

## Release Notes

Bergisch Gladbach, 2024-04-04

### MACSQuantify™ Tyto® Software 3.1

The Software Release Notes shall provide the user with information about software changes, new features, improvements and bug fixes.

In general, the MACSQuantify Tyto Software version 3.1 is designed to migrate the system from the Microsoft® Windows® based operating system (OS) to a more secure and closed Miltenyi Biotec's proprietary MBCore OS, based on Linux®. In addition, this software includes automated features for initial and daily calibration to improve instrument stability and provide standardization across instruments. More importantly, it also includes features such as user management system (UMS), audit trail, run report with e-signature, and lock screen functionality to enable users to be compliant to US FDA 21 CFR Part 11. The 21 CFR Part 11 compliance software is available as an "add-on" for additional costs and needs to be installed by service during the planned visit. Additionally, this release further improves software stability.

Please note: An upgrade of the "Back Scatter Module" which enables scatter-based sorts and sorting with dim markers on the Tyto might be necessary depending on the hardware status of your instrument. Tyto users who have already upgraded their hardware as part of MACSQuantify Tyto Software version 1.0 or higher installation can upgrade their software directly to version 3.1. This software is compatible from MACSQuant Tyto Cell sorters with Abeco 3 PCs with CFast card and higher (from S/N :10041 onwards). Newly produced instruments have this software preinstalled. This software update will be performed during the next, upcoming regular service maintenance visit.

#### Operating system MBCore 0.22.1

The update to our new OS MBCore equips the MACSQuant Tyto Cell Sorter with a Miltenyi-own OS. MBCore is based on a long-term support (LTS) Linux-kernel (for more information please visit [Linux 5.4](#)) and it is intended to replace the currently embedded Windows 7 with Extended Security Updates.

MBCore, manages both hardware and software resources of the MACSQuant Tyto Cell Sorter; it provides a platform for the data acquisition software MACSQuantify Tyto Software 3.1 as well as access to network

resources, data exchange, and live support. The software runs in a kiosk mode, to reduce unauthorized access to the system. This software version supports the exFAT file system; this is also required on external drives for mounting purposes.

## **Security and MBCore**

MBCore is a Miltényi-own OS with an up-to-date cybersecurity concept for client protection against outside attacks to safeguard sensitive information and instrument operability relevant in healthcare and pharmaceutical sector.

MBCore ensures software stability, sustains long-term performance, and data integrity by collecting, transmitting, and storing data according to ALCOA principles ([ALCOA info](#)). MBCore is delivered as an image and forms a container for all other software components. Thus, MBCore is protected from system modification within a running system as well as any permanent virus and rootkits. Moreover, the auto execution for plug-and-play devices is switched off by default, which minimizes the risk of malware spreading. The data acquisition software MACSQuantify Tyto Software 3.1, included in MBCore image, is, hence, a kiosk-mode software, isolated from the operating system level in a container, and executed with read-rights only. Moreover, MBCore itself lacks a user-facing interface by design to ensure (depending on the instrument and software package) audit-trailed traceability as well as enforce data integrity; indeed, only interaction within the designated instrument-software that provides necessary functionalities to the user have been made available.

MBCore has been created within the Yocto Project, widely adopted for medical devices [ref. [Yoctoproject](#)]. MBCore provides concurrently multiple threads of execution on MACSQuant Tyto Cell Sorter built-in PC CPU and, thus, enables better application performance. Also, the main instrument-application is restricted to a maximum of 90% hardware resources, regarding CPU and memory, to prevent the system from freezing. MBCore runs on a “separate-from-customer-data-drive” (industry grade CFast) and has been hardened following Debian hardening guide.

Moreover, MBCore OS updates are encrypted, and the system will only apply image updates if signatures are verified and updates decrypted. Updates of the MBCore OS will be provided within MACSQuantify Tyto Software updates and they will be delivered by Miltényi Biotec upon request. As a security feature, services

run under the unprivileged user, and access to Miltenyi-Biotec service functionalities is restricted via the cryptographic network protocol SSH.

By default, any incoming traffic from outside is blocked. However, the MACSQuant Tyto Cell Sorter can be safely connected to a network to allow a centralized data management as well as enable users to access and store files on remote computers and servers. Remote access is made possible via a temporary communication upon user request: MBCore supports NFS data transfer protocols to push data from instrument to network shares and servers. Pulling data onto the instrument, as well as domain controller integration functionalities are blocked. User rights and permissions are locally managed as part of MACSQuantify Tyto Software in order to allow different user rights. In addition, an improved and secure Live Support is available on the MACSQuant Tyto Cell Sorter. Ports for remote support by Miltenyi Biotec are filtered (port 443 or 5938) so that a connection can be established. Remote access is made possible via a temporary communication and upon user request.

## New Features

1. MACSQuantify Tyto Software version 3.1 employs automated daily calibration to compensate for potential differences in laser performance or PMT sensitivity by adjusting the gains accordingly using the MACSQuant Tyto Calibration Beads (# 130-122-730).
2. The automated calibration described above brings the MACSQuant Analyzer “**Smart gain technology**” to the Tyto cell sorter,
3. Using Smart gain technology simplifies :
  - Performance over time for longitudinal experiments
  - Data reproducibility of intra and inter-instruments assays
4. Smart gain technology with MACSQuantify Tyto Software software version 3.1 allows sharing of instrument settings between MACSQuant Tyto Cell Sorters with same optical bench configuration.
5. MACSQuantify Tyto Software version 3.1 now includes **area** parameter which permits better doublet discrimination using the singlet gates. We recommend using this area parameter for singlet gating's with scatter channels and continue using the **height** parameter for the fluorescent channels.

