Mabtech IRIS™ 2/ASTOR™ 2 system specifications

Introduction

Mabtech IRIS™ 2 FluoroSpot/ELISpot/FociSpot Reader and Mabtech ASTOR™ 2 ELISpot Readers use the Mabtech Apex™ software for exact spot center determination using RAWspot™ technology.

Both readers were developed by Mabtech AB in Nacka Strand, Sweden, whose quality management system complies with ISO 9001:2015 and ISO 13485:2016. The readers are CE-marked for the EU directives for Electromagnetic compatibility, Low voltage, Machinery and Restriction of Hazardous substances directives, and safety approved according to RoHS, REACH, WEEE, FCC, and ICES. The readers themselves are intended for research use only and not for diagnostic procedures. However, the qualities of Mabtech IRIS 2 and Mabtech ASTOR 2 enable use in regulated laboratories after user qualification.

Mabtech IRIS™ 2 and Mabtech ASTOR™ 2 validation

Mabtech IRIS 2 and Mabtech ASTOR 2 are assembled, validated, and calibrated at Mabtech's headquarters in Nacka Strand, Sweden, and distributed to end users worldwide. All readers are calibrated to match the light intensity of reference readers and given unique machine default exposure for each LED. These individually set machine default exposure values are then used by the Mabtech Apex software when reading ELISpot, FluoroSpot, and FociSpot plates. A validation document describing the validation results is supplied with each reader.

Installation Qualification and Operational Qualification (IQOQ)

Qualified Mabtech technicians install Mabtech readers. Installation includes reader set-up, verification of XY table alignment, and operational qualification of optics and light sources. The operational qualification is made using a plate generated at Mabtech containing spots with all fluorophores used in our kits, one for each filter in Mabtech IRIS 2: LED380, LED490, LED550, and LED640. In addition, standard ELISpot plates are utilized for qualification of the White LED used in ELISpot and FociSpot analysis in Mabtech IRIS 2 as well as Mabtech ASTOR 2.

Upon installation, the Mabtech technician makes sure that the plate generates the same spot counts for LED380-, LED490-, LED550- and LED640-excited spots as it did when the reader was assembled and approved at Mabtech headquarters. This ensures that the reader has not suffered from any damage during transport and that the instrument matches reference readers at Mabtech headquarters.

All procedures are documented in an installation qualification and operational qualification document. In addition to installation and operational qualification, Mabtech provides a general introduction to the reader and hands-on training with customer staff.

Performance Qualification

Mabtech offers Performance Qualification (PQ) plates used to ensure that Mabtech ASTOR 2 and Mabtech IRIS 2 perform according to specifications. With the PQ plate, Mabtech Apex software conducts a series of quantitative and qualitative tests that can identify any incorrect or inconsistent operation of the reader. The data obtained is compared to baseline levels set for camera focus, LED light intensities, and spot counting using the RAWspot algorithm. Each PQ plate comes with a unique serial number, which is registered in Mabtech Apex, ensuring correct comparison. A report is automatically generated in non-modifiable PDF format, and the results are saved on the computer.

Mabtech recommends that PQ is performed at regular intervals, and the software will indicate when it is time to perform a test. When not in use, the PQ plate should be stored in its protective case in the dark, protected from dust, at room temperature.

Annual service

Mabtech offers a service package that includes an annual check-up of the reader. The performance is evaluated, and the hardware adjusted if necessary, with the consent of the user.

CFR21 part 11 compliance

The EU and the US (FDA) have established guidelines for the life sciences industry, known as Annex 11 and CFR21 part 11, respectively. These guidelines outline the use of computerized systems in clinical investigations and specify that the quality of source data obtained through these systems must match that of traditional paper records.

The Mabtech Apex™ software has been designed to comply with the following guidelines in § 11.10 Controls for a closed system of CFR21:

1. A start-up test report is automatically generated each time the user starts Mabtech IRIS™ 2 and Mabtech ASTOR™ 2, and the reader goes through the start-up steps (OFF → BOOTING → READY). The user can access the report by clicking on a hyperlink in the software. The reports are also automatically saved locally at C:\ProgramData. This feature enhances the audit trail and makes it possible for users to sign off on reports where the status of the reader has been validated prior to the readout of plates.

2. IQOQ and initial PQ are performed in connection to installation. Subsequent PQ can be performed using PQ Plate IRIS or PQ Plate ASTOR and the PQ function in Mabtech Apex. A timeline is created, and baseline focus, light intensity, and SFU/RSV values are established when registering a new PQ plate. PQ analysis is then performed regularly. Each time a PQ test is performed data is added to the timeline. The new data is compared to the baseline values, ensuring accurate reader performance over time. A PQ report outlining test criteria and results is exported in a PDF format, and the raw data from all PQ measurements are automatically saved locally at C:\ProgramData.

