

Quick Guide

Ikaros

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Distributor

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This Quick Guide is intended for novice users and users, who have been using previous versions of MetaSystems imaging systems, namely laboratory staff operating, maintaining, and analyzing data generated by MetaSystems systems.

The Quick Guide contains important information for the reliable operation of your MetaSystems system:

- Symbols Used
- Safety Instructions
- Product Descriptions
- Important Notices for Setup and Operation
- Instructions for Use

Please familiarize yourself with its content prior to using the system and pay special attention to the hints concerning safe operation of the instrument. The specifications are subject to change; the Quick Guide is not covered by an update service.

Assumptions on Previous Knowledge

The Quick Guide 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, Ikaros, and Isis imaging systems.

How to Obtain More Information

- While this Guide provides just a brief introduction, a comprehensive description about the system functionality is available through manuals and help files:
 - Inside Ikaros, Isis, Metafer press the [F1] key to open a built-in help file.
 - The help file is also available as a printable PDF file. You need a PDF reader software to open, display and print the PDF file. PDF reader software is available from various sources on the Internet.
- In addition to the present Quick Guide and the software manuals, the following operating manuals for optional equipment should also be consulted depending on the configuration:
 - Operating manuals for the computer, monitor, and printer.
 - Operating manual for the microscope, transmitted and reflected light fluorescence illuminator.

Errors and Suggestions

If you spot any mistakes in this online help or if you have any suggestions for improvement, please contact MetaSystems in Germany.

Compliance Notice

Systems by MetaSystems have been designed, produced and tested to meet the requirements regarding:

■ Electrical safety Directive 2006/95/EC for electrical equipment

designed for use within certain voltage limits.

EN 61010-2-101:2002 Safety requirements for electrical equipment for measurement, control, and laboratory use – Part 2-101: Particular requirements for in vitro diagnostic (IVD) medical equipment (IEC 61010-2-101:2002 (Modi-

fied)).

■ Electromagnetic Compatibility

(EMC)

Directive 2014/30/EU for electromagnetic com-

patibility.

EN 61326-2-6:2006 Electrical equipment for measurement, control and laboratory use – Part 2-6: Particular requirements – In vitro diagnostic (IVD) medical equipment (IEC 61326-2-

6:2005).

And meet the requirements of the EU directive 98/79/EC for IVD products (In Vitro

Diagnostics)

Instrumentation identification marking C€ mark

Symbols Used

This product complies with the requirements in the directive 98/79 EC on in vitro diagnostic medical devices.

For in vitro diagnostic use.

Manufacturer.

↑ Caution.

Consult instructions for use.

Safety Instructions

General Provisions

Imaging systems by MetaSystems:

- Are intended for laboratory use only and, thus, may only be operated by qualified and trained persons. MetaSystems or its representatives provide the technical training as part of the service. It is the responsibility of the laboratory to provide and maintain the necessary knowledge of the operator and to utilize all functions in compliance with standard laboratory practice and regulatory guidelines.
- Aid lab technicians in the documentation of microscopic brightfield and fluorescence images.
- PRequire the presence of a hardware token for software protection, also known as 'dongle', 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. Thus, each dongle requires its own individual license key. 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.
- Are only auxiliary components in the complex process of diagnosing the final result. The quality of the final result depends decisively on the process of specimen preparation. Although imaging systems have some capabilities to enhance images captured from difficult specimens but they cannot generally correct or compensate for short-comings or imperfections such as inadequate brightfield staining or fluorescence insitu hybridizations. Some of the system's image enhancement functions may have a distinct influence on the images. The operator should be careful about using them and be aware that when applied excessively or inappropriately they may reduce the quality and result in loss of image details.

It is part of the operator's responsibility to:

- Check the plausibility of each result by reviewing the images on screen and the slide directly under the microscope.
- Follow all procedures and recommendations for keeping the Metafer system within the specifications permanently (□).

Specific Provisions

Your system was built and thoroughly tested according to our quality system. In order to ensure continuous safe and reliable operation please observe the safety notices and caution signs below.



Caution: Laboratory Safety Guidelines!

Before using Ikaros, it is essential to consult applicable laboratory safety guidelines and regulations in their latest versions, particularly those on the use of electric laboratory equipment, glass microscopic slides and potentially hazardous samples.



