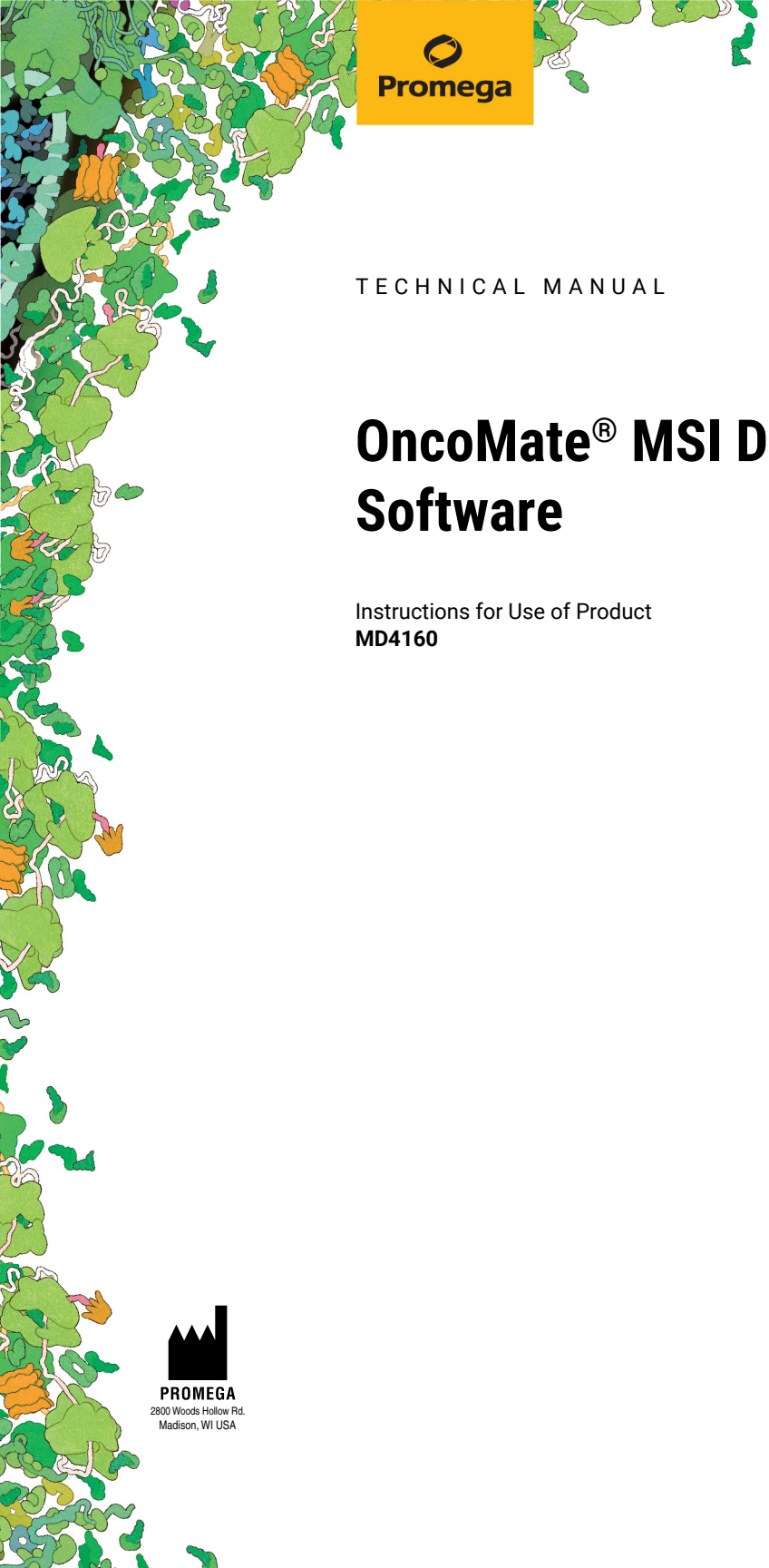


TECHNICAL MANUAL

OncoMate® MSI Dx Analysis Software

Instructions for Use of Product
MD4160

PROMEGA
2800 Woods Hollow Rd.
Madison, WI USA

INSTRUCTIONS FOR USE OF PRODUCT
MD4160
IVD

Rev1
TM680

OncoMate® MSI Dx Analysis Software

All technical literature is available at: www.promega.com/protocols/
Visit the website to verify that you are using the most current version of this Technical Manual.
Email Promega Technical Services if you have questions on use of this system: genetic@promega.com

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Symbols Key

Symbol	Explanation	Symbol	Explanation
	For In Vitro Diagnostic Use		Catalog number
	Manufacturer		Refer to Instructions for Use

1. About This Manual

This reference manual provides information on specific functions and capabilities of the OncoMate® MSI Dx Analysis Software. It is not intended to be a step-by-step guide to using the analysis software. Consult the *OncoMate® MSI Dx Analysis System Technical Manual* #TM543 for step-by-step instructions to analyze and interpret data, and additional information about assay requirements and use.

2. Product Name

OncoMate® MSI Dx Analysis Software
Part No. MD4160

Abbreviations
bp, base pairs
CSV, comma-separated values
DCS, data collection software for the Applied Biosystems® 3500 Dx Genetic Analyzer
FFPE, formalin-fixed, paraffin-embedded
FSA, fragment analysis data file extension
HNPCC, hereditary nonpolyposis colorectal cancer
IT, Information Technology or computer systems professional
MMR, mismatch repair
MSI, microsatellite instability
MSI-H, microsatellite instability high
MSS, microsatellite stable
NA, not applicable
not MSI-H, an MSS result generated by the OncoMate® MSI Dx Analysis Software
PC, personal computer
PCR, polymerase chain reaction
PDF, portable document format
QC, quality control
RFU, relative fluorescence unit
UDF1, user-defined field 1

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3. Product Components

PRODUCT	SIZE	CAT.#
OncoMate® MSI Dx Analysis Software	**1 each**	**MD4160**

The OncoMate® MSI Dx Analysis Software is provided with a product license on a USB drive.

4. Intended Use

The OncoMate® MSI Dx Analysis System is a qualitative multiplex polymerase chain reaction (PCR) test intended to detect the deletion of mononucleotides in five microsatellite loci (BAT-25, BAT-26, NR-21, NR-24 and MONO-27) for the identification of microsatellite instability (MSI) using DNA obtained from formalin-fixed, paraffin-embedded (FFPE) solid tumor specimens, and DNA isolated from matched normal FFPE specimen or whole blood. The OncoMate® MSI Dx Analysis System is for use with the Applied Biosystems® 3500 Dx Genetic Analyzer and OncoMate® MSI Dx Analysis Software.

The OncoMate® MSI Dx Analysis System is indicated for use as a companion diagnostic test to identify patients who may benefit from treatment with the targeted therapies listed in Table 1 in accordance with the approved therapeutic product labeling.

Table 1. OncoMate® MSI Dx Analysis System Companion Diagnostic Indications.

Indication	Biomarker	Therapy
Endometrial Carcinoma	MSS; defined as not MSI-high [not MSI-H]	KEYTRUDA® (pembrolizumab) in combination with LENVIMA® (lenvatinib)
Solid Tumors	MSI-H	KEYTRUDA® (pembrolizumab)

5. Summary and Explanation

Microsatellites are short, repetitive DNA sequences consisting of repeat units of one to six nucleotides [e.g., (A)n, (CA)n, (AAAAG)n]. Microsatellite sequences are distributed throughout the human genome and are prone to copying errors during DNA replication. Normally, copying errors are repaired by the cellular DNA mismatch-repair (MMR) system. Microsatellite instability (MSI) is observed when MMR function is deficient and DNA replication errors are therefore not repaired (1–6). Among microsatellites, mononucleotide repeats are the most likely to show instability, resulting in microsatellite alleles that are typically shorter in MMR-deficient tissue versus matched normal samples. Microsatellite instability may result from several underlying mechanisms, including somatic and germline mutation of MMR genes and alterations to MMR gene promoter regions (6).

The OncoMate® MSI Dx Analysis System is used to determine tumor MSI status with the OncoMate® MSI Dx Analysis Software, which provides an automated MSI analysis from imported raw data files. During analysis, five mononucleotide-repeat microsatellite markers are evaluated to assess MSI status (BAT 25, BAT 26, NR 21, NR-24 and MONO-27) and two pentanucleotide-repeat microsatellite markers are evaluated for quality control (QC) purposes (Penta C and Penta D). Stability is assessed at each of the five mononucleotide-repeat microsatellite markers by comparing allelic profiles from a normal (i.e., noncancerous) and a tumor sample collected from the same patient. MSI is indicated by a reduction in the length of microsatellites within the tumor sample. The stability results for the mononucleotide-repeat marker panel are then collectively interpreted to determine the tumor MSI status. If two or more of the five mononucleotide-repeat markers are unstable, the tumor is classified as MSI-H; if four or more mononucleotide-repeat markers are stable, the tumor is classified as microsatellite stable (MSS or not MSI-H). Because samples with valid results that do not meet the test criteria for MSI-H are considered MSS (one or no unstable markers), the OncoMate® MSI Dx Analysis System MSS test result is a "not MSI-H" result. The pentanucleotide-repeat markers are analyzed to confirm shared identity between the normal and tumor DNA samples. Comparison to a normal sample mitigates incorrect interpretation of instability in individuals exhibiting locus heterozygosity and polymorphisms at mononucleotide-repeat markers and is essential for detecting instability resulting from small deletions.



Refer to the *OncoMate® MSI Dx Analysis System Technical Manual* #TM543 for more information.

6. Quality Controls Summary

The OncoMate® MSI Dx Analysis Software evaluates the quality of the capillary electrophoresis data and includes a variety of additional checks to ensure that the data are sufficient for making a valid MSI determination (see Section 12.1, Sample Batch Definition and Requirements, and Section 15.1, Data Quality Requirements). Positive and negative amplification controls must be analyzed in the same plate with corresponding patient samples during the capillary electrophoresis separation run, and these controls must be identified as "Positive Control" and "Negative Control" in the Applied Biosystems® 3500 Dx Genetic Analyzer data collection software (DCS). If amplification controls are not processed with patient samples, the data import will fail and sample analysis will not be performed. Patient samples must be identified in the Applied Biosystems® 3500 Dx Genetic Analyzer DCS as "Samples" and entered into the DCS as matched normal and tumor pairs following a prescribed sample-naming format. See Section 16 for acceptable sample naming conventions and the *OncoMate® MSI Dx Analysis System Technical Manual* #TM543 for instructions on sample labeling during capillary electrophoresis. All analyzed samples and controls must contain the Size Standard 500 (added prior to capillary electrophoresis), and the size standard peaks analyzed by the software (60, 65, 80, 100, 120, 140, 160, 180, 200, 225, 250, 275 and 300 base pairs) must be present and have peak heights between 175 and 10,000 relative fluorescence units (RFU).

7. Principles of the Procedure

The workflow within the OncoMate® MSI Dx Analysis Software (Figure 1) entails importing samples that define a sample batch, reviewing and approving the MSI results for each sample in the batch and exporting files (PDF and CSV) that report sample and batch results.

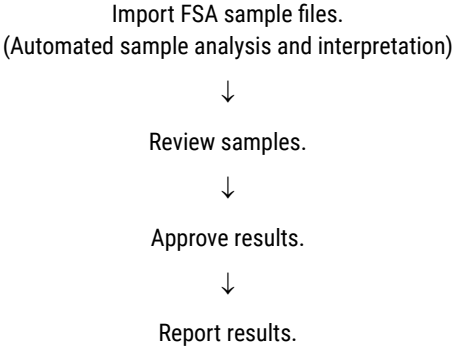


Figure 1. OncoMate® MSI Dx Analysis Software workflow.

To determine tumor MSI status, the OncoMate® MSI Dx Analysis Software imports and analyzes microsatellite fragment data (FSA files) generated by the Applied Biosystems® 3500 Dx Genetic Analyzer during the separation and analysis of OncoMate® MSI Dx Analysis System amplification products.

During data analysis, DNA fragments amplified from seven microsatellite regions (five mononucleotide-repeat and two pentanucleotide-repeat loci) are sized with reference to the Size Standard 500 fragments using the Local Southern method (7). Following fragment sizing, the software analyzes the required positive and negative amplification controls to verify expected PCR and capillary electrophoresis performance and applies additional QC checks to evaluate patient data quality (see Table 17 for a description of all QC tests performed by the software).

The OncoMate® MSI Dx Analysis Software requires data from a paired normal sample (FFPE tissue or blood) to determine tumor MSI status. To confirm correct sample pairing, the software analyzes pentanucleotide-repeat markers; if all Penta C and Penta D alleles detected in the normal sample are also present in the tumor sample, the sample identity check passes. The software then evaluates mononucleotide-repeat loci for evidence of nucleotide deletions indicative of microsatellite instability. A locus is "Unstable" when a new, smaller allele is detected in the tumor sample. Otherwise, the locus is interpreted as "Stable" when no deletion is detected, "No Call" when peak intensities are too low or divergent to make a confident stability assessment, or "Invalid" when other quality control failures are observed. The OncoMate® MSI Dx Analysis System evaluates data from five microsatellite loci for instability to account for tumor heterogeneity within and among individual patients that may affect method sensitivity at any given locus, and locus-level results are interpreted collectively to assign an overall tumor MSI status. A tumor sample is interpreted as "MSI-H" when two or more loci are unstable. A tumor sample is interpreted as "MSS" when four or more loci are interpreted as stable (1). A sample is assigned a MSI result of "Invalid" when the sample identity check fails, any locus-level Invalid results are observed, or No Call locus results preclude sample interpretation (see Section 15, Assay Quality Controls, for additional information).

PCR amplification of a mononucleotide-repeat locus results in a central allele peak that is flanked on both sides by PCR stutter peaks. For heterozygous loci, two peak distributions are observed for a locus. Microsatellite instability at a locus is detected as changes in the size (bp) and abundance, represented by fluorescent intensity (RFU), of these DNA fragments in the tumor sample relative to the same patient's normal sample. These changes are produced when a new shorter-length allele and corresponding stutter products are present in the tumor sample. Depending on the size of the deletion and the tumor content of the sample, these new DNA fragment peaks may be distinct from or superimposed upon the cluster of peaks amplified from the patient's normal allele (Figure 2). The OncoMate® MSI Dx Analysis Software detects deletions ≥2bp in microsatellites when sample requirements are met (implemented in the software as ≥1.75bp to account for the sizing precision of capillary electrophoresis).

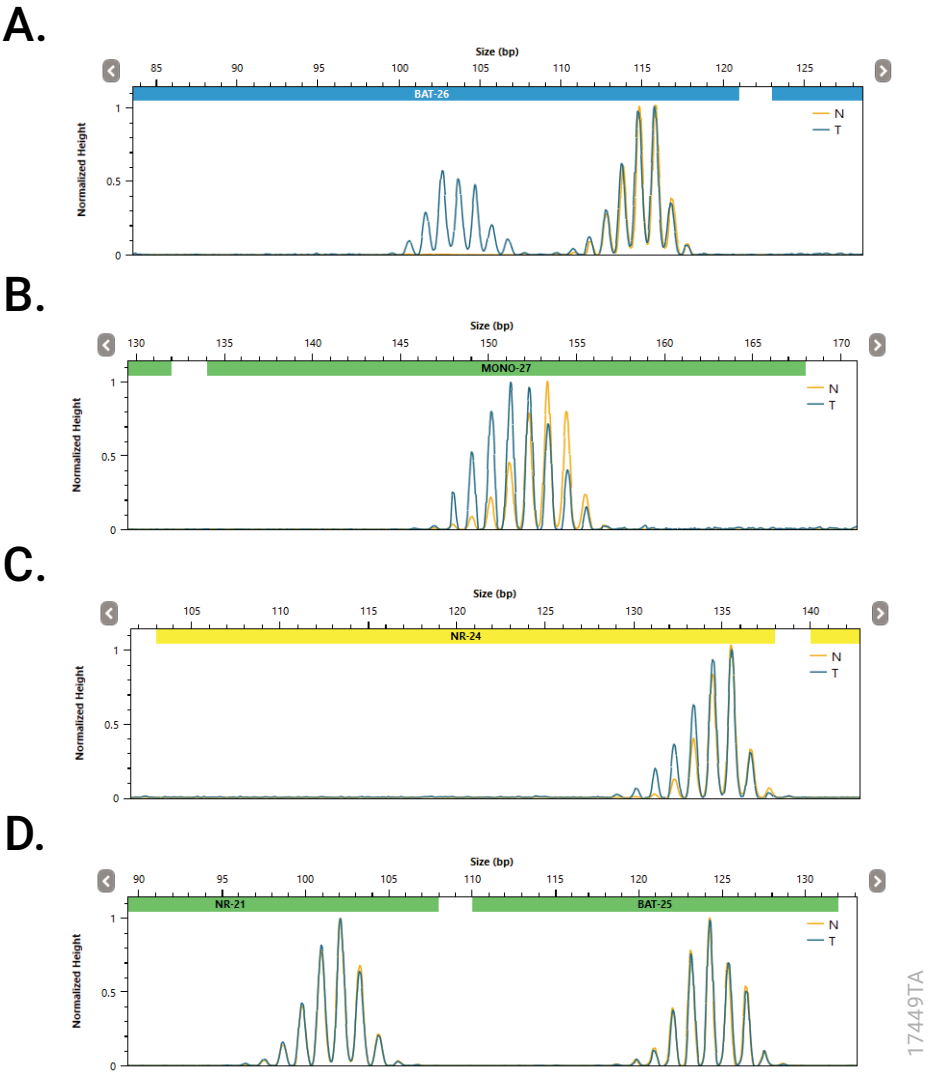


Figure 2. Examples of unstable and stable mononucleotide loci identified by the OncoMate® MSI Dx Analysis Software. Depending on the size of the deletion and the tumor content of the sample, new allele and stutter peaks indicative of instability may be distinct from or overlap the cluster of peaks amplified from the patient's normal allele. **Panel A.** The tumor peaks (blue, -T) are distinct from the normal allele peaks (yellow, -N). **Panels B and C.** The tumor peaks partially overlap the normal allele peaks. **Panel D.** For MSS tumor samples, allelic profiles for the normal and tumor samples fully overlap, showing minimal differences when data are normalized based on peak intensities.

8. Software Installation

8.1 System Requirements and Recommended Security Controls

The system requirements for the OncoMate® MSI Dx Analysis Software are listed in Table 2. Software users must have Modify permissions to the directories used for backing up the application database (Admin user only), archiving or sharing batches (Lab Director users only), and creating reports (Lab Director and Lab Technician users). If multiple users will access the software on a shared PC, all users must have Modify permission to these shared directories according to their software roles.

Note: The "Network Service" user, assigned automatically to the SQL Server, must have Modify permissions to the folder selected for database backups (see Sections 10.6 and 10.7).

Table 2. System Requirements for the OncoMate® MSI Dx Analysis Software.

System Requirement	Recommended
Operating System	Windows® 11 with 64-bit computer
RAM	16GB or higher
Processor	Intel® i5 or newer

The OncoMate® MSI Dx Analysis Software is intended for use as a closed system in clinical laboratories. To maintain cybersecurity and ensure safe and effective software operation, the following environmental security controls are recommended:

Secure Installation Environment

Install and run the software only on the supported Windows® 11 operating system, and keep the operating system up to date with security patches.

Ensure the host computer has an enabled firewall and is running up-to-date commercially available antimalware software. The Oncomate® MSI Dx Analysis Software has been validated for use with the following antivirus and antimalware software:

- Cisco Secure Endpoint
- CrowdStrike Falcon Go
- Windows Defender

Prevent unauthorized connection of removable media to the host computer. If portable media are used to transfer data files, use a drive that is regularly scanned for viruses and malware and restrict use with other computers.

Access Control

Limit access to the host computer and the OncoMate® MSI Dx Analysis Software to authorized personnel using unique user accounts and enforce strong password policies.

Actively maintain user account status' through administration of the host computer and the software.

Network Configuration

Deploy the host computer on a segmented VLAN isolated from general IT traffic.

Configure a stateful firewall to allow only the necessary network ports or connections required for the host computer's function.

Disable unused physical and wireless interfaces (e.g., Bluetooth, Ethernet) at the host or network level.

All data connections should utilize encryption (e.g. HTTPS or other secure protocols) to protect sensitive information in transit.

Monitoring and Incident Response: Stay alert to any unusual behavior from the software. If you suspect a cybersecurity issue, for instance because of unexpected software behavior or repeated login failures, disconnect the host computer from the network if safe to do so, and consult this technical manual for more information on expected software behavior. Contact your local IT support for guidance on next steps and submit the issue to Promega technical support (see Section 17, Troubleshooting). Have an incident response plan so that all users know how to respond to potential security events (e.g. whom to notify in your organization).

Software Updates: Apply software updates as provided by Promega Corporation, which will notify users if a new software version is available and provide instructions for acquiring authorized updates. Only install updates obtained from official channels to ensure authenticity.

Data Backup and Recovery: Follow the instructions in this manual for backing up data. Regularly backup the database and archive batch results in a secure backup location. In the event of an issue, use the provided procedures to restore the software settings from a backup, and only allow authorized personnel to perform restoration operations.

End-of-Support Planning: Stay informed about the software's support lifecycle. Promega Corporation will communicate the expected end-of-support date for the software. After support ends, software updates may no longer be provided. Plan to upgrade or replace the software before it reaches end-of-support so that you continue to receive security updates and maintain a safe operating environment.

Secure Decommissioning: If the software or host computer is to be retired, transferred, or otherwise taken out of service, be sure to securely decommission it. This includes deleting any sensitive data, patient information, or encryption keys stored by the software prior to disposal. If needed, consult your local IT support to ensure that no residual confidential data remains on the system.