   Clarification: Meets paragraph a) in § 11.10 Controls for closed systems.

3. Copies of records are generated in both human-readable form and electronic form throughout the readout and analysis process. Data can be exported in a PDF, Excel, jpg, tiff, pzfx, and raw file format.

   Clarification: Meets paragraph b) in § 11.10 Controls for closed systems.

4. All captured well images are saved and processed as image RAW files. These contain the untouched signal input straight from the image sensor and are free of the user bias that otherwise would be introduced by settings such as sharpness, digital gain, color, hue, and saturation. From the moment of capture, the image RAW files are never changed or altered by the software. As a result, the true RAW data is maintained and cannot be concealed by any user, including the administrator.

   Clarification: Meets paragraph c) in § 11.10 Controls for closed systems.

5. Limited access is handled from the start when users must select a username and provide a unique password. After repeated failed attempts, the user is locked out. The creation of new user accounts is limited to administrators. The administrator controls user access to create new templates and the period of user access. Furthermore, the administrator defines whether to use Machine Default exposure values for LEDs or manually set values. Additional admin-controlled activities include:

   - Admin can export an audit file for each created user, showing all user activity from within the handle user section.
   - Admin can dictate user password complexity.
   - Admin can export individual users through an encrypted file and import it on another desktop computer thereby maintaining user ownership within the history file.
   - Admin controls the number of failed password attempts before user is locked out of Mabtech Apex.
   - Admin can set time of inactivity before the user must input their password again to continue using the system.
   - Admin can give admin privileges to created users.

   Clarification: Meets paragraphs d), f), and g) in § 11.10 Controls for closed systems.

6. Date, time, user, and machineID are always generated and stored for each read and saved plate. History files are automatically created in write-protected PDF format and specify the chronological order of all events from plate creation to last saving. This includes all elements that control source data: users, algorithm settings, spot counts, RSV values, time stamps, machineID, etc. In addition, users can add notes to individual wells informing of mishaps in pipetting or similar. The notes are saved separately and reported within the Excel file and cannot be deleted once created.

   Clarification: Meets paragraph e) in § 11.10 Controls for closed systems.

7. Captured RAW images and count files generated by the RAWspot™ algorithm in Mabtech Apex and the audit trail of each plate are individually validated by a checksum system in the software. Upon reading, each file is automatically passed through a checksum function, and a unique block of data is generated for each file type. Upon saving, the history audit file is given a unique checksum block of data. Every time a plate is opened, the checksum validation is re-run and controlled against the stored copy, making sure that it matches the original checksum value. If any of these image RAW files, count files or history files are removed, altered, or manipulated, the checksum validation will ultimately fail when opening the plate and will provide an integrity warning. If no warnings are provided, data integrity is assured.

   Clarification: Meets paragraph h) in § 11.10 Controls for closed systems.

Good clinical laboratory practice compatibility

Good Clinical Laboratory Practice (GCLP) is a set of standards that provides guidance on implementing Good Laboratory Practice (GLP) and Good Clinical Practice (GCP) principles to the analysis of samples from a clinical trial. GLP is a quality system that covers the organizational process and the conditions under which non-clinical laboratory studies are planned, performed, monitored, recorded, archived, and reported. It aims to promote the generation of valid, high-quality test data. The GCP principles are international, ethical, and scientific quality standards for designing, conducting, performing, monitoring, auditing, recording, analyzing, and reporting clinical trials that involve the participation of human subjects. Compliance with the practices assures that data and reported results are credible and accurate and that the rights, safety, and confidentiality of trial subjects are protected. If a customer would like to apply Mabtech IRIS 2 or Mabtech ASTOR 2 in their GCLP-regulated environment the following need to be taken into consideration:

1. Equipment: Validation of the reader as well as installation, training, and maintenance should be completed in the specific environment for use.
2. Standard Operating Procedures (SOPs) for handling, maintenance, etc. should be established by the user.
3. Computer systems: Procedures for the software such as audit trail, controlled user restrictions, and time stamps should be established.

CE mark

The readers have been tested and approved according to the EU directives for Electromagnetic compatibility, Low voltage, Machinery, and Restriction of Hazardous substances directives. International standards (e.g. IEC 61010-2-101) that regulate the safety requirements for electrical equipment for measurement, control, and laboratory use for in vitro diagnostic medical devices have been applied to ensure compliance.

ISO 9001 and ISO 13485

The Quality Management System at Mabtech AB complies with the quality management standards ISO 9001:2015 and ISO 13485:2016. The compliance is audited annually by external audits and the certificates have been maintained without interruption since 2006 when Mabtech first aimed for certification. The scope of the certificates is as follows: Development, manufacturing, marketing, and sales of monoclonal antibodies and immunoassay instruments for *in vitro* applications in biomedical sciences and service of immunoassay instruments. The ISO certificates are available for download on Mabtech's website.

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