sample platter until it reaches the bottom, then release the button to engage the tool with the platter. While holding the extraction tool, guide the sample platter into the bottom of the chamber. Press down firmly until the sample platter snaps into place. Depress the button on the extraction tool once more to remove it from the sample platter. Place the sample insert into the sample chamber with the wide rim on the top and the vertical groove along the left side. When properly oriented, the sample insert will engage with a pin inside the sample chamber to slide into place.



To remove the sample holder, first slide the sample insert up and out using the finger hole along the rim of the insert, then remove the sample platter by engaging the extraction tool with the platter and pulling upward.



Software

The FMS-Oxygen Headspace Analyzer control software is installed on the computer connected the system. The software has two operating modes: Open and GxP.

Open and GxP Software Modes

The Open mode of the software allows the user to change system parameters and does not force the user to check system accuracy or store data in a designated location. The Open mode includes a session definition creator to allow the user to create definitions for use in the GxP mode.

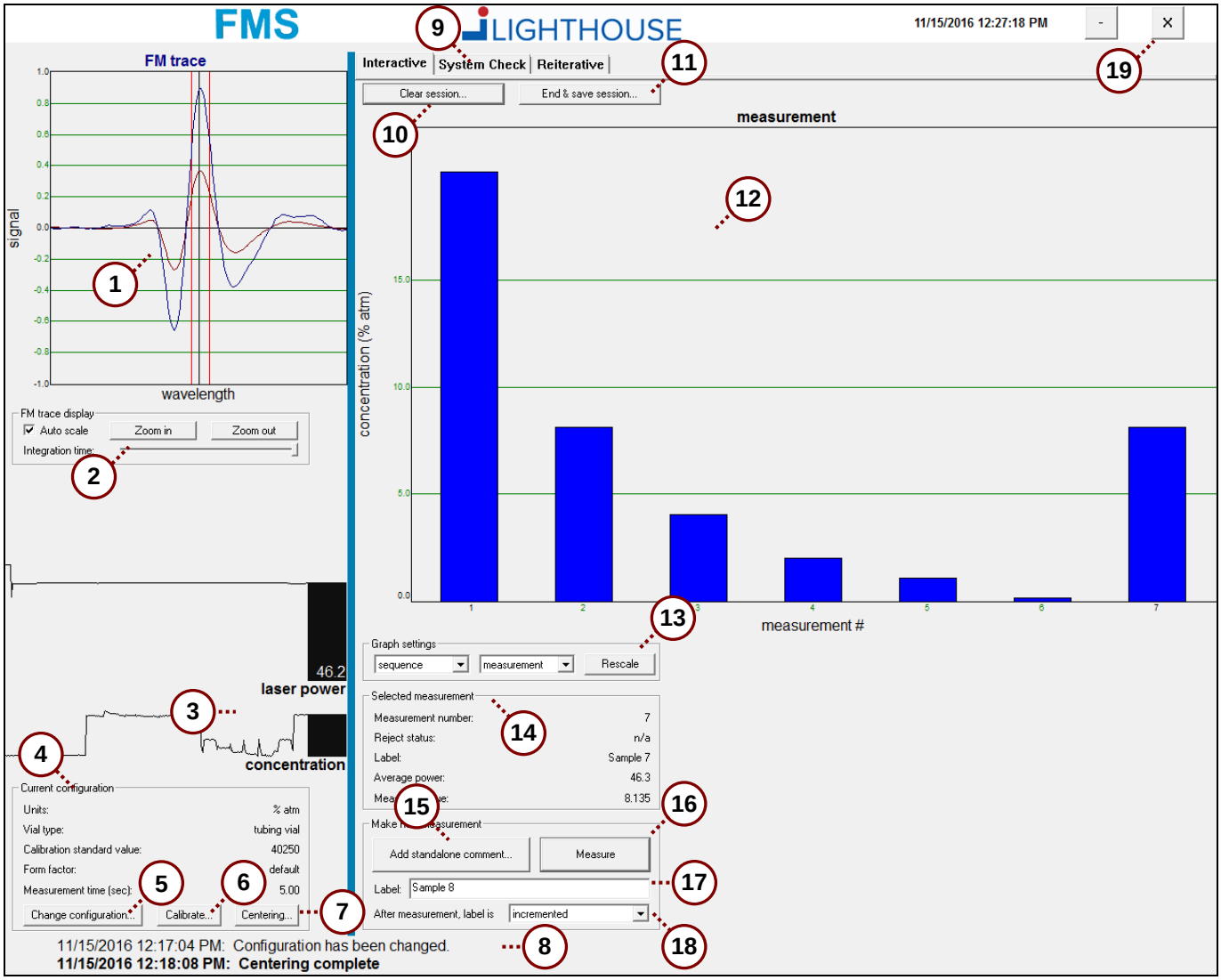
The GxP mode of the software uses pre-defined session definitions to specify all system parameters and force the user to follow a sequence of steps, including:

1) Choosing a session definition
2) Calibrating the instrument
3) Checking system accuracy
4) Measuring samples
5) Saving the data in a designated GxP storage location *or* sending the data to a printer

In order to be compliant with data integrity regulations, the computer should be set up in a GxP-compliant manner. Refer to “Recommended Setup for GxP Compliance” on page 7.

Software Interface

The instrument collects, analyzes, and stores data through the use of configurations and controls in the software interface.



1. Oxygen absorption signal
2. Oxygen signal display options
3. Laser power and oxygen meters
4. Current configuration
5. *Change configuration* button
6. *Calibrate* button
7. *Centering* button
8. Status bar
9. Screen navigation tabs
10. *Clear session* button / *Launch database viewer* button
11. *End & save session* button / *End session* button
12. Measurement results graph
13. Results graph display options
14. Selected Measurement box
15. *Add standalone comment* button
16. *Measure* button
17. Label box
18. Label control options
19. Exit button

The software interface is organized with real-time data and configuration information on the left and measurement results and history on the right. The vertical blue line functions as a divider between the two sections and can slide horizontally by clicking and dragging with the mouse.

The FM trace provides a graphical display of the oxygen absorption signal (1). The blue trace represents the current FM signal and the red trace represents the signal obtained from the previous measurement. The FM trace display options (2) allow the user to auto scale, zoom in

on, or zoom out of the signal; and change the integration time (update frequency) by sliding the bar left or right. These options are related to the display only and have no effect on the measurement.

The laser power and oxygen meters (3) display instantaneous measurements of collected laser power and the headspace oxygen for the container currently in the path of the laser. The display also provides a ticker to show recent power and oxygen levels.

The current configuration information box (4) lists a subset of the settings as established in the Configuration window, and can be modified by clicking the *Change configuration…* button (5). (Note: In the GxP mode this button is replaced with the *GxP Setup…* button, which will display the current configuration without allowing for changes.) The *Calibrate…* button (6) initiates the calibration process for the vial type and SCV code specified. The *Centering* (7) button initiates the centering process to move the FM signal to the correct position for calibration and measurement.

The measurement results graph (12) displays all measurements performed during a session. The results are updated after every measurement. The two drop-down menus (13) allow the user to configure the display to show the laser power or oxygen measurements in sequence or as a function of time.

The navigation tabs (9) provide access to the Interactive Measurement, System Check, and Reiterative Measurement Screens. The *End & save session…* button (11) ends a session and stores all measurements before clearing the data. The *Clear session…* button (10) clears the data without saving. In the GxP mode, the Reiterative Measurements screen and the *Clear Session…* button are disabled. In the GxP Database mode, the *Clear session…* button is replaced with the *Launch database viewer…* button (see “Using the FMS Database Viewer” on page 25) while the *End & save session…* button is replaced with the *End session…* button.

The selected measurement box (14) provides the results of the most recent measurement. The following values will be reported for each measurement:

- Measurement number – a count of the total number of measurements performed since data was last saved or cleared.
- Reject status – indicates accept, reject, indeterminate, or n/a (if pass/fail was not enabled).
- Label – displays the text entered into the Label box (17) at the time of measurement.
- Average power – an expression of the amount of laser light collected by the detector during the measurement.
- Measured value – the measured oxygen of the sample in the units specified in the configuration window.

The *Add standalone comment…* button (15) allows the user to insert a comment which will appear in the data report between the previous measurement and the next measurement. The *Measure* button (16) initiates an oxygen measurement. Any text entered in the Label box (17) will be written in the data report along with the measurement result. This label can be set to clear, increment, or be left intact (18) following a measurement. If the label is set to increment, the last character will increase by one unit — e.g. Sample 1, Sample 2, Sample 3… or 5A, 5B, 5C…

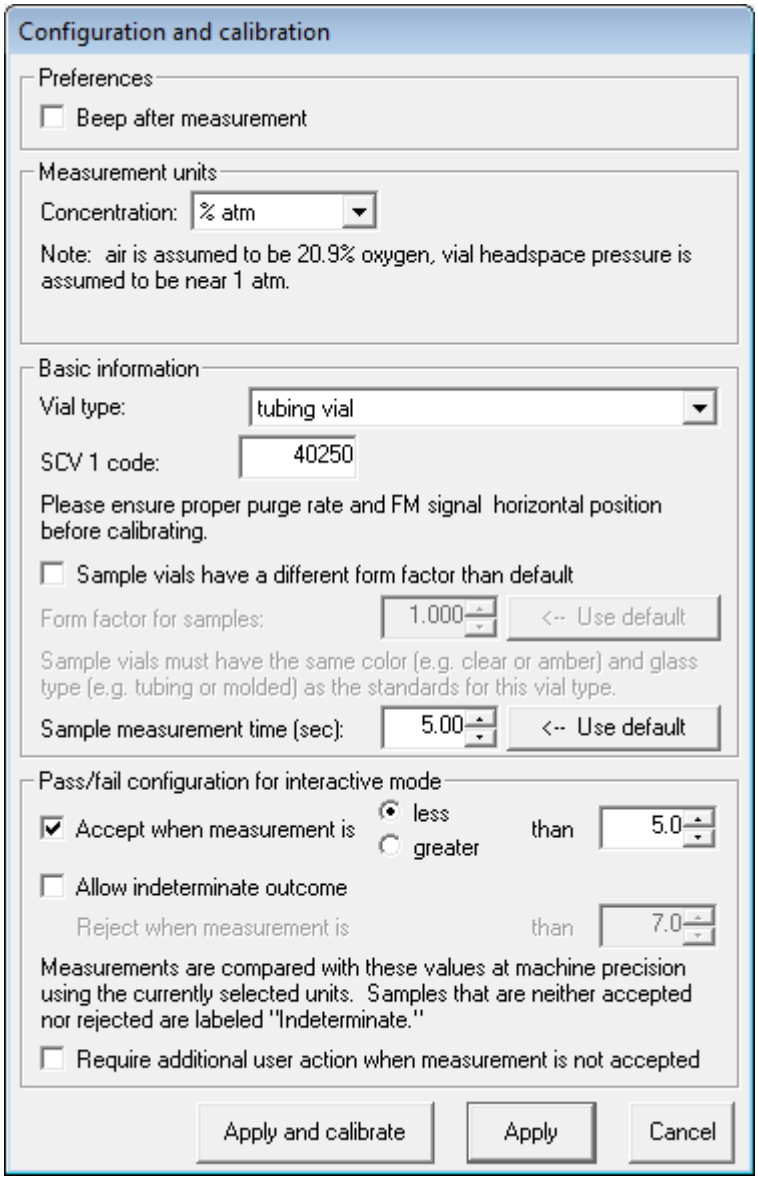
At the bottom of the interface is the status bar (8), which provides messages and alarms during operation. When the instrument is in normal operation, the blue status indicator will flash continuously. The indicator will momentarily change from blue to red when a new message is displayed.

