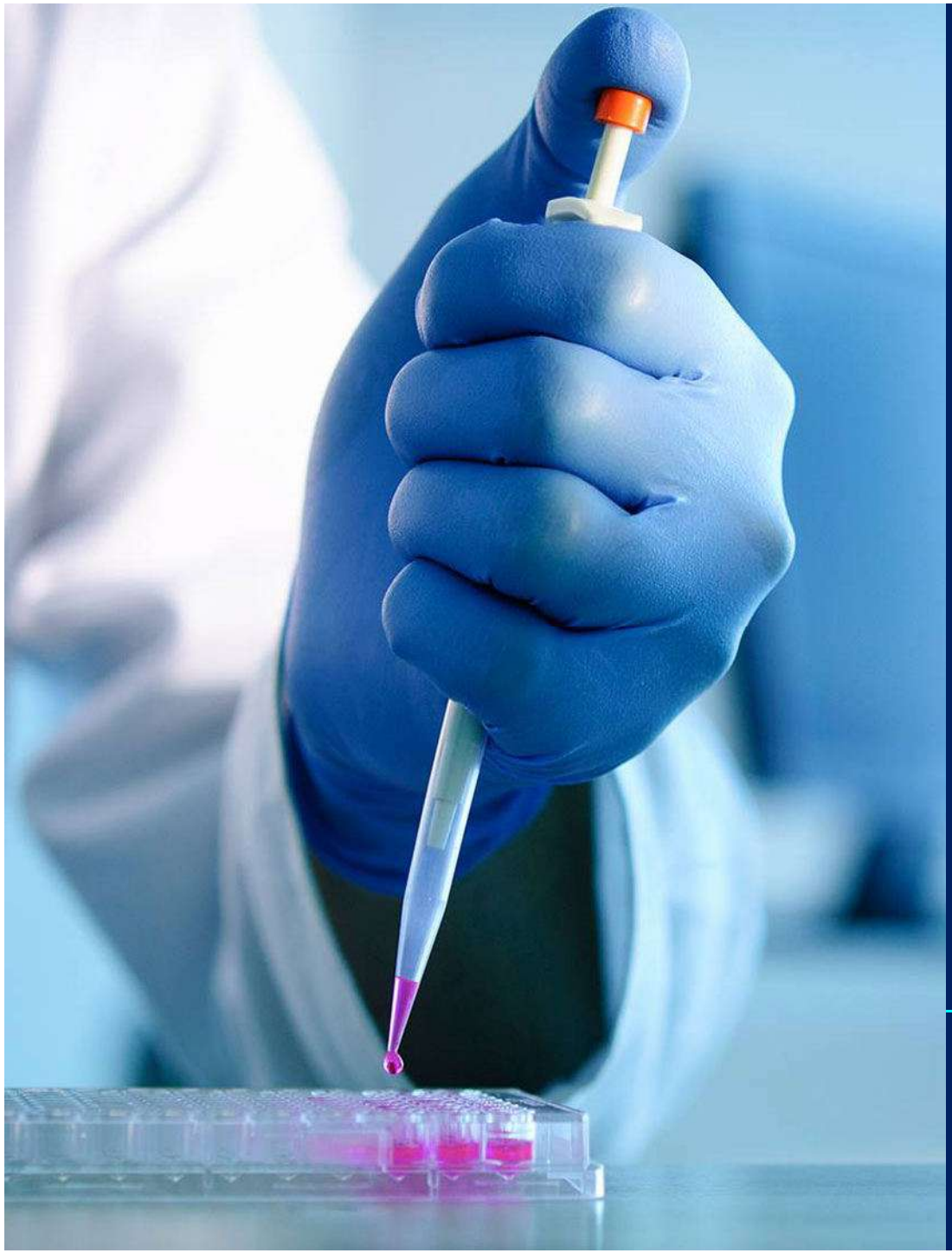
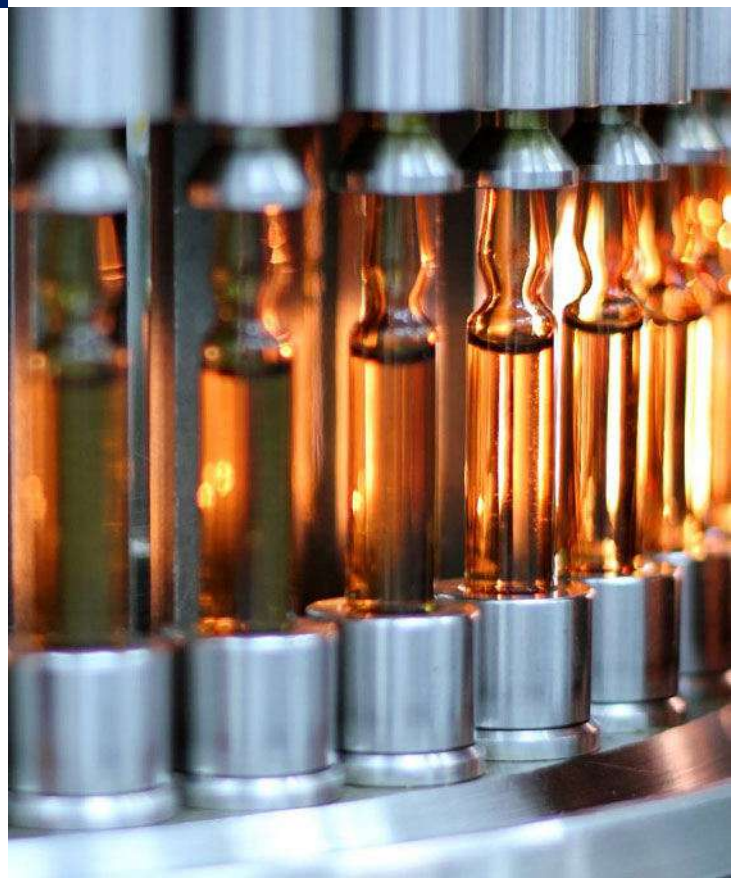


