# Fusion QbD® Software System

# Fusion Inhaler Testing



## The Only Software That Has It All!

- **Can be used for all DUSA and ALL Inhaler Testing work – ACI, MMI, MSLI, FSA, FSI, and NGI®!**

- **Automates LC work on multiple instruments and CDS systems!**

- **Part 11 support for regulatory compliance!**

- **Built-in workflow management system with secure templating!**

- **Reduces or eliminates labor intensive manual data and report review!**

- **Reduces analyst time by a minimum of 40%!**

# Fusion Inhaler Testing™

## The only fully automated off-the-shelf software solution for *in vitro* inhaler testing!

- Exceptional time-savings with validated data import, analysis, and reporting
- Complies with USP Chapter 601 and Ph. Eur. Chapter 2.9.18
- Secure, centrally-managed 21 CFR Part 11 environment

Fusion Inhaler Testing (FIT) is a totally automated, scalable software solution that meets today's regulatory requirements for inhalable drug testing.

### Compliance As It Should Be

Compliance begins with access control and audit trails, and continues with data handling and storage. When testing is finished, one-click completes data analysis and generates the required reports.

Create secure templates for Cascade Impactor and Dose Uniformity testing and analysis. Incorporate email notifications and e-signature control for work review and approval.
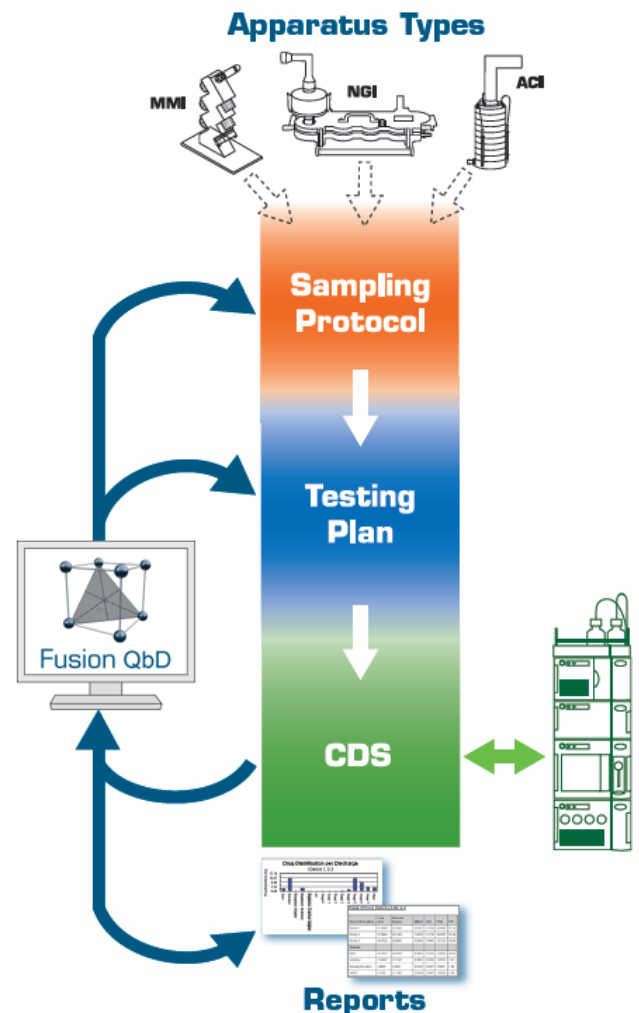
### Dramatically Increases Productivity

Currently, testing of inhalable drug delivery devices to determine aerodynamic particle size distribution (APSD) is a tedious, time-consuming manual process. FIT improves productivity by combining apparatus stage and sampling protocol information into testing plans that are exported to the Chromatography Data Software (CDS) as ready-to-run sample sets or sequences.

Further enhancing productivity, FIT eliminates manual data transcription and checking by automatically importing and analyzing chromatographic data for results calculation and reporting.

### Complete Report Suite

FIT is a full-featured solution that manages the entire work and data flow for analyzing and reporting in vitro inhaler test results. Increase productivity and report quality data with FIT!

