BioResearch

Lonza

4D-Nucleofector™ LogWare Manual

Content

1 Introduction

1.1 Overview 4D-Nucleofector™ LogWare

In addition to the standard software which is automatically implemented on each 4D-Nucleofector™ System, Lonza offers the 4D-Nucleofector™ LogWare suited for use in regulatory environments (Table 1). The 4D-Nucleofector™ LogWare comprises specific features required for the compliance with Title 21 CFR part 11. These features ensure data consistency, enable electronic signatures and create electronic records of the systems usage.

Features comprise:

- User administration rights to create and manage users and allow data export according to Title 21 CFR part 11
- Generation of audit trails
- User login and re-authentication before conducting an experiment
- Logging of every data creation or modification (e.g. creating an experiment) as a specific user activity together with user information and a time stamp
- Logging of experiments with an enhanced result data set containing serial numbers, time stamps and user information
- Reporting of results, failure reporting and detailed failure description. Format of result file allows seamLess export into standard office programs (Word, Excel)
- Generation of encrypted data and reports which are safely stored on the device (deletion is not possible)

Table 1: Overview of differences between standard 4D-Nucleofector™ Software and 4D-Nucleofector™ LogWare

Feature	4D-Nucleofector™ Software	4D-Nucleofector™ LogWa re
Cell Type Programs, representing the optimal settings	+	+
Free program choice	+	+
Condition transfer from 20 µL to 100 µL, 1 mL or 20 mL	+	+
Custom program generation and modification	+	-
Administration mode	-	+
User log in	-	+
Activity logging	-	+
Data encryption	-	+
Audit trail generation and export	-	+
Data corruption detection	-	+
Data handling according Title 21 CFR part 11	-	+
Language/keyboard Settings	German / English	English only

2 Product Components

The 4D-Nucleofector™ LogWare and additional facilitating PC software is provided on a USB memory stick and comes with further accessories for convenient use.

- 4D-Nucleofector™ LogWare USB Stick containing:
  - 4D-Nucleofector™ LogWare (serial number locked)
  - 4D-Nucleofector™ PC Editor (PC Software)
  - 4D-Nucleofector™ Audit Viewer (PC Software)
  - Software manual

NOTE: **We strongly recommend to store the original 4D-Nucleofector™ LogWare USB stick in a safe place and not to use it for regular data transfer to or from the 4D-Nucleofector™ System to have it available in case a system reset is required (see chapter 7)**

- USB hub plus adhesive tape for attachment of the hub to the front panel (see figure 1)
- Flexible silicone QWERTY keyboard
- Software manual

Figure 1: Recommended position for attachment of USB hub

3 Software Features

In this chapter the general software features are described. For software handling, please refer to chapter 4 – 10.

3.1 User Levels and Rights

Following the Title 21 CFR part 11 guidelines users shall not be able to change system settings or alter the system in a way that influences the data created or the performance. Therefore, in the 4D-Nucleofector™ LogWare all adjustable settings have been assigned to the administration dialog to be handled by an administrator only (Table 2).

There are three different user levels:

- Device administrator
- User with standard access
- User with limited access

The administrator level is required to configure the system. An administrator is not able to act as a user and vice versa. A user is allowed to perform the standard operational functions of the 4D-Nucleofector™ System. Neither a device administrator nor a user has the right to delete data such as results, experiments or programs.

3.2 Login, Log Out and Lockout

3.2.1 Login

The maximum number of login attempts is set to three. In case the number of allowed attempts is reached without success, the user is locked out from the system and only an administrator is able to reactivate this user.

3.2.2 Log Out

A user or device administrator can actively log out by pressing the "**LOCK**" symbol in the upper right corner of the software.

Users or device administrators are automatically logged out after 30 minutes of inactivity by default. The time of inactivity can be adjusted by an administrator within the "**Display, Standby and Audio**" section (see chapter 6.7).

