

Quick Guide

Metafer

4.3

Scanning and Imaging Software

This Quick Guide contains important information on your MetaSystems software. Please familiarize yourself with its content prior to using Metafer.



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Change History

Rev. no.	Reason for change	valid from
1.0	New document – for software release according to IVDR	2022-05-25
2.0	New revision - Change of address MetaSystems S.r.l	2024-05-28

1. Symbols Used

Symbol	Remarks
Symbols According to ISO 15223-1:2021	
	<p><i>Caution</i></p> <p>Text boxes marked with the standardized <i>Caution</i> symbol followed by the term CAUTION! indicate a potentially hazardous situation that, if not avoided, may interfere with the integrity of the software installation itself or data generated with the medical device.</p> <p>Text boxes marked with the standardized <i>Caution</i> symbol followed by the term ATTENTION! and should be read with great care to prevent any problem with software or connected standard hardware.</p>
	<p><i>Consult Instructions for Use / Consult electronic Instructions for Use</i></p>
	<p>YYYY-MM <i>Country of Manufacture and Date of Manufacture of the Medical Device</i></p> <p><i>Country of Manufacture – Germany (two-letter country code according to ISO 3166-1), followed by the Date of Manufacture, which is given as Year (YYYY) – Month (MM)</i></p>
	<p><i>Distributor</i></p>
	<p><i>In Vitro Diagnostic Medical Device</i></p>
	<p><i>Manufacturer</i></p>



Translation – This symbol is accompanied by the name and address of the entity that is responsible for the translation activity.

Symbol according to the Regulation (EU) 2017/746 (IVDR)



'CE-mark' – The CE-mark indicates conformity with the *European Union In Vitro Diagnostics Regulation*.

Additional Symbol



Text boxes marked with this information sign contain important technical information or hints on new or revised software features or settings.

2. General

Instructions for Use (IFU)

Instructions for Use for Metafer 4.3 compromise of two types of documents:

IFU	Definition
Quick Guide	Concise Instructions for Use (IFU): product descriptions including Intended Use, safety instructions, notes on setup and operation, and basic instructions for use, and troubleshooting.
Manuals/ Help Files	<p>Comprehensive Instructions for Use (IFU): product Descriptions including Intended Purpose, safety instructions, and extensive instructions for use and configuration. Manuals and Help Files for one software version have identical contents (except for minor format-specific alterations):</p> <ul style="list-style-type: none">■ Manuals are provided as PDF file, which can be viewed and printed with an appropriate reader software (not a MetaSystems product). The content of the manual is identical to the corresponding help file (except for minor format-specific adaptations).■ Help Files are provided as CHM files, which can be opened directly from Metafer. No separate viewer software is required.

Additional Copies

Additional copies of the Quick Guide are available as PDF files or printed copies. Please send an e-mail request to MetaSystems, mentioning the document number (*see front page*).

Assumptions on Previous Knowledge

The IFU assumes you have:

- Basic computer literacy, including a general understanding of data storage, file transfers, and copying and pasting.
- Sufficient knowledge of applicable laboratory techniques to interpret images generated by MetaSystems Metafer software.

How to Obtain More Information and Support

MetaSystems Representatives

MetaSystems is an international company with offices in Germany (headquarters), in Argentina (Buenos Aires), in Hong Kong, in India (Bangalore), in Italy (Milano) and in the U.S.A. (Boston). Additionally, MetaSystems is proud to have a global network of partners, which is covering the local business in almost all regions of the world. Please refer to the front page of this Quick Guide for contact details of your local MetaSystems representative or visit www.metasystems-international.com.

Errors and Suggestions

You may submit electronic comments and suggestions on the IFU at any time for company consideration to MetaSystems (see below). Comments may not be acted upon by MetaSystems until the document is next revised or updated.

Reporting Serious Incidents

If any serious incident occurs in relation to Metafer 4.3, the incident shall be reported to MetaSystems, the competent authority of your country.

3. Product Description

The European In Vitro Diagnostic (IVD) Regulation 2017/746 (IVDR) replaces the In vitro diagnostics Directive (98/79/EC) (IVDD) which has been the regulation framework for products for more than two decades. The IVDR entered in force in May 2017, and the 5-year transition period ends in May 2022.

