



QUANTUM

MULTI-PURPOSE LYOPHILISATION PROCESS
QUANTITATION, ANALYSIS & CONTROL

IMA  **LIFE**
Aseptic Processing & Freeze Drying Solutions

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DETECT, QUANTIFY, CONTROL.



THE SMALLEST INDIVISIBLE MEASURE, BE IT ENERGY, MOMENTUM OR MASS, NOW APPLIED TO FREEZE DRYING.

Lyophilization or freeze-drying involves removal of solvent, typically water, from a frozen solution by sublimation, resulting in a porous (cake like) structure.

The process is inefficient and expensive due to the slow drying rates and the operating expenses associated with the use of chillers and other equipment needed for the process. The bulk of the water vapor is removed during primary drying (sublimation) and the remaining during secondary drying (desorption) at controlled temperatures to avoid irreversible damages to the active ingredient.

Coupled with the value of the products manufactured in each batch of a freeze drying cycle, testing product integrity is of paramount importance.



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Real time in-situ monitoring of the drying process, both during primary and secondary drying at laboratory scale and production scale provide unprecedented process quantitation and control capability through:

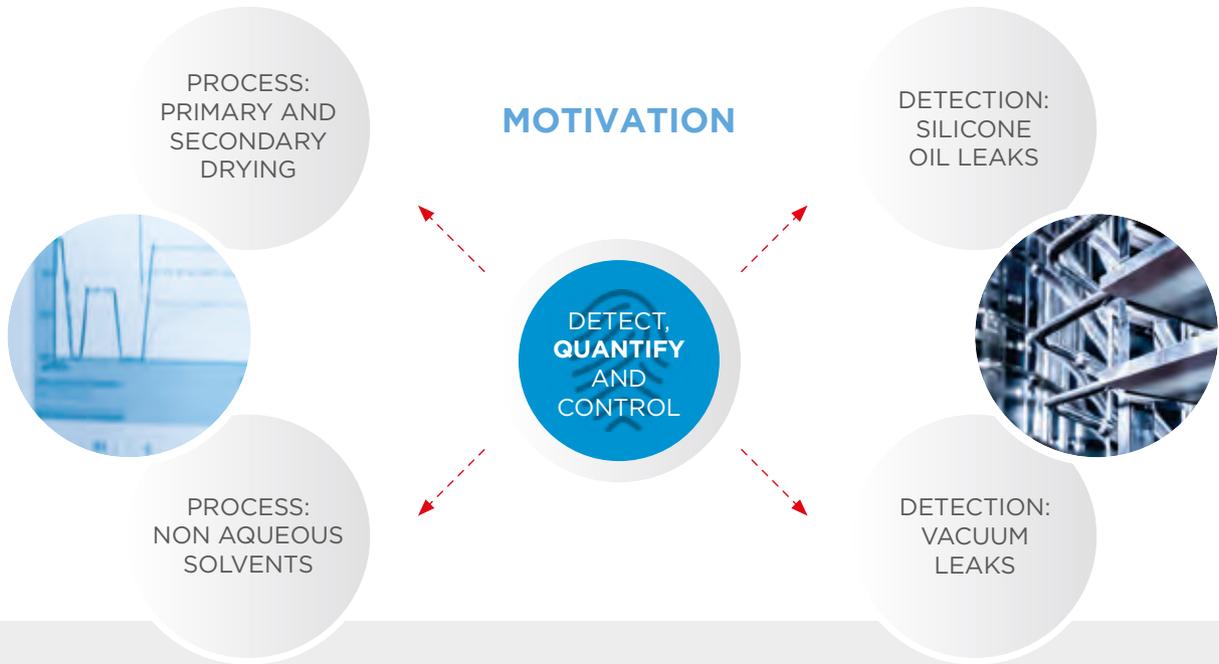
- **Guaranteeing quality assurance** by reducing rejects and maximizing confidence through real-time quantitation of the drying process.
- **Maximizing the return on investment (ROI)** by accurately detecting process endpoints and identifying presence of trace contaminants prior to failure events.



FROM THE FDA'S DOCUMENT ON FREEZE-DRYING INSPECTION (UCM074909)

"It is necessary to **monitor the leak rate** periodically to maintain the integrity of the system. It is also necessary, should the leak rate **exceed specified limits**, to determine the actual leak site for purposes of repair".

