

System Assessment Report
Relating to Electronic Records and Electronic Signatures;
Final Rule, 21 CFR Part 11

System: tiamo 2.3

1 Procedures and Controls for Closed Systems

Ru nno	Ref.	Topic	Question	Yes	No	partly	Comments
1.1	11.10 (a)	Validation, IQ, OQ	Is the system validated?	O			<p>The operator is solely responsible for the validation of the system. The responsibility of the supplier lies in supplying systems which are capable of being validated. This is supported by the internal Metrohm quality control system which can be audited at any time.</p> <p>In this respect Metrohm offers a range of validation services: conformity certificates, prepared documentation for IQ and OQ, carrying out IQ and OQ at the operator's premises, ...</p> <p>Standard methods for system validation are stored in the system.</p>
1.2	11.10 (a)	Audit Trail, Change	Is it possible to discern invalid or altered records?	X			<p>All relevant operator entries are recorded in an automatically generated audit trail with date, time with difference to UTC (Coordinated Universal Time) and user. This time is the client time, which means that the administrator has to take care of the server time having been transmitted to the client.</p> <p>In the report generator, the report can be defined in order to indicate any modified results data (results).</p> <p>For method modifications all former versions are saved in the database and a comment has to be entered. Methods are subject to a version control. This means that modified data of a method leads to a new entry (version) in the database.</p> <p>If the results data are changed (recalculation), all former versions are saved in the database and a comment has to be entered. A version check is implemented for determinations. This means that modified data leads to a new entry in the database.</p> <p>Invalid results can be recognized if limit values have been defined. In case of exceeding this limits it can be defined in the system whether a message is displayed on the screen or a on the report or whether an E-mail is sent. Additionally it can be defined whether the determination has to be canceled.</p>

Ru nno	Ref.	Topic	Question	Yes	No	partly	Comments
1.3	11.10 (b)	Report, Printout, Electronic Record	Is the system able to produce accurate and complete copies of electronic records on paper?	X			<p>Configurable reports can be printed out for determinations (results data). Modifying the report configuration can be disabled for routine users.</p> <p>The automatic printout at the end of an analysis can be defined in the method run. This way it can be ensured, that system operator can reliably follow any modifying, overwriting or deleting of the data of a determination.</p> <p>Each printout is accompanied by a time stamp giving information about the difference to UTC.</p>
1.4	11.10 (b)	Report, Electronic Record, FDA	Is the system able to produce accurate and complete copies of records in electronic form for inspection, review and copying by the FDA?	X			<p>All data can be stored as encrypted XML file and can be evaluated by <i>tiamo</i>.</p> <p>Data can be exported to XML, CSV and SLK format.</p> <p>Via the report generator all reports can be provided in PDF format.</p> <p>The automatic data export at the end of an analysis can be defined in the method run. This way it can be ensured, that the system operator can reliably follow any modifying, overwriting or deleting of the data of a determination.</p>
1.5	11.10 (c)	Electronic Record, Retention Period, Archiving	Are the records readily retrievable throughout their retention period?	O			<p>The operator is solely responsible for storage/archiving.</p> <p><i>tiamo</i> can be installed as local server or client version. The system can permanently store the data in the <i>tiamo</i> database or on the computer or on a network drive by using an archiving system or on paper. The database has an automatic backup function.</p> <p>The data on the storage device is encrypted and provided with a checksum. This way it is protected against accidental and improper modification. Modifications are recognized by the system. The content can be read by the <i>tiamo</i> software at any time.</p> <p>The method used for archiving data and which data are to be archived must be defined by the operator. Interfaces for archiving (XML files) are available in the system.</p>

