

APPLICATION NOTE

Nitrogen purge optimization
and validation of sterile liquid
filling lines ●



INTRODUCTION

Sterile liquid filling lines are increasingly being implemented with nitrogen purge capability during filling. Large molecule biopharmaceuticals can be prone to oxidation and to prevent this from occurring, the headspace is often purged with an inert gas during filling to ensure a longer shelf life. Consistently producing containers with specified headspace oxygen conditions depends on a number of parameters and is not necessarily straightforward. The use of a fast and robust oxygen monitoring method can significantly streamline the set up and validation of a filling line. For these reasons, laser-based headspace analysis is often the method of choice for monitoring headspace oxygen levels during filling.

METHOD HIGHLIGHTS

The LIGHTHOUSE laser-based headspace method shines light through the headspace to measure headspace oxygen concentrations in finished product containers. Based on spectroscopic methods, the measurement is analytical, rapid, and non-destructive. These characteristics enable immediate feedback on the headspace oxygen levels in product containers during filling. This is especially useful during the set-up, optimization, and

qualification of a filling line configured for nitrogen purging. Portable benchtop headspace oxygen analyzers can be implemented at-line to make immediate headspace oxygen measurements as a function of the various nitrogen purging parameters. Robust filling line performance qualification data can be collected efficiently saving both time and resource. Figure 1 shows the measured headspace oxygen in syringes filled and purged on a line being validated in a new parenteral manufacturing

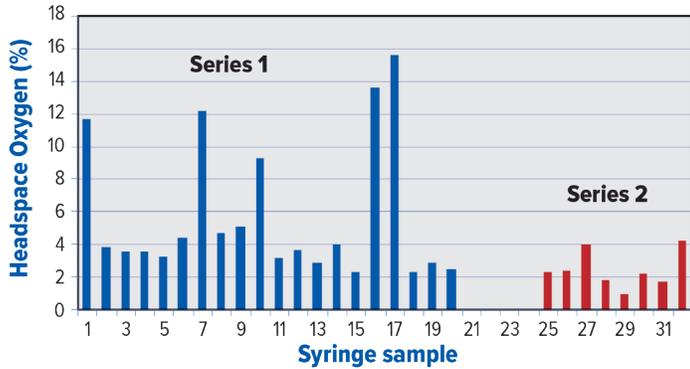


Figure 1: Measured headspace oxygen levels in syringes filled and purged on a line that is being validated in a new manufacturing facility.

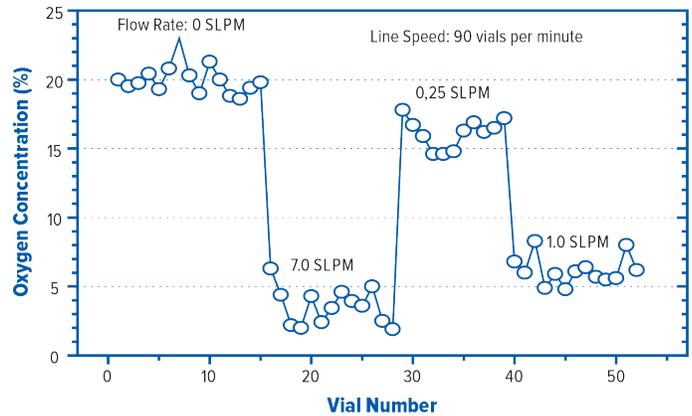


Figure 3: Automated headspace oxygen analysis performed while the nitrogen purging rate is adjusted during filling.

facility. An initial series of syringes analyzed at-line showed some samples having oxygen levels above the 5% specification. After optimization of the filling process, a later series showed syringes being produced with no outliers. It is also possible to implement 100% in-line oxygen monitoring of product on the filling line (Figure 2). Figure 3 shows the results of automated headspace oxygen measurements performed while the nitrogen purging rate was adjusted in real time during filling. The results show that the higher the purging rate in standard liters per minute (SLPM), the lower the oxygen levels in the finished product vials. Automated machine platforms can be implemented in-line after

filling to measure the headspace oxygen levels in 100% of the product containers. Such a 100% oxygen monitoring implementation not only monitors the purging process but also guarantees that 100% of product is purged below specified headspace oxygen levels.

BENEFITS

- Laser-based headspace is analytical, rapid, and non-destructive
- Gives fast feedback on purge performance during filling
- Measurement method is robust and independent of operator
- Enables efficient, accurate optimization and validation of the filling line
- Scalable for 100% monitoring of product during filling

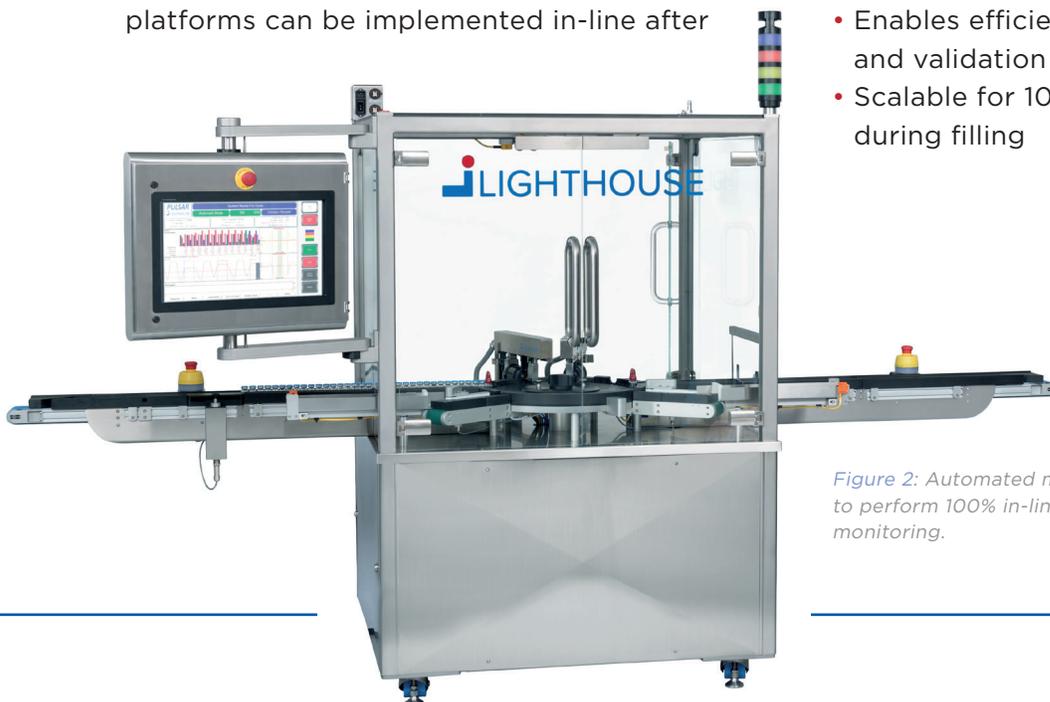


Figure 2: Automated machine to perform 100% in-line oxygen monitoring.

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