Click the □ button in the upper right corner to display the software in a full-screen view, and the – button to exit full screen or minimize the window. The X button (19) closes the software interface. If measurement data is present when this button is clicked, the user will be reminded that data has not yet been saved.

When the software interface is displayed as a window (i.e. not in full-screen), click on the Lighthouse logo in the upper left corner to access software information and create a GxP session definition.

Software Configuration

The software is configured in the Configuration window, which is accessed by clicking the *Change configuration*… button. This provides the user with multiple options for measurement, calibration, and pass/fail mode.



If **Beep after measurement** is selected, the computer will play a sound when a measurement is complete. The tone will vary depending on the pass/fail status of the measurement.

The **measurement units** determine what units will be used when reporting the oxygen concentration. The options are % atmosphere, torr equivalent, and mbar equivalent; and operate under the assumption of a 20.9% oxygen atmosphere and container fill pressure near one atmosphere.

The **vial type** drop-down menu lists all containers that have been configured for use with the analyzer. The correct vial type must be selected when calibrating and performing measurements.

The **SCV code** indicates which standard calibration vial (SCV) is to be used during the calibration process. This code must match the code written on the SCV. A second SCV is used during calibration, but this code is fixed at 0 (0% oxygen).

The **Sample vials have a different form factor than default** option allows the measurement of samples in containers with diameters different than that of the calibration container. If the user wishes to measure a container for which no standards exist, the user may select this option, enter the form factor of the container, and calibrate using an existing standard. The form factor is determined by calculating the ratio of the inner diameter of the new container to that of the existing standard. This option is not available in the GxP mode. *Note: It is recommended that the sample and standard have the same glass color, type, and thickness when using this function.*

The **sample measurement time** can be adjusted to increase or decrease the length of a single measurement (0.25 to 20.00 sec). Because one measurement is comprised of multiple scans, a reduction in the measurement time will decrease the total number of scans and may increase measurement uncertainty. The default and recommended value is 5.00 seconds.

The **pass/fail configuration** allows the user to set a reject condition for measurements. To enable the Pass/Fail mode, click on the first check box in the Pass/fail configuration box to access the parameters. The system can be configured to accept a measurement if it is greater than the specified value or less than the specified value.

In addition, an **indeterminate outcome** can be designated wherein a measurement can fall between an accept value and a reject value. If this option is selected, an additional reject value is specified. When the measured value of a sample is above the prescribed minimum or below the prescribed maximum, the reject status will display “accept”. When the measured value of a sample is below the prescribed minimum or above the prescribed maximum, the reject status will display “reject”. If the measurement of a sample falls between the accept and reject values, the reject status will display “indeterminate”.

When the **Require additional user action when measurement is not accepted** option is enabled and a reject or indeterminate measurement results, a dialog box will appear to alert the user that a sample was not accepted. The user must acknowledge this prompt before another measurement can be performed.

Clicking the ***Cancel* button** will close the window without saving any changes, the ***Apply* button** will close the window and save the changes, and the ***Apply and calibrate* button** will save the changes and begin the calibration process (or centering process if not already performed).

Note: The configuration for the GxP mode is set during creation of the GxP session definition (refer to “Creating a GxP Session Definition” on page 20) and may not be changed when operating in the GxP mode.

System Shutdown

To close the software after use, click the  button in the upper right-hand corner of the software interface. Be sure to turn off the purge when the system is not in use.

To shut down the analyzer, first close the software interface then flip the power switch to the off position.

System Operation in Open Mode

The Open software mode offers the user more flexibility when performing measurements that do not require strict compliance to data integrity regulations. The Open mode is also used to create the session definitions necessary for operating in the GxP mode.

The procedures in this section provide a complete set of instructions to operate the system in the Open mode.

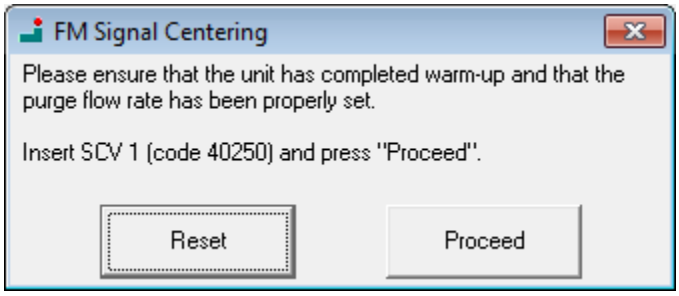
System Startup

1. **Turn on the power switch.** The flowmeter gauge will illuminate when power is on.
2. **After 30 minutes** the system will be warmed up.
3. **Install the sample holder for measurement.** The sample holder positions the container in the proper location for measurements. Refer to “Sample Chamber and Sample Holders” on page 9 for sample holder installation instructions.
4. **Turn on the computer and initiate the software interface.** The computer connected to the instrument controls all the data acquisition, analysis, and display of results. After the computer is turned on and the Windows desktop is displayed, double click the *FMS Oxygen Open* shortcut to initiate the FMS software interface in the Open mode.
5. **Set the vial type and SCV code** from the Configuration window (see “Software Configuration” on page 12). The SCV code in the software must match the SCV code on the calibration standard.
6. **Turn on the nitrogen purge from the front panel** and adjust the purge flow rate to at least 3.0 SLPM before centering the signal, calibrating, and making measurements.
7. **Center the signal and calibrate the instrument before use** (see “Centering the Absorption Signal” on page 15 and “Calibrating the Instrument” on page 16).

Centering the Absorption Signal

The oxygen absorption signal must be positioned correctly to ensure that the signal analysis is performed accurately. When the centering process is initiated, the software positions the peak of the absorption signal at the center of the two vertical red lines. As long as the signal peak remains between these two lines, the measurements will be performed correctly. The centering process must be repeated should the signal drift outside of this window.

1. **Click the *Centering…* button.** The FM Signal Centering dialog appears. The user is prompted to ensure that the unit has completed warm up and the purge flow is properly set.
2. **Insert SCV 1** corresponding to the SCV code displayed in the dialog.
3. **Click the *Proceed* button.** The dialog will display “Centering in progress. Please wait.”
4. **When the signal is centered**, the dialog will disappear.



If, during subsequent centering attempts, the software is unable to position the signal, the centering parameters may need to be reset. This can occur if the system was not allowed to completely warm up or if the ambient temperature has changed by more than 5°C. Click the *Centering…* button then the *Reset* button. Click *Yes* on the subsequent prompt to reset the centering. The system must be recalibrated following a reset.

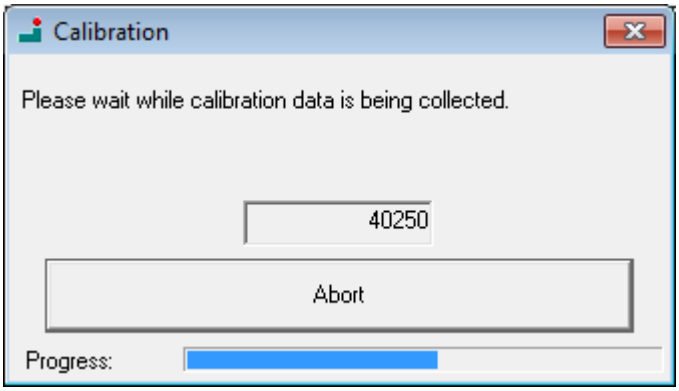
Calibrating the Instrument

The instrument must be calibrated before making measurements when the software is first initialized or when the vial type configuration is changed.

1. **Click the *Calibrate…* button.** The Calibration dialog appears.

   Note: If the Calibrate… *button is pressed before the centering process has been performed, the software will automatically display the FM Signal Centering prompt. Once the centering process is completed the software will then initiate the calibration process automatically.*

2. **Click the *OK* button.** The user is prompted to insert the SCV corresponding to the SCV code displayed in the dialog.
3. **Insert SCV 1** corresponding to the SCV code displayed in the dialog.
4. **Click the *OK* button.** The system collects data for 10 seconds. The user is then prompted to insert the SCV with SCV code 0.
5. **Insert SCV 0**.
6. **Click the *OK* button.** The system collects data for 10 seconds and stores the calibration information. When the calibration process is completed the dialog will disappear.