8.2 Installing the OncoMate® MSI Dx Analysis Software

The OncoMate® MSI Dx Analysis Software is provided on a USB drive. These instructions describe software installation on a single computer. To install the software on additional computers, repeat the installation process for each computer. Do not install the OncoMate® MSI Dx Analysis Software on a network drive or on the computer that controls the Applied Biosystems® 3500 Dx Genetic Analyzer.

Installing the OncoMate® MSI Dx Analysis Software requires a Windows® user account with continuous administrator privileges. Confirm that the user installing the software has administrative privileges in the Windows® Operating System with read, write and execute permissions.

1. Check the host PC for Windows updates and run any queued updates prior to installing the OncoMate® MSI Dx Analysis Software. Queued but uninstalled Windows® updates can interfere with the software installation.
2. Locate the OncoMate Setup.exe file on the USB drive containing the OncoMate® MSI Dx Analysis Software, and copy it to the computer on which you want to install the software. Double-click on the .exe file to begin software installation.
3. Read the end user license agreement (See Figure 3). Select "I accept the agreement" and **Next** to continue with software installation or **Cancel** to cancel the software installation. If you chose "I do not accept the agreement", select **Cancel** to exit the installer.

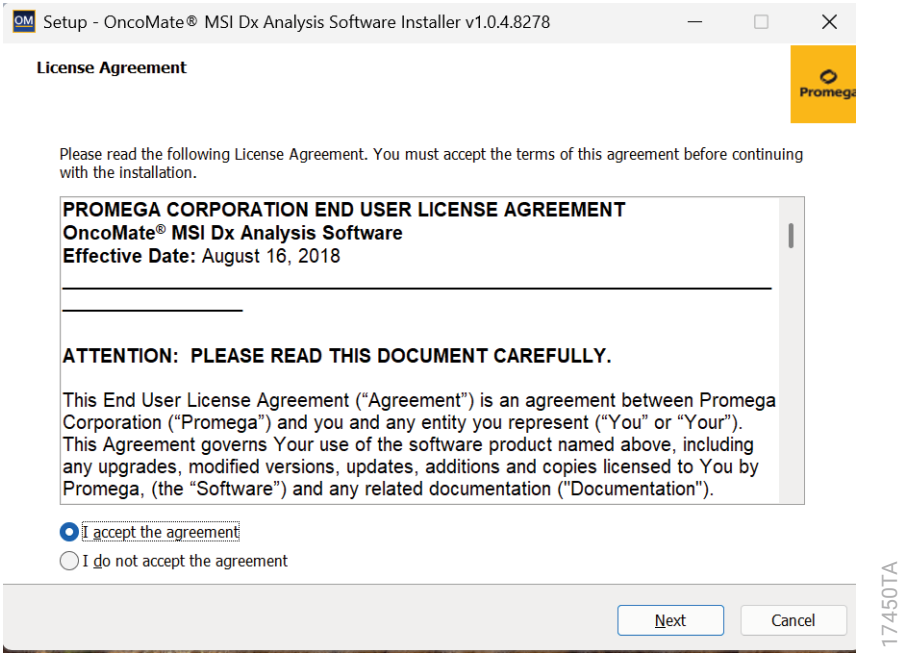


Figure 3. Reading the end-user license agreement.

4. Choose a password for the Administrator account, and type the password into the 'Password' and 'Confirm Password' fields (Figure 4). The password must be at least eight characters long and is case-sensitive.

   Note: The Administrator password is required to customize software configurations and access administrative functions. See Section 10, Software Administration and Configuration, for more information.

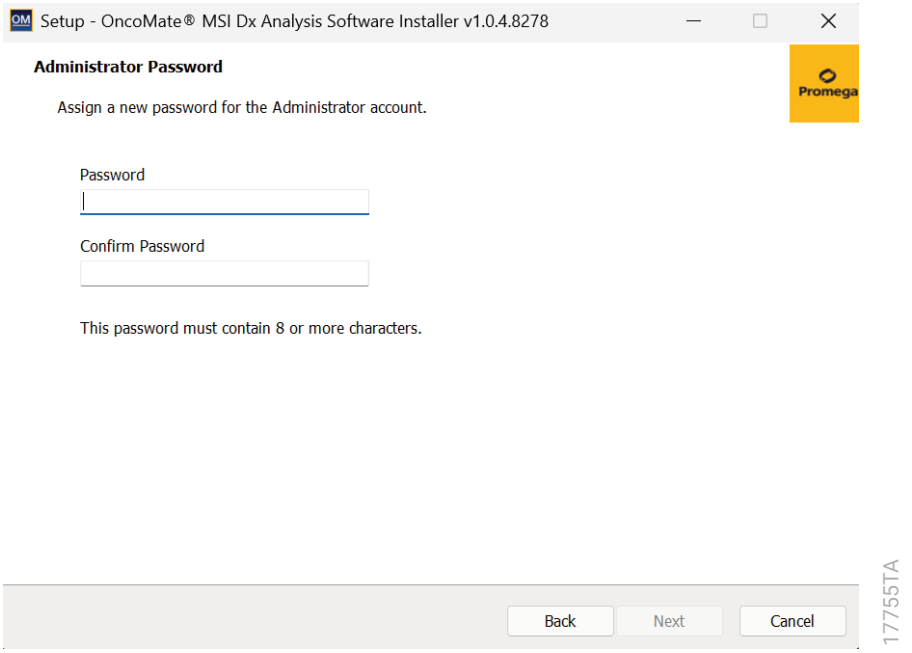


Figure 4. Assigning a password for the Administrator account.

5. Select **Next** to continue with software installation. Select **Back** to return to the previous window or **Cancel** to cancel the software installation.
6. Choose a security key for instance-specific data encryption, and type the key into the 'Security Key' and 'Confirm Security Key' fields. The Security Key must be at least eight characters long and is case-sensitive.
7. Select **Next** to continue with software installation. Select **Back** to return to the previous window or **Cancel** to cancel the software installation.
8. The installer may request that you restart the PC in order to continue. If requested, restart your PC. When you sign back into Windows following the restart, the installer will auto-start, again request agreement with the EULA, require reentry of the Administrator password and security key, and then continue with the installation.

9. A window will appear to notify you that the software is installed (Figure 5). Select **Finish** to proceed to the OncoMate® MSI Dx Analysis Software License window. A shortcut for the software is automatically created on your desktop.

   Note: By default, the "Run OncoMate.exe" check box is checked so that the software opens after the License Key is entered and applied (Steps 10–12). Uncheck the "Run OncoMate.exe" check box if you do not want the software to open after finishing the installation and licensing process.

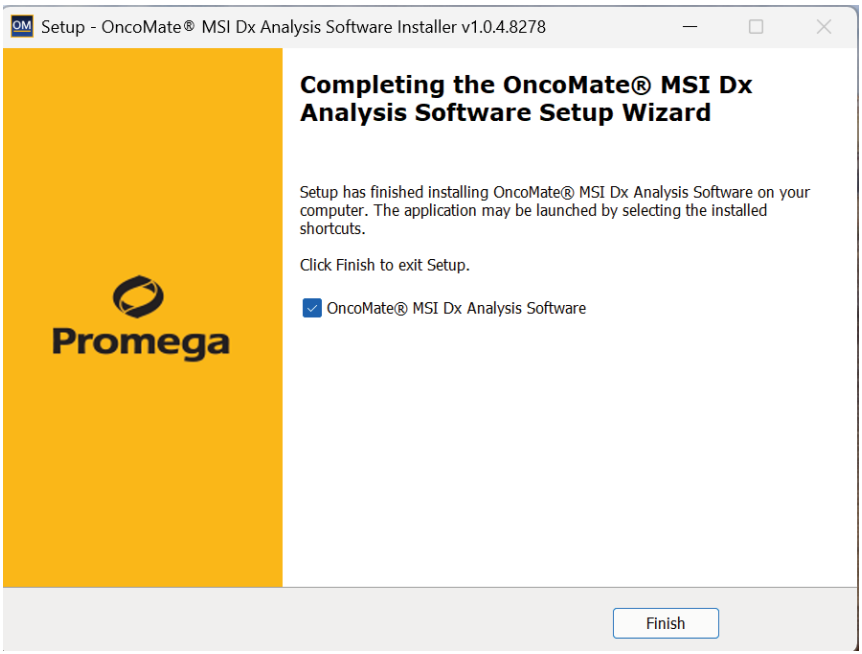


Figure 5. Notification that installation of the OncoMate® MSI Dx Analysis Software is complete.

10. Enter your first name, last name, company name and license key (Figure 6) in the OncoMate® MSI Dx Analysis Software License window. A label containing the license key can be found affixed to the USB drive. The license key field is highlighted in red in Figure 6. Once the license key is entered in the separate fields below 'Serial number', the applicable serial number will automatically appear in the 'Serial number' field.

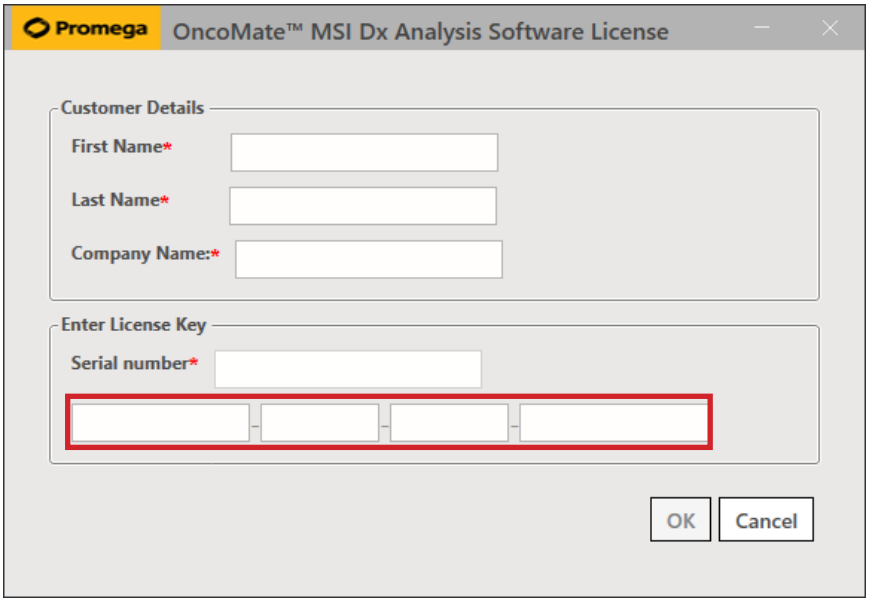


Figure 6. The OncoMate® MSI Dx Analysis Software License window prompts you to enter your details and the software license key.

11. Select **OK** to continue or **Cancel** to close the OncoMate® MSI Dx Analysis Software License window. If **Cancel** is selected, the user will be returned to the license window each time the OncoMate® MSI Dx Analysis Software is launched until a valid license key is entered, all required fields are populated, and **OK** is selected.

12. A message will appear to notify you that the license is now applied to the OncoMate® MSI Dx Analysis Software. Select **OK**.

    If the "Run OncoMate.exe" check box was checked in Step 5, the software will open and prompt you to login. To login, use the password selected in Step 3 and the Admin username.

9. User Roles Within the OncoMate® MSI Dx Analysis Software

Permissions to access functions and customize configurations within the OncoMate® MSI Dx Analysis Software are controlled by user roles assigned within the software. The software is configured with three user roles with different functionalities and permission levels, as described below:

Administrator ("Admin") User Role

1. Create new user accounts.
2. Reset user passwords.
3. Lock and unlock user accounts.
4. Edit existing user accounts.
5. Manage the OncoMate® MSI Dx Analysis Software database, including backing up and restoring the database.
6. Manage user and password preferences.
7. View an audit of user activities within the software and generate audit reports.

Note: There is a single Administrator user account, and this role may not be deleted or edited.

Lab Technician User Role

1. Create new sample batches and add samples to a new batch
2. Analyze samples in a batch.
3. Start, resume and complete sample reviews.
4. Add notes in the Result Notes field for a sample or batch.
5. Export sample and batch summary reports following sample approval by a Lab Director user.
6. Export Technical Support Package files.

Lab Director User Role

A user with the role of lab director can perform the same functions as a lab technician user with the following additional permissions:

1. Approve sample MSI results.
2. Archive batches and restore batches from the archive.
3. Share batches and restore shared batches.

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10. Software Administration and Configuration

10.1 Logging in and Navigating as the Software Administrator

The Administrator (“Admin”) user account enables the software administrator to add and edit user accounts, manage the OncoMate® MSI Dx Analysis Software database, reset user passwords, lock and unlock user accounts, configure the software to fit the needs of the laboratory and users, view and search a list of actions recorded in the audit log, and generate audit reports.

The user name for the Administrator account is “Admin”. The password for the Admin account is set by the user during software installation (Section 8.2). The user name for the Admin user account cannot be changed.

Note: After 10 minutes of inactivity, the OncoMate® MSI Dx Analysis Software session will end, and you will be required to log in again. “Auto logoff time” in the bottom left corner of the screen indicates when the software will log out the current user due to inactivity. The “Auto logoff time” resets after any activity within the software, including moving the cursor.

1. Double-click the icon for the OncoMate® MSI Dx Analysis Software on the computer desktop. 

2. At the Login screen, enter the user name “Admin”, and your password. Select **Login**.

Note: Passwords are case-sensitive.

Once logged in , the Admin user is presented with the Users screen by default, with the task pane in the left margin (Figure 7). The ‘Users’ screen lists the first name, last name, organization, user name, role and status (active or inactive) for all user accounts.

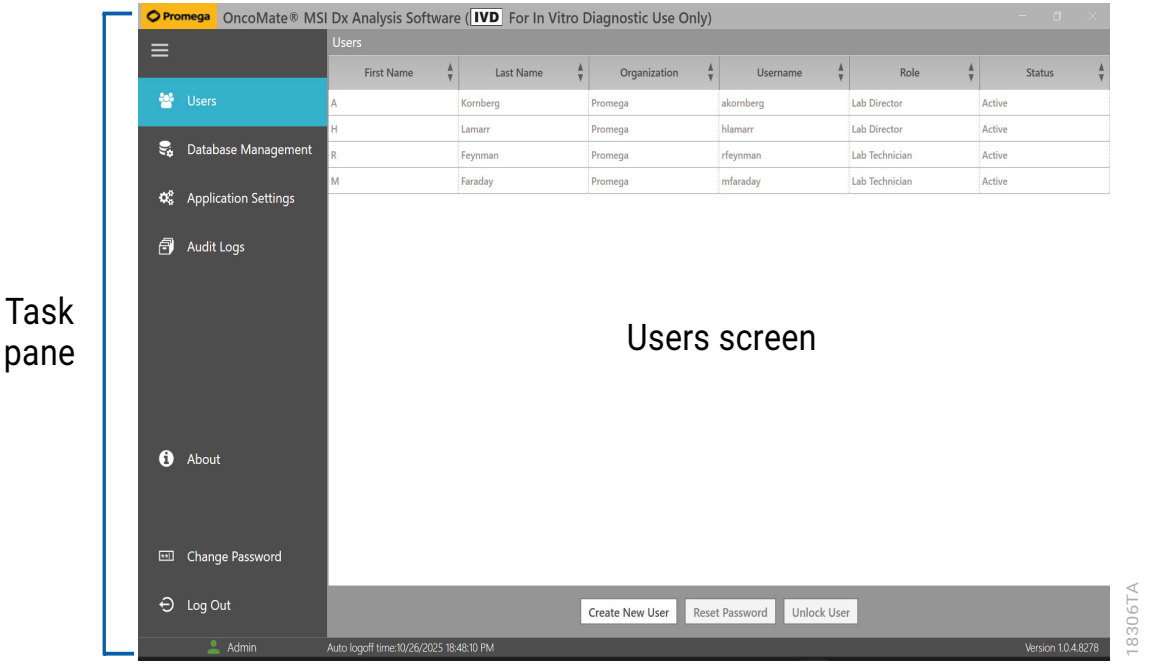
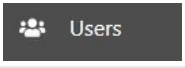
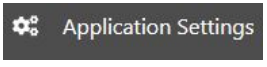
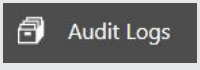
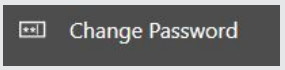
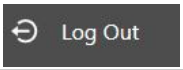


Figure 7. The 'Users' screen is displayed when the Admin user logs in.

The task pane presented to the software administrator includes the buttons described in Table 3.

Table 3. Buttons in the Admin Task Pane.

Button	Description
	**Menu Bar:** Toggle between an expanded task pane or collapsed task pane. When the Menu Bar is used to expand or collapse the task pane, the content of the task pane does not change; only the width of the task pane changes
	**Users:** View the 'Users' screen, which lists the first name, last name, organization, user name, role and status (active or inactive) for all user accounts.
	**Database Management:** Create an archive (i.e., backup) copy of the database, and restore the database to an archived version of the database. See Section 10.2.
	**Application Settings:** Customize software settings, password requirements and preferences, the location where reports and data export files are saved and other attributes. See Section 10.3
	**Audit Logs:** View the audit log, a list of auditable actions and changes tracked by the OncoMate® MSI Dx Analysis Software for data integrity purposes, and generate audit reports. See Sections 10.8 and 10.9.

Button	Description
	**About:** View the 'About' screen for OncoMate® MSI Dx Analysis Software. The 'About' screen provides the software version number, license status and additional information. The End-User License Agreement can be viewed from the 'About' screen by clicking on the PDF icon, which opens the End-User License Agreement as a PDF document in a separate window. The 'About' screen is identical for all user roles (Admin, Lab Technician and Lab Director).
	**Change Password:** Change the password for the active user. For more information, see Section 11.3.
	**Log Out:** Log out of the OncoMate® MSI Dx Analysis Software. For more information, see Section 11.4.

10.2 Creating a New User Account

Before the software can be used to analyze, review or approve sample data, the software administrator must login and create unique user accounts. Each new user is assigned the role of Lab Technician or Lab Director (see Section 9).

1. To create a new user account, log in as the Admin user, and select the **Create New User** button at the bottom center of the Users screen to display the 'Create New User' window (Figure 8).



Figure 8. The 'Create New User' window. Fields with a red asterisk are required.

2. Enter the user's first name, last name and organization. Select the user role (Lab Technician or Lab Director) from the Role drop-down menu. Enter a user name, which the user will use to log into the software.
3. Select **Save User**. A window with a system-generated temporary password appears.
4. Select **Copy to clipboard** and temporarily record this password in a secure location to share with the new user. The Admin will need to share the temporary password with the user outside of the OncoMate® MSI software application since the temporary password is required when the new user logs into the software for the first time.

   Note: The temporary password will be overwritten if new content is copied to the clipboard before the password is shared with the new user. If this occurs, the administrator can reset the user's password as described in Section 10.6.
5. Select the **X** in the upper right corner to close this window and return to the Users screen.

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10.3 Editing a User Account

The software administrator can edit the first name, last name, organization, role and user name for an existing user account. Changes made to a user account are captured in the audit log.

1. To edit an existing user account, log in as the Admin user, and from the Users screen, double-click anywhere on the row of the user account to be edited. The 'Edit User' window appears and is populated with the first name, last name, organization, role and user name associated with the existing user account.
2. Make the desired changes to the First Name, Last Name, Organization and/or User Name fields. To edit the user role associated with the existing user account, select a different role from the Role drop-down menu.
3. Select **Save User**.

   Note: Following any saved change(s) to an account, the affected lab technician or lab director user will be prompted to change the account password during their next login.
4. Select the **X** in the upper right corner to close this window and return to the Users screen.

10.4 Resetting a Password

The Admin user can reset the password for any user accounts. For example, the administrator will need to reset the password for any user who has forgotten a password or was locked out of a user account after three unsuccessful login attempts.

1. To reset a user's password, log in as the Admin user, and from the 'Users' screen, select the user account you wish to edit. The user account is highlighted in blue, and the **Reset Password** button near the bottom of the screen is active.
2. Select **Reset Password**. A message appears asking you to confirm that you want to reset the password. Select **Yes** to reset the password for the highlighted user account. Select **No** to cancel the password reset and return to the Users screen.
3. If you select **Yes** to reset the password, the software will generate a new temporary password for that user account.
4. Select **Copy to clipboard** and temporarily record this password in a secure location to share with the new user. The Admin will need to share the temporary password with the user outside of the OncoMate® MSI software application since the temporary password is required when the new user logs into the software for the first time.

   Note: The temporary password will be overwritten if new content is copied to the clipboard before the password is shared with the new user. If this occurs, the administrator can reset the user's password as described above.
5. Select the **X** in the upper right corner to close this window and return to the Users screen.

10.5 Locking and Unlocking a User Account

The administrator can lock and unlock user accounts. User accounts also will be locked after three unsuccessful login attempts. User accounts that are locked will have a status of "Inactive" in the Users screen and must be unlocked by the software administrator before that user is able to log into the OncoMate® MSI Dx Analysis Software. User accounts that are unlocked will have a status of "Active" in the Status column.

Locking a User Account

1. Log in as the Admin user, and from the Users screen, select the user account you wish to lock. The user account is highlighted in blue, and the **Lock User** button near the bottom of the screen is active.
2. Select **Lock User**. A message appears asking you to confirm that you want to lock the selected user account. Select **Yes** to lock the selected user account. Select **No** to cancel the action and return to the Users screen.

