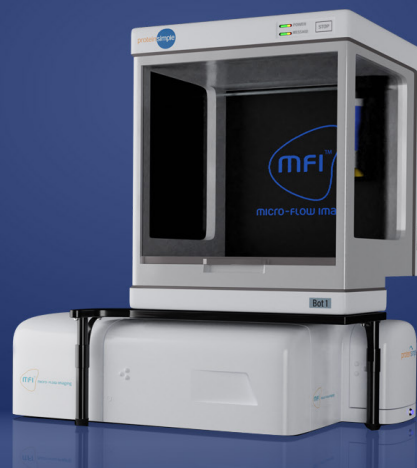# STAYING 21 CFR PART 11-COMPLIANT WITH MICRO-FLOW IMAGING VIEW SYSTEM SOFTWARE AND MFI IMAGE ANALYSIS

INTRODUCTION

Micro-Flow Imaging™ (MFI) lets you analyze particles in solutions that contain your therapeutic product by using image-based detection, making MFI ideal for biotherapeutic characterization. That also means that when you're using MFI in a GMP environment, you need to be compliant with the FDA Title 21 Code of Federal Regulations (CFR) Part 11 to ensure the authenticity and integrity of electronic data. Procedural controls like training notifications and SOPs need to be in place along with technical controls in the software to maintain data security. Micro-Flow Imaging View System Software (MVSS), the software package MFI uses to acquire, manage and analyze data, has all the tools required for 21 CFR compliance so there'll be no concern about analyzing biotherapeutics by MFI in a regulated environment.

MICRO-FLOW IMAGING VIEW SYSTEM SUITE DATA WORKFLOW

MFI gives you image-based subvisible particle analysis for your pharmaceutical products. This means collecting the size, count and morphological information that helps you make important decisions about the development and manufacture of your product.

The MFI software suite gives you the tools you need to analyze individual samples or cohorts of data to make the right decisions during your research. In this application note, we'll focus on the 21 CFR Part 11 tools integrated into MFI for method and batch execution, data processing and audit trails. For more details on exactly how MVSS supports 21 CFR Part 11 compliance, check out the "Micro-Flow Imaging View System Software 21 CFR Compliance Checklist".

GETTING STARTED

To use the MVSS CFR features, you'll first need a user account. User accounts are set up in MVSS by a site administrator designated by your company/ institute who manages user accounts and assigns user privileges (FIGURE 1). Administrator accounts are distinct from the Windows local administrators group. The MVSS user group hierarchy is initially populated with three groups: Administrator, User and Viewer. These groups are umbrellas under which individual users can be easily assigned a predetermined set of privileges within the software.

ADDING USERS

Users can be assigned to a group by an administrator. New users will be provided with a unique Username and Password and assigned to a specific group and/or be given specific user permissions (FIGURE 2). Controls in MVSS ensure the uniqueness of each username, and password expiration can be defined in accordance with your IT policy. Permissions not assigned to a user will be disabled.

USER PERMISSIONS

MVSS comes preconfigured with three different user levels: Administrator, User and Viewer. These groups contain the permissions relevant for that level of operator responsibility and can be reconfigured as needed by the system administrator (TABLE 1). The preset permissions provide users with access to the different features of MVSS and MFI Image Analysis software.

FIGURE 1. MVSS user group settings where administrators can manage the features of both MVSS and MFI Image Analysis to which different user groups have access.

FIGURE 2. The Administrator can add users to the hierarchy and designate them to a specific group using the Add User Account function in MVSS.

RUNNING METHODS AND BATCHES IN MVSS

LOGGING IN

MVSS will require you to log in with your username and password every time the software is launched (**FIGURE 3**). You'll get three tries before the system locks you out, but the site Administrator can unlock your account if this happens. Once you've logged in, MVSS will display your unique user information in the status bar at the top of the main window.

