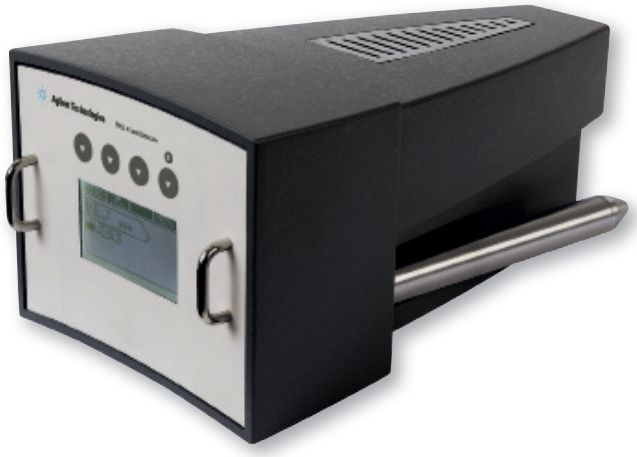
Application Note

Agilent
Trusted Answers

Leak Testing for Biopharmaceutical Applications

PHD-4 portable helium leak detector for biopharmaceutical applications



Agilent Portable Helium Leak Detector prevents product loss

The biopharmaceutical industry uses fermenter and bioreactor vessels to produce a myriad of products. These vessels can be quite large and typically have many wall penetrations. The penetrations can include stirrers, process instrumentation, vents, and fill and drain connections. Between process runs, the vessels are commonly drained, then steamed out before being “buttoned up” for the next campaign.

Infinitesimal leaks can be created during the cleaning process when valves are operated, and/or clamp fittings are opened and closed. In addition, as valves and other seals wear over time, they can develop leaks. Small leak paths will allow bacteria to enter the vessel, and ruin the batch.

Traditional Methods of Leak Detection

The biopharmaceutical industry has traditionally used pressure decay and/or visual (bubble testing) leak detection methods (such as the use of "Snoop®") to detect leaks in process vessels.
Both leak detection methods present major drawbacks:

- **Pressure Decay** uses compressed air to elevate the vessel pressure, and then relies on the ability of an operator to discern a change (decay) on a pressure gauge reading over a set period of time.
  Furthermore, pressure decay just indicates that there is a leak, but does not help the operator locate the leak!
- **Bubble Testing** uses a solution of soap and water squirted over various vessel penetrations, in an effort to identify leaks by seeing bubble formation at the leak site.
  While the bubble test method can find larger leaks, it is a crude and highly subjective leak detection method, which rarely provides repeatable results.
  Bubble testing cannot show small leaks or leaks in places like internal valve seals (valves are often installed in a horizontal position, and would have to be flooded with the soap solution in order to show the leak).

Agilent PHD-4, the solution...

What it is…

Agilent Technologies' PHD-4 is a portable leak indicator, which detects helium tracer gas that has been injected into the vessel, as it escapes the vessel through a leak path.
The sensitivity of the PHD-4 in finding leaks is about **three orders** of magnitude greater than conventional bubble testing methods.

Why helium as a tracer gas…

Helium is present in only small amounts (5 ppm) in the ambient air. This results in low background noise and makes helium a very attractive gas for leak detection applications.
In addition, helium is:

- readily available on a worldwide basis.
- not toxic or flammable
- an inert gas.

Helium can be easily obtained in cylinders of various sizes and only needs to be of welding-grade purity.

The application…

The vessel is pressurized slightly and filled with a diluted concentration of helium. This will reduce the amount of helium used while still providing adequate sensitivity. Testing can start immediately after pressurization. The operator moves the PHD-4 flexible "sniffer" probe over suspected leak sites and into valve areas. The PHD-4 will provide both a visual (helium concentration) and audio (similar to a Geiger counter) indication of not only a leak, but the relative size and location of the leak found. The PHD-4 can measure concentrations generally down to as low as 2 ppm/helium, but practically, readings of 20 ppm and higher represent leaks that can be repaired, prior to returning the process vessel to service.

What is the pay back?

