Quantum

Multi-purpose lyophilisation process quantitation, analysis & control

May 2018

IMA LIFE
Aseptic Processing & Freeze Drying Solutions

CHALLENGES IN FREEZE DRYING
冻干过程遇到“挑战”

From the FDA’s guideline on Freeze-Drying process (UCM074909)
FDA指南中对冻干工艺过程中泄漏的“顾虑与要求”

- 要**定期**检查系统完整性:

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.”

- 泄漏“源头”究竟是什么？:

“Leakage into a lyophilizer 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…”

CHALLENGES IN FREEZE DRYING
冻干过程遇到“挑战”

Silicone oil detection 硅油检测

- Silicone oil can originate from silicone oil shelf circuit or from the product itself (stoppers).
- Small leakage in large system can be hard to detect.
- Once detected, not only the last produced batch may be lost, as suspicion can be raised on previous batches too.

Vacuum leaks 真空泄漏

- Vacuum system must be monitored periodically.
- Searching for Vacuum leak is always a time consuming operation impacting the turn around time.

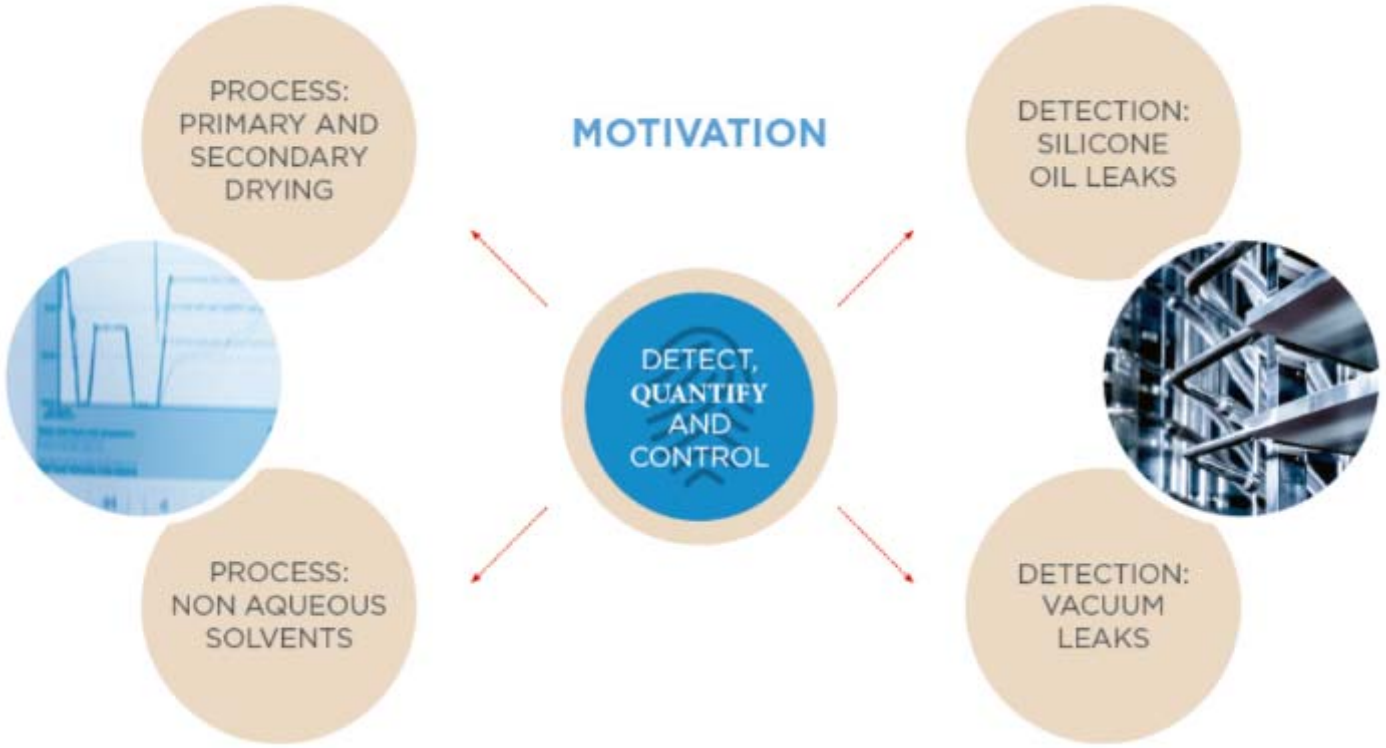
Monitoring primary and secondary end points 初次干燥和二次干燥终点监测

- Present solutions are indirect measurements with insufficient accuracy.
- Absence of methods to determine Secondary Drying end with quantification of residual moisture.