GMP Requirements

21 CFR Compliance

Content

1 Good Manufacturing Practice

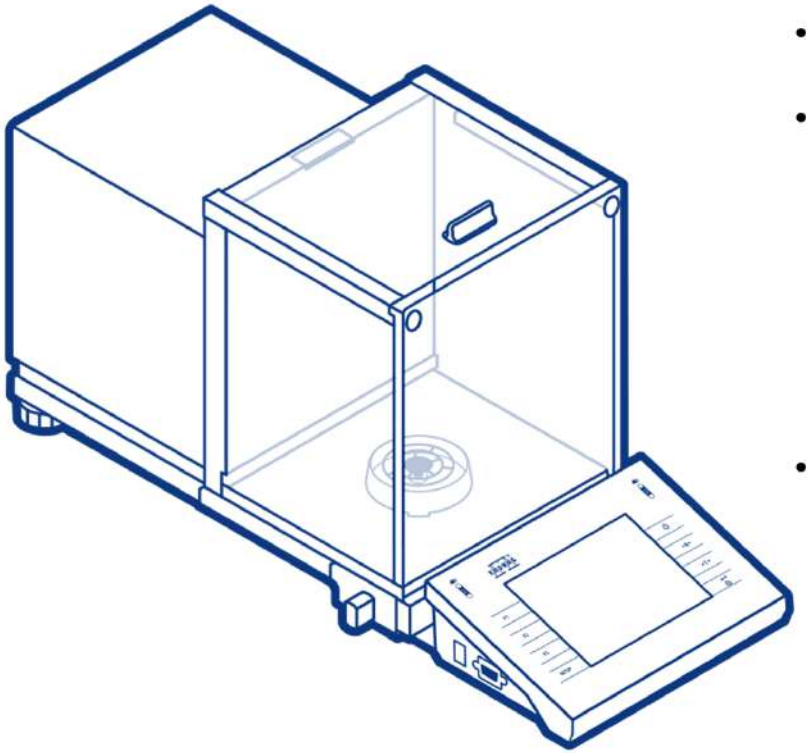


GMP or similar systems are defined as a set of rules which assure proper product manufacturing practice. They ensure strict supervision over weighing processes, sample weight control, sample dosing or checkweighing, selection etc. GMP procedure's function is to organize the control process in a way providing the user with a safe finished product (which RADWAG balances offer).

In pharma industry safety refers to use of certain medicines and for motor industry safety means security and reliability when it comes to use of particular mechanisms regarding operation of a vehicle and its subassemblies.

Content

2 In terms of balance



In terms of balance GMP focus needs to be put on balance life cycle which consist of:

- Evaluation of user's needs
- Choice of balance, selecting solution potentially assuring required weighing accuracy. The evaluation of parameters crucial for a specific weighing procedure. Choice of customized solution connected with weighing process.
- Balance installation, which means assessing working conditions regarding the manufacturers recommendations, matching or selecting best location for balance operation – concerning reading unit. Staff training, raising qualifications etc. Influence of ambient conditions on weighing.

2 In terms of balance

Balance Calibration:

Verification of device's measuring possibilities which are possible to achieve in certain working environment. Analysis of the results obtained in the weighing process – what that means in practice. How it should be interpreted. Choice of balance, selecting solution potentially assuring required weighing accuracy. The evaluation of parameters crucial for a specific weighing procedure. Choice of customized solution connected with weighing process.

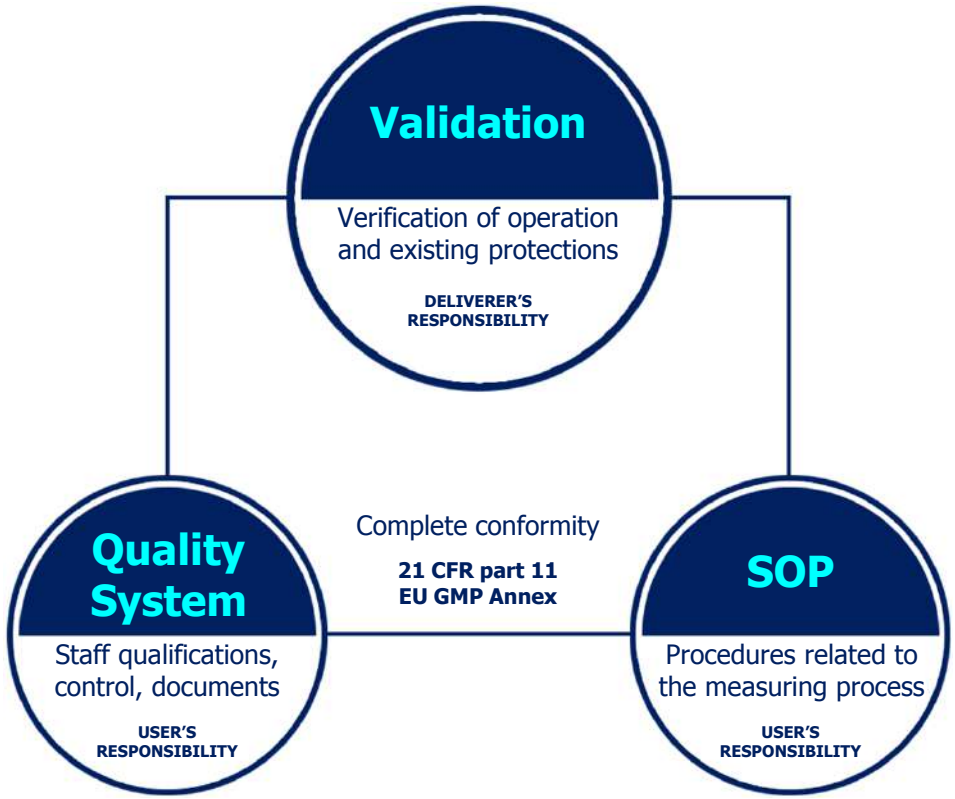
Routine operations, measuring equipment (balance) supervision:

