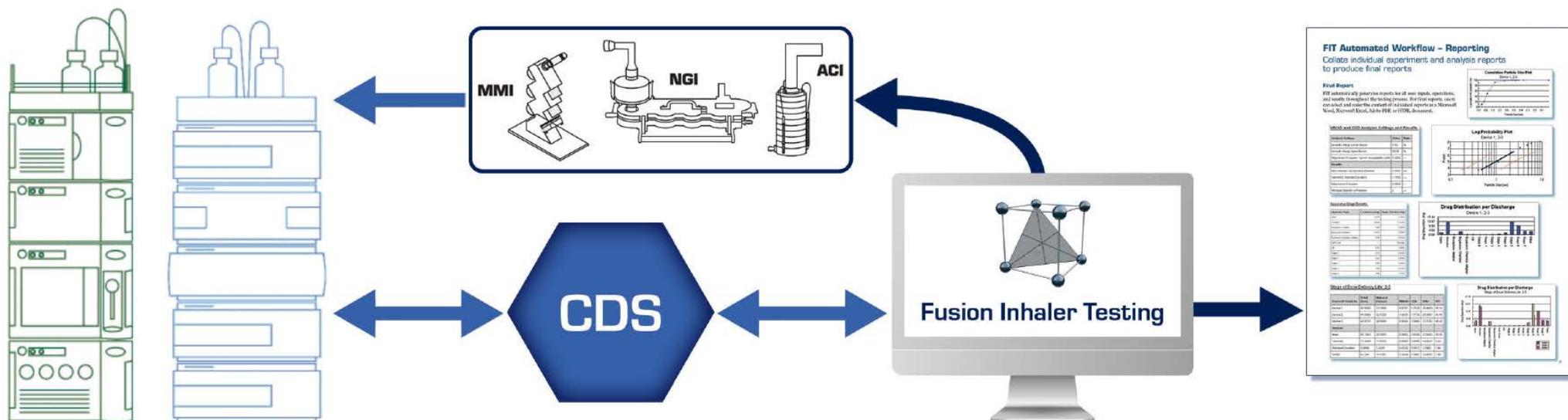


Fusion Inhaler Testing



The Only Fully Automated Software Solution for
Orally Inhaled and Nasal Drug Product R&D and QC



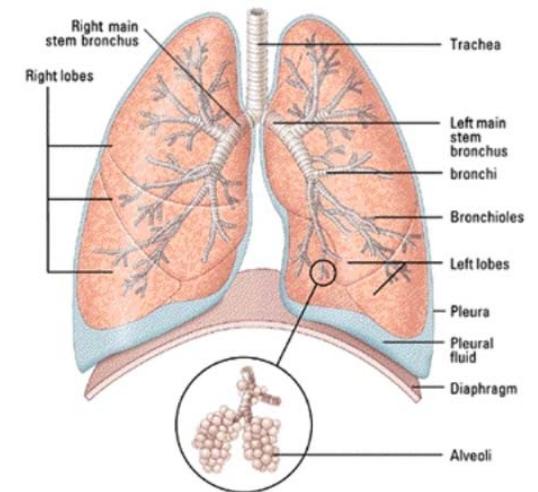
The lung represents an excellent non-invasive systemic drug delivery route. The high surface area available for absorption, allows a drug to easily pass into the bloodstream, rising to rapid onset of action and improved efficacy.

Ensuring the drug reaches the required parts of the lung is essential if a good clinical response is to be achieved. **Particle size** plays a critical role here.

The characterization of the **aerodynamic size distribution** to be inhaled, is therefore essential during drug formulation, inhaler device design, and stability trials.

The **aerodynamic size distribution** of particles is measured **in-vitro** using apparatus that simulate the human lung.

These Impactors test the **'fine particle' dose** based on the mass of the active component capable of reaching the lung and indicate where inhaled particles would be deposited within the lungs.



In-vitro cascade impaction testing is characterized by the generation of large numbers of samples all requiring LC analysis. This in turn generates large quantities of individual test results which require collation, calculation, and reporting in accordance to **USP Chapter 601** or **Ph.Eur. Chapter 2.9.18** guidelines.

Until now the tools available to help perform this task have been limited to “**off-line**” applications, that are not integrated into the LC testing and data acquisition workflow.

The consequence is a large **financial overhead** due to time spent **transcribing** results and **reviewing** those transcriptions for errors, along with manual, or at best semi-automated analysis and reporting using non-GXP compliant software tools.

Fusion Inhaler Testing

Fusion Inhaler Testing (FIT) manages the entire work and dataflow.



From generation of the sampling plan, via **file-less** data exchange with the LC data system, to result collation, calculation and report compilation, FIT has it automated in accordance to **USP Chapter 601** or **Ph.Eur. Chapter 2.9.18**, within a **21 CFR p11** compliant environment.

FIT - Complete Apparatus Support

FIT supports the Anderson Cascade Impactor (ACI) and the Next Generation Impactor (NGI) –
All Configurations!

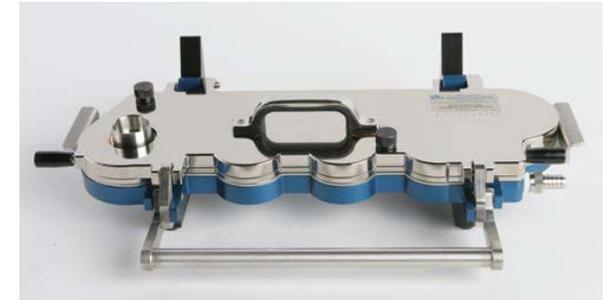
ACI



FIT also supports these other apparatuses:

- NGI configured with a Pre-separator
- FSI (Fast Sampling Impinger)
- FSA (Fast Screening Anderson Impactor)
- MMI (Marple-Miller Impactor)
- MSLI (Multi-Stage Liquid Impinger)
- DUSA (Dosage Unit Sampling Apparatus) – including all calculations required to verify Delivered Dose Uniformity (DDU).

NGI



Supports All Install Environments

Install Environment

FIT

Standalone (Workstation)



Network (Enterprise)



Citrix Ready Certified



Fully Qualifiable for GXP Environments*



- * – Fusion QbD is operating in the GxP environments of international pharmaceutical companies worldwide.

How Fusion Inhaler Testing Assures Compliance

Required Features

FIT

Full integration of **all e-record** and **all e-signature** features and functions required to support full 21 CFR 11 compliance.



Integrated Project Management System.



Full audit trail, including all data exchanges with the CDS.



Why Audit Trail is Important!

What CDS Project
did this data come
from?



Who entered this
data – was the
data modified?

Filter Options

Date

Enable

Starting Date:

March 2020						
Sun	Mon	Tue	Wed	Thu	Fri	Sat
23	24	25	26	27	28	29
1	2	3	4	5	6	7
8	9	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28
29	30	31	1	2	3	4

Ending Date:

March 2020						
Sun	Mon	Tue	Wed	Thu	Fri	Sat
23	24	25	26	27	28	29
1	2	3	4	5	6	7
8	9	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28
29	30	31	1	2	3	4

Users

Enable

Available:

Administrator

Included:

Events

Enable

Available:

- Print Reports
- Experiment Setup
- Enable User Defined Option
- Generate Design
- Export Experiment Design
- Export Testing Design
- Matrix Master Wizard
- Edit Run No. Labels
- Robustness Simulator
- Create Testing Design
- Delete Testing Design
- Response Reductions

Included:

- Import Responses
- Create/Edit Response Data

OK Cancel ?

