Laboratory medicine – mandatory quality controls are self-evident

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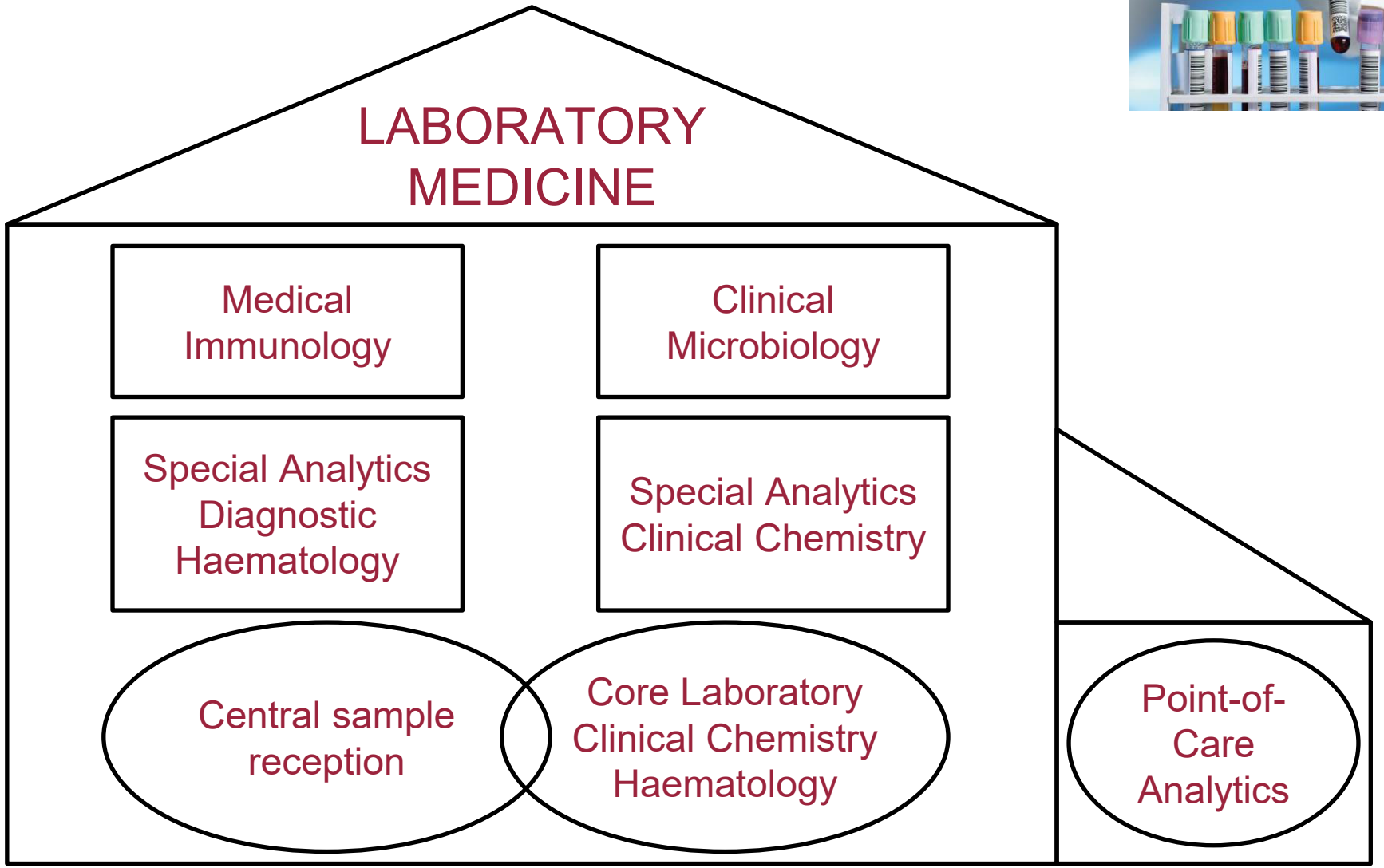
Eurachem Workshop 2023
Berne
23.5.2023