### Saves Time and Improves Data Quality

*FIT increases productivity with automated testing plans, data analysis, and reports that meet regulatory requirements.*

# Manage the Entire Workflow with FIT

## Compatibility & flexibility from sampling protocol to final reports

### Universal Applicability

- Full compatibility with USP Apparatus 1-6 and Ph. Eur. 2.9.18 Apparatus C, D, and E

- Automatically creates testing plans for ACI, MMI, MSLI, FSA, FSI, and NGI®

- Seamlessly interfaces with LC instruments controlled by the Agilent ChemStation/OpenLAB, Thermo Scientific Chromeleon, Varian Galaxie, and Waters® Empower™ chromatography data software systems

### Easily Create Reusable Testing Plan Templates

- Eliminates user errors with coordinated device sampling protocols

- Flexible, template-driven input of device and LC set-up parameters, including standards and system suitability samples

- File-less export of testing plans to chromatography data software as ready-to-run sample sets

### Quickly Collate LC Results with File-less Data Exchange

- Automates import and analysis of chromatographic results data via a simple wizard

- One-click analysis. Results include apparatus stage averages, Mass Balance, Fine Particle Dose, Fine Particle Fraction, MMAD, and GSD

- Additional user-settable groupings by stage or particle size

### Automatically Generated Reports

- USP and Ph. Eur. report formats available

- Graphical formats include histogram, Cumulative Summation Chart (CUSUM), and log probability (probit) plots

- Arranges selected individual reports in any order as Microsoft Word, Microsoft Excel, Adobe PDF, or HTML documents

### Total Compliance and Workflow Management

- Fully supports 21 CFR Part 11 compliance requirements for closed systems

- Control user access, roles, permissions, review/approval loops, and email notifications through Fusion Administrator

### Complete Compatibility

*FIT automatically generates testing plans for and analyzes data from USP Apparatus 1-6 and Ph.Eur. 2.9.18 Apparatus C, D, and E. [Images used with permission of Copley Scientific.]*
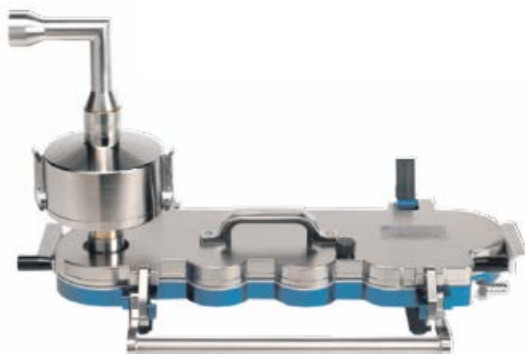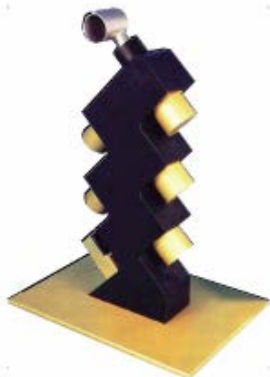
# FIT Intelligent Dataflow

## Reduces manual user inputs – fewer human errors

### Stores Apparatus and Product-specific Testing Protocol Data

Individual apparatuses can be predefined. Apparatus and stage IDs can be stored and included in final reports for mapping results data to specific apparatus configurations providing complete transparency of analysis.

For each stage, FIT can use either the Nominal Cut-off Diameter, or store the stages Effective Diameter as determined by mensuration. This is then used to calculate the Effective Cut-off Diameter (ECD) for use in subsequent calculations. The use of ECDs increases both accuracy and precision of results. Mensuration expiration dates can be defined with warnings.