Supported Apparatuses

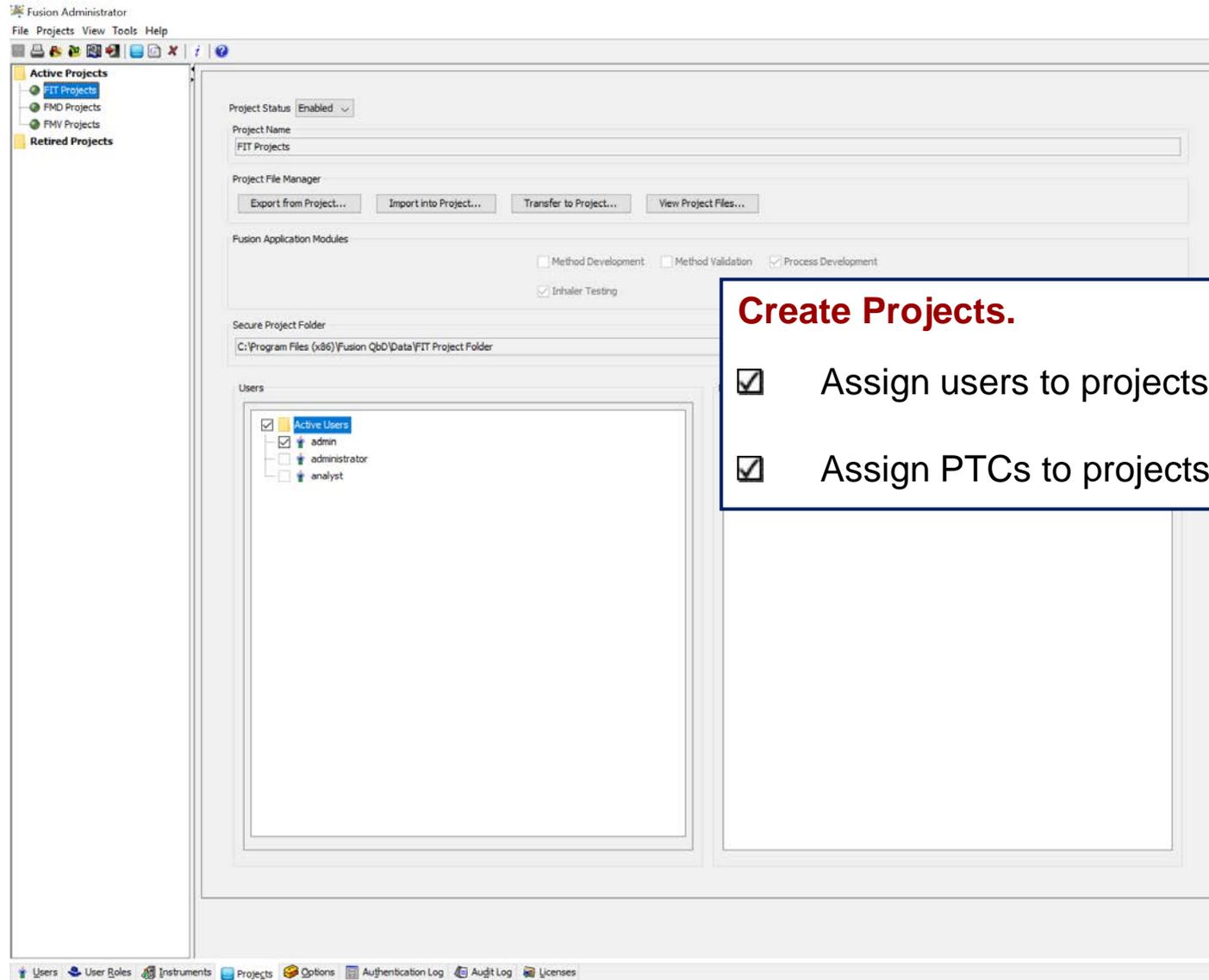
- ACI – without Pre-separator (USP 1) and with Pre-separator (USP 3)
- NGI – with Pre-separator (USP 5) and without Pre-separator (USP 6)
- MMI (USP 2), MSLI (USP 4), FSA, FSI

Chromatography Data Software (CDS) Systems

- Agilent ChemStation and OpenLab 1 – ChemStation Edition
- ThermoFisher Chromeleon™
- Waters® Empower™

Operating Systems

- Windows® 10, 11
- Windows® Server 2008 R2, 2012 R2, 2016, 2019, 2022



Create Projects.

- Assign users to projects.
- Assign PTCs to projects for product testing.

Fusion Administrator – Product Testing Configuration (PTC) Setup

Fusion Administrator
File Instruments View Tools Help

All Instruments

- ChemStation
- Chromleon 7
- Empower
- Generic
- Inhaler Testing
 - NGI - Ph. Eur. E
 - NGI with Pre-separator, Ph. Eur. E
 - Tutorial Apparatus**
- Common Instruments**
- ChemStation
- Chromleon 7
- Empower
- Generic
- Inhaler Testing
- S-Matrix ADL
- Empower
- Waters_Fad
- Empower

Associated Product Testing Configurations



Status	Configuration Name
<input checked="" type="checkbox"/>	Tutorial PTC
<input type="checkbox"/>	Default Config. NGI with Pre-separator, Ph. Eur. E
<input type="checkbox"/>	Product Testing Configuration 1

All Product Testing Configurations

State	Status	Configuration Name	Apparatus type
●	Assigned	Default Config. NGI with Pre-separator, Ph. Eur. E	NGI with Pre-separator
●	Assigned	Product Testing Configuration 1	NGI with Pre-separator
●	Assigned	Tutorial PTC	NGI with Pre-separator

Delete New

Product Testing Configuration

Configuration Name: Tutorial PTC Apparatus Type: NGI with Pre-separator

General Settings

Dose Delivery Mode: Oral

Device Type: MDI/DPI

Sampling Flow Rate: 60.00 ± 1.000 L/min Apply Specification Limits

Mass Balance Calculation Method: Target Delivered Amount

Perform Uniformity Testing

Data Treatment Settings

Missing Peaks: Use Zero

Perform LOQ Testing in FIT

Data Below LOQ: Use Zero

Compound Data Settings

Number of Compounds: 1

Compound Name	Delivered Amount Target	(Editable in FIT) <input checked="" type="checkbox"/>	Target Units **	Target Precision	LOQ Value (µg/mL)	LOQ Precision
API	80.00		µg	2	0.250	3

* - Each response data value entered into FIT must represent a single actuation test result for correct analysis and reporting.

Impactor Sample Properties Wash Volume Precision

Stage Name	Stage Type	Wash Volume (mL)	AutoFill...
<input checked="" type="checkbox"/> Device	Device	10.00	
<input checked="" type="checkbox"/> Throat	Apparatus	10.00	
<input checked="" type="checkbox"/> Pre-separator	Apparatus	10.00	
<input checked="" type="checkbox"/> Stage 1	Apparatus	10.00	
<input checked="" type="checkbox"/> Stage 2	Apparatus	10.00	
<input checked="" type="checkbox"/> Stage 3	Apparatus	10.00	
<input checked="" type="checkbox"/> Stage 4	Apparatus	10.00	
<input checked="" type="checkbox"/> Stage 5	Apparatus	10.00	
<input checked="" type="checkbox"/> Stage 6	Apparatus	10.00	
<input checked="" type="checkbox"/> Stage 7	Apparatus	10.00	
<input checked="" type="checkbox"/> MOC	Apparatus	10.00	

Instrument Manager Status

- Number of Instruments: 19. Limit: 20.
- Number of Instruments: 6. Limit: 10.
- Number of Instruments: 7. Limit: 10.
- Number of Instruments: 1. Limit: No Limit.
- Number of Instruments: 3. Limit: No Limit.

Create Product Testing Configuration.

- Flexible template accommodates the required apparatus type & testing configuration data.
- Specify Compound data, testing parameters, and Acceptance limits for product testing.

Simple Sampling Plan Setup and Design

Create New Work File

Project
 Select Project: FIT Projects
 Project Name: FIT Projects

Product Testing Configuration
 Product Testing Configuration 1

Experiment Type
 Cascade Impaction

Name: Product Testing Configuration 1

Apparatus Type: NGI with Pre-separator
Sampling Flow Rate: 60.00
Control Limit: 1.000
Apply Specification limit: Yes
Dose Delivery Mode: Oral
Calculation Method: Uniformity
Perform Uniformity Testing: No
Missing Peaks Treatment: Use Zero
Perform LOQ Test in FIT: Yes
Data Below LOQ Treatment: Use Zero

Compound Settings

Compound Name	Uniformity Target	Editable in FIT	Target Units *	Target Precision	LOQ Value (µg/mL)	LOQ Precision
API	45.00	No	µg/actuation	2	0.020	3

* - Each response data value entered into FIT must represent a single actuation test result for correct analysis and reporting.

Stage Name	Wash Volume (mL)
Device	1.000

OK Cancel

Step 1. Select the PTC

Select the PTC for the project from a list of PTCs permitted for the user.



Simple Sampling Plan Setup and Design

Inhaler Testing - Inhaler Testing Tutorial.smae

File Edit Activity Tools Window Help

Sampling Plan Setup Generate Sampling Plan

Sampling Plan Setup

- Create Sampling Plan
- Sampling Plan Reports

Data Management / Analysis

- Data Management
- Data Analysis

Reporting Toolkit

- Fusion Reporter
- Audit Log Reporter

Project Name: Project 1 Sampling Plan Name: Sampling Plan 1 Product Testing Configuration: Tutorial PTC

Product Documentation: Cascade Impactor

Product Information

No. of Data Fields: 3

Name	Value
Product Code	A1A
Batch ID No.	B2B
LIMS No.	C3C

Include Device Storage Conditions

Stability Time Point: Amount: 30 Units: Days

Device Orientation: Upright

Temperature and Humidity (Deg. C / %RH): 25/60

Step 2. Product Documentation

Document all required product identity and sampling point information.

Simple Sampling Plan Setup and Design

Inhaler Testing - Inhaler Testing Tutorial.smae

File Edit Activity Tools Window Help

Sampling Plan Setup Generate Sampling Plan ?

Project Name: Project 1 Sampling Plan Name: Sampling Plan 1 Product Testing Configuration: Tutorial PTC

Product Documentation: **Cascade Impactor**

Replication Scheme

No. of injections per sample: 1

Obtain all injection repeats from the same vial

Actuation Settings

Total Number of Actuations (shots) per Test: 5

Number of Actuations (shots) per Dose: 1

Nesting Hierarchy

Tier 1: Stage of Life Tier 2: Device

Stage of Life Settings

No. of Stages: 1

Block on Stage of Life

Device Settings

No. of Devices: 3

Block on Device

Stage of Dose Delivery Life	Device ID
Start	Device 1
Start	Device 2
Start	Device 3

Step 3. Sampling Plan Setup

- Set up the specified protocol for actuations, devices, and stages of dose delivery life.

Inhaler Testing - Inhaler Testing Tutorial.smae

File Edit Activity Tools Window Help

Edit Run No. Labels Standards Setup Import Report Delete Report ?