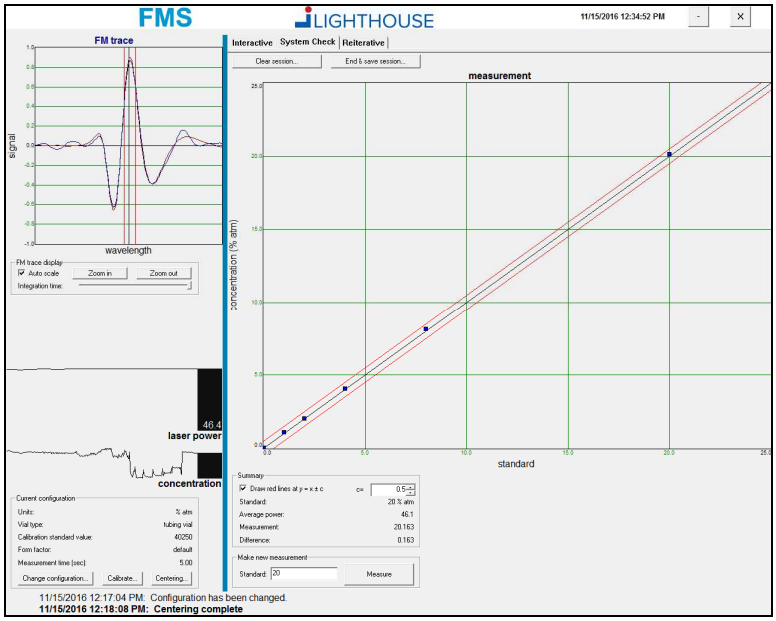


System Check Procedure

The reference standards supplied with the instrument can be measured to verify that the system was calibrated properly and is making accurate measurements.

1. **Select the System Check tab** to access the System Check Screen.
2. **Set the maximum deviation** by clicking the up and down arrows or directly entering a value for c. This parameter specifies the maximum allowable deviation of the measured value from the known value of the standard.
3. **View the maximum deviation boundaries** on the results graph by selecting the “Draw red lines at y = x ± c” check box. (Optional)
4. **Place the standard in the sample holder** and enter the known value of the standard in the *Standard* text box next to the *Measure* button. Each standard has the known value written on the top.
5. **Click the *Measure* button**.
6. **If the measurement falls within the limits**, a blue dot will appear between the two red lines on the results graph. The average power, measured value, and difference from the known value will be displayed in the Summary box.

   If the measurement does not fall within the limits, a blue dot will appear outside of the two red lines on the results graph. The average power, measured value, and difference from the known value will be displayed in the Summary box.
7. **Data can be cleared** by clicking the *Clear session…* button above the results graph. **Data can be saved** by clicking the *End & save session…* button. Data is stored as a tab-delimited text file (.dat file extension) and can be imported into a suitable text viewer such as Microsoft Excel.

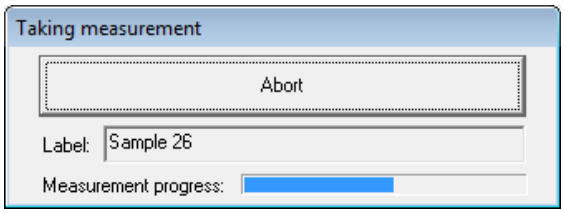


Measurement Procedures

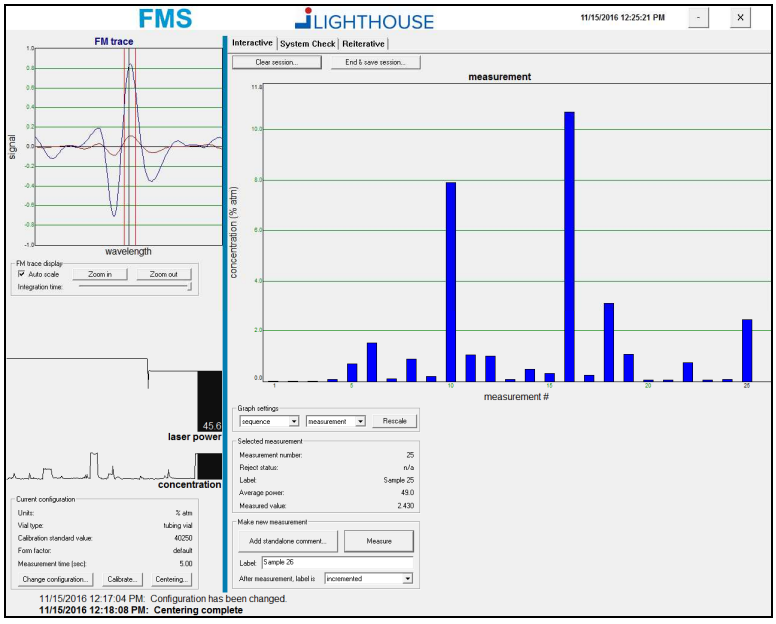
Measurements can be performed with two methods: interactive or reiterative. The interactive method is used when individual measurements are performed on multiple samples. The reiterative measurement is used to make continuous measurements on a single sample. Reiterative measurements are not available in the GxP mode.

Interactive Measurements

1. **Select the Interactive tab** to access the Interactive Measurements Screen.
2. **Place the sample in the sample holder.** Check the Power meter to ensure light is passing through the container unobstructed. Laser power below 20 may indicate a blockage of light and can reduce measurement accuracy.
3. **Enter a sample label** in the Label text box. The label can be set to clear, increment, or be left intact following the measurement. (Optional)
4. **Click the *Measure* button** to acquire a measurement of the sample. The measurement dialog displays the measurement progress and allows the user to abort the measurement if desired. Once the measurement is complete, the Selected Measurement box will display the measurement number, pass/fail status (if enabled), label (if entered), average power, and measured value. The measured value is also plotted on the results graph.

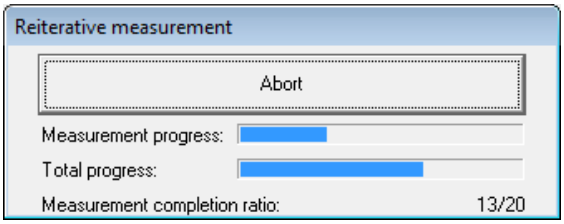


5. **Repeat steps 2 through 5** for the remaining samples.
6. **When all measurements are complete** the data can be cleared by clicking the *Clear session…* button, or the data can be saved by clicking the *End & save session…* button. Data is stored as a tab-delimited text file (.dat file extension) and can be imported into a suitable text viewer such as Microsoft Excel.

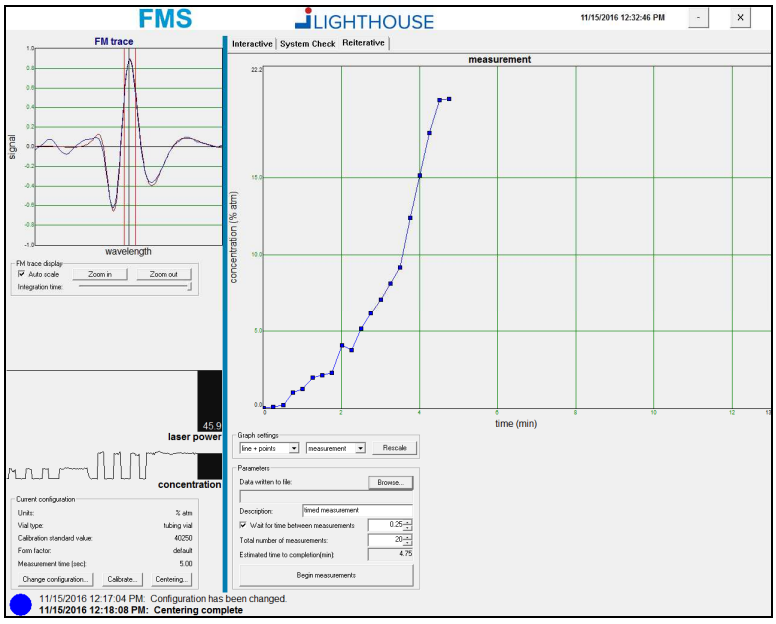


Reiterative Measurements

1. **Select the Reiterative tab** to access the Reiterative Measurements Screen.
2. **Enter a description** of the measurement in the Description text box. (Optional)
3. **Set the measurement interval**, if desired, by enabling the wait time check box and entering the number of minutes in the value box (minimum value of 0.25). This parameter specifies the time between consecutive measurements. If the wait time is not enabled, each measurement will be made immediately after the previous measurement is completed. (Optional)
4. **Enter the total number of measurements** to be performed. An estimated time to completion of all measurements will be displayed below.
5. **Place the sample in the sample holder**. Check the Power meter to ensure light is passing through the container unobstructed. Laser power below 20 may indicate a blockage of light and can reduce measurement accuracy.
6. **Click the *Begin measurements* button**. The measurement dialog will indicate current measurement progress and total progress, and allow the user to abort the measurement session if desired.