Compared to the IVDD, the IVDR raises the bar significantly higher for IVD products, manufacturers and other stakeholders.

The new EU In Vitro Diagnostics Regulation (EU IVDR) is not radically different from the current IVD Directive (IVDD), but adds some additional requirements for products:

- Four new classes of devices A, B, C, and D, associated with increasing risk;
- New device classification rules;
- Additional requirements, e. g. for Post Market Surveillance (PMS);
- A system and database for device identification over its entire life cycle: Unique Device Identification (UDI).

Intended Purpose

Metafer is a software intended to control microscope and accessory hardware, to acquire digital images, and to assist the operator in the detection, classification, and counting of cells of human or other origin and other objects in microscopic specimen.

Metafer is intended for use in in vitro diagnostic procedures by clinical and non-clinical laboratories in accordance with their established procedures. Slide scanning and analysis conditions can be adapted to a variety of specimen, including, but not limited to, cultured and stained cells in their interphase or metaphase state. The analytical and clinical performance has not been established.

Legal Classification in the EU



Metafer carries a self-declared CE mark according to the EU Regulation 2017/746 on in vitro diagnostic medical devices (IVDR).



Metafer 4.3 has been classified as an IVD product according to the IVDR (2017/746).

Legal Classification outside the EU

MetaSystems products are used in many countries worldwide. Depending on the regulations of the respective country or region, some products may not be used for clinical diagnostic use. Please ask our local contact for further information in regard to the regulatory status in your country. Please visit www.metasystems-international.com for information on local MetaSystems representatives.

License Protection and Software Feature Control by Hardware Token

MetaSystems software requires the presence of hardware copy protection modules, also known as 'dongles', to be started and executed. Failure to plug in the dongle will result in the software not running. A MetaSystems' dongle does not only work as a security key, but also as a physical license key, which enables particular features in the MetaSystems software.

- Each dongle has an individual serial number.
- Only features enabled by the license key are available in the respective software. All other software features are disabled, but can be enabled after purchasing the respective license and reprogramming the dongle.
- The software periodically performs checks for a valid dongle and license key.
- The required **Update Expiry Date** for Metafer 4.3 is *June 2021 (0621)*.

4. Safety Information

General Precautions

For professional laboratory use only.

Table: General Precautions



CAUTION: Power Point! The computer running Metafer 4.3 shall be connected only to properly grounded electrical outlets. Consult also the safety instruction in the product information supplied with all electric instruments and components.



CAUTION: Operation by qualified personnel only! The software must be operated only by qualified and trained laboratory personnel.



CAUTION: Motorized Focus Drive! Risk of Personal Injury and System Damage! On microscopes with a motorized focus drive do not place your hand or any object between microscope stage and objectives, while the stage is moving upwards. The same care should be taken when the stage is moving downward. You may be injured and/or damage the microscope in both instances. Please consult the safety and operating instructions of the microscope manufacturer.



CAUTION: Risk of Ineffective Safety Measures! If it is determined that protective measures are no longer effective, the device must be taken out of service and secured against inadvertent operation, to avoid the risk of injury. Contact MetaSystems or its representative to have the device repaired.



ATTENTION! If a search is terminated due to a hardware error, please follow the instructions in the displayed error message and check the identity and plausibility of all slide names which are part of the current aborted scan job.



ATTENTION! Consult Laboratory Safety Guidelines and Instructions for Use for all installed hardware components! Before using Metafer it is essential to familiarize yourself with all applicable laboratory safety guidelines and regulations

in their latest versions, and the instructions for use (IFUs) of all installed hardware components.