Sampling Plan Setup

- Create Sampling Plan
- **Sampling Plan Reports**

Data Management / Analysis

- Data Management
- Data Analysis

Reporting Toolkit

- Fusion Reporter
- Audit Log Reporter

Sampling Plan Reports

Sampling Plan

Name: Administrator
Company: S-Matrix Corporation
Project: Project 1
Date: 18 SEP 2024 16:26:17 PDT [UTC-07:00]

Sampling Plan - Sampling Plan 1

Experiment Constants

Constant Name	Constant Value	Units
Stage of Life	Start	

Sampling Plan Matrix

Run No.	Device	Apparatus Stage
Start_Device 1_Device	Device 1	Device
Start_Device 1_Throat	Device 1	Throat
Start_Device 1_Pre-separator	Device 1	Pre-separator
Start_Device 1_Stage 1	Device 1	Stage 1
Start_Device 1_Stage 2	Device 1	Stage 2
Start_Device 1_Stage 3	Device 1	Stage 3
Start_Device 1_Stage 4	Device 1	Stage 4
Start_Device 1_Stage 5	Device 1	Stage 5

Step 4. Generate Sampling Plan

FIT instantly generates the sampling plan with one click.

Simple Standards Setup

Standards Setup

Selected CDS: Empower
 Standards Strategy: Multi-level Bracketing - Overlap

Settings:

Levels per Bracket: 5

No. of Repeat Injections per Level: 1

No. of Check Standard Levels per Bracket: 1

No. of Unknown Injections within Brackets: 10

Experiment Design

	Run No.	Device	Apparatus Stage
1	CAL - L1.1.a	---	---
2	CAL - L2.1.a	---	---
3	CAL - L3.1.a	---	---
4	CAL - L4.1.a	---	---
5	CAL - L5.1.a	---	---
6	CHK - L1.1.a	---	---
7	Start_Device 1_Device	---	---
8	Start_Device 1_Throat	---	---
9	Start_Device 1_Pre-separator	---	---

Validation Status: Your settings are valid.

Clear Reset Next >> Cancel ?

Step 5. Standards Protocol Setup

- Select the Specified Standards Protocol supported by your CDS.



Step 6. Closed-loop Automation

☑ Export Design and Import Chromatogram Results in the Following Simple Steps.

1. Complete the FIT template with the relevant information
2. FIT creates a Sampling Plan for the required cascade impaction testing
3. FIT exports the Sampling Plan to the CDS
4. The CDS runs the exported Sampling Plan sequence
5. FIT imports and analyzes the CDS results
6. FIT creates final reports and graphs



ChemStation
OpenLab



(See next slides)

FIT Export Automation – Empower Example



Automatically Generates Sampling Plan

Automatically Builds Sequence and All Instrument Methods

Empower CDS

RD2 Optimization in S-Matrix\Internal Development\FMD\RD2 - Optimization - 9_9_0 as System/Administrator - Sample Set Method Editor

File Edit View Help

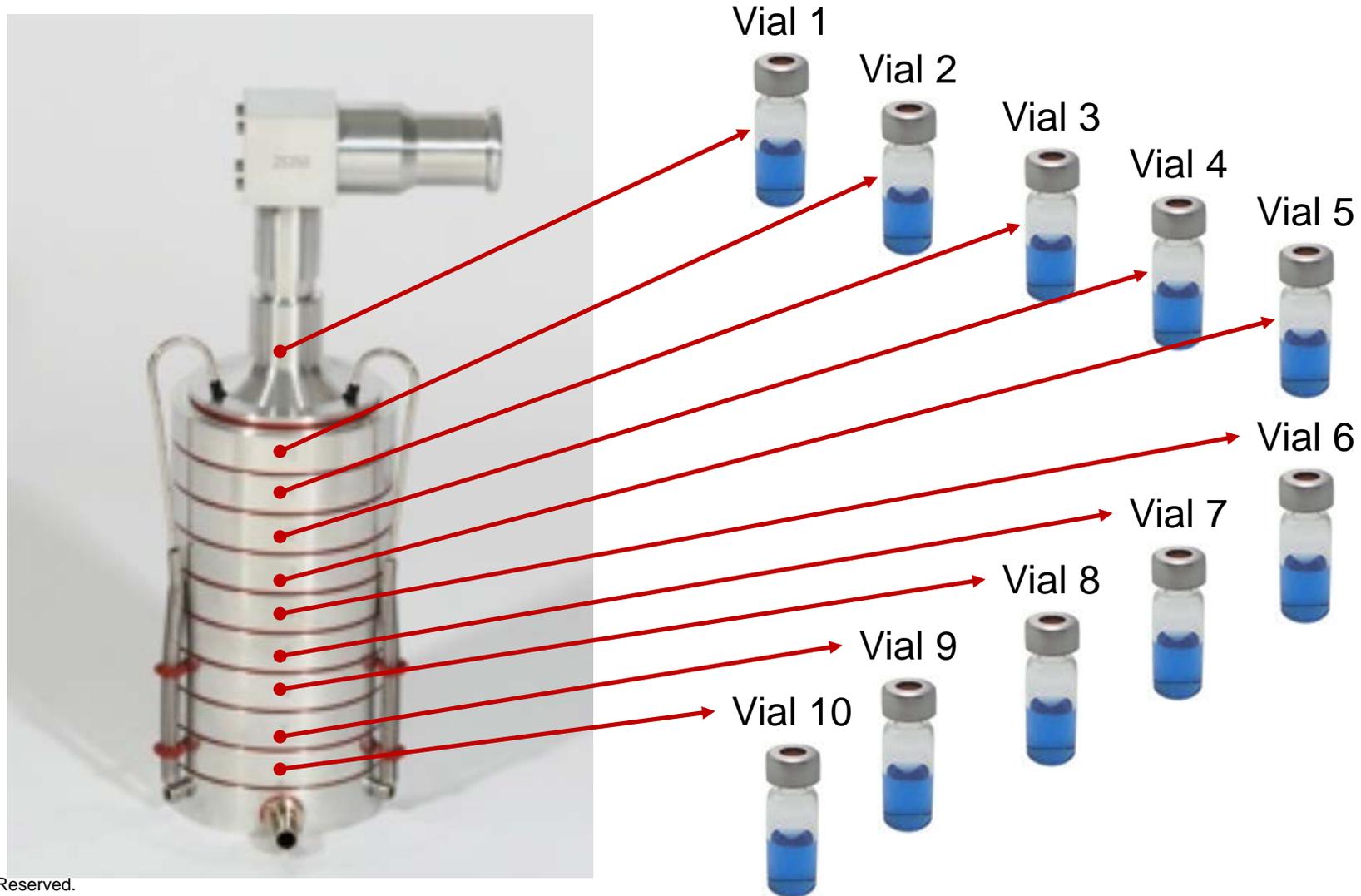
Apply Table Preferences Sample Set Method

	Plate/Well	Inj Vol (uL)	# of Injs	Label	SampleName	Level	Function	Method Set / Report or Export Method	Label Reference	Processing	Run Time (Minutes)	Data Start (Minutes)	Next Inj Delay (Minutes)	MS Tune Method	MS Calibration Method	Column Position	Auto Additions	SampleWeight	Dilution
1							Condition Column	RD2 Optimization 001_031			6.60					Position 5			
2							Equilibrate	RD2 Optimization 001_001			4.00					No Change			
3	1:A,1	2.0	1	Unk-001-001	1		Inject Samples	RD2 Optimization 001_001		Normal	17.60	0.00	3.50					1.00000	1.00000
4							Equilibrate	RD2 Optimization 001_002			4.00					No Change			
5	1:A,1	2.0	1	Unk-001-002	2		Inject Samples	RD2 Optimization 001_002		Normal	9.60	0.00	3.50					1.00000	1.00000
6							Equilibrate	RD2 Optimization 001_003			4.00					No Change			
7	1:A,1	2.0	1	Unk-001-003	3		Inject Samples	RD2 Optimization 001_003		Normal	17.60	0.00	3.50					1.00000	1.00000
8							Equilibrate	RD2 Optimization 001_004			4.00					No Change			
9	1:A,1	2.0	1	Unk-001-004	4		Inject Samples	RD2 Optimization 001_004		Normal	9.60	0.00	3.50					1.00000	1.00000
10							Equilibrate	RD2 Optimization 001_005			4.00					No Change			
11	1:A,1	2.0	1	Unk-001-005	5		Inject Samples	RD2 Optimization 001_005		Normal	9.60	0.00	3.50					1.00000	1.00000
12							Equilibrate	RD2 Optimization 001_006			4.00					No Change			
13	1:A,1	2.0	1	Unk-001-006	6		Inject Samples	RD2 Optimization 001_006		Normal	9.60	0.00	3.50					1.00000	1.00000
14							Equilibrate	RD2 Optimization 001_007			4.00					No Change			
15	1:A,1	2.0	1	Unk-001-007	7		Inject Samples	RD2 Optimization 001_007		Normal	17.60	0.00	3.50					1.00000	1.00000
16							Condition Column	RD2 Optimization 001_032			6.60					Position 5			
17							Equilibrate	RD2 Optimization 001_008			4.00					No Change			
18	1:A,1	2.0	1	Unk-001-008	8		Inject Samples	RD2 Optimization 001_008		Normal	13.60	0.00	3.50					1.00000	1.00000
19							Condition Column	RD2 Optimization 001_033			6.60					Position 5			
20							Equilibrate	RD2 Optimization 001_009			4.00					No Change			
21	1:A,1	2.0	1	Unk-001-009	9		Inject Samples	RD2 Optimization 001_009		Normal	9.60	0.00	3.50					1.00000	1.00000
22							Equilibrate	RD2 Optimization 001_010			4.00					No Change			
23	1:A,1	2.0	1	Unk-001-010	10		Inject Samples	RD2 Optimization 001_010		Normal	9.60	0.00	3.50					1.00000	1.00000
24							Equilibrate	RD2 Optimization 001_011			4.00					No Change			
25	1:A,1	2.0	1	Unk-001-011	11		Inject Samples	RD2 Optimization 001_011		Normal	17.60	0.00	3.50					1.00000	1.00000
26							Equilibrate	RD2 Optimization 001_012			4.00					No Change			
27	1:A,1	2.0	1	Unk-001-012	12		Inject Samples	RD2 Optimization 001_012		Normal	17.60	0.00	3.50					1.00000	1.00000
28							Condition Column	RD2 Optimization 001_034			6.60					Position 5			
29							Equilibrate	RD2 Optimization 001_013			4.00					No Change			
30	1:A,1	2.0	1	Unk-001-013	13		Inject Samples	RD2 Optimization 001_013		Normal	13.60	0.00	3.50					1.00000	1.00000
31							Condition Column	RD2 Optimization 001_035			6.60					Position 5			
32							Equilibrate	RD2 Optimization 001_014			4.00					No Change			
33	1:A,1	2.0	1	Unk-001-014	14		Inject Samples	RD2 Optimization 001_014		Normal	13.60	0.00	3.50					1.00000	1.00000
34							Equilibrate	RD2 Optimization 001_015			4.00					No Change			
35	1:A,1	2.0	1	Unk-001-015	15		Inject Samples	RD2 Optimization 001_015		Normal	13.60	0.00	3.50					1.00000	1.00000
36							Equilibrate	RD2 Optimization 001_016			4.00					No Change			
37	1:A,1	2.0	1	Unk-001-016	16		Inject Samples	RD2 Optimization 001_016		Normal	9.60	0.00	3.50					1.00000	1.00000
38							Equilibrate	RD2 Optimization 001_017			4.00					No Change			