"Leakage into a lyophiliser may originate from various sources. As in any vacuum chamber, leakage can occur from the atmosphere into the vessel itself. Other sources are media employed within the system to perform the lyophilizing task. These would be the **thermal fluid circulated through the shelves** for product heating and cooling..."



QUANTUM smart miniature **Mass Spectrometer (MS)** is a non-invasive technique capable of performing quantitative real-time process relevant measurements.

It is a multi-purpose device designed ground-up for use in pharma freeze dryers **detecting contaminants and process gases at concentrations down to ppm levels.**

Not only does this allow for **silicone oil detection** and for **non-aqueous solvent detection**, but **QUANTUM** can also be used as a **system leak detection tool** and as a **process analytical tool for scale-up and development studies.**

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FEATURES AND PERFORMANCES OF QUANTUM SMART SPECTROMETER™

QUANTUM is a miniaturized fully integrated small footprint process mass spectrometer. At the heart of QUANTUM is a pre-calibrated modular sensor comprising a long lasting ion source, a multichannel quadrupole array mass filter and the Faraday Cup detector (FC). In addition, the QUANTUM assembly houses the sampling sub-system all control electronics and the complete vacuum pumping system.

The system is out-of-the-box plug-and-play **ready in less than 5 minutes** and supports an Internet-of-Things (IoT) ready Ethernet port communications and easy to use web browser based software user interface.

SMALL FOOTPRINT WITH INTEGRATED ELECTRONICS

The unique filtration system prevents oil contamination and increases life and measurement reproducibility.