Product Testing Protocol parameters including apparatus stage configuration, delivery mode, target flow rate, APIs and their LOQs can be defined and stored for use with specific apparatuses.
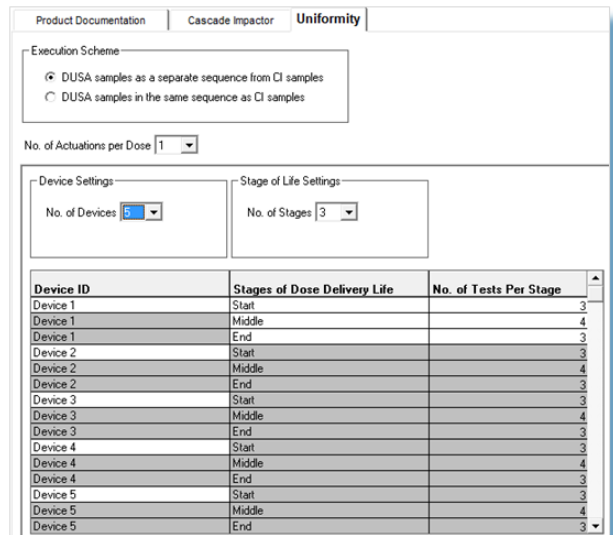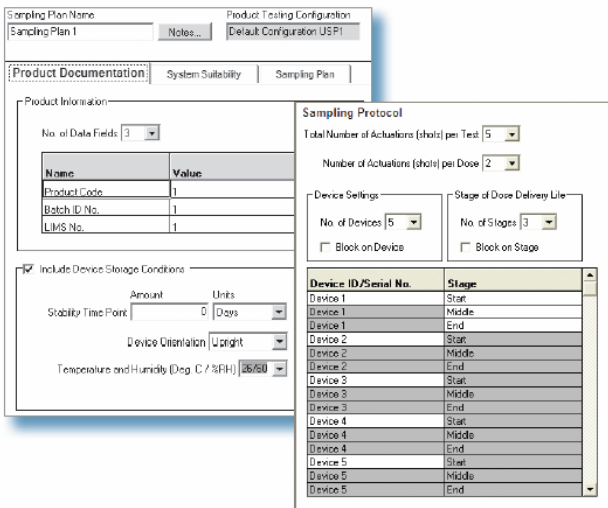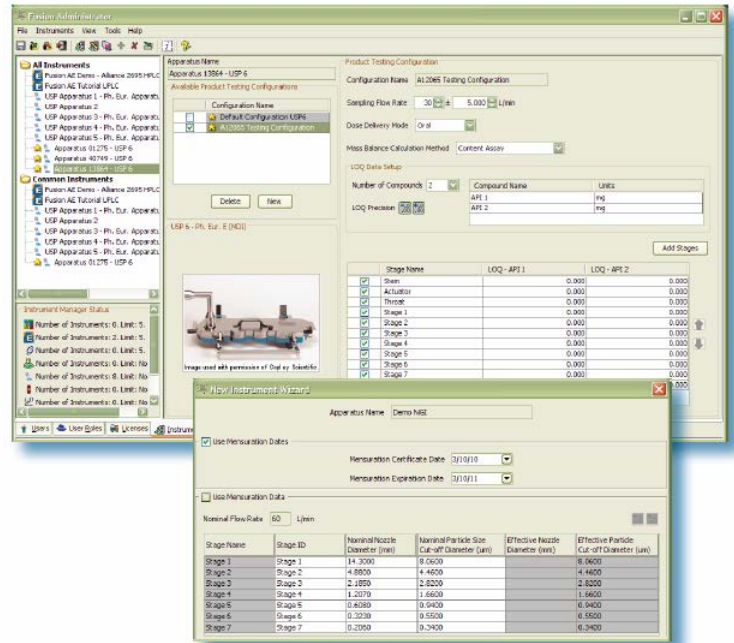


### Flexible Data Entry

User settable metadata fields exist to enter information about the inhalation product under test. If required, stability trial fields can be enabled, with standard storage conditions available via dropdown menus to ensure accurate data entry.

### Uniformity Testing

You can set the number of devices and stages of dose delivery life, and export the DUSA injections separately or as part of the overall testing protocol.

# FIT Automated Workflow – Testing Plan

## Exports testing plans as ready-to-run CDS sequences

### Testing Plan to CDS Sample Set Automatically

Sampling requirements including the number of devices under test, actuations per device, and device stages of life are defined and test plans quickly generated. Standard injections can be inserted before test plans are exported to the CDS as ready to run sample sets or sequences.