Table 2: Overview of device administrator and user rights

Feature		Chapter	Device Administrator	User with Standard Access	User with Limited Access
Perform a firmware update		6.5	+	–	–
Export / view result files		6.3	+	+	+
Set or change date and time		6.8	+	–	–
User management	– Create user accounts	6.1	+	–	–
	– Create further administrators				
	– Lock or unlock user accounts				
	– Activate and deactivate accounts				
	– Generate new temporary passwords				
Update of "Lonza Programs" (i.e. the set of Optimized Protocols)		6.4	+	–	–
Export audit trails (unfiltered or filtered by time period)		6.2	+	–	–
Perform a system backup		6.6	+	–	–
View firmware version and serial number of all attached 4D-Nucleofector™ Units		6.9	+	+	+
Adjust display brightness		6.7	+	–	–
Adjust duration of inactivity until the software automatically logs out the current user		6.7	+	–	
Generation and import of experiments		8	–	+	–
Run experiments		8	–	+	+
Perform a device cleaning		8	–	+	+
Restart system		8	–	+	+
Activate the transport mode		8	–	+	+

3.2.3 Inactivity (User Only)

A user who is inactive for more than 60 days will be set to "**inactive**". In order to be able to access the software again an administrator needs to activate the user again by removing the "**inactive**" checkbox for the corresponding user in the "**User Management**" section (see chapter 6.1.2).

3.2.4 Lockout

In case of entering a wrong password repeatedly (default: 3 times) the user or device administrator will be locked out of the system. At each login the user will be informed about the last unsuccessful login (if such happened) including time and date of attempt.

If a locked user tries to log in a notification is shown that the user is locked out and a device administrator needs to be contacted to reactivate the user account.

In order to be able to access the software again an administrator needs to unlock the user. Unlocking a user automatically generates a new temporary password (to be provided to the user by the administrator) that has to be changed by the user within one day and can only be used once.

For resetting the default administrator account in case of a lockout see chapter 7.

3.3 Data Handling

3.3.1 Data Logging

The 4D-Nucleofector™ LogWare logs all user activities relevant for the system use together with a time and date stamp, the operator's user name, user level and serial numbers of 4D-Nucleofector™ Units connected:

- User creation or edits
- User login successful or failed
- User log out
- User lock out
- Experiment saving, run, abortion, finish
- Result saving
- Password change
- Time/date change
- Standby
- System check
- System backup
- Use of device cleaning mode
- Firmware update
- "Lonza Programs" update

3.3.2 Data Storage

The system stores all data generated without allowing the user to delete specific data. In case of low system memory (<25 MB) the user will be notified to contact the system administrator. Even with every day usage this limit won't be reached before a minimum of 10 years of use. In case the low system memory status is reached please contact Lonza for help to free up memory.

To avoid the loss of data it is recommended to regularly create a system backup as described in section 6.6. Store the backup files on a secured hard disk drive or server network. In case of system damage Lonza can restore the system with the data from the most recent backup.

4 Getting Started

Table 3 below provides a quick start guide describing the required steps to set up the system. For more details on the single steps please refer to the indicated chapters of this manual or the general 4D-Nucleofector™ Manual.

Table 3: Quick start guide

Step	Description	More Details See Chapter
1	Turn on 4D-Nucleofector™ System on the rear side of the Core Unit. A system check will be performed after each start.	4D-Nucleofector™ Manual, 2.7.1
2	Install the 4D-Nucleofector™ LogWare using provided USB stick.	5
3	Login as administrator using first login settings. User: administrator Password: PASSWORD1 Press "LOGIN"	Figure 2
4	At your first login as administrator the system asks to change the password. Change your administrator password according to password rules. The initial administrator password is invalid after change to the individual administrator password.	6.1.1, Table 4
5	Login with the new administrator password. The number of inactive or locked users will be displayed and there will be a warning if memory is low.	
6	Setup date and time.	6.8
7	Enter users and note user name and temporary password.	6.1.1, Table 4
8	Login as user with your temporary password.	
9	Change your user password according to password rules. The number of inactive or locked users will be displayed and there will be a warning if memory is low	6.1.1, Table 4
10	After changing the password and login you can now access the standard operational functions as described in the 4D-Nucleofector™ Manual , i.e. – Define an experiment – Execute an experiment (requires user re-authentification) – View results	4D-Nucleofector™ Manual, 2.7.4 – 2.7.6
11	Turn off system when not in use anymore. **NOTE: Activate transport lock in case any transport of the 4D-Nucleofector™ System is planned.**	4D-Nucleofector™ Manual, 2.7.7

Figure 2: Login screen

5 Installation of the 4D-Nucleofector™ LogWare

This software can be installed on each 4D-Nucleofector™ System comprising of Core, X and/or Y Unit and/or LV Unit and will replace the standard software which is installed by default. Existing experiment or result files will not be overwritten and are still valid.

