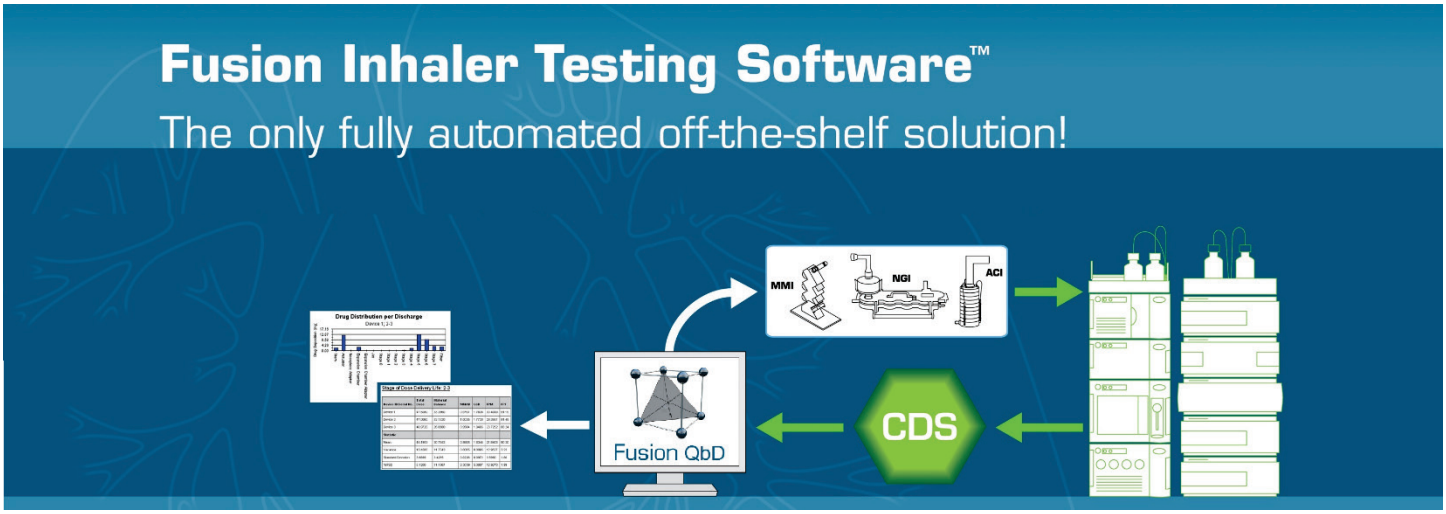
S-Matrix®

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, FSA, FSI, MM, MSLI, and NGI!**
- **Automates LC work on multiple instruments and CDS systems!**
- **Full Part 11 support for regulatory compliance!**
- **Built-in workflow management system with secure templating!**
- **Reduces or eliminates labor intensive manual data entry 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 oral and nasally delivered drug products.

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.