Unlocking a User Account

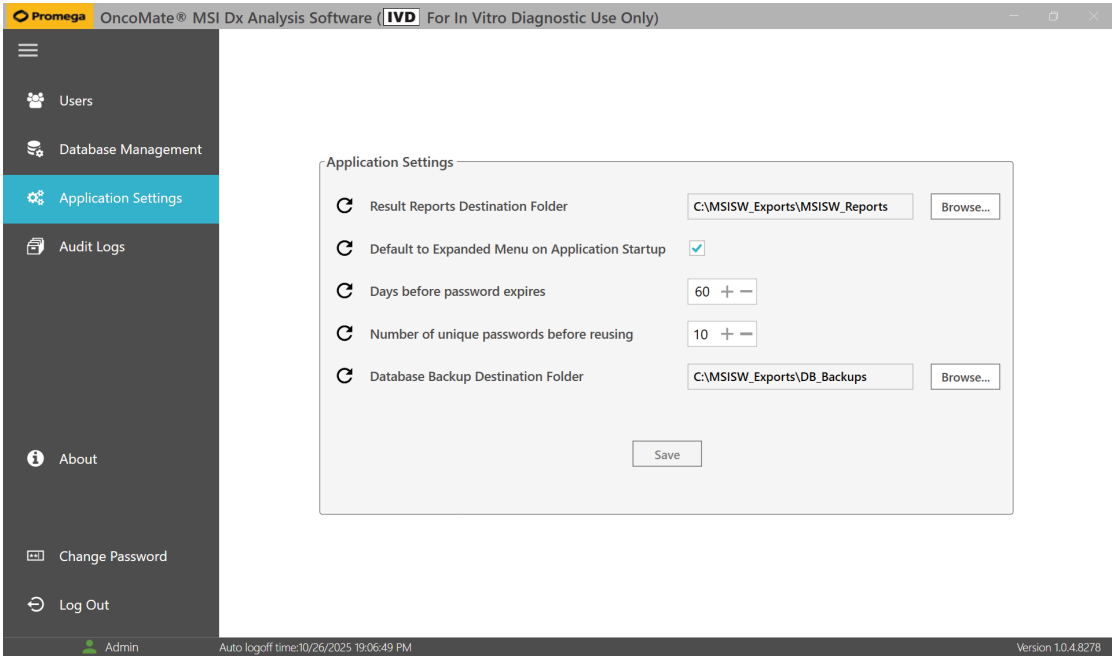
1. Log in as the Admin user, and from the 'Users' screen, select the user account you wish to unlock. The user account is highlighted in blue, and the **Unlock User** button near the bottom of the screen is active.
2. Select **Unlock User**. A message appears and ask you to confirm that you want to unlock the selected user account. Select **Yes** to unlock the selected user account. Select **No** to cancel the action and return to the Users screen.

   Note: Selecting **Yes** will reset the password to a temporary password.
3. Once the user account is unlocked, a message with a system-generated temporary password appears. Select **Copy to clipboard** and temporarily record this password in a secure location to share with the new user. The Admin will need to share the temporary password with the user outside of the OncoMate® MSI software application since the temporary password is required when the user logs into the software.

   Note: The temporary password will be overwritten if new content is copied to the clipboard before the password is shared with the new user. If this occurs, the administrator can reset the user's password as described in Section 10.6.
4. Select the **X** in the upper right corner to close this window and return to the Users screen.

10.6 Configuring Application Settings

The **Application Settings** button on the task pane is used to customize software settings, password requirements and preferences, the location where reports and data export files are saved and other attributes to meet the laboratory's needs. Selecting **Application Settings** displays the 'Application Settings' screen (Figure 9), which includes the options described below to configure the software. Only the Admin user can configure application settings.



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Figure 9. The 'Application Settings' screen.

Application Setting Descriptions

Result Reports Destination Folder: This function allows the Admin user to select the default location where result reports, data export files and technical support files are saved. See Section 14.

Note: Assign the reports destination to a directory on the host workstation for which all OncoMate® MSI Dx Analysis software users have Modify permissions. This includes the "Network Service" user assigned automatically to SQL Server 2022. If a directory within a specific Windows user account is selected as the report destination location (e.g., C:\Users\bsmith\OncoMateReports), other OncoMate® MSI Dx Analysis software users signed onto the PC with their unique Windows® credentials will not have access to the reports destination folder and report creation will fail.

Default to Expanded Menu on Application Startup: This check box determines whether the task pane is expanded or collapsed by default when users log into the OncoMate® MSI Dx Analysis Software. By default, the check box is checked and the task pane will be displayed in the wider, expanded form. Uncheck the check box to display the task pane in a narrower, collapsed form.

Days Before Password Expires: This field allows the Admin user to control how often users must change their password and choose a new password. By default, users are required to change their passwords every 60 days. The maximum interval is 365 days, and the minimum is 60 days.

Number of Unique Passwords Before Reusing: This field determines how many unique passwords must be used before a user can reuse a previous password. By default, a user must create ten different new passwords before an old password can be reused for that user account. The maximum is 25 new passwords, and the minimum is 10.

Database Backup Destination Folder: This function allows the Admin user to select the default location where database backup files are saved. See Section 10.7.

Configuring Application Settings

1. To configure user preferences and software settings, log in as the Admin user, and select **Application Settings** from the task pane.
2. Change any or all settings on this screen to meet the needs of the laboratory.
3. After customizing the settings, select **Save**.

   Note: The Admin user may reset an application setting to its default value by selecting the Reset icon to the left of the setting. 

10.7 Database Management

The Database Management function allows the software administrator to archive data by creating a backup copy of the current OncoMate® MSI Dx Analysis Software database and restore an archived copy of the database to the current database.

Restoring a backup version of the database will overwrite the current database. Any new user accounts created since the database backup file was saved will be lost and must be recreated. We recommend creating a backup copy of the current database as described below prior to restoring a backup version.

In accordance with best practices, we recommend that the OncoMate® Administrator backup the application database prior to any Microsoft® SQL Server updates being applied. OncoMate® software should also be shut down during the update.

Database Backup

1. To create a backup copy of the current database, log in as the Admin user, and select **Database Management** from the task pane. The 'Database Operations' window appears.

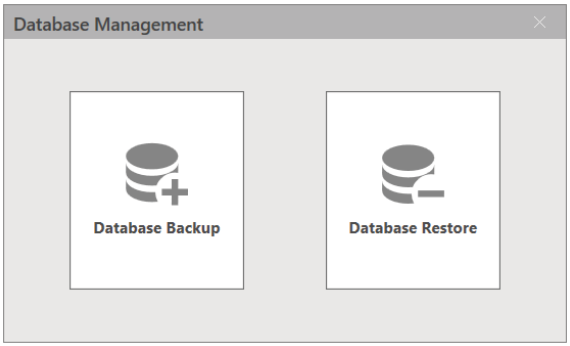


Figure 10. The 'Database Operations' window.

2. Select **Database Backup** to start the backup process.

3. Select **OK** to close the message window informing you that the database backup was successful (Figure 11). The software will save a copy of the current database as a .ODB file to the backup destination defined in the Application Settings in a new folder labeled with the backup date as follows: DatabaseBackup-YearMonthDay. The software assigns the .ODB file a name based on the date when the backup file was created as follows: YearMonthDayTimeDatabaseBackup.odb. Do not change the name of the database backup file as doing so will result in a failure when restoring the database.

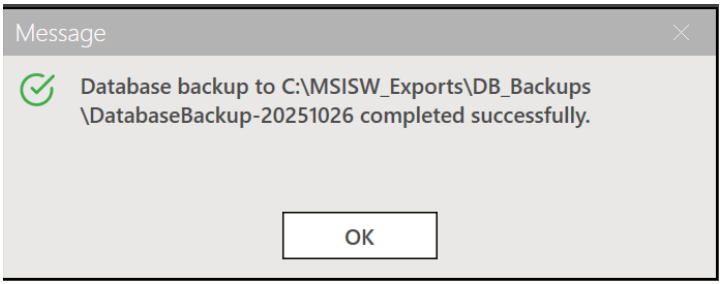


Figure 11. A Message window informs you that a backup copy of the OncoMate® MSI Dx Analysis Software database was saved successfully to the indicated file location.

Database Restore

1. To restore the current database to an archived backup copy, log in as the Admin user, and select **Database Management** from the task pane. The 'Database Operations' window appears (Figure 10).

2. Select **Database Restore**.

3. A Windows® Explorer window opens. Navigate to the location of the desired backup copy of the database that you wish to restore. Select the desired backup file and Select **Open**.

4. A message warns you that restoring the database will replace the current database with the selected backup copy of the database and overwrite all existing records. Select **OK** to continue with the database restoration process. Choose **Cancel** to cancel database restoration and return to the Admin User screen.

5. A second message warns that restoring the database will erase all current records and recommends creating a backup copy of the current database prior to restoring the database to a previous version. Select **Yes** to continue with the database restoration process. Select **No** to cancel database restoration.

6. After selecting **Yes**, the software will overwrite the current database with the backup copy of the database chosen in Step 3.

   Note: If database restoration is successful, a notification message will appear (Figure 12). If database restoration is not successful, a message will notify you of the failure and describe the root cause of the failure if known.

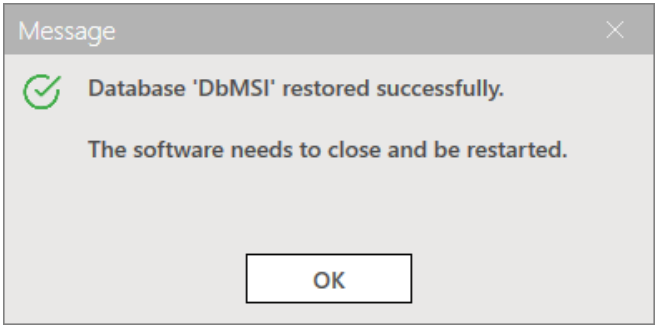


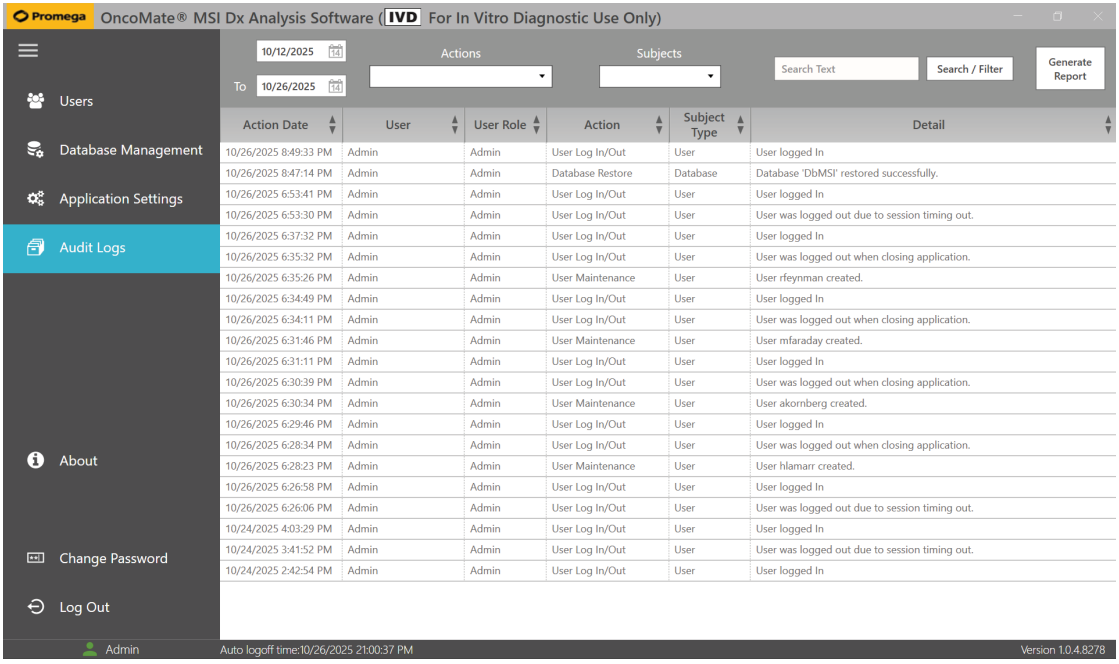
Figure 12. A message showing that database restoration was successful.

7. Select **OK**. The OncoMate® MSI Dx Analysis Software will restart, and you are required to log in again. The software will now use and display content of the restored database.

   Note: Any data, actions, batch reviews and approvals, and other database content recorded after the restored backup copy was created is no longer accessible by the OncoMate® MSI Dx Analysis Software. To access more recent database content, repeat this process to restore a more recent backup copy of the database.

10.8 Viewing Software Audit Records

The OncoMate® MSI Dx Analysis Software includes an auditing function that tracks actions that affect batches, samples, user accounts and the OncoMate® MSI Dx Analysis Software database for traceability purposes. Only the Admin user can view the list of audited actions, which is displayed on the Audit Logs screen (Figure 13). By default, the audit log displays all auditable actions recorded within the past two weeks.



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Figure 13. The Audit Logs screen.

For each auditable action, the Audit Logs screen displays the attributes shown in Table 4.

Table 4. Action Attributes Displayed on the Audit Logs Screen.

Attribute	Description	
Action Date	The date and time when the action was initiated within the software	
User	The user name of the user who performed the action	
User Role	The user role of the user who performed the action	
Action	The type of action performed. Actions are organized into the categories described below:	
	Batch Definition	A user created a new batch, added samples to a batch or imported an existing batch of samples. The names of the affected batch and samples are recorded in the Details field.
	Batch Archive **Batch Share** **Batch Restore**	A user archived, shared or restored a batch of samples. The name of the batch and whether the batch was restored, shared or archived is recorded in the Details field.
	Batch Analysis	The software performed a QC evaluation of the batch to determine if a batch met the quality control requirements described in Section 15.1 and designated the batch as “Pass” or “Fail”.
	Database Backup **Database Restore**	The software administrator archived the Onco-Mate® MSI Dx Analysis Software database or restored the database to an archived version.
	Data Report/Export	A user generated data reports. The name of the batch and the type of report generated is recorded in the Details field.
	Review/Approval	A user reviewed or approved a sample. Review and approval of each sample is recorded as a separate action in the audit log. The sample name and whether the sample was reviewed or approved is recorded in the Details field. This category includes adding a note to a sample.
	User Login/Out	A user logged into the software or logged out of the software. This includes instances where a user was logged out by the software due to inactivity.
	User Maintenance	The software administrator created a new user account or made changes to an existing user’s account.

Attribute	Description	
Subject Type	The subject of the action. An action can affect the following subjects:	
	Batch	A change was made to a batch of samples.
	Database	A change was made to the software database.
	Sample	A change was made to a sample.
	User	A change was made to a user account.
Detail	A more detailed description of the action. This field provides additional information such as the name of user, batch(es), sample(s) and database affected by the action.	

By default, actions recorded in the audit log are ordered chronologically by date and time, with the most recent change at the top. Actions can be sorted in ascending or descending order by action date, user name, user role, action type or action subject by clicking on the corresponding column heading. Arrow icons in the column heading indicate whether audit actions are sorted, as described in Table 5.

Table 5. Sorting Options in the Audit Log.

Option	Description
	The order is not determined by content in this column. Choose this icon to arrange actions in ascending order.
	The order is determined by content in this column, and actions are displayed in ascending order. Select this icon to arrange actions in descending order.
	The order is determined by content in this column, and actions are displayed in descending order. Choose this icon to arrange actions in ascending order.

The software administrator can search the audit log and limit the actions displayed on the Audit Logs screen several ways:

Date: The Admin user can limit the actions displayed in the audit log by selecting a specific date range in the upper left corner of the Audit Logs screen. Manually type the search start and end dates, using the format mm/dd/yyyy, or select the  icon to choose start and end dates from the calendar. Once start and end dates are defined, select the **Search/Filter** button in the upper right corner to execute the search. The actions listed in the audit log will be limited to only those actions performed within that date range.

Text: The Admin user can search the content of the Audit Log by entering a specific keyword or string of text into the Search Text field at the top of the screen and selecting the **Search/Filter** button. The software will search the User and Detail fields of audit actions and list in the audit log only those actions that contain those search terms. To clear the search results and remove the search filter, delete all text from the Search Text field and select **Search/Filter**. The software's search function is not compatible with Boolean operator or wildcard characters.

Actions: The Admin user can limit actions displayed in the audit log to a specific type of action by choosing an action type from the Actions drop-down menu at the top of the screen. The action types in the drop-down menu are listed in Table 4.

Subjects: The Admin user can limit actions displayed in the audit log to a specific action subject by choosing a subject type from the Subjects drop-down menu at the top of the screen. The types of action subjects in the drop-down menu are listed in Table 4.

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10.9 Generating Audit Reports

Only the Admin user can create a report of auditable actions. This report (PDF format) includes the software user that generated the report, the name of the software (i.e., OncoMate® MSI Dx Analysis Software), the computer's IP address, the date and time when the report was generated, the type of report (OncoMate® MSI Dx Audit Log Report) and the user name of the Windows® user logged into the computer when the report was generated followed by a list of the actions displayed in the audit log. The actions included in the audit log report reflects any searches, filters or sorting applied to the actions when the report was generated.

1. To generate an audit log report, log in as the Admin user, and select **Audit Logs** in the task pane.
2. If desired, sort or filter the audit log to display the audit actions of interest. See Section 10.8 for more information.
3. Select **Generate Report** in the upper right corner of the screen. The 'Save As' window will appear.
4. Navigate to the desired location of the audit log report, and enter a file name.
5. Select **Save**. A message will appear to inform you that the audit report was successfully created.

11. Logging Into and Out of the Software as a Lab Technician or Lab Director

This section provides instructions on how to log into and out of the OncoMate® MSI Dx Analysis Software as a lab technician or lab director. To log in as the software administrator, see Section 10.1.

Note: After 10 minutes of inactivity, the OncoMate® MSI Dx Analysis Software session will end, you will be logged out and you will be required to log in again. "Auto logoff time" in the bottom left corner of the screen indicates when the software will log out the the current user due to inactivity. The "Auto logoff time" will be reset after any activity within the software, including moving the cursor.

11.1 Logging into the OncoMate® MSI Dx Analysis Software

This section describes the standard login process. To login using a temporary password because your user account is new, your password expired or the administrator locked and unlocked your account, see Section 11.2.

1. Double-click the icon for the OncoMate® MSI Dx Analysis Software on the computer desktop.
2. At the Login screen, enter your user name and password to activate the Login button. Select **Login** to enter the OncoMate® MSI Dx Analysis Software.

   To exit the application without logging in, select the **X** in the upper right corner of the Login screen.

   Notes:

   a. Passwords are case-sensitive.

   b. When entering the user name or password, do not include spaces or other characters that are not part of the user name or password, as these unnecessary characters will cause the login attempt to fail.
3. If the login attempt is successful, you will see the 'Batches' screen, with the task pane in the left margin and the batches table.

   If the login attempt is not successful, the Invalid Username or Password window is displayed. Select **Ok** to return to the Login screen. Re-enter your user name and password, and select **Login** to enter the OncoMate® MSI Dx Analysis Software.

   Note: After three unsuccessful login attempts, your user account will be locked and can be unlocked only by the software administrator. If your user account becomes locked, contact your software administrator to unlock your user account and obtain the temporary password.

11.2 Logging in With a Temporary Password

The software assigns a temporary password to all new user accounts, user accounts with an expired password and user accounts that were required to be unlocked by the software administrator. To access your account, log in using this temporary password. If you do not know the temporary password, contact the software administrator. Once you've logged into the software using a temporary password, you will be prompted to change your password.

When logging into a new user account for the first time, you will also need to know your user name. If you do not know your user name, contact the software administrator.

As your password expiration date approaches, you will be notified by a pop-up window and given an opportunity to change your password at each login (Figure 14). Select **Remind me later** to log into the software without changing the password at this time. You will continue to be notified until your password is changed or expires. Select **Change Now** to open the 'Proceed to Change Password' window and change your password. The software administrator determines how often passwords expire by adjusting user preferences.

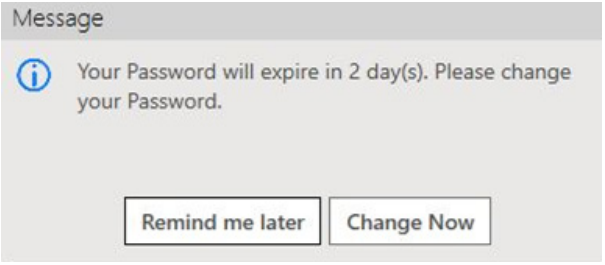


Figure 14. A notification that your password will soon expire will appear upon login beginning 1 week before your password expires.

1. Double-click the icon for the OncoMate® MSI Dx Analysis Software on the computer desktop.

2. At the Login screen, enter the user name and temporary password. Select Login. To exit the application without logging in, select the **X** in the upper right corner of the Login screen.

   Notes:

   a. Passwords are case-sensitive. When entering the user name or password, do not include spaces or other characters that are not part of the user name or password, as these unnecessary characters will cause the login attempt to fail.

   b. If the login attempt is not successful, the 'Invalid Username or Password' window is displayed. Select **Ok** to return to the Login screen. Re-enter your user name and password, and select **Login** to enter the OncoMate® MSI Dx Analysis Software. After three unsuccessful login attempts, your user account will be locked and can be unlocked only by the software administrator.

3. You will be prompted to change your password. In the 'Proceed to Change Password' window, enter the temporary password in the 'Old Password' field. Enter a new password in the New Password field. Enter your new password in the 'Confirm Password' field. Select **Change Password**.

   Note: The new password must contain a minimum of 8 characters.

4. If the passwords entered in the New Password and Confirm Password fields match, a message appears to confirm that the password was successfully changed.

   If the passwords do not match, you will be prompted to re-enter the old and new passwords.

5. Select **Ok**. The software will close, and a new login screen will appear. Enter your user name and the new password to log into the OncoMate® MSI Dx Analysis Software.

Once you've successfully logged into the OncoMate® MSI Dx Analysis Software, the 'Batches' screen will appear.

11.3 Changing a User Password

You can change your login password at any time by selecting the **Change Password** button on the task pane.

1. To change your password, select **Change Password** from the task pane.
2. In the 'Proceed to Change Password' window, enter the old password, enter a new password and confirm the new password. Select **Change Password** to change the password. Select the **X** in the upper right corner of the window to exit this screen without changing the password.