Caution: Operation by qualified personnel only!

The system must be operated only by qualified and trained laboratory personnel, who have been advised on the risks of operating a microscope and performing the respective assay.



Caution: Power Point! Risk of electric Shock!

Plug the individual system components into properly grounded electrical outlets. The cables are equipped with 3-prong plugs to ensure proper grounding (protective earth conductor). If you must use an extension cable, although it is not recommended, use a 3-wire cable with properly grounded plugs. Do not remove the grounding prong from a cable. Consult also the safety instruction in the product information supplied with the individual components.

In case of error there is a risk of contact with life-threatening voltage.



Caution: Motorized Focus Drive! Risk of Personal Injury and System Damage!

On microscopes with a motorized focus drive, it is imperative one does not place a 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 personally injured and/or damage the microscope in both instances. Please consult the safety and operating instructions of the microscope manufacturer (🗐).



Caution: Gas Discharge Lamps! Risk of Personal Injury and System Damage!

Microscopes with fluorescence equipment, used in conjunction with MetaSystems systems, may include gas discharge lamps. They can explode if safe handling and operation is not observed. Gas discharge lamps emit ultraviolet radiation that may burn the eyes and skin.

Please follow the safety and operating instructions given by the microscope manufacturer (II).

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.



Caution: Build-up of Heat! Risk of Fire

Obstruction of vents may cause a build-up of heat in one of the system components. This may cause damage or fire in extreme circumstances. Ensure that the vents are always kept clear of obstructions (min. distance 15 cm).

Notes on Warranty

All MetaSystems systems are covered by a one-year warranty. The manufacturer and its representative guarantee that the instrument is free of material or manufacturing defects upon installation. Any defects must be reported immediately and steps taken to minimize damage. If such a defect is reported, the manufacturer shall be obliged to correct the fault, either by repairing the device or by replacing it with a new one, at the manufacturer's discretions. No warranty is given for defects caused by normal wear and tear (particularly of moving parts) and improper use of the device.

The manufacturer shall not be liable for damage caused by misuse, negligence or any other tampering with the device, particularly the removal or replacement of device components, or the use of unapproved accessories from other manufacturers. Service and maintenance may only be carried out by trained personnel of MetaSystems. Improper use or modification of the hardware in any manner may void the warranty.

Maintenance and service is to be carried out only by MetaSystems or individuals authorized by MetaSystems. In the event of a problem with the device, please contact MetaSystems or its representative.

Warranty extensions and/or service contracts for software and hardware are available on request.

Setup and Operation

Ambient conditions — The ambient conditions as outlined under Technical Data should be adhered to. Select an installation site which is as temperature-stable as possible.

Fluorescence preparations — When documenting fluorescence preparations, do not expose the microscope to direct sunlight. This helps minimize the influence of stray light.

Staining / FISH— Although imaging software has some capabilities to enhance difficult specimens, it cannot generally correct or compensate for shortcomings or imperfections caused

Quick Guide

by inadequate staining and/or FISH (*fluorescent in situ hybridization*). Follow your evaluated laboratory protocols and applicable SOPs.

Avoid Vibrations — For prolonged experimental procedures using the microscope choose an installation location with minimum vibration. Vibration stemming e. g. from forced ventilation, floor impact or other shocks can lead to reduced image quality and experimental errors. To reduce vibrations at the installation location, engage suitable damping measures.

Minimal space requirements — The minimal area required for setting up your system is 100 cm \times 60 cm [Metafer 150 cm \times 60 cm] (width \times depth). Observe the applicable national regulations for visual display unit work stations and EN ISO 9241.

Power supply — If the electricity is subject to local voltage fluctuations, we recommend the usage of a UPS (<u>u</u>ninterrupted <u>p</u>ower <u>supply</u>). Please note: Laser printers must NOT be connected to a UPS due to their high initial current peak during warm up.

Computer network — Several systems can be networked together using "Cat. 5" cables with standard RJ-45 connections. The required data transfer rates are at least 100 Mbps. Please note: The network installation is not included in the system price.