Protection of Personal Data

MetaSystems guarantees confidentiality of all medical or patient related data and herewith confirms to fulfil the requirements according to Regulation (EU) 2016/679 *On the protection of natural persons with regard to the processing of personal data* (General Data Protection Regulation) as follows:

Personal data will be:

- Processed lawfully, fairly and in a transparent manner in relation to the data subject.
- Collected for specified, explicit and legitimate purposes and not further processed in a manner that is incompatible with those purposes.
- Adequate, relevant and limited to what is necessary in relation to the purposes for which they are processed.
- Kept in a form which permits identification of data subjects for no longer than is necessary for the purposes for which the personal data are processed.
- Processed in a manner that ensures appropriate security of the personal data, including protection against unauthorized or unlawful processing and against accidental loss, destruction or damage, using appropriate technical or organizational measures.

If you have any questions concerning the MetaSystems' Privacy Policy statement, please contact MetaSystems.

Cybersecurity

Supported Operating System



ATTENTION! Metafer 4.3 has been developed and tested exclusively for use with the Windows™ 10/64-bit and Windows™ 11/64-bit operating system (OS).

Microsoft™ has discontinued the support for all operating system versions prior to Windows™ 10. These versions do not receive updates and security patches any longer and bear a high level of vulnerability against cybersecurity threads. We explicitly recommend running our software only on computers with Windows™ 10/64-bit.

Although our software may technically be able to run on older operating systems (for example Windows™ 7), this will be entirely at your own risk. MetaSystems does not take any responsibility for errors arising due to the use of non-approved operating systems.

User Access

MetaSystems offers different levels of user login modes. Depending on the security policies of the institution where Metafer is installed, user access modes can be selected from low to high security. For details on the login modes, please refer to the product help or manual.

Local Mode

If network resources hosting the case data or shared configuration folder are (temporarily) not accessible, Metafer 4.3 can be operated in a 'local emergency mode'. This mode allows to continue to work with data stored on the local computer. After the normal operation mode has been restored, data can be manually transferred to the preferred data storage location.

Hardware

Hardware Requirements

Table: Minimal Hardware Requirements for Computer Running Metafer 4.3

Hardware Components	Description
PC	A scanning PC should meet these specifications: Intel Core i7 (8 cores) 16 GB DDR4 SDRAM, 512 GB SSD, 550 W power supply. Demanding applications, e. g. virtual slide scanning, may require advanced hardware specification. Please inquire, MetaSystems will assist you in finding the optimal configuration depending on the actual Metafer software license(s).
Monitor	Minimum resolution: Full HD (1920 x 1080)
Mouse	3-button mouse (or equivalent ergonomic input device)

Supported Standard Hardware Components

The Metafer software can control selected standard hardware components.

The typical Metafer workstation configurations differ in their hardware setup:

Hardware Components	Metafer Slide Scanning	Metafer Analysis
Powerful PC and monitor	☑	–
ZEISS microscope	☑	–
High-resolution digital camera	☑	–
Märzhäuser scanning stage	☑	–
Trackball for manual stage movements	☑	–

Hardware Components	Metafer Slide Scanning	Metafer Analysis
3-button mouse	☑	☑
Copy Protection & License Management Device (Dongle)	☑	☑
<u>Optional</u>		
Slide Feeder	(☑)	-
External, configurable keyboard	(☑)	(☑)
Graphics board for deep neural network calculations	(☑)	(☑)

Supported Microscope Models

Microscopes are not part of MetaSystems systems. The camera and microscope must be connected by a C-mount adapter for CCD cameras (not included). Please contact your microscope representative for details. MetaSystems software supports a number of motorized microscopes. Suitable control cables are available from the microscope manufacturers (not included).

Metafer supports several microscope models. The ZEISS Axio Imager Z2 is the recommended choice due to its high-precision focus drive with 'heavy duty' support for motorized slide scanning stages.

ZEISS Microscope Models		
Axio Imager Z2	Axio Imager M2	Axioplan2 Imaging E
Axio Imager Z1	Axio Imager M1	Axioplan2 Imaging
AxioVert 200	Axioplan2 MOT	


Supported Camera Models

Metafer supports several camera models. Cameras are not included in the Metafer software package and must be ordered separately.