- Periodic control tests – what should or shouldn't be checked?
- Adjusting as a process improving the accuracy of measurements.
- Risk as an element of measuring cycle, risk analysis meaning documents like ICHQ9 (QbD – Quality by Design) or alike for the pharmaceutical industry.
- Measuring uncertainty as a factor related to the weighing process, analysis of the major components of such parameter, its influence on a final result.

2 In terms of balance

Closed measuring systems such as 3Y, 4Y series balances or HY 10 terminals can be operated wherever compliance with 21 CFR Part 11 is required. Compliance with 21 CFR Part 11 means conformity with EU GMP Annex 11.

Relevant provisions of Annex 11 define computerised system as a set of software and hardware components which together fulfill certain GMP-specified functionalities. When it comes to 3Y, 4Y, HY 10 the said components are in-built elements and along with the balance they constitute one integral device.



2 In terms of balance

Conformity with CFR 21 requires more than just adherence of the weighing device to the regulations. Complete compliance is ensured when some of the requirements are met by the manufacturer and some by the user of the equipment.

Technical verification §11.10 (a,b,c,d), is to be carried out by the manufacturer, who installs the device. It aims to evaluate correctness of operation, control protections introduced in order to verify changes or access to various levels of application, and to enable verification of electronic signatures and documents. All these actions are part of validation of a weighing system.

Complete conformity

21 CFR part 11 / EU GMP Annex

2 In terms of balance

Procedural control §11.10 (e,f,g,h), is to be carried out by the user and it should cover Standard Operating Procedures which refer to measurement process issues. The SOP procedures should not be complicated, they must provide effective operation.

Complete conformity

21 CFR part 11 / EU GMP Annex

2 In terms of balance

Administrative monitoring §11.10 (i,j,k,l) is to be carried out by the user, it covers issues such as settings and parameters of both the device and the system.

Administrative monitoring means also staff trainings, control measures for access and distribution, procedures of control over changes (introduced modifications).

Complete conformity

21 CFR part 11 / EU GMP Annex

Content

3 Annex 11

Requirements of 21 CFR are applied only when there is a need to achieve conformity for products introduced into the USA market. 21 CFR is a document released by FDA – Food and Drug Administration.

European Commission has published a similar document, GMP (4) Annex 11, referring to computerised systems. Requirements of both 21 CFR and GMP (4) are practically likewise.

21 CFR part 11

3 Annex 11

Complete conformity with 21 CFR Part 11 is ensured by the following: mechanisms implemented on a balance, SOP procedures, administrative procedures being a part of Quality management system. The above statement refers to all measuring systems regardless of measured quantity.

Complete conformity

21 CFR part 11 / EU GMP Annex

3 Annex 11

Radwag offers balances and terminals (3Y, 4Y, HY) which ensure achieving conformity with CFR 21. Radwag has implemented all of the below presented provisions:

- **§ 11.10** Controls for closed systems
- **§ 11.50** Signature manifestations
- **§ 11.70** Signature/record linking
- **§ 11.100** Subpart C: General requirements, electronic signatures
- **§ 11.200** Subpart C: Electronic signature components and controls
- **§ 11.300** Subpart C: Controls for identification codes/passwords

Content

4 Technical Verification

11.10 (a-d)

All Radwag measuring systems are designed with reference to strict requirements of ISO 9001 introducing regulations for designing and production. The regulations guarantee reliability and functionality of each system, which system can be optimised in order to meet unique requirements of a particular working environment.

Any activity of any user of the system gets recorded in an Audit Trail, wherein the Audit Trail may be freely overviewed.

4 Technical Verification

11.10 (a-d)

In measuring systems of 4Y series all single records related to the weighing process are recorded in balance database, access to which is protected by use of passwords and respective access levels. Any data can be printed or exported at any time in format read by a spreadsheet program.

4 Technical Verification

11.10 (a-d)

All data is permanently stored in a database based on SQL. Database content may be periodically archived on a freely selected device in accordance with adopted time schedule.

4 Technical Verification

11.10 (a-d)

Upon start-up, the weighing system although active requires logging in. Each user has unique access code to the system.

There are 4 access levels:

- Guest
- User
- Advanced user
- Administrator

Each access level permits the user to carry out particular set of operations, e.g. printing, settings modification, designing printouts, designing methods, etc.

