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PyroButton Solution Products for Stability Process Management

Introduction

Stability evaluation of products is a critical requirement in the determination of their safety, quality and efficacy.

FDA & ICH guidance include in the design of stability study the following considerations:

- Container/closure specification and its effect on product stability
- Storage conditions for products in general relative to various temperature and humidity requirements:
  - Long term studies at 25 ± 2 ºC and 60 ±5 % RH (for a period of 12 months)
  - Intermediate studies at 30 ± 2 ºC and 65 ±5 % RH (for a period of 6 months)
  - Accelerated studies at 40 ± 2 ºC and 75 ±5 % RH (for a period of 6 months)
  - Stress studies may be conducted by increasing the temperature of the Accelerated test conditions at 10 ºC intervals (e.g., 50 ºC, 60 ºC, ..) and 75 %RH.
- Storage conditions for products intended to be stored in refrigerators relative to various temperature and humidity requirements:
  - Long term studies at 5 ± 3 ºC (for a period of 12 months)
  - Accelerated studies at 25 ± 2 ºC and 60 ±5 % RH (for a period of 6 months)
- Storage conditions for products intended to be stored in freezers relative to various temperature and humidity requirements:
  - Long term studies at 20 ± 5 ºC (for a period of 12 months)
- Storage conditions for products intended to be stored semi-permeable containers relative to various temperature and humidity requirements:
  - Long term studies at 25 ± 2 ºC and 40 ±5 % RH (for a period of 12 months)
  - Intermediate studies at 30 ± 2 ºC and 35 ±5 % RH (for a period of 6 months)
  - Accelerated studies at 40 ± 2 ºC and 25 ±5 % RH (for a period of 6 months)
- Storage conditions for emulsions relative to various temperature and humidity requirements:
  - Heating & cooling cycles should performed between 4 ºC & 45 ºC

Opulus provides various levels of solution products based on PyroButton-X self-powered data-loggers, communication systems, and integrated software to meet the requirement for Temperature and Humidity Mapping of the Stability Chambers, Validation of the Storage Conditions, Temperature & Humidity Tracking of Products, Permeability Studies of Containers/Closures, Challenge Studies of Containers/Closures, Calibration of Stability Chambers, Maintenance, Qualification & Re-Qualification of Stability Chambers.

Vendor Suitability Analysis

What suitability criteria should be considered during selection of the vendor?

- **Q(1): Is the Vendor experienced in the understanding and interpretation of the applicable regulations in Design Qualification, Installation Qualification, Operational Qualification, Performance Qualification, 21 CFR Part 11, Process Validation, and Method Validation?**
  A(1)*: Opulus employees have over 30 years of background and actual experience in the development and design of products & services for the FDA & EU regulated industries, including pharmaceutical, biotech & medical device companies, and research institutes.*

- **Q(2): Is the development of products follow life cycle process and based on meaningful SOP(s)?**
  A(2)*: Opulus development is based on life cycle process & relevant SOPs, that include Product Concept, Requirements Analysis, Requirements Specification, Preliminary Design, Detailed Design, Implementation, Integration, Verification & Validation.*

- **Q(3): Is the Vendor experienced in the creation & development of competency training & SOP(s) for the products & services?**
  A(3)*: Opulus has developed competency training & SOP(s) for all of their products and services.*

- **Q(4): Is the Vendor competent & experienced in the support of system set up and completion of DQ-IQ-OQ-PQ?**
  A(4)*: Opulus provides competent support for the set up and completion of DQ-IQ-OQ-PQ.*

- **Q(5): Is the Vendor competent & experienced for the compliance verification of 21 CFR Part 11?**
  A(5)*: Opulus provides competent support for the compliance verification of 21 CFR Part 11 requirements. Opulus has consulted others in the assessment, gap analysis, and resolution relative to 21 CFR Part 11 compliance.*

- **Q(6): Is the Vendor competent & experienced in the calibration, maintenance and full system validation processes?**
  A(6)*: Opulus provides competent support for the calibration, maintenance, and validation of the system. Opulus can integrate these requirements with SOP(s) and competency training.*

