



LIGHTHOUSE

The Science of Pharmaceutical Manufacturing



The Power of LIGHTHOUSE headspace inspection

In today's sterile operations, ensuring the stability and sterility of finished drug product are critical objectives. Current quality concepts involve not only 100% inspection of the final finished product, but also the generation of data during development to ensure process design quality and the generation of in-process data to monitor process robustness. In both development and manufacturing environments, data needs to be generated on both the product and the process to ensure overall quality.

Unfortunately, many traditional analytical methods used to inspect finished sterile product are costly to maintain, difficult to validate, and do not give direct quantitative

insight into the process. On the other hand, rapid non-destructive headspace analysis from LIGHTHOUSE is a powerful analytical tool for science-based product & process studies in development and for performing in-process monitoring & automated 100% final product inspection in fill & finish operations.

LIGHTHOUSE helps Clients generate science-based data in many ways:

- Manufacture, implementation, and validation of headspace inspection systems
- Analytical Services for Client samples sent to LIGHTHOUSE laboratory facilities for analysis
- LIGHTHOUSE Application Scientists on-site at Client facilities to support short term headspace inspection activities



Groups that have benefited from headspace analysis include filling & packaging departments, QC, and process & formulation development groups for a broad range of applications. These include 100% leak detection, container closure studies, in-process control of headspace oxygen levels, batch release testing, lyophilization cycle development, and product stability studies.



What are the benefits?

The rapid and non-destructive inspection of headspace oxygen, moisture, and vacuum levels can guarantee finished product quality and enable monitoring of sterile manufacturing processes. In development, non-destructive characterization of the headspace conditions enables accurate & efficient stability studies, saving expensive product material. Science-based process studies verify the quality of process design and enable process optimization before scale-up.

LIGHTHOUSE develops and supplies non-destructive measurement systems that have revolutionized headspace inspection in pharmaceutical manufacturing, QC, and R&D. We also work closely with our customers on a project basis, either through measurement services offered from our headspace laboratories or through short term leasing of headspace equipment on a per project basis.

The experience and knowledge gained from analyzing millions of sterile product samples from facilities around the world makes LIGHTHOUSE a trusted partner. Our science-based approach enables us to help customers characterize their processes and finished product quality. Some of the proven benefits realized by our clients are outlined below.

Non-destructive measurement technique

- No expensive product is destroyed
- 100% inspection of product is enabled providing deep insight into process robustness and quality of finished product
- Multiple measurements can be made on a sample over time, reducing material needed for development and stability studies

Rapid measurement time

- Enables real time process monitoring
- Enables in-line 100% inspection at production speeds
- Gives fast feedback for efficient process optimization
- Reduces time and effort required for development studies

Robust and Quantitative results

- Systems are easy to use and require minimal operator training
- Quantitative and accurate results
- Results are independent of operator skill
- straightforward method validation against NIST traceable standards

Quantitative insight into finished product and packaging conditions enables the design of robust manufacturing processes. This lowers the risk of costly process upsets and helps ensure the quality of finished product. Whether your application is in manufacturing, QC, or development, LIGHTHOUSE platforms generate a return on investment that is real and measurable.