Changing system settings — The system settings are preconfigured by MetaSystems or it's representatives. These settings should only be changed by MetaSystems personnel or by experienced users. Pleased make a note of any changes made as some modifications may cause severe software malfunctions Please consult the accompanying manuals and contact MetaSystems (I).

Dust - Protect the microscope and camera from dirt and dust, which may impair with the functionality of the camera and other system components. If you remove the camera from the microscope, please ensure that the sensor is pointing downwards. The sensor is not protected by a glass filter. Do not touch the sensor and do not try to clean the camera yourself. Cameras should only be cleaned by the camera manufacturer or by MetaSystems

Cleaning — Shut down all pieces of equipment belonging to the device and remove the power cord of all system components prior to cleaning. Only use a soft damp cloth for cleaning. Never employ liquid or spray cleaner containing inflammable substances.

Sensitive Fluorescence Filters — If your microscope is equipped with fluorescence filters, you should be aware that they are particularly sensitive to heat radiation. Prolonged exposure to fluorescence light may cause irreversible damage leading to a complete loss of functionality. Ensure that proper heat protection filters are positioned in the light path between lamp and fluorescent filters. Please follow the guidelines of the filter manufacturer with regard to filter maintenance and cleaning (🗓).

Software updates — Software updates are available free of charge for 1 year during the initial free upgrade period after installation. You can update the software yourself following the detailed installation instruction included. You may receive new software version electronically or on CD-ROM.

Warming up of the Camera — Cameras can get warm during operation. This may lead to a poorer signal-to-noise ratio causing a reduction in image quality. Ensure a tight connection between camera and microscope (camera adapter) to dissipate this heat energy through the microscope.

Product Descriptions

MetaSystems products consist of software modules, hardware components and accessories in different configurations.

The entire system subject to this declaration consisting of specified, verified and validated hardware components, software modules and their accessories after commissioning by system specialists or authorized third parties.

Only components, modules and accessories specified, verified and validated by MetaSystems can be replaced by MetaSystems specialists or authorized third parties as part of maintenance or servicing.

Intended Use

The Ikaros system provides the tools for complete karyogram analyses on a computer.

Clinical Application

The Ikaros system is intended to be used for karyotyping with real-time microscopic 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 preand postnatal diagnosis of birth defects, chromosome abnormalities, genetic diseases, cancer, and for the follow up of cancer treatment.

General Precautions

The Ikaros system is intended for use in cytogenetic laboratories and requires a trained operator, generally a cytogenetic technician. Specific training should provide sufficient levels of both the technical knowledge needed to operate the instrument and familiarity with the process of karyotyping and the local requirements for the handling of medical data. MetaSystems or its representatives provide the technical training as part of the installation. It is the responsibility of the laboratory to provide and maintain the necessary cytogenetic knowledge of the operator and to utilize all function in compliance with standard laboratory practice and regulatory guidelines.

The Ikaros system aids the cytogenetic specialist in the preparation of karyotypes. However, the system is only one of the tools in the process and the quality of the final result depends heavily on other tools as the microscope and on the process of specimen preparation. The Ikaros software has some capabilities to enhance difficult specimens but it cannot generally correct or compensate for shortcomings or imperfections caused by the other tools, such

Quick Guide

as poorly focused images, or introduced through the handling of the specimen, such as inadequate banding.

The Ikaros software includes a variety of functions that support the process of metaphase interpretation and karyotyping at the discretion of the operator. Some of these functions, such as filtering, have a distinct influence on the chromosome images. The operator should be careful about using them and be aware that- when applied excessively or inappropriately - they may reduce the quality of karyotypes and result in insufficient resolution or other loss of the details which are necessary for correct diagnosis.

The system does not suggest an interpretation of the karyotype, a diagnosis, or a treatment. In general, it is likely that there will be one or more errors in any automatically computer-generated data. Therefore, the system does not relieve the qualified cytogenetic personnel from their responsibilities and from using their understanding to examine, edit as necessary, and interpret the chromosome images and every karyotype. Results must be verified by microscopic inspection of the analyzed cells and interpreted by a competent cytogeneticist who is expected to exercise his judgment in the use of the provided information when formulating the final diagnosis.