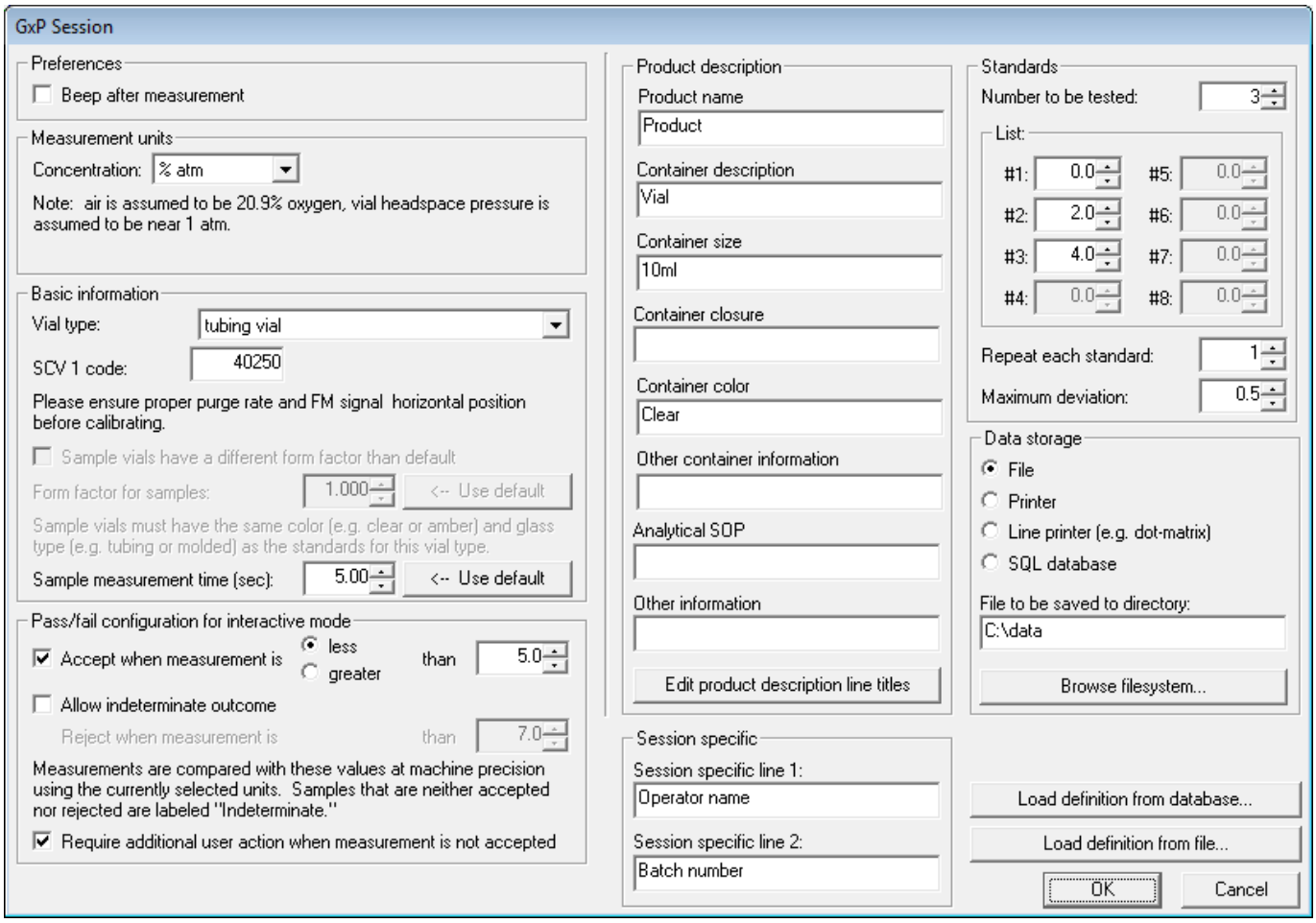
7. **The display can be changed** during the measurement to show either the measured value or the laser power on the results graph in a number of different plot types (sequence, line + points, line only, area + points, area only). These options can be selected using the two drop-down menus in the graph settings box.
8. **To stop the acquisition** before the total number of measurements has been completed, click the *Abort* button. The current measurement in the set will be canceled, though all previous measurements will remain intact.
9. **To save the measurement data** click the *Browse* button, select a storage location, and enter a file name. This may be performed at any time during the data acquisition. Data is stored as a tab-delimited text file (.dat file extension) and can be imported into a suitable text viewer such as Microsoft Excel.



Creating a GxP Session Definition

In order to use the instrument in the GxP mode, a session definition must be created to outline the specific parameters to be followed by the user during a measurement session. This information cannot be changed by the user when operating in the GxP mode. Session definitions are created by a user operating in the Open software mode.

The database storage option discussed in this section is only available on systems with the GxP Database software package installed. Please contact Lighthouse Instruments for additional information.



1. **Click on the Lighthouse logo** in the upper left-hand corner of the software interface and select “Create a GxP definition…” from the menu. The GxP Session window will appear.
2. **Load the settings of an existing definition**, if desired, by clicking the *Load definition from database…* or *Load definition from file…* button. This will not overwrite the stored definition; it will only use the stored definition as the template for a new definition.
3. **Set the system configuration** on the left side of the window. See “Software Configuration” on page 12 for a description of configuration options.
4. **Enter product description information** in the applicable text boxes. The titles may be customized by clicking the *Edit product description line titles* button and entering new titles in the text boxes. Click the button again to store the new titles.
5. **Enter the desired session-specific information**. These two fields will become the titles for text boxes to be filled in by the user at the start of every GxP session. The default titles are “Operator name” and “Batch number”.

6. **Indicate the number of standards** to be used in the required System Check (0 to 8). This will activate the value boxes below.

7. **Enter the value of each standard** to be used in the System Check.

8. **Set the number of measurements** to be performed on each standard during the System Check by changing the value in the “Repeat each standard” box (1 to 10).

9. **Set the maximum deviation** for the System Check. This parameter specifies the maximum allowable deviation of the measured value from the known value of the standard. If this deviation is exceeded, the session will be ended and further measurements will not be possible until a new session is started and the system is calibrated again.

10. **Select the data storage location** from one of the following options:

File:	data is saved as a tab-delimited text file in a designated storage location (local or network) at the end of the session
Printer:	data is sent to a printer (local or network) at the end of the session
Line printer:	data is sent to a line printer (e.g. dot matrix) after each measurement
SQL database:	data is stored in a secure SQL database (local or network) after each measurement

    If file storage is selected, click the *Browse filesystem…* button to select the directory location where GxP session data is to be stored.

11. **Click the *OK* button** to save the session definition. If file storage or printing is selected, the definition is saved as a file with a unique filename. The file must be saved in the designated location for GxP definition files — the default location is “C:\GxP session definitions”. If the computer is configured for GxP compliance, the definition storage location is specified during the computer setup (see “Recommended Setup for GxP Compliance” on page 7).

    If SQL database storage is selected, the session definition will be given a description by the user and saved in the SQL database. The user will be prompted to select an available server to be used for storage of the definition as well as any data generated using that definition. The Windows user must be a member of the FMS Supervisor or FMS Administrator user group in order to save a new session definition to the database. Refer to “Group Management” on page 27 for instructions on assigning user groups.

System Operation in GxP Mode

The GxP software mode is used when measurements are required to be compliant with data integrity regulations. The user is forced to choose a session definition, calibrate the instrument, check system accuracy, and store data in a pre-defined location. In order to meet data integrity requirements, it is recommended that the computer be set up in a GxP-compliant manner. Refer to “Recommended Setup for GxP Compliance” on page 7 for information on configuring the computer to meet these requirements.

The database storage option discussed in this section is only available on systems with the GxP Database software package installed. Please contact Lighthouse Instruments for additional information.

Executing a GxP Session

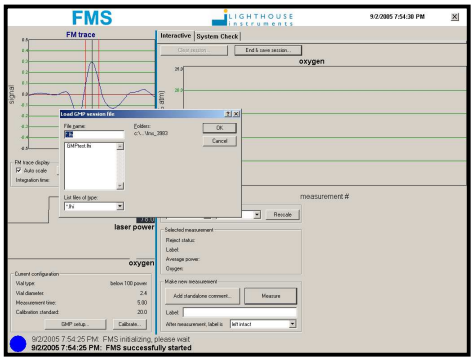
Below is a complete set of instructions to collect data in the GxP mode.

1. **Turn on the power switch.** The flowmeter gauge will illuminate when power is on.
2. **After 30 minutes** the system will be warmed up.
3. **Turn on the nitrogen purge from the front panel** and adjust the purge flow rate to at least 3.0 SLPM.
4. **Install the sample holder for measurement.** The sample holder positions the container in the proper location for measurements. Refer to “Sample Chamber and Sample Holders” on page 9 for sample holder installation instructions.
5. **Turn on the computer and initiate the software interface.** The computer connected to the instrument controls all the data acquisition, analysis, and display of results. After the computer is turned on and the Windows desktop is displayed, double click the *FMS Oxygen GxP* or *FMS Oxygen GxP Database* shortcut to initiate the FMS software interface in the GxP mode

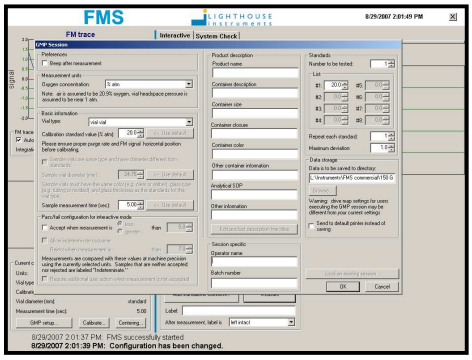
   *Note: If storing data in the database, the Windows user must be a member of an FMS user group in order to begin a GxP session. Refer to “*Group Management*” on page 27 for instructions on assigning user groups.*

6. **Choose a session definition** from the displayed list. After clicking the *OK* button, the GxP definition configuration will display but cannot be altered.

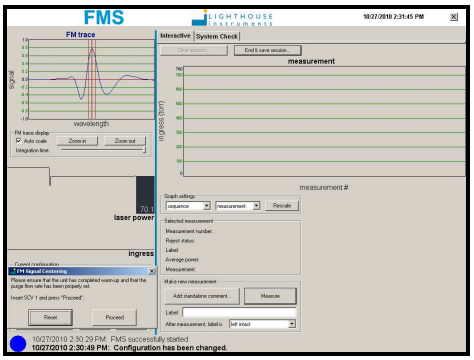
   Note: Additional session definitions may be created using the Open software mode. Refer to “Creating a GxP Session Definition” on page 20.



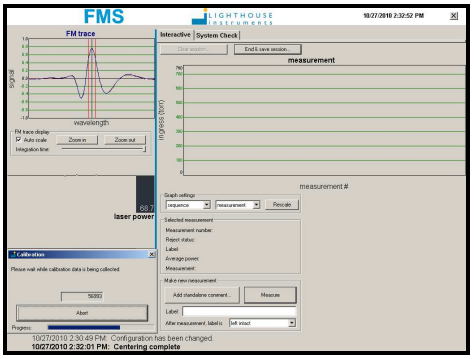
7. **Enter the session specific information** (the default fields are operator name and batch number) for the measurement session. If no session specific information is provided, the software will insert “(not given)”. Click the *OK* button to close the GxP Session window and open the FMS Signal Centering dialog.



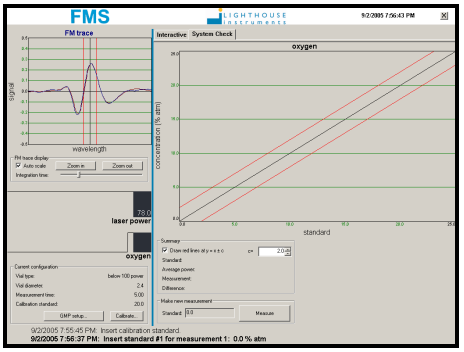
8. **Center the absorption signal.** Insert SCV 1 then click the *Proceed* button. When the centering process is complete, the system will automatically start the calibration process.



9. **Calibrate the instrument.** When the calibration data for SCV 1 has been collected, insert the SCV with SCV code 0 and click the OK button.