6. MACSQuantify Tyto software version 3.1 includes following audit trail entries for the Research Use Only (RUO) default version without 21 CFR Part 11 add-on including the general instrument specific and user management activities
- User login (including failed logins)
  - User logout
  - Run finished (sort & calibration)
  - Export of system audit trail (only csv format)
  - Users added, Role assigned/unassigned
  - Set user inactive/reactivate user
  - Change user details
  - Role added/changed
  - User login including failed logins/lock user
  - Change password
  - Modify password policy including password expiration
7. MACSQuantify Tyto Software version 3.1 offers features to support compliance enabling according to 21 CFR Part 11 (#160-003-602, to order please visit [www.miltenyibiotec.com](http://www.miltenyibiotec.com)), i.e. lightweight directory access protocol (LDAP) connection, full user management system (UMS) with configurable user permissions, signature of run Reports with a signature reason, new audit trail entries as well as lock screen and lock screen timer functionality. The audit trail report can be viewed and exported for documentation in a human readable format. In particular, the following user activities are tracked in the Audit Trail:
- Instrument Specific activities:
    - ◆ User login (including failed logins)
    - ◆ User logout
    - ◆ Screen locked/unlocked
    - ◆ Create files
    - ◆ Errors
    - ◆ Software crash
    - ◆ Run started/finished/paused/resumed
    - ◆ Sort started/finished

- ◆ Calibration started/finished
- ◆ Run report created/signed
- ◆ Ventilation started/stopped
- ◆ Export of system audit trail
- ◆ Copy files
- ◆ Export of system audit trail
- ◆ Delete files
- ◆ Save files
- ◆ Sample export to csv
- ◆ Change data and time
- User management activities:
  - ◆ Users added, role assignments
  - ◆ Set user inactive/reactivate user
  - ◆ Change user details
  - ◆ Roles added, changed or deleted
  - ◆ User login including failed logins/lock user
  - ◆ Change password
  - ◆ Modify password policy including password expiration
  - ◆ Create LDAP group including role assignments

#### 8. MACSQuantify Tyto software version 3.1 with 21 CFR part 11 compliance add-on

- Lock screen timeout functionality enabled with 21 CFR Part 11 compliance add-on, can be configured according to the user requirements or can be initiated manually from the main user interface.
- As part of 21 CFR Part 11 compliance add-on, setting the maximum MQD file limit is possible, while for the default users it still remains to be 16 MQD files saved for one run.
- 21 CFR Part 11 compliance add-on enables audit trail report export to PDF or csv format and also offers filtering different descriptions.
- Customers LDAP or Windows Active Directory can be connected to User Management System.

## Improvements

### MACSQuantify Tyto software version 3.1

- The Network Time Protocol (NTP) is disabled during the run to ensure no unexpected time changes occur.
- The user file storage is now divided between public (accessible to any user) or private (accessible to the named user). Users with rights to write to both locations will be presented with a choice of which to use for their session.

## Bug fixes

| Bug description                                                                                                           | Status |
|---------------------------------------------------------------------------------------------------------------------------|--------|
| 1. Hardware error " Vacuum Pump not running while activated"                                                              | fixed  |
| 2. A rare bug during workspace import from SW 0.5.1 to SW 1.0 causing MD5 validation failed error message                 | fixed  |
| 3. End of sample trigger not working properly on some standard cartridges                                                 | fixed  |
| 4. Real Time Sort Statistics graphs are not updating, due to change in time zone                                          | fixed  |
| 5. Number of events displayed on the plots are inconsistent                                                               | fixed  |
| 6. Network setup in Options default had inconsistent behavior with IP address                                             | fixed  |
| 7. Run Report and Real Time Sort Statistics are not uniform when run is stopped right after the Pause button is activated | fixed  |
| 8. MACSQuant Tyto cartridge detected message closed immediately without the user interaction                              | fixed  |
| 9. Experiment tab disappearing when Esc button is pressed                                                                 | fixed  |
| 10. USB drive eject after copying a large file cause SW crash                                                             | fixed  |
| 11. Problems during loading an analysis template                                                                          | fixed  |
| 12. Critical error during undo action performed on the plot changes                                                       | fixed  |

## Known Issues

| Bug description                                                                       | Workaround                                                                                                                                                       |
|---------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1. SW freezes when NFS server is stopped and user logs out                            | Reboot the instrument after the NFS shut down                                                                                                                    |
| 2. New workspace overwrites the old workspace, if the save dialogue is cancelled      | Save the old workspace before opening the new workspace                                                                                                          |
| 3. Run Report shows inconsistent Real Time Sort Statistics-due to change in time zone | Reboot the instrument every time with a change in time zone                                                                                                      |
| 4. USB not shown in Copy dialogue, if its inserted before the startup                 | Remove and reinsert the USB drive                                                                                                                                |
| 5. Backup data on a server location needs user credentials                            | Currently no workaround, will be fixed in the next Software release (version 3.2)                                                                                |
| 6. Few dialog boxes seem to appear twice                                              | This issue is rather a cosmetic & trivial<br>Currently no workaround, will be fixed in the next Software release (version 3.2)                                   |
| 7. Occasional SW crashes observed while shut down procedure                           | No impact to data or sample integrity. User will have to reinitiate the shutdown after the SW restarts. Will be fixed in the next Software release (version 3.2) |