CHALLENGES IN FREEZE DRYING
冻干过程遇到“挑战”

- A Mass spectrometer, customized for freeze drying application. 为冻干所“定制”的质谱仪
- A multi purpose analyzer. 让其成为一个多用途分析仪器
  - ✓ PAT tool for primary and secondary drying monitoring.
    作为初次干燥和二次干燥过程分析的工具
  - ✓ Monitoring non aqueous solvents.
    监测非水溶媒
  - ✓ Routine checks for potential silicone oil and/or vacuum leaks of the freeze dryer.
    用于例行检查冻干机的潜在硅油/真空泄露
- A device adapted for both pilot scale and production scale freeze dryers.
  通用于**中试**和**生产型**冻干机
- Usable in new or existing freeze dryers.
  适用于**现有**和**新造**冻干机

QUANTUM – MASS SPECTROMETER
QUANTUM – 质谱仪



QUANTUM – MASS SPECTROMETER
QUANTUM – 质谱仪

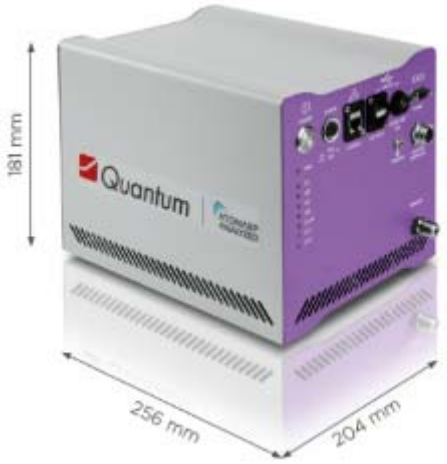
Mass spectroscopy device: well-proven technology since the last 25 years.
质谱分析仪器应用已经是25年的成熟技术

Today, the new miniaturized QUANTUM device allows for:
如今，新型紧凑设计的QUANTUM可以带来：

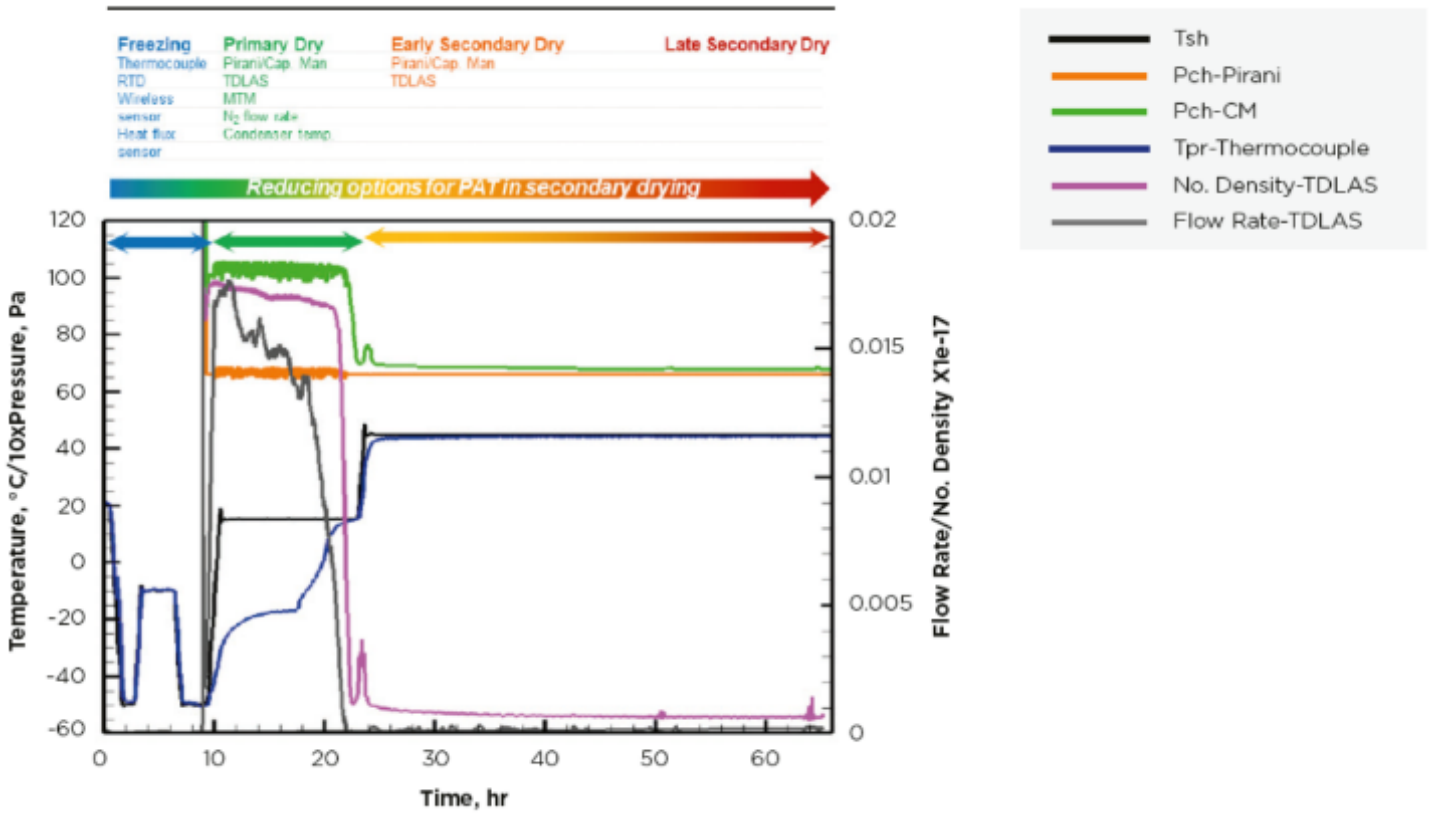
- An economically viable solution.
  一个经济灵活的方案
- A customized device for freeze-dryers within an aseptic environment.
  针对无菌冻干机的定制设备