Ru nno	Ref.	Topic	Question	Yes	No	partly	Comments
1.6	11.10 (d)	Login, Access Protection, Authorization User, Administrator	Is the system access limited to authorized individuals?	X			<p>The system is provided with a login system with an unlimited number of profiles (access rights / user groups). The access rights for the single user groups can be arbitrarily defined by the administrator.</p> <p>The persons responsible for the system (administrators) must ensure that access rights are assigned to authorized persons only.</p> <p>All changes of access rights are recorded in the audit trail.</p>
1.7	11.10 (e)	Audit Trail, Electronic Record, Operator Entries	Is there a secure, computer generated, time stamped audit trail, that logs the date and time of those user entries and actions which create, modify or delete electronic records?	X			<p>The audit trail documents all user entries and actions on electronic records with date, time with difference to UTC and user.</p> <p>Additionally, all modifications of security settings, user administration or configuration data are recorded in the audit trail.</p>
1.8	11.10 (e)	Electronic Record, Overwriting data, Change	If modifying electronic records, is previously recorded information still available in the system (i.e. is it not overwritten by the modification)?	X			<p>Yes, a new version is automatically created, if methods or determination data are changed and saved.</p>
1.9	11.10 (e)	Audit Trail, Retention Period	Is the audit trail of an electronic recording retrievable throughout the retention period of the record?	X			<p>As long as the audit trail has not been deleted it is kept. The disk space is the limiting factor here. The audit trail can only be deleted after it has been archived. The audit trail is being archived as a text file with a checksum.</p> <p>The operator is solely responsible for the storage of the archived audit trail.</p>
1.10	11.10 (e)	Audit Trail, FDA, Inspection	Is the audit trail available for review and copying by the FDA?	X			<p>The audit trail can be exported to a text file with a checksum and is therefore available in electronic form and on paper. Via the checksum, the integrity of the Audit Trail can be verified.</p> <p>Additionally, a read-only PDF file of the audit trail can be created.</p>

Ru nno	Ref.	Topic	Question	Yes	No	partly	Comments
1.11	11.10 (f)	Sequence of steps, Sequence, Plausibility Check, Devices	If the sequence of system steps or events is important, is it enforced by the system (e.g. as it would be the case in a process control system)?	X			<p>In the system, plausibility checks are already carried out when a determination is started, for example, a check is made whether all necessary devices are present.</p> <p>The sequence of the determination is programmed in the method and must be strictly maintained.</p> <p>Maintaining the sequence is supported by using the sample assignment table or the automatic sample data request. Only the functions to be carried out are accessible.</p>
1.12	11.10 (g)	Login, Access Protection, Authorization, User, Administrator	Does the system ensure that only authorized persons can use the system, electronically sign records, access the functions, the computer system input or output device, can modify a record or perform other operations?	X			<p>The user can be identified by the login function. (The persons responsible for the system (administrators) must ensure that access rights are assigned to authorized persons only). The administrator function can be clearly separated from user roles, see also 11.10 (d), No. 1.6. Methods and determinations can be signed and therefore be released electronically. There are two signature levels. The system demands that the reviewing and the releasing person is not the same.</p>
1.13	11.10 (h)	Balance, Connection, Terminals, Input data, Devices	<p>Does the system control the validity of connected devices?</p> <p><i>If it is a system requirement that input data or instructions can only be received by certain input devices (e.g., terminals) does the system check the validity of the source of any data or instructions received?</i></p> <p><i>(Note: This applies where data or instructions can be received from more than one device, and therefore the system must verify the integrity of the source, such as a network of balances or remote controlled terminals).</i></p>	X			<p>During the IQ all the devices connected are entered into the list of devices and are subsequently checked.</p> <p>Metrohm devices are recognized, their validity is being checked and they are automatically entered into the list of devices.</p> <p>Balance: In the system the configuration of the balance is saved. In order to check that the correct balance is connected, the operator must carry out an IQ after a system installation or modification. The data obtained is checked for the correct identification and position of the weight in the character string.</p> <p>Validation of the devices connected is carried out as part of the system validation (see also 11.10 (a), No. 1.1) by the operator.</p>

Ru nno	Ref.	Topic	Question	Yes	No	partly	Comments
1.14	11.10 (i)	Training, Support, User, Administrator	Is there documented training, including training on the job, for system users, developers, IT support staff?	X/O			The operator is responsible for training the users and administrators. Metrohm offers standard training courses for all application fields. Individual training courses can be arranged separately. Metrohm product developers and service personnel are trained on a regular basis.
1.15	11.10 (j)	Policy, Responsibility, Electronic Signature	Is there a written policy that makes individuals fully accountable and responsible for actions initiated by their electronic signatures?	O			If electronic signatures are used the operator must have a policy which clarifies the equality of handwritten and electronic signatures.
1.16	11.10 (k)	Documentation, Distribution of Documentation, Access to Documentation, System Documentation, Logbook, Manuals	Is the distribution of, access to, and use of systems operation and maintenance documentation controlled?	O			The system has a comprehensive online help supporting the user and the service personnel. The operator is responsible for distributing paper-based documentation.
1.17	11.10 (k)	SOP, Documentation, Manuals, System Documentation, Audit Trail, Logbook	Is there a formal change control procedure for system documentation maintaining an audit trail which records modifications with a time sequence?	X/O			The system documentation is unambiguously assigned to a system and a software version. Release notes are kept with each software version. However, the operator must maintain a device logbook and note any changes in the documentation and the software. Templates of these documents are supplied by Metrohm.

