21 CFR Part 11 Compliance
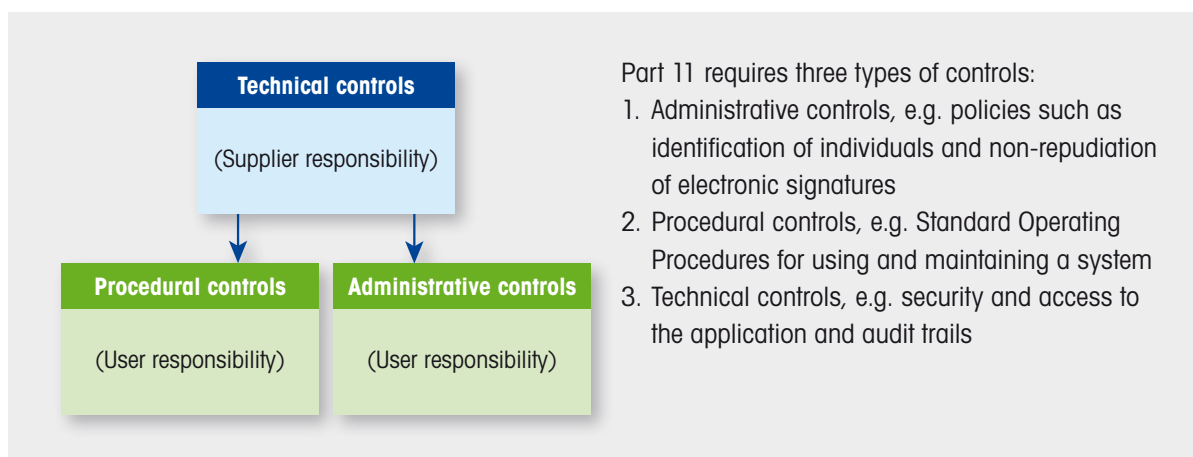## Electronic Records and Signatures

The U.S. Federal Food and Drug Administration (FDA) has issued regulations that provide criteria for acceptance by the FDA, under certain circumstances, of electronic records and electronic signatures as equivalent to paper records and handwritten signatures executed on paper.

Electronic records can therefore replace paper records
• for FDA submission
• for FDA inspection
• for archiving purposes
The purpose of the regulation is to ensure the integrity, the trustworthiness and the reliability of electronic records and, where used, electronic signatures.

Technical controls

(Supplier responsibility)

Procedural controls

(User responsibility)

Administrative controls

(User responsibility)

Part 11 requires three types of controls:
1. Administrative controls, e.g. policies such as identification of individuals and non-repudiation of electronic signatures
2. Procedural controls, e.g. Standard Operating Procedures for using and maintaining a system
3. Technical controls, e.g. security and access to the application and audit trails

The Electronic Records and Electronic Signatures final rule (FDA 21 CFR Part 11) became effective on August 1997. All systems that come under FDA regulations are impacted by the regulation.

The CFR STAR^e software ensures that the technical controls are compliant. Full 21 CFR Part 11 compliance is, however, only established when all three types of control are in place.

Features and benefits

• **Access control** – restricts system access to authorized individuals only
• **User Level Management** – customize user access profiles to reduce the probability of data manipulation
• **Electronic signatures** – replaces traditional signatures
• **Audit trail** – records all activities and changes to data

METTLER TOLEDO

FDA 21 CFR Part 11
Definitions

Electronic records

Electronic record means any combination of text, graphics, data, audio, pictorial, or other information representation in digital form that is created, modified, maintained, archieved, retrieved, or distributed by a computer system.

Electronic signature

Electronic signature means a computer data compilation of any symbol or series of symbols executed, adopted, or authorized by an individual to be the legally binding equivalent of the individual's handwritten signature.
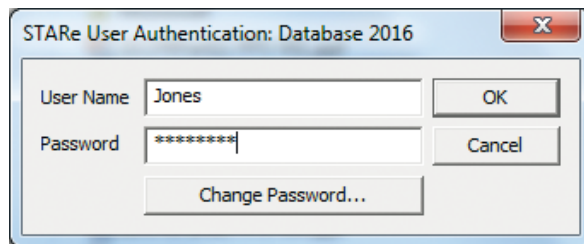
The ST**A**R^e software login box.

