LIGHTHOUSE

THE SCIENCE
OF PHARMACEUTICAL
MANUFACTURING

CASE STUDY

Quality Stability Testing: Oxygen Monitoring During Shelf Life

Background

- A manufacturer of a syringe product received complaints about discolored product that was nearing the end of shelf life.
- A root cause investigation was started and product syringes were put on stability. The headspace oxygen levels were monitored over time.
- Laser-based headspace analysis is a useful tool to check package integrity and for the presence of reactive headspace gases that can degrade the formulation.

Stability Study

Headspace oxygen of syringe product samples with three different fill levels (Level 1 = low, Level 2 = medium, Level 3 = high) was monitored over a period of 12 months. The initial levels of oxygen in the product samples were low.
In the filling process, a nitrogen overlay was used to fill the headspace with nitrogen in order to protect the formulation from degradation by air.

The results (Figure 1) show increased levels of headspace oxygen after 6 months. This can be explained by air permeating into the product syringes, and oxygen therefore coming into the headspace. Initially the oxygen is consumed by the product, but when the formulation became saturated with oxygen, it started to degrade and the oxygen consumption could no longer keep up with the permeation rate into the syringe. The headspace oxygen levels then started to rise (note that saturation occurred for the lower fill levels but not the high fill level).

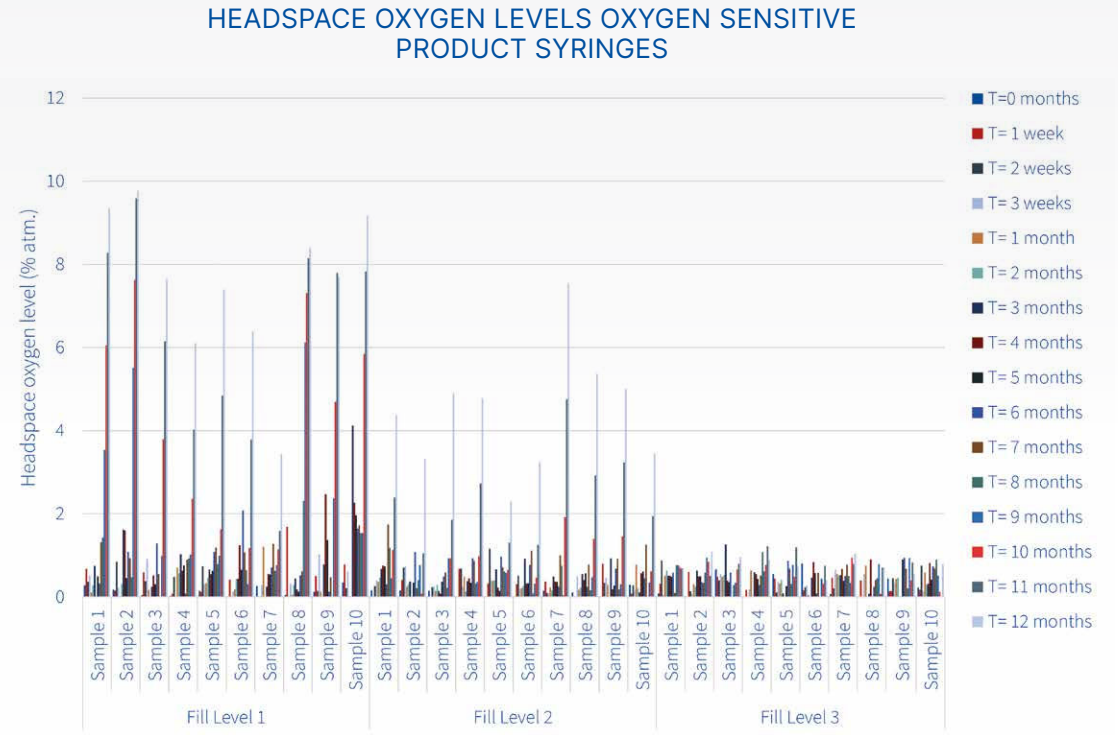

Figure 1: Results of stability study showing headspace oxygen levels during a period of 12 months.

Conclusion

The stability study showed that syringe samples with lower fill levels (and less product) demonstrated an earlier increase of headspace oxygen. If there is less product in the syringe, oxygen saturation will occur faster and headspace oxygen levels will rise sooner, eventually leading to discoloration of the product.

This study provided an opportunity to extend the product shelf life, either by optimizing the formulation or by improving the packaging to provide a better barrier for gas permeation over the shelf life.

Pharmaceutical QC laboratories working with oxygen-sensitive formulations benefit greatly from using LIGHTHOUSE FMS-Oxygen Headspace Analyzers.

Replacing traditional destructive methods that use electrochemical sensors, gas chromatography, or invasive sensors with accurate non-destructive laser-based headspace analysis saves valuable product samples for other tests and avoids product disposal and contamination issues.

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