2 Additional Procedures and Controls for Open Systems

Ru nno	Ref.	Topic	Question	Yes	No	partly	Comments
2.1	11.30	Data, Encryption, Data Transfer	Can methods and determinations be securely transferred from one system to another? Is the data encrypted on its way from the sender to the receiver?	N/A			Access to <i>tiamo</i> via the Internet is not provided. The data are stored as a file, encrypted and provided with a checksum. This protects the data against unauthorized modification. In case of a modification the data become useless. Even if corrupted data are transferred to another system this is recognized.
2.2	11.30	Electronic Signature	Are electronic signatures used?	N/A			Access to <i>tiamo</i> via the Internet is not provided. Methods and determinations can be signed and therefore be released electronically. There are two signature levels. The system demands that the reviewing and the releasing person is not the same.

3 Signed Electronic Records

Ru nno	Ref.	Topic	Question	Yes	No	partly	Comments
3.1	11.50	Electronic Signature	Do the signed electronic records contain the following related information? - Full name of signer - Date and time of the signature - Meaning of the signature (as approval, review, responsibility)	X			In case of methods and determinations all signatures contain the full name of the signer, date and time of the signature and the reason (out of a list box) for signing. Additionally, a comment on a signature can be entered, which is saved together with the electronic signature. There is no obligation to sign user data or audit trail data, therefore these data are not signed.
3.2	11.50	Electronic Signature	Is the information mentioned above shown on displayed and printed copies of the electronic record?	X			Full signature data are shown on the display and on printouts.

Ru nno	Ref.	Topic	Question	Yes	No	partly	Comments
3.3	11.70	Electronic Signature	Are signatures linked to their respective electronic records in order to ensure not being cut, copied or otherwise transferred by ordinary means for the purpose of forgery?	X			The signature is inseparably linked to the method or determination. Forgery is therefore impossible. User information is completely assumed in the signature. When displaying the signature, this information is always readable in plain text.

4 Electronic Signature (General)

Ru nno	Ref.	Topic	Question	Yes	No	partly	Comments
4.1	11.100 (a)	Electronic Signature	Are electronic signatures unambiguously assigned to a person?	X			Yes, by unique relation between login name and person within the system. It must operationally be ensured, that user names are used only once (the system monitors the unambiguity of the login name).
4.2	11.100 (a)	Electronic Signature	Are electronic signatures ever reused by, or reassigned to, anyone else?	O			A login name used is assigned to one person. It must operationally be ensured, that this login name is not assigned to another person. A reactivation is not affected by this.
4.3	11.100 (a)	Electronic Signature	Does the system allow transferring the authorization of electronic signatures (representatives)?	O			The assignment of representatives has to be carried out by the administrator. Here, operational arrangement is necessary.
4.4	11.100 (b)	Electronic Signature	Is the identity of a person verified before an electronic signature is allocated?	O			The organisational process of the authorization request has to ensure, that the requesting person is the correct one.

5 Electronic Signatures (Non-biometric)

Ru nno	Ref.	Topic	Question	Yes	No	partly	Comments
5.1	11.200 (a) (1)(i)	Electronic Signature	Does the signature consist of at least two components, such as an identification code (e.g. user name) and a password, or an identification card and a password?	X			Yes (login name and password).
5.2	11.200 (a) (1)(ii)	Electronic Signature	When several signings are made during a continuous session, is the password requested for each signing? (Note: Both elements must be named when firstly signing a session).	X			The password has to be entered with each signature.
5.3	11.200 (a) (1)(iii)	Electronic Signature	If signings are not made during a continuous session, would still both elements of the electronic signature be requested?	X			The login name and the password have to be entered with each signature.
5.4	11.200 (a) (2)	Electronic Signature	Are non-biometric signatures used by their genuine owners only?	O			The operator has to ensure that a user only uses his own signature
5.5	11.200 (a) (3)	Electronic Signature, Falsify Electronic Signature	Would an attempt to falsify an electronic signature require the collaboration of at least two persons?	X			Yes (the data of the database are encoded in a format non-readable for humans).