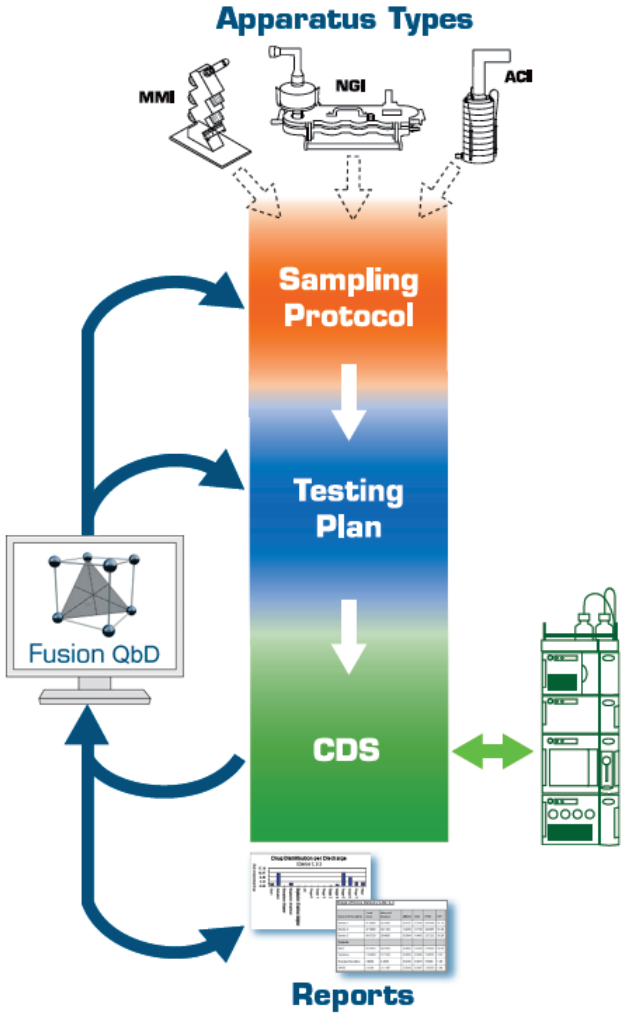
Dramatically Increases Productivity

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

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.



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 plan (testing protocol) to final reports

Universal Applicability

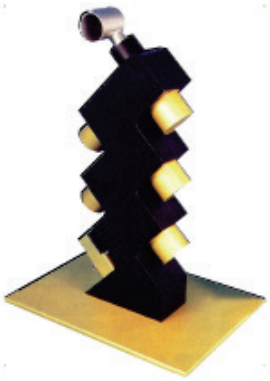
- Full compatibility with all USP Apparatuses (ACI. FSA, FSI, MM, MSLI, NGI), Ph. Eur. Apparatuses C, D, and E
- Automatically creates testing plans for all apparatuses
- Seamlessly interfaces with LC instruments controlled by the Agilent ChemStation/OpenLab 1.x, Thermo Scientific Chromeleon 7.2.x and later, 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

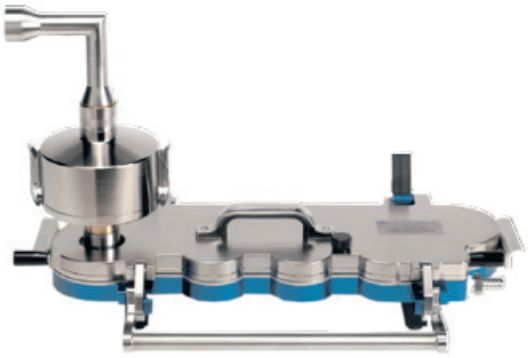


Automatically Generated Reports

- 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 all USP Apparatuses (ACI. FSA, FSI, MM, MSLI, NGI), Ph. Eur. Apparatuses C, D, and E