METHOD CONTROLS

Methods created in MVSS are saved as controlled files. Once a method has been executed for the first time, the file gains its controlled designation. Methods can be run multiple times, but they may not be edited directly. Instead, to edit a Method file, a user must save the method with a unique name. Once the file has been given a unique name, the parameters of the method cannot be edited. This ensures that the method referenced in a compliant report is always valid.

BATCH CONTROLS

Batches created in MVSS are also saved as controlled files. Similar to Method files, once a batch has been executed for the first time, it gains its controlled status. To edit the parameters of a batch, the file must be resaved with a unique name. This preserves the original parameters of the batch.

Previously run controlled batches can be used again but can't be overwritten. If you want to make changes to the batch, save it under a different batch file name after you've made changes.

DATA PROCESSING

Once the run is complete, no raw data processing is needed—your data is ready for analysis. All run files generated are stored as controlled files in the system repository, and any steps taken when analyzing the data are logged in the Audit Trail.

PRIVILEGE	ADMINISTRATOR	USER	VIEWER
Perform Analysis	X	X	
Open Report	X	X	X
Export Report	X		
View Image	X	X	
View Audit Trail	X	X	X
Import/Export Delete Audit Trail	X		
Analyze Multiple Samples	X	X	X
Edit Multi-Sample Filters	X		
Import/Export Methods	X		
Import/Export Batches	X		
Create Method	X		
Create Group	X		
Create Account	X		
Create Batch	X		
Import/Export Projects	X		
View/Export Logs	X		
Delete Data (Projects, Logs)	X		
Hardware Setting	X		
Flow Cell Focus	X		
Flow Cell Integrity Check	X		

TABLE 1. Permissions for the Administrator, User and Viewer groups as defined the default settings in MVSS.
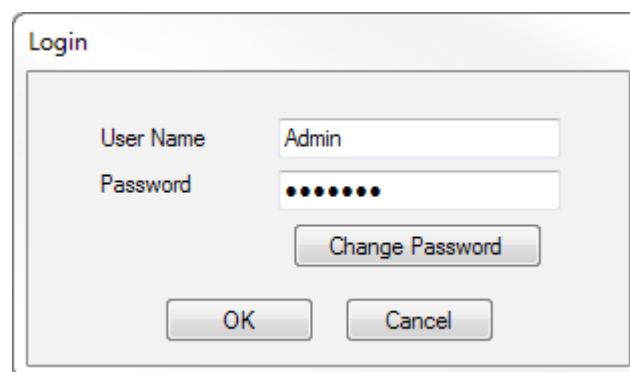

FIGURE 3. MVSS log-in screen.

THE REPOSITORY

All data acquired by MFI is stored in the repository. The repository functions as a secure location for data storage, ensuring that files cannot be modified or deleted without authorization.

EXPORTING DATA

To move data out of the repository, there are two export functions available:

COMPLIANT EXPORT

Exporting compliant data creates proprietary (.data) files, which are compatible with the MFI repository. These files contain barriers to being edited and record any modification(s) that occur.

NON-COMPLIANT EXPORT

Copies of data can also be exported in non-compliant form. These exports can then be used to analyze data in MVAS (the legacy software), or by using MFI Image Analysis tools on third-party computers. Non-compliant exports are logged in the audit trail and do not modify the original data file in any way.

AUDIT TRAIL AND REPORTS

MVSS generates an audit trail for inspections and audits. Each audit trail includes these action categories:

- Hardware Setting Changes – Records changes to the system configuration. Examples include changing com ports, pump calibrations and Bot1 calibrations.

- File – Records the creation of, or changes to, files. Examples include generating or exporting methods and batches.

- Filters – Creating, modifying, deleting and importing/exporting filters are all captured in the audit trail.

- Software Updates

- Operation Failures

Audit trail logs these actions for all users; it is a secure log that can't be altered or disabled and is date- and time-stamped. Users with the appropriate permission can view an audit trail by going to the View menu in MVSS and selecting **View Audit Trail**. Audit trails can then be printed in PDF format or hard copy (**FIGURE 4**).