Laboratory Medicine



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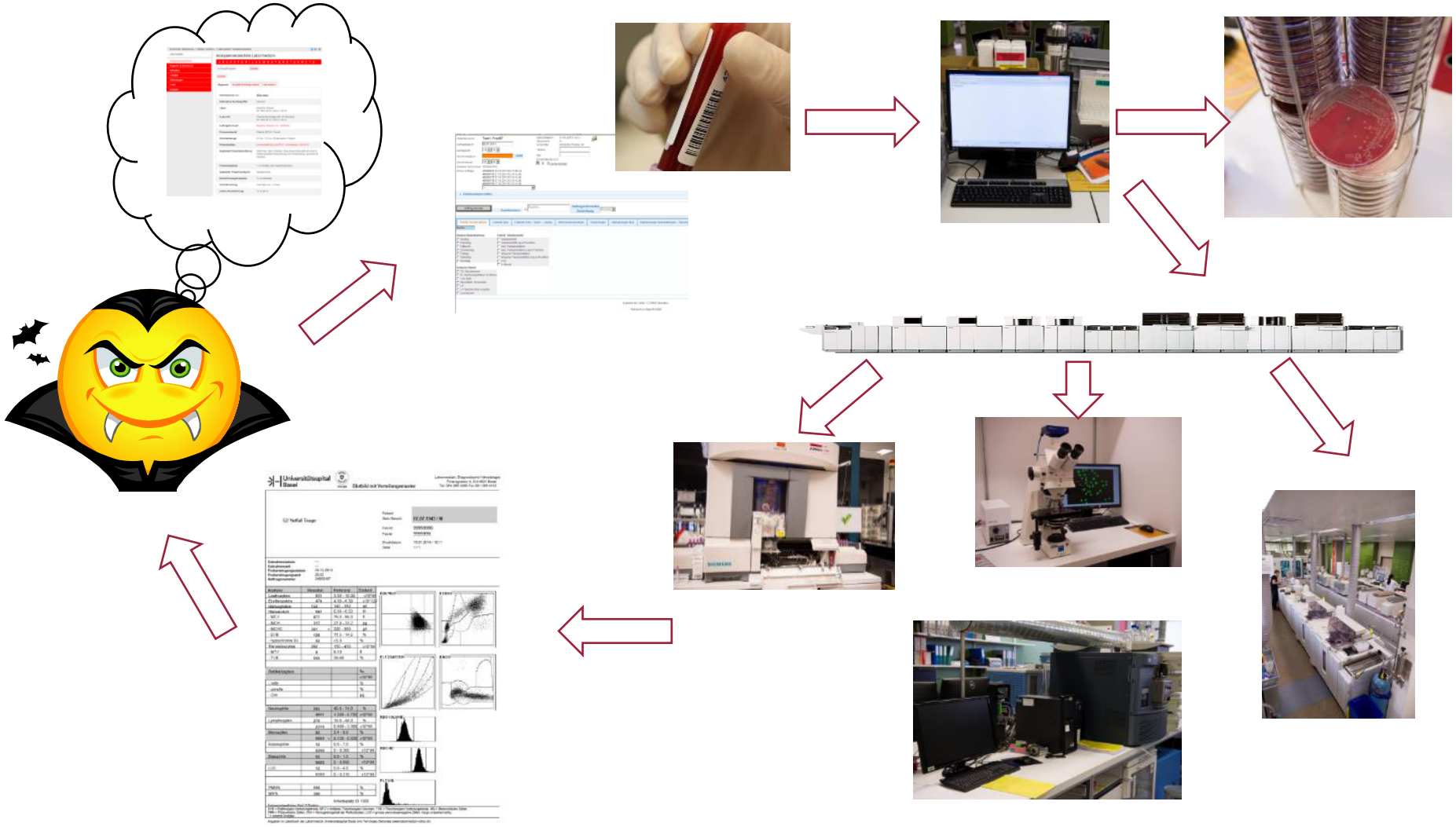
Laboratory Medicine

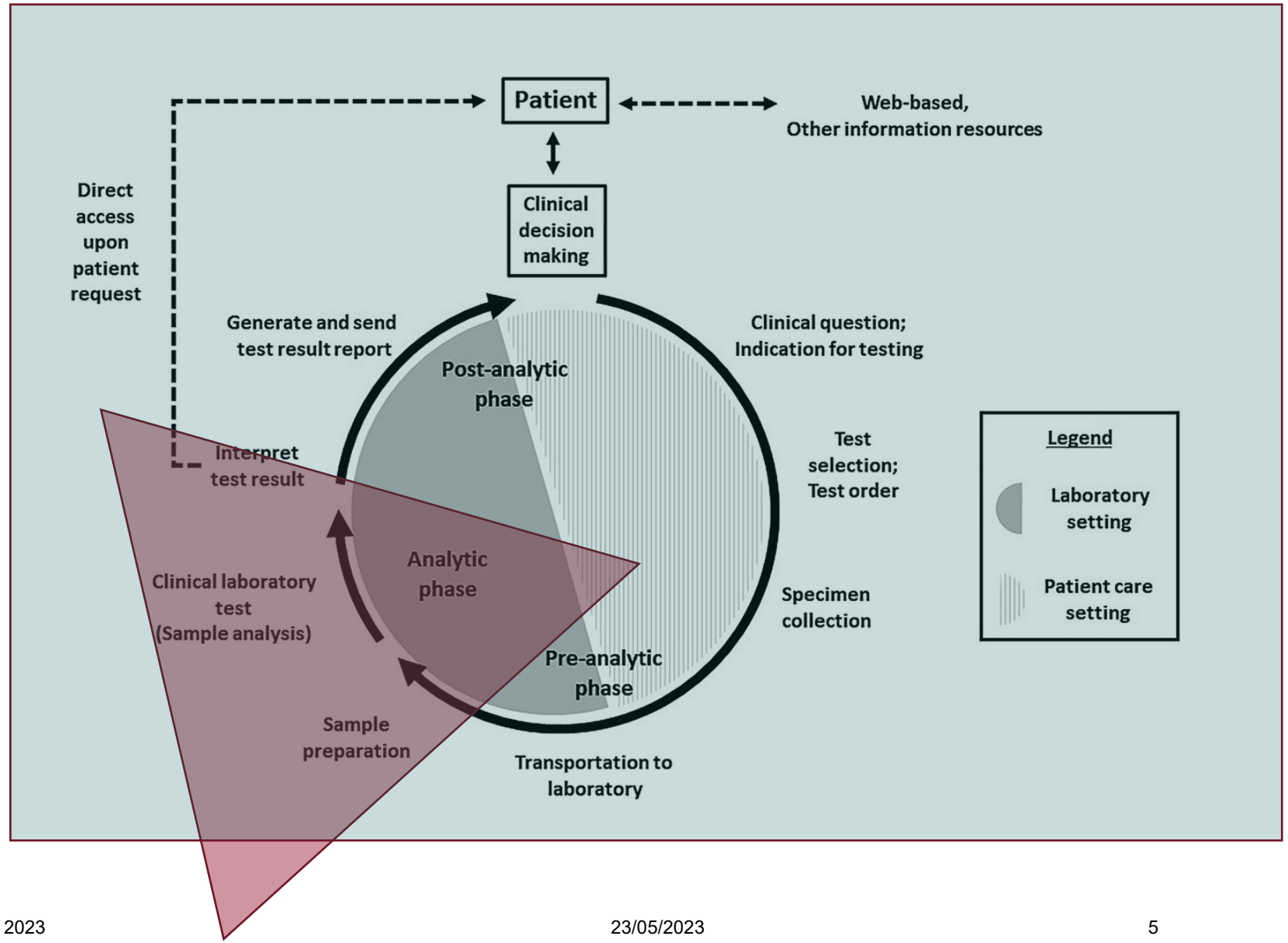
Some numbers from the Laboratory Medicine in the University Hospital Basel:

