LIGHTHOUSE

THE SCIENCE
OF PHARMACEUTICAL
MANUFACTURING

CASE STUDY

# CCI Test Method Validation for Pre-filled Syringes

# Background

- Regulators are paying closer attention to the proper design of robust Container Closure Integrity (CCI) studies and the validation of CCI test methods.
- A method was developed for CCI testing of pre-filled syringes and then validated.
- The purpose of Method Validation is to demonstrate sufficient accuracy and reproducibility of a method, in this case to detect CCI defects at the plunger seal of a pre-filled syringe.
- The developed CCI test method uses Headspace Gas Ingress analysis to identify changes in the headspace content of the syringe that result from gas ingress through a leak.

# The Method

The method applied uses an FMS Headspace Gas Analyzer and a CCI Test Vessel, offering a robust solution for CCI Testing. This method utilizes Headspace Gas Ingress analysis to measure changes in the headspace gas composition of the syringe that result from gas ingress through a leak.

The CCI Test Vessel creates an environment that accelerates gas ingress through an open defect. Samples are placed inside the vessel and exposed to a tracer gas (in this case carbon dioxide).
In the case of a closure defect, $CO_2$ will leak into the syringe headspace and will be detected by performing headspace analysis.

## METHOD VALIDATION

Three operators performed headspace analysis, each on 5 samples of every control group.

Before measurement, the samples were pre-conditioned in the CCI Test Vessel for 30 minutes at 1.3 atm of $CO_2$ overpressure and subsequent headspace analysis of all the samples was easily performed in less than 15 minutes.

Sample overview:

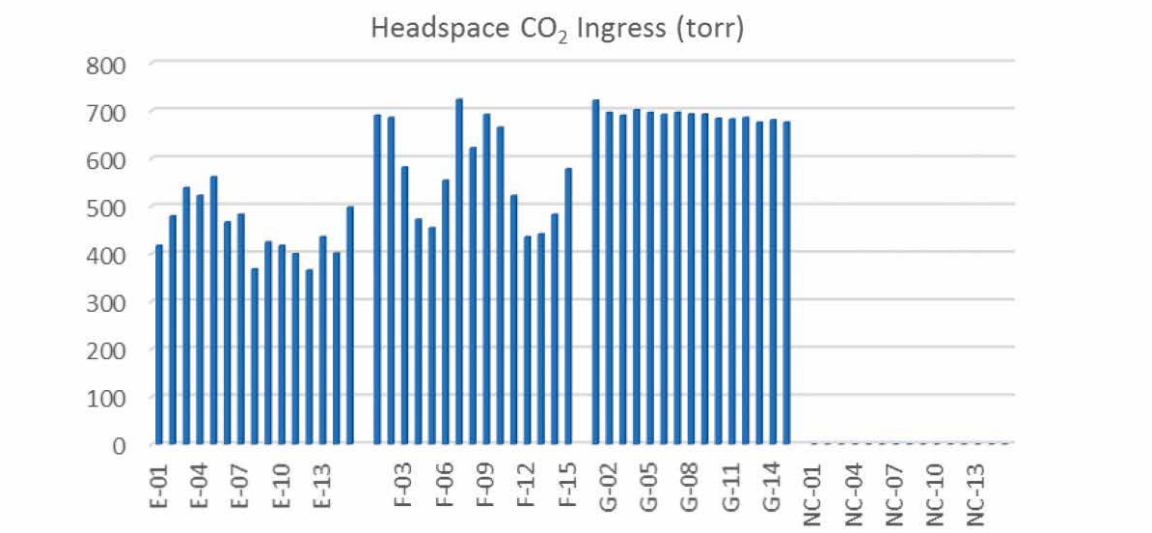
| NUMBER OF SAMPLES | CONTROL GROUPS |
|---|---|
| 15 | Positive Control - small defect - empty (Figure 1) |
| 15 | Positive Control - small defect - formulation |
| 15 | Positive Control - small defect - empty |
| 15 | Negative Control |

Figure 1
Positive control with a tungsten microwire creating a small defect.

# Conclusions

The purpose of the Method Validation was to demonstrate that the method is sufficient for accurately and reproducibly detecting critical defects at the plunger seal. All the positive controls in this study measured more than half an atmosphere of $CO_2$ ingress into the syringe headspace. All negative controls measured no $CO_2$ ingress.

This headspace gas ingress CCI testing method was shown to be validated for the detection of a critical leak for a specific product configuration. The parameters of the method can be straightforwardly optimized to generate robust CCI data on other products if appropriate.




| 1 ML SYRINGES | $CO_2$ INGRESS (TORR) | LEAK | CCIT |
|---|---|---|---|
| | AVERAGE | DETECTED | RESULT |
| Positive Control - empty | 451 | 15/15 | 100% Pass |
| Positive Control - filled | 573 | 15/15 | 100% Pass |
| Gross Defect | 690 | 15/15 | 100% Pass |
| Negative Control | 0 | 0/15 | 100% Pass |

## CONTACT US

- Lighthouse Instruments, LLC
  2050 Avon Court
  Charlottesville, VA 22902
  United States of America
  Office • +1 (434) 293-3081
  Email • info@lighthouseinstruments.com

  www.lighthouseinstruments.com

- Lighthouse Instruments B.V.
  Wisselwerking 22
  1112 XP Diemen
  The Netherlands
  Office • +31 (0)20 7051 050
  Email • euinfo@lighthouseinstruments.com