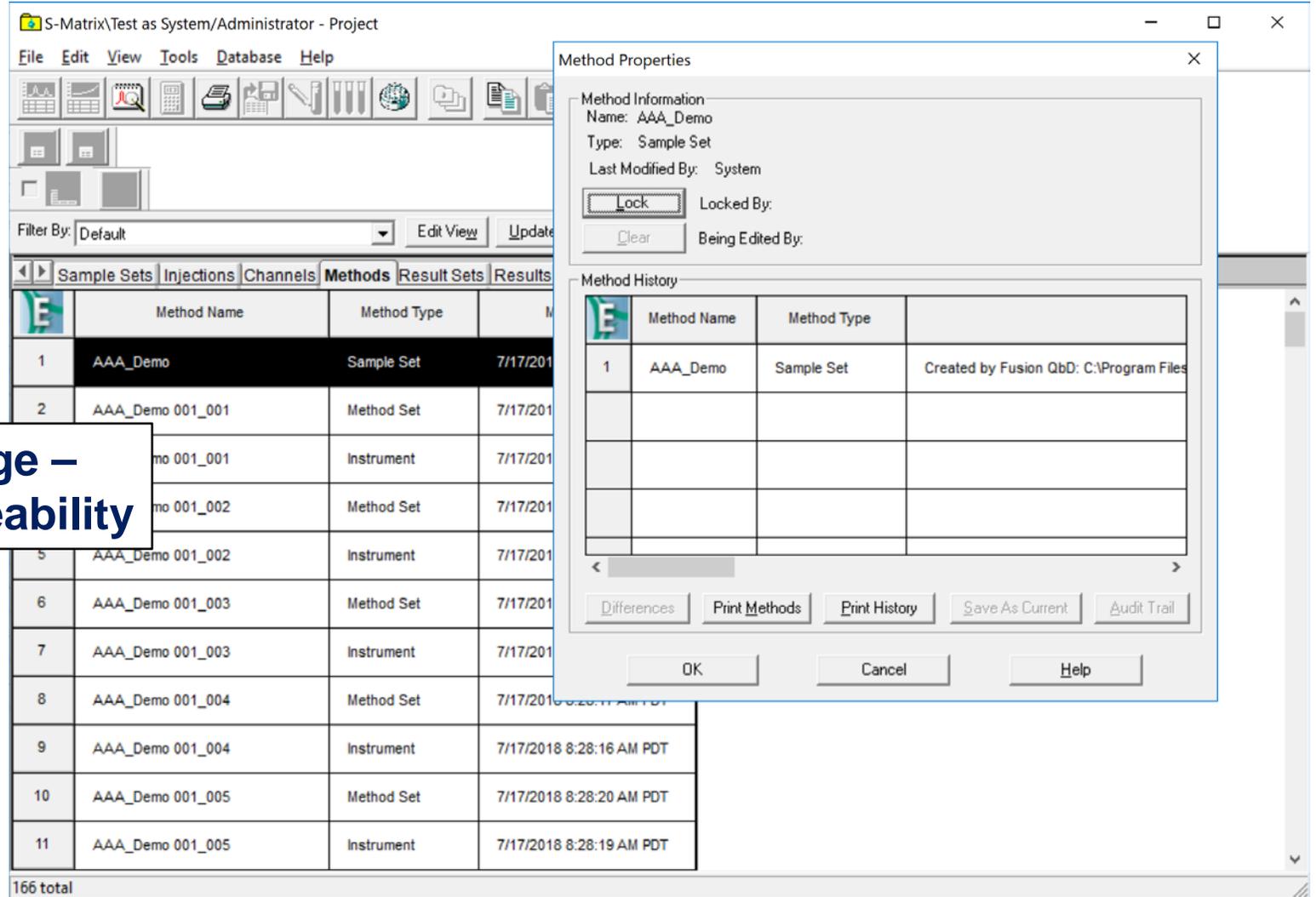
For Help, press F1

FIT Export Automation

Ready-to-Run Sequences with Correct Vial Positions for Standard and Sample Injections



Automated, Audited Data Exchange – Preserves Data Integrity and Traceability



The screenshot displays the S-Matrix software interface. The main window shows a 'Methods' table with the following data:

	Method Name	Method Type	
1	AAA_Demo	Sample Set	7/17/2018
2	AAA_Demo 001_001	Method Set	7/17/2018
	AAA_Demo 001_001	Instrument	7/17/2018
	AAA_Demo 001_002	Method Set	7/17/2018
5	AAA_Demo 001_002	Instrument	7/17/2018
6	AAA_Demo 001_003	Method Set	7/17/2018
7	AAA_Demo 001_003	Instrument	7/17/2018
8	AAA_Demo 001_004	Method Set	7/17/2018 8:28:17 AM PDT
9	AAA_Demo 001_004	Instrument	7/17/2018 8:28:16 AM PDT
10	AAA_Demo 001_005	Method Set	7/17/2018 8:28:20 AM PDT
11	AAA_Demo 001_005	Instrument	7/17/2018 8:28:19 AM PDT

The 'Method Properties' dialog box is open, showing the following information:

- Method Information:**
 - Name: AAA_Demo
 - Type: Sample Set
 - Last Modified By: System
 - Buttons: Lock, Clear
 - Fields: Locked By, Being Edited By
- Method History:**

	Method Name	Method Type	
1	AAA_Demo	Sample Set	Created by Fusion QbD: C:\Program Files
- Buttons:** Differences, Print Methods, Print History, Save As Current, Audit Trail, OK, Cancel, Help