| Run No. | Stage of Life | Device | Apparatus Stage |
|---------|---------------|--------|-----------------|
| CAL - L1.1.a | --- | --- | --- |
| CAL - L2.1.a | --- | --- | --- |
| CAL - L3.1.a | --- | --- | --- |
| CAL - L4.1.a | --- | --- | --- |
| CAL - L5.1.a | --- | --- | --- |
| CHK - L1.1.a | --- | --- | --- |
| 1_D1_L1_S1 | Start | Device 1 | Stem |
| 2_D1_L1_S2 | Start | Device 1 | Actuator |
| 3_D1_L1_S3 | Start | Device 1 | Throat |
| 4_D1_L1_S4 | Start | Device 1 | Inlet Cone |
| 5_D1_L1_S5 | Start | Device 1 | Stage 0 |
| 6_D1_L1_S6 | Start | Device 1 | Stage 1 |
| 7_D1_L1_S7 | Start | Device 1 | Stage 2 |
| 8_D1_L1_S8 | Start | Device 1 | Stage 3 |
| 9_D1_L1_S9 | Start | Device 1 | Stage 4 |
| 10_D1_L1_S10 | Start | Device 1 | Stage 5 |
| | | | Stage 6 |
| | | | Stage 7 |
| | | | Filter |

### Effortlessly Builds Ready-to-Run Sequences

Through FIT, select an LC system and assay method. FIT then communicates with the CDS to build the ready-to-run sequence, including all required calibration standard and system suitability check injections.

| | Plate/Well | Inj Vol (uL) | # of Injs | Label | SampleName | Function | Method Set / Report Method | Processing | Run Time (Minutes) | SampleWeight | Dilution |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 1:A,1 | 10.0 | 1 | Unk-000-000 | Blank - 1 | Inject Samples | Fusion QbD Tutorial UPLC | Don't Process or Report | 10.00 | 1.00000 | 1.00000 |
| 2 | | | | | | Clear Calibration | Fusion QbD Tutorial UPLC | Normal | | | |
| 3 | 1:A,2 | 10.0 | 1 | CAL-001-001 | CAL - L1.1.a | Inject Standards | Fusion QbD Tutorial UPLC | Don't Process or Report | 10.00 | 1.00000 | 1.00000 |
| 4 | 1:A,3 | 10.0 | 1 | CAL-001-002 | CAL - L2.1.a | Inject Standards | Fusion QbD Tutorial UPLC | Don't Process or Report | 10.00 | 1.00000 | 1.00000 |
| 5 | 1:A,4 | 10.0 | 1 | CAL-001-003 | CAL - L3.1.a | Inject Standards | Fusion QbD Tutorial UPLC | Don't Process or Report | 10.00 | 1.00000 | 1.00000 |
| 6 | 1:A,5 | 10.0 | 1 | CAL-001-004 | CAL - L4.1.a | Inject Standards | Fusion QbD Tutorial UPLC | Don't Process or Report | 10.00 | 1.00000 | 1.00000 |
| 7 | 1:A,6 | 10.0 | 1 | CAL-001-005 | CAL - L5.1.a | Inject Standards | Fusion QbD Tutorial UPLC | Don't Process or Report | 10.00 | 1.00000 | 1.00000 |
| 8 | 1:A,7 | 10.0 | 1 | CHK-001-001 | CHK - L1.1.a | Inject Controls | Fusion QbD Tutorial UPLC | Don't Process or Report | 10.00 | 1.00000 | 1.00000 |
| 9 | 1:A,8 | 10.0 | 1 | Unk-001-001 | 1_D1_L1_S1 | Inject Samples | Fusion QbD Tutorial UPLC | Don't Process or Report | 10.00 | 1.00000 | 1.00000 |
| 10 | 1:B,1 | 10.0 | 1 | Unk-001-002 | 2_D1_L1_S2 | Inject Samples | Fusion QbD Tutorial UPLC | Don't Process or Report | 10.00 | 1.00000 | 1.00000 |
| 11 | 1:B,2 | 10.0 | 1 | Unk-001-003 | 3_D1_L1_S3 | Inject Samples | Fusion QbD Tutorial UPLC | Don't Process or Report | 10.00 | 1.00000 | 1.00000 |
| 12 | 1:B,3 | 10.0 | 1 | Unk-001-004 | 4_D1_L1_S4 | Inject Samples | Fusion QbD Tutorial UPLC | Don't Process or Report | 10.00 | 1.00000 | 1.00000 |
| 13 | 1:B,4 | 10.0 | 1 | Unk-001-005 | 5_D1_L1_S5 | Inject Samples | Fusion QbD Tutorial UPLC | Don't Process or Report | 10.00 | 1.00000 | 1.00000 |
| 14 | 1:B,5 | 10.0 | 1 | Unk-001-006 | 6_D1_L1_S6 | Inject Samples | Fusion QbD Tutorial UPLC | Don't Process or Report | 10.00 | 1.00000 | 1.00000 |
| 15 | 1:B,6 | 10.0 | 1 | Unk-001-007 | 7_D1_L1_S7 | Inject Samples | Fusion QbD Tutorial UPLC | Don't Process or Report | 10.00 | 1.00000 | 1.00000 |
| 16 | 1:B,7 | 10.0 | 1 | Unk-001-008 | 8_D1_L1_S8 | Inject Samples | Fusion QbD Tutorial UPLC | Don't Process or Report | 10.00 | 1.00000 | 1.00000 |
| 17 | 1:B,8 | 10.0 | 1 | Unk-001-009 | 9_D1_L1_S9 | Inject Samples | Fusion QbD Tutorial UPLC | Don't Process or Report | 10.00 | 1.00000 | 1.00000 |
| 18 | 1:C,1 | 10.0 | 1 | Unk-001-010 | 10_D1_L1_S10 | Inject Samples | Fusion QbD Tutorial UPLC | Don't Process or Report | 10.00 | 1.00000 | 1.00000 |
| 19 | 1:C,2 | 10.0 | 1 | Unk-001-011 | 11_D1_L1_S11 | Inject Samples | Fusion QbD Tutorial UPLC | Don't Process or Report | 10.00 | 1.00000 | 1.00000 |
| 20 | 1:C,3 | 10.0 | 1 | Unk-001-012 | 12_D1_L1_S12 | Inject Samples | Fusion QbD Tutorial UPLC | Don't Process or Report | 10.00 | 1.00000 | 1.00000 |
| 21 | 1:C,4 | 10.0 | 1 | Unk-001-013 | 13_D1_L1_S13 | Inject Samples | Fusion QbD Tutorial UPLC | Don't Process or Report | 10.00 | 1.00000 | 1.00000 |
| 22 | | | | | | Clear Calibration | Fusion QbD Tutorial UPLC | Normal | | | |

