Rapid Non-Destructive Headspace Vacuum Analysis of COMPANY XYZ Vacuum Vials

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COMPANY XYZ

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INTRODUCTION

Headspace pressure levels of vacuum vial samples were measured using a Lighthouse Instruments FMS-1400 Headspace Pressure/Moisture Analyzer as part of a proof of principle demonstration for COMPANY XYZ.

INSTRUMENTATION AND METHOD

Laser Absorption Spectroscopy: General Background Information

Laser absorption spectroscopy is an optical measurement method for rapid and non-invasive headspace gas analysis of parenteral containers. The technique can measure a number of physical parameters within the headspace of a parenteral container, including gas concentrations and total headspace pressures.

Light from a near-infrared semiconductor laser is tuned to match the internal vibrational frequency of the target molecule. The light is passed through the headspace region of a container, scanned in frequency and detected by a photodetector. The amount of light absorbed is proportional to the target molecule concentration.

The instruments incorporate a high sensitivity detection method known as frequency modulation spectroscopy.

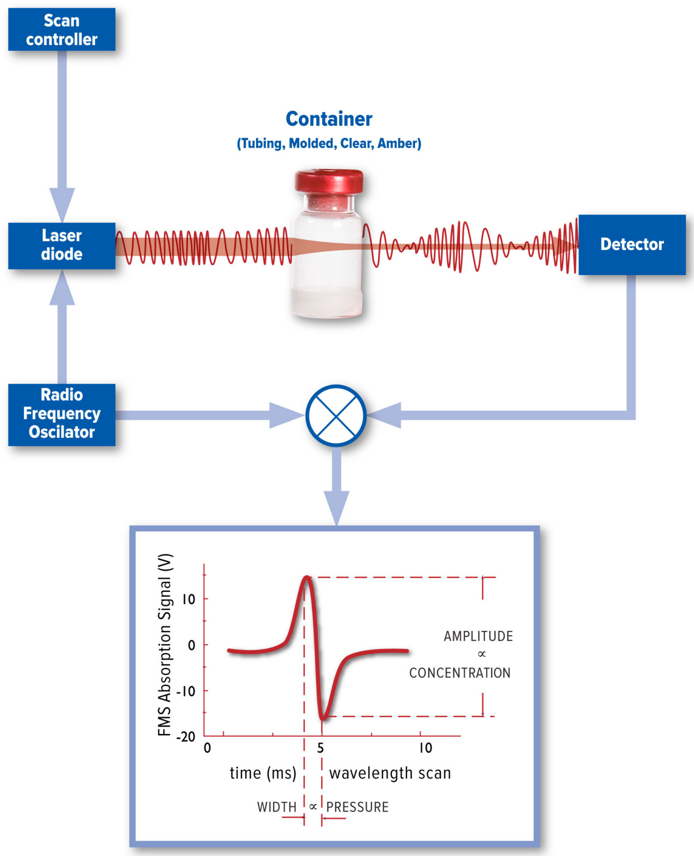

Figure 1. Schematic of frequency modulation spectroscopy

Water Vapor Absorption Spectroscopy: General

Water vapor absorbs near infrared light in a band of transitions around 1.382 µm. The water vapor 101 band is a series of ro-vibrational transitions that combine the symmetric stretch (ν_1 3657 cm^{-1}, 2.734 µm) and asymmetric stretch (ν_3 3756 cm^{-1}, 2.662 µm).

HEADSPACE MOISTURE AND VACUUM MEASUREMENTS

Measurement Principle

The FMS-1400 Headspace Moisture/Pressure Analyzer operates on the principle of optical absorption spectroscopy. Light from a near infrared diode laser is directed through the headspace region of a parenteral container. The laser light is tuned in frequency to match the internal absorption frequency of moisture molecules at 1400 nm. The width of the absorption signal is proportional to the headspace pressure while the area is proportional to the headspace water vapor concentration. Figures 2 and 3 show a set of spectra for several different headspace pressures and moistures.

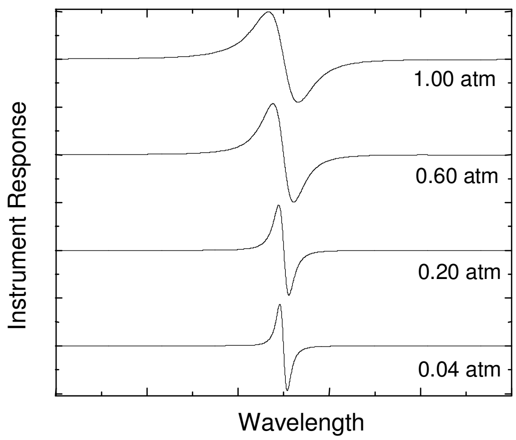

Figure 2: Absorption spectra for several known headspace pressures. Note that the signal width varies as a function of pressure.