The measurements accuracy meets the required goals:
其精确的测量可达到以下使用目标

- PAT tool for primary and secondary drying.
  初次和二次干燥的过程分析技术工具
- Silicone oil & vacuum leak detection.
  检测硅油和真空泄露

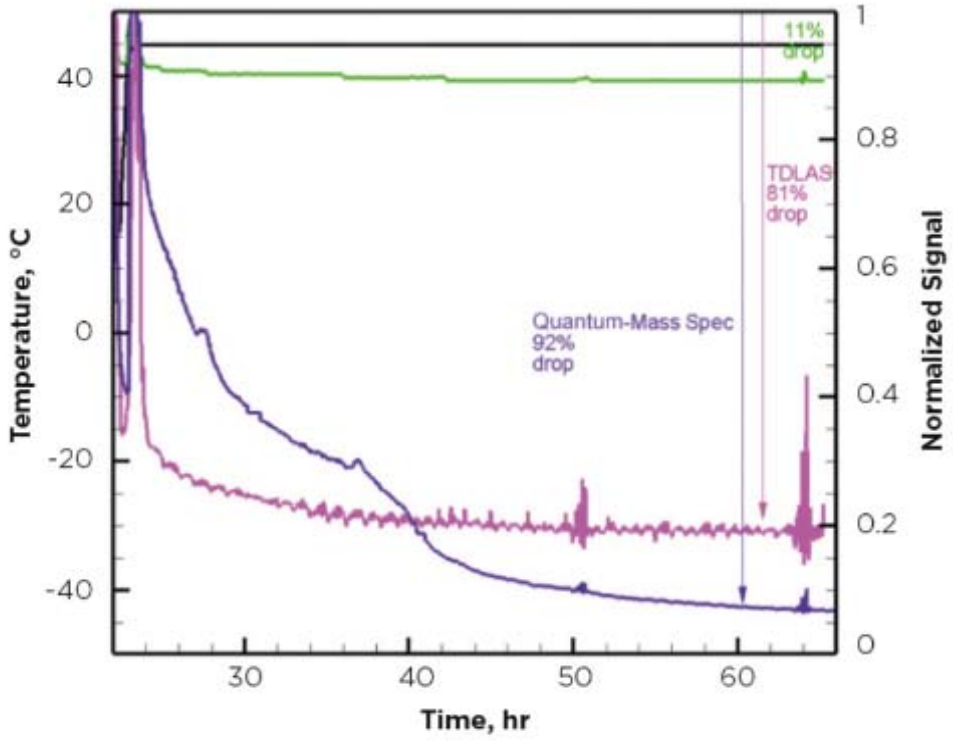


QUANTUM


Freezing
Thermocouple
RTD
Wireless
sensor
Heat flux
sensor
Primary Dry
Pirani/Cap. Man
TDLAS
MTM
N2 flow rate
Condenser temp
Early Secondary Dry
Pirani/Cap. Man
TDLAS
Late Secondary Dry