- Opening time:
  - Core Lab: 24/24h, 365/365d
  - Specialized labs: Mo – Fr, 8 – 17, some of them also Saturday and Sunday
- 1089 different analytes according of the accreditation list
- 423 SOPs describing analytical methods
- 2022: 7.1 million lab results
- 250 employees
- Turn-around time for emergency samples (~30% of all samples): < 1 hour

From blood collection to the report of results



The total testing process in the medical laboratory



Accreditation ISO 15189

Quality control

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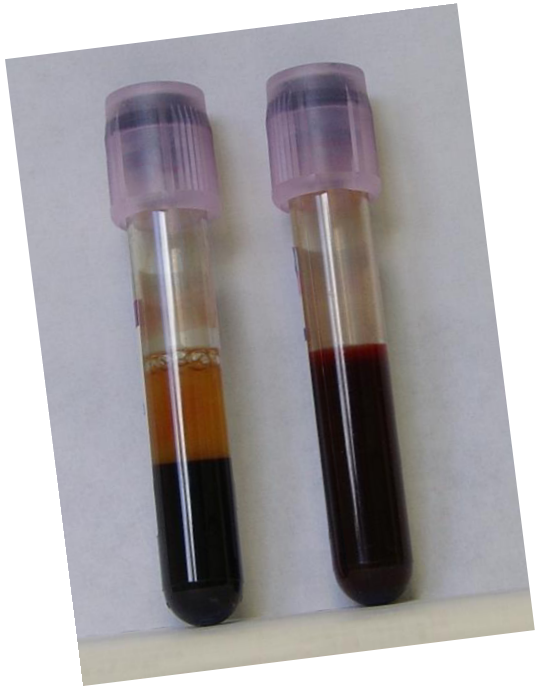
Analytical methods in the medical laboratory

- Wide spectrum of analytical techniques:
  - Photometry
  - Immunoassays
  - Ion selective electrodes, amperometry
  - Microscopy
  - Culture
  - HPLC/GC coupled to UV-, fluorescence or mass spectrometry detectors
  - Flow cytometry
  - PCR
  - Next generation sequencing (NGS)
  - Atomic absorption spectroscopy, ICP-MS
  - Electrophoresis
  - ……..

Sample materials in the medical laboratory



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Source of the analytical methods used in the medical laboratory

- Commercial kits with dedicated methods, reagents, calibrators and controls in connection with a fully automated specific instrument
- Commercial kits which are applied on different commercial instruments or are performed manually (e.g. ELISA's, LC-MS/MS kits)
- In-house developed assays which are performed on different instruments (e.g. LC-MS/MS methods, PCR methods)
- Fully manual tests (e.g. microscopy with or without coloring of the preparation)

Information on a sample available in the medical laboratory

- Name, sex and birthday of the individual
- Sender (general physician's office, outpatient clinic, inpatient department, intensive care unit, emergency station, ……)

- Optimally: Time of sampling
- Sometimes: Results of earlier samples from the same patient

✓No information on clinical symptoms, no information on medical treatment and actual drug therapy

✓Plausibility of the test results can only be checked with the comparison of different assays in the same sample

➢The medical laboratory needs special measures to control the quality of its results during 24/24h

The medical laboratory

- Laboratory medicine is an analytical field with a wide variety of very complex and extremely variable samples
- The «target» value of the sample is always unknown
- With the combination of different results in the same sample, plausibility of a test result can be estimated

- The laboratory in most cases does not have any information on the patient's symptoms

- A large number of analytical methods are used with different levels of traceability

Legal regulation of medical analyses

- Operating permit
- Accounting permit to send bill to the health insurances

- Requirements for the laboratory (e.g. qualification of the personnel, safety measures to protect the environment)
- Requirements for the analytical quality (e.g. mandatory accreditation, mandatory quality controls)