FIT Import Automation – Empower Example

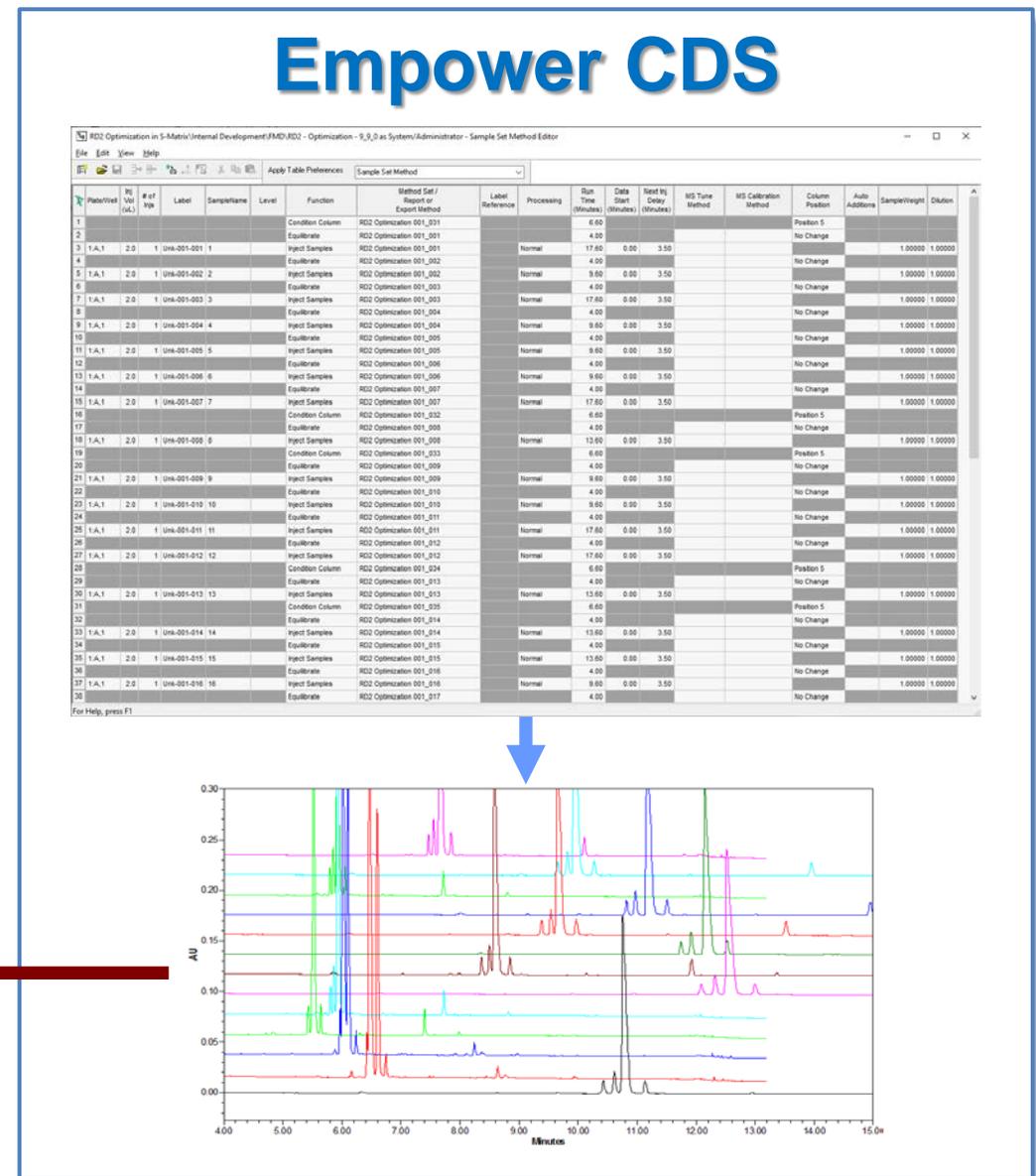


Fusion QbD®

Automatically Retrieves All Chromatogram Results Data

Automated analysis, graphing, and reporting.
 Report formats:
 RTF, DOC, HTML, PDF, XLSX, XML

Empower CDS



Run/Vol	# of Inj	Label	Sample Name	Level	Function	Method Set / Report or Export Method	Label Reference	Processing	Run Time (Minutes)	Data Start (Minutes)	Inject Delay (Minutes)	MS Tune Method	MS Calibration Method	Column Position	Auto Addition	Sample Weight	Dilution
1					Condition Column	RD2 Optimization 001_001			6.00					Position 5			
2					Equilibrate	RD2 Optimization 001_001			4.00					No Change		1.00000	1.00000
3	1.A.1	2.0	1	106-001-001	1	Inject Samples	RD2 Optimization 001_001	Normal	17.00	0.00	3.50			No Change		1.00000	1.00000
4					Equilibrate	RD2 Optimization 001_002			4.00					No Change		1.00000	1.00000
5	1.A.1	2.0	1	106-001-002	2	Inject Samples	RD2 Optimization 001_002	Normal	9.00	0.00	3.50			No Change		1.00000	1.00000
6					Equilibrate	RD2 Optimization 001_003			4.00					No Change		1.00000	1.00000
7	1.A.1	2.0	1	106-001-003	3	Inject Samples	RD2 Optimization 001_003	Normal	17.00	0.00	3.50			No Change		1.00000	1.00000
8					Equilibrate	RD2 Optimization 001_004			4.00					No Change		1.00000	1.00000
9	1.A.1	2.0	1	106-001-004	4	Inject Samples	RD2 Optimization 001_004	Normal	9.00	0.00	3.50			No Change		1.00000	1.00000
10					Equilibrate	RD2 Optimization 001_005			4.00					No Change		1.00000	1.00000
11	1.A.1	2.0	1	106-001-005	5	Inject Samples	RD2 Optimization 001_005	Normal	9.00	0.00	3.50			No Change		1.00000	1.00000
12					Equilibrate	RD2 Optimization 001_006			4.00					No Change		1.00000	1.00000
13	1.A.1	2.0	1	106-001-006	6	Inject Samples	RD2 Optimization 001_006	Normal	9.00	0.00	3.50			No Change		1.00000	1.00000
14					Equilibrate	RD2 Optimization 001_007			4.00					No Change		1.00000	1.00000
15	1.A.1	2.0	1	106-001-007	7	Inject Samples	RD2 Optimization 001_007	Normal	17.00	0.00	3.50			No Change		1.00000	1.00000
16					Condition Column	RD2 Optimization 001_012			6.00					Position 5			
17					Equilibrate	RD2 Optimization 001_008			4.00					No Change		1.00000	1.00000
18	1.A.1	2.0	1	106-001-008	8	Inject Samples	RD2 Optimization 001_008	Normal	13.00	0.00	3.50			No Change		1.00000	1.00000
19					Condition Column	RD2 Optimization 001_013			6.00					Position 5			
20					Equilibrate	RD2 Optimization 001_009			4.00					No Change		1.00000	1.00000
21	1.A.1	2.0	1	106-001-009	9	Inject Samples	RD2 Optimization 001_009	Normal	9.00	0.00	3.50			No Change		1.00000	1.00000
22					Equilibrate	RD2 Optimization 001_010			4.00					No Change		1.00000	1.00000
23	1.A.1	2.0	1	106-001-010	10	Inject Samples	RD2 Optimization 001_010	Normal	9.00	0.00	3.50			No Change		1.00000	1.00000
24					Equilibrate	RD2 Optimization 001_011			4.00					No Change		1.00000	1.00000
25	1.A.1	2.0	1	106-001-011	11	Inject Samples	RD2 Optimization 001_011	Normal	17.00	0.00	3.50			No Change		1.00000	1.00000
26					Equilibrate	RD2 Optimization 001_012			4.00					No Change		1.00000	1.00000
27	1.A.1	2.0	1	106-001-012	12	Inject Samples	RD2 Optimization 001_012	Normal	17.00	0.00	3.50			No Change		1.00000	1.00000
28					Condition Column	RD2 Optimization 001_024			6.00					Position 5			
29					Equilibrate	RD2 Optimization 001_013			4.00					No Change		1.00000	1.00000
30	1.A.1	2.0	1	106-001-013	13	Inject Samples	RD2 Optimization 001_013	Normal	13.00	0.00	3.50			No Change		1.00000	1.00000
31					Condition Column	RD2 Optimization 001_035			6.00					Position 5			
32					Equilibrate	RD2 Optimization 001_014			4.00					No Change		1.00000	1.00000
33	1.A.1	2.0	1	106-001-014	14	Inject Samples	RD2 Optimization 001_014	Normal	13.00	0.00	3.50			No Change		1.00000	1.00000
34					Equilibrate	RD2 Optimization 001_015			4.00					No Change		1.00000	1.00000
35	1.A.1	2.0	1	106-001-015	15	Inject Samples	RD2 Optimization 001_015	Normal	13.00	0.00	3.50			No Change		1.00000	1.00000
36					Equilibrate	RD2 Optimization 001_016			4.00					No Change		1.00000	1.00000
37	1.A.1	2.0	1	106-001-016	16	Inject Samples	RD2 Optimization 001_016	Normal	9.00	0.00	3.50			No Change		1.00000	1.00000
38					Equilibrate	RD2 Optimization 001_017			4.00					No Change		1.00000	1.00000

Automated, Audited Data Exchange – Preserves Data Integrity and Traceability

Method Development - FMD Tutorial - Optimization - Part 2 - 991 533.smae

File Edit Activity Tools Window Help

Generate Audit Log

- Design of Experiments
 - Create a Design
 - Design Reports
- Data Entry / Analysis
 - Data Entry
 - Data Analysis
- Best Answer Searches
 - Best Overall Answer
 - Acceptable Performance Region
 - Point Predictions
- Visualization Graphics
 - Single Response Series
 - Multiple Response Series
- Reporting Toolkit
 - Fusion Reporter
 - Audit Log Reporter**

Name: Administrator
Company: S-Matrix Corporation
Project: Project 1
Date: 07 MAY 2022 15:13:56 PDT [UTC-07:00]



Audit Log

20 JUN 2021 10:13:51 PDT [UTC-07:00] - Administrator

Event Type: Import Responses

Import Response Settings

Setting	Value
Target CDS	EMPOWER
Empower Version	Empower 3 Software Build 3471 SPs Installed: Service Release 3 DB ID: 2484307300
Empower Database	(local)
Empower User	system
Project Name	RD2 - Optimization - 9_9_0
Result Set(ID)	RD2 Optimization (9001)
Processed Channel	PDA Ch1 225nm@4.8nm, Time offset by 0.020 mins.
Activate PeakTracker	Checked
Raw PDA Channel	Unchecked
Raw MS Channel	QDa Positive Scan
MS Time Offset(min)	0.02
MS Intensity Threshold	100000
Processed MS Channel	QDa Positive Scan MS TIC, Smoothed by 59 point Savitzky-Golay Filter. (QDa Positive(+) Scan (100.00-1250.00)Da, Centroid, CV=15)
Track Non-absorbing Peaks	Checked
Auto-imported Response(s)	Height, RetentionTime, WidthAt50Pct, USPTailing, WidthAtTangentUSPResolution, Area
Import Chromatogram Trace Data	Checked
Import Prediction Chromatogram Data	Checked
Total Import Time	00:06:42
Locale	English (United States)