NOTE: **The software is serial number locked, thus it will only work with the specific Core Unit serial number that needs to be provided during the ordering process.**

To install the 4D-Nucleofector™ LogWare following steps are required:

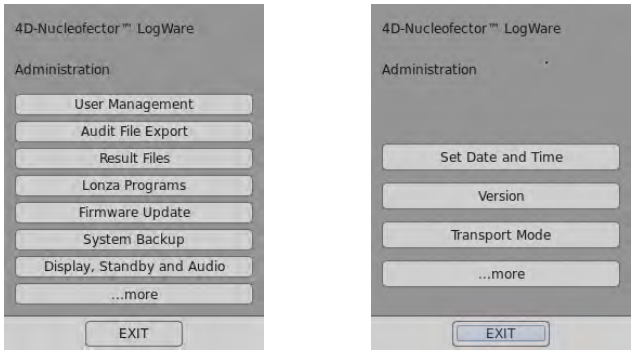
- Start the 4D-Nucleofector™ System
- The "**Choose a Device**" main screen will appear
- Click on the Core Unit icon
- Select "**Firmware Update**" within the "**Settings**" menu
- A dialog box will appear asking to plug in the USB stick, i.e. the original 4D-Nucleofector™ LogWare USB Stick
- Plug in the USB stick and press "**OK**"
- Follow the instructions on the screen to update the firmware

For future firmware updates of the 4D-Nucleofector™ LogWare see chapter 6.5.

6 Administrator Settings

After log in as administrator a menu is displayed which contains all tasks related to user management and system settings (Figure 3). The items of the administration menu are described in their order of appearance. The second menu page can be accessed by pressing "**more**".
The menu items can be either accessed via the touchscreen or the keyboard. When using the keyboard the arrow keys allow navigating through the menu and pressing "**ENTER**" opens the menu item.
To leave a submenu press "**BACK**".
If text entry is required this can be either done via the touch screen or the keyboard. The tab key can be used to walk through the fields or buttons.
Leave the administrator settings menu by pressing "**EXIT**". Now standard users can log in.

Figure 3: Menu "Administration"



6.1 User Management

6.1.1 Creation of a New Account

For adding a new user (Figure 4 and 5), press the "**NEW**" button.

Figure 4: Menu "User Management"

Figure 5: Generating a new user

- Enter user name (see table 4 for guidelines), first name and last name. Once a user has been created selected user name, first and last name cannot be edited anymore. If a change is required a new user has to be created.
- Define user level using the drop-down list (for further information on user rights see 3.1):

Limited access:	Users with this access level are only allowed to execute predefined experiments, export and view results and view software versions.
Standard access:	These users are allowed to setup and run experiments, export and view results and view software versions
Administrator:	Administrative tasks as described in this section.

- A temporary password is displayed. Note that password and provide it to the new user
- Press "**CREATE**"

The successful creation is acknowledged by a message. The temporary password is again displayed.
After pressing "**OK**" one can continue creating further users by repeating the steps described above or leaving the menu by pressing "**BACK**".

Table 4: Guidelines for user names and passwords

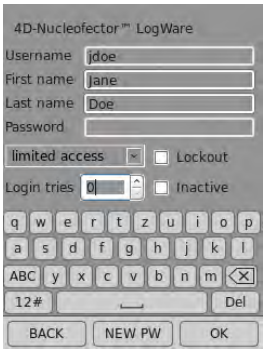
Definition of user name	User names should be unique on the system and identify a person, not being generic for multiple users. The length should be between minimum 3 to maximum 12 characters. A user name can only contain letters (a-z, A-Z) and numbers (0-9), but no special characters. The user name is case sensitive.
Temporary passwords	Upon generation of a new account or release of a locked account a temporary password is automatically generated by the software. This password should be noted and used for the first login. Temporary passwords must be changed upon the first login, they cannot be kept for future logins. A temporary password has a limited validity of 1 day only!
Individual passwords	Each user will be asked to define his individual password after first login using the temporary password. The individual password must have – a minimum length of 8 and a maximum length of 12 characters – contain upper and lower case letters – contain numeric characters – contain special characters (for example: . " £ ^ * & !) Words from English dictionaries and combinations like 12345678, 00000000, abcdefgh, aaaaaaaa etc. are NOT allowed. The software contains a library of prohibited terms, names, words and combinations to check conformity of the password selected with the rules described above. Each password has a default period of 90 days after which the password has to be changed. Re-use of the same password is prohibited for a period of 365 days. Passwords characters are displayed as dots only.