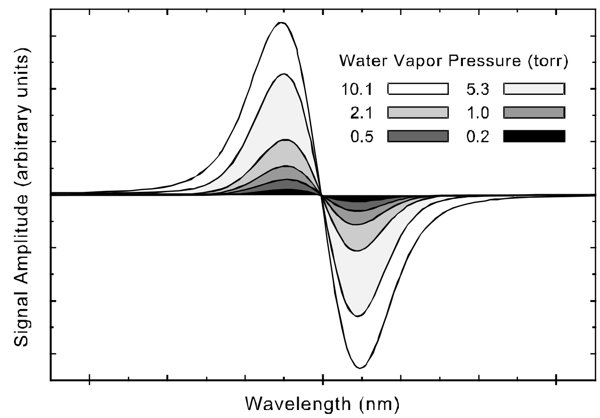

Figure 3: Absorption spectra for several known headspace moistures at constant background pressure.

COMPANY XYZ SAMPLE SET

A 25 ml vacuum vial from COMPANY XYZ was used for a proof of principle experiment demonstrating rapid non-destructive vacuum analysis. The vacuum vial was of the type used for drying UTKs in the hot lab. The vacuum vial contained 0.2 – 0.4 g water for injection and was expected to be stoppered under vacuum with some small amount of sterile air.

MEASUREMENT PROTOCOL

Headspace pressure measurements were performed using a Lighthouse Instruments FMS-1400 Headspace Moisture/Pressure Analyzer (SN 1400-212). Calibration was performed using certified standards manufactured by Lighthouse Instruments.

A sample holder fitting the COMPANY XYZ 25ml vial was used to enable efficient purging of environmental humidity in the instrument measurement cell. The sample holder was adjusted so that the laser light went through the empty headspace of the vial.

Each headspace pressure measurement was stored electronically. Three consecutive measurements were made on the vacuum vial to collect statistical data for determining standard deviations of the measurement.

A syringe was then used to inject consecutive amounts of approximately 3ml of air into the vacuum vial. After each 3ml injection of air the headspace pressure was again measured three consecutive times. This proof of principle experiment demonstrated the ability of the system to accurately measure pressure in the vacuum vial from near full vacuum up to one atmosphere.

Graphical representations of the results are presented in the following section. A detailed overview of the raw data can be found in the Appendix at the very end of this report.

THE LIGTHOUSE FMS-1400 HEADSPACE MOISTURE/PRESSURE ANALYZER

RESULTS

Below is a graphical representation of the headspace pressure measurements made on the COMPANY XYZ vacuum vial after consecutive injections of approximately 3ml of air.

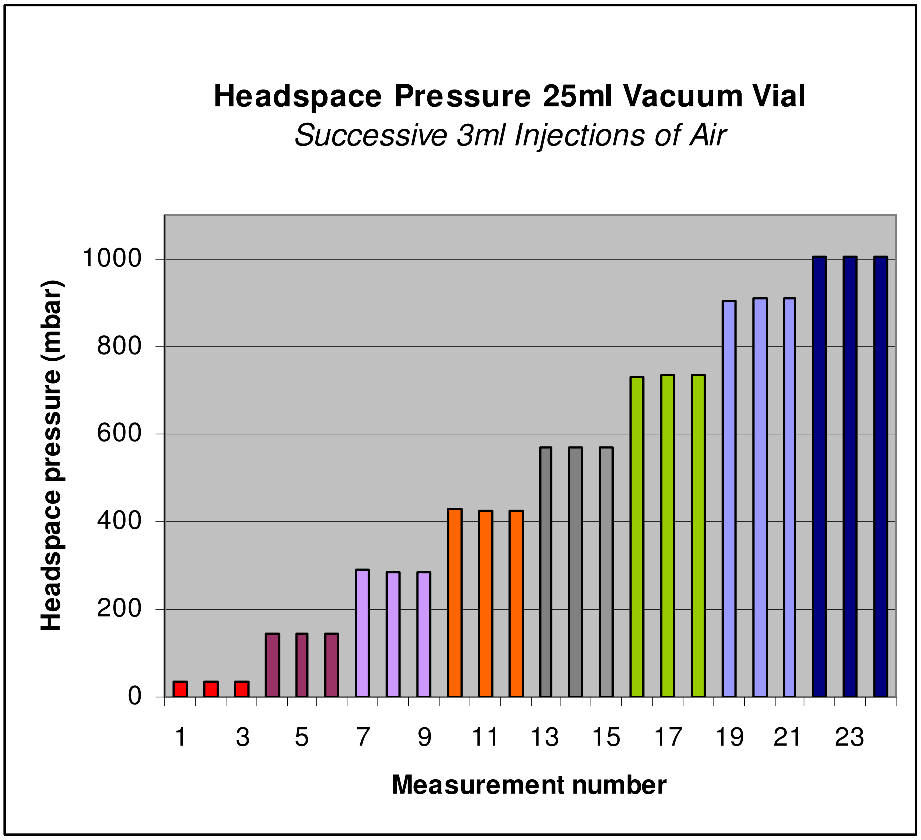

Figure 1: Plot of the headspace pressure measurements made on the COMPANY XYZ vacuum vial. Three headspace pressure measurements were made on the 25ml vacuum vial followed by three measurements made after each injection of 3ml of air into the vial until atmospheric pressure was reached in the vacuum vial.