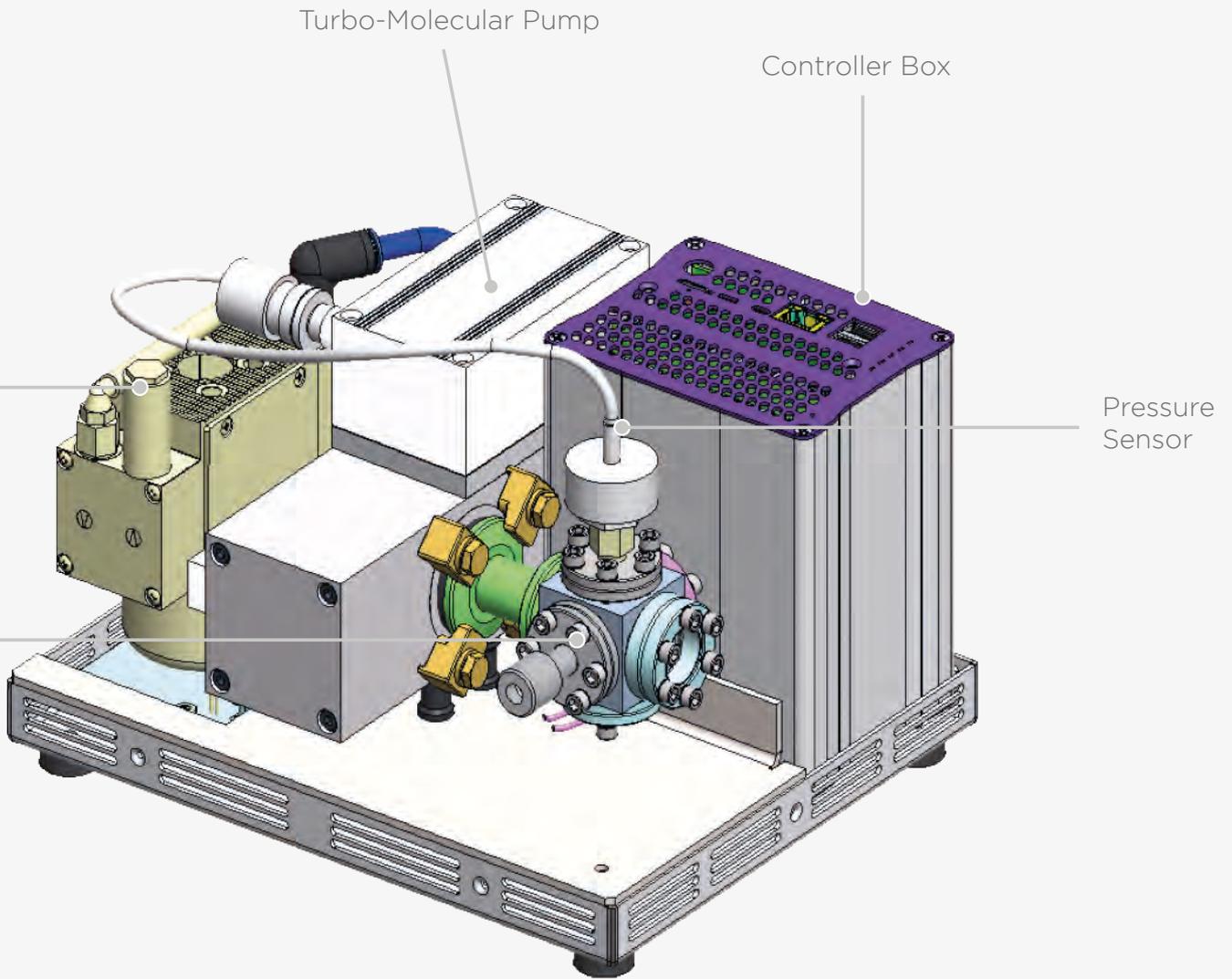
Diaphragm Pump

Gas Analysis Subsystem



CONTAINED PUMPING SYSTEM: TURBO + ROUGHING PUMPS

181 mm H x 256 mm L x 204 mm W



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UNIQUE KEY FEATURES

Ultra-Compact Form Factor: unlike typical residual gas analyzers that require external pumps to operate at low pressure, **QUANTUM is pumped by the small turbo and roughing pumps fully integrated within the enclosure.** This is possible due to miniature distributed array of micro-quadrupoles (rod length comparable to the gas molecules mean-free-paths) allowing high pressure operation (3 orders of magnitude compared to standard RGAs).

Higher pressure with Use of Non-Drifty Detector: the high pressure operation results in higher ion currents from use of a rugged and non-drifty FC detector with state-of-the-art circuitry down to ppm concentration levels spanning 6+ decades of dynamic range.



Quantitative and Accurate: QUANTUM is unique in its **ability to deliver highly accurate measurements in the order of sub-1%**. This unique advantage is made possible due to its innovative electronics and signal processing. Further, its operation allows calibration within the same pressure range against the gold standard Capacitance Diaphragm Gauge (CDG).

Remote Browser-Based SW Control: QUANTUM Graphic User Interface (GUI) provides its operator with the convenience of remote log-in via a browser-based software control. The GUI dashboard offers advanced features to support routine operation of the basic user while empowering the skilled user to add some customized capabilities.



OPERATION AND PERFORMANCES

It is designed to be robust and reliable. Due to its **miniature quadrupole array design** QUANTUM operates at high pressure with abundant generation of ions allowing the ubiquitous utilization of the rugged Faraday Cup detector with stable detector sensitivity over the operational time compared to an Electron Multiplier detector.

It provides **essential quantitative data** when detecting trace amounts of silicone oil, helium, water vapor, nitrogen and oxygen levels.

Patented algorithms then calculate the mole fraction of each gas component giving high accuracy quantitative data.

Fit for both **pilot scale** and **production scale Freeze Dryers**, it is a highly customized viable solution with easy integration in new or existing Freeze Dryers.

Inherently precise, QUANTUM Smart Spectrometer™ provides a complete process analytical tool for pharmaceutical lyophilisation; **it provides real-time data for process optimization and end-point detection.** The proprietary Silicone Oil filtration system allows the detection of Si-Oil contamination during the freeze-dry process, while protecting QUANTUM instrumentation from degradation due to Si-Oil deposition.

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WHY USE QUANTUM SMART
SPECTROMETER™ TO MONITOR
THE LYOPHILIZATION PROCESS.



QUANTITATIVE CONTAMINANT DETECTIONS

- **Safe detection of traces of contaminating silicone oil** from shelf heat transfer fluid) through QUANTUM's unique, miniaturized mass spectrometer augmented with a patented silicone oil filtration system for instrument protection.
- **Detecting and monitoring the evolution** of known, as well as previously unknown, **contaminants**.

Benefits: Trace levels of contaminants in large systems are often left undetected.