### Control Multiple Systems from Different Vendors

FIT seamlessly interfaces with LC instruments controlled by Agilent ChemStation/OpenLAB, Thermo Scientific Chromeleon, Varian Galaxie, and Waters® Empower™.
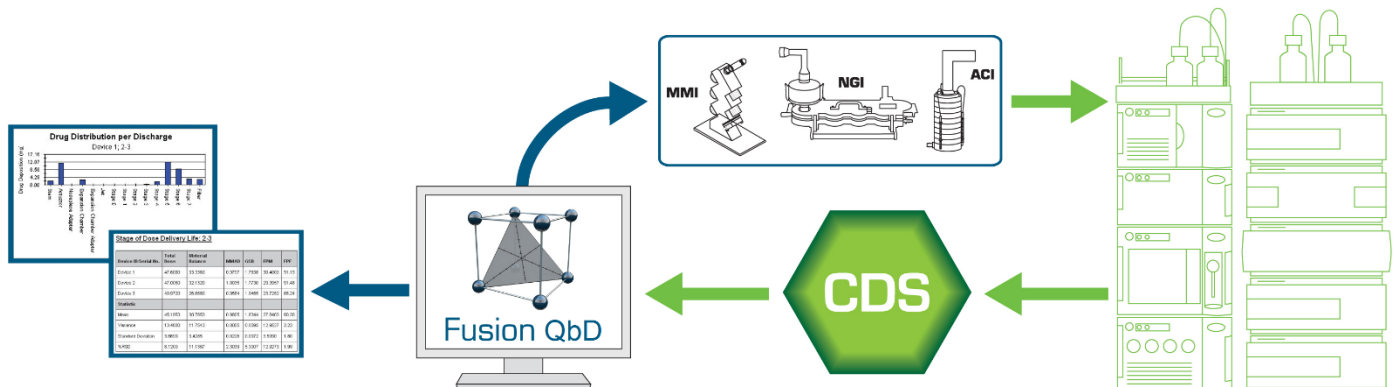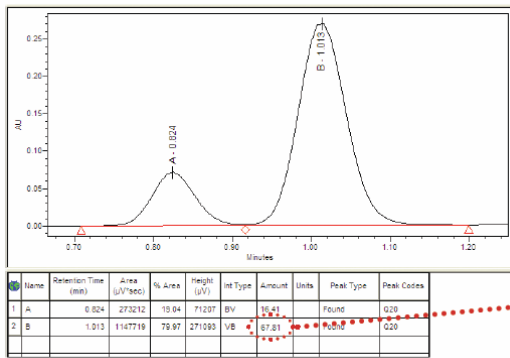
# Automated Workflow – Data Import & Analysis