MFI IMAGE ANALYSIS SOFTWARE

MFI Image Analysis Software can integrate into the compliance features when it is launched from MVSS 5.0 or higher on the instrument computer. This includes integration into the permission structure of MVSS and the audit trail. MFI Image Analysis can also directly reference the repository when launched from MVSS.

ACCESSING DATA

When MFI Image Analysis is launched from MVSS 5.0 or higher, it can source compliant data from the system repository. This ensures that all data maintain the highest level of integrity throughout the entire analysis workflow.

PERMISSIONS IN MFI IMAGE ANALYSIS

MFI Image Analysis takes advantage of the existing permission structure available to system administrators. These options are permission features and allow access to the different functionalities in MFI Image Analysis:

Analyze Multiple Samples: This permission gives users access to the MFI Image Analysis package in MVSS.

Edit Multi-Sample Filters: The user's right to edit filters in the MFI Image Analysis software will be controlled through the Edit Multi-Sample Filter permission.

Export Report: This permission controls the user's ability to operate the Sample Report function in MFI Image Analysis software as well as the export function in each analysis window.

AUDIT TRAIL ENTRIES FOR MFI IMAGE ANALYSIS

When launched from MVSS, MFI Image Analysis can record events in the system audit trail to maintain compliance throughout the data analysis workflow. The events recorded by MFI Image Analysis in the audit trail include:

- Launching/closing MFI Image Analysis

- Exporting data

- Creating a report

- Importing/creating/editing/deleting a filter

System Model : **MFI5200**
System Serial # : **3009**

#	Date	Time	User Name	First Name	Last Name	Action	Status	Previous Val...	New Value	Description
1	2012/02/29	15h01m10s				Login	-	-	-	-
2	2012/03/09	12h04m10s	Admin	First Name	Last Name	Login	-	-	-	-
3	2012/03/09	12h04m10s	Admin	First Name	Last Name	Login	-	-	-	-
4	2012/03/09	12h04m25s	Admin	First Name	Last Name	The micrometer was not detect...	-	-	-	The micrometer was not detected
5	2012/03/09	12h06m01s	Admin	First Name	Last Name	System Com Port Updated	-	1	5	
6	2012/03/09	12h06m01s	Admin	First Name	Last Name	Pump Prime Speed Updated	-	0.00	6.00	-
7	2012/03/09	12h06m01s	Admin	First Name	Last Name	System Serial Number Updated	-	-	3060	-
8	2012/03/09	12h06m06s	Admin	First Name	Last Name	Close Application	-	-	-	-
9	2012/03/09	12h06m19s	Admin	First Name	Last Name	Login	-	-	-	-
10	2012/03/09	12h26m47s	Admin	First Name	Last Name	Pump Calibration	-	0.00	2.55	Pump Verification Volume(ml)
11	2012/03/09	12h26m47s	Admin	First Name	Last Name	Pump Calibration	-	0.00	4.30	Pump Calibration Volume(ml)
12	2012/03/09	12h26m47s	Admin	First Name	Last Name	Pump Calibration	Passed	-	-	
13	2012/03/09	12h38m19s	Admin	First Name	Last Name	Create Method	-	-	-	Video Run Method
14	2012/03/09	12h39m18s	Admin	First Name	Last Name	Flow Cell Focus	-	-	-	Flow Cell Focus
15	2012/03/09	12h39m54s	Admin	First Name	Last Name	Flow cell Serial# updated	-	-	3010	-
16	2012/03/09	12h48m12s	Admin	First Name	Last Name	Flow Cell Focus	-	0	4974	Flow Cell #3010 Focus Position Updated
17	2012/03/09	12h50m30s	Admin	First Name	Last Name	Close Application	-	-	-	-
18	2012/03/09	12h52m03s	Admin	First Name	Last Name	Login	-	-	-	-
19	2012/03/09	12h55m43s	Admin	First Name	Last Name	Close Application	-	-	-	-
20	2012/03/09	12h56m04s	Admin	First Name	Last Name	Login	-	-	-	-
21	2012/03/09	12h56m22s	Admin	First Name	Last Name	Close Application	-	-	-	-
22	2012/03/09	12h56m36s	Admin	First Name	Last Name	Login	-	-	-	-
23	2012/03/09	12h56m41s	Admin	First Name	Last Name	Bot1 Detected	-	-	-	-
24	2012/03/09	12h57m22s	Admin	First Name	Last Name	Bot1 Calibrated	-	-	-	X = 0.0000, Y = 0.0000, Z = 0.0000
25	2012/03/09	12h57m40s	Admin	First Name	Last Name	Bot1 Calibrated	-	-	-	X = 0.0000, Y = 0.0000, Z = 0.0000
26	2012/03/09	12h58m20s	Admin	First Name	Last Name	Close Application	-	-	-	-
27	2012/03/09	12h58m42s	Service Account	First Name	Last Name	Login	-	-	-	-
28	2012/03/09	12h58m42s	Service Account	First Name	Last Name	Login	-	-	-	-
29	2012/03/09	12h58m47s	Service Account	First Name	Last Name	Bot1 Detected	-	-	-	-
30	2012/03/09	12h59m18s	Service Account	First Name	Last Name	Close Application	-	-	-	-
31	2012/03/09	12h59m29s	Admin	First Name	Last Name	Login	-	-	-	-
32	2012/03/09	12h59m34s	Admin	First Name	Last Name	Bot1 Detected	-	-	-	-
33	2012/03/09	12h59m47s	Admin	First Name	Last Name	Bot1 Calibrated	-	-	-	X = 0.0000, Y = 0.0000, Z = 0.0000
34	2012/03/09	13h02m07s	Admin	First Name	Last Name	Bot1 Calibrated	-	-	-	X = -0.5710, Y = 0.2385, Z = 2.4845
35	2012/03/09	13h08m09s	Admin	First Name	Last Name	Begin Batch Execution.	Success	-	-	Video Demo Batch
36	2012/03/09	13h10m11s	Admin	First Name	Last Name	Batch Execution cancelled by t...	-	-	-	-