6.1.2 Editing a User

For editing a user press the **"EDIT"** button (Figure 4). Editing a user account (Figure 6) might be required for

- Activating or deactivating users (users who have been inactive for more than 60 days are set to inactive and they are not able to log into the system without an administrator having them activated again)
- Re-activating locked users after repeated unsuccessful login attempts (in this case a new temporary password is generated that has to be changed by the user within the next 1 day)
- Assigning a new temporary password

Figure 6: Editing a user



6.2 Audit File Export

In addition to experiment and result files, the system generates log files for audit trails. These log files are chronological records of all relevant user interactions with time stamp, device information and reference to the user involved in that action (for interaction types that are logged, please refer to 3.3.1).
A log file can be exported from the 4D-Nucleofector™ System to a USB stick in order to view or print it with help of the PC-based **4D-Nucleofector™ Audit Viewer** which is provided on the original 4D-Nucleofector™ LogWare USB Stick.

6.2.1 Installation of the 4D-Nucleofector™ Audit Viewer

It is not required to run an installation routine to install the 4D-Nucleofector™ Audit Viewer on a PC. Just follow the steps below to copy the software onto the hard disk drive:

- Insert 4D-Nucleofector™ LogWare USB Stick into a PC
- Copy the folder called "**4D-Nucleofector™ Audit Viewer**" onto the PC hard disk
- Open the folder, search the file called "**4D-Audit-Viewer.exe**" and double click on it to start the software

6.2.2 Export and Printing of Log Files

For exporting and printing log files enter the **"Audit File Export"** menu. One can either export all logged events or events within a defined time frame (Figure 7). For exporting the log files insert a USB stick into the USB port of the 4D-Nucleofector™ Core Unit and press "**EXPORT**". Exported log files are named "**4DN-yyyy-MMM-dd.NAT**" where yyyy-MMM-dd is reflecting the industry standard for the date of the audit trail export (e.g. "4DN 2013-NOV-12.NAT").

For viewing or printing the log file
- Start the Audit Software
- Select "**OPEN**" in the upper left corner of the software
- Navigate to the respective folder on USB stick and select the previously exported audit trail file (Figure 8)
- In the bottom section of the Software window the report can be filtered by time period, activity and user
- To print the report press "**PRINT**" in the upper right corner of the software window (Figure 9)

Figure 7: Audit file export

Figure 8: Open audit trail file

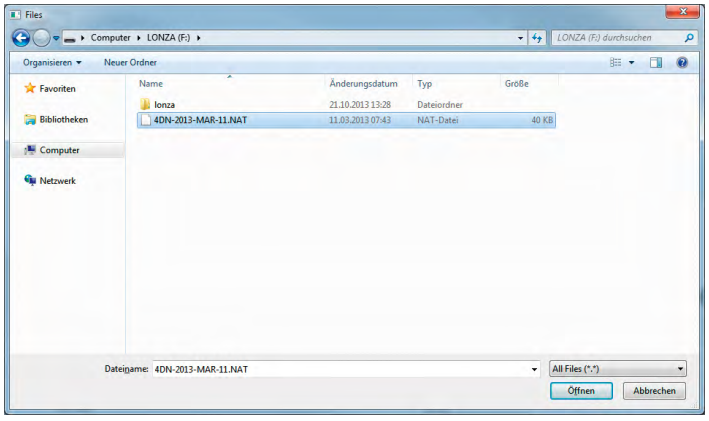
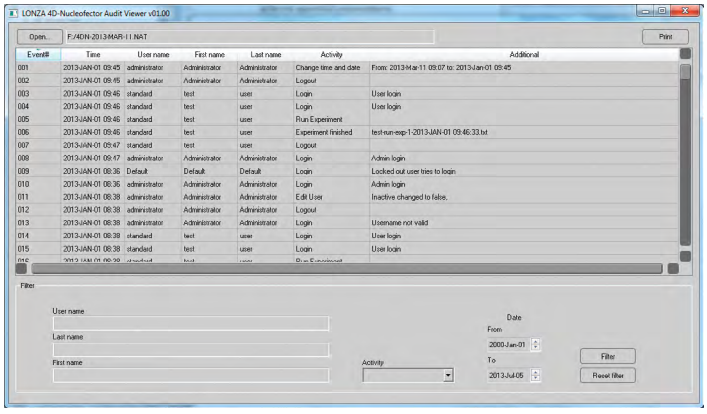