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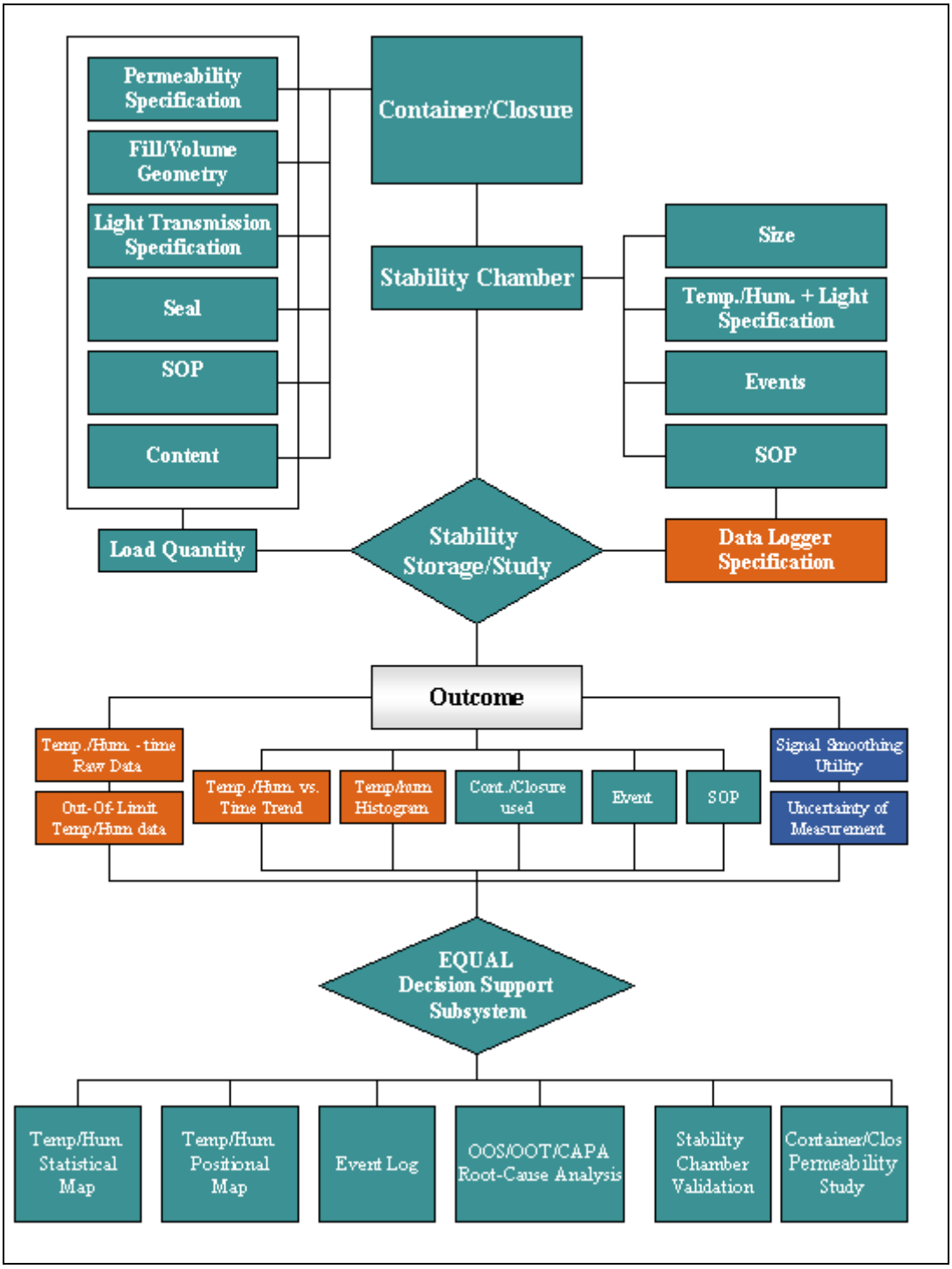
PyroButton Stability Process Management Model