Closed system

Closed system means an environment in which system access is controlled by persons who are responsible for the content of electronic records that are on the system.

Key features

The ST**A**R^e software has been designed to work as a closed system. Its key features are:
• Access Control to the application (password)
• User Level Management (user rights)
• Electronic Records (file integrity)
• Audit Trail (change and system history)
• Electronic Signatures (status of electronic records)
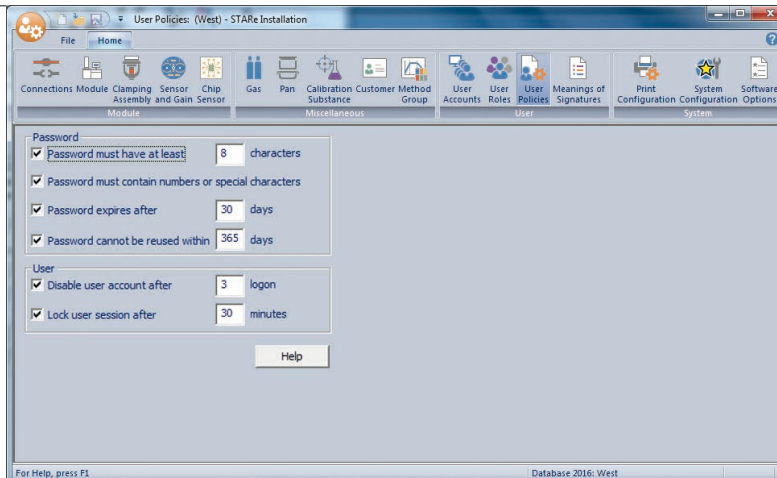
User policy definition.

Access control

The primary role of access control is to limit system access to authorized individuals. The STAR^e software can therefore only be used if the login is successful. Every user is unique and has a user name and a specific password.

Multiuser system

For multiuser purposes, each user must have a Windows and a STAR^e account. The Windows account allows the user to start the operating system; the STAR^e account allows the STAR^e software to be used.

If more than one user uses the STAR^e software, the automatic Windows screen saver lock must be switched off. A STAR^e user is automatically logged off after a certain period of inactivity (defined by the administrator).

Password policies

User identification restrictions:
- No two individual users can have the same login (unique user name)
- Old accounts can be disabled but not deleted

Users cannot be deleted or renamed, even if no other records refer to this user. In this way, the STAR^e software ensures that the entries in the audit trail can be uniquely assigned to a user. As a result, it is not possible to have more than one distinct user with the same identification throughout the lifetime of the STAR^e database.

The administrator has the options to define:
- The minimum password length
- Password with/without special characters (for enhanced security)
- Password age control
  - expiration date (password must be periodically changed)
  - reuse period for passwords, if allowed
- Maximum number of logon attempts (account lockout after an administrator-defined number of failed logins)
- Deactivation time (for the STAR^e screen saver lock)

The administrator can reset the password of any user.

User Account Creation

User account creation.

Electronic records

Electronic record means any combination of text, graphics, data, audio, pictorial, or other information representation in digital form that is created, modified, maintained, archieved, retrieved, or distributed by a computer system.

File integrity
Electronic records must be protected against intentional or accidental modification or deletion.

All electronic records are stored in the STAR^e software in a relational Ingres database. This means that only authorized STAR^e users can access data via the STAR^e software. A Windows user cannot access data in the database via the operating system. This provides more enhanced security compared with a file-based system.

Electronic copies
Copies in human readable paper form and in electronic form can be generated of all electronic records that can be signed. The content is the same as in the textual or graphical printouts. Electronic copies for inspection by internal or external auditors (e.g. the FDA) are generated in a non-editable format. For the STAR^e software, this is the .pdf file format.