## At last, totally automated data import with one-click analysis!

### Validated LC Results Import

Chromatogram results are imported directly from the CDS vendors' validated software development kit (SDK). For example, an Anderson analysis with five devices, three stages of life and two API generates 390 individual results. FIT extracts these results with 100% accuracy – no intermediate files, no transcription errors, and no checking!



### Comprehensive Data Analysis

The Data Analysis Wizard guides the user through the calculation options that can be locked to restrict user access. USP Chapter 601, Ph. Eur. 2.9.18, and FDA requirements are supported. One-click data analysis produces reports in USP, Ph.Eur., and/or general formats.
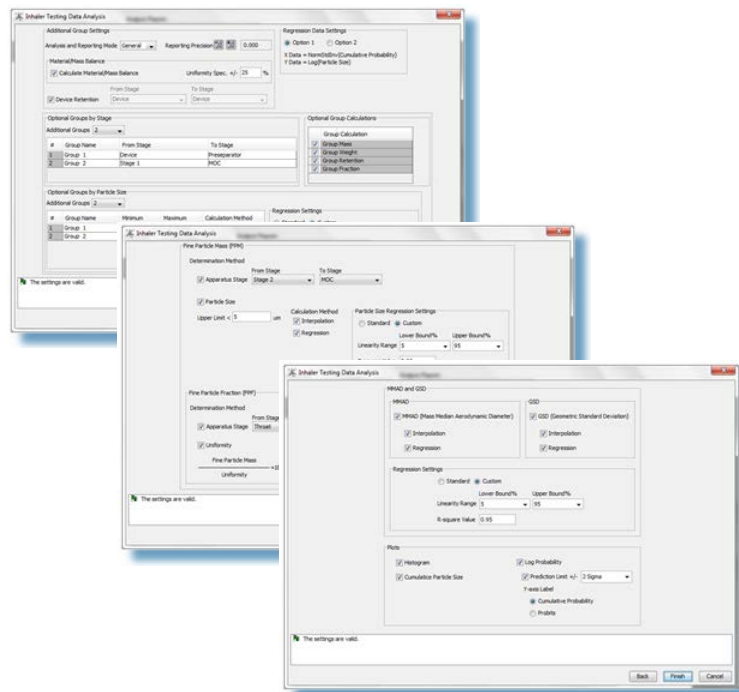


*Dose Uniformity – Complete Calculation Suite*

*Cascade Impactor – Calculations Include:*
- *Material Balance*
- *Mass Balance*
  - *by Delivered Dose (Content) Uniformity*
  - *by Label Claim/Target Delivered Dose*
  - *by Content Assay*
- *Total Dose*
- *Emitted Dose*
- *Fine Particle Dose*
  - *by Apparatus Stage*
  - *by Particle Size*
- *Interpolation*
- *Regression*
- *Fine Particle Fraction*
  - *by Emitted Dose*
  - *by Label Claim/Target Delivered Dose/Content Assay*
- *Additional Groupings*
  - *by Stage*
  - *by Particle Size*
- *Mass Median Aerodynamic Diameter (MMAD)*
- *Geometric Standard Deviation (GSD)*
- *Shot Weight, Stage and Group Statistics*
  - *Mean*
  - *Variance*
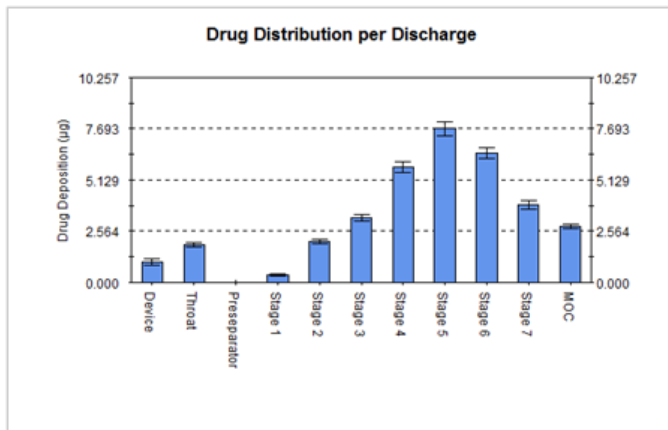  - *Standard Deviation*
  - *% RSD*