4 Technical Verification

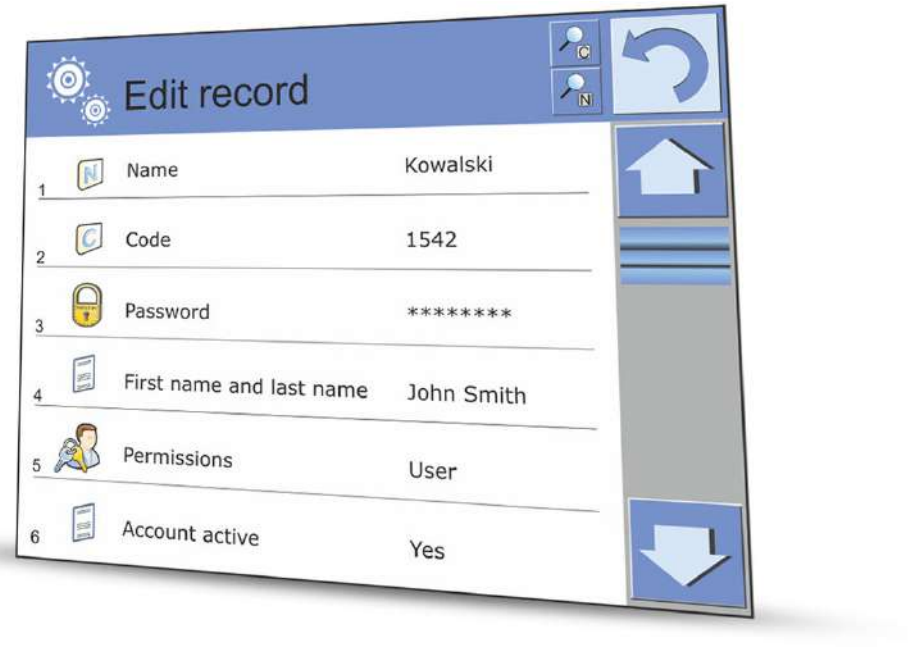
11.10 (a-d)

Weighing system's administrator can enforce password length, uppercase and lowercase, letters quantity or digits quantity. Besides the administrator can enforce user logout upon passage of specified amount of time. He/she is also entitled to lock the accounts.

4 Technical Verification

11.10 (a-d)

User-related data provides the following: name, code, password, first name and last name, permissions, status of the account, menu language, RFID card ID. When logging in it is necessary to confirm identity by entering access code.



4 Technical Verification

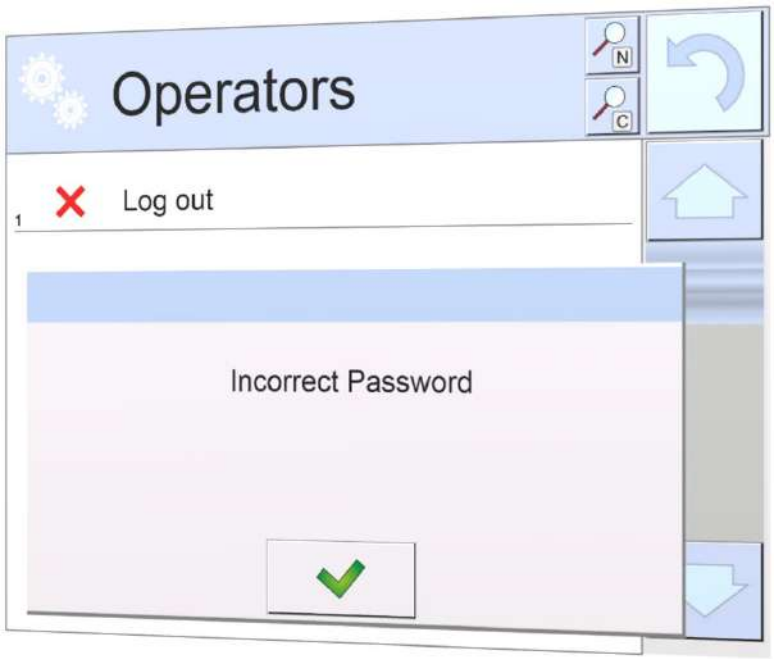
11.10 (a-d)

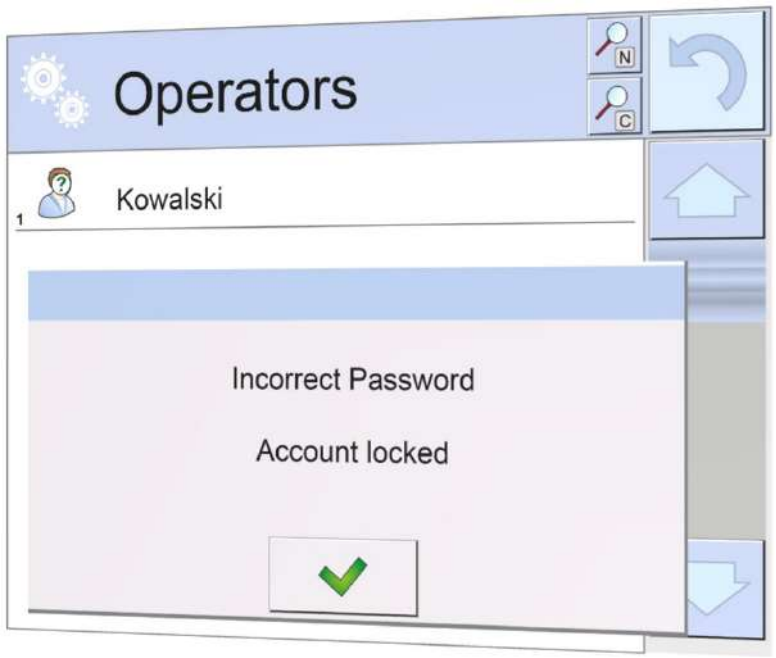
Persons who use electronic signatures based upon use of identification codes in combination with passwords shall employ controls to ensure their security and integrity. Balance software guarantees maintaining the uniqueness of each combined identification code and password, such that no two individuals have the same combination of identification code and password.

