LIGHTHOUSE

THE SCIENCE
OF PHARMACEUTICAL
MANUFACTURING

CASE STUDY

Manufacturing: Filling Line Nitrogen Purge Qualification

Background

- A client had an existing filling line and wanted to optimize the nitrogen purge process to decrease headspace oxygen levels to 2%.
- In addition, frequent line stoppages resulted in a need to identify and reject high oxygen vials that had lost the nitrogen headspace during the stoppage.
- A purging process qualification study was performed using rapid non-destructive headspace oxygen analysis in an at-line set-up with samples being measured immediately from the line.

Purge Qualification Study

The existing filling line consisted of a pre-purge, and a post purge where nitrogen would be blown into the vials after filling of the product (Figure 1, right to left).

As shown in the schematic there is a 'dead space' before stoppering occurs. This residence time before stoppering allowed nitrogen gas to escape. The client was aiming to reduce the headspace oxygen to 2% but could do no better than 5% headspace oxygen because nitrogen was escaping before the vials were stoppered.

A suggestion, from the filling line manufacturer, was to introduce a Nitrogen Overlay System in the dead space (see Figure 1). However, the nitrogen 'tunnel' made the situation worse and the headspace oxygen could not be purged lower than 7%. The Nitrogen Overlay System caused turbulent gas flow around the open vials, pulling air from around the vials into the headspace and preventing efficient purging. The solution was an extended post purge arm (Figure 2, right to left). Post purge was done closer to the stoppering, reducing the residence time and allowing less nitrogen to escape.

The extended post purge arm allowed the client to achieve the targeted 2% headspace oxygen. Figure 3 shows the measured headspace oxygen levels as a function of the residence time.

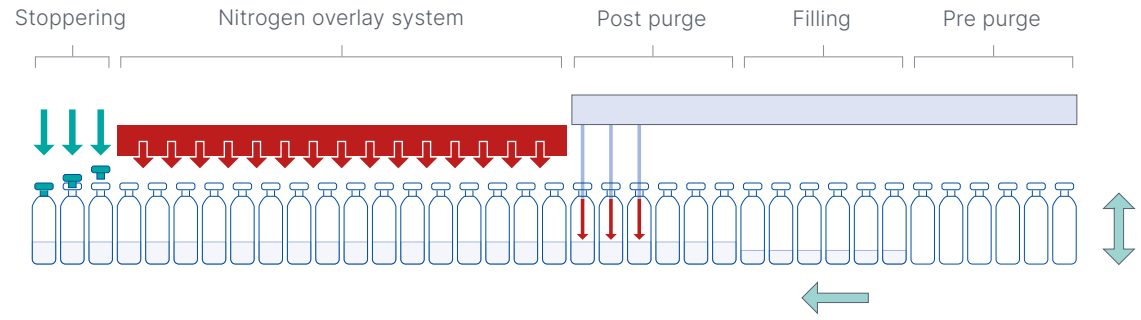

Figure 1: Filling line schematic illustrating the Nitrogen Overlay System in the 'dead space'.

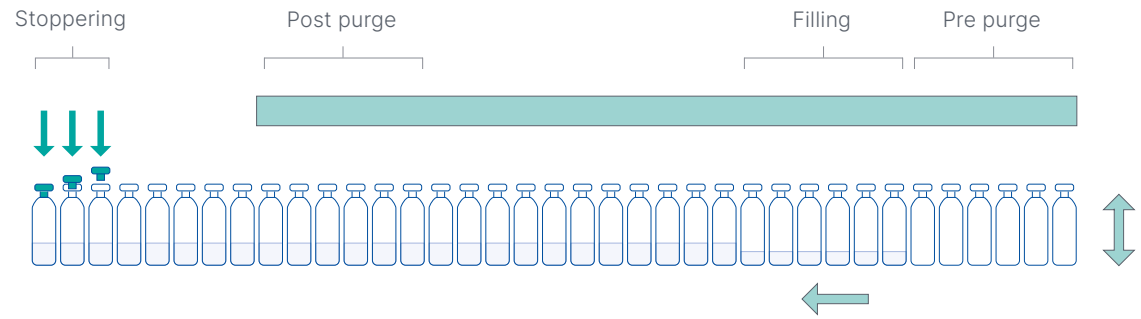

Figure 2: Filling line schematic including an extended post purge arm to purge closer to the stoppering.

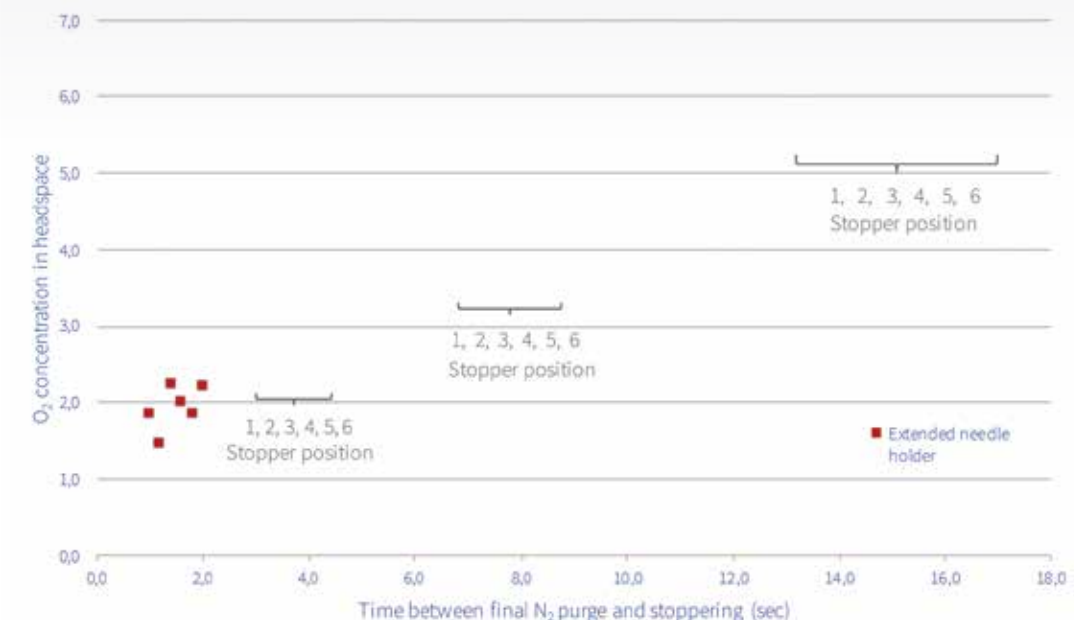

Figure 3: Headspace oxygen levels as a function of the residence time, comparing the filling process using a standard needle holder with using an extended post purge arm. The targeted 2% headspace oxygen is achieved using the post purge arm (extended needle holder).

Conclusion

Use of the at-line headspace oxygen analyzer during the purge qualification study enabled:

- Efficient purge optimization and validation.
- Optimal purge performance at ~2% headspace oxygen.
- Validation of a software solution to reject a fixed number of vials after a line stoppage.
- Ultimately, a significant reduction in production downtime.

Manufacturing departments filling oxygen-sensitive formulations benefit greatly from using LIGHTHOUSE FMS-Oxygen Headspace Analyzers. At-line configurations give operators the ability to quickly and accurately determine headspace oxygen levels. This in turn streamlines filling line optimization and qualification during set-up and enables in-process control measurements during routine production.

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