Imported Data Source

Sample Name	ResultID	MS ResultID	TIC (ID/Type)	MS-Spectra (ID/Type)	UV-Spectra (ID/Type)
1	9155	9153	MS_TIC (9004/2D)	QDa Positive Scan (7036/3DMS)	
10	9048	9189	MS_TIC (9050/2D)	QDa Positive Scan (7063/3DMS)	
11	9191	9193	MS_TIC (9055/2D)	QDa Positive Scan (7066/3DMS)	
12	9058	9195	MS_TIC (9060/2D)	QDa Positive Scan (7069/3DMS)	

Ready

Inhaler Testing Data Analysis

Mass Balance Calculation Settings

Calculation Method: Target Delivered Amount

Response Settings

Select	Response Name	Units	Amount
<input checked="" type="checkbox"/>	API - Amount	µg	35.000

Apparatus Settings

Sampling Flow Rate: 60.00 ± 1.000 L/min

#	Device ID	Stage of Dose Delivery Life	Testing Apparatus Name	Testing Date	Sum Shot Weight (mg)	Actual Flow Rate (L/min)	Pressure Drop (kPa)
1	Device 1	Start	Tutorial Apparatus	09/18/2024	456.00	60.000	3.998
2	Device 2	Start	Tutorial Apparatus	09/18/2024	447.00	60.000	4.012
3	Device 3	Start	Tutorial Apparatus	09/18/2024	449.00	60.000	4.064

The settings are valid.

Back Next Cancel

Step 1. Enter Sample & Test Data

- Enter the dates and the executed testing conditions.

Inhaler Testing Data Analysis

Additional Group Settings
 Analysis and Reporting Mode: **General**
 Reporting Precision: 0.000
 Calculate Material/Mass Balance
 Uniformity Spec. +/- 15.00 %
 Device Retention
 From Stage: Device To Stage: Device

Regression Data Settings
 Option 1 Option 2
 X Data = NormStdInv(Cumulative Probability)
 Y Data = Log(Particle Size)

Optional Groups by Stage
 Additional Groups: 0

#	Group Name	From Stage	To Stage

Optional Group Calculations

Group Calculation
<input checked="" type="checkbox"/> Group Mass
<input type="checkbox"/> Group Weight
<input type="checkbox"/> Group Retention
<input type="checkbox"/> Group Fraction

Optional Groups by Partide Size
 Additional Groups: 2

#	Group Name	Minimum (µm)	Maximum (µm)	Use Cut off	Calculation Method
1	Size Group 1	0.00	8.06	<input type="checkbox"/>	Regression
2	Size Group 2	0.00	8.06	<input type="checkbox"/>	Interpolation

Regression Settings
 Within Bounds Extended
 Linearity Range: Lower Bound% 15.70 Upper Bound% 84.30
 R-square Value: 0.95
 Probit 4 = 15.70% Probit 6 = 84.30%

The settings are valid.

Back Next Cancel

Step 2. Enter Group Settings

- Material / Mass Balance
- Optional Groupings
 - by Stage
 - by Particle Size
- Optional Group Calculations
 - Group Mass
 - Group Weight
 - Group Retention
 - Group Fraction

All Wizard settings can be **Pre-set** and **LOCKED** in re-usable templates.

Inhaler Testing Data Analysis

Fine Particle Mass (FPM)

Determination Method

Apparatus Stage From Stage: Stage 2 To Stage: MOC

Particle Size

Upper Limit < 5.00 μm

Calculation Method

Interpolation Regression

Particle Size Regression Settings

Within Bounds Extended

Linearity Range: Lower Bound%: 15.70 Upper Bound%: 84.30

R-square Value: 0.95

Probit 4 = 15.70% Probit 6 = 84.30%

Prediction Limit +/- 2 Sigma

Fine Particle Fraction (FPF)

Determination Method

Apparatus Stage From Stage: Throat To Stage: MOC

Target Delivered Amount

$$\frac{\text{Fine Particle Mass}}{\text{Target Delivered Amount}} \times 100$$

The settings are valid.

Back Next Cancel

Step 3. Enter FPM & FPF Settings

- Determination Methods
 - by Stage
 - by Particle Size
- Calculation Method for Particle Size
 - Interpolation
 - Regression

All Wizard settings can be **Pre-set** and **LOCKED** in re-usable templates.

Inhaler Testing Data Analysis

MMAD and GSD

MMAD

- MMAD (Mass Median Aerodynamic Diameter)
- Interpolation
- Regression

GSD

- GSD (Geometric Standard Deviation)
- Interpolation Only
- Interpolation - Regression (ISO 27427)
- Regression Only

Regression Settings

Within Bounds Extended

Linearity Range: Lower Bound% Upper Bound%

R-square Value

Probit 4 = 15.70% Probit 6 = 84.30%

Plots

- Histogram
- Cumulative Particle Size
- Log Probability
- Prediction Limit +/-
- Y-axis Label: Cumulative Probability Probits

The settings are valid.

Back Finish Cancel

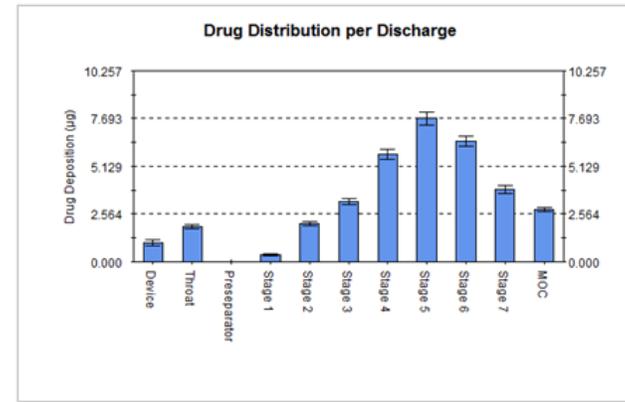
Step 4. Enter MMAD & GSD Settings

- Determination Methods
 - Interpolation
 - Regression
- Plot Settings
 - Histogram
 - Cusum
 - Log Probability

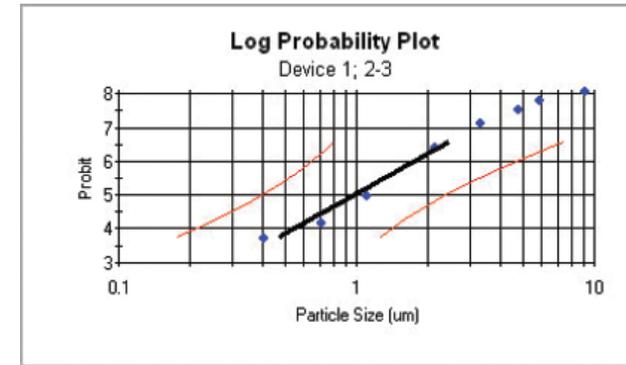
All Wizard settings can be **Pre-set** and **LOCKED** in re-usable templates.

Instant, Automated Analysis and Graphing

Stage Deposition per Actuation (µg)											
Device - Stage of Life	Device	Throat	Preseparator	Stage 1	Stage 2	Stage 3	Stage 4	Stage 5	Stage 6	Stage 7	MOC
Device 1 - Start	1.163	1.954	0.000	0.349	2.154	3.251	5.617	7.390	6.157	3.635	2.733
Device 2 - Start	1.102	1.935	0.000	0.438	2.059	3.377	6.103	7.616	6.633	4.071	2.750
Device 3 - Start	0.824	1.745	0.000	0.362	1.960	3.055	5.594	8.072	6.605	3.959	2.921
Mean	1.030	1.855	0.000	0.363	2.055	3.225	5.772	7.693	6.465	3.950	2.801
Variance	0.033	0.016	0.000	0.002	0.009	0.026	0.083	0.121	0.071	0.051	0.011
Std. Dev.	0.181	0.126	0.000	0.048	0.097	0.162	0.287	0.348	0.267	0.226	0.104
%RSD	17.54	6.70	—	12.99	4.72	5.00	4.95	4.52	4.13	5.82	3.71