The following table contains a summary of the headspace pressure measurements made on the COMPANY XYZ vacuum vial. The mean pressure value represents the average of three consecutive measurements made on the sample. The third column in the table lists the standard deviation of these three measurements.

Sample Label	Measured Mean Pressure (mbar)	St Dev (mbar)
vacuum vial	36.7	0.46
vacuum vial + 3ml air	145.6	0.10
vacuum vial + 6ml air	287.6	0.35
vacuum vial + 9ml air	427.4	0.27
vacuum vial + 12ml air	570.7	0.19
vacuum vial + 15ml air	733.3	1.43
vacuum vial + 18ml air	909.8	2.32
vacuum vial + 21ml air	1004.3	0.95

DISCUSSION

Rapid non-destructive headspace pressure measurements were easily made on the COMPANY XYZ 25ml vacuum vial with low standard deviations of the measurement showing very good precision for measuring the vacuum levels in the vial. The initial headspace pressure reading of 36.7 mbar for the vacuum vial was as expected.

CONCLUSION

Headspace pressure measurements made on the COMPANY XYZ 25ml vacuum vial using a rapid non-destructive laser-based headspace method demonstrate that the LIGHTHOUSE headspace measurement platform can robustly determine vacuum levels ranging from near full vacuum up to one atmosphere.

As the recognized market leader for laser-based headspace analysis, LIGHTHOUSE uses extensive experience in inspecting product from sterile facilities around the world to support clients with a science-based approach for rapid non-destructive headspace inspection solutions.

REFERENCES FOR FURTHER READING

[1] LIGHTHOUSE White Paper: "Introduction to Laser-Based Headspace Inspection and the Application to 100% Container Closure Inspection of Sterile Pharmaceutical Containers"
Downloadable at http://www.lighthouseinstruments.com/NewFiles/whitepaper.php

[2] Veale, J. "New Inspection Techniques for Aseptic Processing" Chapter 11 of Practical Aseptic Processing, Fill and Finish, Vol. 1, edited by Jack Lysfjord
Can be ordered at
https://store.pda.org/bookstore/ProductDetails.aspx?productabbreviation=17283

APPENDIX

An overview of the raw data file is found below:

Lighthouse Instruments Headspace Moisture/Pressure Analyzer Model FMS-1400
FMS version: 4.5.3.0, (c) 2002-2009 Lighthouse Instruments, LLC
Serial number: 212, License holder: Lighthouse Instruments

Original filename: C:\Documents and Settings\customer\My Documents\Lighthouse\Sample reports\COMPANY XYZ\COMPANY XYZ vacuum vial 28dec2010.dat

Current time: 12/28/2010 2:30:10 PM

Config: Configuration:
Config: Pressure units: millibar
Config: Moisture concentration units: millibar
Config: Vial type: small head tubing vial
Config: Sample measurement time (sec): 5.00
Config: Buffer gas: nitrogen
Config: Show buffer gas partial pressure instead of total pressure: OFF
Config: Primary measurement for pass/fail and system check: pressure
Config: Pass/fail configuration: disabled
Calibration: Calibration performed with SCV codes 1046 and 10002013.

label	power	pressure (mbar)	date/time
vacuum vial	36.6	37.11	12/28/2010 14:22
vacuum vial	18.5	36.2	12/28/2010 14:22
vacuum vial	19.6	36.64	12/28/2010 14:22
vacuum vial 3 ml air	35.5	145.69	12/28/2010 14:23
vacuum vial 3 ml air	21.1	145.66	12/28/2010 14:23
vacuum vial 3 ml air	20.1	145.51	12/28/2010 14:24
vacuum vial 6 ml air	20.1	288	12/28/2010 14:24
vacuum vial 6 ml air	20.9	287.41	12/28/2010 14:24
vacuum vial 6 ml air	21.2	287.39	12/28/2010 14:24
vacuum vial 9 ml air	21.2	427.68	12/28/2010 14:25
vacuum vial 9 ml air	21.5	427.43	12/28/2010 14:25
vacuum vial 9 ml air	21.6	427.14	12/28/2010 14:25
vacuum vial 12 ml air	21.9	570.88	12/28/2010 14:25
vacuum vial 12 ml air	22	570.82	12/28/2010 14:25
vacuum vial 12 ml air	21.9	570.53	12/28/2010 14:26
vacuum vial 15 ml air	22.3	731.85	12/28/2010 14:26
vacuum vial 15 ml air	25.9	733.27	12/28/2010 14:26
vacuum vial 15 ml air	27	734.71	12/28/2010 14:26
vacuum vial 18 ml air	30.2	907.16	12/28/2010 14:27
vacuum vial 18 ml air	29.9	910.47	12/28/2010 14:27
vacuum vial 18 ml air	29.8	911.62	12/28/2010 14:27
vacuum vial 21 ml air	34.3	1004.05	12/28/2010 14:28
vacuum vial 21 ml air	47.2	1005.28	12/28/2010 14:28
vacuum vial 21 ml air	29	1003.42	12/28/2010 14:28