4 Technical Verification

11.10 (a-d)

Radwag balances cannot be operated by an operator who has entered wrong password few times in a row. Such an attempt results with an account lock.





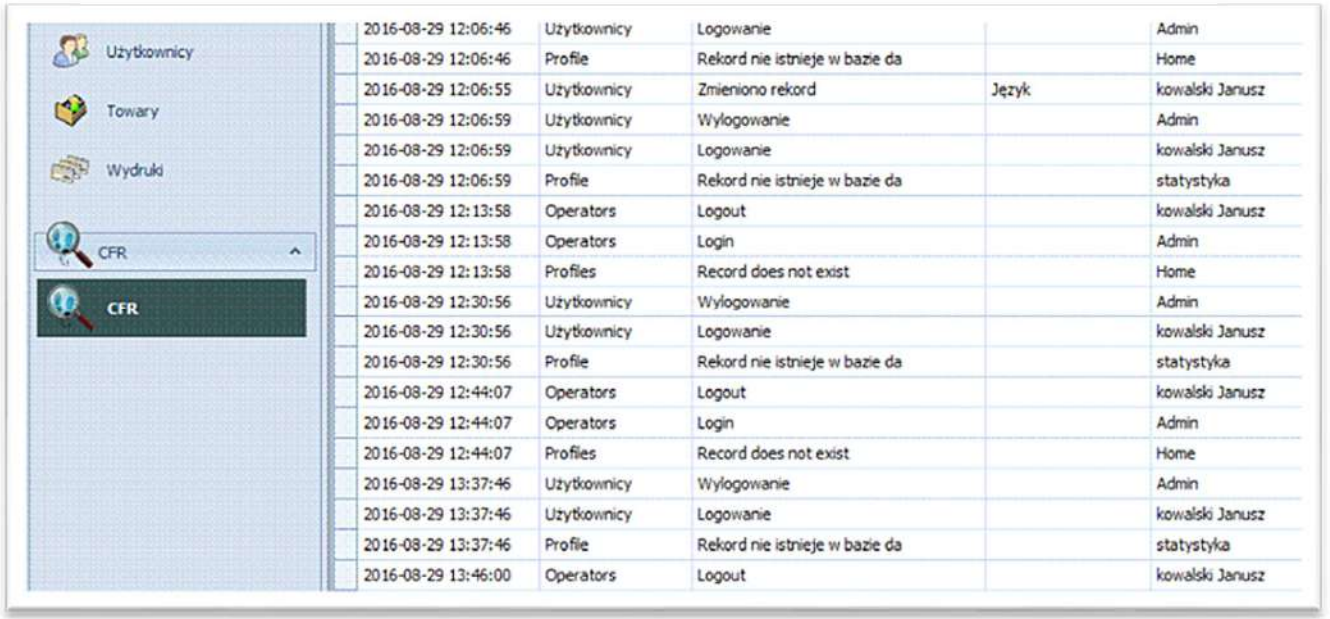
Content

5 Procedural Control – Audit Trial

11.10 (e-h)

Audit Trail has been designed to retrace all modifications concerning weighing instrument or its databases. It registers information on creating each record in the database, its modification (archiving previous and new value) or deleting. All Audit Trail records are linked with respective operator in order to easily recreate the history of weighing instrument operation. Time of carried out modification is saved with an information about possible change of the time on the weighing instrument.

The Audit Trail file cannot be modified. It is possible to export the file to a USB drive. Audit Trail Reader program enables reading the data stored in Audit Trail using PC. Audit Trail Reader allows to filter, manage and export data (as a report) to various files (PDF, XLS, CSV or HTML).



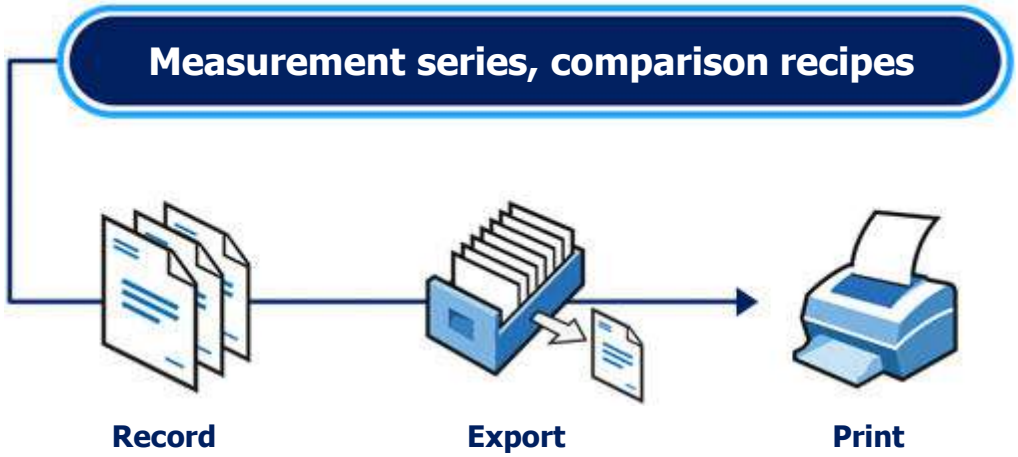
2016-08-29 12:06:46	Użytkownicy	Logowanie		Admin
2016-08-29 12:06:46	Profile	Rekord nie istnieje w bazie da		Home
2016-08-29 12:06:55	Użytkownicy	Zmieniono rekord	Język	kowalski Janusz
2016-08-29 12:06:59	Użytkownicy	Wylogowanie		Admin
2016-08-29 12:06:59	Użytkownicy	Logowanie		kowalski Janusz
2016-08-29 12:06:59	Profile	Rekord nie istnieje w bazie da		statystyka
2016-08-29 12:13:58	Operators	Logout		kowalski Janusz
2016-08-29 12:13:58	Operators	Login		Admin
2016-08-29 12:13:58	Profiles	Record does not exist		Home
2016-08-29 12:30:56	Użytkownicy	Wylogowanie		Admin
2016-08-29 12:30:56	Użytkownicy	Logowanie		kowalski Janusz
2016-08-29 12:30:56	Profile	Rekord nie istnieje w bazie da		statystyka
2016-08-29 12:44:07	Operators	Logout		kowalski Janusz
2016-08-29 12:44:07	Operators	Login		Admin
2016-08-29 12:44:07	Profiles	Record does not exist		Home
2016-08-29 13:37:46	Użytkownicy	Wylogowanie		Admin
2016-08-29 13:37:46	Użytkownicy	Logowanie		kowalski Janusz
2016-08-29 13:37:46	Profile	Rekord nie istnieje w bazie da		statystyka
2016-08-29 13:46:00	Operators	Logout		kowalski Janusz

