

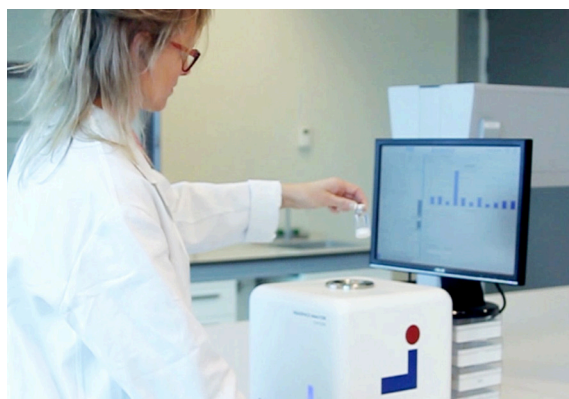


Container Closure Integrity Testing

PRODUCT NOTE 302

The new USP<1207> Sterile Product Packaging-Integrity Test chapter scheduled for release in August 2016 revises the test methods recommended for use to detect leaks or loss of integrity in sterile pharmaceutical product containers.

In the new chapter, microbial immersion and dye ingress methods are classified as probabilistic methods which require a series of sequential events with random outcomes to qualitatively determine if a package has leaked. Due to the risk of false negatives, these probabilistic methods require that both positive and negative controls are used for every measurement test session. The new recommendations in the chapter describe and recommend the use of deterministic methods, which predictably and quantitatively measure



a physical or chemical endpoint, for all new container closure integrity (CCI) tests.

Laser-based headspace analysis is described as a non-destructive deterministic method that uses laser spectroscopy to detect gas flow through a container defect. Having introduced this method into the pharmaceutical industry more than fifteen years ago, LIGHTHOUSE supports customers who are preparing to implement deterministic CCI testing methods.

CCI TESTING SUPPORT SERVICE OPTIONS

Feasibility studies	Samples sent to LIGHTHOUSE lab facility for CCI feasibility studies
CCI method development	LIGHTHOUSE Application Scientist performs outsourced CCI method development
CCI validation protocols	Customized protocols provided for CCI validation
Troubleshooting inspection	Lease equipment available for on-site CCI testing of commercial product

MEASUREMENT CAPABILITIES

Headspace parameters	Headspace oxygen, pressure (vacuum), carbon dioxide for CCI testing
Containers	Sealed vials, ampoules, bottles, syringes (tubing, molded, clear, amber, clear plastic)



Container Closure Integrity Testing

PRODUCT NOTE 302

Key Points in the new USP<1207> chapter

- Definition of deterministic vs. probabilistic CCI test methods.
- Recommendation that only deterministic methods be used unless no deterministic method exists or in special cases where a package requires a direct microbial assessment.
- No requirement to compare the new deterministic method to existing microbial immersion or dye ingress methods.

Why choose LIGHTHOUSE as a CCI test method partner?

- Expertise in the laser-based headspace method having originally developed it with funding from the Food and Drug Administration
- CCI Application experts provide support with CCI studies, test method choice, as well as

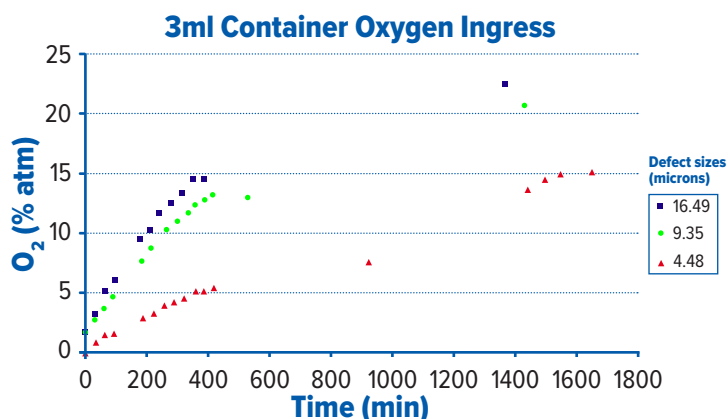


Figure 1: The rise in oxygen levels in nitrogen-purged containers having known defect sizes measured with the non-destructive headspace method from LIGHTHOUSE.

method development and validation.

- LIGHTHOUSE platforms have inspected the closure integrity of millions of finished product containers.
- For commercial product batches, support is also available for CCI troubleshooting or for the lease of equipment for on-site testing.

NEW USP CHAPTER <1207> DEFINITIONS OF CCI TEST METHODS

<i>Deterministic</i>	<i>Probabilistic</i>
Predictable & quantitative	Qualitative
Physical-Chemical endpoint	Relies on series of sequential events with random outcomes
Non-destructive	Destructive
No sample prep	Requires manual sample prep
Validated for reproducible leak detection	Requires positive & negative control in every test