Figure 9: Log file report

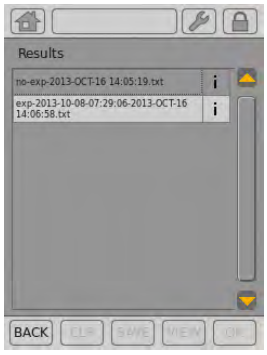


6.3 Result Files

Via this menu administrators are able to view result and export them to a USB stick for the transfer to the PC Editor (see chapter 9) in order to print them. To generate a printable result report with the PC Editor the following steps are required:

- Start the 4D-Nucleofector™ System and login as user or administrator
- Plug in a USB stick
- Click on the "**Core Unit**" icon (users only)
- Select "**Result Files**" within the "**Settings**" or "**Administration**" menu (Figure 3)
- Select the result to be printed (Figure 10) and press "**VIEW**"
- Then click "**SAVE**" and double click "**USBA**" to open the root directory of the USB stick
- Navigate to the desired folder on the USB stick and press "**OK**"

Figure 10: Result file list



- Start the 4D-Nucleofector™ PC Editor
- The "**Choose a Device**" main screen will appear.
- Click on the "**Core Unit**" icon.
- Select "**Result Files**" within the "Settings" menu
- Select "**LOAD**" and navigate to the directory where the desired result file has been stored.
- Select the desired result and press "**OPEN**".
- The encrypted result file is now copied to the PC editor
- Select
  - "**VIEW**" to view the result
  - "**PRINT**" to print the result
  - "**LOAD**" to load another exported result file from the **USB stick**

6.4 Lonza Programs

The "**Lonza Programs**" menu shows the currently installed version of programs and cell type codes. A new program list can be uploaded via this menu by navigating to the appropriate update file on a USB stick plugged into the 4D-Nucleofector™ System. The program update file is always named "**4D-Nucleofector-PV.pd**". The most recent list of Lonza programs will be always installed during a regular firmware update.

6.5 Firmware Update

The 4D-Nucleofector™ System may require an update of its firmware due to new optimized protocols added to the Lonza program list or technical improvement of the operation software. A new firmware will be provided by Lonza on a USB stick. To update the firmware proceed as follows:

- Start the 4D-Nucleofector™ System and login as administrator
- Select "**Firmware Update**" within the "**Settings**" menu
- A dialog box will appear asking to plug in the USB stick
- Plug in the 4D-Nucleofector™ LogWare USB stick with the update files and press "**OK**"
- Follow the instructions on the screen to update the firmware

6.6 System Backup

A complete backup of data can be stored as an encrypted package onto a USB stick. To create a backup select "**System Backup**" from the administration screen and press "**Backup all data to USB device**". The system will copy an encrypted file to the USB stick containing all experiments, results, logs and system files required to restore the system.

6.7 Display, Standby and Audio

In this menu following settings can be adapted by a device administrator (Figure 11):

- Display brightness
- Duration of inactivity until the system automatically switches into standby mode and logs out users or administrators
- Acoustic signal for touchscreen user interaction

Figure 11: Display, standby and audio

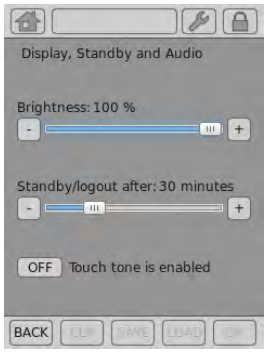
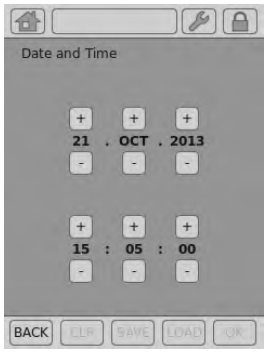


Figure 12: Set date and time



6.8 Set Date and Time

By entering the menu currently set date (dd-MMM-yyyy) and time (hh:mm:ss) are displayed (Figure 12). Both can be changed by using the "+" and "–" buttons. Keeping the buttons pressed allows for faster scrolling. New time and date is acknowledged by pressing "**OK**".