Reducing options for PAT in secondary drying
Temperature, °C/10xPressure, Pa
Flow Rate/No. Density X1e-17
Time, hr
120
100
80
60
40
20
0
-20
-40
-60
0.02
0.015
0.01
0.005
0
0
10
20
30
40
50
60
Tsh
Pch-Pirani
Pch-CM
Tpr-Thermocouple
No. Density-TDLAS
Flow Rate-TDLAS

COMPARISON OF SECONDARY DRYING SIGNAL BETWEEN PIRANI / TDLAS AND MASS SPEC

二次干燥时皮拉尼 / TDLAS 与 质谱 信号的比较



Tsh

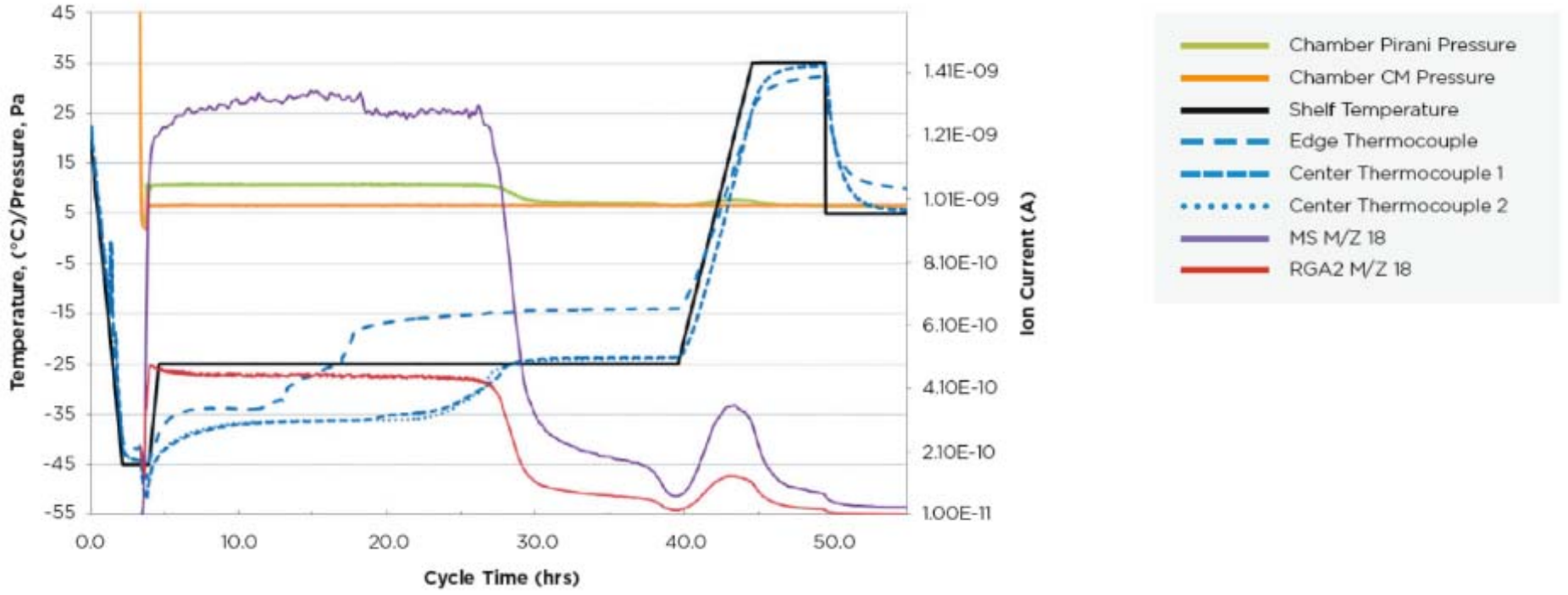
Norm-Pirani (11% drop in signal)

