
Headspace oxygen measurement in vials and ampoules with the Orbisphere PharmaPack in the pharmaceutical industry

Application description



Small volume parenteral (SVP) solutions are packaged in different ways depending on their intended use: as heat-sealed ampoules, vials sealed with a rubber closure, or prefilled syringes.

In some cases oxygen may have negative effects on the product such as:

- oxidative degradation of the active drug substance
- decrease drug potency and reduce product shelf life
- product discoloration, changes in dissolution rate and profile, precipitation
- generation of foul odors and flavors
- generation of adverse pharmacological properties, including those associated with toxicity or negative side effects

In order to avoid this phenomenon the ampoule or vial is flushed internally with nitrogen before filling. Depending on the ampoule/vial shape and line speed, starts and stops, this operation cannot avoid residual air content in the final headspace.

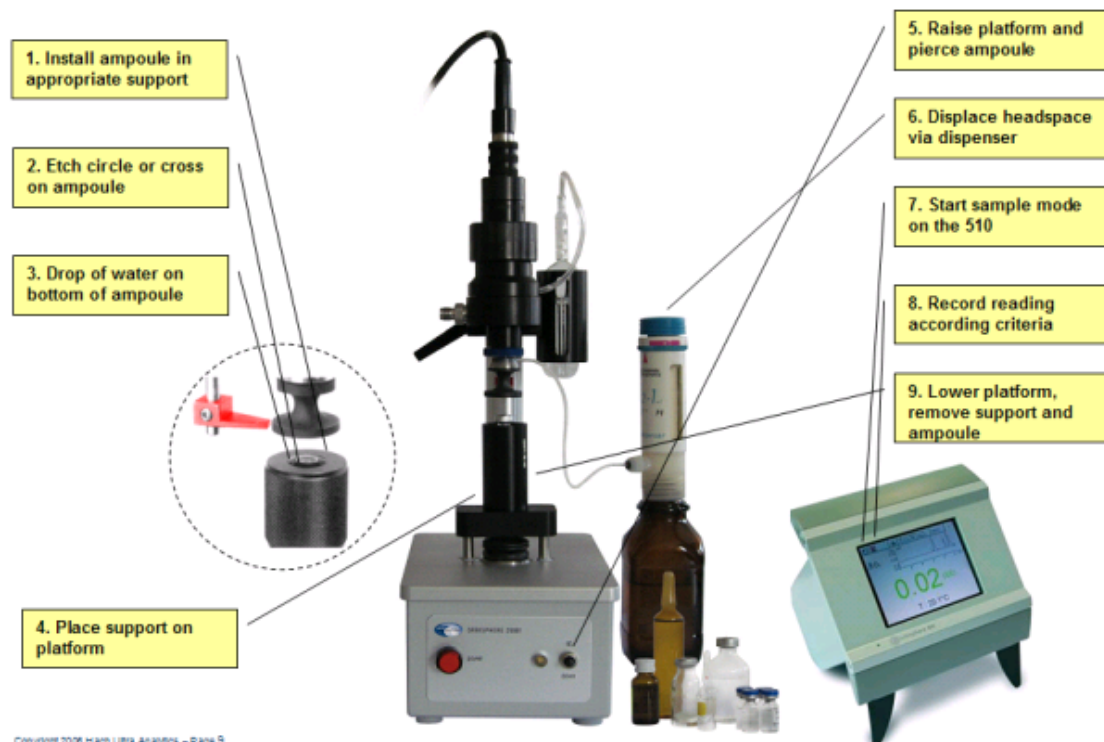
The Orbisphere 29981 (PharmaPack) associated with the model 510 instrument, deliver a reliable analysis of oxygen content in the headspace of any ampoule or vial.

Why choose the Orbisphere PharmaPack 29981?

- Semi-automated sampling, no operator influence, excellent repeatability
- Reduced bench space, suitable for at-line work
- Fast headspace O₂ analysis in < 1 minute, quick information to check on-spec production
- High sensitivity, measures O₂ down to 0.001 %, reduces false alarms
- Proven EC technology in O₂ analysis for ampoules and vials, trusted data for accurate product acceptance decisions
- Continuous nitrogen purged system, allows excellent repeatability for all operating conditions
- New integrated purge gas bubbler, avoids water suction when measuring ampoules with internal vacuum (generated by the heat sealing step)

Operating procedure

Vials or ampoules are installed on a specific support available in all sizes. The whole procedure includes 9 steps (see following illustration) with a headspace analysis completed in less than a minute. Results are given by the 510 instrument and can be exported via the USB port for further analysis.



Which analysis strategy to apply?



The analysis strategy is identified first by quality standard procedures defined in each company. The main parameters to look at are: amount of samples from the line, frequency, acceptance criteria, out of spec procedures. The ISO 2859 is also an excellent source to define the rules of a quality control plan.

