LIGHTHOUSE
The Science of Pharmaceutical Manufacturing

Technical Note 204

Detection of microbial contamination in sterile containers using headspace analysis

INTRODUCTION

Sterility testing in the pharmaceutical industry has long been based on growth media culture methods. The general approach is to incubate for 14 days and then determine potential contamination with a visual inspection of the media sample. Over the last decade a number of Rapid Microbial Methods based on various analytical techniques have been implemented. These provide quicker, more sensitive, accurate, and reproducible test results when compared with conventional, growth-based methods. Recently, it has been demonstrated that laser-based headspace provides yet another alternative approach for detecting microbial contamination in sterile pharmaceutical product. Applications for this method include automated media fill inspection and rapid non-destructive contamination testing directly in finished product containers.

METHOD HIGHLIGHTS

The LIGHTHOUSE laser-based headspace method shines light through the headspace to measure headspace gas concentrations in finished product containers. Based on spectroscopic methods, the measurement is analytical, rapid, and non-destructive. When microorganisms grow inside a pharmaceutical container, they consume oxygen (for aerobic growth) and/or produce carbon dioxide. The changes that result in the headspace gas composition of the pharmaceutical container can be dramatic. Figure 1 shows how headspace oxygen and carbon dioxide levels of growth media vials evolve during a 14 day incubation period after inoculation with a microorganism. In this particular case, the analytical headspace measurement detects headspace oxygen con-

sumption and carbon dioxide production from the growing microorganisms after 24 hours of incubation. The headspace measurements show that oxygen inside the media vial has been fully consumed, and corresponding maximum levels of carbon dioxide reached, after 72 hours of incubation. Microbiological applications for the laser-based headspace method include automated media vial inspection and non-destructive finished product inspection in support of sterility failure troubleshooting and investigations.

BENEFITS

- Laser-based headspace is analytical, rapid, and non-destructive
- Method can be automated to achieve inspection speeds of several hundred samples per minute
- Measurements of headspace oxygen and carbon dioxide provide two independent analytical measurements to identify microbial growth
- Measurement method is robust and independent of operator

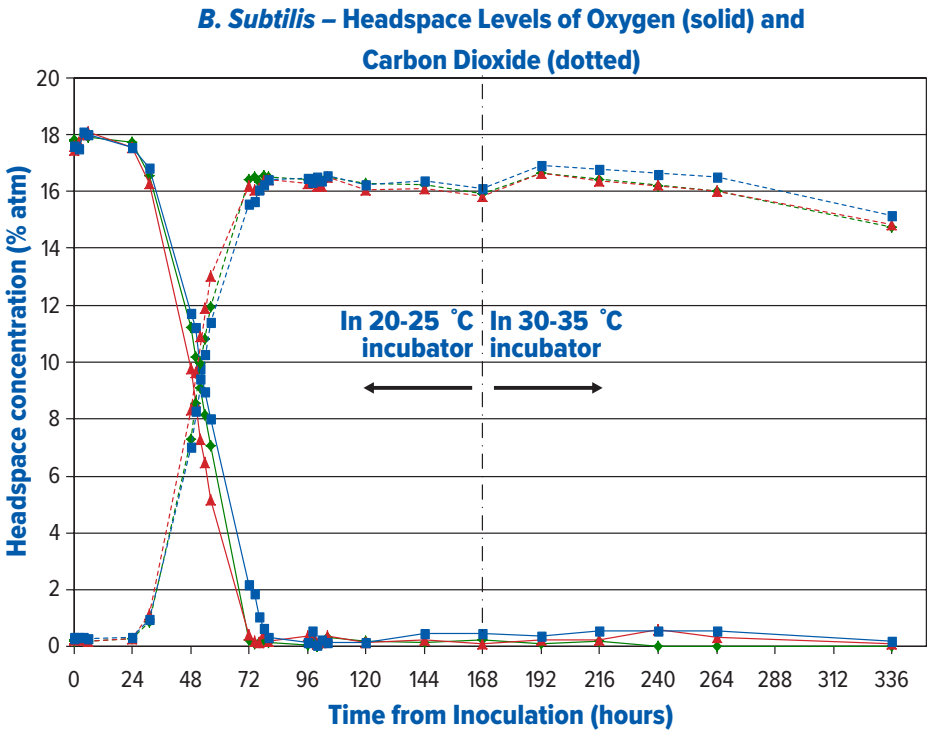

Figure: Headspace oxygen and carbon dioxide concentrations in three media vial samples injected with < 100 CFU of Bacillus subtilis (ATCC 6633) plotted over the 14 day incubation period. Growth is detected after 24 hrs with the headspace conditions changing drastically in the first 72 hrs.