Current Camera Models

CoolCube 1	CoolCube 1m / CoolCube 1c*
CoolCube 1P	CoolCube 1Pm / CoolCube 1Pc*
CoolCube 4 (TEC) /4P	CoolCube 4m (TEC) / CoolCube 4c (TEC) and CoolCube 4Pm / CoolCube 4Pc* (Available with passive (standard) or thermo-electric (TEC) cooling)

* m: monochrome version / c: color version (w/ Bayer RGB filter mask).

Metafer also supports some legacy analog and digital camera models. Please refer to the Metafer 4.3 Help / Manual for details (.


Supported Other Hardware Components

Hardware Components

Tango Controller	Stepping motor controller for 1, 2, or 3 axes, e. g. for motorized stages. Available as internal (PCIe card) or external unit; 1.25A; RS232.
Slide Feeder	SlideFeeder 80 (SF 80). The original slide feeder model has a capacity of up to 80 slides (10 frames with 8 slides each). SlideFeeder x80 (SF x80). The advanced successor model of the slide feeder. Various configurations: capacity: 80 - 480 slides, barcode reader, passive oil reservoir or active AutoOiler (immersion oil).
FastWheel	External filter wheel for microscopes. Different product variants are available which differ in filter diameter (25/32mm) and number of filters receptacles (8/10), USB2.0 interface (USB2COM adapter in connector); mounting adapters (flanges) available for major microscope brands.

Hardware Components

AutoOiler Software-controlled pump for immersion oil.

For further details and addresses of hardware component manufacturers, please refer to the Metafer 4.3 Help / Manual ()

5. Pre-Installation Requirements

Workspace Requirements

- **Prepare the Workspaces** – Ensure that the installation site is clean and empty and that all objects that are not required for setting up the MetaSystems devices are removed.
- **Provide Power Supply** – Provide a CEE 7/4 socket (*Schuko*) with 100V-240V, 50-60Hz or a respective adapter for each computer.
- **Make Sure There is Enough Space** – The recommendation for just a computer workstation is a workspace of 90 x 70 cm (w x d). If the workstation is combined with a microscope, the available workspace should not be smaller than 130 x 80 cm (w x d). Please observe also the applicable national regulations for visual data workstations and EN ISO 9241-1.
- **Inform Us about Your Existing Microscope(s)** – If an existing microscope shall be used with Metafer, please provide some details prior to the installation: (i) the brand and the model of the microscope, (ii) the illumination devices, (iii) the objective lenses, (iv) the camera adapter, and (v) if applicable, the fluorescence filters available.
- **IT Infrastructure Requirements** – You will generate some image and case data with Metafer. Please make sure that there is enough storage space available on your data server. We recommend to estimate your weekly/monthly workload and the requirement for storage space on the server. Please involve your IT department.
- **Data Management** – Data is indexed automatically with the help of a software called NeonServer which runs as a Windows service.
For all installations, except for a stand-alone computer, NeonServer should be installed on a separate PC with at least 4 cores, 16 GB RAM, and 100 GB disk space. Dedicated server hardware is not required, but recommended. The computer network should allow fast data transfer (1 Gb/low-latency).
For more detailed information, please refer to these documents: *MetaSystems Pre-installation Requirements* and *Supported Operating System for MetaSystems Devices* in their current version. Please contact MetaSystems.

6. Installation

- **Appoint ,Super-Users'** – Determine one or two persons among the users who are responsible for the systems and are available as our contact persons. These persons should be allowed to coordinate and communicate the requests and wishes of the users and to make short-term decisions regarding the system configuration.
- **Provide IT Support** – Ensure that IT staff are available for the duration of the installation to respond quickly to any issues related to the IT infrastructure.
- **Provide Temporary Administrator Account** – During the installation phase, our employees require temporary administrator access. This access can be deactivated after the installation and is used to carry out the necessary installations and to test the interoperability of the systems.
- **Installation and Training by MetaSystems Personnel** – We offer installation and training of laboratory staff as a service.
We are aware that installation and training may interfere with your daily laboratory routine in one way or the other. Therefore, we suggest making appropriate arrangements which allow your personnel attend the training sessions. Together we can draw up a training plan in advance to address the general and particular training requirements for every operator of the Metafer software.
- **Provide Suitable Samples** – Ideally, we use your own samples to create training cases as close as possible to your routine work. This will also allow to customize parameter within the software to achieve good results.
- **Training Scope Metafer** – In brief, the training covers:
 - **Start and end Metafer / user login.**
 - **Settings** – Data folders, paths, security settings, user groups, reporting.
 - **Navigation** – create case, case data import.
 - **Cases** – View, search, filter, sort, and group cases.
 - **Cases** – Rename, delete to 'trash', and restore from 'trash'