# FIT Automated Workflow – Reporting

## Collate individual analysis reports to produce final reports

### Final Report

FIT automatically generates reports for all user inputs, operations, and results throughout the testing process. For final reports, users can select and order the content of individual reports as a Microsoft Word, Microsoft Excel, Adobe PDF, or HTML document.

**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 | 1.984 | 0.000 | 0.349 | 2.154 | 3.251 | 5.617 | 7.390 | 6.157 | 3.636 | 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 | 1.888 | 0.000 | 0.383 | 2.058 | 3.228 | 5.772 | 7.693 | 6.465 | 3.888 | 2.801 |
| Variance | 0.033 | 0.016 | 0.000 | 0.002 | 0.009 | 0.026 | 0.063 | 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 | — | 12.59 | 4.72 | 5.03 | 4.96 | 4.52 | 4.13 | 5.82 | 3.71 |



Drug Distribution per Discharge

**Dose Content Uniformity through Container Life - API**

| Device | Device 1 | | | Device 2 | | | Device 3 | | |
|---|---|---|---|---|---|---|---|---|---|
| Stage of Life | Dose (μg) | % Target | Result | Dose (μg) | % Target | Result | Dose (μg) | % Target | Result |
| Start | 35.44545 | 101.27271 | Pass | 35.03182 | 100.09091 | Pass | 32.16818 | 91.90909 | Pass |
| Start | 32.48636 | 92.81817 | Pass | 32.83636 | 93.81817 | Pass | 33.18636 | 94.81817 | Pass |
| Start | 32.39091 | 92.54546 | Pass | 34.30000 | 98.00000 | Pass | 32.93182 | 94.09091 | Pass |
| Start-Mean | 33.44091 | 95.54545 | Pass | 34.05606 | 97.30303 | Pass | 32.76212 | 93.60606 | Pass |
| Middle | 36.14545 | 103.27271 | Pass | 35.47727 | 101.36363 | Pass | 36.24091 | 103.54546 | Pass |
| Middle | 34.30000 | 98.00000 | Pass | 32.48636 | 92.81817 | Pass | 35.63636 | 101.81817 | Pass |
| Middle | 38.08636 | 108.81817 | Pass | 35.85909 | 102.45454 | Pass | 40.18636 | 114.81817 | Pass |
| Middle | 37.51364 | 107.18183 | Pass | 37.70455 | 107.72729 | Pass | 35.54091 | 101.54546 | Pass |
| Middle-Mean | 36.51136 | 104.31818 | Pass | 35.38182 | 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 | 39.00909 | 111.45454 | Pass | 36.24091 | 103.54546 | Pass | 38.72273 | 110.63637 | Pass |
| End | 37.51364 | 107.18183 | Pass | 37.70455 | 107.72729 | Pass | 35.54091 | 101.54546 | Pass |
| End-Mean | 36.85606 | 105.30303 | Pass | 37.08940 | 105.96970 | Pass | 36.07121 | 103.06061 | Pass |
| No. of Test Results > ≥ 20.0% of Target | 0 | Pass | | 0 | Pass | | 0 | Pass | |
| No. of Test Results > ≥ 25.0% of Target | 0 | Pass | | 0 | Pass | | 0 | Pass | |
| Mean Result > ≥ 15.0% of Target | | Pass | | | Pass | | | Pass | |