PROCESS MONITORING

- **Monitoring water vapor** for quantitatively accurate real-time process endpoint detection of primary and secondary drying phases.

Benefits: Current solutions exist for primary drying or qualitative secondary drying monitoring. The unique instrumentation augmented with the calibration against gold standard capacitance manometer gauges allows quantitative accuracy for Lyo process gases.

VACUUM LEAKS DETECTIONS

- System-wide **helium leak check**.
- Periodic and accurate vacuum system monitoring.

OTHER ADVANTAGES OF QUANTUM IN THE FREEZE-DRYING APPLICATION OVER CONVENTIONAL SOLUTIONS INCLUDE:

- The ability **to probe strategic locations** on the freeze-dryer, given its conducive compact size for ease of placement.
- **Quantitative measurements** for Lyo specific species of interest.
- Generation of **real time self-diagnostics and instrument health** for a reliable high uptime operation.

THE IMPORTANCE OF A MULTI-PURPOSE SYSTEM TECHNOLOGY:

- **Product quality assurance** by detecting trace contaminants and reducing product rejects at the onset of system leaks including Oxygen, silicone oil by alerting operators, triggering mitigating actions sooner.
- **Optimizing the lyophilization process** and minimizing engineering batch line-time usage from laboratory to production environment.

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OPERATION MODE: STAND ALONE

Maintenance mode used for silicone oil and He leak detection:

- Run mass spec pre CIP/SIP
 - Open valve to mass spec, run CIP/SIP, load batch
- Not recommended for in process use (eg. water vapor)
- Data sent to stand alone computer
- Alarms (visual) generated based on silicone oil levels

OPERATION MODE: INTEGRATED

In process mode used for silicone oil, water vapor, He leak and non aqueous solvent detection:

- Data sent to freeze dryer SCADA with historian backup
- Alarms (visual) generated based on analyte levels directly on FD SCADA
- Run mass spec pre CIP/SIP or during cycle in continuous operation

TECHNICAL SPECIFICATIONS

MEASUREMENT SPECIFICATION	CONDITIONS/UNITS
Installation	Complete in 2 working days
Mass Range	1-100 amu
Mass Resolution	FWHM: 1 (m/z = 28)
Communication Interfaces	Ethernet (wi-fi upon request)
Mass Number Stability	0.1 amu
Sensitivity	5e-6 A/Torr
Linear Response Range	1e-9 Torr - 5e-3 Torr at 400 μ A emission for N2
Minimum Detectable Partial Pressure	1e-9 Torr for N2 / 1e-8 Torr for He / 1e-9 Torr for Ar
Minimum Detectable Concentration (LoD)	1 ppm for N2 at 1mTorr
Maximum Operational Pressure	5e-3 Torr for N2
Scan Speed per amu	10 msec/amu to 10 sec/amu adjustable
Sampling Pressure Range	1e-5 Torr - 1e+3 Torr (8 decades P range)
Operating Temperature	10°C to 35°C
Electron Energy	25 V - 100 V (70 V default setting)
Emission Current	0.01 - 1mA (0.4mA default setting)
Accuracy	< 1% of reading
Startup-up time	3' from out of the box
Weight	9.0 kg
Ambient temperature	5°C to 35°C , no air conditioning
Power Consumption	DC24V, <100W