FIGURE 4. An example of an audit trail generated in MVSS

CONCLUSION

Our MVSS and MFI Image Analysis software gives you many tools to ensure data authenticity and integrity, including (but not limited to) restricted access and secure computer-generated time-stamped audit trails. The software also gives you 21 CFR Part 11-compliant data exports. Full compliance requires procedural controls like SOPs and proper training to be in place, and the 21 CFR Part 11-compliant features of MVSS, along with the high-quality data generated by its robust methods, makes MFI the go-to system for analyzing particles in a regulated environment.
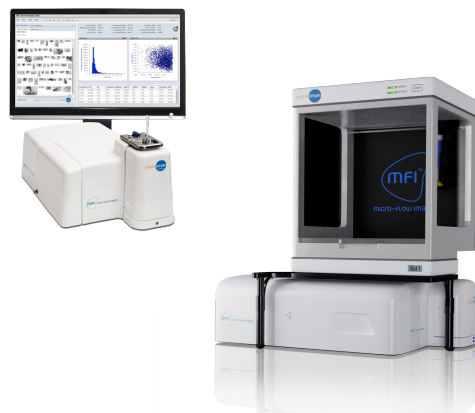
Learn more | proteinsimple.com/mfi_5000.html

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WHERE SCIENCE
INTERSECTS INNOVATION™

At ProteinSimple, we're changing the way scientists analyze proteins. Our innovative product portfolio helps researchers reveal new insight into proteins, advancing their understanding of protein function. We enable cutting-edge research to uncover the role of proteins in disease and provide novel approaches to develop and analyze protein-based therapeutics. We empower you to make your next discovery by eliminating common protein analysis workflow challenges.

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