6.9 Version

This section of the administration menu provides version information regarding the installed firmware of each connected unit as well as the version of the Lonza Programs containing the Lonza Optimized Protocols.

6.10 Transport Mode

A transport lock is mandatory when transporting the 4D-Nucleofector™ System to protect interior fragile parts against damage. The "**Transport Mode**" menu enables the activation of the transport lock when being logged in as administrator.

7 Reset of Administrator Account

In case the default administrator has been locked out, the "**administrator**" account can be reset by starting the 4D-Nucleofector™ System with the original 4D-Nucleofector™ LogWare USB Stick inserted.

- Enter the USB stick (serial number locked) during booting process
- The application recognizes the update files and the serial number and prompts "**Do you want to reset the default administrator?**"
- When the operator selects "**Yes**" the password for "**administrator**" is reset to the temporary password "**PASSWORD1**".

Existing user accounts are not affected when resetting the default administrator.

NOTE: The original 4D-Nucleofector™ LogWare USB Stick should remain with a device administrator to be available in case the device administrator has been locked out or forgot the password.

8 Operating the System (Users)

For defining and running Nucleofection™ Experiments on the 4D-Nucleofector™ System, please refer to the 4D-Nucleofector™ System Manual. The handling of the system is identical when using the 4D-Nucleofector™ LogWare with few exceptions related to user rights (for overview, also see 3.1):

- Starting an experiment requires user re-authentification
- Setting up and saving experiments is only allowed for users with standard access level
- Settings do not allow for
  - Changing date and time
  - Firmware update
  - Changing display, standby and audio

9 PC Editor Software

The 4D-Nucleofector™ LogWare is accompanied by a dedicated PC Editor version which is also provided on the original 4D-Nucleofector™ LogWare USB Stick. This PC editor can be used to

- Conveniently program experiments for subsequent upload to the 4D-Nucleofector™ LogWare
- Print result files that have been exported from the 4D-Nucleofector™ LogWare as a table including date and time of the experiment, user, additional information and individual results per well.

The PC Editor has been adapted to the changes made to the standard 4D-Nucleofector™ Software in order to be compatible to the Title 21 CFR part 11 implications in the 4D-Nucleofector™ LogWare. These changes do not include the need to login into the software, since the generation of experiments or printing of results does not have to be linked to a specific user.

9.1 Installation of the PC Editor

It is not required to run an installation routine to install the 4D-Nucleofector™ LogWare PC Editor on a PC. Just follow the steps below to copy the software onto the hard disk drive:

- Insert 4D-Nucleofector™ LogWare USB Stick into a PC
- Copy the folder called "**4D-Nucleofector™ PC Editor**" onto the PC hard disk
- Open the folder, search the file called "**4D-Nucleofector_Editor.exe**" and double click on it to start the software
- A window will appear displaying a graphical user interface of the 4D-Nucleofector™ that allows to:
  - set up, store and export experiments to a USB drive
  - load, view and print result files from a USB drive
  - update to the "**Lonza Programs**" list

9.2 Generating a Printable Result Report

To generate a printable result report with the PC Editor, please refer to chapter 6.3.

10 Troubleshooting

For transfection results troubleshooting, sample rescue and error codes please refer to 4D-Nucleofector™ System Manual, chapter 3 and 4. Here only potential issues specific to the 4D-Nucleofector™ LogWare are described.

What Happened?	Procedure
I am locked out	Contact your administrator to unlock you.
I lost my user password	Contact your administrator to generate a new password.
I lost my administrator password	Reset the administrator account as described in chapter 7.
I want to change my password	Contact your administrator to generate a new password.

www.lonza.com/research
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