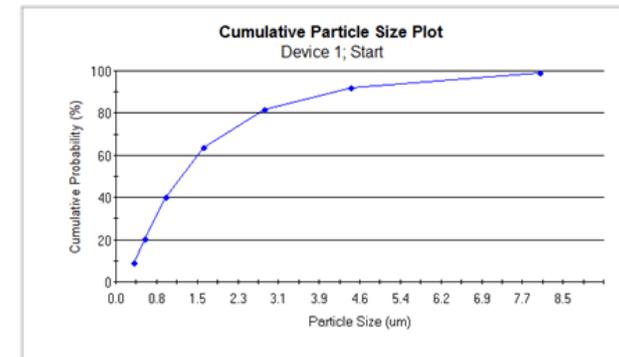
Dose Content Uniformity through Container Life - API									
Device	Device 1			Device 2			Device 3		
	Dose (µg)	% Target	Result	Dose (µg)	% Target	Result	Dose (µg)	% Target	Result
Start	35.44545	101.27271	Pass	35.03182	100.09091	Pass	32.16515	91.90909	Pass
Start	32.48636	92.81817	Pass	32.83636	93.81817	Pass	33.18636	94.81817	Pass
Start	32.39091	92.54545	Pass	34.30000	95.00000	Pass	32.93182	94.09091	Pass
Start-Mean	33.44291	95.54545	Pass	34.05636	97.30000	Pass	32.76212	93.60606	Pass
Midline	36.14545	103.27271	Pass	35.47727	101.36363	Pass	36.24091	103.54545	Pass
Midline	34.30000	95.00000	Pass	32.48636	92.81817	Pass	35.63636	101.81817	Pass
Midline	35.05636	105.81817	Pass	35.85909	102.45454	Pass	40.18636	114.81817	Pass
Midline	37.51364	107.18183	Pass	37.70455	107.72729	Pass	35.54091	101.54545	Pass
Midline-Mean	36.51136	104.31818	Pass	35.35182	101.09091	Pass	36.90114	105.43181	Pass
End	34.04545	97.27271	Pass	37.32273	106.63637	Pass	33.95000	97.00000	Pass
End	39.09090	111.45454	Pass	36.24091	103.54545	Pass	38.72273	110.63637	Pass
End	37.51364	107.18183	Pass	37.70455	107.72729	Pass	35.54091	101.54545	Pass
End-Mean	36.85606	105.30000	Pass	37.05940	105.96970	Pass	36.07121	102.06061	Pass
No. of Test Results > ± 20.0% of Target	0	Pass	0	0	Pass	0	0	Pass	0
No. of Test Results > ± 25.0% of Target	0	Pass	0	0	Pass	0	0	Pass	0
Mean Result > ± 15.0% of Target	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass



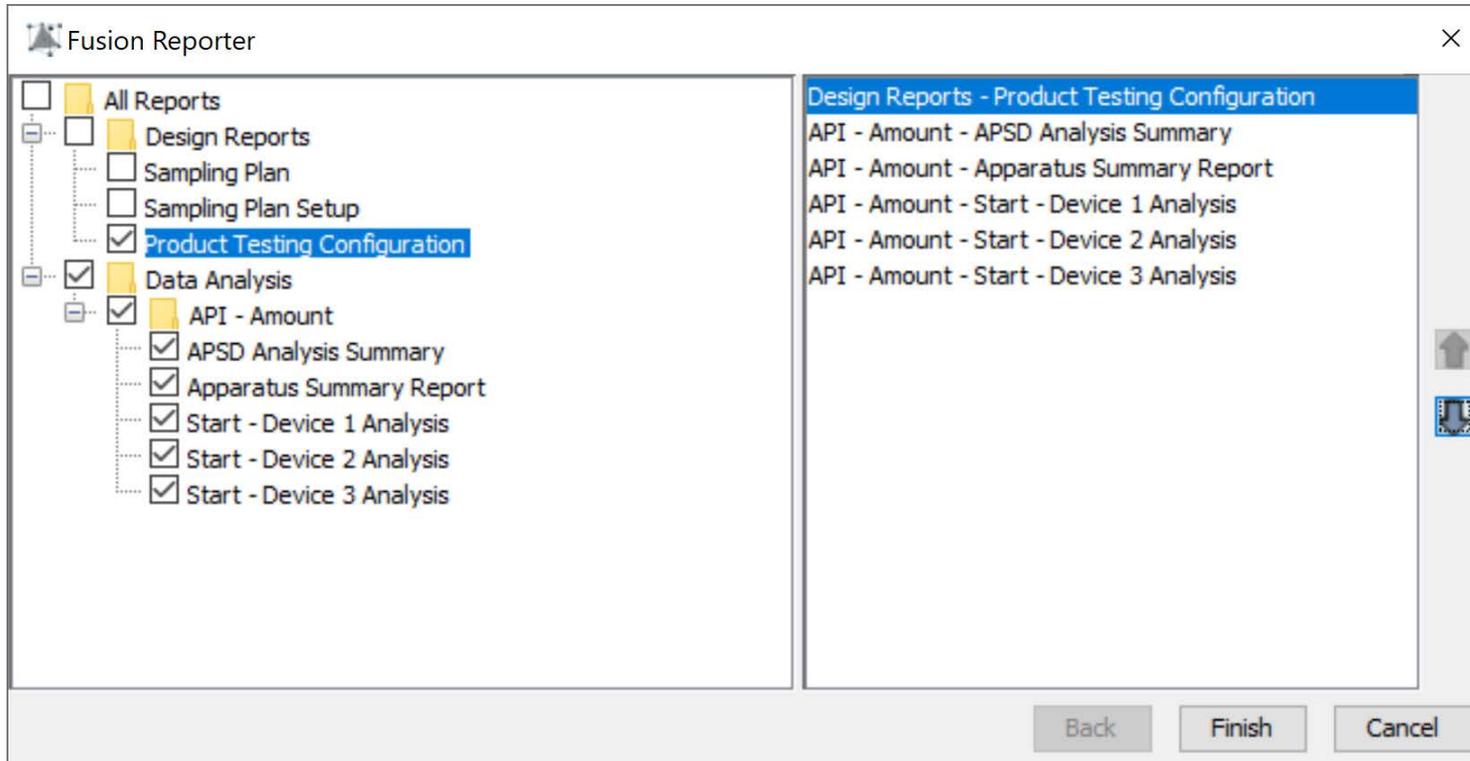
Mass Data (µg)				
Device - Stage of Life	Total Dose	Emitted Mass	FPM(1)	FPF(4)
Device 1 - Start	64.291	57.801	37.234	64.417
Device 2 - Start	31.700	31.700	28.554	90.074
Device 3 - Start	31.996	29.263	26.226	89.622
Mean	42.665	39.555	30.671	81.371
Variance	351.025	280.267	33.650	215.624
Std. Dev.	18.736	15.820	5.801	14.654
%RSD	43.91	39.96	18.91	18.05

Size Distribution (µm)					
Device - Stage of Life	MMAD(2)	GSD(4)	Log(Particle Size) - N1CP Intercept	Log(Particle Size) - N1CP Slope	R ²
Device 1 - Start	2.505	3.476	0.399	0.541	0.964
Device 2 - Start	0.824	2.342	-0.054	0.370	0.991
Device 3 - Start	0.623	—	-0.208	0.555	0.893
Mean	1.315	2.909	0.037	0.459	0.949
Variance	1.068	0.643	0.102	0.011	0.003
Std. Dev.	1.034	0.802	0.320	0.103	0.051
%RSD	78.43	27.57	872.67	21.14	5.36

*N1CP - Normal Inverse Cumulative Probability.



Flexible Report Collation and Output



- Any or all Individual reports may be included into an automatically compiled final report.
- Individual reports can be arranged in any order.
- An “Import Image” function allows chromatogram images to be incorporated into any individual report.
- The compiled final report can be output in a variety of final formats.



Security

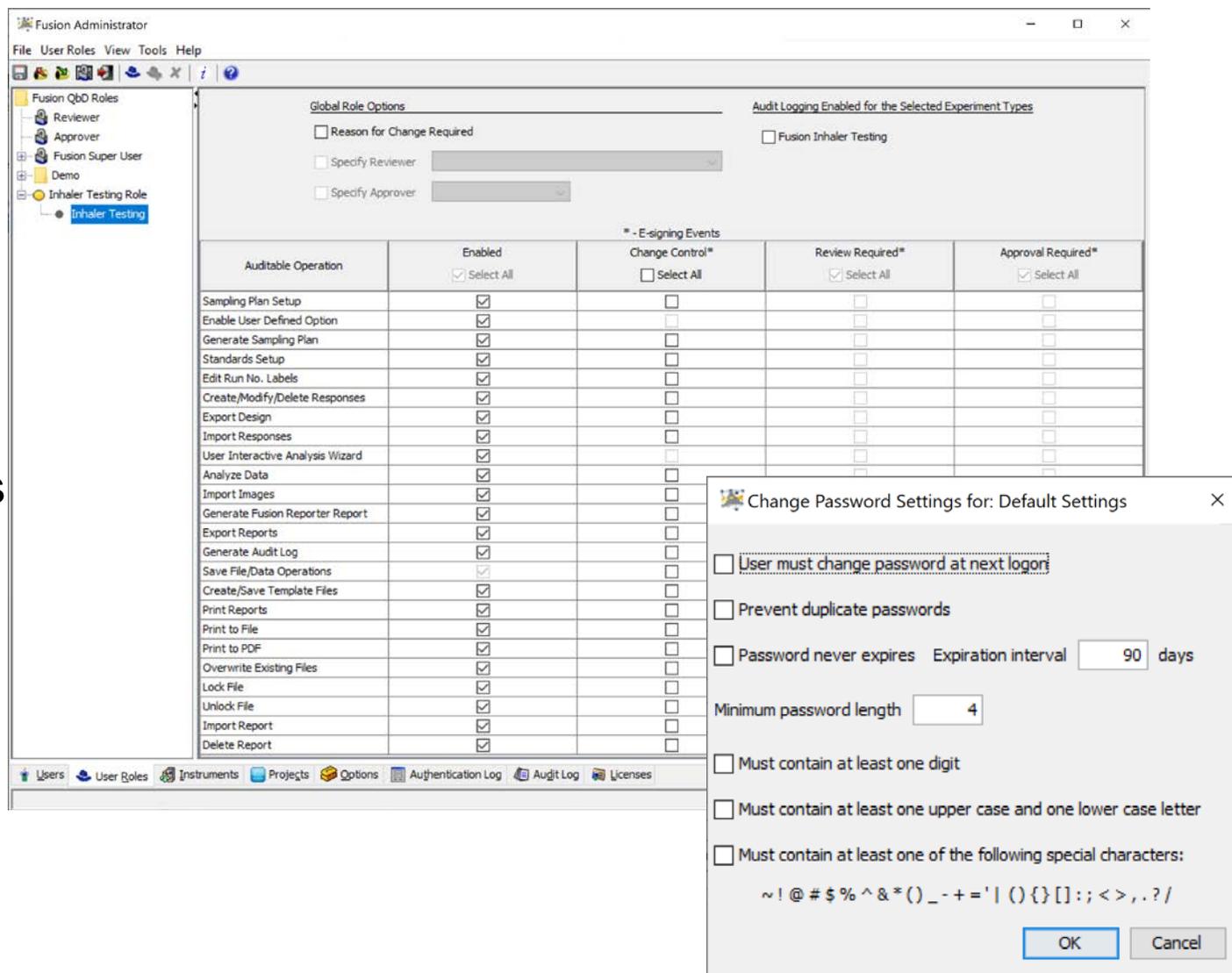
- Access Controls
- User role-based permissions