A short look back on the development of proficiency testing in Switzerland

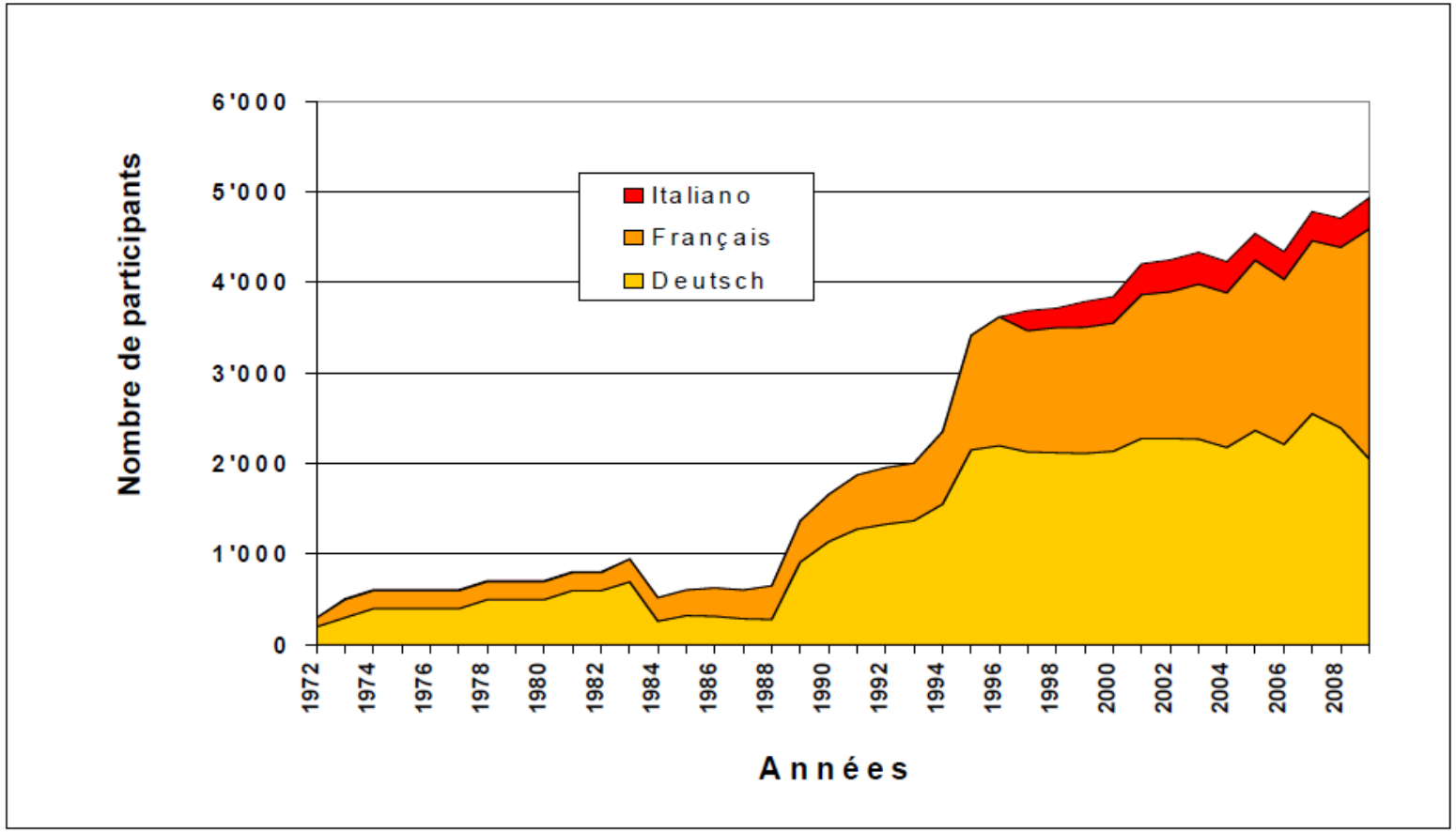

Figure 1 : Evolution du nombre de laboratoires participants aux EEQ du CSCQ de 1972 à 2010

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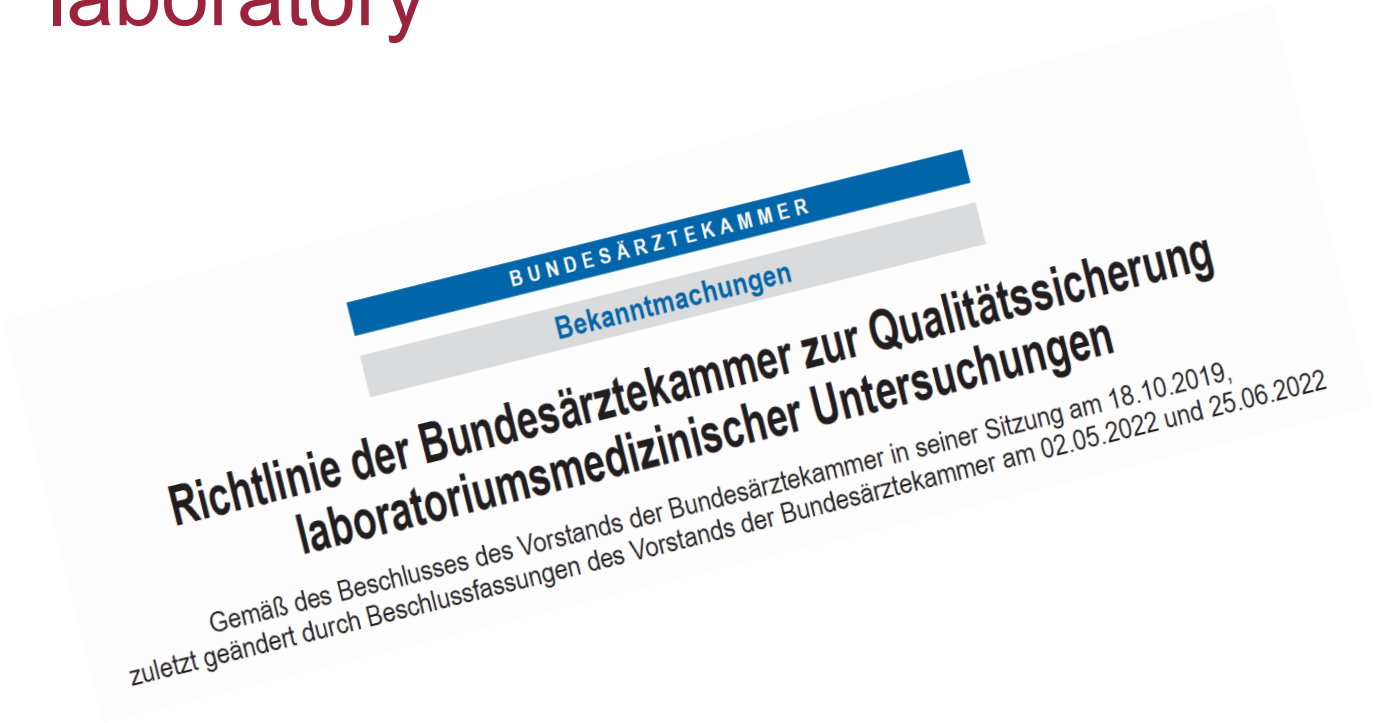
Measures to be taken to control the quality of the results in the laboratory