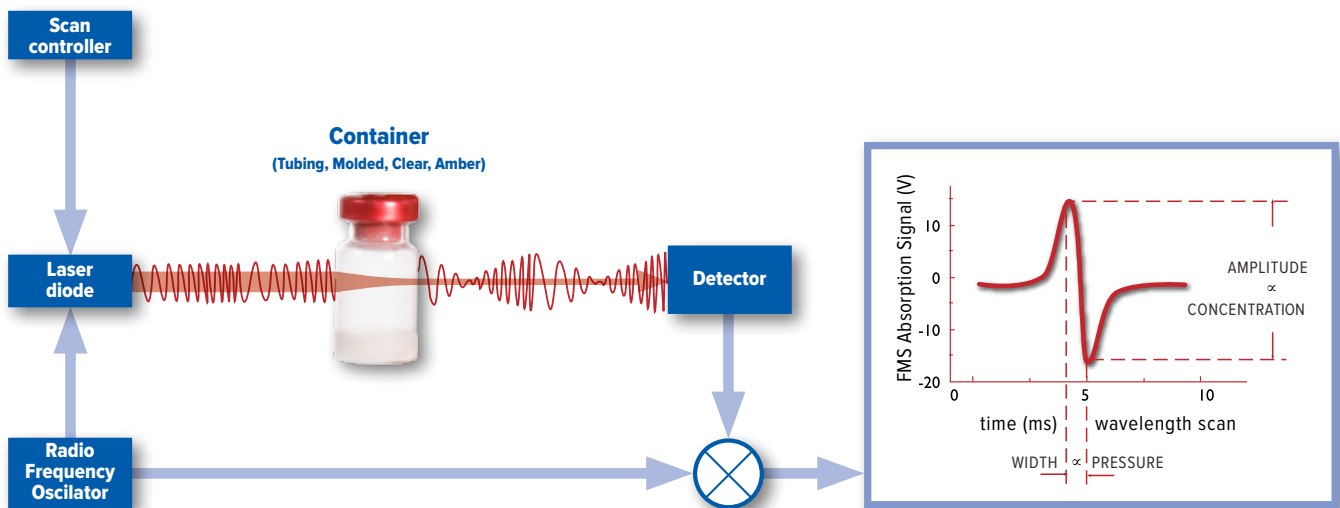
Technology

LIGHTHOUSE scientists pioneered the use of diode laser absorption spectroscopy for performing headspace inspection of pharmaceutical packages. Commercialized with funding from the Food & Drug Administration, patented platforms from LIGHTHOUSE make use of a high-sensitivity laser absorption technique called Frequency Modulation Spectroscopy (FMS). The technique measures a number of physical parameters within the headspace of a parenteral container including gas concentration (oxygen and moisture) and total headspace pressure (vacuum level).

Rapid and non-destructive headspace inspec-

tion is accomplished by transmitting diode laser light through the container headspace at a wavelength matching the absorption wavelength of the molecule of interest (760 nm for oxygen and 1400 nm for moisture). Applying sophisticated modulation and signal processing techniques, the systems achieve measurement sensitivities that are 10,000 times greater than standard NIR absorption.

A wide variety of containers can be inspected using laser absorption spectroscopy including tubing, molded, clear and amber glass vials & ampoules, bottles, cartridges, syringes, and translucent plastic containers.



Make the right choice for your application

A wide variety of applications have been validated and implemented using rapid non-destructive headspace analysis. The table below indicates what type of headspace measurement can be used to address each application.

	VISTA Inspection machine			FMS Benchtop		
	Oxygen	Pressure	Moisture	Oxygen	Pressure	Moisture
MANUFACTURING / PACKAGING						
100% Container Closure Integrity Inspection lyophilized product	•	•				
100% Container Closure Integrity Inspection liquid product	•					
100% Vacuum Detection of lyophilized product		•				
100% Moisture Inspection of lyophilized product			•			
100% Oxygen Monitoring purged liquid / Lyo product		•				
At-line Oxygen monitoring purged liquid product				•		
Off-line Vacuum Detection of lyophilized product					•	
Off-line Container Closure Testing				•	•	
QUALITY CONTROL						
Release testing headspace oxygen levels				•		
Release testing headspace vacuum levels					•	
Container closure testing of lyophilized product				•	•	
Product stability testing oxygen				•		
Product stability testing moisture						•
Water Activity solid dosage form						•
PACKAGING DEVELOPMENT						
Container closure integrity studies				•	•	
Vacuum retention studies					•	
Rubber stopper moisture desorption studies						•
Rubber stopper oxygen permeation studies				•		
End of shelf life study oxygen content				•		
PROCESS DEVELOPMENT						
Liquid filling line nitrogen purge validation				•		
Lyo cycle optimization						•
Lyo chamber moisture mapping						•
FORMULATION DEVELOPMENT						
Product stability determination oxygen				•		
Product stability determination moisture						•
Product stability determination water activity						•

Products and Services

Measurement Systems From R&D to Manufacturing



VISTA™ Series

In-line 100% inspection systems for non-destructive headspace analysis of oxygen, moisture and pressure

- Automatic calibration and continuous system check with certified standards
- Compatible with vials/bottles/ampoules/cartridges/syringes
- Compatible with tubing/molded/clear/amber glass and translucent plastics
- Can be configured for containers ranging from 1ml to 2L
- No tool changeover
- Throughputs up to 500 vials per minute
- Available with full set of validation protocols

The VISTA Machine Platform can be configured to meet specific application requirements. Examples of configuration options are:

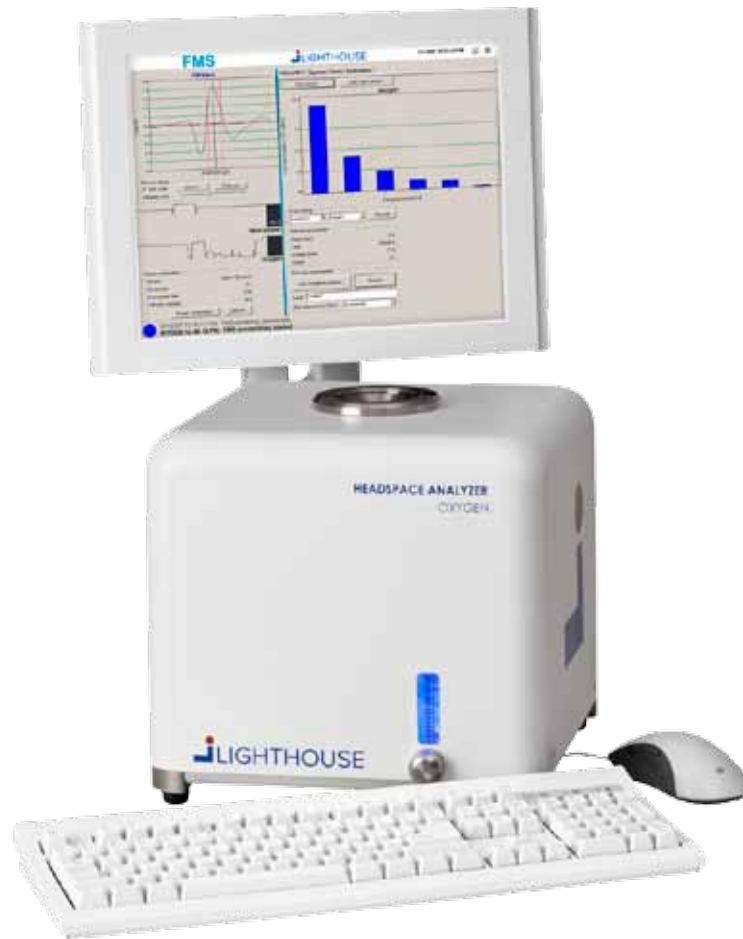
- Sensor heads for measurement of head-space oxygen, pressure, and/or moisture
- Multiple sensors depending on throughput and sensitivity requirements
- Rotary tables, buffer tables, tray on/off depending on infeed/outfeed requirements
- Label printing and print vision inspection
- Integration into packaging or filling lines
- 21 CFR part 11 compliant electronic data storage





CAUTION

IP65



FMS™ Series

At/off-line inspection systems for non-destructive headspace analysis of oxygen, carbon dioxide, moisture and pressure

- Non-destructive headspace measurement in a few seconds
- Compatible with vials/bottles/ampoules/cartridges/syringes
- Compatible with tubing/molded/clear / amber glass and translucent plastics
- Can be configured for containers ranging from 0.5ml to 2L
- Full set of validation protocols
- 21 CFR part 11 compliant

The FMS Series is available in several configurations

FMS-Oxygen Headspace Analyzer

Configured for measuring headspace oxygen

FMS-Moisture/Pressure Headspace Analyzer

Configured for measuring headspace pressure and moisture

FMS-Carbon Dioxide Headspace Analyzer

Configured for measuring carbon dioxide

FMS-Water Activity Analyzer

Configured for measurement of water activity



Measurement Services in Support of R&D and Manufacturing

LIGHTHOUSE offers a broad range of measurement services for determining headspace oxygen, moisture, and vacuum in sterile product containers. Headspace measurement services are carried out by our laboratory facilities in Charlottesville, Virginia and Amsterdam, The Netherlands. Clients requiring rapid non-destructive headspace analysis can choose from several service options. Samples can be sent to LIGHTHOUSE for analysis, equipment can be brought to the client and analysis performed on site by LIGHTHOUSE Application Scientists, or equipment can be implemented at the client on a project basis for a short term lease. Measurement Services clients take advantage of the expertise at LIGHTHOUSE gained from analyzing millions of samples from sterile



drug facilities all over the world to address the following applications:

Applications include:

- 100 % container closure integrity batch inspection
- Container closure studies and leak rate modeling
- Headspace oxygen stability studies
- Nitrogen purge optimization & validation
- Lyo chamber moisture mapping
- Lyo cycle optimization
- Packaging permeation studies

We regularly apply our expertise in headspace inspection to support customers in pharmaceutical development and manufacturing quality assurance groups investigating customer complaints and product recalls. On-site measurement services utilize our benchtop FMS™ Series instruments and/or our VISTA™ In-line Series systems at the client location. We have supported pharmaceutical customers for the rework of clinical and commercial batches enabling the release of product.