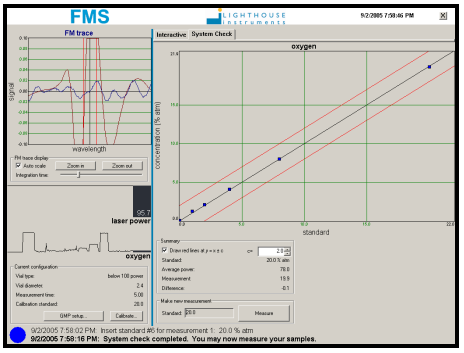


10. **Perform the system check.** Follow the steps in the FMS status bar at the bottom of the software interface. The user will be instructed to sequentially insert and measure the standards listed in the session definition.



11. **If the system check is successful,** the software interface switches to the Interactive Screen and the user is allowed to make sample measurements.

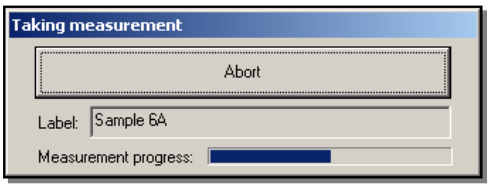
    If the system check fails, no further measurements may be performed. The user must end the session and begin a new one.



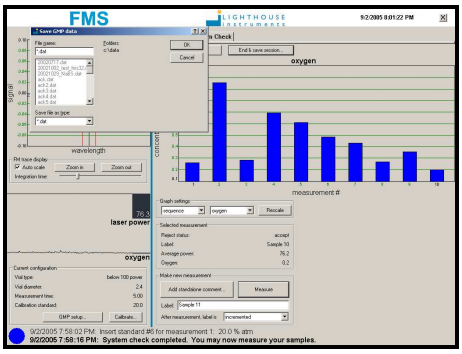
12. **Place the sample in the sample holder.** Check the Power meter to ensure light is passing through the container unobstructed. Laser power below 20 may indicate a blockage of light and can reduce measurement accuracy.

13. **Enter a sample label** in the Label text box. The label can be set to clear, increment, or be left intact (default) following the measurement.

14. **Click the *Measure* button** to acquire a measurement of the sample. The measurement dialog displays the measurement progress and allows the user to abort the measurement if desired. Once the measurement is complete, the Selected Measurement box will display the measurement number, pass/fail status (if enabled), label (if entered), average power, and measured value. The measured value is also plotted on the results graph.



15. **When a measurement session is complete**, the user will end the session by clicking the *End & save session…* button or, if storing data in a database, the *End session…* button. The data from the session will be stored according to the settings prescribed in the definition. The action required upon ending the session will depend on the data storage settings:



    - For file storage, the user will assign a unique filename and the data will be saved in the storage directory specified in the definition. Data is stored as a tab-delimited text file (.dat file extension) and can be imported into a suitable data viewer such as Microsoft Excel.
    - For printed data, the user will select the printer where the data will be sent.
    - For database storage, data is recorded in the database following each measurement. When the user ends the session, the end of the session is logged to the database and no additional measurements can be added. Data can be viewed using the FMS Database Viewer software (see “Using the FMS Database Viewer” on page 25).

16. **Start a new GxP measurement session** by clicking the *GxP Setup…* button. The user will be prompted to select another GxP session definition.

Using the FMS Database Viewer

The FMS Database Viewer software allows the user to interact with data stored in the database during a GxP session. The database viewer can be used to view data reports, export a report to another format, review and approve a report, manage user access, enable or disable definitions, and view the activity log.

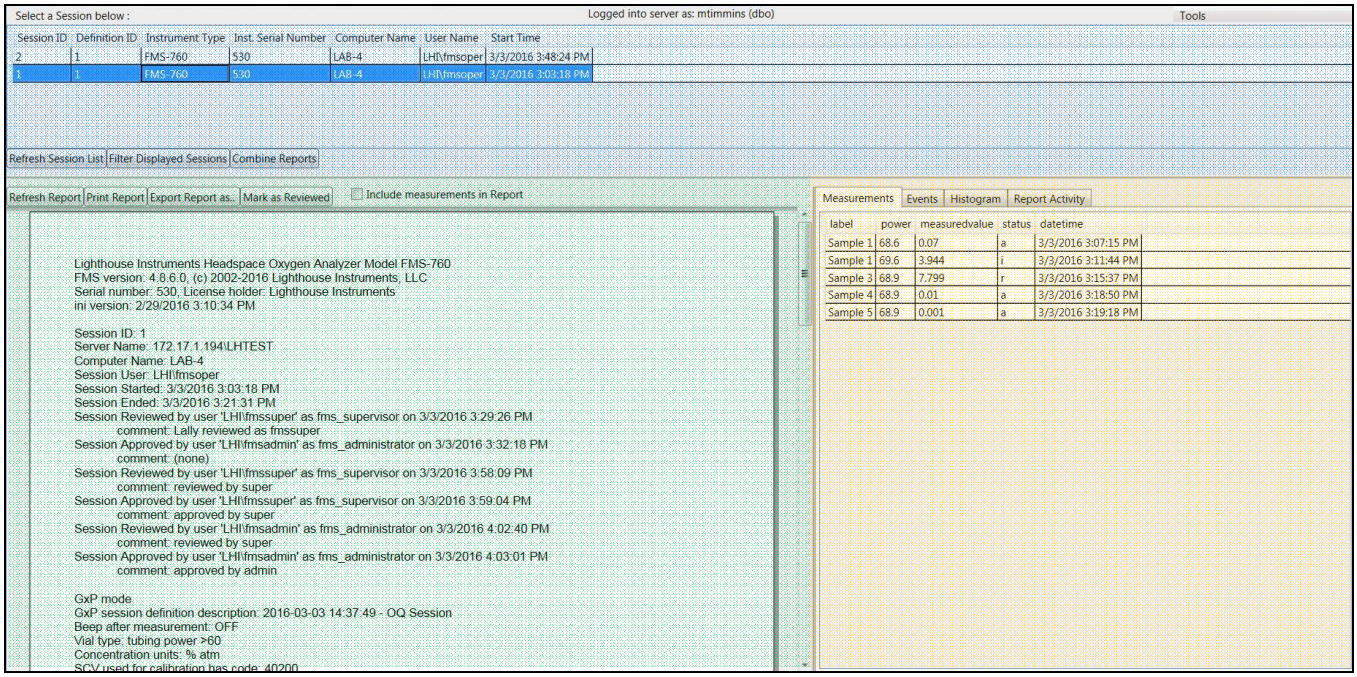
This section is only applicable to systems with the GxP Database software package installed. Please contact Lighthouse Instruments for additional information.

Launching the Database Viewer

The database viewer is launched by double-clicking on the *FMS Database Viewer* shortcut on the Windows desktop. If access to the Windows desktop is not permitted, the viewer can be launched from the FMS software in the GxP mode by clicking the *Launch database viewer…* button above the measurement results graph. In this case, the user can switch between the database viewer and the FMS software by pressing the ALT+TAB keys on the keyboard. The database viewer can be used at any time during a GxP session to view data that has already been collected.

When the database viewer is launched, the user will be automatically logged in to the software using their Windows account. The user must be a member of an authorized user group in order to access the Database Viewer. Refer to “Group Management” on page 27 for instructions on assigning user groups. The group membership will determine which functions are available to the user.

The database viewer software is divided into three windows. The session list in the top window (highlighted below in blue) provides a list of all measurement sessions stored in the database. The session report in the bottom left window (highlighted below in green) generates a full report of the selected measurement session. The session details in the bottom right window (highlighted below in orange) present additional information about the selected measurement session. Additional windows are available from the *Tools* menu in the upper-right corner.



Viewing a Session Report

The session list displays all measurement sessions that have been stored in the database. Each row corresponds to one session and the columns contain the following information about each session:

Session ID	unique numeric identifier of the session
Definition ID	unique numeric identifier of the definition used for a session — this number can be cross-referenced in the Session Definition table (see “Session Definition Viewer” on page 29)
Instrument Type	model number of the FMS system
Inst. Serial Number	serial number of the FMS system
Computer Name	name of the computer connected to the FMS system
User Name	Windows user logged in when collecting data
Start Time	date and time when the session was started

The session list can be sorted on any of these fields by clicking the header of the column.

Filtering the Session List

To find a specific session within the database, filters can be applied to the session list to display sessions that meet user-defined conditions:

1. Click the *Filter Displayed Sessions* button to display the filter options.
2. Click the *Add Filter Clause* button.
3. Select one of the session list headers from the drop-down menu to filter against this parameter. In addition to the session list headers, the “GxPSessionInfo” filter is available to compare against the GxP information stored in the session. This information represents any field included in the GxP Session window displayed at the start of a session, including vial type, product description fields, and session-specific fields (by default, user name and batch number).
4. Select the appropriate comparison condition from the drop-down menu. The comparison conditions are explained in the box to the right. For non-numeric filters (InstrumentType, ComputerName, UserName, GxPSessionInfo) the only condition available is “Equals” and means the filter text must match exactly as it exists in the database — a partial match is not possible.

Comparison Conditions

==	equals
!=	does not equal
>	greater than
<	less than
>=	greater than or equal
=<	less than or equal

5. Type the comparison value in the text box to complete the filter clause. For example, the filter clause “UserName Equals lh\jsmith” will display all sessions executed by user “lh\jsmith”, or the filter clause “StartTime < 1-25-2016 11:00” will display all sessions started before January 25, 2016, at 11:00 AM. If no time is specified for a “StartTime” filter, the comparison will be made at the beginning of that day (midnight or 00:00).
6. Click the *Add Filter Clause* button to filter on additional values. Choose the AND operator between the two clauses to display sessions that meet all conditions; choose the OR operator to display sessions that meet any of the conditions. For example, the filter clause “UserName Equals lh\jsmith AND StartTime < 1-25-2016 11:00” will display all sessions started by user “lh\jsmith” before January 25, 2016, at 11:00 AM.
7. Click the *Run Filter* button to apply the filter to the session list.
8. Click the *Filter Displayed Sessions* button again to modify the current filter. Click the *Clear Filter* button to remove the filter from the session list.

Session Report Functions

Click on a row in the session list to view the report for that session. The report will be displayed in the bottom left window. The report contains all information relevant to the measurement session, including user identification, hardware and software identification, system settings, product description, error messages, user comments, and all measurements on standards and samples.