User Level Management
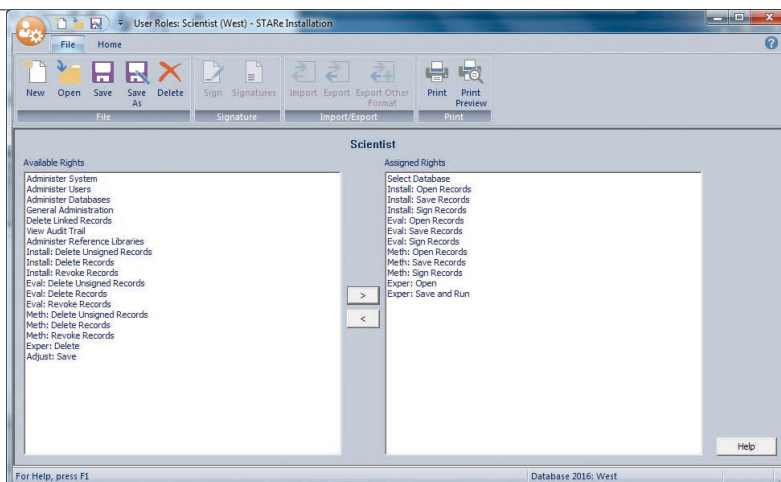
User role definition.
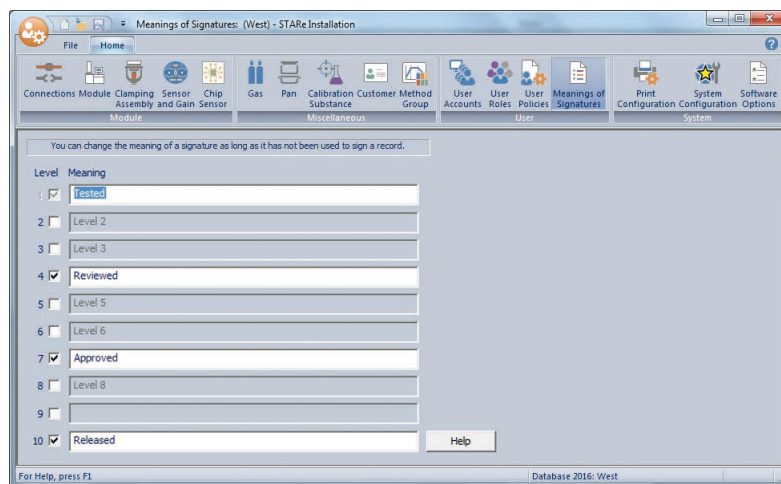
Signature levels and signature meanings.

User	Role	Signature level	Meaning
Jones	Lab Manager	10	Released
Widman	Senior Scientist	7	Approved
Miller	Scientist	4	Reviewed
Frazer	Lab Technician	1	Tested

User rights

Up to 30 different rights can be granted as appropriate to an unlimited number of diffenrent user roles.

User roles

Each user is assigned a user role. The user role defines the group of rights granted to that particular user (for example the administrator, lab manager, lab technician, operator).

Signature level

Each user is assigned a user role and signature level that corresponds to the user's daily business requirements. This means that a user can only sign a record if he has the basic right to sign and also has the appropriate signature level (i.e. higher than the actual status of the electronic record = last signature level).

Example

Once user Miller has signed a record, only users with the right of signature and with a signature level higher than 4 can additionally sign the same electronic record (in this example, Widmann or Jones, because they have signature levels of 7 or 10).

Electronic Signatures
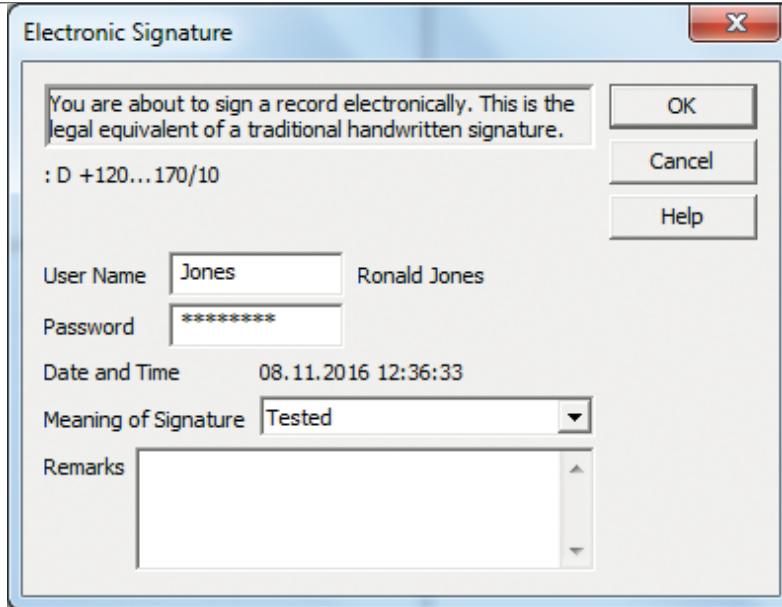
Electronic signature user authentification.