Workflow Management

- Change control
- e-Review / e-Approve control loops
- Email notifications

21 CFR 11 Compliance

- e-Signature
- Audit Logging
- Data Audit Trail

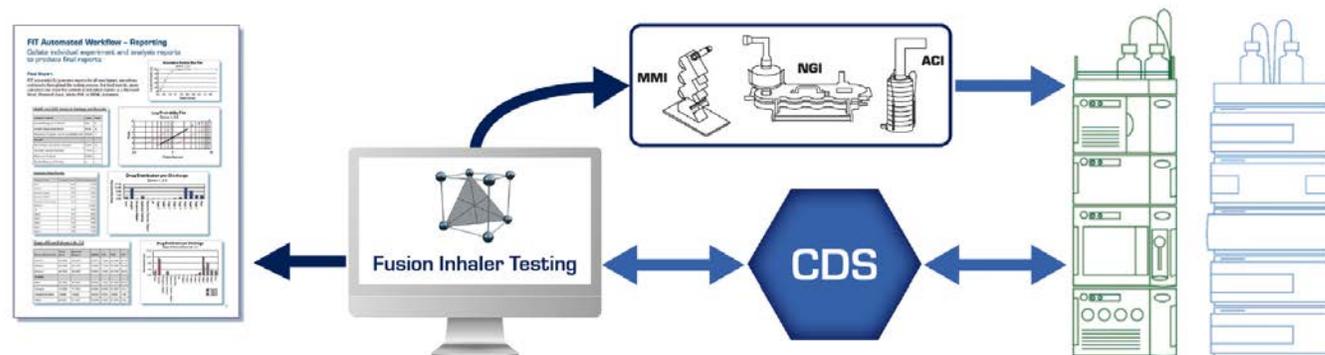


The screenshot displays the Fusion Administrator interface. On the left, a tree view shows the hierarchy: Fusion QbD Roles > Reviewer > Approver > Fusion Super User > Demo > Inhaler Testing Role > Inhaler Testing. The main window shows 'Global Role Options' with checkboxes for 'Reason for Change Required', 'Specify Reviewer', and 'Specify Approver'. A table below lists 'Auditable Operation' with columns for 'Enabled', 'Change Control*', 'Review Required**', and 'Approval Required**'. A dialog box titled 'Change Password Settings for: Default Settings' is open, showing options like 'User must change password at next login', 'Prevent duplicate passwords', 'Password never expires' (with a 90-day interval), and 'Minimum password length' (set to 4).

Auditable Operation	Enabled <input checked="" type="checkbox"/> Select All	Change Control* <input type="checkbox"/> Select All	Review Required** <input checked="" type="checkbox"/> Select All	Approval Required** <input checked="" type="checkbox"/> Select All
Sampling Plan Setup	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Enable User Defined Option	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Generate Sampling Plan	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Standards Setup	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Edit Run No. Labels	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Create/Modify/Delete Responses	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Export Design	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Import Responses	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
User Interactive Analysis Wizard	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Analyze Data	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Import Images	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Generate Fusion Reporter Report	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Export Reports	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Generate Audit Log	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Save File/Data Operations	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Create/Save Template Files	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Print Reports	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Print to File	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Print to PDF	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Overwrite Existing Files	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Lock File	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Unlock File	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Import Report	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Delete Report	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

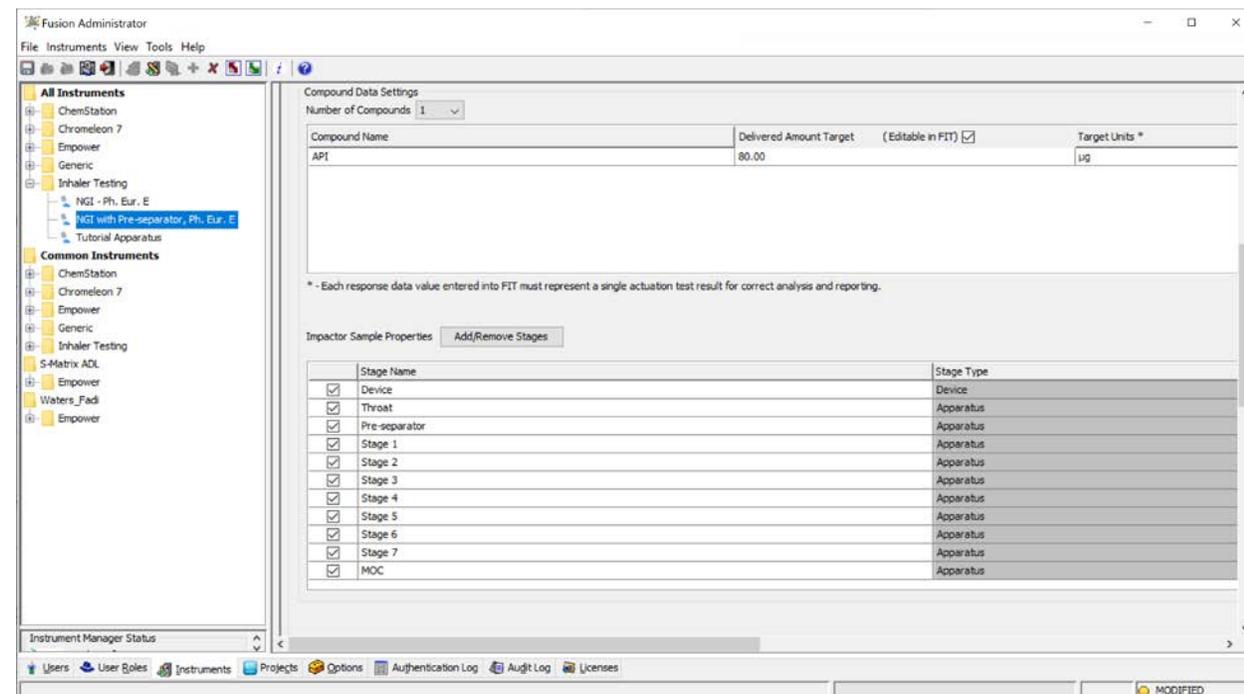
CDS Automation

- No transcriptions required
- No transcription checks required
- No chance of transcription error
- Large time savings
- Improvements in data quality



Stored Apparatus Definitions

- Reliable identification and assignment
- Stored mensuration data – no transcriptions means no checks required
- Warnings when out of “calibration”



Stage Name	Stage Type
<input checked="" type="checkbox"/> Device	Device
<input checked="" type="checkbox"/> Throat	Apparatus
<input checked="" type="checkbox"/> Pre-separator	Apparatus
<input checked="" type="checkbox"/> Stage 1	Apparatus
<input checked="" type="checkbox"/> Stage 2	Apparatus
<input checked="" type="checkbox"/> Stage 3	Apparatus
<input checked="" type="checkbox"/> Stage 4	Apparatus
<input checked="" type="checkbox"/> Stage 5	Apparatus
<input checked="" type="checkbox"/> Stage 6	Apparatus
<input checked="" type="checkbox"/> Stage 7	Apparatus
<input checked="" type="checkbox"/> MOC	Apparatus

Proven Return on Investment !

International Pharma Co. Benchmarking Project

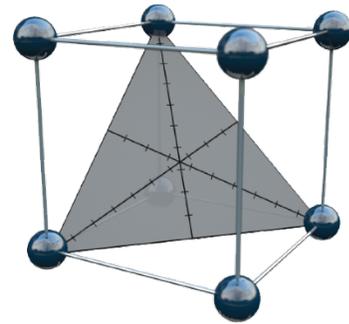
Realized Savings = 2+ Days per Week per Analyst *

Fusion Inhaler Testing™ delivers

- Large time savings
- Improved data quality
- Regulatory compliance
- Increased productivity
- Lower costs
- Increased competitiveness
- Business growth

* - on average 2.5 FTE equivalent years spent in method validation support work over 10-year life span of drug.

End of Presentation



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