A science based approach to method evaluation



LIGHTHOUSE uses a science-based approach when evaluating the best method for meeting the analytical measurement and process monitoring needs of sterile product development and manufacturing. The key to this approach is the generation of informative analytical data. Quantitative insight into a product or process forms the basis for a meaningful and objective discussion with the client. LIGHTHOUSE facilities are set up with the full range of headspace measurement platforms to generate data so that clients receive quick and valuable feedback for the following types of activities:

Feasibility study (Platform evaluation)

Clients considering the implementation of a LIGHTHOUSE platform build business cases to support capital equipment purchases and need evidence that the platform's performance ad-

equately addresses their critical applications. Feasibility studies using in-line and off-line headspace inspection platforms are performed at LIGHTHOUSE using real product samples and certified standards manufactured from the client's containers. The generation of meaningful quantitative data provides the client with a complete picture of the platform's performance for the application of interest, ensuring a solid basis for an informed purchase decision.

Analytical services (Optimization)

We are regularly contacted by clients to help them investigate container closure issues, determine appropriate vial/stopper combinations, optimize nitrogen purging systems, and determine moisture and oxygen permeation properties of stoppers and packaging materials. These activities fall under our Measurement Services and support our clients' strategies for generating data so that quality can be designed into the process and product. Our scientific approach and experience across a broad range of sterile product and process applications allows us to address current issues as well as support clients in determining long-term process and product solutions.



World-class automation engineering capabilities

LIGHTHOUSE has assembled a world class team for designing, developing, and supporting the VISTA series of automated headspace inspection machines. A strategic partnership between LIGHTHOUSE and DMW Automation combines unparalleled expertise in laser measurement physics and industrial automation engineering. Physicists, electrical, and mechanical engi-

neers from LIGHTHOUSE work as one team with automation engineers from DMW Automation. The LIGHTHOUSE automated VISTA Headspace Inspection Machines are designed and supported by a team having more than thirty years of experience in industrial implementations for the global pharmaceutical industry.



Photo of VISTA staging floor courtesy of DMW Automation

About Us

LIGHTHOUSE is the leading manufacturer and provider of optical, non-destructive headspace inspection systems for in-line, at-line, and R&D applications specific to the pharmaceutical industry. LIGHTHOUSE developed the non-destructive headspace inspection systems with funding from the Food and Drug Administration. We have over 300 laser based systems installed around the world at some of the world's leading pharmaceutical, biopharmaceutical, and contracting manufacturing companies including: Amgen, Baxter, Bayer, Boehringer Ingelheim, BMS, Datwyler, DSM, Eli Lilly, Genentech, GlaxoSmithKline, Hospira, Johnson & Johnson, Merck, Novartis, Patheon, Pfizer, Roche, Serum Institute of India, Sankyo, Sanofi-Aventis, TEVA, West Pharmaceutical Services, and Wyeth.

Contact Us

North America

LIGHTHOUSE Instruments, LLC
2020 Avon Court Suite 2
Charlottesville, VA 22902
Tel: +1 434 293 3081
Fax: +1 434 293 7773

Europe

Technical Sales & Support Center
LIGHTHOUSE Instruments B.V.
Science Park 408
1098 XH Amsterdam
The Netherlands
Tel: +31 6 2017 6502
euinfo@lighthouseinstruments.com

Head European Sales Office
Monkhurst House, Office 1, Sandy Cross Lane
Heathfield, East Sussex TN21 8QR
UK
Tel: +44 1435 869033
euinfo@lighthouseinstruments.com

German Local Office

Mr. Jens Hoellein
Tel: +49 173 634 8290
euinfo@lighthouseinstruments.com

Japan

Dencom Corporation 1-5-10 Honcho
Kawasaki, Kanagawa 210-0001
Japan
Tel: +81 44 201 1418
Fax: +81 44 201 1465
sales@dencomjapan.com

India

SPINCO BIOTECH Pvt Ltd
No. 4, Vaidyaram Street, T. Nagar
Chennai 60017 India
Tel: +91 44 2340174
Fax: +91 44 2340761
www.spincotech.com
info@spincotech.com