- **Case datasheet** – Enter data, customize data sheet
- **Case structure** – Hierarchical levels: case, scans, cells, culture, slide, region; data on each hierarchical level
- **Case history**
- **Cells** – Cell List, Cell Gallery, and Combined Karyogram
- **Workflows** – Manual / automatic (triggered/conditional) workflow progression
- **Reporting** – Printing reports, different report types, customizing reports
- **Problems** – solve problems and report unsolvable problems (XReports)
- **Get Help** – Look-up shortcuts, open / navigate / search Help file
- **Installation and Training Are Documented** – For your and our reference we will ask you to sign an Installation / Service Report after training is completed to document the trained software features (*System Installation / Service Report – MSC-SysInstRep-2019-10-02-X.PDF*). The same report is also used to document any service / maintenance work, if necessary.
- **Software Installations Backups** – MetaSystems software comes with built-in routines to create backups of the current software installation. Backups are stored (a) locally on the computer running Metafer, (b) on a network resource chosen by the customer, and (c) at MetaSystems. The latter backup copy helps us to look up configuration details, even if a remote support is not feasible. Software installation can be restored from backups.
- **Using Metafer** – Please refer to the:
 - Metafer 4.3 Manual / Help for in-depth coverage of the Metafer program functions for slide scanning and imaging.
 - Neon 1.3 Manual / Help for detailed description of the case management, data management, and reporting options.

7. Post-Installation

- **Allow Us to Support You Remotely** – For fast and professional online support, we offer a remote support software tool TeamViewer (branded as 'MetaSystemsQS'). Please note, that remote support by MetaSystems requires a signed Remote Support Agreement form, which is available on request (*Remote Support Agreement*).

TeamViewer is a highly secure remote maintenance solution using fully encrypted data channels. In its latest version, it includes encryption based on 2048 RSA private/public key exchange and AES (256-bit) session encryption. This technology is based on the same standards as https/SSL and meets today's standards for security. The key exchange also guarantees full client-to-client data protection. Access from outside requires a session token which is generated on start-up of the QuickSupport module. This token is only valid during one single session; it is not possible to access the device from outside without it. Do not start the remote access module unless asked by a MetaSystems staff member to do so.

You can download the tool from the MetaSystems website:

- 1. Scroll down to Support and click on Online Support Tool; the download will start automatically.*
- 2. Double-click the TeamViewerQS.exe to install. Follow the on-screen instructions.*

- **Make sure that your device(s) is/are protected against malware and viruses** – Likewise, we support the installation and maintenance of anti-virus software through your IT department. You should also take all necessary measures to protect the device and your network from harmful influences (e.g., by a network firewall). Please note that the above measures are part of on-site network maintenance, and that MetaSystems assumes no responsibility for damage or data loss caused by inadequate protective measure.

- **Software Updates Fixing Software Errors – Despite our thorough testing regime, certain software errors may remain undetected until after the initial release of a software version** – We are committed to fix known software errors.

For this purpose, we will release minor software updates, indicated by the third part of the version number (e.g., 4.3.0 -> 4.3.1).

Major issues compromising the proper operation of Metafer must be reported to the Notified Body and to the Authorities having jurisdiction together with a plan for corrective actions. In this instance, you will be informed

- **Pay attention to regular updates of security relevant drivers and software** – We strongly recommend updating computers regularly and to keep the drivers and operating system (OS) up to date. If we become aware of any OS patches that may compromise the intended operation of our software, we will inform you and recommend corrective actions.

- **Service and Maintenance Plans** – Metafer 4.3 does not require maintenance at fixed intervals.