   Note: A password must contain a minimum of 8 characters.
3. If the passwords entered in the New Password and Confirm Password fields match, a message appears to confirm that the password was successfully changed.

   If the passwords do not match, you will be prompted to re-enter the old and new passwords.
4. Select **Ok**. The software will close, and a new login screen will appear. Enter your user name and the new password to log into the OncoMate® MSI Dx Analysis Software.

11.4 Logging Out and Closing the Software

This section describes the standard logout process.

1. To log out of the software, select the **Logout** button in the task pane.
2. A confirmation window appears. Select **Yes** to continue logging out, and then select **Ok** to acknowledge the successful logout. Select **No** to continue using the software.
3. After you have logged out of the software, the login window appears, allowing a different user to log in and start an active session.
4. To close the software, simply select the gray **X** in the upper right corner.

12. Navigating and Managing Batches

12.1 Sample Batch Definitions and Requirements

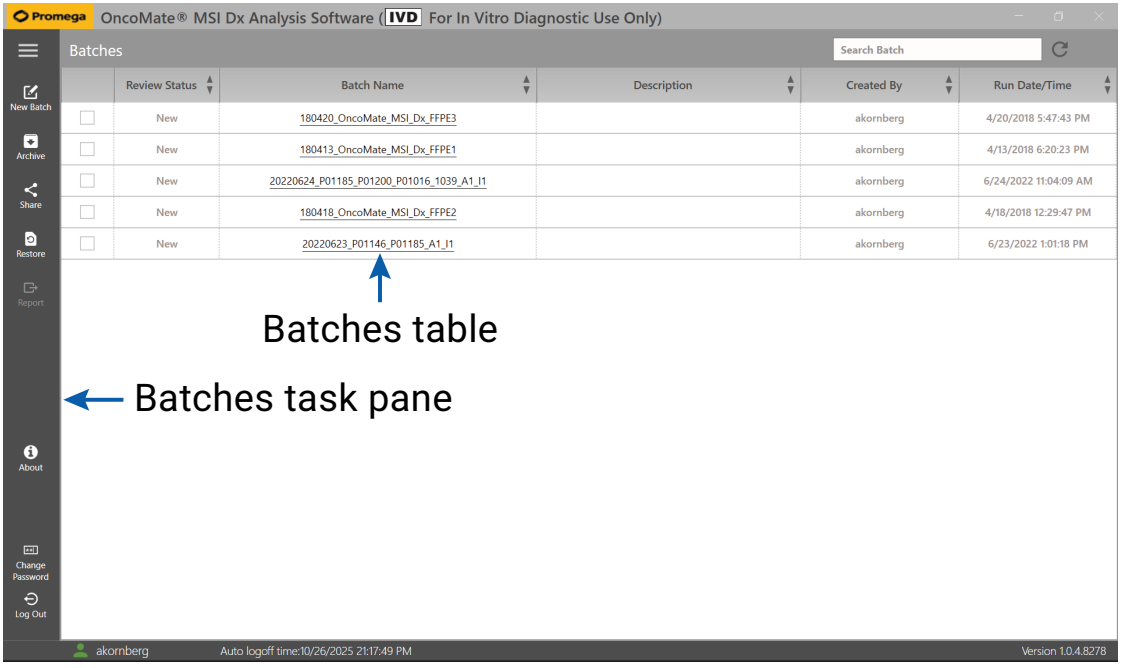
The OncoMate® MSI Dx Analysis Software organizes samples that were analyzed during the same capillary electrophoresis run into batches. Batches are named automatically by the software according to the plate name assigned during capillary electrophoresis setup. A batch cannot contain patient samples or controls analyzed during different capillary electrophoresis runs. Batches must meet a minimum set of requirements to be considered valid for interpretation:

- Each batch must include both a positive amplification control and a negative amplification control, and these controls must be designated "Positive Control" and "Negative Control" in the Sample Type field during capillary electrophoresis run setup in the Applied Biosystems® 3500 Dx Genetic Analyzer DCS.
- Patient samples must be identified as "Sample" in the Sample Type field during capillary electrophoresis run setup and must be analyzed as matched normal and tumor sample pairs throughout the OncoMate® MSI Dx Analysis System workflow.
- During capillary electrophoresis run setup, information for paired samples (Sample Name and normal/tumor designation) must be entered following prescribed conventions. Acceptable conventions are described in Section 16. Improperly identified samples cannot be paired by the OncoMate® MSI Dx Analysis Software and will not be imported or analyzed. The software will reject importing FSA files with other Sample Type designations available in the capillary electrophoresis DCS (e.g., "HiDi", "Blank").
- All analyzed samples and controls must contain the Size Standard 500 (added prior to capillary electrophoresis), the size standard peaks analyzed by the software (60, 65, 80, 100, 120, 140, 160, 180, 200, 225, 250, 275 and 300 base pairs) must be present and have peak heights of ≥175RFU and ≤10,000RFU, and the 100, 200 and 300 base pair peaks must have intensities that are local maximums (i.e., that exceed the two neighboring peaks).


See the *OncoMate® MSI Dx Analysis System Technical Manual* #TM543 for information about the laboratory analysis of samples and controls and use of the Size Standard 500 during capillary electrophoresis.

12.2 The 'Batches' Screen

When login is successful, Lab Technician and Lab Director users are presented with the 'Batches' screen. The 'Batches' screen consists of the batches task pane in the left margin and the batches table (Figure 15).



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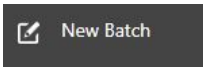
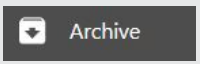
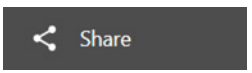
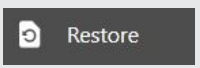
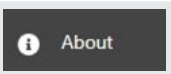
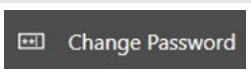
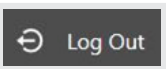
Figure 15. The two main areas of the 'Batches' screen: The batches task pane and batches table. This example shows the 'Batches' screen for lab director users.

The Batches Task Pane

The batches task pane (Figure 15) includes tools to create a new batch, share or archive an existing batch, restore a shared or archived batch, generate reports, change a password, and view the end user license agreement and additional information about OncoMate® MSI Dx Analysis Software. The functions in the task pane are described in Table 6. Some of these functions are available only to users with the role of lab director, as indicated below.

Note: The task pane does not include a Save function. The software automatically saves a batch after any auditable actions occur; see Section 10.8 for more information on audit records.

Table 6. Functions in the Task Pane of the OncoMate® MSI Dx Analysis Software.

Button	Description
	**Menu Bar:** Toggles between an expanded task pane and collapsed task pane. The task pane is shown in the collapsed view in Figure 5 and in the wider, expanded form in Figure 9. When the Menu Bar is used to expand or collapse the task pane, the content of the task pane does not change; only the width of the pane changes.
	**New Batch:** Creates a new batch for analysis. For instructions on how to create a new batch, see Section 12.3.
	**Archive:** Archives a batch and removes the batch from the 'Batches' screen. This button is available only to lab director users. For instructions on how to archive a batch, see Section 12.5.
	**Share:** Shares a batch for viewing in a different instance of the software. This button is available only to lab director users, and shared batches are not removed from the Batches screen. For instructions on how to share a batch, see Section 12.7.
	**Restore:** Restores an archived batch from a file location. Restored batches are displayed on the 'Batches' screen. This button is only available to lab director users. For instructions on how to restore a batch, see Section 12.6.
	**Report:** Generates reports and data exports for the selected batch. See Section 14 for more information.
	**About:** Displays the 'About' screen for OncoMate® MSI Dx Analysis Software. The 'About' screen provides the software version number, license status and additional information. The End-User License Agreement can be viewed from the 'About' screen by selecting the PDF icon, which opens the End-User License Agreement as a PDF document in a separate window. The 'About' screen is identical for all users.
	**Change Password:** Allows a user to change the password for the active user account. To change a password, see Section 11.3.
	**Log Out:** Logs out the active user from the software. For more information, see Section 11.4.

The Batches Table

The batches table (Figure 9) displays a list of all active batches, regardless of which user created the batch. This list includes all imported and restored batches; batches that have been archived are not shown in the batches table. The batches table will be empty until batches of samples are created or restored from the archive. Each batch is displayed as a separate row that includes the following attributes:

Review Status: Indicates the current review status of the batch. The batch review status can be New, Under Review, Reviewed and Approved as follows:

New: No samples in the batch are reviewed.

Under Review: At least one sample in the batch is reviewed.

Reviewed: All samples in the batch are reviewed.

Approved: All samples in the batch are approved.

Batch Name: Indicates the name of the batch. The software assigns a batch name based on the capillary electrophoresis Plate name stored in the FSA file.

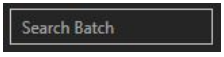
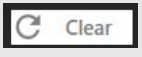
Description: Provides a field where users can enter a brief description of the batch following import. A batch description is optional.

Created By: Displays the user name for the user who created the batch.

To open a batch and view a list of samples in that batch, select the underlined batch name in the Batch Name column. To select one or more batches for subsequent actions (e.g., prior to archiving or generating reports), place a check mark in the check box in the first column or click anywhere on the row for that batch. Selected batches will be highlighted in blue.

To search active batches, use the **Search Batch** button in the upper right corner of the screen. See Table 7 for more information about search capabilities.

Table 7. Search Functions in the Batches Screen of the OncoMate® MSI Dx Analysis Software.

Function	Description
	**Search Batch:** Enter one or more keywords in the Search Batch field in the upper right corner of the 'Batches' screen. The software will search the list of batch names in the 'Batches' screen for those keywords and display only those batches with batch names that begin with the keyword(s). **Note:** The Search Batch function will only return batches with names that begin with the search keyword(s). Batches with names that contain the keyword(s) elsewhere in the batch name will not be included in the search results.
	**Clear:** Select **Clear** to clear the Search Batch field and remove the search filter to display a complete list of active batches in the 'Batches' screen.

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12.3 Creating a New Batch (Importing Sample Data)

The **New Batch** button in the task pane of the 'Batches' screen allows lab technician or lab director users to create a new batch of samples by importing the corresponding FSA files into the OncoMate® MSI Dx Analysis Software. The user must be aware of the following when importing FSA files to create a new batch:

- Only data from FSA files generated on Applied Biosystems® 3500 Dx Genetic Analyzer instruments can be imported into the software; data from other file types and FSA files from other capillary electrophoresis instruments are not appropriate. If portable media are used to transfer data files from the Applied Biosystems® 3500 Dx instrument to the OncoMate® MSI Dx Analysis Software, use a drive that is regularly scanned for viruses and malware and restrict use with other computers.
- The software will import only one batch of samples at a time. During data import, the OncoMate® MSI Dx Analysis Software will confirm that patient samples and controls were analyzed during the same capillary electrophoresis run and share the same unique plate name and run date. The software will not import data from any files that were not analyzed during the same capillary electrophoresis run.
- During import, data from sample and control FSA files are read into the software, but individual FSA files are not stored in the software database. The laboratory is responsible for the retention and management of FSA files produced by the capillary electrophoresis instrument.
- Successful data import requires FSA files for both the normal and tumor samples of each sample pair. If either the tumor or matched normal samples is absent, or if one of the prescribed sample-naming conventions was not followed (see Section 16), import of the corresponding sample will fail.
- If a batch includes more than one positive or negative amplification control or multiple patient samples with the same sample name, the software will import only the first files encountered of each type or name.
- Batch creation depends on the presence of appropriately identified positive and negative amplification control files. If one or both amplification control files is absent, the software will not import patient sample files.
- When data import fails for one or more FSA files, the software will display a message to inform you which file(s) failed to import and the reason(s) for failure. See Section 17, Troubleshooting, for guidance on resolving import failures.

1. To create a new batch, select the **New Batch** button in the task pane. 

2. In the file tree window that appears (Figure 16, blue box), navigate to the desired sample data folder or individual FSA files one of two ways:

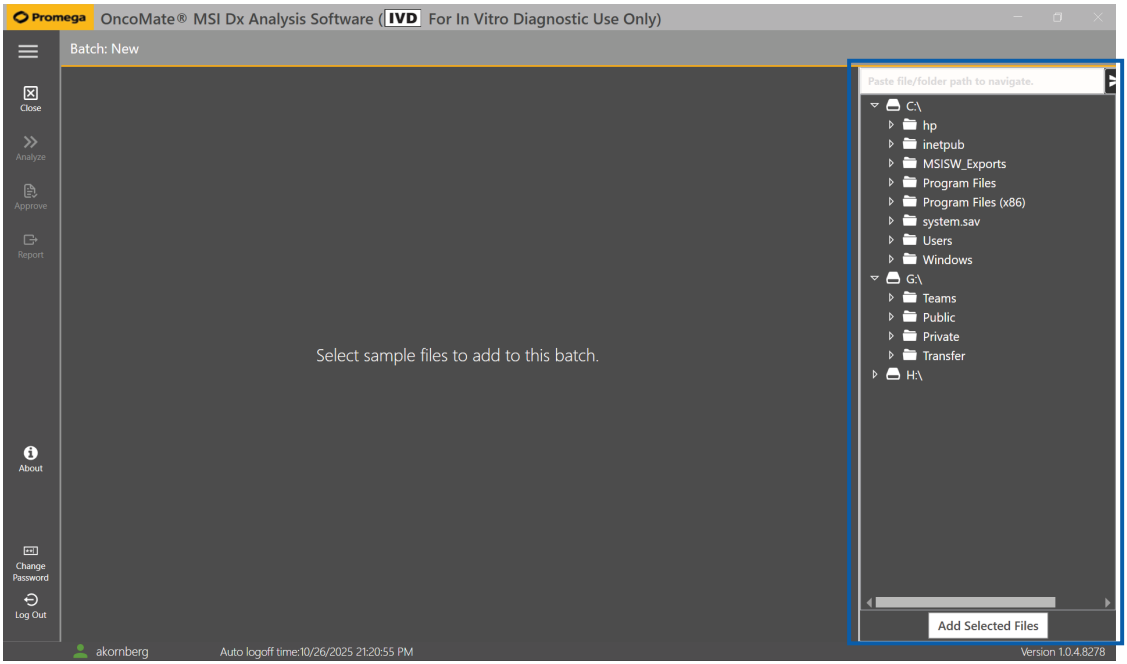
   - Type or paste the file path of the target folder into the empty field at the top of the file tree. Choose the **Go** icon.  The file tree will expand to that file location.
   - Navigate to the desired folder or files using the file tree by double-clicking on the drive name where the desired sample files are saved or selecting the small arrow to the left of the drive name. This will expand the view to include all folders on that drive. Continue to expand the file tree by clicking on the small arrows or double-clicking on folders within the file tree to navigate to the desired folder or FSA files.

   Notes:

   a. When importing samples into a batch, you can select a folder containing the FSA files or individual FSA files. When a folder is selected, all FSA files within that folder will be added to the batch.

   b. Selecting the **Reset** icon  will refresh the screen and cause the file tree to revert back to the initial file tree structure.

   c. Mapped drives are visible in the folder tree. Cloud drives, such as Microsoft® OneDrive, are not accessible.



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Figure 16. Adding samples to a new batch. The file tree is outlined in blue.

3. Select the desired sample folder or FSA files in the file tree, being sure to include the positive and negative controls and normal and tumor samples for each patient.

4. Select **Add Selected Files** at the bottom of the file tree to initiate import. To exit this screen without selecting FSA files for the new batch, select **Close** in the task pane to return to the 'Batches' screen.

   Note: While samples are being imported, the software displays a message that the sample import is in progress. Once import is finished, the 'Sample Summary' screen (Section 13.1) loads automatically and displays samples comprising the new batch.

5. Once samples are added to a new batch, analyze sample data immediately by selecting **Analyze** in the task pane on the Samples screen. See Section 13.3 for more information.

12.4 Adding Samples to an Existing Batch

Lab technician or lab director users can add patient samples to an existing batch. To be added, samples must have been analyzed during the same capillary electrophoresis run as the samples and controls in the existing batch. When adding samples to a batch, you must include both the normal and tumor samples from the same patient.

If a file is not added successfully, a message will appear to inform you which file failed to import and the reason(s) for failure. See Section 17, Troubleshooting, for guidance on resolving import failures.

1. To add additional samples to a batch, open the batch by selecting the name of the existing batch in the Batch Name column. The Samples screen appears and displays a list of samples in that batch (Figure 17).

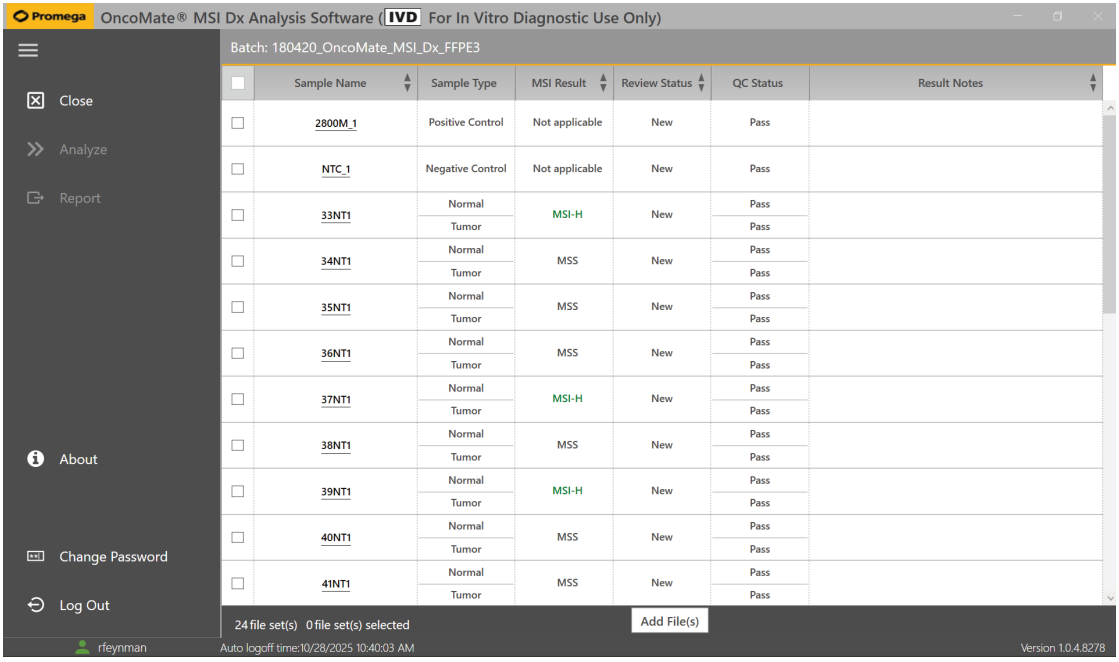


Figure 17. The Samples screen with a list of samples in the selected batch.

2. Select the **Add File(s)** button near the bottom center of the screen. A file tree will appear in the right margin (Figure 16).
3. Navigate to the desired sample data folder or FSA files one of two ways:
   - Type or paste the file path of the target folder into the empty field at the top of the file tree. Choose the **Go** icon.  The file tree will expand to that file location.
   - Navigate to the desired folder or files using the file tree by double-clicking on the drive name where the desired sample files are saved or selecting the small arrow to the left of the drive name. This will expand the view to include all folders on that drive. Continue to expand the file tree by clicking on the small arrows or double-clicking on folders within the file tree to navigate to the desired folder or FSA files.

   Notes:

   a. When adding samples to a batch, you can select a folder containing the FSA files or individual FSA files. When a folder is selected, all FSA files within that folder will be added to the batch.

   b. Selecting the **Reset** icon  will refresh the screen and cause the file tree to revert back to the initial file tree structure.
4. Select the desired sample folder or FSA files in the file tree, being sure to include the normal and tumor samples for each patient.
5. Select **Add Selected Files** at the bottom of the file tree to initiate import. To exit this screen without selecting FSA files, select **Close** in the task pane to return to the 'Batches' screen.

   Note: While samples are being imported, the software displays a message that the sample import is in progress. The batch now includes the additional sample files. The newly added samples have an MSI Result of "Unanalyzed".
6. Once samples are added to an existing batch, select **Analyze** in the task pane on the Samples screen to immediately analyze sample data. See Section 13.3 for more information.

   Note: Existing samples that were previously analyzed may appear to be reanalyzed but their results are unaffected.

12.5 Archiving a Sample Batch

Archiving is used to remove completed or unwanted batches from the OncoMate® MSI Dx Analysis Software. Archiving batches improves the overall speed of the OncoMate® MSI Dx Analysis Software. Therefore, we recommend that users archive batches regularly to ensure efficient software performance and to streamline the batches table.

Batches can be archived at any point in the workflow without the need for review. Archived data will retain the individual sample and control data associated with a batch, the review status of each sample and the batch review status. Note that data from sample and control FSA files are read into the software, but the FSA files are not retained or archived by the software. Archived batches can be restored later using the Restore function detailed in Section 12.6. Only lab director users can archive and restore batches.

Follow the instructions below to archive batch data.

1. Select the desired batch from the 'Batches' screen by placing a checkmark in the check box in the first column or selecting anywhere on the row for the batch. The selected batch will be highlighted in blue.

   Note: To select multiple batches, hold down the **Shift** or **Ctrl** key and select other batches in the 'Batches' screen.

2. Select **Archive** in the task pane. The 'Archive Batches' window will appear, giving you the option to archive all batches or the selected batches.
3. Choose your preference and select **Archive** to proceed or **Cancel** to close the 'Archive Batches' window.
4. A Windows® Explorer window will appear. Navigate to the desired location, and select **OK** to archive the batch(es) or **Cancel** to close with explorer window. The software will return a message, indicating that the selected batches were archived successfully. Select **OK** to close the message window. The software will save each archived batch as a separate .oba file in a new folder labeled with the archive date as follows: BatchArchives-YearMonthDay. Do not change the name of the batch archive file as doing so will result in a failure when restoring the batch.