A row of buttons at the top of the report provides access to the available functions:

Refresh Report	update the report to include any additional measurements that were added to the session since the report was loaded — this is only applicable to sessions that are still in progress
Print Report	send the report to a printer
Export Report as…	select from the drop-down menu to export the report to a DAT file (tab-delimited text file for importing into Excel) or PDF file
Mark as Reviewed	log an event (and optional comment) in the report indicating that the current user has reviewed the report; the user must enter his or her Windows username and password in order to mark the report as reviewed
Mark as Approved	log an event (and optional comment) in the report indicating that the current user has approved the report; the user must enter his or her Windows username and password in order to mark the report as approved **Only available to members of the FMS Supervisor and FMS Administrator groups*
Include measurements	check this box to display the individual measurements in the report — this may result in the report loading slower, especially for sessions with a large number of measurements ** measurements are always displayed in the Session Details window*

To zoom in or zoom out on the report, click on the report with the mouse cursor then press the *CTRL* key and the plus (+) or minus (-) keys.

Session Details

The bottom right window contains details about the session, divided into four tabs:

Measurements	table of all interactive measurements from the session with measurement label, laser power, pass/fail status (a = accept, i = indeterminate, r = reject, n = not enabled) and time & date stamp — each row represents one measurement
Events	all events that occurred during the session with a time & date stamp — events include user comments, system calibration/centering, and failed measurements
Histogram	a histogram of all interactive measurements — left-click and hold the mouse to identify a value, right-click and drag to move the axes, scroll mouse wheel to zoom, middle-click and drag to zoom area, change the bin size in the text box at the bottom
Session Activity	all events of user interaction with the session report, including reviewing, approving, printing, and exporting

Data from the tables can be copied by clicking on the upper left corner of the table to select all cells then pressing *CTRL+C* on the keyboard. The histogram can be copied by clicking in the histogram window then pressing *CTRL+C* on the keyboard.

Combine Session Reports

Multiple reports can be combined into a single printout or exported file. The combined reports will contain all information found in each of the individual session reports:

1. Click the *Combine Reports* button under the session list.
2. Select “Enable Report Selection” from the drop-down menu. A column of check boxes will appear to the left of the session list.
3. Identify the session reports to be combined, and click the check box for that session in the session list.
4. Click the *Combine Reports* button and select “Export Combined Reports to PDF” or “Print Combined Reports”.

Group Management

The FMS software applications offer a tiered set of privileges depending on the FMS group type. The table below outlines the software functions available to each FMS group type:

Software function	FMS Operator	FMS Supervisor	FMS Administrator
Execute session	●	●	●
View report	●	●	●
Export/print report	●	●	●
View the Activity Log	●	●	●
Mark report as reviewed	●	●	●
Mark report as approved	-	●	●
Create definitions	-	●	●
Enable/disable definitions	-	●	●
Modify viewer settings	-	●	●
Add/remove groups	-	-	●

All usernames, passwords, and password policies are managed with Windows authentication (local or domain). Access to the FMS database and software is based on the Windows user logged in when the software is launched. The Windows user must be a member of a Windows local or domain group that has been designated as one of the three FMS group types (Operator, Supervisor, and Administrator).

To assign an FMS group type to a new Windows group:

1. Access the FMS Database Viewer as an FMS Administrator.
2. Select *Group Management* from the *Tools* menu.
3. Click the *Add New Group* button.
4. Type the Windows group into the “GroupName” field, including the local computer or domain name — for example, “domain_name\group_name” or “computer_name\group_name”.
5. Select the desired FMS group type from the “GroupType” drop-down menu.
6. Click the *Accept* button. If the Windows group is not valid, an error message will display.

Repeat this process to assign an FMS group type to all relevant Windows groups. Multiple Windows groups can be designated as the same FMS group type, but a single Windows group can not be designated as multiple FMS group types.

Session Definition Viewer

All GxP session definitions stored in the database can be viewed by selecting *Session Definition Viewer* from the *Tools* menu. The window displays the following information:

Definition ID	Unique numeric identifier of the definition — the same number is shown in the session list when the definition was used for a session
Description	description entered when the definition was created
Created By	user logged in when creating the definition
Creation Date	date and time when the definition was created
Instrument Type	FMS system model number compatibility
Inst. Serial Number	FMS system serial number compatibility
Ini Version	FMS software configuration file compatibility
Software Version	FMS software version compatibility
Enabled	uncheck this box to disable the definition **Only available to FMS Supervisors and FMS Administrators*

When the FMS software is launched in the GxP mode, the user will be presented with a list of available session definitions. Definitions will only be made available for use if they share the same instrument type and serial number of the connected system, as well as the same software version and configuration file of the installed FMS software. Incompatible definitions and disabled definitions will be hidden from the list.

Database Viewer Settings

Settings for the session reports are accessed by selecting *Settings* from the *Tools* menu:

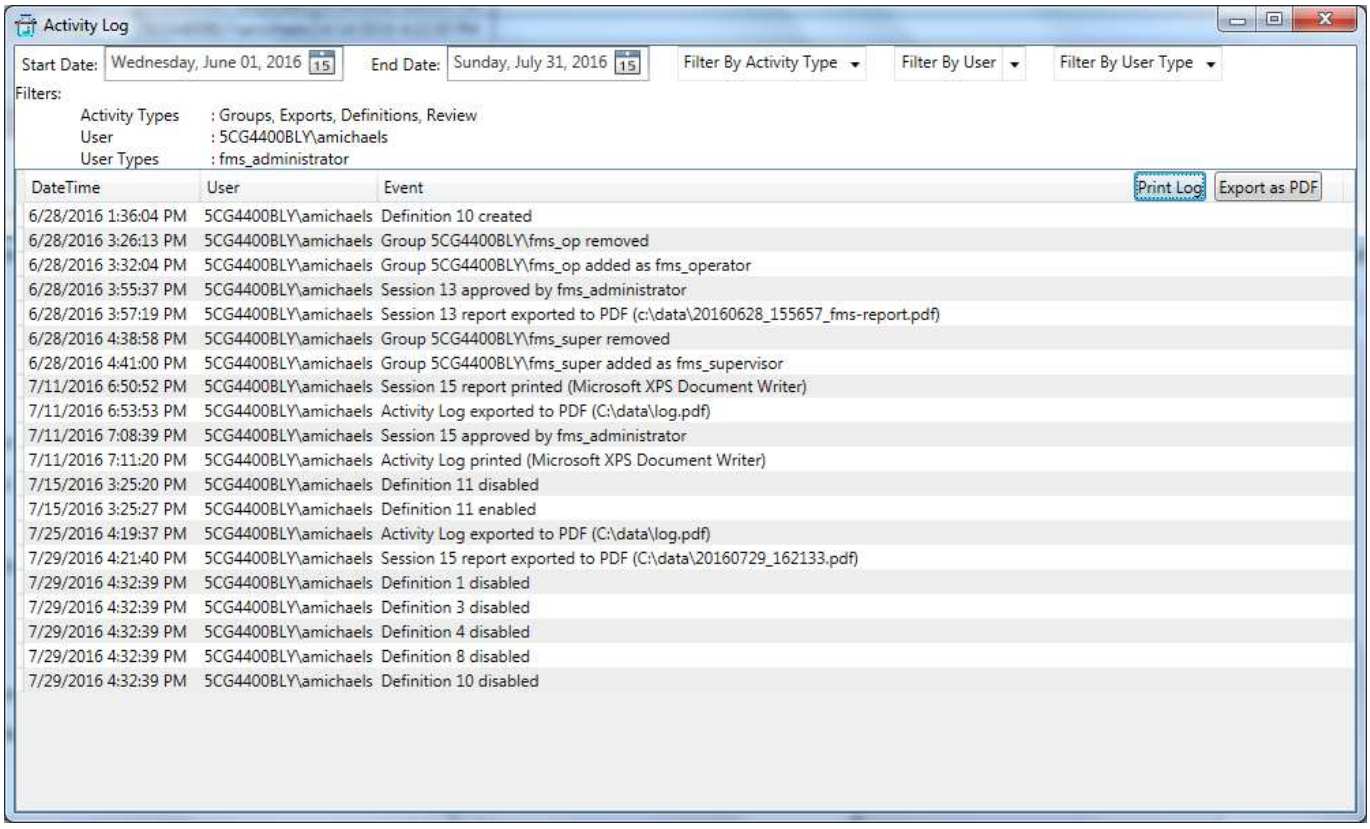
Content	
Default to include measurements at startup	sets the default value for the “Include measurements” option in the session report
Lock to default setting	prohibits the user from changing the “Include measurements” option from the default value
Formatting	
Page format	sets the paper size for printed reports and reports exported to PDF
Export Control	
Default directory	default storage location for exporting session reports
Default filename	default filename for exporting session reports — the date and time will be added as a prefix in the format YYYYMMDD_hhmmss
Lock filename and directory to default settings	prohibits the user from changing the storage location and filename from the default when exporting session reports

The database viewer settings are not stored in the database but on the local computer on a per-user basis. The settings must be individually configured for each user on each client running the database viewer software. The Settings window is available to all users, but changes made by an FMS Operator must be approved by an FMS Administrator or FMS Supervisor using his or her Windows username and password.

Activity Log

The Activity Log displays a list of all user actions performed on the system. Each action is logged with a date/time stamp, user name, and description of the event.

To access the Activity Log, select *Activity Log* from the *Tools* menu. Choose a start date and end date by clicking on the respective calendars to display all events that occurred from the beginning of the first date (midnight or 00:00) to the beginning of the second date.



The Activity Log can also be filtered by Activity Type, User, and User Type (fms_operator, fms_supervisor, or fms_administrator) using the drop-down menus on the top row of the window. The available Activity Types are listed below:

Activity Type	Included events
Sessions	starting and ending measurement sessions
Groups	adding and removing groups
Exports	exporting and printing session reports and the activity log
Settings	changes to database viewer settings
Definitions	creating, disabling, and enabling definitions
Review	reviewing and approving session reports

Multiple activity types and user types can be selected by clicking on individual checkboxes in the drop-down menus. The Activity Log in its current view can be printed by clicking the *Print Log* button or exported to a PDF file by clicking the *Export as PDF* button. The printout or file will include the details of the filters used.