6 Electronic Signatures (biometric)

Ru nno	Ref.		Question	Yes	No	partly	Comments
6.1	11.200 (b)	Electronic Signature, Biometric Electronic Signature	Has it been proved that biometric electronic signatures can be used by their genuine owner only?	N/A			There is no use of biometric signatures with the system.

7 Control of Identification Code and Password

Ru nno	Ref.	Topic	Question	Yes	No	partly	Comments
7.1	11.300 (a)	Identification Code, Uniqueness, Password, Identification, Login, Access Protection	Are there controls in order to maintain the uniqueness of each combination of identification code and password, such as no person can have the same combination of identification code and password?	X / O			<p>The system ensures that every identification code (user name) is used only once within the system and therefore each combination of identification code and password can also only exist once. Modification of names has to be organizationally administered by the operator.</p> <p>The system can be run as client server system. This ensures that all identification codes are identical on all clients. It is recommended to use unambiguous identification codes (e.g. personnel number or initials) covering the entire organization.</p> <p>Generally it is recommended setting guidelines for the whole organization in which creating of user accounts and using passwords (length, period of validity, ...) are defined.</p>
7.2	11.300 (b)	Identification Code, Password, Validity, Identification, Login, Access Protection	Are there procedures ensuring that the validity of identification codes are periodically checked?	O			The operator is responsible for checking the identification codes.

Ru nno	Ref.	Topic	Question	Yes	No	partly	Comments
7.3	11.300 (b)	Password, Validity, Password Expiry, Identification, Login, Access Protection	Do passwords periodically expire and need to be revised?	X			The validity period of the password can be defined by the administrator. Values between 30 and 90 days are common. A long validity period represents a security risk. A validity period which is too short means that the users have to remember a new password frequently and may write it down. The system saves the password history and therefore reusing passwords is impossible.
7.4	11.300 (b)	Identification Code, Password, Validity, Disable User Access, Identification, Login, Access Protection	Is there a procedure for recalling or disabling identification codes and passwords if a person leaves or changes its workplace?	O			The procedure has to be set up by the operator. The corresponding user can be removed from the system by the administrator, but remains saved in the system as part of the group "removed users" without any access rights.
7.5	11.300 (c)	Identification Code, Password, Validity, Disable User Access, Identification, Login, Access Protection, Loss of ID card	Is there a procedure for electronically disabling an identification code or password if it is potentially insecure or has been lost?	O			The procedure has to be set up by the operator. The corresponding user can be removed from the system by the administrator, but remains saved in the system as part of the group "removed users" without any access rights.
7.6	11.300 (d)	Unauthorized Use, Login, Access Protection	Is there a procedure for recognizing attempts of misuse and for notifying the security authority?	X			After n incorrect attempts (number can be defined by the administrator) a message is displayed, saying that the maximum number of unsuccessful login attempts has been reached and the user is disabled. A corresponding message can be sent to the management by E-mail.
7.7	11.300 (d)	Unauthorized Use, Login, Access Protection	Is there a procedure for reporting repeated or serious attempts of misuse to the management?	O			A method for reporting to the management must be defined by the operator. After n incorrect attempts a message is displayed, saying that the maximum number of login attempts has been reached and the user is disabled. A corresponding message can be sent to the management by E-mail.
7.8	11.300 (c)	Loss of ID card, ID card, Unauthorized Use, Access Protection	Is there a loss management procedure if identification hardware (e.g. ID card) is lost or stolen?	N/A			There is no hardware for identification.

Ru nno	Ref.	Topic	Question	Yes	No	partly	Comments
7.9	11.300 (c)	Loss of ID card, Electronically Disabling ID card, ID card, Unauthorized Use, Access Protection	Is there a procedure for electronically disabling such hardware if it is lost, stolen or potentially insecure?	N/A			There is no hardware for identification.
7.10	11.300 (c)	ID card, Access Protection	Are there controls for the issuing of temporary and permanent replacements of this hardware?	N/A			There is no hardware for identification.
7.11	11.300 (e)	Testing of ID cards, ID card, Access Protection	Is there initial and periodic checking of identification tokens and cards?	N/A			There is no hardware for identification.
7.12	11.300 (e)	Modification of ID cards, ID card, Unauthorized Use, Access Protection	Does this checking also control that there have been no unauthorized modifications?	N/A			There is no hardware for identification.

O = The operator is responsible.