   Note: It may take several minutes for the selected batches to be archived by the software.

12.6 Restoring an Archived Batch

Batches that were previously archived can be restored to the list of active batches on the 'Batches' screen. Only users with a lab director role can restore an archived batch. Follow the instructions below to restore an archived batch to the active data set.

1. From the 'Batches' screen, select **Restore** in the task pane.
2. A Windows® Explorer window will appear. Navigate to the archived batch, and select the archive file (.oba format).

   Note: To select multiple batches, hold down the **Shift** or **Ctrl** key and select the archive file for each additional batch.
3. Select **Open** to restore the archived batch or **Cancel** to close the Explorer window. The software will return a message indicating that the selected batch was successfully restored. Select **OK** to close the message window.

12.7 Sharing a Sample Batch

Sharing is used to view analyzed batches in a different instance of the OncoMate® MSI Dx Analysis Software. Batches can be shared at any point in the workflow following analysis. Sharing is not intended for batches that were imported but not analyzed.

Shared batches will retain the individual sample and control data associated with a batch, the review status of each sample and the batch review status. Note that data from sample and control FSA files are read into the software, but the FSA files are not retained or shared by the software. Shared batches can be restored later using the Restore function. See Section 12.8 for more information. Only lab director users can share and restore batches. Follow the instructions below to share batch data.

1. Select the desired batch(es) from the 'Batches' screen by placing a check mark in the check box in the first column or selecting anywhere on the row for the batch. The selected batch(es) will be highlighted in blue.
2. Select **Share** in the task pane. The 'Share Batches' window will appear, giving you the option to share all batches or the selected batches.
3. Choose your preference and select **Share** to proceed or **Cancel** to close the 'Share Batches' window.

4. A Windows® Explorer window will appear. Navigate to the desired location and select **OK** to share the batch(es) or **Cancel** to close with explorer window. After selecting **OK**, the 'Batch Share' window will appear, requiring you to create a security key to encrypt and export the batch to share.
5. Enter a security key in the 'Security Key' field. Enter the same security key in the 'Confirm Security Key' field. Select **OK**. The software will return a message, indicating that the selected batches were successfully shared.

   Note: The security key must contain a minimum of eight characters. Retain this security key, as it is required to decrypt the shared batch in other instances of the software.
6. Select **OK** to close the message window. The software will save each shared batch as a separate .obs file in a new folder labeled with the share date as follows: BatchShare-YearMonthDay. Do not change the name of the batch share file, as doing so will result in a failure when restoring the batch.

   Note: It can take several minutes for the software to create .obs files for the selected batches.

12.8 Restoring a Shared Batch

Batches that were shared can be restored to the list of active batches on the 'Batches' screen by following the instructions below. Only users with a lab director role can restore a shared batch. Do not change the name of the batch share file, as doing so will result in a failure when restoring the batch.

1 From the 'Batches' screen, select **Restore** in the task pane.

2. A Windows® Explorer window will appear. Navigate to the shared batch and select the shared file (.obs format).
3. Select **Open** to restore the shared batch or **Cancel** to close the Explorer window. After selecting **Open**, the 'Batch Restore' window will appear, requiring you to enter a security key to import the shared batch.
4. Enter the security key assigned when the shared batch file was created in the Security Key field and select **OK**. If the correct security key is entered, the software will return a message indicating that the batch was successfully restored and that the software must close to complete the restore process.

   Note: The security key is assigned by the user who originally shared the batch. Restoration of a shared batch will fail if the correct security key is not entered.
5. Select **OK** to close the software and finish restoring the shared batch.

13. Navigating and Managing Samples

13.1 The Samples Screen

Once a batch of samples is imported or restored in the OncoMate® MSI Dx Analysis Software, you can view a list of sample pairs in that batch on the Samples screen.

The Samples screen loads automatically once initial sample import is finished, prior to sample analysis. To open the Samples screen for a previously analyzed batch, click on the underlined batch name on the 'Batches' screen (Figure 15). The Samples screen is composed of two main areas: the samples task pane and samples table (Figure 18).

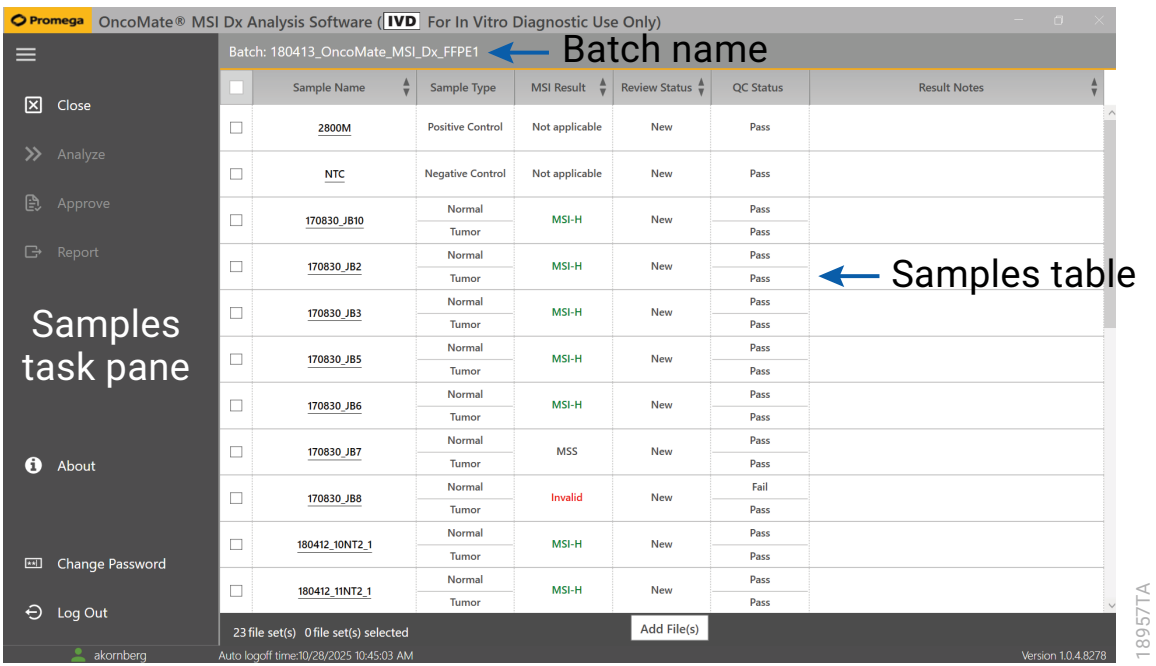
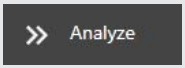
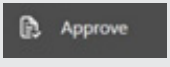
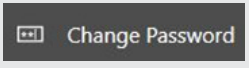
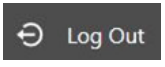


Figure 18. The Samples screen. The samples task pane and samples table are indicated. The Batch Name is displayed above the Samples table.

The Samples Task Pane

The samples task pane includes a series of buttons to manage samples within a batch. These buttons are described in Table 8.

Table 8. Buttons in the Samples Task Pane on the Samples Screen.

Button	Description
	**Menu Bar:** Toggles between an expanded task pane and collapsed task pane. When the Menu Bar is used to expand or collapse the task pane, the content of the task pane does not change; only the width of the pane changes.
	**Close:** Close the Samples screen and return to the Batches screen. Any changes made to a sample's review status will be saved automatically when selecting **Close**.
	**Analyze:** Analyze all samples within the batch, including performing the QC evaluation and assigning marker stability and sample MSI results.
	**Report:** Generates sample reports for the selected sample(s). See Section 14 for more information.
	**Approve:** Approve a batch that is analyzed and reviewed. This button is available only to lab director users. See Section 13.6 for more information.
	**About:** Displays the 'About' screen for OncoMate® MSI Dx Analysis Software. The 'About' screen provides the software version number, license status and additional information. The End-User License Agreement can be viewed from the 'About' screen by selecting the PDF icon, which opens the End-User License Agreement as a PDF document in a separate window.
	**Change Password:** Change the password for the active user account. See Section 11.2 for more information.
	**Log Out:** Log out of the OncoMate® MSI Dx Analysis Software.

The Samples Table

The samples table lists all sample pairs in the selected batch. Each sample is displayed as a separate row that includes the following information:

Sample Name: The sample name assigned to this sample pair in the Applied Biosystems® 3500 Data Collection Software during capillary electrophoresis.

Sample Type: The sample types are Positive Control, Negative Control, Normal or Tumor. Sample type is designated during setup of the capillary electrophoresis run. See Section 16 for a discussion of acceptable sample-naming conventions, including how to identify normal and tumor samples during capillary electrophoresis run setup. If sample type is not assigned correctly, the software will not recognize and analyze the affected sample pair(s).

MSI Result: The MSI result assigned to the sample pair (MSS, MSI-H or Invalid) during data analysis. The MSI result displayed for the negative and positive controls is "Not Applicable".

Unanalyzed: Until samples are analyzed, the MSI Result for each sample pair will be "Unanalyzed". To analyze sample pairs, see Section 13.3.

MSI-H: Microsatellite instability high (MSI-H) indicates that two or more mononucleotide-repeat markers were identified as unstable.

MSS: Microsatellite stable (MSS) indicates that four or more mononucleotide-repeat markers were identified as stable. A sample interpreted as "MSS" by the software is a not MSI-H result.

Invalid: Invalid indicates that the quality of the sample data is unacceptable due to a critical QC failure or insufficient data at the marker level (see Section 18).

Review Status: The sample pair's review status.

New: The sample pair was imported and is awaiting review by a lab technician or lab director user.

Reviewed: The sample pair was reviewed and is awaiting approval by a lab director user.

Approved: The sample pair was approved.

QC Status: The sample pair's QC status. The OncoMate® MSI Dx Analysis Software assigns QC Status by evaluating several quality attributes associated with the controls and patient samples to determine whether the samples are of sufficient quality for MSI interpretation. These quality attributes are described in Section 15.1.

Pass: All data quality attributes have passed.

Fail: The data has failed to meet data quality criteria for analysis so"Invalid" is assigned as the MSI result.

Result Notes: Notes associated with a sample pair. Result notes are added by the user from the Sample Data screen (see Section 13.2).

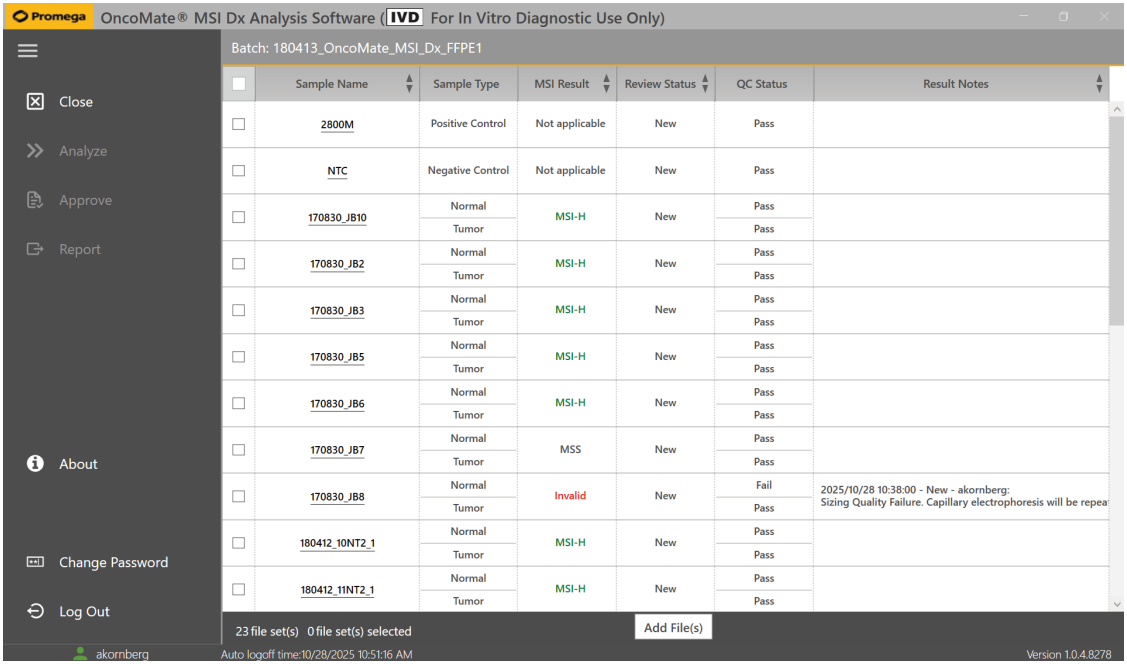


Figure 19. The Samples screen showing the MSI results for analyzed samples.

By default, the negative and positive controls are displayed at the top of the samples table, and the other sample pairs in the batch are listed in alphanumeric order. Normal and tumor samples from the same patient are grouped together. Sample pairs can be sorted in ascending or descending order by sample name, MSI result and sample review status by selecting the corresponding column heading. Arrow icons in the column heading indicate whether samples are sorted, as described in Table 9. Sample pairs cannot be sorted by sample type or QC status.

Table 9. Sample-Sorting Options in the Samples Table.

Option	Description
	Sample order is not determined by content in this column. Choose this icon to arrange samples in ascending or descending order. To change the order in which samples are displayed in the samples table, select the column heading.
	Samples in the samples table are displayed in descending order.
	Samples in the samples table are displayed in ascending order.

You can view more detailed information about a sample pair by clicking on the underlined sample name in the Sample Name column in the Samples table to access the Sample Data Screen (Section 13.2).

13.2 The Sample Data Screen

Once a batch of samples is analyzed in the OncoMate® MSI Dx Analysis Software, you can view sample results on the Sample Data screen.

The Sample Data screen displays detailed information about a sample pair, including electropherograms for the samples and Size Standard 500, results of the QC evaluation, sample-level and marker-level MSI results, and information about the consumables used during capillary electrophoresis. To view the Sample Data screen for a sample pair or positive or negative control, select the underlined sample name in the Sample Name column of the Samples screen.

The Sample Data screen is composed of five main areas: The task pane, Title Bar, Results View, QC Table and Run Information section (Figure 20). Each of these sections is discussed below. By default, the Sample Data screen opens with the Results View expanded to display superimposed electropherograms for the normal and tumor samples, a table with stability calls for the MSI markers and any result notes. The Results View, QC Table and Run Information sections can be expanded by selecting the Down Arrow icon  and hidden by selecting the Up Arrow icon .



Figure 20. The Sample Data screen.

When an unanalyzed sample pair or control is selected, only the task pane and Title Bar are displayed, along with the message “This sample has not yet been analyzed”. The Results view, QC table and Run Information sections are not displayed. To analyze samples, see Section 13.3. Once all samples in the batch are analyzed, all five sections of the Sample Data screen are visible.

The Task Pane of the Sample Data Screen

The task pane of the Sample Data screen includes the Menu Bar and **Close** button (Table 10).

Table 10. Buttons in the Task Pane of the Sample Data Screen.

Button	Description
	**Menu Bar:** Toggles between an expanded task pane and collapsed task pane. The content of the task pane does not change; only the width of the pane changes.
	**Close:** Close the current Sample Data screen and returns you to the Samples screen. Any changes made to the display are not saved.

Title Bar

The Title Bar displays the Sample ID, Sample MSI Result and Sample Review Status. At the right edge of the Title Bar, there are two arrows that you can use to display the Sample Data screen for the previous sample or next sample in the batch. See Table 11 for more information.

Table 11. Sample Attributes and Buttons Displayed on the Title Bar of the Sample Data Screen.

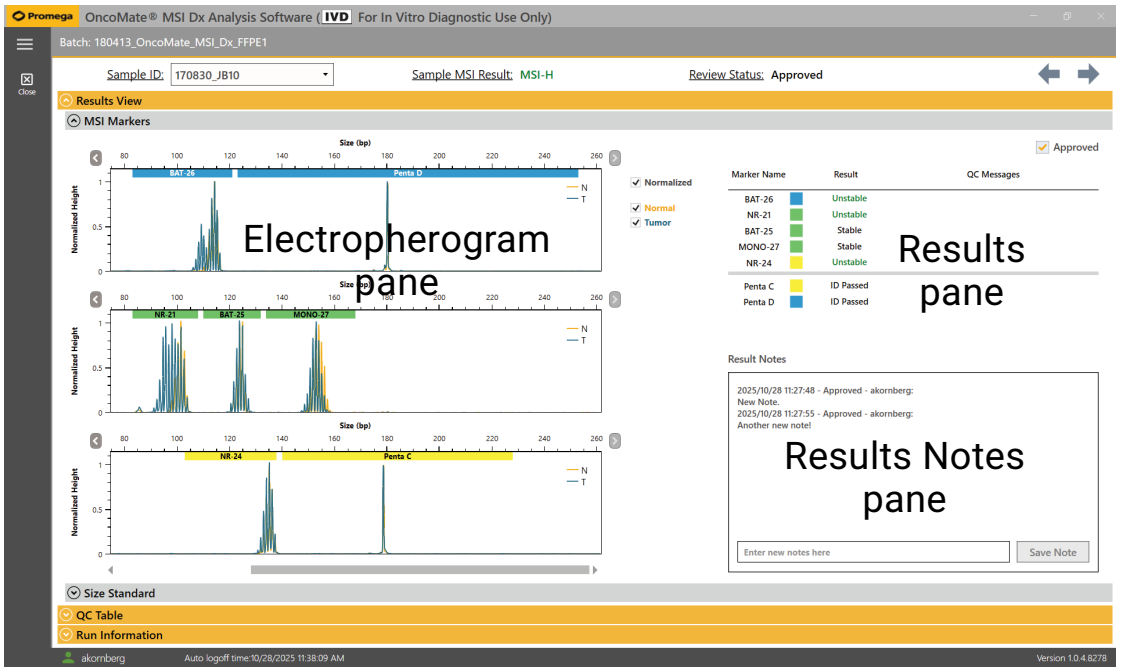
Attribute or Button	Description
Sample ID	Displays the sample name assigned to this sample pair in the Applied Biosystems® 3500 Data Collection Software during capillary electrophoresis.
Sample MSI Result	Displays the MSI result assigned to the sample pair (MSS, MSI-H or Invalid). The MSI result for the negative and positive controls is “Not Applicable”. See Section 13.1 for more information about MSI results.
Sample Review Status	Displays the sample review status assigned to the sample pair (New, Analyzed, Reviewed or Approved). See Section 13.1 for more information about the sample review status.
	**Previous Sample:** Displays the Sample Data screen for the previous sample.
	**Next Sample:** Displays the Sample Data Screen for the next sample.

Results View

The Results View is composed of two main sections: MSI Markers and Size Standard. Each section is defined by a gray heading with an **Up Arrow** icon to expand the section or a **Down Arrow** icon to hide the section.

MSI Markers

The MSI Markers section is composed of three main areas: the Electropherogram pane, Results pane and Result Notes pane (Figure 21).



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Figure 21. The MSI Markers section of the Sample Data screen.

Electropherogram Pane

The Electropherogram pane displays electropherograms for the selected sample pair or control. All three dye channels for the mononucleotide and pentanucleotide markers are shown, with the marker panels (i.e., size ranges) indicated at the top of each dye channel. The marker panels are color-coded to reflect the dye channel:

- The fluorescein-labeled BAT-26 and Penta D loci are shown in blue.
- The JOE-labeled NR 21, BAT 25 and MONO 27 loci are green.
- The ET-TMR-labeled NR 24 and Penta C loci are black.

Across dye channels, data for the normal sample are displayed in yellow, and data for the tumor sample are displayed in blue.

The Electropherogram pane includes three check boxes that allow you to customize the display (Table 12). By default, electropherograms are visible for both the normal sample and tumor sample, as indicated by checkmarks in both the "Normal" and "Tumor" check boxes, and peak intensity data are normalized.

Table 12. Check Boxes in the Electropherogram Pane.

Check Box	Description
☑ Normalized	**Normalized Check Box:** When this check box is marked, peak heights are displayed as normalized values, where peak intensities are displayed on a relative scale of 0 to 1. The tallest peak of every marker for each normal or tumor sample is assigned an intensity of "1". To view the peak intensities as absolute values in RFU, uncheck the "Normalized" check box.
☑ Normal	**Normal Check Box:** When this check box is marked, the electropherogram for the matched normal sample is visible in yellow in the Results View. Uncheck this box to hide the electropherogram for the matched normal sample.
☑ Tumor	**Tumor Check Box:** When this check box is marked, the electropherogram for the tumor sample is visible in blue in the Results View. Uncheck this box to hide the electropherogram for the tumor sample.

Note: These check boxes affect the display for the blue, green and yellow dye channels but not for the Size Standard 500.

The horizontal axis above the marker panels is the Base Pair Axis, which indicates fragment size in base pairs. The default view for each dye channel encompasses a size range of approximately 80–260bp and includes all marker panels. To move to the left and view data at less than 80bp, select the icon for the dye channel. To move to the right, select the icon. Alternatively, use the scroll bar at the bottom of the Electropherogram pane to move all dye channels to the left or right simultaneously.

The vertical axis is the Height Axis, which indicates peak intensities (i.e., peak heights). Peak intensities can be displayed as absolute values in RFU or normalized values based on the tallest peak in each marker for a given sample. By default, peak intensity is displayed as Normalized. To view the peak intensities as absolute values in RFU, uncheck the "Normalized" check box.

To zoom in to a narrower fragment size range, click anywhere within one of the dye channels, and when the double-headed diagonal arrow appears, drag the cursor to the left or right to encompass the desired size range. The arrow will change to a double-headed horizontal arrow ⟺ and the selected size range will be highlighted in yellow (Figure 22, Panel A). Likewise, you can change the scale of the Height Axis by dragging the cursor up or down. The double-headed diagonal arrow will change to a double-headed vertical arrow ⇕, and the selected size range will be highlighted in yellow (Figure 22, Panel B).