Norm-TDLAS (No. Dens.) (81% drop)

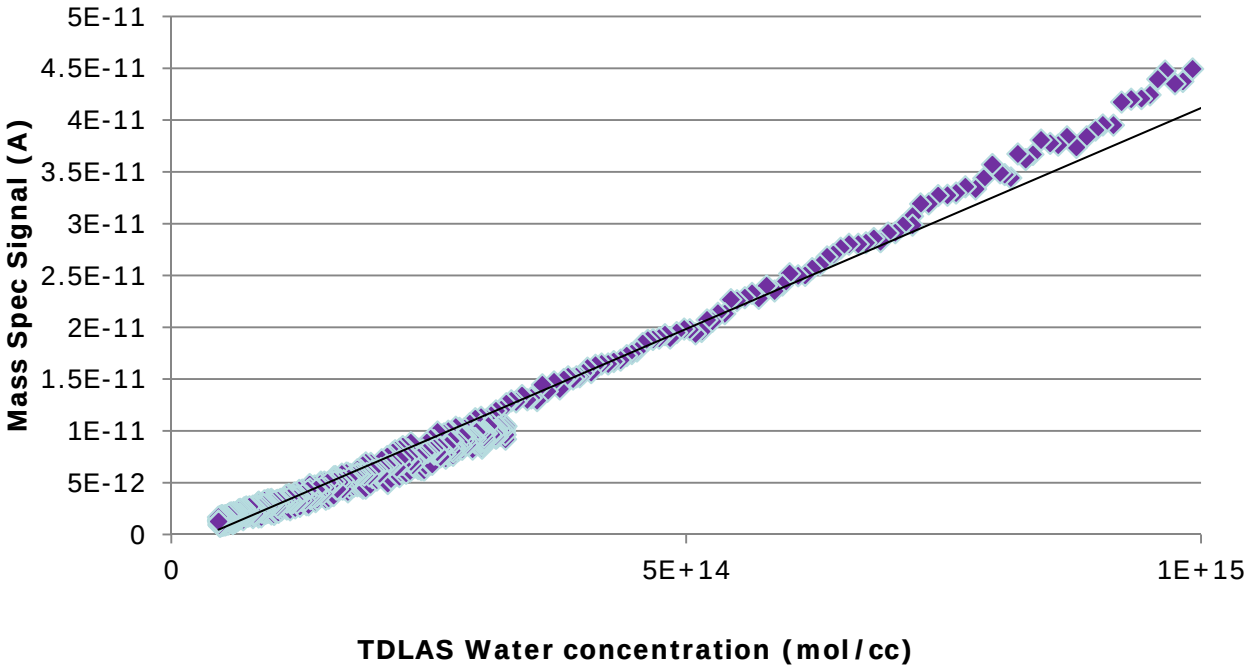
Norm Quantum (92% drop)