5

Procedural Control Audit Trail

11.10 (e-h)

Radwag measuring system is a system in which sequence of events for all weighing processes has been planned. Upon completed measurement all data is automatically saved to balance database. Next the data can be printed or exported.



5

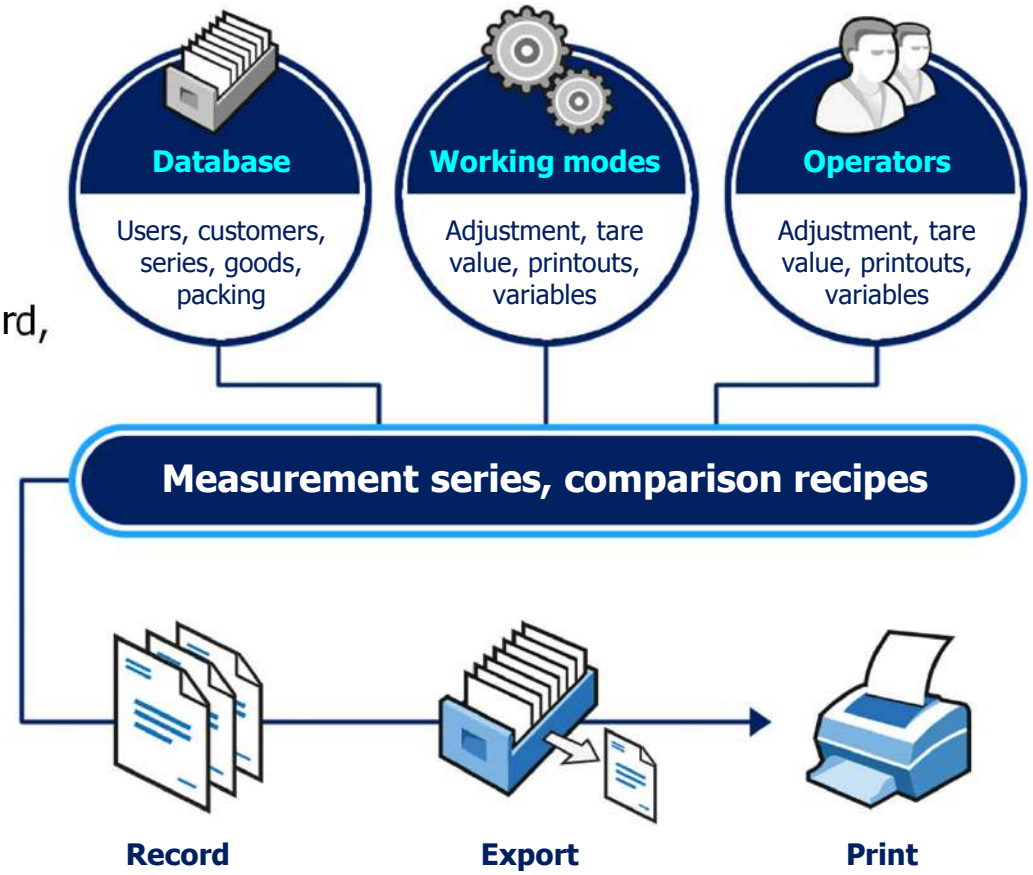
Procedural Control – Audit Trial

11.10 (e-h)

Measuring processes based on methods such as:

- series of measurements,
- differential weighing,
- formulations,
- comparison with mass standard,

enforce particular sequence of operations which cannot be altered. When carrying out measuring processes that are not based on any particular method, the sequence of operations and events shall be accordant with SOP regulations reflecting process and system requirements.



5

Procedural Control – Audit Trial

11.10 (e-h)

