

Quick Guide

Ikaros

6.3

Image acquisition and processing for cytogenetic analysis

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



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Change History

| Rev. no. | Reason for change | valid from |
|----------|--|------------|
| 1.0 | New document – for IVD software product registration in Malaysia | 2024-12-09 |

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> |
|  | <i>Consult Instructions for Use / Consult electronic Instructions for Use</i> |
|  YYYY-MM | <p><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> |
|  | <i>Distributor</i> |
|  | <i>Importer</i> |
|  | <i>In Vitro Diagnostic Medical Device</i> |



Manufacturer



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

Symbol according to the Directive (EU) 98/79/EC (EU IVDD)



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

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 Ikaros 6.3 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 Ikaros. No separate viewer software is required. |

Additional Copies

Additional copies of the Quick Guide are available as PDF files. 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 Ikaros 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 China, in Hong Kong, in India (Bangalore), in Italy (Milano), in Japan, 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 Ikaros 6.3, the incident shall be reported to MetaSystems and the competent authority of your country.

3. Product Description

Intended Use

Monochrome Mode

The Ikaros system is intended to be used for karyotyping with real-time microscope images from cultured and stained cell specimens in their metaphase. By transferring images of chromosome spreads from the microscope to a computer the labor-intensive manual processing of photographs is eliminated. Karyotypes are assembled by the operator with the support of image processing software. The results are documented in hardcopy and archived for later review.

The system works with brightfield and fluorescent samples with all currently applied banding techniques including G- and Q-banding. All specimens suitable for banding analysis including amniotic fluid, peripheral blood, chorionic villus, bone marrow, and tissue can be used without limitation to specific diseases. Karyotyping is normally applied for the pre- and postnatal diagnosis of birth defects, chromosome abnormalities, genetic diseases, cancer, and for the follow up of cancer treatment.

Color Mode

The color fluorescence (Isis) mode allows fast and easy acquisition, processing, archiving, and documentation of microscopic fluorescent images.

Legal Classification in the EU



Ikaros carries a self-declared CE mark according to the EU Directive 98/79/EC on in vitro diagnostic medical devices (IVDD).



Ikaros 6.3 has been classified as an IVD product according to the IVDD (98/79/EC).

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 Ikaros 6.3 is *June 2021 (0621)*.

4. Safety Information

General Precautions

For professional laboratory use only.

Table: General Precautions



CAUTION: Power Point! The computer running Ikaros 6.3 shall be connected only to properly grounded electrical outlets. Also consult 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: 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! Consult Laboratory Safety Guidelines and Instructions for Use for all installed hardware components! Before using Ikaros 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. Please study the IFUs supplied with the components.

Observe the Guidelines for Cytogenetic Analyses

Cytogenetic associations and boards in various countries have published guidelines on how to conduct cytogenetic analyses. In unison, these guidelines emphasize the role and responsibility of experienced cytogenetics in establishing the final diagnosis, for example the European Cytogeneticists Association:

Checking of all cases by a second qualified cytogeneticist is essential. This independent check should involve a single comparison of every set of homologues as a minimum at the required quality for reason the referral reason). The same cells as the primary

analyst may be used for the check. A senior supervisor or an experienced cytogeneticist must check the analysis. An independent 'blind' analysis where the checker does not know the first analyst's finding is recommended. (...)

Interphase FISH results must be independently scored by an appropriately trained person. The checker should examine 30-70% of the total of cells used by the primary analyst. If the analyst and checkers' primary scores differ significantly then a third person (if necessary, from another laboratory) must be called in to provide a resolution. This person should normally be informed of the previous scores. For metaphase FISH the same procedures must be used as for checking conventional chromosome analysis. (...)

Interpretation of results requires supervision by an appropriately trained physician or cytogeneticist.

ECA General Guidelines and Quality Assurance for Cytogenetic (2012)

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! Ikaros 6.3 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 Ikaros 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, Ikaros 6.3 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 Ikaros V6.3

| Hardware Component | Description |
|--------------------|--|
| PC | Standard PC (processor speed: 2 GHz, RAM size: 2 GB system memory, hard disk space: 32 GB, display: 1920 x 1080) |
| Monitor | Minimum resolution: Full HD (1920 x 1080) |
| Mouse | 3-button mouse (or equivalent ergonomic input device) |

Supported Standard Hardware Components

Table: A Selection of Standard Hardware Components Supported by Ikaros V6.3

| Hardware Component | Description |
|---------------------------------|---|
| PC | PC model specifications: Intel Core i5-10505 CPU (6 Cores, 3.2 to 4.65 GHz), HD Graphics 630), 8 GB DDR4 SDRAM 2666 MHz Non-ECC Dual Channel, 512GB M.2 PCIe-NVMe-SSD drive; DVD +/-RW; 260W Power Supply, standard keyboard. Note: Other PC models with similar specification could be suitable as well. Standard PC hardware can be obtained from well-established manufacturers like Dell, HP, Lenovo, and others. |
| Monitor | Monitor model specifications: 61 cm (24") LED monitor with a resolution of 1920 x 1080 Pixels, monitor settings calibrated Note: Other monitor models with equivalent specification could be suitable as well. |
| Copy Protection Device (Dongle) | Pre-programmed WibuKey Codemeter CM copy protection device (USB Type-A plug). |
| Graphics Card | CUDA-enabled GPU board 4GB Single Slot / Double Slot. |
| CoolCube 1 | CoolCube 1m / CoolCube 1c* |

| Hardware Component | Description |
|-----------------------|--|
| 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) |
| 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. |
| 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) |

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

Microscopes

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 several motorized microscopes. Suitable control cables are available from the microscope manufacturers (not included).

For addresses of hardware component manufacturers, please refer to the Ikaros 6.3 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 Ikaros, 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 Ikaros. Please make sure that there is enough storage space available on your data server. The table below gives you an estimate on the amount of data to expect:

Table: Estimation of digital storage space per case

| Scenario | No. of Scans/Images | Min. Space Requirement |
|--|--------------------------|------------------------|
| Karyotyping Case | 20 - 25 images | ~20-25 MB |
| Karyotyping Case (with scanned slides (Metafer)) | 5 Scans + 20 - 25 Images | ~100-120 MB |

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 Ikaros 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 Ikaros** – In brief, the training covers:
 - **Start and end Ikaros / 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*). 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 Ikaros, (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 Ikaros** – Please refer to the:
 - Ikaros 6.3 Manual / Help for in-depth coverage of the Ikaros program functions for image acquisition, image processing and karyotyping.
 - 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 startup 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., 6.3.0 -> 6.3.1).

Major issues compromising the proper operation of Ikaros 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** – Ikaros 6.3 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 center 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 sudden is not recognized anymore | 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). |
| 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. |

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



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