Troubleshooting Guide

General Troubleshooting

Problem	Possible Cause	Corrective Action
The power indicator light does not illuminate when the instrument is turned on.	The power cord is not connected.	Ensure the power cord is firmly inserted into the rear panel of the instrument and into the proper power source.
	A fuse is blown.	With the power cord unplugged, use a flathead screwdriver to extract the fuse drawer located in the power entry module. Replace with a new fuse of the same specifications.
The FM signal is not visible in the software interface.	The system has not completely warmed up.	Allow the system to warm up for 30 minutes prior to performing measurements.
	No test sample is present.	Insert a SCV 1 to verify the presence of the FM signal.
	The FM signal has drifted from center.	Click the *Centering…* button to center or reset the signal.
	The system has been disconnected or powered off.	Reconnect and power on the system. Restarting the software may be necessary.
Measured values are inconsistent or not as expected.	The purge is not on.	Turn on the purge and set flow rate to at least 3.0 SLPM.
	The FM signal has drifted from center.	Click the *Centering…* button to center or reset the signal.
	The sample holder is not installed properly or the incorrect sample holder is installed.	Verify that the sample holder is properly installed and corresponds to the container being analyzed.
	The system was not properly calibrated.	Make sure the system is calibrated for the container being analyzed. The system must be calibrated with the purge on using the correct standards and sample holder.
	The incorrect configuration is selected.	Ensure that the correct vial type and form factor are set in the configuration window.
	The sample is not rotating during measurement.	Verify that the sample holder is properly installed and corresponds to the container being analyzed.
	One of the standards is damaged.	Inspect the standards for damage and replace if necessary.
	The FM signal is continuously drifting from center even after warm-up.	Contact Lighthouse Instruments for service.

General Troubleshooting

Problem	Possible Cause	Corrective Action
Noise and/or vibration from the instrument.	This is normal and to be expected due to the laser vibration motors and sample rotation motor.	None.

FMS Error Messages

Error Message	Possible Cause	Corrective Action
Calibration error occurred: laser power is too low	The laser power was too low when calibrating the system.	Make sure the sample holder is installed properly and the standard is positioned in the path of the laser.
Could not make a new entry in database	Communication between the FMS and the database server could not be established.	Attempt to restore communication to the server then press the *Retry* button. If communication is restored the data will not be lost.
Data acquisition hardware is unavailable	The system is not properly connected to the computer.	Ensure the USB cable is firmly inserted into the rear panel of the instrument and the computer.
		Connect the USB cable to a different USB port on the computer.
		Replace the USB cable.
	The data acquisition hardware has failed.	Contact Lighthouse Instruments for service.
Failed measurement: low power	The laser power of the previous measurement was below the minimum value.	Make sure the sample holder is installed properly and no product or label is blocking the path of the laser.
FM signal too small	The FM signal is smaller than expected when attempted to center the signal.	Only use SCV 1 to center the signal.
		Ensure that the correct vial type is selected in the configuration window.
		Make sure the sample holder is installed properly and the standard is positioned in the path of the laser.
FMS fatal error XX code YY	There is a problem with the hardware.	Record the error code and contact Lighthouse Instruments for service.
GxP session definition is corrupt or from a different software version	The GxP definition file has been corrupted or was created with an older version of the software.	Create a new GxP definition using the current version of the software.

FMS Error Messages

Error Message	Possible Cause	Corrective Action
GxP session halted: system check failed.	One of the standards failed the system check by measuring outside the required limits.	End and save the session then start a new session. If the system check fails repeatedly, refer to General Troubleshooting for possible causes and corrective actions.
Hardware initialization file is missing or corrupt	The hardware initialization file (fms.ini) has been removed or corrupted.	Reinstall the software.
Instrument disconnected or unpowered	The system has been turned off.	Turn the system back on.
	The USB cable has been disconnected.	Reconnect the USB cable.
Instrument not found or has been disconnected for too long	The system has been disconnected or turned off for more than 60 seconds.	Save any unsaved data and restart the software with the system connected and powered on.
Laser drive error	There is a problem with the hardware.	Contact Lighthouse Instruments for service.
Measurement interrupted for some reason: please check laser power	The measurement failed for an unknown reason.	Check the laser power and repeat the measurement.
	The system was disconnected during the measurement.	Reconnect and power on the system. Restarting the software may be necessary.
Measurement interrupted for some reason: please restart calibration procedure	The calibration failed for an unknown reason.	Restart the calibration procedure.
	The system was disconnected during calibration.	Reconnect and power on the system. Restarting the software may be necessary.
Motor failure error	The system has been disconnected or turned off	Reconnect and power on the system. Restarting the software may be necessary.
	The internal motors have failed.	Contact Lighthouse Instruments for further support.
Unable to locate GxP configuration file XXXX. FMS will close.	The specified GxP definition file or location could not be located.	Verify that the GxP definition file or location exists. Ensure that the current user has access to the file or location.
Unable to reconnect to FMS database	Communication between the FMS and the database server could not be established.	Attempt to restore communication to the server then press the *Retry* button. If communication is restored the data will not be lost.
You are not permitted to change directories	The defined GxP data file storage location could not be accessed.	Verify that the storage location exists. Ensure that the current user has access to the storage location.

FMS Informational Messages

Message	Description
Configuration has been changed.	The user has made a change in the configuration window.
Instrument has been reconnected.	The system has been reconnected after being disconnected or powered off for 60 seconds or less.
Measurement was not in accepted range.	A measurement was marked as “reject” or “indeterminate”. This message will only be displayed if the “Require additional user action if the measurement is not accepted” option is enabled in the configuration window.
Measurement was not saved to database.	Communication between the FMS and the database server was lost and could not be restored. The previous measurement was not saved to the database and will not be saved even if communication is restored.
System check complete. You may now measure your samples.	The GxP system check was successfully completed, indicating that all standards measured within the required limits.
Unable to increment label.	The label could not be incremented because the last character in the label was a space or a non-alphanumeric character.
You must calibrate the unit before making measurements.	The system must be calibrated when the software is first started or when the vial type is changed in the configuration window.
Your GxP session has ended. No further measurements may be made.	Once a GxP session has ended, no addition measurements can be made. A new GxP session must be started.

Appendix

Theory of Operation

Laser Absorption Spectroscopy

Laser absorption spectroscopy is an optical measurement method useful for rapid and noninvasive inspection of parenteral containers. The technique can measure a number of physical parameters within the headspace of a parenteral container, in particular gas concentrations and total headspace pressures.

Light from a near infrared semiconductor laser is tuned to match the internal vibrational frequency of the oxygen molecule. The light is passed through the headspace region of a container, scanned in frequency and detected by a photodetector after exiting the container. The instrument records which laser frequencies are absorbed and how much light at each frequency is absorbed. The number of laser frequencies absorbed (width of the signal) is proportional to total headspace pressure and the amount of light absorbed (height of the signal) is proportional to the oxygen concentration. The FMS-Oxygen Headspace Analyzer incorporates a high sensitivity signal processing method, known as frequency modulation spectroscopy, to enhance the signal to noise ratio.

Frequency Modulation Spectroscopy

Frequency modulation spectroscopy (FMS) is a high sensitivity laser absorption technique that is useful for noninvasive monitoring of gas concentrations in sealed containers. The physical basis of the technique is to encode molecular absorption information into the sidebands of a frequency modulated diode laser. The concept is analogous to the way voice, video, and data information is encoded in the sidebands of a radio transmission. By shifting the detection bandwidth to high frequency, laser intensity noise is reduced towards the shot noise limit and the signal to noise ratio is increased. Figure 1 shows a schematic diagram of the FMS technique.

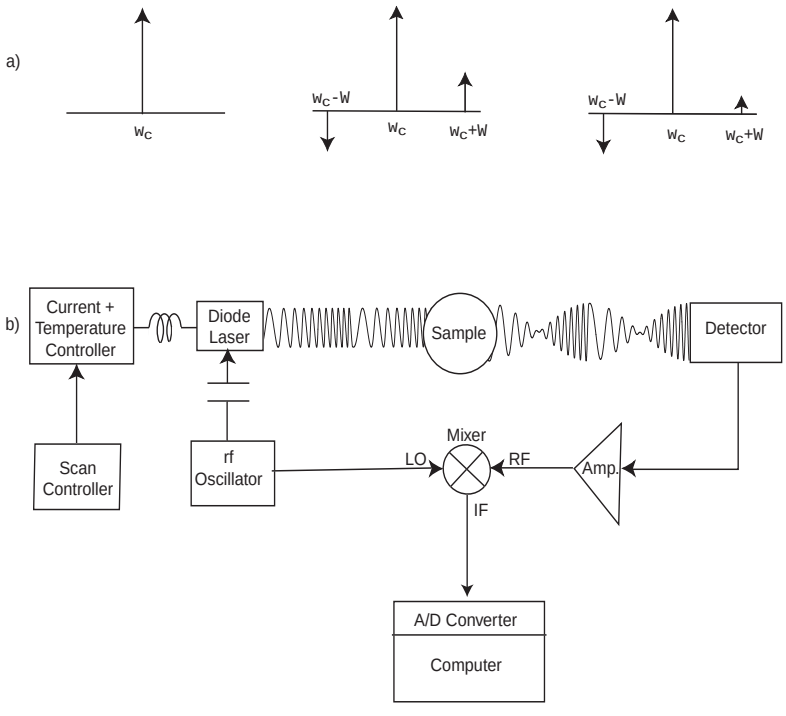


Figure 1: a) Frequency and intensity profile of a diode laser beam: Unmodulated, Modulated with no absorption, and Modulated with absorption. b) Schematic diagram of the frequency modulation spectroscopy technique.

A diode laser is frequency modulated by superimposing a radio frequency oscillation, Ω, onto the diode injection current. The spectral output of a frequency modulated diode laser, shown at the top of Figure 1, consists of a carrier frequency ω_c and side band frequencies, $\omega_c \pm \Omega$. When the laser frequency is tuned through a molecular resonance, the amount of light absorption, which is proportional to the gas concentration, is "written" into the side band frequencies. This is shown schematically as a decrease in the amplitude of the upper side band ($\omega c+\Omega$) at the top of Figure 1. The absorption information is extracted using phase sensitive detection techniques. A mixer demodulates the radio frequency signal and outputs a voltage proportional to gas concentration. The demodulated absorption feature is shown in Figure 2. The gas concentration is proportional to the peak-to-peak amplitude of the FM signal.