Zooming in will change the display of all three dye channels. To reset both the Base Pair Axis and Height Axis to the default settings for all dye channels, right-click on either axis for one of the dye channels and choose **Reset All**. The size range and peak height range will revert to the default ranges for all dye channels. To reset the size range to the default settings for all dye channels, right-click on the Base Pair Axis and choose **Reset Base Pair Axis**. To reset the peak height range to the default settings for all dye channels, right-click on the Height Axis and choose **Reset Height Axis**.

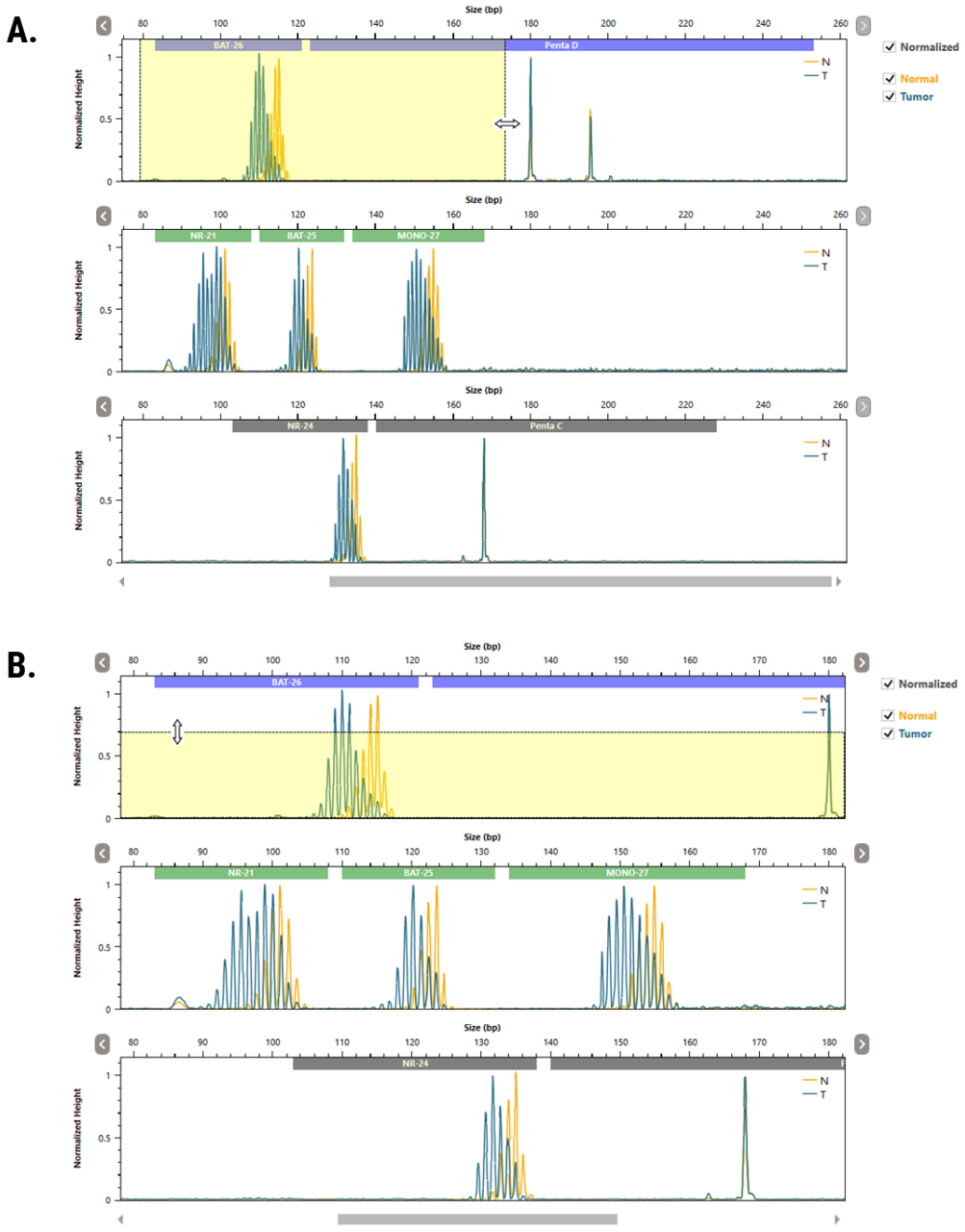


Figure 22. Zooming in on an electropherogram. Panel A. Changing the fragment size range. **Panel B.** Changing the peak height range.

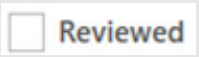
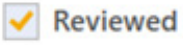
The Results Pane

The Results pane consists of a table of results and a separate check box used to acknowledge sample review by the user.

The results table shows the stability result (Stable, Unstable, No Call or Invalid) for each mononucleotide-repeat marker and the sample identity QC result (ID Passed or ID Failed) for the pentanucleotide-repeat markers. The dye label for each marker is identified by a colored box between the marker name and result: Blue for the fluorescein-labeled BAT-26 and Penta D; green for the JOE-labeled NR 21, BAT 25 and MONO 27; and yellow for the ET-TMR-labeled NR 24 and Penta C. The results table includes a QC Messages column. When a QC test failure is observed, the QC Messages column displays a brief message indicating the failure(s). You can view more details about sample QC failures in the QC Table section of the Sample Data Screen, as discussed below. QC evaluations performed by the software are described in Section 15. The results table is not shown for the positive and negative controls.

The check box in the upper right corner of the Results pane is provided for the user to record the review of a sample's results (Table 13). Information about the sample review and approval workflow is provided in Section 13.5.

Table 13. Sample Review Status Check Box in the Results Pane.

Check Box	Description
	The absence of a checkmark in the "Reviewed" check box indicates that the user has not yet completed sample review. The user acknowledges completion of the sample review by checking this check box (see Section 13.5).
	The presence of a checkmark in the "Reviewed" check box indicates that the user has completed sample review.

The Result Notes Pane

The Result Notes pane is provided to allow the user(s) to record comments about the results of a sample pair. This field may be used, for example, to describe proposed troubleshooting steps when an Invalid sample result is observed. All notes added to a sample pair are displayed in the Result Notes pane and the Result Notes column of the Samples Screen. Notes added by the user are also included in sample and batch reports.

To add a new note to a sample pair, enter the note in the field labeled "Enter new notes here" and select **Save Note**. The software will append the date, time, sample review status when the note was added, and the name of the user who added the note. Once you select **Save Note**, the note cannot be edited or deleted. However, more than one note may be added by the same or separate users.

Size Standard

The Size Standard section, located at the bottom of the Results View section, displays the superimposed electropherograms for the Size Standard 500 for both the tumor and matched normal samples (Figure 17). The section is collapsed in the default view. To expand and display the Size Standard, select the Size Standard. The horizontal axis is the Base Pair Axis. By default, the range of approximately 35–335bp is displayed. The Size Standard 500 includes size standard peaks at 60, 65, 80, 100, 120, 140, 160, 180, 200, 225, 250, 275, 300, 325, 350, 375, 400, 425, 450, 475 and 500 base pairs, but the software evaluates only the size standard peaks in the range of 60–300 base pairs during analysis.

Use the and icons to view peaks that are smaller than 35bp and larger than 335bp, respectively. The vertical axis is the Height Axis. Peak intensities are displayed as absolute values in relative fluorescent units (RFU).

You can zoom in on a specific fragment size range or peak height range by selecting and dragging within the Electropherogram pane as described above for the blue, green and yellow dye channels. To reset both the Base Pair Axis and Height Axis to the default settings, right-click on either axis and choose **Reset All**. To reset the size range, right-click on the Base Pair Axis and choose **Reset Base Pair Axis**. To reset the peak height range, right click on the Height Axis and choose **Reset Height Axis**.

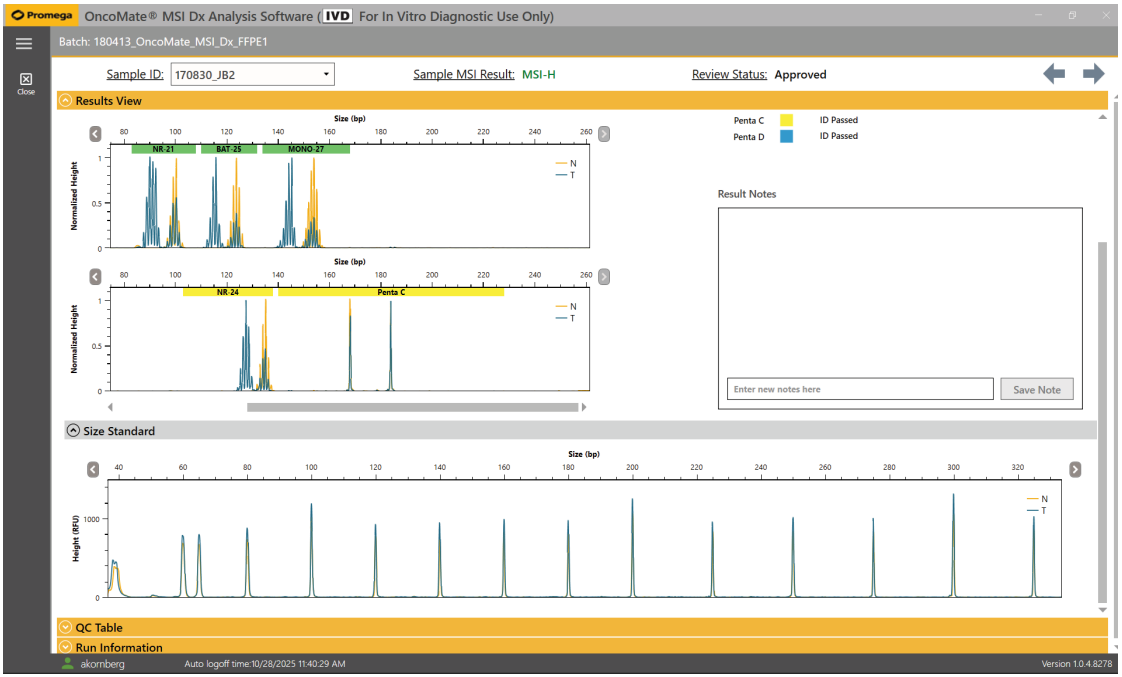
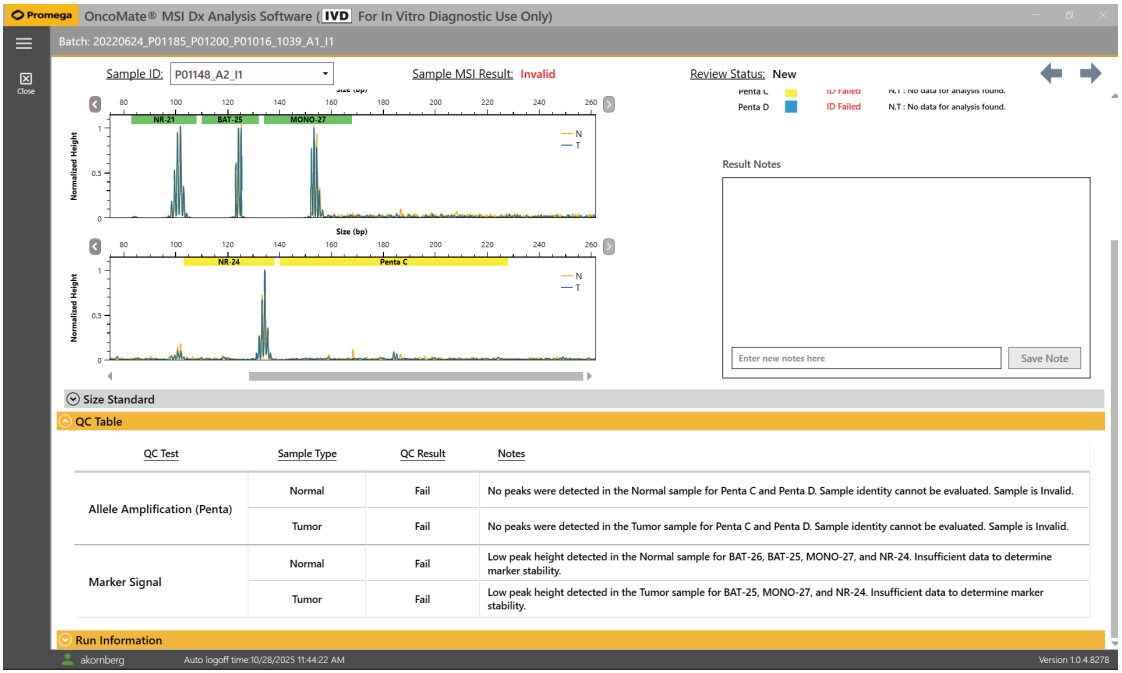


Figure 23. The Size Standard section. Expanding this section allows you to view the Size Standard 500 for the tumor and matched normal samples as superimposed electropherograms.

QC Table

The OncoMate® MSI Dx Analysis Software evaluates numerous quality attributes associated with patient samples and positive and negative controls to determine whether the batch and samples are of sufficient quality for MSI interpretation. The section is collapsed in the default view. To expand and display the QC Table, select QC Table. See Section 15.1 for more information. The results of this QC evaluation are displayed in the QC Table section (Figure 24). When all QC tests have passed, the QC Table section displays the message "All QC assessments passed". Information reported in the QC table is intended to provide information on the failure to help guide the user during troubleshooting of samples with Invalid results.



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Figure 24. The QC Table section. Expanding this section allows you to view the QC evaluation results for the selected sample.

Run Information

The Run Information section displays information about the capillary electrophoresis run and the consumables used (Figure 25). This information is extracted from the FSA file and is organized by run, capillary array, polymer, anode buffer and cathode buffer. Table 14 summarizes the information displayed in the Run Information section. The section is collapsed in the default view. To expand and display the Run Information, select Run Information.



Figure 25. The Run Information section. Expanding this section allows you to view information about the capillary electrophoresis run and capillary electrophoresis consumables.

Table 14. Content of the Run Information Section.

Run	Description
Name	The name of the run assigned during capillary electrophoresis setup in the Applied Biosystems® 3500 Dx Genetic Analyzer data collection software.
Start date/time	The date and time when the capillary electrophoresis run was initiated.
Batch name	The name of the batch. The software assigns a batch name based on the capillary electrophoresis plate name assigned for capillary electrophoresis.
Plate creator	The username of the account signed into during capillary electrophoresis.
Assay	The capillary electrophoresis assay name (e.g., OncoMate MSI Dx Assay v2.0).

Run	Description
Instrument	The instrument model, data collection mode and serial number used during capillary electrophoresis
Dye set	The dye set used to analyze the OncoMate® amplification products during capillary electrophoresis.
Data collection version	The version of the Applied Biosystems® 3500 Dx Genetic Analyzer data collection software used to collect the data.
Sample name (Normal)	The Sample Name entered into the 3500 Dx data collection software for the normal sample.
Sample name (Tumor)	The Sample Name entered into the 3500 Dx data collection software for the tumor sample.

Capillary Array	Description
Lot number	The lot number of the capillary array used to analyze the selected sample.
Serial number	The serial number of the capillary array used to analyze the selected sample.
Expiration	The expiration date of the capillary array used to analyze the selected sample.
Runs processed	The number of injections on the capillary array when the selected sample was analyzed.
Capillary array length	The length of the capillary array.
Total # of capillaries	The total number of capillaries in the capillary array.
Capillary number	The number of the capillary used to analyze the selected sample.

Polymer	Description
Type	The name of the polymer installed on the capillary electrophoresis instrument during the run.
Lot number	The lot number of the polymer.
Installed	The date and time when the polymer was installed on the capillary electrophoresis instrument.
Expiration	The expiration date for the polymer used to analyze the selected sample.
Runs processed	The number of the runs since the polymer was last changed.

Anode Buffer	Description
Type	The name of the anode buffer installed on the capillary electrophoresis instrument during the run.
Lot number	The lot number of the anode buffer.
Installed	The date and time when the anode buffer was installed on the capillary electrophoresis instrument.
Expiration	The expiration date for the anode buffer used during the capillary electrophoresis run.
Runs processed	The number of the runs since the anode buffer was last changed.

Cathode Buffer	Description
Type	The name of the cathode buffer installed on the capillary electrophoresis instrument during the run.
Lot number	The lot number of the cathode buffer.
Installed	The date and time when the athode buffer was installed on the capillary electrophoresis instrument.
Expiration	The expiration date for the cathode buffer used to analyze the selected sample.
Runs processed	The number of the runs since the cathode buffer was last changed.

13.3 Analyzing Samples

Once samples are added to a new or existing batch, these samples must be analyzed immediately by selecting **Analyze** in the task pane on the Samples Screen. Any user with the role of lab technician or lab director can analyze samples.

During analysis, the software evaluates batch and sample quality (Section 18) and assigns an MSI result of "MSI-H", "MSS" or "Invalid" to all matched normal and tumor sample pairs. The positive and negative controls are assigned an result of "Not Applicable". Until a sample is analyzed, the sample review status on the Samples Screen is "New", the MSI result is "Unanalyzed" and the QC status is undetermined (i.e., neither "Pass" or "Fail"). Once samples are analyzed, the sample review status changes to "Analyzed" and the QC status changes to "Pass" or "Fail". Analyzed samples are ready for review and approval (Section 13.5).

13.4 Marker and Sample Results

The OncoMate® MSI Dx Analysis Software analyzes microsatellite data from normal and tumor samples to assess the stability of five mononucleotide-repeat markers and assign an overall sample MSI status. Pentanucleotide repeat markers are analyzed to assess identity between the normal and tumor samples.

Table 15 and Table 16 summarize the marker stability calls and sample MSI results, respectively, returned by the analysis software. Refer to Section 15.1, Quality Controls, for information on QC checks that may affect marker stability calls and sample MSI results.

For information related to the OncoMate® MSI Dx Analysis Software results, including guidance on user troubleshooting of Invalid samples, consult the *OncoMate® MSI Dx Analysis System Technical Manual* #TM543. The methods used by the OncoMate® MSI Dx Analysis Software to determine MSI results are described in Section 7, Principles of the Procedure.

Table 15. Marker-Level Stability Calls Provided by the OncoMate® MSI Dx Analysis Software.

Value	Description
Unstable	Microsatellite instability was detected for the marker. For the mononucleotide-repeat region analyzed, the differences identified between the normal and tumor samples indicate a deletion of ≥2 nucleotides in the tumor sample.
Stable	Microsatellite instability was not detected for the marker. For the mononucleotide-repeat region analyzed, any differences identified between the normal and tumor samples did not result from a deletion of ≥2 nucleotides.
No Call 	No Call indicates that the marker stability could not be determined due to a data quality issue (see Section 15, Assay Quality Controls). View the QC Table for information about failed QC tests for the sample. See the *OncoMate® MSI Dx Analysis System Technical Manual* #TM543 for guidance on troubleshooting QC failures that lead to No Call results.
Invalid 	Invalid indicates that the quality of the sample data is unacceptable due to a critical QC failure (see Section 15, Assay Quality Controls). View the "QC Table" for for information about failed QC tests the sample or the controls. See the *OncoMate® MSI Dx Analysis System Technical Manual* #TM543 for guidance on resolving QC failures that lead to invalid results.
NA	For pentanucleotide markers, stability is not assessed, and a result of "NA" (not applicable) is reported.

Table 16. Sample-Level MSI Results Provided by the OncoMate® MSI Dx Analysis Software.

Value	Description
MSI-H	MSI-H (MSI high) indicates that two or more mononucleotide-repeat markers were identified as unstable.
MSS	MSS (MSI stable) indicates that four or more mononucleotide-repeat markers were identified as stable. Because samples with valid results that do not meet the test criteria for MSI-H are considered MSS (one or no unstable markers), the OncoMate® MSI Dx Analysis System MSS test result is a not MSI-H result.
Invalid 	Invalid indicates that the quality of the sample data is unacceptable due to a critical QC failure (see Section 15, Quality Control for Sample Batches). When a batch is marked QC Failed due to an issue with a control sample, all samples within that batch are marked as Invalid. View the QC Table for the sample or for the controls for information about failed QC tests. See the *OncoMate® MSI Dx Analysis System Technical Manual* #TM543 for guidance on resolving QC failures that lead to invalid results.

13.5 Releasing Test Results

To release test results for reporting outside the OncoMate® MSI Dx Analysis Software, the results must be reviewed and approved. The software allows the two-step process to be completed either by a single or multiple users. Lab Technician users have permissions to review a result. Lab Director users have permissions to review and approve a result. Sample and batch reports are unavailable for export from the software until a sample has been formally reviewed and then approved.

Reviewing Sample Results

Once samples are analyzed, the associated data must be reviewed by a Lab Technician or Lab Director user. Except in the case of a positive or negative amplification control QC failure (see below), the user must acknowledge the sample review by placing a check mark in the Reviewed check box in the Results pane of the Sample Data Screen (see Section 13.2, Figure 15). Any Lab Director or Lab Technician user can open batches created by other Lab Director or Lab Technician users and review samples with a status of "New". Sorting the samples by the Review Status column will help identify samples that are ready for review.

When the positive or negative amplification control fails any QC test, the result of "Invalid" is assigned to all samples in the batch. When this occurs, the user is not required to place a check mark in the Reviewed check box for samples, and the Approve button is active immediately for Lab Director users following sample analysis (see Approving Sample Results, below).

Once a sample is marked "Reviewed", the sample review status changes from "New" to "Reviewed" on the Samples screen and the Sample Data screen. All samples, including samples with an MSI result of "Invalid", must be reviewed and marked as "Reviewed" before they can be approved, except when a control fails a QC test.

Once one or more samples in a batch are marked "Reviewed" by the user, the batch review status changes to "Under Review". When all samples in a batch are reviewed, the batch review status changes to "Reviewed".

Follow the instructions below to review samples in a batch.