TYPICAL OPERATING CHARACTERISTICS

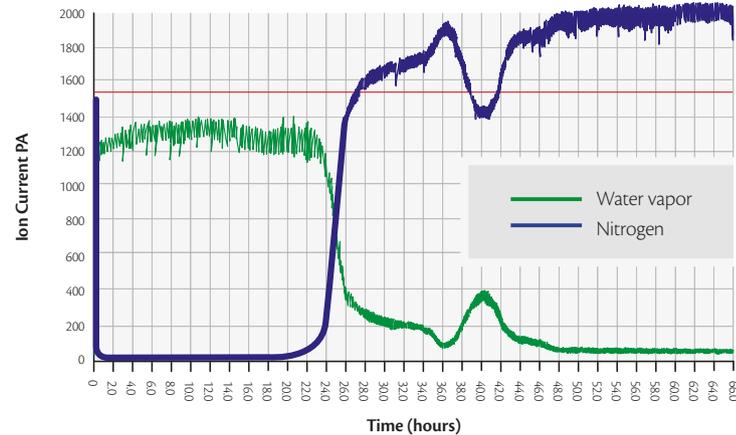
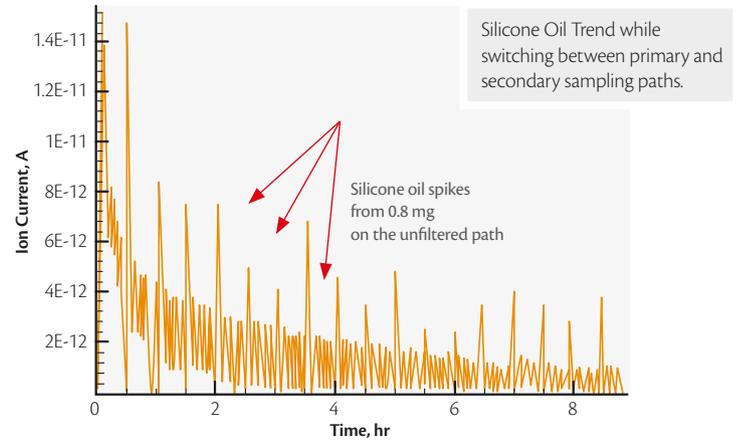
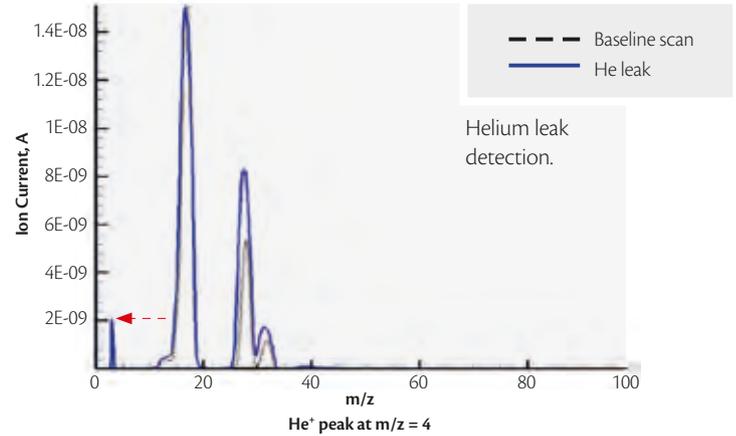
REAL TIME DATA COLLECTION

- IN-LINE MEASUREMENTS
- RAPID SCAN CAPABILITY
- CONTINUOUS DATA BACKUP

USER FRIENDLY INTERFACE



Typical Applications: end-point detection Water vapor, N₂, CO₂, He and O₂ detection and Si-Oil contamination detection.



Primary and secondary drying monitoring with water vapor (green) and nitrogen concentration (blue).

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GLOBAL SERVICE TEAM

The **IMA Life Service Team** can deploy qualified personnel with the expertise, experience and instrumentation to carry out tests and assure a technical assistance at your site on your Freeze Drying equipment. Our network has an active presence all over the world. Our comprehensive support extends far beyond natural borders and cultural barriers. **No matter when or where you need us: you provide the challenge, we address the rest.**

Service Assistance worldwide for Freeze Dryers:

- BOLOGNA (Italy)
- MILANO (Italy)
- DUBLIN (Ireland)
- DONGEN (The Netherlands)
- PARIS (France)
- TONAWANDA, TEMPE, PALM BEACH, WINTERVILLE (USA)
- HATILLO (Puerto Rico)
- SAN PAOLO (Brazil)
- BEIJING (China)
- TOKYO (Japan)
- MUMBAI, HYDERABAD, AHMEDABAD, BANGALORE, VADODARA, GOA AND VISHAKAPATNAM (India)
- JAKARTA (Indonesia)





DUBLIN

DONGEN

PARIS

MILANO

BOLOGNA

BEIJING

TOKYO

AHMEDABAD

VADODARA

HYDERABAD

MUMBAI

GOA

BANGALORE

VISHAKAPATNAM

JAKARTA

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QUANTUM solution was developed in collaboration between IMA Life, Atonarp and a major pharma company with purpose-built quantitative instrumentation for the application of freeze-drying and aseptic processing.



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IMA S.p.A. reserves the right to make any changes to the described machine characteristics.

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