Legal Classification

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. In Europe, MetaSystems products are CE-labeled as in vitro diagnostic devices (IVD):

| | Australia | Brazil | Canada | Japan | U.S.A |
|--------|----------------|------------------|-------------------|-----------------|------------------|
| lkaros | Class 3 / TGA | Class 1 / Anvisa | Class 3 / License | MAH License no. | Class 2 / |
| | ARTG inclusion | DOU entry | (SOR-98-282) | 13B3X10527 | 510(k) clearance |

Product Variants

Ikaros is available in different configurations:

| Reference No. | Description |
|---------------|--|
| Class 3 | |
| P-0000-003-MS | Ikaros Karyotyping System (1st) - Primary system with software and camera |
| P-0000-004-MS | Ikaros Karyotyping System (Sat) - Satellite system with software and camera |
| P-0010-001-MS | Ikaros Analysis System - Analysis station with software (image processing functions) |
| P-0020-002-MS | Ikaros Capture System - Capture station with software (image acquisition functions) |

Hardware Components

All hardware components are carefully selected and tested to ensure compatibility. Wherever possible, standard components from qualified manufacturers are used in order to ensure consistently high quality, availability of spare parts and low maintenance costs.

Systems from MetaSystems comprise the following components:

| Component | Comment |
|----------------------------|--|
| PC / operating system | Standard office PC, model selected and tested by MetaSystems |
| Computer mouse | Computer wheel mouse |
| Camera with USB connection | Optional for systems with capture functionality |
| Monitor | Min. 24" TFT monitor (Full HD) |

Instructions for Use -How to get to the first karyogram

All main functions for image acquisition and processing are accessible directly through command buttons on the right-hand side of the screen. Most functions can be activated and completed with a three-button mouse. A function is started with a left mouse click and confirm it with a right click. Shortcut keys are also available for many functions. A complete summary of all command buttons, menu commands, mouse clicks and key shortcuts can be found in the accompanying manuals (🗓).

- Start the PC and turn on the microscope. Optional: Wait until the boot sequence of a motorized microscope is completed.
- On the Windows desktop, click on the Ikaros program icon.
- Load a case or setup a new one by typing the case name into the 'Case' field.
- Click on the 'Capture' button and adjust the focus, stage position and illumination in the 'live' image. Finalize the image acquisition by pressing the right mouse button.
- The functions 'Object threshold' and 'Separate' can be used to separate the chromosomes. Additional processing functions can be used to enhance the chromosomes and to analyze the metaphase (see the accompanying manual).
- By clicking on the empty karyotype form in the upper right corner of the screen you can switch to the karyotype view.
- Use the 'Assign' function to move chromosomes into their corresponding classes.
- Other functions can be used for further optimization and evaluations (🕮).
- The command 'View Case Data' opens the integrated case data sheet, in which you can fill in patient details, type of analysis and diagnosis.
- Print a report with a left mouse click on the printer icon.
- Save images and case data by selecting 'File Save'.
- You can exit the program by selecting 'File Quit'.

Microscopes

Microscopes are not part of MetaSystems systems. The camera and microscope must be connected by a *C*-mount adapter for 2/3" 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).

A detailed description of supported microscopes and system configuration can be found in the accompanying manuals (🕮).

Köhler Illumination

It is common knowledge among microscopists that correctly adjusted microscope is essential for good image quality and, hence, the basis for a successful analysis of microscope slide. The *Köhler* illumination provides a homogeneously illuminated field of view, reduced optical glare from the light source and an increase in optical resolution. The prerequisite for *Köhler* illumination is a vertically adjustable, centerable condenser with iris diaphragm. It is recommended to check the illumination on a regular basis (according to laboratory SOPs):

- 1. Move up condenser with the top lens swung in (if available).
- 2. Focus on specimen with a low power objective (e.g. 10x or 16x).
- 3. Close down the lamp field stop (diaphragm in the microscope stand) while viewing.
- 4. Lower condenser slightly until the diaphragm (lamp field stop) image is in focus.
- 5. Center diaphragm image using the condenser centering screws.
- 6. Open diaphragm to the edge of field of view, then fine focus and open it further to just clear the field.
- 7. Adjust contrast using the condenser aperture diaphragm.
- 8. Remove eyepiece and check to see that 75% of visible aperture is filled with light.