BUNDESÄRZTEKAMMER

Bekanntmachungen

Richtlinie der Bundesärztekammer zur Qualitätssicherung laboratoriumsmedizinischer Untersuchungen

Gemäß des Beschlusses des Vorstands der Bundesärztekammer in seiner Sitzung am 18.10.2019,
zuletzt geändert durch Beschlussfassungen des Vorstands der Bundesärztekammer am 02.05.2022 und 25.06.2022

Clinical Laboratory Improvement Amendments

QUALAB

QUALAB – Schweizerischer Verein für Qualitätsentwicklung im medizinischen Laboratorium
QUALAB – Association suisse pour le développement de la qualité dans les laboratoires médicaux
QUALAB – Associazione svizzera per la promozione della qualità nei laboratori medici

ACCREDITATION

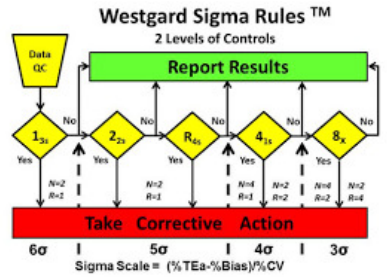
Measures to be taken to control the quality of the results in the laboratory

- Internal quality control:
  - Commercial samples accompanied by a leaflet from the manufacturer containing target values and acceptable ranges for each analyte (often method dependent information)

- External quality control
  - Classical proficiency testing
    - Some analytes are (very) unstable in biological matrices

- General challenges:
  - Matrix effect dependency of most methods
  - In most cases «normal» samples cannot be used due to instability of most of the analytes
    - Addition of stabilizers
    - Solution of analytes in an artificial matrix

Internal quality control: regulation in Switzerland

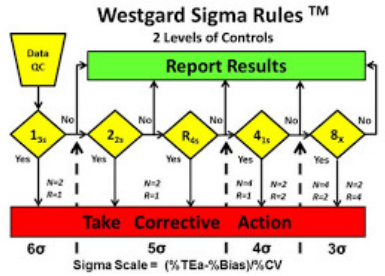


- For every analyte determined in a laboratory internal quality control samples need to be measured

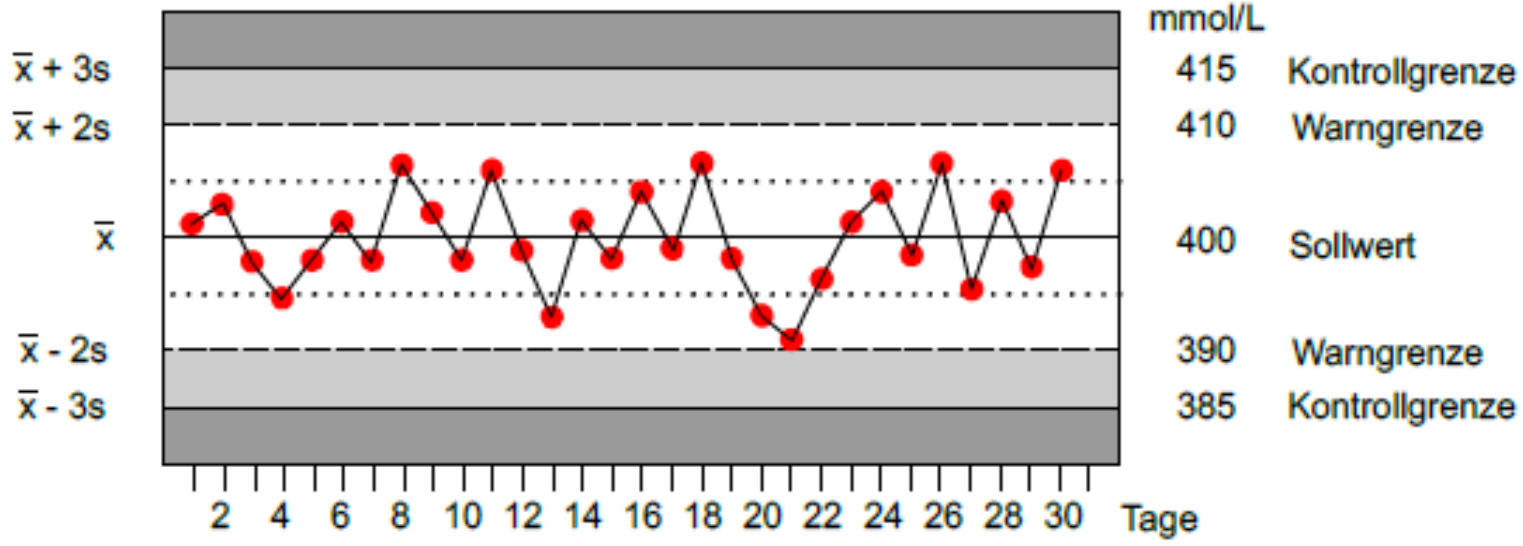
- The target value is usually defined by the manufacturer
- The allowed deviation from the target value is defined in the regulations. For a defined list of analyses (~ 70 parameters) the maximal tolerance is defined by the Qualab