Log Probability Plot
Device 1; 2-3
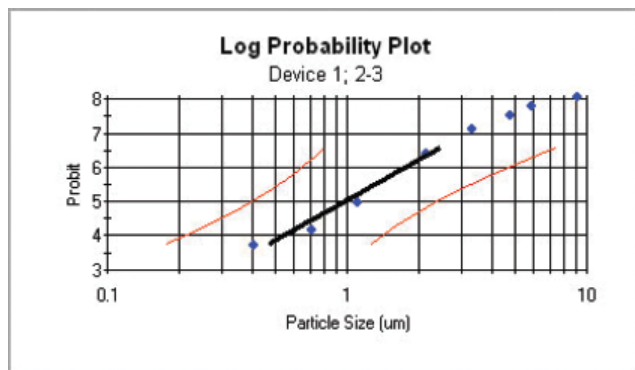
**Mass Data (μg)**

| Device - Stage of Life | Total Dose | Emitted Mass | FPM(1) | FPF(4) |
|---|---|---|---|---|
| Device 1 - Start | 64.296 | 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 | 39.588 | 30.671 | 81.371 |
| Variance | 351.025 | 250.267 | 33.655 | 215.624 |
| Std. Dev. | 18.736 | 15.820 | 5.801 | 14.684 |
| %RSD | 43.91 | 39.96 | 18.91 | 18.05 |
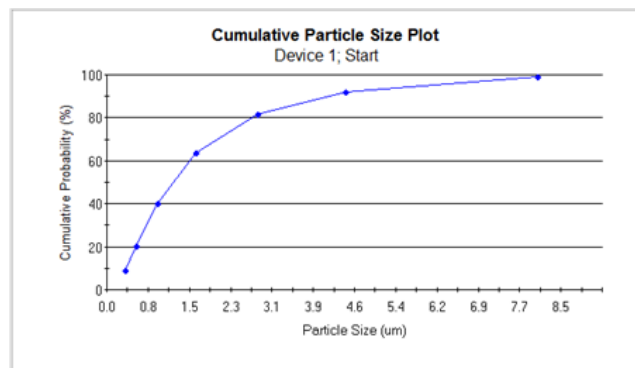
**Size Distribution (μm)**

| Device - Stage of Life | MMAD(2) | GSD(4) | Log(Particle Size) - NICP Intercept | Log(Particle Size) - NICP Slope | R^2 |
|---|---|---|---|---|---|
| Device 1 - Start | 2.506 | 3.476 | 0.399 | 0.541 | 0.964 |
| Device 2 - Start | 0.824 | 2.342 | -0.064 | 0.370 | 0.991 |
| Device 3 - Start | 0.623 | — | -0.205 | 0.555 | 0.893 |
| Mean | 1.318 | 2.909 | 0.037 | 0.489 | 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 |

¹NICP - Normal Inverse Cumulative Probability.



Cumulative Particle Size Plot
Device 1; Start

# S-Matrix Software Products and Support

S-Matrix Corporation develops advanced Design of Experiment based-software that automates R&D experimental work according to Quality-by-Design principles and methodologies. S-Matrix's Fusion QbD platform automates and redefines experimentation in Analytical R&D, Chemical and Process R&D, Formulation, and Product R&D.

## Fusion QbD Software System Product Suite

■ **Fusion LC Method Development**
Fully automated QbD experimenting on your LC system, integrated DOE, automated robustness simulation & chromatography data modeling. Chemistry screening without the need for peak tracking.

■ **Fusion Analytical Method Validation**
Meet regulatory guidelines with a best-practices approach toward LC method validation with comprehensive reporting. Also supports formal validation of Non-LC methods (e.g. GC, CE, Q-NMR).

■ **Fusion Inhaler Testing**
Create sampling plans, export and import data from your CDS via validated data exchange, calculate particle size distribution results, and generate reports according to USP 601, Ph.Eur. 2.9.18, and ISO 27427.

■ **Fusion Product Development**
The perfect QbD software for formulation & product development – automated experimental design selection, sophisticated analysis tools, including automated modeling and simulation, comprehensive reporting, with a full 21 CFR 11 compliance toolset.

## Sales and Support

Sales: Tel: 800-336-8428 (Outside the USA: 707-441-0406). Email: Sales@smatrix.com
Customer Support: Tel: 707-441-0407. Fax: 707-441-0410. Email: Support@smatrix.com

## On-site and Web Training

S-Matrix offers on-site training programs for installed systems. Training includes experiment strategies, experimental design (DOE), data analysis, graphical visualization and ranking of effects, numerical and graphical optimization, and QbD Reporting.

S-Matrix also offers interactive web training which covers software features and operation, along with general principles of DOE and QbD. Web training programs can be tailored to suit your individual focus and information requirements.

To arrange an on-site or web-based training program, call 707-441-0406.

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