PyroButton-SQL v.4 for Optimal Stability Process Management

Introduction

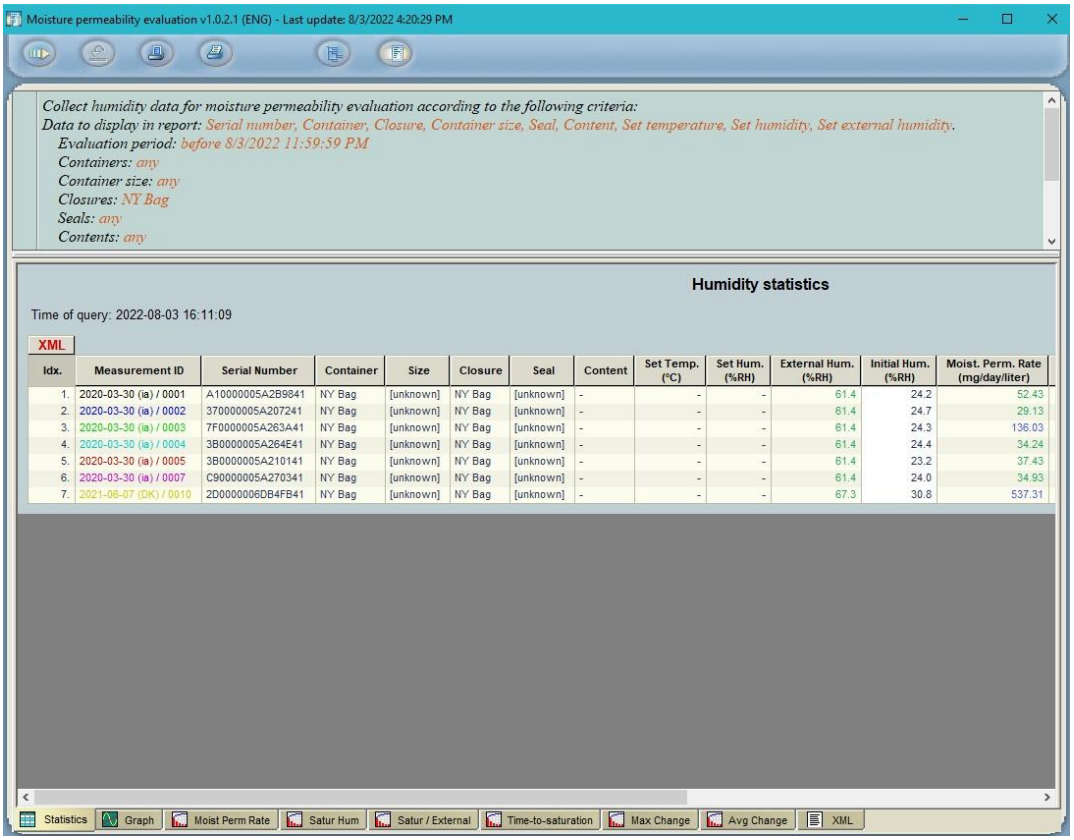
PyroButton-SQL v.4 integrates self-powered data-logger measurements with SQL database, application modules, and Decision Support Sub-system. The system is suitable for the stability process management and temperature/humidity tracking of the stability chambers, containers/closures, and products.
The benefits of a single integrated solution include:

- Consistent validation of the stability storage
- Integration & comparative analysis of multiple stability chambers
- Consistent tracking of temperature & humidity across the various stability chambers
- Improved reliability and increased speed for permeability tests of containers/closures
- Consistent Performance Qualification & Re-Qualification of the Stability Chambers
- Scalable and modular implementation
- Effective & efficient OOS, OOT, & CAPA compliance
- Highest Return-On-Investment

The following application modules are included in PyroButton-SQL v.4: Applications, Basic, Clean Room, Equipment, Facilities, Meteorological, Process, Stability Chamber, Sterilization, Transportation.
PyroButton-SQL v.4 is the only out-of-the-box solution product that encompasses self-powered data-logger operations with SQL based information management, & Decision Support Sub-system for temperature/humidity mapping, validation, qualification, and in situ permeability analysis of containers.

Key Benefits to the User

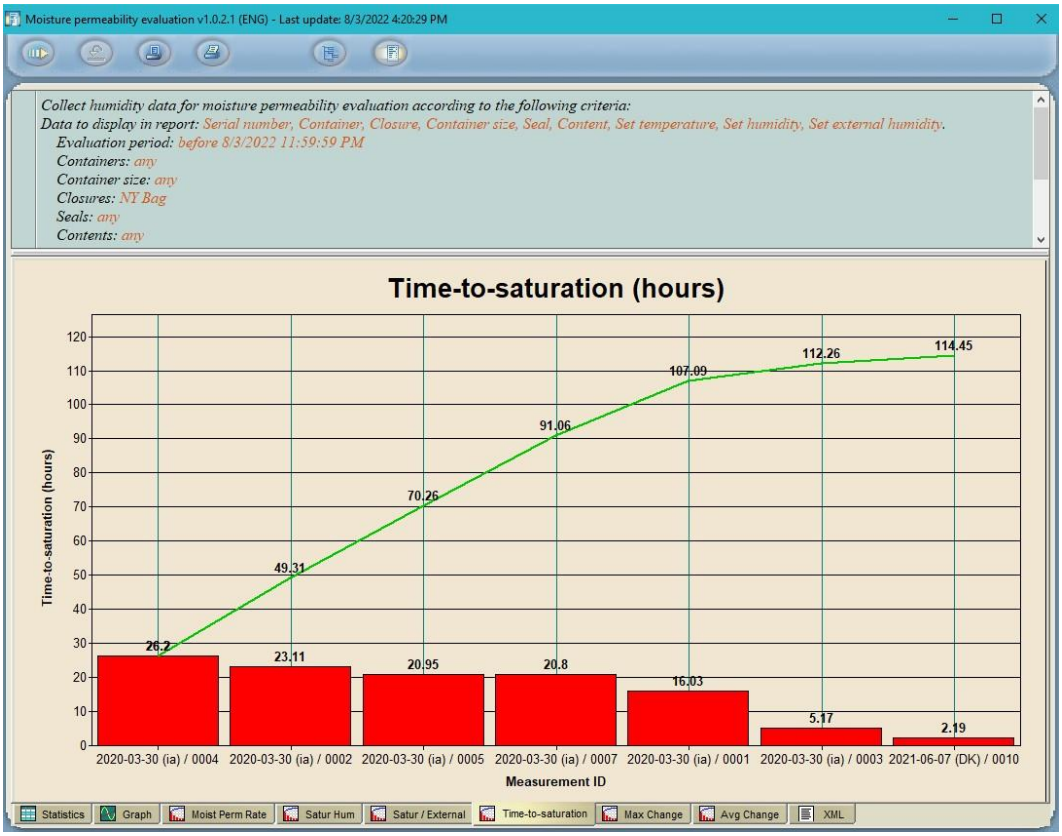
- Temperature & humidity tracking of
  - Multiple Stability chambers
  - Products relative to storage requirements
  - Stability Chambers relative to load quantity
- Temperature Sensor Pattern Analysis
- Calibration & maintenance
- Re-qualification (scheduled & unscheduled)
- Heat/humidity distribution
- Heat/moisture penetration relative to heat/moisture load
- Thermal monitoring & diagrams
- Humidity monitoring & diagrams
- In situ permeability analysis of containers/closures
- Events management