Oxygen Absorption Spectroscopy

Oxygen absorbs near infrared light in a band of transitions centered at 762 nm. The oxygen A-band is a series of rotational transitions within the 0-0 vibrational band of the $X^3\Sigma^-_g \leftarrow b^1\Sigma^+_g$ magnetic dipole transition. It is structured in two branches – the R-branch and P-branch – and consists of pairs of rotational transitions that progress to longer and shorter wavelengths from the band origin. The P-branch extends towards longer wavelengths and the first 10 pairs of transitions cover the range 762 – 766 nm. The R-branch extends towards shorter wavelength and the first 10 pairs of transitions cover the range 762 – 760 nm.

The narrow spectral linewidth (50 MHz) and tunability (0.1 nm/°C, 0.01 nm/mA) of a diode laser allow monitoring of individual, atmospherically broadened (1.5 GHz halfwidth) oxygen rotational transitions. Lasers used in the FMS-Oxygen Headspace Analyzer are tuned to match one of the stronger individual transitions in either the R- or P -branch depending on the manufactured laser specifications. The strongest line in the R-branch is the (R7Q8) transition at 760.89 nm, which has an integrated line strength of 7.7x10-24 cm/molecule. In the P-branch, the strongest line is the (P7P7) transition at 763.43 nm, which has an integrated line strength of 7.3x10-24 cm/molecule.

Headspace Oxygen Concentration Measurement

The amount of laser light absorbed by an individual rotational transition in the oxygen A-band is proportional to the oxygen concentration in the headspace of a parenteral container. The laser frequency is repeatedly scanned over the absorption feature and successive scans are averaged to improve the signal to noise ratio. The averaged light absorption signal (examples shown in Figure 2) and the total power are then multiplied by a calibration constant to yield the headspace oxygen concentration.

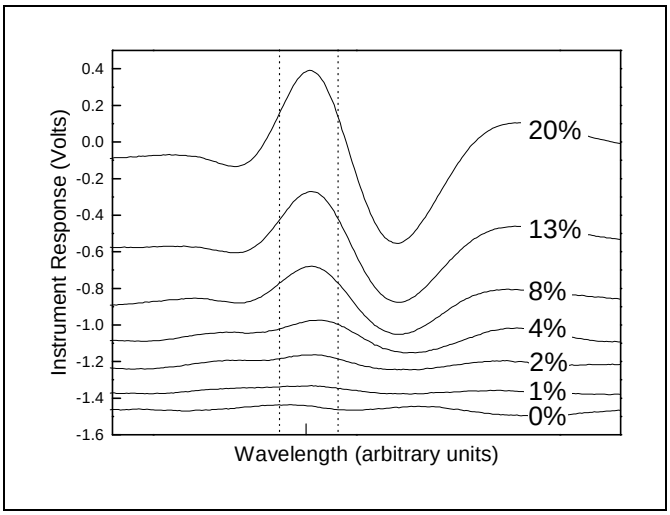


Figure 2: Frequency modulation signals from oxygen absorption. The peak-to-peak amplitude of each spectrum is proportional to the oxygen concentration (noted to the right of each scan). These spectra were taken through 1" diameter glass containers filled with certified gas mixtures of oxygen and nitrogen.

GxP Setup for FMS Software Using Network File Storage

Scope

This procedure describes the relevant Microsoft Windows settings that restrict a GxP user to running only the FMS software and saving data files in a network directory.

Responsibilities

1. The person following these instructions needs to have at least partial system administrator experience with Windows 7 and, in particular, with the safe and proper use of the operating system registry and system policy editors.
2. User information technology group or equivalent (hereafter referred to as IT) must configure the server for proper operation.
3. A GxP supervisor must create GxP session definitions using the software interface running in Open mode and save them to the server.
4. A GxP operator executes the GxP session definitions and saves the acquired data to the server.

Materials, Supplies and Equipment Needed

1. Lighthouse Instruments FMS-Oxygen Headspace Analyzer
2. Attached computer, connected to internal company LAN, running Windows 7 and FMS software v4.6.0.0 or later
3. SMB file server(s) (i.e. Windows Server or Unix compatible server running Samba) on LAN
4. Network resource to store GxP session definitions, e.g. “\\server\gxp_def”
   - GxP supervisor has full control (read, create, modify/delete permissions)
   - GxP operator has read permission only
5. Network resource to store data, e.g. “\\server\gxp_data”
   - GxP operator has create permission
   - GxP supervisor, GxP operator, or anyone else has read permission at the discretion of the GxP supervisor, IT group, and/or quality/validation managers
   - No one (outside of the IT administrators group) has modify/delete permission

Safety Precautions

1. Note that these instructions are for Windows 7 only, though they may also apply to Windows XP with little or no modification.
2. Follow all user LAN security protocols.

Procedure

1. Log in to Windows as a Windows administrator. Configure the display and other hardware settings as desired, confirm that network resources are available, and verify that the GxP supervisor can run the FMS software in the Open mode and save GxP definitions into “\\server\gxp_def”.

2. Add a user with a password following your local security policies. The username must match that used on your server(s) from which you will be reading GxP definitions and onto which you will be storing your GxP data. For example, we’ll take this username to be “gxp_op”.

3. Log in as user “gxp_op” and map the required network resources such that they are persistent. For example, “\\server\gxp_def” can be mapped to local drive letter “K:” and “\\server\gxp_data” can be mapped to local driver letter “M:”. If you are storing the executable on a network share, be sure to map it as well.

4. Using the registry editor, select the key “HKEY_CURRENT_USER\Software\Microsoft\Windows NT\CurrentVersion\Winlogon” and add or change a string value called “Shell”. Set its value to (using our example):

   ```
   "%ProgramFiles(x86)%\Lighthouse Instruments\fms\fms.exe" -gmp "K:\"
   ```

   You must replace the “K:\” with the actual mapped directory (from the perspective of “gxp_op”) containing the GxP definitions. If it is preferred that “gxp_op” run only a particular definition, it may be replaced with the definition filename, e.g. “K:\Sessions\MyProduct.lhi”. If the FMS executable is located somewhere other than the default location, be sure to reflect this in the registry entry, as well.

5. Log in as a Windows administrator and open the Group Policy Editor: press Win+R, type “gpedit.msc” and click OK. Remove the ability to run task manager from the recovery console by changing “Local Computer Policy\User Configuration\Administrative Templates\System\Ctrl+Alt+Del Options\Remove Task Manager” to “Enabled”.

6. Log in as user “gxp_op”. Verify that the FMS software in the GxP mode runs automatically, Windows key or Ctrl+Esc does not activate the Start Menu, Ctrl+Shift+Esc does not activate the Task Manager, and Ctrl+Alt+Del does not offer the option to run the Task Manager. Finally, confirm that user “gxp_op” is logged off when the FMS software is closed.

7. Refer to “Creating a GxP Session Definition” on page 20 to create a definition for this configuration. The data storage option should be set to “File” and the selected directory must match the mapped directory from the perspective of “gxp_op”; in this example, the K: drive. The definition file must be saved in the “\\server\gxp_def” location.

GxP Setup for FMS Software Using Printed Reports

Scope

This procedure describes the relevant Microsoft Windows settings that restrict a GxP user to running only the FMS software and printing the data report at the end of a session.

Responsibilities

1. The person following these instructions needs to have at least partial system administrator experience with Windows 7 and, in particular, with the safe and proper use of the operating system registry and system policy editors.
2. A GxP supervisor must create GxP session definitions using the software interface running in Open mode and save them to a local directory.
3. A GxP operator executes the GxP session definitions and prints the acquired data.

Materials, Supplies and Equipment Needed

1. Lighthouse Instruments FMS-Oxygen Headspace Analyzer.
2. Attached computer running Windows 7 and FMS software v4.6.0.0 or later. Computer filesystem(s) must support permissions, e.g. NTFS but not FAT.
3. Printer attached to computer or on LAN.
4. Local directory to store GxP session definitions, e.g. “C:\gxp_def”
   - GxP supervisor has full control (read, create, modify/delete permissions)
   - GxP operator has read permission only

Safety Precautions

1. Note that these instructions are for Windows 7 only, though they may also apply to Windows XP with little or no modification.

Procedure

1. Log in to Windows as a Windows administrator. Configure the display and other hardware settings as desired and verify that the GxP supervisor can run the FMS software in the Open mode and save GxP definitions into “C:\gxp_def”.
2. Add a user with a password following your local security policies. For example, we’ll take this username to be “gxp_op”. Confirm that user “gxp_op” has read permissions for “C:\gxp_def”.
3. Log on as user “gxp_op” and set the appropriate printer to be used by default.
4. Using the registry editor, select the key “HKEY_CURRENT_USER\Software\Microsoft\Windows NT\CurrentVersion\Winlogon” and add or change a string value called “Shell”. Set its value to (using our example):

   ```
   "%ProgramFiles(x86)%\Lighthouse Instruments\fms\fms.exe" -gmp "c:\gxp_def"
   ```

   If it is preferred that “gxp_op” run only a particular definition, it may be replaced with the definition filename, e.g. “C:\gxp_def\MyProduct.lhi”. If the FMS executable is located

somewhere other than the default location, be sure to reflect this in the registry entry, as well.

5. Log in as a Windows administrator and open the Group Policy Editor: press Win+R, type “gpedit.msc” and click OK. Remove the ability to run task manager from the recovery console by changing “Local Computer Policy\User Configuration\Administrative Templates\System\Ctrl+Alt+Del Options\Remove Task Manager” to “Enabled”.

6. Log in as user “gxp_op”. Verify that the FMS software in the GxP mode runs automatically, Windows key or Ctrl+Esc does not activate the Start Menu, Ctrl+Shift+Esc does not activate the Task Manager, and Ctrl+Alt+Del does not offer the option to run the Task Manager. Execute an example GxP definition and verify that the printer works. Finally, confirm that user “gxp_op” is logged off when the FMS software is closed.

7. Refer to “Creating a GxP Session Definition” on page 20 to create a definition for this configuration. The data storage option should be set to “Printer”. The definition file must be saved in the “C:\gxp_def” location.

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