N/A = Not applicable to the system

January 13, 2009 a physical audit has been performed based on the tiemo 2.0 version. According to Metrohm AG, the implemented changes in the current version are not relevant with regard to 21 CFR Part 11 or compliant with 21 CFR Part 11 (see Release Notes 8.101.8017EN, 8.101.8027EN and 8.101.8039EN). Therefore, this update does not require a physical re-audit.

8 Indices

References to the page number:

A

Access Protection	4, 5, 10, 11, 12
Access to Documentation.....	6
Administrator	4, 5, 6
Archiving	3
Audit Trail	2, 4, 6
Authorization	4, 5

B

Balance	5
Biometric Electronic Signature	10

C

Change.....	2, 4
Connection	5

D

Data	7
Data Transfer	7
Devices	5
Disable User Access	11
Distribution of Documentation	6
Documentation	6

E

Electronic Record	3, 4
Electronic Signature	6, 7, 8, 9, 10
Electronically Disabling ID card	12
Encryption	7

F

Falsify Electronic Signature	9
FDA	3, 4

I

ID card	11, 12
Identification	10, 11
Identification Code	10, 11
Input data	5
Inspection	4
IQ	2

L

Logbook	6
Login	4, 5, 10, 11
Loss of ID card	11, 12

M

Manuals	6
Modification of ID cards	12

O

Operator Entries	4
OQ	2
Overwriting data	4

P

Password	10, 11
Password Expiry	11

Plausibility check	5
Policy	6
Printout	3

R

Report	3
Responsibility	6
Retention Period	3, 4

S

Sequence	5
Sequence of steps	5
SOP	6
Support	6
System Documentation	6

T

Terminals	5
Testing of ID cards	12
Training	6

U

Unauthorized Use	11, 12
Uniqueness	10
User	4, 5, 6

V

Validation	2
Validity	10, 11

References to the run number of the entry:

A

Access Protection ... 7.12, 7.11, 7.10, 7.9, 7.8, 7.7, 7.6,
7.5, 7.4, 7.3, 7.2, 7.1, 1.12, 1.6
Access to Documentation..... 1.16
Administrator 1.14, 1.12, 1.6
Archiving 1.5
Audit Trail 1.17, 1.10, 1.9, 1.7, 1.2
Authorization 1.12, 1.6

B

Balance 1.13
Biometric Electronic Signature 6.1

C

Change..... 1.8, 1.2
Connection 1.13

D

Data 2.1
Data Transfer 2.1
Devices 1.13, 1.11
Disable User Access 7.5, 7.4
Distribution of Documentation 1.16
Documentation 1.17, 1.16

E

Electronic Record..... 1.8, 1.7, 1.5, 1.4, 1.3
Electronic Signature..... 6.1, 5.5, 5.4, 5.3, 5.2, 5.1, 4.4, 4.3,
4.2, 4.1, 3.3, 3.2, 3.1, 2.2, 1.15
Electronically Disabling ID card..... 7.9

Encryption 2.1

F

Falsify Electronic Signature 5.5
FDA..... 1.10, 1.4

I

ID card 7.12, 7.11, 7.10, 7.9, 7.8
Identification..... 7.5, 7.4, 7.3, 7.2, 7.1
Identification Code 7.5, 7.4, 7.2, 7.1
Input data 1.13
Inspection 1.10
IQ 1.1

L

Logbook 1.17, 1.16
Login 7.7, 7.6, 7.5, 7.4, 7.3, 7.2, 7.1, 1.12, 1.6
Loss of ID card..... 7.9, 7.8, 7.5

M

Manuals 1.17, 1.16
Modification of ID cards 7.12

O

Operator Entries 1.7
OQ 1.1
Overwriting data..... 1.8

P

Password 7.5, 7.4, 7.3, 7.2, 7.1
Password Expiry 7.3

Plausibility Check 1.11
Policy 1.15
Printout 1.3

R

Report..... 1.4, 1.3
Responsibility 1.15
Retention Period..... 1.9, 1.5

S

Sequence 1.11
Sequence of steps..... 1.11
SOP 1.17
Support..... 1.14
System Documentation 1.17, 1.16

T

Terminals..... 1.13
Testing of ID cards 7.11
Training 1.14

U

Unauthorized Use..... 7.12, 7.9, 7.8, 7.7, 7.6
Uniqueness 7.1
User..... 1.14, 1.12, 1.6

V

Validation..... 1.1
Validity 7.5, 7.4, 7.3, 7.2