1. Open the batch by selecting the underlined batch name in the 'Batches' screen.
2. Select the underlined sample name in the Sample Name column to open the Sample Data screen for that sample.
3. Review the sample data, including sample and size standard electropherograms, QC evaluation results, stability calls for MSI markers, and the sample MSI result.

   Notes:

   a. We recommend reviewing electropherograms with the "Normalized" check box unchecked, as well, to detect peak height differences that may be of interest to the laboratory or useful for troubleshooting QC failures.

   b. If a QC failure was observed for the positive or negative amplification control, resulting in "Invalid" results for all samples, the user reviewing the batch should consult the QC Table for the control data to determine relevant troubleshooting steps.
4. **Optional:** Record comments about the sample review (e.g., proposed troubleshooting steps for Invalid samples) using the "Enter new notes here" field of the Result Notes pane, and select **Save Note**. Notes may be added to a sample at any point during or after the review or approval.

5. Record the sample review by placing a check mark in the "Reviewed" check box in the upper right corner of the screen.

   Note: The check mark placed in the "Reviewed" check box is saved by navigating to a different sample (i.e., selecting the right or left arrow icon) or selecting **Close** in the task pane. Until then, you can remove the check mark from the check box and the sample review status will remain "New".

6. To review additional samples in the batch, use the right or left arrow in the upper right corner to navigate to the next or previous sample, respectively. To return to the Samples screen, select **Close** in the task pane.

The reviewed samples are now ready for approval. For lab director users, the **Approve** button in the task pane is now active.

Approving Sample Results

Samples with a review status of "Reviewed" must be approved by a Lab Director user; sample approval is unavailable to Lab Technician users. Any Lab Director user can perform the complete review and approval workflow alone. Alternatively, a Lab Director user can open batches created by other Lab Director or Lab Technician users and approve samples with a status of "Reviewed". Sorting the samples by the Review Status column will help identify samples that are ready for approval. Until a sample is approved, sample and batch reports are unavailable for export from the software.

When the positive or negative amplification control fails any QC test, the result of "Invalid" is assigned to all samples in the batch. When this occurs, the user is not required to place a check mark in the "Reviewed" check box for samples, and the **Approve** button is active immediately for Lab Director users following sample analysis.

Once a sample is approved, the sample review status changes from "Reviewed" to "Approved" on the Samples screen and the Sample Data screen and the **Reviewed** check box icon changes to an **Approved** check box icon. Once all samples in a batch are approved, the batch review status on the 'Batches' screen changes to "Approved".

Follow the instructions below to approve samples in a batch.

1. Navigate to the Samples screen.
2. Select the samples to be approved.

   Notes:

   a. Samples can be selected by placing a check mark in the check box in the first column of the samples table or by selecting anywhere on the row for the sample. Select all samples by checking the check box in the title bar. Alternatively, hold down the **Ctrl** and **Shift** keys to select multiple sample rows.

   b. If a QC failure was observed, including for the positive or negative amplification control resulting in "Invalid" results for all samples, the Lab Director user approving the sample(s) may view the QC Table on the Sample Data screen to identify the cause of the QC failure.

   c. Additional comments about a sample may be recorded by the approving Lab Director by using the "Enter new notes here" field on the Sample Data screen and selecting **Save Note**.

3. From the samples task pane, select **Approve**.

4. Enter your password in the "Approve Result(s)" pop-up window to electronically sign the sample results and finalize the approval workflow.

   Note: Sample approval requires an electronic signature. The software considers the user name and password combination to be an electronic signature.

14. Reports and Data Export Files

The OncoMate® MSI Dx Analysis Software allows users with the role of Lab Technician or Lab Director to generate sample and batch reports and data export files.

Reports and data export files are saved in the Result Reports Destination Folder set by the software administrator in the Application Settings (Section 10.6). The software saves all files for a particular batch in a batch-specific folder, which is automatically created by the software and shares the same name as the batch. If reports and data export files are generated for multiple batches, the software creates multiple new folders, one for each batch.

The files that may be exported from the software are described below.

14.1 Sample Report

The OncoMate® MSI Dx Analysis Software enables Lab Technician or Lab Director users to generate a sample report for one or more approved samples in a batch, including the positive and negative controls. A separate sample report is generated for each approved sample, and each sample report is saved as a PDF document. Each page of a sample report is labeled with the user name of the person who generated the report, creation date and time, and page count.

A sample report includes the following information:

Value	Description
Sample Name (Pair)	The sample name displayed by the software for the sample pair (see Section 16).
MSI Result	The sample's MSI result.
Review Notes	Comments about the results of a sample pair added by any user to the Result Notes pane.
Batch Name	The batch name.
Run Start Date/Time	The date and time when the capillary electrophoresis run was started.
Batch QC Status	The results of the QC evaluation, either Pass or Fail.
Sample Name (Normal)	The Sample Name entered into the 3500 Dx DCS for the normal sample.
Sample Name (Tumor)	The Sample Name entered into the 3500 Dx DCS for the tumor sample.
Sample Reviewer	The user name of the person who reviewed the sample.
Reviewer Role	The user role of the person who reviewed the sample.
Review Date/Time	The date and time that the sample was reviewed.
Sample Approver	The user name of the person who approved the sample.
Approver Role	The user role of the person who approved the sample.

Value	Description
Approval Date/Time	The date and time that the sample was approved.
Marker Stability Results	Each MSI marker is listed, along with the dye color and the MSI result (Stable, Unstable or Invalid) for that locus.
QC Messages	Comments recorded as a result of the QC evaluation for each MSI marker if applicable.
Electropherograms	The electropherogram for each dye channel, with the normal and tumor samples overlaid and the marker panels labeled; normalized and non-normalized data are displayed.
Run Information	Information about the capillary electrophoresis run and consumables used to analyze the sample, including information about the capillary array, polymer, anode buffer and cathode buffer.

Sample report files are named by the software according to the report creation date and time and the sample name using the following format: [YYYYMMDDHHmm]_[sample name].pdf. For example, a sample report generated on September 7, 2021, at 10:07am for sample "101NT" is named "202109071007_101NT.pdf".

Instructions for creating sample reports are provided in Section 14.4.

14.2 Batch Summary Report

The OncoMate® MSI Dx Analysis Software enables Lab Technician or Lab Director users to generate a batch summary report for all samples in a batch. This report is available for export once all samples in the batch have been approved. The user can choose to export the batch summary report in PDF, CSV or both file formats. Identical information is provided in the PDF and CSV versions of the report.

A batch summary report includes the following information for each sample in the batch:

Batch Information	
Run Start Date/Time	The date and time when the capillary electrophoresis run was started.
Data Collection Software Version	The version of the Applied Biosystems® 3500 Data Collection Software used to gather the capillary electrophoresis data.
Batch ID	The batch name.
Run Name	The name of the capillary electrophoresis run used to generate the data.
Batch QC Status	The results of the QC evaluation, either Pass or Fail.
OncoMate Version	The version of OncoMate® MSI Dx Analysis Software used for data analysis.
Assay	The name of the assay: OncoMate® MSI Dx Analysis System.
Plate Creator	The user name of the person who was logged in to set up the 96-well plate for capillary electrophoresis analysis.
Report Date/Time	The date and time that the summary export report was created by the OncoMate® MSI Dx Analysis Software.
Reported by	The user name of the person who generated the report.

Sample Information	
Sample ID	The sample name displayed by the software for the sample pair (see Section 16).
Sample Type	The sample type. For tumor and matched normal sample pairs, the sample type is “Sample”. For positive controls, the sample type is “Positive Control”, and for negative controls, the sample type is “Negative Control”.
Sample QC Status	The result of the QC evaluation. The QC status is “Pass” or “Fail”. See Section 15 for more information about QC status.
MSI Result	The sample’s MSI result (MSI-H, MSS or Invalid).
Status	The sample’s review status.
Well	The plate well that contained the sample during capillary electrophoresis analysis. Two wells are listed for tumor and matched normal sample pairs, and one well is listed for positive and negative controls.
BAT-26	The stability call for the BAT-26 marker.
NR-21	The stability call for the NR-21 marker.
BAT-25	The stability call for the BAT-25 marker.
MONO-27	The stability call for the MONO-27 marker.
NR-24	The stability call for the NR-24 marker.
Review Date/Time	The date and time when the sample was marked as “Reviewed”.
Review User Name	The user name of the sample reviewer.
Approval Date/Time	The date and time when the sample was marked as “Approved”.
Approval User Name	The user name of the sample approver.
Review Notes	Any user comments entered during the sample review and approval processes if applicable.

Batch summary report files are named by the software according to the report creation date and time and the batch name using the following format: [YYYYMMDDHHSS]_[batch name]. For example, depending on the file format selected for the batch summary (PDF or CSV), a batch summary report generated on September 7, 2021, at 10:07am for batch “2021.09.01_OncoMateMSI” is named “202109071007_2021.09.01_OncoMateMSI.pdf” or “202109071007_2021.09.01_OncoMateMSI.csv”.

Instructions for creating batch summary reports are provided in Section 14.4.

14.3. Technical Support Export Files

Lab Technician and Lab Director users can create a data export file for troubleshooting purposes: the Technical Support Package. This file is saved as an encrypted TSE file, which can be decrypted only by Promega Technical Services Scientists. The Technical Support Package is available for export immediately following data analysis (i.e., without prior sample review or approval) and includes data for all samples and controls in a batch.

Instructions for creating the Technical Support Package file are provided in Section 14.4.

14.4 Generating Reports and Data Export Files

Generating Sample Reports from the Samples Screen

Sample reports for approved samples may be generated using the Report option in the Samples Screen task pane:

1. From the 'Batches' screen, open the batch that contains the samples of interest.
2. Select the samples of interest on the Samples screen and select **Report** from the task pane.

   Note: For the **Report** button on the task pane to be active, both controls and at least one of the selected samples must have a review status of "Approved".
3. The 'Sample Reports' window will appear (Figure 26). Select **All Approved Samples** or **Selected Approved Samples** and then **Report**. The software generates a sample report for either all approved samples or the selected subset of approved samples, depending on the option chosen. A pop-up window informs you of the location of the batch-specific folder that contains the reports.

   Select **Cancel** to return to the Samples screen without generating sample reports.

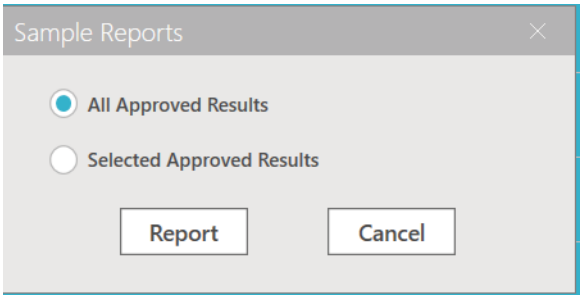


Figure 26. The 'Sample Reports' window.

Generating Reports and Exports from the 'Batches' Screen

Software reports and exports may be generated individually or all together using the Report option in the 'Batches' screen task pane. When using this option:

- Sample Reports are only generated for approved samples and controls.
- Batch Summary Reports are only generated once all samples and controls in the batch are approved.
- Technical Support Export files may be generated at any point following batch analysis.

To generate reports and exports from the 'Batches' screen:

1. Select the batch(es) of interest on the 'Batches' screen and select **Report** from the task pane.

   Note: To select multiple batches, hold down the **Shift** or **Ctrl** key and select other batches in the 'Batches' screen.

2. The 'Reports' window will appear (Figure 27). Select the reports you wish to generate and then **Report**. The software generates the requested reports and exports, and a pop-up window informs you of the location of the batch-specific folder that contains the files.

   Select **Cancel** to return to the 'Batches' screen without generating sample reports.

   Note: If none of the samples in the selected batch have a review status of "Approved", an error message informs you that no samples are available for reporting. However, if the Technical Support Package option was selected, these reports will still be created in the destination folder. Select **Ok** to return to the 'Batches' screen.

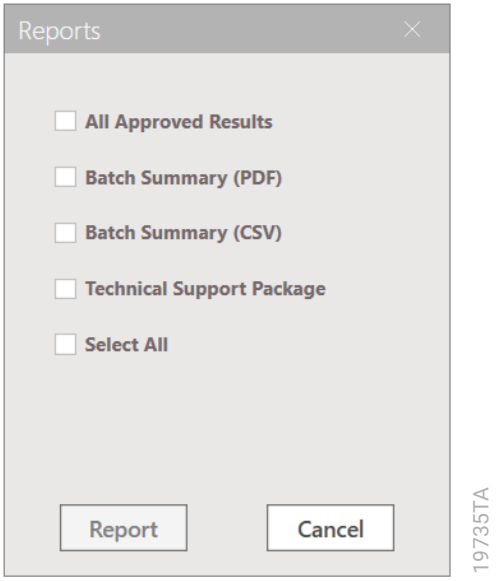


Figure 27. In the 'Reports' window, choose the type(s) of reports and/or data export files to create.

15. Assay Quality Controls

The OncoMate® MSI Dx Analysis Software analyzes controls and interprets normal and tumor samples in the context of the capillary electrophoresis plate on which they were processed. Samples and controls are assigned to a sample batch based on the capillary electrophoresis Plate name assigned during capillary electrophoresis setup. Each sample within a batch consists of a normal and tumor sample, which are labeled during capillary electrophoresis setup following prescribed conventions (see Section 16) that are used by the software to correctly pair samples. Additional requirements are necessary to define a set of samples and amplification controls as a complete and valid sample batch. See Section 12.1, Definition of a Sample Batch, and Section 15.1, Quality Control Requirements, for information about these requirements.

See the *OncoMate® MSI Dx Analysis System Technical Manual* #TM543 for instructions on sample labeling during capillary electrophoresis setup.

15.1 Data Quality Requirements

The OncoMate® MSI Dx Analysis Software evaluates several quality attributes associated with control and patient samples to determine whether the batch and samples are of sufficient quality for MSI interpretation. Data quality checks performed by the software and the consequences of failures are summarized below and detailed in Table 17.

Any QC failure observed for an amplification control will result in a batch QC failure, and all patient samples within the batch will have a sample result of Invalid. QC failures for patient samples can have the following outcomes:

- Most QC failures detected by the software are considered severe; marker and sample results of Invalid will be returned in response to these failed tests.
- QC failures for three tests, Mononucleotide Amplification QC, Marker Signal QC and Intensity Difference QC, relate to insufficient data at the marker level and return a marker result of No Call.

  Note: When No Call marker results are observed, a sample result of MSI-H is returned if two or more mononucleotide-repeat markers were identified as unstable, and a sample result of MSS is returned if four or more mononucleotide-repeat markers were identified as stable. When these criteria are not met, a sample result of Invalid is returned because the sample interpretation is ambiguous.

When a sample or control fails one or more QC tests, the failure reason is displayed on the Sample Data screen in abbreviated form in the “QC Messages” column of the results table and in full form in the QC Table. The QC Table is accessed by selecting QC Table and expanding the QC Table section (see Figure 21).

See the *OncoMate® MSI Dx Analysis System Technical Manual* #TM543 for guidance on resolving QC failures that lead to Invalid sample results.

Note: Data analysis using the OncoMate® MSI Dx Analysis Software is more sophisticated than the basic analysis performed within the Applied Biosystems® 3500 Dx Genetic Analyzer data collection software. Quality warnings displayed in the DCS may be triggered by broad peaks, signal spikes, etc., that are ignored by the OncoMate® software or that occur outside of the analysis range relevant for MSI status determination. Therefore, analyze all samples using the OncoMate® MSI Dx Analysis Software as the final assessment of data quality.

Table 17. Automated Data Quality Control Tests Implemented in the OncoMate® MSI Dx Analysis Software. Invalid results are assigned at the marker and sample levels in response to critical QC failures (i.e., failures that require repeated sample analysis), while No Call marker results are assigned for non-critical QC Failures associated with insufficient information for a given marker. When a control sample fails any QC test, a sample result of Invalid is assigned to all patient samples in the batch. Consult the Troubleshooting section of the *OncoMate® MSI Dx Analysis System Technical Manual* #TM543 for guidance on resolving QC failures.

QC Test	Description of QC Test and QC Message Returned by the Software When a Failure is Observed[1]	Sample Types Evaluated[2]	Patient Sample Result for Failed QC Test[3]
Sizing Quality QC (Size Standard 500)	Quality of the Size Standard 500 fragments is assessed based on peak shape, size matching, and a size calling curve. "Poor sizing quality observed in the [control] [normal/ tumor/ normal and tumor] sample(s). Poor quality data cannot be used to determine sample MSI Status. [Sample batch is Invalid] [Sample is Invalid]."	+, –, N, T	Sample Invalid[3]
Negative Control QC (All markers)	For negative amplification controls, there must be no peaks detected above the analytical threshold. "Peaks were detected in the negative amplification control. Artifact(s) present or the batch may be contaminated with DNA. Sample batch is Invalid."	–	All Samples Invalid
Control Identity QC (Pentanucleotide markers)	For the positive amplification control, the alleles present in the pentanucleotide markers must match the expected alleles for the 2800M control DNA within ±1.5 base pairs. "2800M Control DNA was not used as the positive amplification control or an electrophoresis issue was encountered. Sample batch is Invalid."	+	All Samples Invalid
Off-Scale Peak QC (All Markers)	The intensity (RFU) of peaks in a marker must not exceed the maximum detectable range of the capillary electrophoresis instrument. "Marker peak height is too high to evaluate in the [control] [normal/ tumor/ normal and tumor] sample(s). Data with excessive peak intensity cannot be used to determine sample MSI Status. [Sample batch is Invalid] [Sample is Invalid]."	+, N, T	Marker Invalid Sample Invalid[3]
Spectral Pull-Up QC (All Markers)	Allele peaks that are aligned by length in separate dye channels are evaluated for spectral pull-up (i.e., signal bleed-through between dye channels). "Spectral pull-up (bleed-through) detected in the [control] [normal/ tumor/ normal and tumor] sample(s). Poor quality data cannot be used to determine sample MSI Status. [Sample batch is Invalid] [Sample is Invalid]."	+, N, T	Marker Invalid Sample Invalid[3]

QC Test	Description of QC Test and QC Message Returned by the Software When a Failure is Observed[1]	Sample Types Evaluated[2]	Patient Sample Result for Failed QC Test[3]
Broad Peak QC[4] (All Markers)	The width of peaks must not exceed the value assigned for MSI analysis. "Broad peak(s) detected in the [control] [normal/ tumor/ normal and tumor] sample(s). Poor quality data cannot be used to determine sample MSI Status. [Sample batch is Invalid] [Sample is Invalid]."	+, N, T	Marker Invalid Sample Invalid[3]
Pentanucleotide Amplification QC (Pentanucleotide markers)	At least one allele above the analytical threshold (RFU) must be present within each pentanucleotide-repeat marker. "No peaks were detected in the [control] [normal/ tumor/ normal and tumor] sample(s). [Sample batch is Invalid] [Sample identity cannot be evaluated. Sample is Invalid]."	+, N, T	Marker Invalid Sample Invalid[3]
Mononucleotide Amplification QC (Mononucleotide markers)	At least one allele above the analytical threshold (RFU) must be present within each mononucleotide-repeat marker. "No peaks were detected in the [control] [normal/ tumor/ normal and tumor] sample(s). [Sample batch is Invalid] [Insufficient data to determine marker stability]."	+, N, T	Marker No Call[3,5]
DNA Contamination QC (Pentanucleotide markers)	For each pentanucleotide marker, there can be no more than two alleles present in the normal sample. "More than two alleles were detected in the [control] [normal] sample. Artifact(s) present or the [batch] [sample] may be contaminated with DNA. [Sample batch is Invalid] [Sample is Invalid]."	+, N	Marker Invalid Sample Invalid[3]
Patient Sample Identity QC (Pentanucleotide markers)	For each pentanucleotide marker, the alleles identified in the normal sample must be present in the tumor sample (within ±1.5 base pair). "An allele in the normal sample is missing from the tumor sample. Samples from different patients may have been paired. Sample is Invalid."	T	Marker Invalid Sample Invalid
Marker Signal QC (Mononucleotide markers)	For mononucleotide markers that have been interpreted as stable, allele peak height(s) in the normal and tumor samples must be ≥700 RFU to ensure assay sensitivity. "Low peak height detected in the [normal/ tumor/ normal and tumor] sample(s). Insufficient data to determine marker stability."	N, T	Marker No Call[5]

QC Test	Description of QC Test and QC Message Returned by the Software When a Failure is Observed[1]	Sample Types Evaluated[2]	Patient Sample Result for Failed QC Test[3]
Intensity Difference QC (Mononucleotide markers)	For mononucleotide markers that have been interpreted as stable, the ratio of peak heights, N/T, must be <10 to ensure assay accuracy; for mononucleotide markers with subtle shifts that have been interpreted as unstable, the ratio of peak heights, T/N, must be <10 to ensure assay accuracy. "An excessive intensity difference was observed between the normal and tumor samples. Marker stability cannot be determined."	Sample pair	Marker No Call[5]
Unexpected Peak(s) QC (Mononucleotide markers)	For mononucleotide markers, DNA fragments indicative of instability must be absent from the normal sample. "Unexpected peaks detected. Artifact(s) present, or the normal and tumor samples may have been switched. Sample is Invalid."	Sample pair	Marker Invalid Sample Invalid

[1]The QC messages returned by the software vary when a control sample or a patient sample (normal, tumor, or normal and tumor) fails a QC test. Bracketed statements within the messages, displayed above, indicate the specific language returned for a control or patient sample failure.

[2]N, normal sample; T, tumor sample; +, positive control; –, negative control

[3]The MSI result is Invalid for all patient samples in a batch when a control sample fails any QC test.

[4]The known broad-peak artifact in NR-21 (approximate range 83bp to 90bp) is unrelated to instability and ignored by the OncoMate® MSI Dx Analysis Software. The software will return a result of Invalid when a broad peak other than the known NR-21 artifact is observed.