The process of signing consists of:
- User authentication
- Check of the signature right
- Check of the signature level
- Setting the level to the new signature level
- Selection of a meaning out of an administrator-defined list (max. 10 meanings)
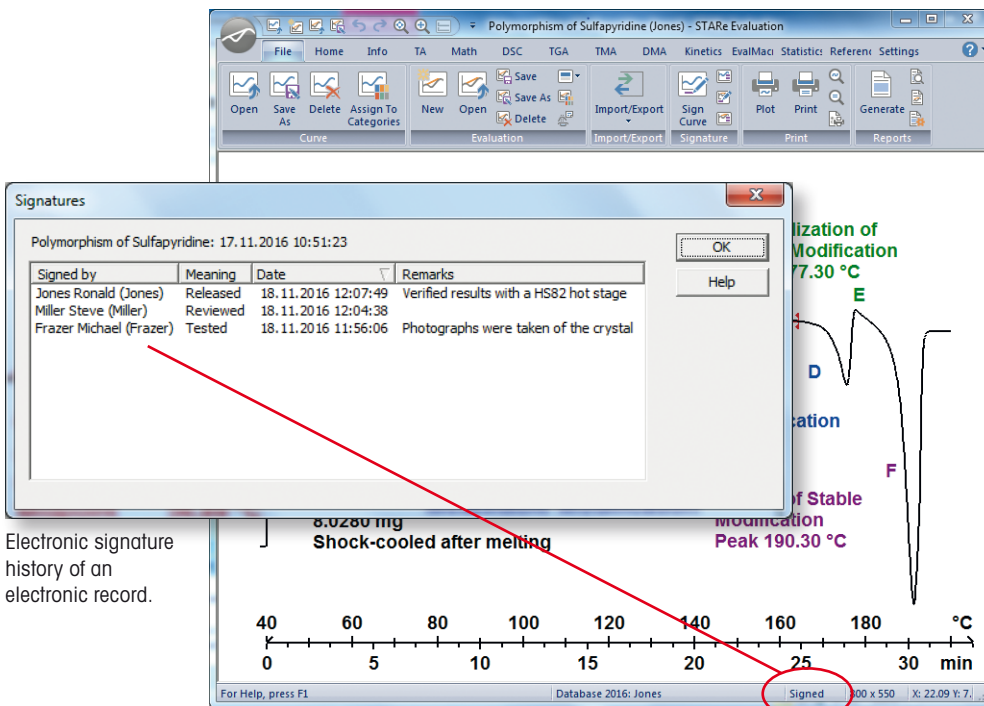- Adding an optional remark

It generates:
- Printed name of the signer
- Date and time of the execution
- History of all signatures related to this electronic record

The electronic signature (status) is visible in the electronic display as well as on the printout of each electronic record.

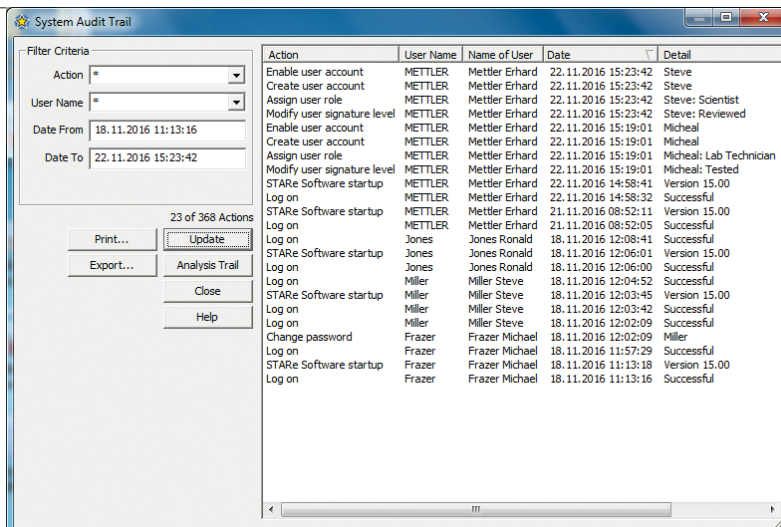For more details, you can select File ⇨ Electronic signature …

The following information appears and is automatically included in a printout.