A filling machine normally includes many sub lines where vials and ampoules are prepared (nitrogen flushed), filled and sealed.

Each sub line has to be controlled and therefore one to three samples should be taken for control, according to the known variance of each sub line. At the end, a total of 20 samples can be collected for analysis.

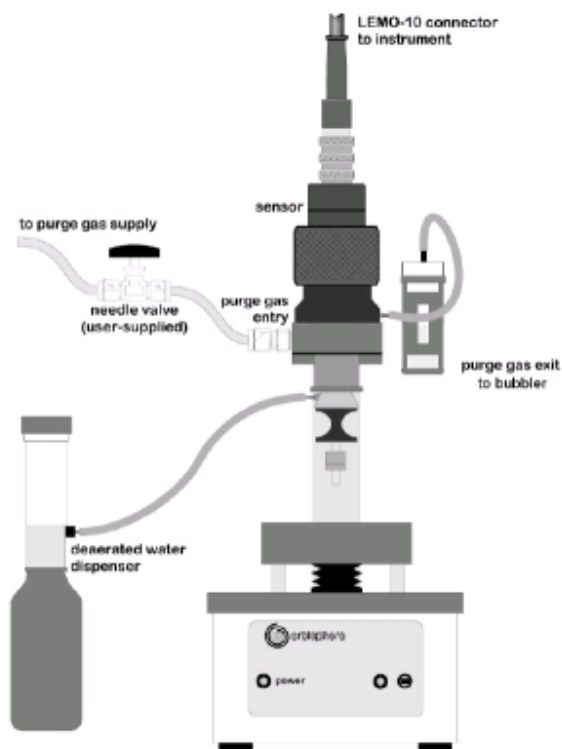
The frequency of sampling has to be linked to the frequency of possible changeovers in the line and also the line stability and the risk of out-of-spec production. It can go from one sample batch every hour, to up to 6 hours.

Acceptance criteria for maximal oxygen content are defined by proper product constraints. Herewith are some values defined in a pharmaceutical company for several oxygen sensitive products:

Product A:	$1.5 \pm 0.5 \%$
Product B:	$4.0 \pm 0.5 \%$
Product C:	$5.0 \pm 1.0 \%$
Product D:	$7.0 \pm 1.0 \%$

Finally, the procedure to apply to production problems has to ideally follow a flowchart of troubleshooting actions and controls. This allows for a maximum reactivity and a low impact on production efficiency.

System installation recommendations



The whole system requires less than 20 dm² and can be located close to the filling line.

Nitrogen (better than 99.99% purity) is required to continuously purge the system.

Installation and Operation Qualifications of the whole can be performed by our technical staff following precise SOP's.

Recommended systems components

The following table describes the complete set of items required for package analysis. The piercing head is different for vials and ampoules. Swapping piercing heads is simple and done in a matter of seconds without further setup modification, calibration or system shutoff.

Model	Description
510/A00/T1C00000	Orbisphere 510 oxygen (EC) instrument, portable, 85-264 VAC, three 0/4-20mA analog outputs, RS485
31110A.02	EC Sensor, Substance measured: Oxygen, Sensing head material: PEEK, Guard ring: Silver, Maximum pressure: 20 bar, O-Ring: EPDM, Fast response to change in temperature.
29981	Package sampler for vials and ampoules. Flow chamber 32017, and piercing needle assembly 280582 (ampoules) and/or 280583 (vials) must be ordered separately.
32017	Flow chamber for use with 29981. Must be ordered separately.
32505.03	3 meter sensor cable for all new TCD sensors, and for all sensors for 2620, 2640 and 264xx instruments. Supplied with 2 connectors. 10 wires, black sleeve.
29872	Test and verification chamber for 29980 & 29981.
32919	Spare part and tool kit for 29981 sampler. Includes 28301, 28302, 28303, 32916, 28042, and 32917.
32918	Water separation filter, Goretex, 32mm diameter (10 pieces). For 29981.
28300	Dispenser for sampler 29980 and 29981.
32703	Maintenance Kit for oxygen electrochemical sensors. Includes membranes 2956A, electrolyte 2959, membrane holding ring 29228, and tools for sensor maintenance.
32305	Measurement certificate, indicating that the system performs within specific measurement norms for the system in question.
280582 or 280583	Piercing needle assembly (blue) for ampoules. For use with 29981. Piercing needle assembly (yellow) for vials. For use with 29981.
3300x	Power supply cable for portable 510 instruments (x = 1: Europe; x = 2: US; x = 3: CH; x = 4: UK)
IQOQ-PHP-510	IQ-OQ / Orbisphere PharmaPack with 510