- At least one (1) internal quality control sample needs to be run:
  - Every 50 samples for analysers that run in random access mode
  - Every 12 hours if the number of samples during 12 hours is < 50
  - With every batch if the assay is run batch-wise
  - Every two (2) weeks for a short list of very simple instruments not needing calibration or manual pipetting (e.g. pregnancy rapid test)

Internal quality control: regulation in Switzerland



- The data of the internal quality control sample measurement need to be interpreted by the Westgard rules
  - Everything under control



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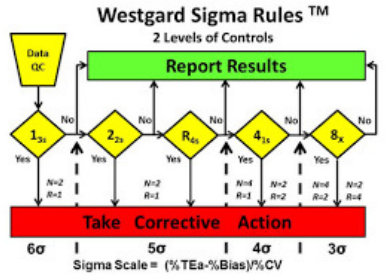
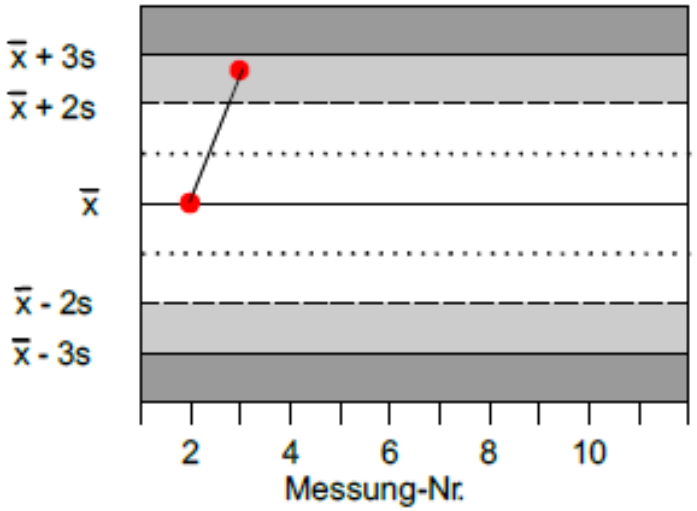
Internal quality control: regulation in Switzerland



- The data of the internal quality control sample measurement need to be interpreted by the Westgard rules
  - Warning



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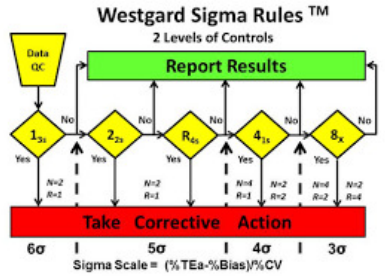
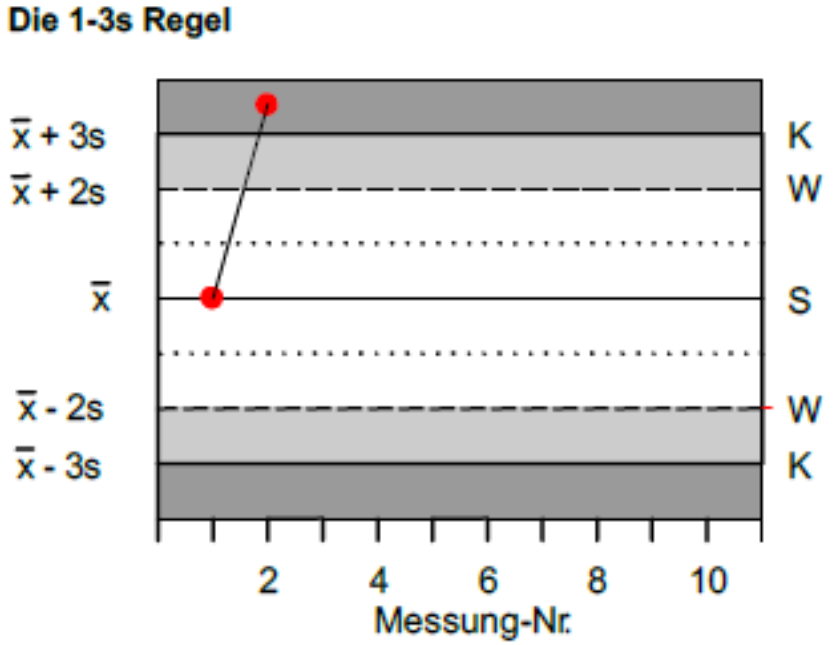
Internal quality control: regulation in Switzerland



- The data of the internal quality control sample measurement need to be interpreted by the Westgard rules
  - Method out of control: absolute deviation too high



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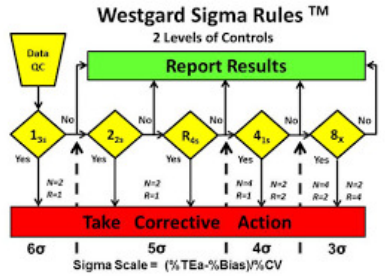
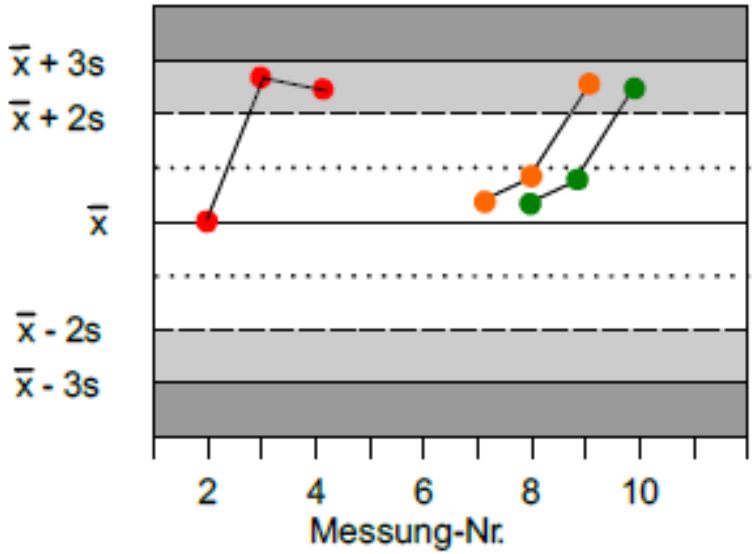
Internal quality control: regulation in Switzerland