Once you decide to sign an electronic record, user authentication takes place (user name and password).

The signature is linked to the record you sign and cannot be removed, copied or transferred.
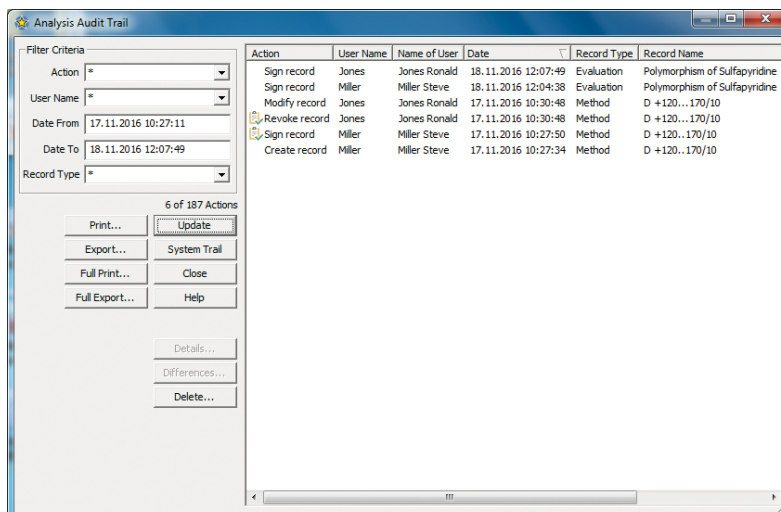

Electronic signature history of an electronic record.

Signed evaluation.

Audit Trail

Excerpt from the system audit trail.

Excerpt from the analysis audit trail.

Computer-generated time-stamped audit trails
METTLER TOLEDO has implemented two audit trails in the STARᵉ software: the system audit trail and the analysis audit trail.
Each has a specific function within the software.

System audit trail
The system audit trail keeps detailed records of all system changes (login attempts, software version changes, backup and restore, user creation, …).

General audit trail functions

Filter functions
Filter functions allow you to quickly find the appropriate part of the audit trail, to facilitate review or inspection.

Filter functions available are:
- Action (why)
- User (who)
- Date (when)
- Item (what)

Printout/Export
Copies of the audit trail or part of it can be generated in human read-able but non-editable form, and in electronic form (.pdf). The same filter criteria as above can be applied. Furthermore, the audit trail can be printed and exported as a text file. Export as a text file is protected by a special user right that needs a user procedure to state when this can be used.

For the analysis audit trail, printouts and exports can be generated that include or exclude some specific details.

System Validation

This ensures that it is not possible to make changes to data outside a compliant system and to bring the data back into a compliant system. The audit trail keeps track of such actions. An old database that was used in a non-CFR compliant system can be restored in a compliant system.

From this point onward, old records are treated as being identical to new records.

Analysis audit trail

The analysis audit trail keeps detailed records of all significant changes of electronic data objects. It documents the creation, modification and deletion of any electronic record.

The audit trail records what, how, who, when, where and why:
• What was changed (indicates the record type)
• How shows the previous and the new value (difference)
• Who made the changes (user and user name)
• When the change occurred (date and time of the change: computer generated time-stamp)
• Where the change was made (electronic record identification)
• Why the change was made (the reason – if there is one)

System validation

The STAR^e software has been developed and validated according to a certified Quality Management System which conforms to ISO 9001 guidelines. The software development life cycle follows ISO guidelines.

METTLER TOLEDO offers in addition Installation Qualification (IQ) and Operational Qualification (OQ) and will be pleased to assist you with Performance Qualification (PQ).