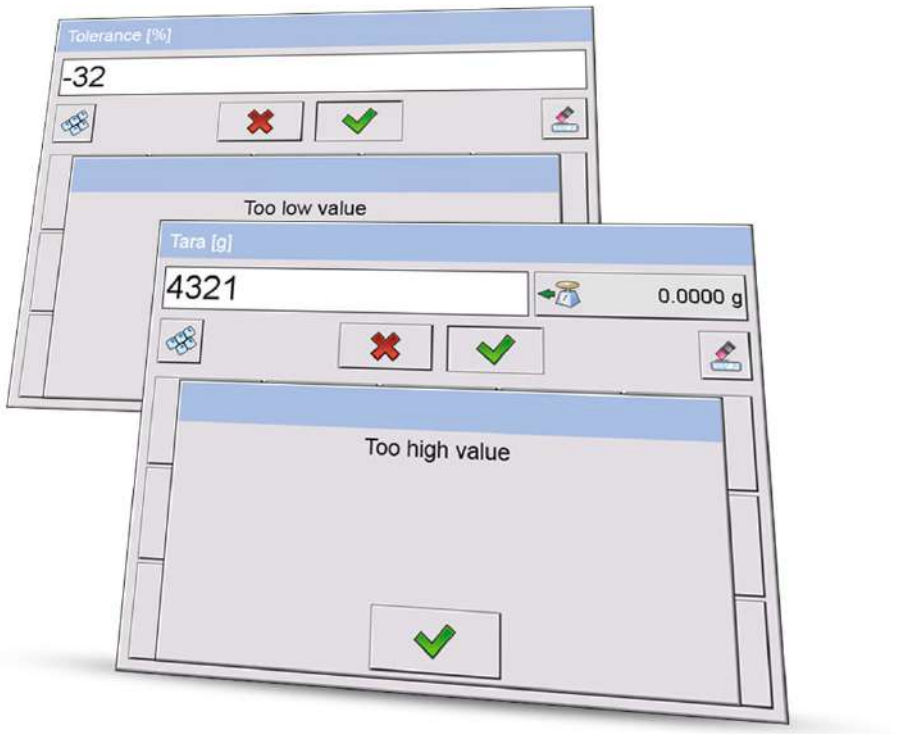
Measuring system of 3Y, 4Y, HY 10 series is protected by multi-level authorization system. In the course of the first logging in, password change is required. Such requirement is one of many safety precautions pre-venting unauthorised access.

5

Procedural Control – Audit Trial

11.10 (e-h)

On Radwag manufactured balances all input data is entered to the system by an operator. An attempt to enter any out of range data is clearly signaled to the operator thus entering too low or too high values is prevented.



Content

6

Administrative Monitoring

11.10 (i-k)

Continuous increase of professional qualifications is an inevitable element of development of each quality system. Radwag offers trainings providing the participants with knowledge on typical applications and dedicated system solutions. Participation is always confirmed with an appropriate certificate. Activity within this area is covered by ADMINISTRATION related operations performed by people monitoring the measuring system.

6 Administrative Monitoring

11.10 (i-k)

System related documents shall cover any issues concerning operation of the weighing system, i.e. technical control, periodical calibration and tests checking the functionality. Radwag offers the above listed services for each weighing system.

- Calibration
- Validation IQ/OQ/PQ
- Periodical technical control

Autotest GLP Report	
Balance type	MYA 4Y
Balance ID	257975
Operator	Admin
Application revision	L1.4.15.K
Date	2016.07.21
Time	10:12:14
Number of measurements	10
Balance weighing interval	0.000001 g
Internal weight mass	17.673852 g
Filter	Slow
Value release	Fast and reliable
Temperature: Start	23.99°C
Temperature: Stop	23.96°C
Humidity: Start	58 %
Humidity: Stop	58 %
Deviation for Max	0.000004 g
Repeatability	0.0000017 g

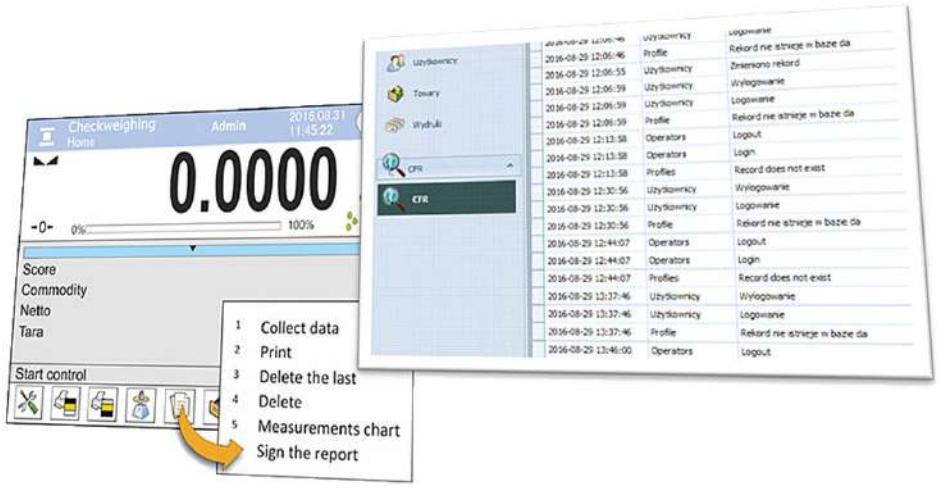
Content

7

Signature Manifestations

Signature signs

Every single weighing record, confirmed by PRINT button, is saved to the database. It is associated with currently logged in operator and product (providing that product has been selected).