Idx.	Measurement ID	Serial Number	Container	Size	Closure	Seal	Content	Set Temp. (°C)	Set Hum. (%RH)	External Hum. (%RH)	Initial Hum. (%RH)	Moist. Perm. Rate (mg/day/liter)
1.	2020-03-30 (ia) / 0001	A10000005A2B9841	NY Bag	[unknown]	NY Bag	[unknown]	-	-	-	61.4	24.2	52.43
2.	2020-03-30 (ia) / 0002	370000005A207241	NY Bag	[unknown]	NY Bag	[unknown]	-	-	-	61.4	24.7	29.13
3.	2020-03-30 (ia) / 0003	7F0000005A263A41	NY Bag	[unknown]	NY Bag	[unknown]	-	-	-	61.4	24.3	136.03
4.	2020-03-30 (ia) / 0004	3B0000005A264E41	NY Bag	[unknown]	NY Bag	[unknown]	-	-	-	61.4	24.4	34.24
5.	2020-03-30 (ia) / 0005	3B0000005A210141	NY Bag	[unknown]	NY Bag	[unknown]	-	-	-	61.4	23.2	37.43
6.	2020-03-30 (ia) / 0007	C90000005A270341	NY Bag	[unknown]	NY Bag	[unknown]	-	-	-	61.4	24.0	34.93
7.	2021-06-07 (DK) / 0010	2D0000006DB4FB41	NY Bag	[unknown]	NY Bag	[unknown]	-	-	-	67.3	30.8	537.31

Container/Closure Permeability Statistics

Container/Closure Permeability Graph



Pareto Diagram - Container/Closure Permeability Study

Return-On-Purchase-Investment (ROPI)

- Low purchase cost ensures rapid Return-On-Purchase-Investment
- Low calibration cost ensures low cost of compliance
- Low maintenance cost ensures low cost of operation
- 21 CFR Part 11 compliance ensures investment security

Components of the PyroButton System

- Data-logger for temperature monitoring,
- Docking Station for data communication and
- 21 CFR Part 11 compliant software for data-acquisition programming, reading of data and evaluation & interpretation of results.

System Requirements

- Intel(R) Core i3 (Intel(R) Core i5 is recommended)
- 2 GB RAM
- DVD drive for installation
- Mouse
- 1680x1050 display resolution, High Color

- 3 GB free hard disk space
- Windows 10 (32bits, 64bits) operating system

DQ-IQ-OQ-PQ

DQ supports the functional & quality specifications designed into PyroButton. Documentary proof of DQ compliance includes:

- IQ-OQ-PQ protocols
- 21 CFR Part 11 Verification Summary,
- Measurement Performance Design Summary, and
- NIST Traceable Calibration Summary

IQ (Installation Qualification) - IQ supports the requirement for proper installation and acceptance qualification for PyroButton. Documentary proof of IQ compliance includes:

- Receipt & acceptance checklist,
- Physical & electrical compliance checklist,
- Environmental compliance checklist,
- Training compliance checklist, and
- Final IQ Summary

OQ (Operational Qualification) - OQ supports the specification compliant functioning of the system. Documentary proof of OQ compliance includes:

- 21 CFR Part 11 operational specification checklist,
- Software operational specification checklist,
- Instrument interface operational specification checklist,
- Instrument operational specification checklist, and
- Final OQ Summary

PQ (Performance Qualification) - PQ supports quality evaluation & quality compliance management of the system. PQ compliance models include:

- 21 CFR Part 11 compliance models,
- Simulation models for data-acquisition optimization, and
- SQC models for measurement qualification review.