FIT Intelligent Dataflow with Workflow Full Templating

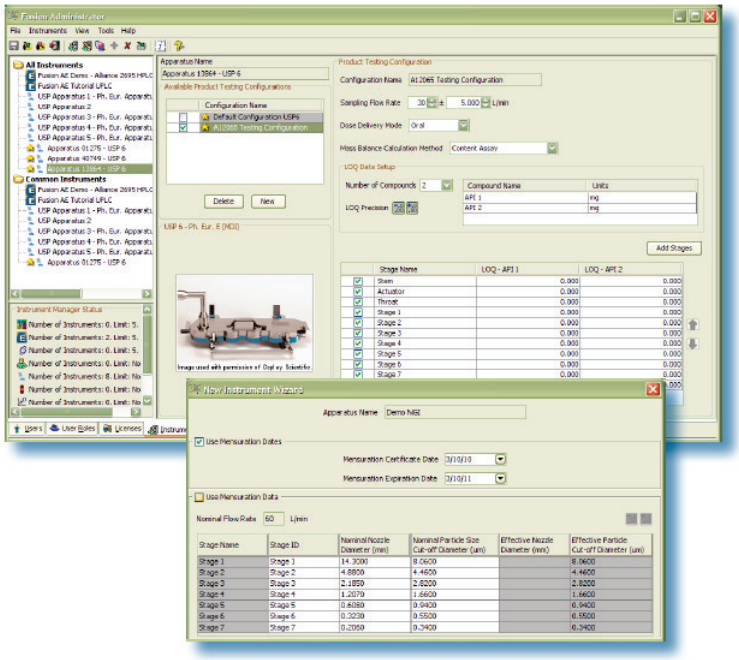
Minimizes manual transcription errors

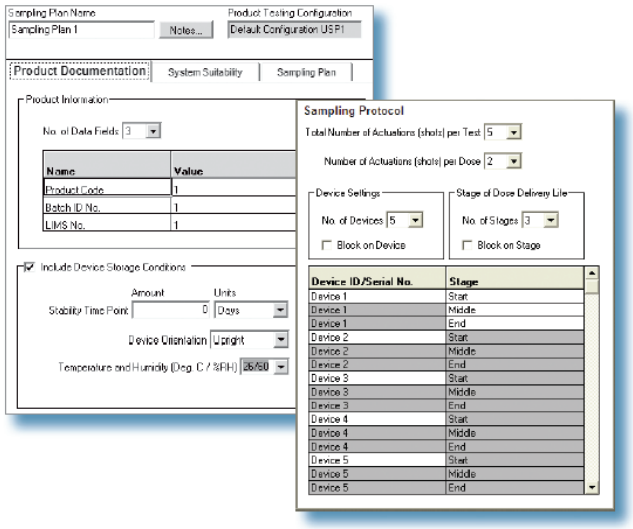
Maintains Apparatus and Product-specific Testing Protocol Data

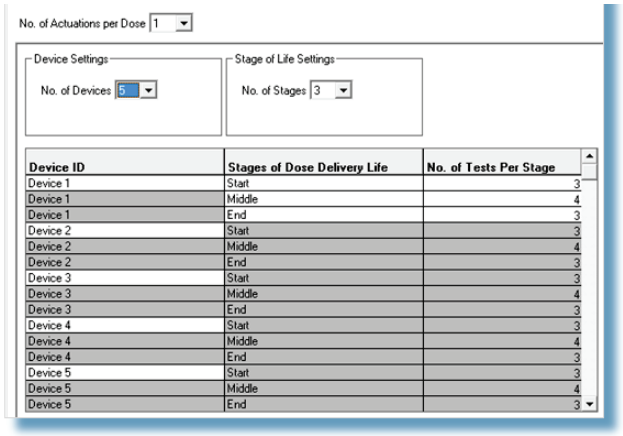
Individual apparatuses can be predefined. Apparatus and stage IDs can be stored and included in final reports for mapping results data to specific apparatus configurations providing complete transparency of analysis.

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 Plans

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

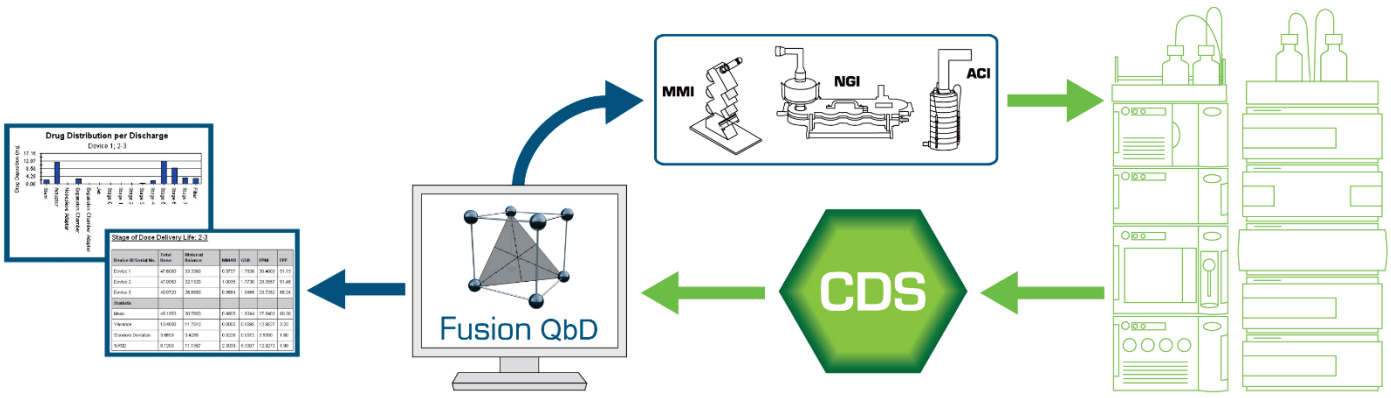
Effortlessly Builds Ready-to-Run Sequences

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 – ChemStation Edition, Thermo Scientific Chromeleon 7.2.x and later, and Waters® Empower™.