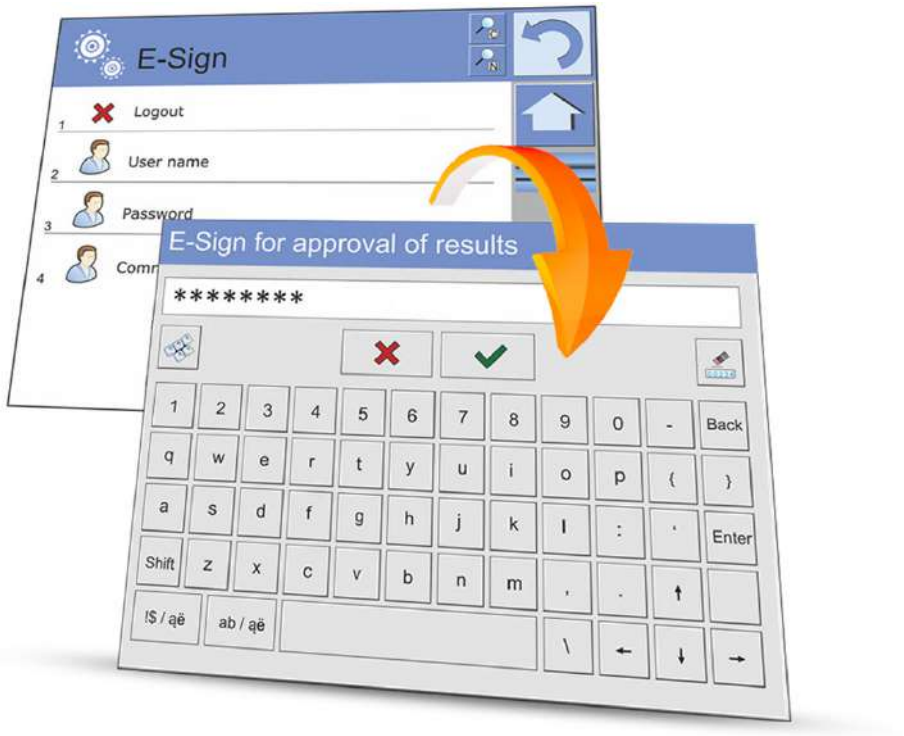


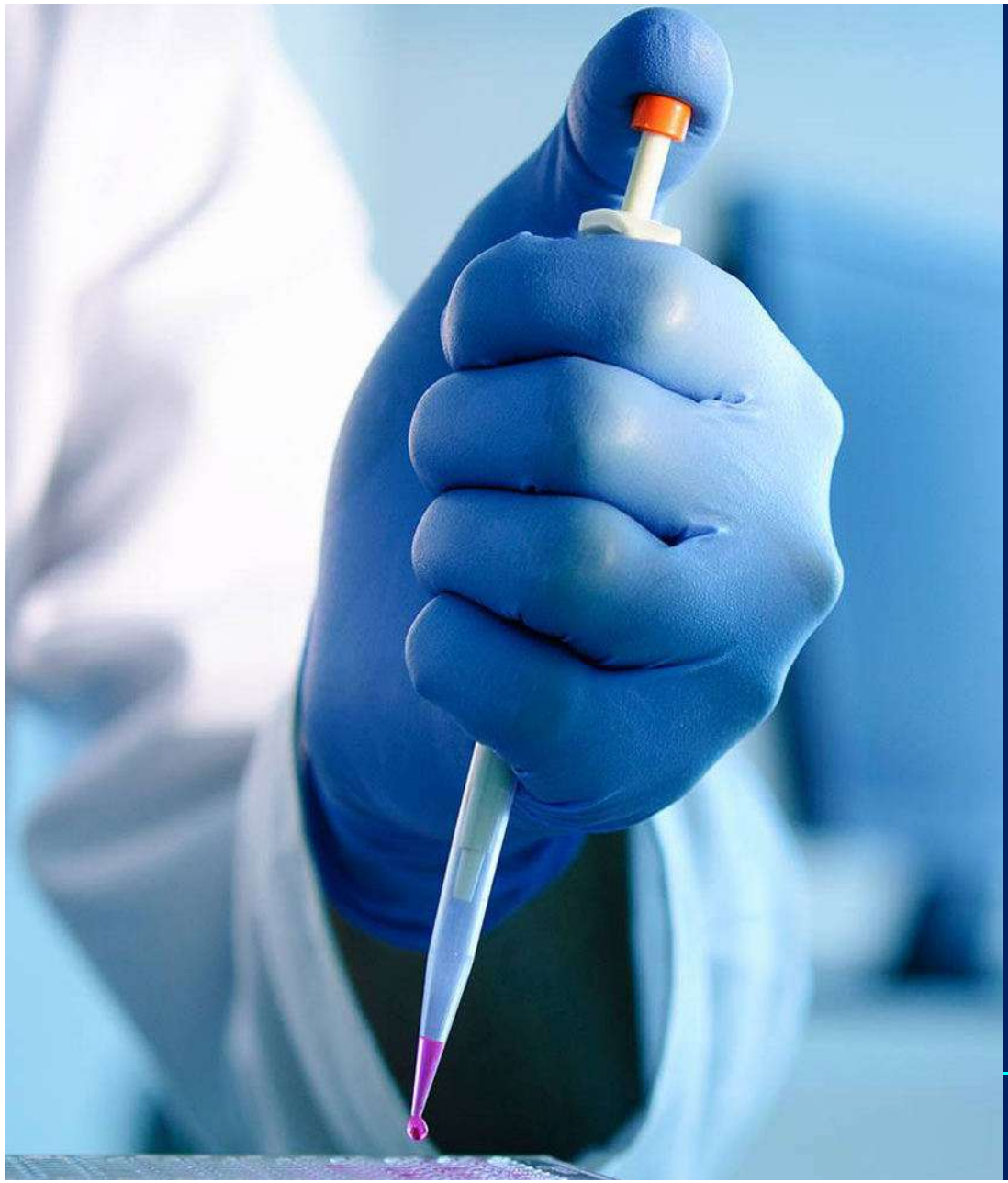
All changes, also those concerning electronic records, are recorded permanently. The changes can by analysed using Audit Trail file.

7 Signature Manifestations

Signature signs

More advanced solution is report on weighing or weighing series. The report is generated automatically for all weighing methods (statistics, SQC, differential weighing, formulations, etc.). Upon completed series each report is saved to reports database where it gets stored permanently. Report can be signed (author) or verified (supervisor).





RADWAG®

Thank you for your attention

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