LIGHTHOUSE
The Science of Pharmaceutical Manufacturing

Technical Note 202

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. 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.

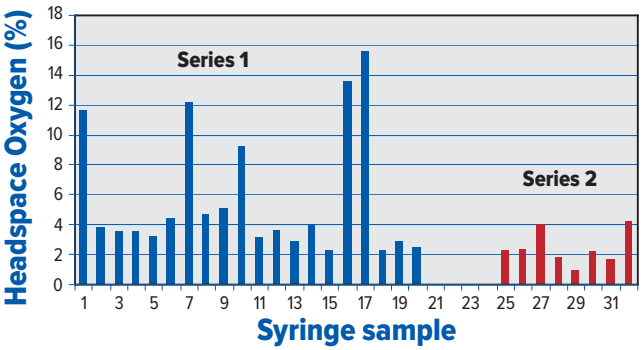

Figure 1

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 allow oxygen analysis to be implemented at-line for immediate feedback on the oxygen levels as a function of nitrogen purging parameters. Figure 1 shows the

measured headspace oxygen in syringes filled and purged on a line being validated in a new parenteral manufacturing 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 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. However, it is apparent that little purging efficiency is gained when increasing the rate from 1.0 to 7.0 SLPM.

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

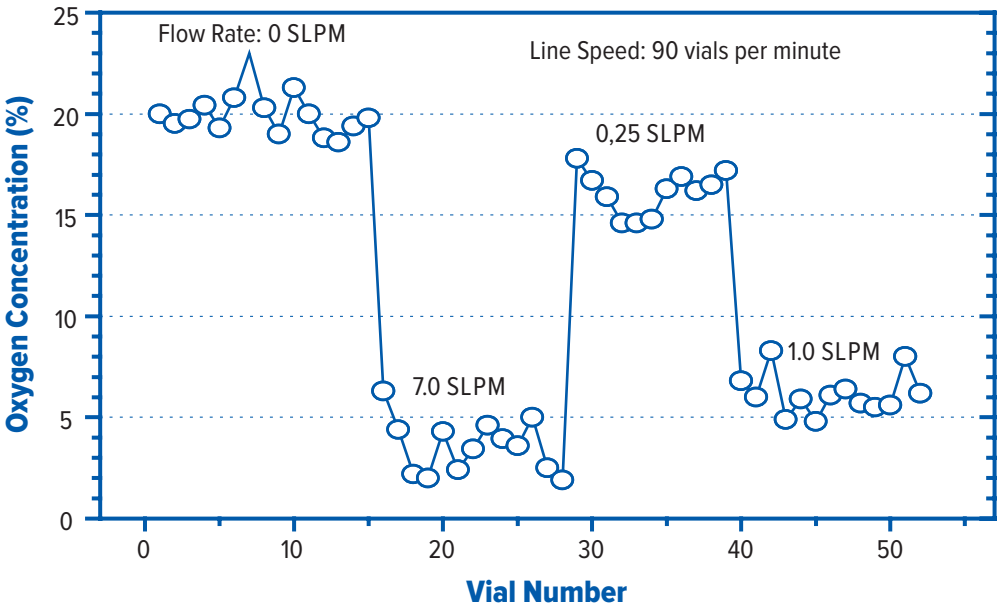

Figure 2