Performance Data and Validation Strategies for the VISTA/O™ In-Line Oxygen Detection System

LIGHTHOUSE
The Science of Pharmaceutical Manufacturing

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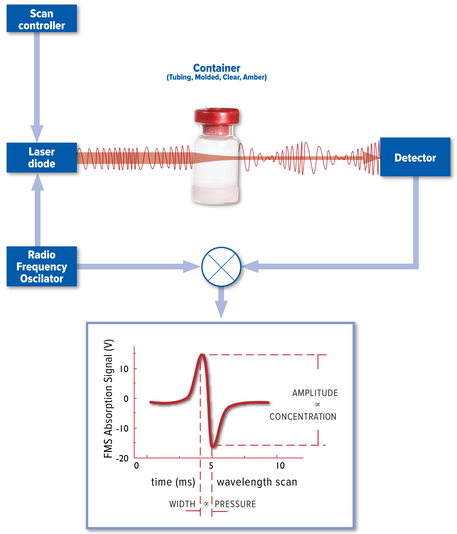
Introduction

Many lyophilized pharmaceutical products are packaged under vacuum in clear, amber, tubing and molded glass containers. Novel process analytical technologies are needed for 100% leak testing. Here we demonstrate the validity of a non-destructive real-time method for measuring headspace oxygen as a means of assessing container closure integrity.

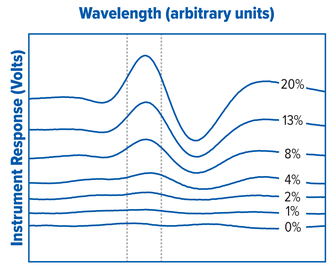
Method

Six pharmaceutical containers (10cc) were filled to atmospheric pressure with 0, 2, 4, 8, and 20% oxygen with a balance of nitrogen using certified gas mixtures (NIST traceable). Multiple headspace oxygen measurements were made on each container. The results were compared with the known values to determine accuracy, precision, linearity, and measurement range for the method using the USP 24 General Test <1225> guidelines.



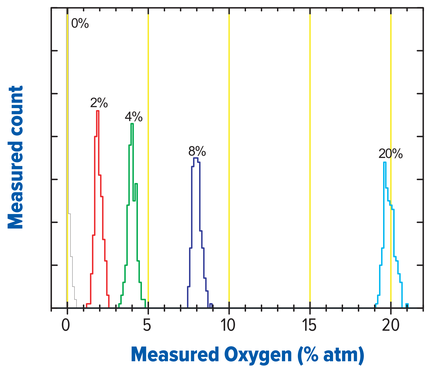
Automation

Headspace oxygen is measured with a Lighthouse VISTA Headspace Oxygen Detection System. The VISTA/O system measures the absorption of laser light by oxygen molecules in the container headspace. The absorption signal amplitude is dependent on the oxygen concentration. The laser absorption signal at varying oxygen concentrations is depicted to the right. The laser system is integrated into a vial transport system for high speed inspection and rejection. The data in this study was collected at 120 vpm.



Data

In-line Headspace Oxygen Histograms
Histograms plotting the results of 100 consecutive in-line measurements of known oxygen standards at a line speed of 120 vials per minute show clear discrimination between the various levels of headspace oxygen.



Precision
The precision of an analytical procedure expresses the closeness of agreement between a series of results obtained from the multiple sampling of the same homogeneous sample under the exact conditions required for performance of the method. This quantity is usually expressed in terms of the relative standard deviation measured during the multiple series of measurements.

The table below presents the standard deviation and relative standard deviation for 100 separate measurements of each oxygen standard.

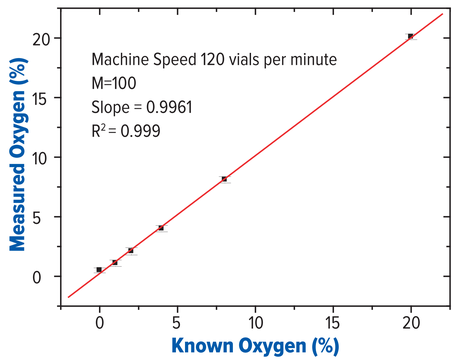
MEAN OXYGEN(%)	ST (N=100)	RSD %
0.07	0.12	n/a
1.99	0.23	12
4.06	0.26	6
8.07	0.26	3
19.96	0.34	4

Accuracy
The accuracy of an analytical procedure expresses the closeness of agreement between the value found using the method and the value that either is accepted as a conventional true value or is an accepted reference value.

The table below shows a comparison of known oxygen to measured oxygen for N=100 measurements at 120 vials per minute. The accuracy is stated as the absolute difference between the two.

MEAN OXYGEN(%)	ST (N=100)	ACCURACY
0	0.07	0.07
2	1.99	0.01
4	4.06	0.06
8	8.07	0.07
20	19.96	0.04

Linearity
The linearity of an analytical procedure is its ability to yield test results that are directly proportional to the concentration of an analyte in samples in a given range. Linearity is expressed in terms of the variance around the slope of the line (calculated using standard linear regression) from test results obtained via the analysis of samples containing varying concentrations of analyte.



Results

Accuracy: +/- 0.07%
Precision: +/- 0.34%
Linearity:
0.9961 slope
0.999 linear correlation coefficient
Range of Measurement:
Present Study: 0 to 20%
Method Capability: 0 to 100%

Conclusion

The measurements demonstrate a novel method for automated and non-destructive monitoring of oxygen in the headspace of parenteral containers. The VISTA/O system complements the award winning, FDA registered VISTA/P headspace pressure detection system. Among the many uses of these systems are leak detection of lyophilized product, process monitoring for oxygen sensitive liquid product, and container closure integrity studies.