5% SUCROSE: COMPARISON OF SECONDARY DRYING SIGNAL BETWEEN PIRANI AND MASS SPEC

5%蔗糖溶液冻干时，皮拉尼与质谱信号的比较

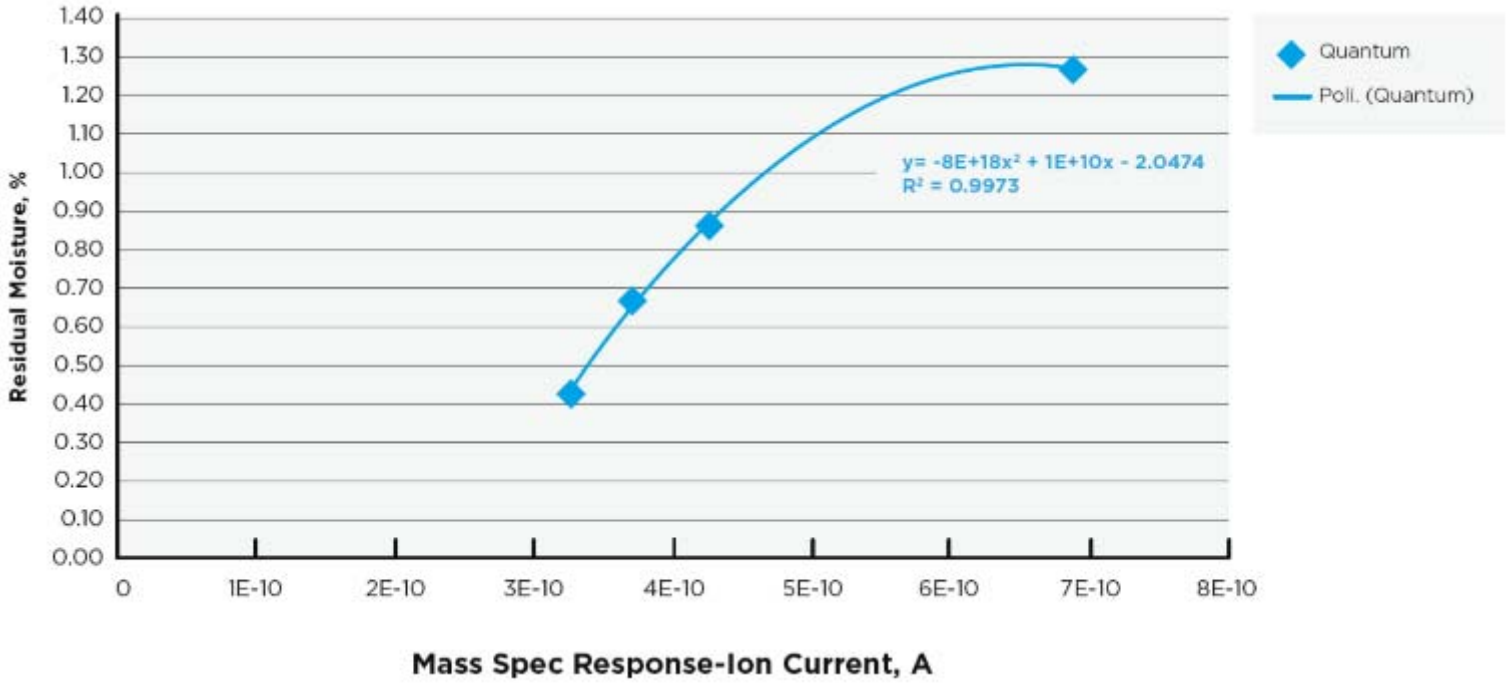


COMPARISON WITH TDLAS
与TDLAS的比较

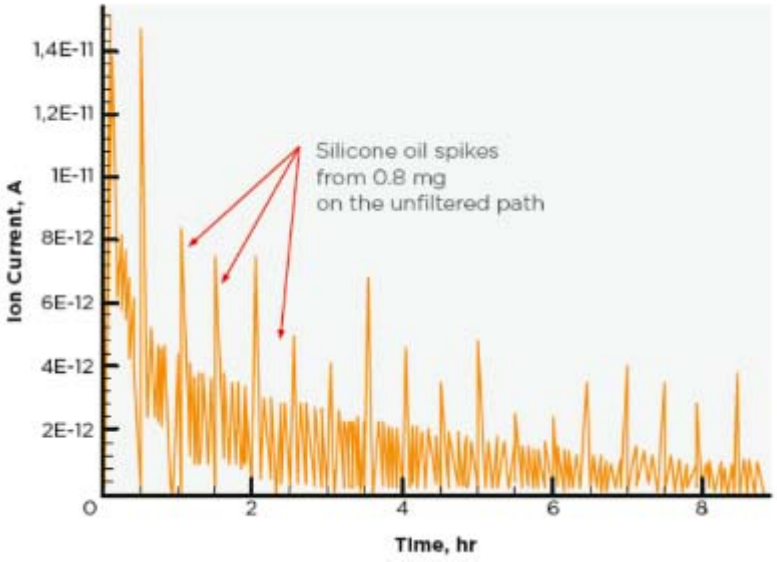


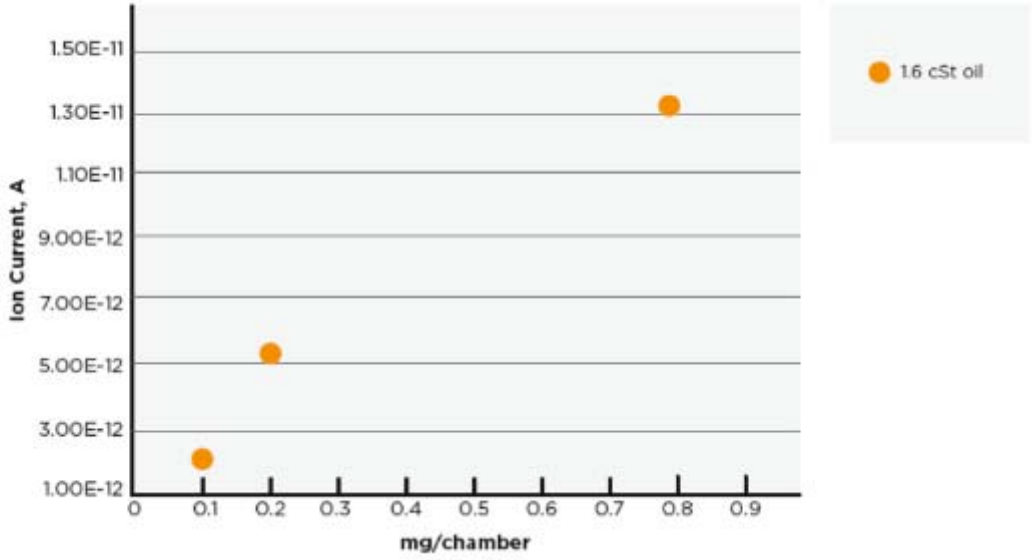
Nearly linear (very close) comparison between TDLAS signal and QUANTUM data.

MASS SPEC TO PREDICT RESIDUAL MOISTURE
质谱用于对残留水分的预判



SILICONE OIL CALIBRATION