Troubleshooting

The following table list some of the most common problems:

| Problem | Potential Cause | Action | |
|--|---|--|--|
| System does not u 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. | |
| Monitor does not u display an image. | Monitor is turned off. The cable connecting the monitor to the PC is not plugged in correctly. | Please check that the power cord and the monitor cable are plugged in correctly and that the monitor is switched on. | |
| Error message on Inon-responding hardware components during software initialization | Systems with motorized microscope: communication cable unplugged, microscope is switched off or boot sequence not yet completed, wrong firmware versions installed in microscope stand. Systems with camera: camera cable(s) unplugged on system, corrupt camera driver, wrong camera type selected. | Check cable connection between system and microscope. Shut down software, switch on microscope and wait until boot sequence completed. If problem persists, contact MetaSystems or representative. Shut down system, wait 30 seconds and restart. If problem persists, contact MetaSystems or representative. | |
| No live image is displayed when the 'Capture' (Ikaros/Isis) or the 'Scan' (Metafer) command is selected. | Microscope illumination uturned off. Light path to the camera is closed. | 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. | |

| Quick Guide | |
|--|--|
| Live image too dark. | Transmitted light: Light source not properly Center light source and adjust centered. Köhler illumination (see above). Luminous-field or condenser aperture diaphragms closed too far. |
| | ■ Light level on the microscope too low. ■ Live image exposure time too short. ■ Increase light intensity on microscope. ■ Increase live image exposure time (☐ see Ikaros or Metafer manuals). |
| | ■ Light source operating beyond recommended livespan. ■ Live image integration time too short. ■ Replace light source (burner, light guide, if applicable, see light source manual). ■ Increase live image integration time (□ see lkaros/lsis or Metafer manuals). |
| Image not in focus / Manual Focusing is impossible | Dobjective damaged. Check objective's front lens for signs of damage. For immersion objectives: Check, whether 'cushion' mechanism is working properly (front less is moving inwards when a gentle force is applied). Objectives can only be repaired by microscope manufacturer. |
| | ■ No coverslip. ■ Use coverslips for coverslip-corrected objectives. |
| | ■ Specimen too thick or une- ven. Prepare fresh samples with reduced and homogenous thickness. |
| | ■ Not sufficient immersion oil ■ Use more immersion oil. for high magnification oil objectives. |
| | ■ Wrong immersion oil (immersion oil specified by mersion objectives). Use immersion oil specified by microscope manufacturer for the particular objective. For fluorescence (FL) applications use only FL-compatible immersion oil, e. g. ZEISS 518F. |
| | ■ Motorized microscope: ■ Consult microscope manual stage was lowered to 'Load' how to return to correct focus |

plane.

to Focus Plane' command from

was switched off. Metafer **U** Metafer systems: Apply 'Move

position before microscope

use the current focus (Z) po-

sition as default focus plan

| | and limits the focus movement range for safety reasons. | the 'Tools' menu (🕮 <i>See Meta-fer manual</i>). |
|---|--|--|
| Images have poor scontrast. | Weak staining | Repeat staining, if possible. Prepare fresh specimen with prolonged staining. |
| | | Check system capabilities with (commercial) control slides: if results are better with control slides, check FISH protocol, all reagents and temperature of water baths and heating plates. If results are similar, check reflected light path on the microscope (filters, light source), check software configuration parameter. |
| No printout is ob- utained. | Printer is switched off. The cable connecting printer and PC is not plugged in correctly. Network printer: printer is not 'shared'. Printer is not selected in the MetaSystems program. | Please check that the power and printer cables are plugged in correctly and that the printer is switched on. Verify that the network share for a network printer is configured properly. Check the program settings to ensure the desired printer is selected (see also accompanying manuals). |
| Warning messages: insufficient disk space. | The amount of data on the storage drive has reached a critical level (usually 90 % full) | Archive cases with MetaArchive software and free disk space with built-in software functions (III see MetaArchive manual). |

If this does not solve the problem, or your problem is not listed, please contact MetaSystems.

Technical Data

| Dimensions (w | idth x depth): |
|----------------------|----------------|
|----------------------|----------------|

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