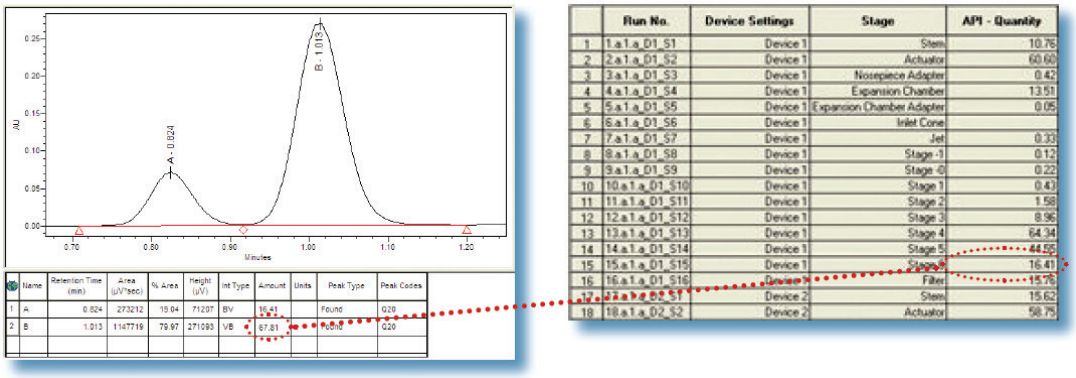


Automated Workflow – Data Import & Analysis

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!

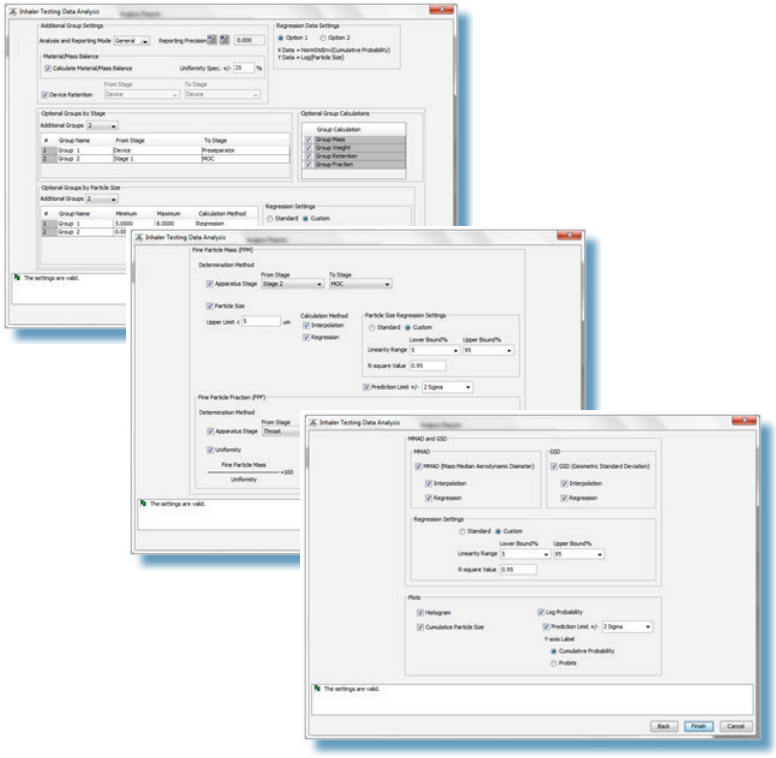


Name	Retention Time (min)	Area (uV*sec)	% Area	Height (uV)	Int Type	Amount	Units	Peak Type	Peak Codes
1 A	0.824	273212	15.04	71207	BV	16.41		Found	Q20
2 B	1.013	1147719	79.97	271093	VB	67.81		Found	Q20

	Run No.	Device Settings	Stage	API - Quantity
1	1.a1.a_D1_S1	Device 1	Stem	10.76
2	2.a1.a_D1_S2	Device 1	Actuator	60.60
3	3.a1.a_D1_S3	Device 1	Nosepiece Adapter	0.42
4	4.a1.a_D1_S4	Device 1	Expansion Chamber	13.51
5	5.a1.a_D1_S5	Device 1	Expansion Chamber Adapter	0.05
6	6.a1.a_D1_S6	Device 1	Inlet Cone	
7	7.a1.a_D1_S7	Device 1	Jet	0.33
8	8.a1.a_D1_S8	Device 1	Stage -1	0.12
9	9.a1.a_D1_S9	Device 1	Stage -0	0.22
10	10.a1.a_D1_S10	Device 1	Stage 1	0.43
11	11.a1.a_D1_S11	Device 1	Stage 2	1.58
12	12.a1.a_D1_S12	Device 1	Stage 3	8.96
13	13.a1.a_D1_S13	Device 1	Stage 4	64.34
14	14.a1.a_D1_S14	Device 1	Stage 5	44.55
15	15.a1.a_D1_S15	Device 1	Stage F	16.41
16	16.a1.a_D1_S16	Device 1	Filter	15.76
17	17.a1.a_D2_S1	Device 2	Stem	15.62
18	18.a1.a_D2_S2	Device 2	Actuator	58.75