Over the past twenty years, the PHD-4 technology has proven to be a valuable tool for bio-pharmaceutical companies. Until now undetectable with "Snoop®" or pressure decay methods. PHD-4 has helped to virtually eliminate lost product due to bacteria entering through undiscovered leaks in the process. The leak testing time is drastically cut, and the probability of identifying important leaks is greatly enhanced. Generally the value of the first batch of product saved using the PHD-4, will pay for its cost many times over.

Comparison and Conclusion

The PHD-4 can be viewed as a qualitative and quantitative tool, similar to "Snoop®", but 1000 times more sensitive than "Snoop®" in finding leaks.
Engineers from a large U.S. pharmaceutical company using the PHD-4 have called it the "best practices" method for finding leaks in bioreactors and fermenters.

Reactor and fermenter vessels require more rigorous ways to find and eliminate leaks then the widely-used pressure decay and/or Snoop® methods. Agilent Technologies' PHD-4 portable helium leak detector offers the solution.

PHD-4 Display

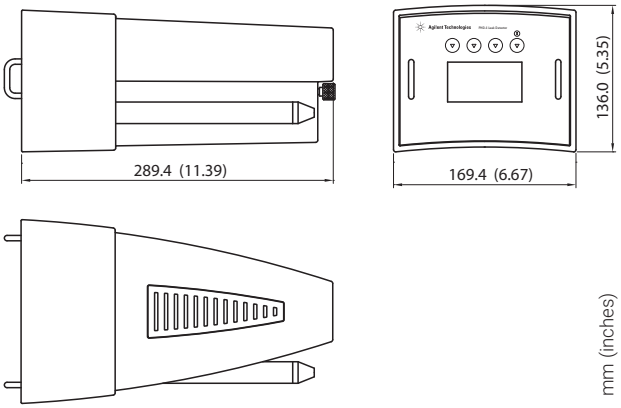
PHD-4 - Principal of Operation

The object or vessel to be tested is filled with a helium-air mixture at a pressure level exceeding ambient conditions. The PHD-4 probe is then passed over the suspected leak area(s), and a gas sample is continuously drawn through a flexible hose by the PHD-4 sampling pump. This pump pulls the gas sample over a special silica capillary which blocks atmospheric gases but allows helium molecules to permeate into the sensor (ion pump based) because of their small size. The sensor output signal indicating the helium presence is processed by dedicated software and allows a direct read-out of helium concentration on the display.

Portable Helium Leak Detector

AGILENT PHD-4 - FEATURES AND BENEFITS	
High Selectivity	PHD-4 is sensitive only to helium. There are no false signals due to the presence of any other gases.
High Sensitivity	PHD-4 is nearly as sensitive to small leaks as a more expensive mass spectrometer leak detector used in the sniffing mode. It will find the leaks in bioreactors and fermenters that need to be addressed.
Battery Operated	PHD-4 can be operated without a main power supply. Up to 4 hours on a single charge.
Simple Operation	PHD-4 is very easy to use and does not require any special operator training. All the active menus of the PHD-4 are available in four languages.
Very Low Maintenance	Replacement of sampling line filters is straightforward and requires only a screwdriver.
Portable	PHD-4 is lightweight, portable and easy to carry, even to the most difficult leak check locations. It weighs only 2.6 kg.

OUTLINE DRAWING



AGILENT PHD-4 - TECHNICAL SPECIFICATION	
Lowest Detectable Helium Concentration:	2 ppm (parts per million)
Lowest Detectable Helium leak:	5 x 10^{-6} atm cc/s 5 x 10^{-6} mbar l/s 5 x 10^{-7} pa m^3/s
Response Time:	< 2 sec
Recovery Time:	<10 sec (from 50 ppm to 0 ppm)
Start up time, including self check-up:	3 min approx.
Electrical Supply:	Rechargeable Battery included Power Supply included 110-240 V 50-60 Hz
Battery operation Time:	4 hours
Maximum Signal Drift:	10 ppm/10 min
Operating Conditions	Temperature: +5°C to +35°C Humidity: 90% maximum relative humidity
Storage Conditions	Temperature: -20°C to +60°C Weight: 2,6 Kg (5.7 lbs)
Compliance to Norms:	CE, CSA/UL approved

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