- The data of the internal quality control sample measurement need to be interpreted by the Westgard rules
  - Method out of control: tendency of the results



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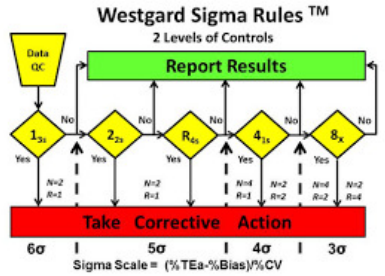
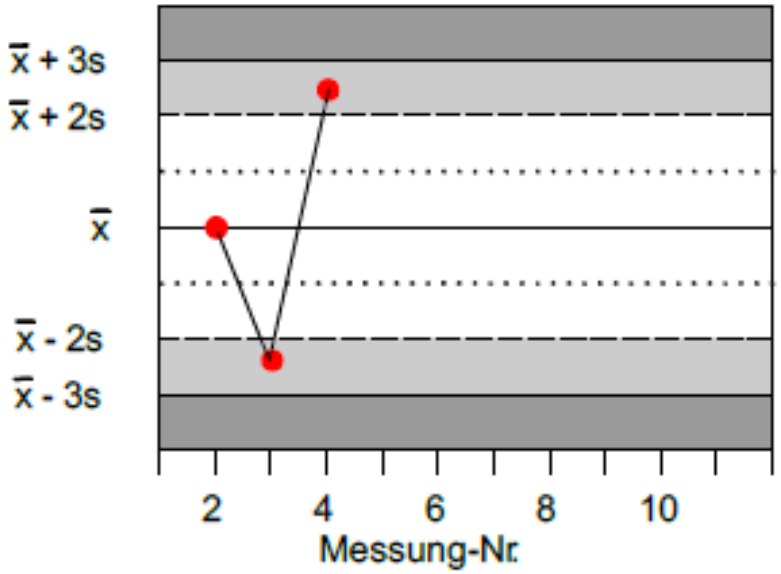
Internal quality control: regulation in Switzerland



- The data of the internal quality control sample measurement need to be interpreted by the Westgard rules
  - Method out of control: huge variation between 2 following results



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External quality control in Switzerland

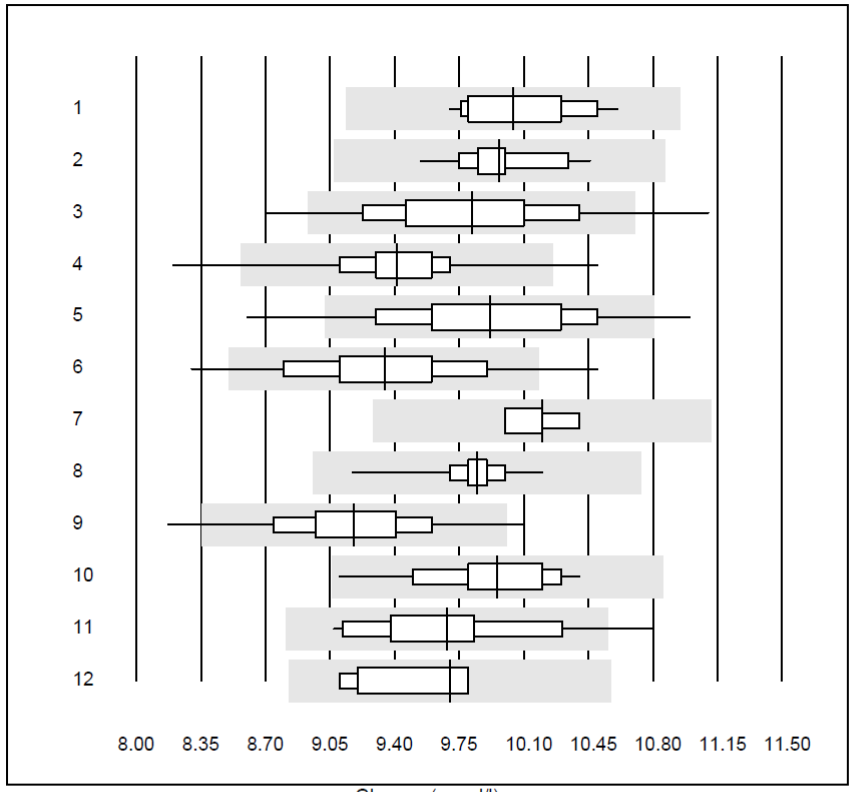
- For a defined list of analyses (~ 250 parameters) the participation at an external proficiency testing scheme is mandatory in every laboratory (including physicians practices). The proficiency testing institution must be accredited and accepted by the Qualab.
- The target value is defined by the consensus values for an analyte and partially method specific (differences between matrix effects of different methods/instruments)
- The allowed deviation from the target value is defined in the regulations