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*

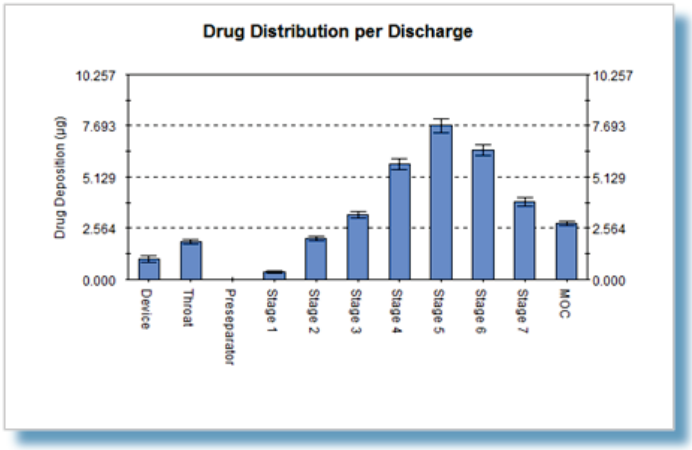
FIT Automated Workflow – Reporting

Final Reports

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.

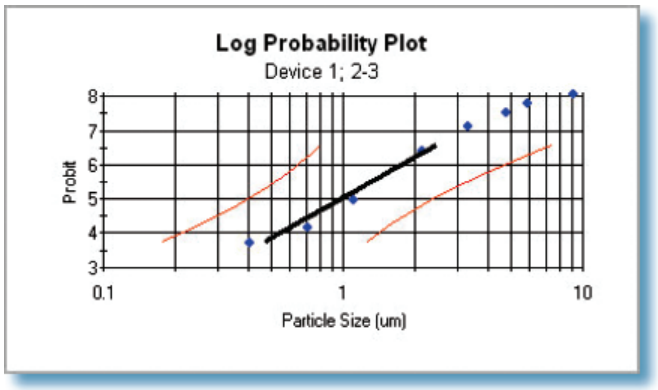
Stage Deposition per Actuation (µg)

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	3.068	5.594	8.072	6.606	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	0.061	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	4.98	4.52	4.13	5.82	3.71



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	38.54091	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	38.54091	101.54546	Pass
End-Mean	36.85606	105.30303	Pass	37.09840	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		



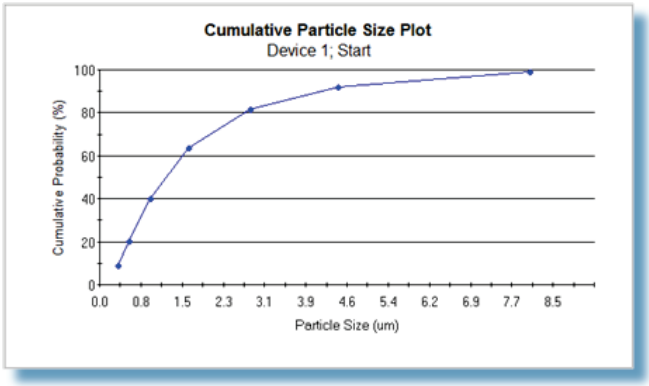
Mass Data (µg)

Device - Stage of Life	Total Dose	Emitted Mass	FPM(1)	FPF(4)
Device 1 - Start	64.290	57.801	37.234	64.417
Device 2 - Start	31.700	31.700	28.564	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	260.267	33.655	215.624
Std. Dev.	18.736	16.820	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	0.624	2.342	-0.084	0.370	0.991
Device 3 - Start	0.623	---	-0.206	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

*NICP - Normal Inverse Cumulative Probability.



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 Process Development – the Perfect R&D Companion Module to FIT**
  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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