MetaSystems and its distribution partners are offering service and maintenance service plans, which include installation of minor software updates and/or preventive maintenance of supported standard hardware components (cameras, microscopes, etc.). Please inquire.

8. Troubleshooting

Problem	Potential Cause	Action
<i>Associated Standard Hardware Components</i>		
Computer does not work.	Interrupted power. System is not turned on.	Please check that all power cords are connected correctly and that all system components are switched on.
Computer works, but MetaSystems application trigger error messages.	Drivers for connected standard hardware components are not (properly) installed.	Open Device Manager, check for problems indicated (yellow question/exclamation marks).
	The hard disk(s) in the local computer or on network resources are almost full.	Open My Computer, open Properties of hard drives and check for available free disk space (> 10% of total disk space) and for any problems indicated.
	Shared network resources are not available.	Open Network and Sharing centre in task bar and check for indicated problems.
Monitor does not display an image.	Monitor is turned off. The cable connecting the monitor to the PC is not plugged in correctly.	Please check that power and monitor cables are plugged in correctly and that the monitor is switched on.
	Monitor has been damaged.	Check monitor for damages.
	Monitor settings have been altered.	Check Control panel / Display for correct settings
No live image is displayed when 'Capture' is selected.	Microscope illumination turned off. Light path to the camera is closed.	Check, whether the microscope is switched off.
		Please check that the required microscope lamp is on and that the light path to the camera is open.
		For fluorescence applications please verify that the correct filter is positioned in the light path.
Camera gets 'lost': camera has been working correctly, but all of a	Energy-saving scheme sends USB port to 'power save' mode.	Go to the Windows Device Manager and deactivate all energy saving options for USB connections (requires admin rights).

Problem	Potential Cause	Action
sudden is not recognized anymore		
Live camera image is displayed, but there seems to be 'dirt' in the light path	Dust particles can settle on different surfaces in the microscope or in the camera.	Clean readily accessible glass surfaces as described by the microscope manufacturer. While the software is in the live image mode: Switch among objectives: is the dust stationary (regardless the different magnifications)? If so, this would exclude the objectives. To check, whether the dust particles are in the camera, please do this: (i) defocus slightly, (ii) move the slide carefully. Is the dust stationary? If so, this would indicate that the dust is inside the camera. In this instance, please contact MetaSystems for camera cleaning.
Live image in brightfield illumination is lacking resolution and contrast	Microscope is not adjusted correctly	Please consult the microscope manual for instructions on <i>Koehler</i> illumination. Check, whether all optical components are correctly mounted and fastened.
Software		
Software cannot connect to NeonServer	Computer running NeonServer is not on and/or not connected to the network. NeonServer is not properly installed 'as a service'. NeonServer service is not started.	Start computer running NeonServer with correct user account. Check, whether NeonServer is listed as 'Service' under Windows. If not, re-install NeonServer (requires admin rights). Start NeonServer service.
Software starts, but data folders are not accessible	Computer hosting data is not on and/or not connected to the network.	Ask your IT dept. to check, whether this computer is properly connected to the network domain and folders are shared correctly.

Problem	Potential Cause	Action
	Your Windows user account does not have read/write access to the respective network resources.	Ask your IT dept. to upgrade your user rights on the network accordingly.
Software problems	indicated	Open Diagnostics (press [F10]) and check details on Problems.
		Check dongle for available licenses.
Software apparently does function as expected.	Software bug.	Create Exception Report (XReport) and forward it to MetaSystems (automatic transfer, if configured accordingly).
	Wrong configuration.	Open Diagnostics (press [F10]) and check details on Problems. Restart Metafer. Restart computer. Rerun Neon installer package. Check program settings.
Cases seem to be missing in the Case List	Case List has been filtered.	Check, whether filter conditions are active for the Case List.
	Data are not fully indexed.	Refresh Case List. Check physical data folder for presence of case subfolder. Reindex data.
Scans / cells seem to be missing in a case	Case has been filtered.	Check, whether filter conditions are active for cells.
	Data are not fully indexed.	Reindex case.



If your problem is not listed here, please consult the Manuals and corresponding Help file before contacting your local MetaSystems distribution partner.