[5]The software will return a sample-level MSI result for samples with No Call marker results when sufficient data are available to make a call (≥2 Unstable markers or ≥4 Stable markers) and no Invalid results are observed. The software assigns an MSI result of Invalid when marker results are ambiguous.

15.2 Description of OncoMate® MSI Dx Analysis Software Quality Control Tests

Sizing Quality QC

The OncoMate® MSI Dx Analysis Software analyzes Size Standard 500 DNA fragment data to evaluate the sizing quality of each sample and control. Sizing quality issues are typically associated with an injection failure during capillary electrophoresis. In these cases, failures are observed in data collected from a single capillary. Sizing quality failures observed in data collected from every capillary of an injection may indicate user error in the preparation of the capillary electrophoresis loading cocktail.

When a sizing quality failure is observed, no data are displayed for the failing normal or tumor sample by the OncoMate® MSI Dx Analysis Software, and the user must review the sample electropherogram using the Applied Biosystems® 3500 Dx Genetic Analyzer Data Collection Software (DCS) to guide troubleshooting. Samples exhibiting a sizing quality QC failure commonly display no (or few) size standard peaks or peaks that deviate from the expected size standard performance. Most commonly, a sizing quality failure will be observed as peaks that broaden (i.e., lose resolution) with increasing size (Figure 28). However, a sizing quality failure will also be returned for size standard fragments that show an unexpected pattern of peak heights, when an electrophoresis artifact is detected between the 60bp and 300bp size standard fragments, and/or when one or more size standard peaks exceeds 10,000 RFU. Data quality is not evaluated for size standard fragments >300bp, as these fragments are not used for sizing of OncoMate® MSI Dx Analysis System amplicons.

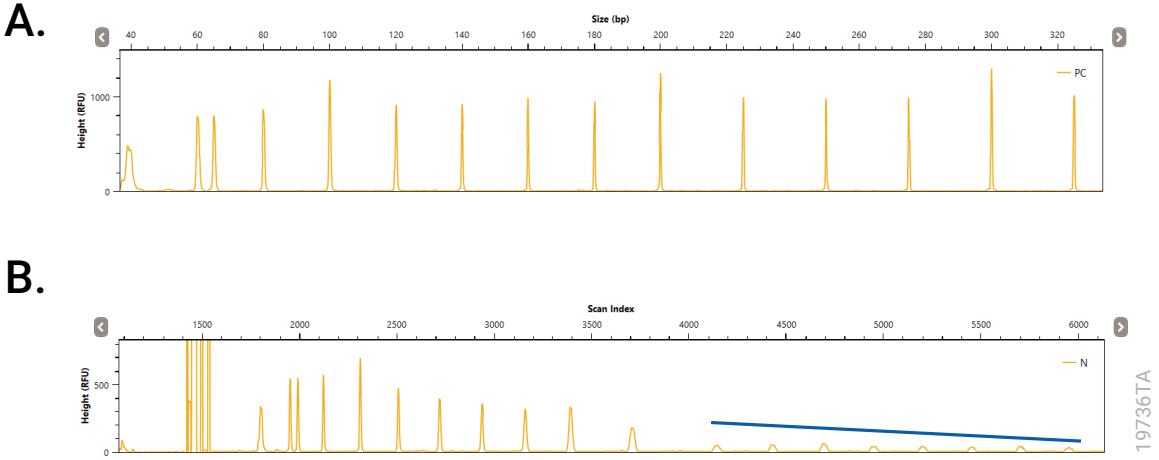


Figure 28. Expected and failing Size Standard 500 performance. Panel A. Thirteen Size Standard 500 DNA fragments between 60bp and 300bp are analyzed in each sample or control. Size Standard 500 DNA fragments >300bp are not used for sizing by the OncoMate® MSI Dx Analysis Software. **Panel B.** Size Standard 500 DNA fragment peaks broaden and decrease in intensity as fragment size increases, this downward slope of Size Standard 500 DNA fragment peaks (blue line) leads to a decrease in the number of expected peaks and a Sizing Quality QC failure.

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Negative Control QC

A negative amplification control must be analyzed as part of every sample batch. The OncoMate® MSI Dx Analysis software evaluates the negative amplification control for fragment peak(s) above the 175 RFU analytical threshold in the sample dye channels (blue, green and yellow/black). A Negative Control QC failure indicates that batch contamination may have occurred, compromising the integrity of all samples in the batch. Therefore, all samples in a batch with a failed negative control sample will have an MSI result of "Invalid".

Control Identity QC

A positive amplification control sample, prepared with 2800M Control DNA, must be analyzed as part of every sample batch. The OncoMate® MSI Dx Analysis software evaluates the Penta D and Penta C markers in the positive amplification control to verify that 2800M Control DNA was used for the positive amplification control. The 2800M positive amplification control exhibits two alleles at each pentanucleotide-repeat marker. The Control Identity QC test requires that these alleles are detected within the following size ranges (bp):

a. Penta D: 193.5–196.5 and 199–202

b. Penta C: 176.5–179.5 and 182–185

A failure of the positive control to meet these criteria indicates potential data quality issues for the entire batch of samples. Therefore, the OncoMate® MSI Dx Analysis software will assign an MSI result of "Invalid" to all patient samples analyzed in a batch when a positive control identity QC failure is observed.

Off-Scale Peak QC

Capillary electrophoresis instruments have a limited range to detect fluorescent signals from dye-labeled DNA fragments. In some situations, the fluorescent signal from OncoMate® MSI Dx Analysis System amplification products may exceed the upper limit of the fluorescent detector on the instrument. When this happens, an Off-Scale Peak QC flag will be returned by the capillary electrophoresis instrument and an Off-Scale Peak QC failure will be reported by the OncoMate® MSI Dx Analysis Software. Off-scale peak intensities may result in assay artifacts, and signal bleed-through into other dye channels may be mistaken for an allele in a normal or tumor sample, compromising MSI analysis. Therefore, patient samples with off-scale peaks will have an MSI result of "Invalid". Off-scale peaks observed for the 2800M positive amplification control indicates a systemic issue when preparing or amplifying OncoMate® MSI Dx Analysis System reactions and potential data quality issues for the entire batch of samples being tested. Therefore, the OncoMate® MSI Dx Analysis software will assign an MSI result of "Invalid" to all patient samples analyzed in a batch when an Off-Scale Peak QC failure is observed in the 2800M positive control.

Spectral Pull-Up QC

When off-scale results are observed or when spectral calibration of the capillary electrophoresis instrument is inadequate (e.g., after moving the instrument or because of adjustments to the instrument optics during a service call), fluorescent signals from dye-labeled fragments may be detected outside of the intended color channel. This situation is referred to as spectral pull-up or bleed-through and results in compromised MSI data quality. The OncoMate® MSI Dx Analysis Software evaluates all samples and the positive amplification control for spectral pull-up. Patient samples with spectral pull-up peaks will have an MSI result of "Invalid". Spectral pull-up observed for the 2800M positive amplification control indicates a systemic quality issue with the capillary electrophoresis run. Therefore, the OncoMate® MSI Dx Analysis software will assign an MSI result of "Invalid" to all patient samples analyzed in a batch when a spectral pull-up QC failure is observed in the 2800M positive control.

In some situations, genuine fragment peaks may be aligned across dye channels and confused for bleed-through during data review. For aligned, tentative bleed-through peaks, the lower-intensity potential pull-up peak is accepted as a genuine peak when present at ≥10% of the peak height of the higher-intensity source-peak.

Broad Peak QC

Broad fragment peaks may be observed sporadically in OncoMate® MSI Dx Analysis System data because of abnormal PCR amplification or capillary electrophoresis analysis. These peaks exhibit a gentle rise and fall pattern that spans several base pairs and are easily distinguished from genuine fragment peaks, which rise and fall sharply across a 1bp to 2bp span. Patient samples with one or more broad peaks will have an MSI result of "Invalid". Broad peaks observed for the 2800M positive amplification control potentially indicate a broader issue with PCR amplification or the capillary electrophoresis run. Therefore, the OncoMate® MSI Dx Analysis software will assign an MSI result of "Invalid" to all patient samples analyzed in a batch when a Broad Peak QC failure is observed in the 2800M positive control.

A known broad-peak amplification artifact is observed between 83bp and 90bp in the OncoMate® MSI Dx Analysis System NR-21 marker. This artifact is automatically ignored by the OncoMate® MSI Dx Analysis Software.

Pentanucleotide Amplification QC

The OncoMate® MSI Dx Analysis software evaluates the Penta C and Penta D markers in patient samples and the 2800M positive control for amplification (i.e., the presence of one or more DNA fragment peaks ≥175 RFU, the system analytical threshold). When no allele is detected for one or more pentanucleotide-repeat markers, the identity of the normal and tumor sample pair cannot be verified. This situation results in a Pentanucleotide Amplification QC failure, a Sample Identity QC failure, and an "Invalid" sample MSI result. Missing pentanucleotide-repeat alleles in the 2800M positive amplification control indicate potential data quality issues for the entire batch of samples. Therefore, in batches where the positive control fails the Pentanucleotide Amplification QC, all samples in the batch are assigned an MSI result of "Invalid".

Mononucleotide Amplification QC

The OncoMate® MSI Dx Analysis software evaluates the five mononucleotide-repeat markers in patient samples and the 2800M positive control for amplification (i.e., the presence of one or more DNA fragment peaks ≥175 RFU, the system analytical threshold). For patient samples, when no allele is detected for a mononucleotide-repeat marker in the normal and/or tumor sample, the stability of the affected marker cannot be determined, and the software will assign a "No Call" result for that marker. Missing mononucleotide-repeat alleles in the 2800M positive amplification control indicate potential data quality issues for the entire batch of samples. Therefore, in batches where the positive control sample fails the Mononucleotide Amplification QC, all samples in the batch are assigned an MSI result of "Invalid". Note that "No Call" marker stability results do not automatically lead to an "Invalid" sample result. An "Invalid" MSI result is assigned to a sample with "No Call" marker results when the interpretation of sample MSI status is ambiguous (i.e., when a sample MSI result cannot be determined from the marker stability results).

DNA Contamination QC

The OncoMate® MSI Dx Analysis Software evaluates the pentanucleotide-repeat markers in the normal sample and the 2800M positive control for extra peaks that may indicate sample contamination. The DNA Contamination QC fails when three or more alleles are detected for Penta C or Penta D. This situation suggests that the normal sample has been contaminated at some point during the assay workflow with human DNA or amplified product. DNA Contamination QC failure observed in the 2800M positive amplification control sample indicates potential data quality issues for the entire batch of samples. Therefore, in batches where the positive control fails the DNA Contamination QC, all samples in the batch are assigned an MSI result of "Invalid". Note that genomic instability associated with certain tumors may result in more than two alleles being present in a tumor sample. Therefore, tumor samples are not evaluated for the DNA Contamination QC. However, the potential for >2 Penta alleles in the tumor sample can lead to a DNA Contamination QC failure if a tumor sample exhibiting genomic instability is switched, physically or in silico, with a normal sample at some point during the assay workflow.

Patient Sample Identity QC

The OncoMate® MSI Dx Analysis Software compares the normal and tumor alleles detected in each pentanucleotide-repeat marker to provide confidence that the normal and tumor sample pair were derived from the same patient. The Patient Sample Identity QC passes when all alleles identified in the normal sample are also present in the tumor sample. Patient Sample Identity QC fails when an allele identified in the normal sample is missing from the tumor sample and/or when other upstream QC failures affecting pentanucleotide-repeat markers prevent sample identity assessment. Genomic instability associated with certain tumors may result in more or fewer alleles being present in the tumor sample relative to the normal sample. The presence of additional alleles in the tumor sample has been observed and does not result in Patient Sample Identity QC failure. Additional alleles in the tumor sample at the Penta markers does not indicate MSI. On the other hand, a missing allele in the tumor sample may indicate a sample switch or loss of heterozygosity (LOH) at the marker. Sample pairs that fail the Patient Sample Identity QC are assigned an MSI result of "Invalid".

Marker Signal QC

For each mononucleotide-repeat marker tentatively interpreted as stable, the OncoMate® MSI Dx Analysis software evaluates the peak intensities of the normal and tumor samples to confirm the stable call. The Marker Signal QC fails when peak intensity is <700 RFU for the normal and/or tumor sample. A Marker Signal QC failure indicates that the sample peak intensity is insufficient to ensure the assay's sensitivity to detect differences indicative of instability. The software assigns a "No Call" result for the marker stability in response to a Marker Signal QC failure. Note that "No Call" marker stability results do not automatically lead to an "Invalid" sample result. An "Invalid" MSI result is assigned to a sample with "No Call" marker results when marker interpretation is ambiguous.

Intensity Difference QC

The OncoMate® MSI Dx Analysis Software compares the peak intensities in the normal and tumor samples for each mononucleotide-repeat marker to ensure the accuracy of the marker stability call. When peak heights differing by ≥10-fold are observed for the normal and tumor samples, changes to the allelic profile are possible that may either a) obscure subtle peak difference indicative of instability (observed when the peak intensity is greater for the normal sample than the tumor sample), or b) mimic subtle peak difference indicative of instability (observed when the peak intensity for the tumor sample is greater than the normal sample). Once a tentative stability result is determined for a marker, the OncoMate® MSI Dx Analysis Software evaluates marker peak heights using the following two-part logic: 1. For mononucleotide markers that have been interpreted as stable, the ratio of peak heights, N/T, must be < 10 to ensure assay accuracy; 2. For mononucleotide markers exhibiting subtle shifts that result in an unstable call, the ratio of peak heights, T/N, must be <10 to ensure assay accuracy. The software assigns a "No Call" result for the marker stability in response to an Intensity Difference QC failure. Note that "No Call" marker stability results do not automatically lead to an "Invalid" sample result. An "Invalid" MSI result is assigned to a sample with "No Call" marker results when the interpretation of sample MSI status is ambiguous (i.e., when a sample MSI result cannot be determined from the marker stability results).

Unexpected Peaks QC

The OncoMate® MSI Dx Analysis Software assesses differences observed between the normal and tumor samples for each mononucleotide-repeat marker to ensure the accuracy of tentatively stable marker results. The most common causes of an Unexpected Peaks QC failure are the presence of an unexpected artifact peak in the normal sample or the presence of peaks indicative of instability in the normal sample. The latter situation typically results from the accidental switching, physically or in silico, of an unstable tumor sample for the normal sample from the same patient at some point during the assay workflow. Sample pairs that fail the Unexpected Peaks QC are assigned an MSI result of "Invalid".

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16. Sample-Naming Conventions

During capillary electrophoresis run setup, information for paired samples (sample name and normal/tumor designation) must be entered into the Applied Biosystems® 3500 Dx Genetic Analyzer DCS following prescribed conventions. Two conventions are recognized by the software, and the user may choose between these based on the laboratory's workflow and preferences. The analysis software will correctly identify and import normal and tumor sample pairs when either of the following conventions is used:

Option 1: Identical sample names, normal and tumor designation in user defined field #1

When identifying sample pairs using option 1, matched normal and tumor samples must be assigned identical sample names in the Sample Name field in the Applied Biosystems® 3500 Dx Genetic Analyzer DCS. Additionally, an N or T must be placed in user defined field #1 (UDF1) to indicate the normal or tumor sample, respectively. The N or T designation is case-insensitive and should not be used for amplification controls. See the *OncoMate® MSI Dx Analysis System Technical Manual* #TM543 for instructions on sample identification and labeling using the UDF1 field.

Option 2: All identifying information in the sample name

When identifying patient sample pairs using option 2, all necessary sample information is entered in the Sample Name field in the Applied Biosystems® 3500 Dx Genetic Analyzer DCS. Using option 2, the user may include other sample metadata in UDF1 so long as a single N or T is not entered. The information entered in the Sample Name field consists of three parts, [Part 1]_[Part 2]_[Optional Part 3], described as follows:

- **Part 1:** Matched normal and tumor samples must be assigned identical Part 1 portions of the sample name. The text in Part 1 is case-sensitive. The Part 1 text is the Sample Name displayed in the OncoMate® MSI Dx Analysis Software.
- **Part 2:** An N or T must be placed in the Part 2 portion of the sample name to indicate the normal and tumor sample, respectively. The N or T designation is case-insensitive. While underscores are shown in the introductory text (above), spaces (" "), underscores ("_"), or dashes ("-") may be used as the delimiter character surrounding Part 2 of the sample name. Additionally, mixed delimiter characters may be used, as shown in the examples below.
- **Optional Part 3:** The Part 3 portion of the sample name may contain additional sample information desired by the laboratory. The Part 3 portion of the sample name may differ between the normal and tumor samples and can be empty for one or both members of the sample pair. When no text is entered for Part 3, the delimiter following the N or T is not required.

The following are just a few examples of acceptable text for paired samples when using option 2:

"Sample 1_N_5hdjdw8" and "Sample 1_T_5hdjdw9" (Sample name displayed: "Sample 1")

"2-N" and "2_T asi873nmx-12n8" (Sample name displayed: "2")

"Patient_3-N-9iujkgrj83r" and "Patient_3_T" (Sample name displayed: "Patient_3")

Note: Improperly identified samples cannot be paired by the OncoMate® MSI Dx Analysis Software and will not be imported or analyzed. Ensure patient privacy when labeling or naming samples. Do not include any protected health information, such as names, dates of birth, medical record numbers, or other identifiers that could directly or indirectly be used to identify an individual.

17. Troubleshooting

For questions not addressed here, please refer to the *OncoMate® MSI Dx Analysis System Technical Manual* #TM543 or contact your local Promega Branch Office or Distributor. Contact information available at: **www.promega.com**. Email: **genetic@promega.com**

Symptoms	Causes	Comments and Corrective Actions
During software installations, a restart is requested but the installer does not automatically reinitiate after the PC restarts	Continuous administrator privileges are required during software installation.	Programs such as Admin By Request, which grant temporary administrator privileges to non-admin users, may cause installation failures. This can occur when the OncoMate® MSI Dx Analysis Software installer requires a system restart, but the temporary admin rights are not reactivated promptly afterward, preventing the installer from resuming. If this issue occurs, restart the PC and have a user with full administrator privileges log in with their Windows® account. The installer will then restart automatically and continue the installation.
After selecting a button or menu item, the desired function does not occur.	Not all functions are available at all times or by all users within the OncoMate® MSI Dx Analysis Software.	Consult the section in this technical manual that describes the function to see whether there are restrictions on how and when it can be used and by whom.
Sample FSA files will not import.	Sample files do not conform to specific requirements necessary for import and analysis by the OncoMate® MSI Dx Analysis Software.	See Section 12.1, Sample Batch Definition and Requirements, and Section 16, Sample-Naming Conventions, for instructions on importing FSA files and the requirements to which they must conform. Sample files with errors in the Sample Name or UDF1 field(s) can be opened, edited and saved using the Applied Biosystems® 3500 Dx Genetic Analyzer data collection software. See the *Applied Biosystems® 3500 Dx Genetic Analyzer and 3500xL Dx Genetic Analyzer IVD User Guide* for additional information.

Symptoms	Causes	Comments and Corrective Actions
Not all sample FSA files were imported.	An error was made when entering sample information into the Applied Biosystems® 3500 Dx Genetic Analyzer DCS.	Sample files with errors in the Sample Name or UDF1 field(s) can be opened, edited and saved using the Applied Biosystems® 3500 Dx Genetic Analyzer data collection software. See the *Applied Biosystems® 3500 Dx Genetic Analyzer and 3500xL Dx Genetic Analyzer IVD User Guide* for additional information.
	The Reinject option was used in the Applied Biosystems® 3500 Dx Genetic Analyzer DCS during an active capillary electrophoresis run and reinjected samples were not imported.	Samples that are reinjected using the Reinject option in the DCS will have the same sample names as those analyzed during the initial injection. Open the FSA files for the reinjected samples in the DCS, and rename the matched Normal and Tumor samples (e.g., add a "_RI" suffix to the sample name). Repeat the import operation in the OncoMate® MSI Dx Analysis Software. Archiving the batch may be required for successful import of renamed samples.
User cannot log in to the OncoMate® MSI Dx Analysis Software.	The user account may be suspended because the maximum number of failed login attempts allowed in the OncoMate® MSI Dx Analysis Software was exceeded.	Consult with the software Administrator to amend the status of the user account. Reactivating suspended accounts is described in Section 10.7, Locking and Unlocking a User Account.
	The user account was inactivated by the site administrator.	
When defining a new password for a user account, the new password is not accepted.	The attempted password is not eight or more characters or fails to conform to the additional requirements set by the site administrator.	Consult with the software Administrator and Section 10.3, Configuring Application Settings, to determine minimum requirements for password use and reuse.
The list of sample batches is excessive, affecting usability or software performance.	Approved batches have not been Archived.	Sample batches can be archived and purged from the OncoMate® MSI Dx Analysis Software. See Section 12.5, Archiving a Sample Batch, for information. Best practice is to Archive a few batches at a time. Attempting to Archive too many batches at one time may cause the software to timeout before the archiving process is finished.

Symptoms	Causes	Comments and Corrective Actions
When opened, Technical Support Export files do not contain understandable information.	Technical Support Export files are encrypted and are only readable by Promega Technical Services.	Not applicable.
The database backup operation fails with a reported error.	The user and/or SQL database have insufficient access to the database backup destination folder set by the Admin user in the Application Settings.	Consult with your local IT group to ensure that the OncoMate® software Admin assigns a Database Backup Destination Folder where Windows® users and the "Network Service" user, which is assigned to the SQL Server, have Modify permissions.

18. References

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19. Summary of Changes for Rev1

1. Updated the Intended Use text in Section 4.
2. Updated first paragraph in Section 5.
3. Added references to Section 18.
4. Renumbered existing tables.

Promega



PROMEGA
2800 Woods Hollow Rd.
Madison, WI USA

Updated 10/26

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