硅油检测



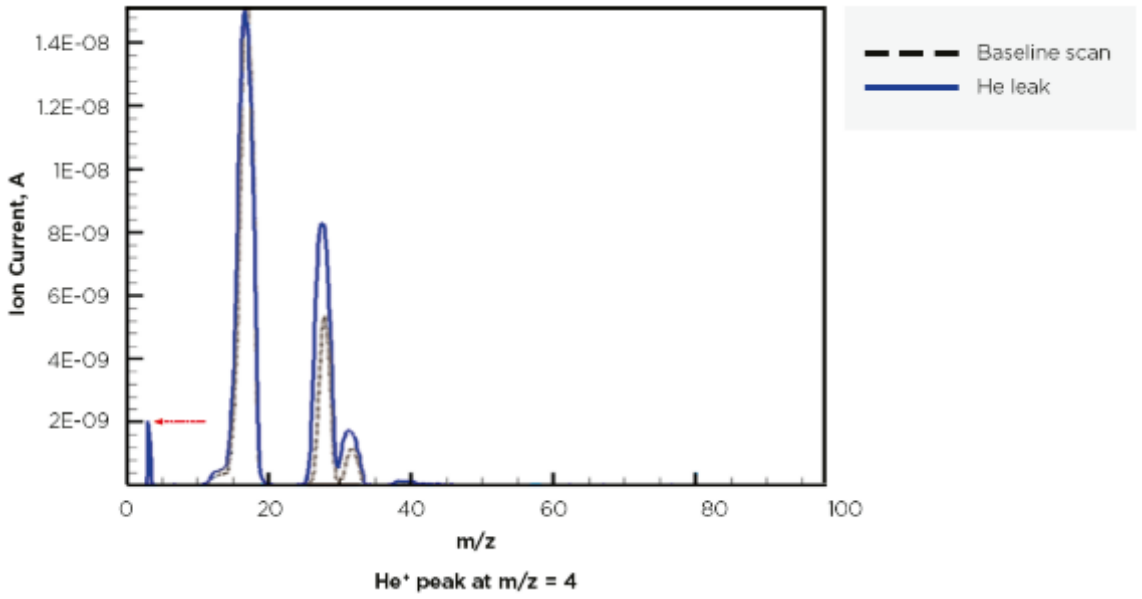


Detection down to 0.1 mg in 1.0 m^3 chamber.

SYSTEM LEAK CHECK: HE LEAK DETECTION
真空漏率检测:氦质谱

- Tested here using an external **He supply at the source of the leak** and sensed using a **mass spec system** connected to the side of the **production dryer chamber.**

- **测试用外部氦气源和连接在冻干箱测的质谱仪来检查漏点**



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