External quality control in Switzerland

- Depending on the discipline 1 – 4 samples need to be determined during a year

- Depending on the discipline between 75 and 100% of the results need to be correct
- If an external quality control result is incorrect, a continuous improvement process has to be started by the lab
- If the problem is not solved after 2 years, the reimbursement of the test(s) concerned by the health insurance will be stopped

Glucose



QUALAB Toleranz : 9 %

Nr.	Methode	Total	% OK	% ungen.	% Ausr	Zielwert	VK%	Typ
1	nasschemisch	26	100.0	0.0	0.0	10.0	2.7	e
2	Cobas	29	100.0	0.0	0.0	10.0	2.1	e
3	Reflotron	119	89.9	5.9	4.2	9.8	4.6	e
4	Fuji Dri-Chem	1068	98.7	0.5	0.8	9.4	2.4	e
5	Spotchem SP-4430	105	88.6	9.5	1.9	9.9	5.2	e
6	Spotchem D-Concept	524	94.8	4.8	0.4	9.3	4.3	e
7	Dimension	4	100.0	0.0	0.0	10.2	1.6	e
8	Piccolo	77	100.0	0.0	0.0	9.8	1.5	e
9	Cholestech LDX	286	96.5	2.1	1.4	9.2	3.8	e
10	Selectra Pro	17	88.2	0.0	11.8	10.0	3.3	e
11	Autolyser/DiaSys	19	94.7	5.3	0.0	9.7	4.2	e
12	andere Methoden	7	85.7	0.0	14.3	9.7	3.3	e*
13	iStat Chem8	7	100.0	0.0	0.0	9.2	1.2	e

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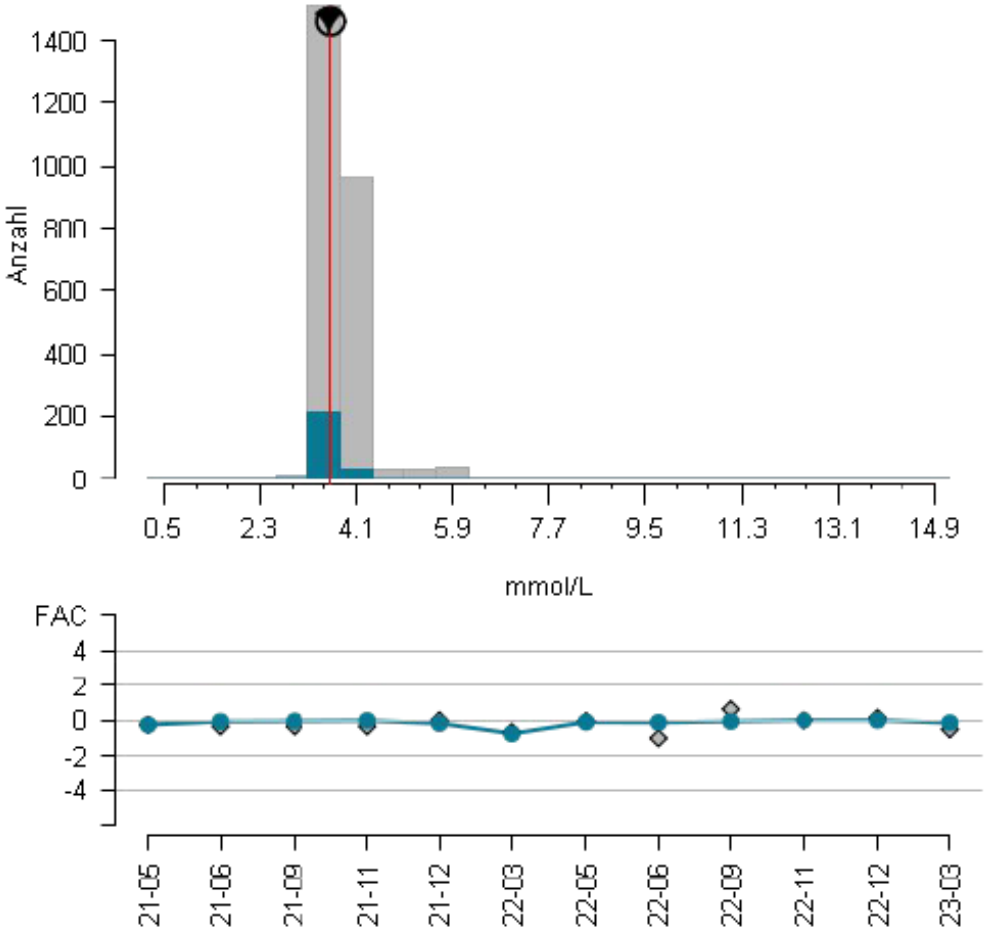
S-Glucose [11]



Ihre Resultate :

Gerät :	Cobas 8000	
Resultat :	3.6 mmol/L	
QUALAB Auswertung :	Konform	
QUALAB Bereich :	[3.3-4.0] (9%)	
FAC-Wert :	-0.14 (Ausgezeichnet)	-0.5
Z-Score :	-0.47	-0.45

Methode	**Hexokinase** [147]	**Alle**
Anzahl Teilnehmer :	248	2587
Zielwert :	3.6 mmol/L	3.7 mmol/L
Unsicherheit :	< 0.1 mmol/L	
SD :	0.07 mmol/L	0.22 mmol/L
VK :	2.04 %	6.01 %

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U02 Urin Teststreifen/HCG

	Zielwert	negativ	positiv	% Erfüllt
Schnelltest	positiv	16	1150	98.63
andere Methoden	positiv	0	4	100.00
hCG+, Abbott	positiv	0	1	100.00
Quick Vue Plus	positiv	0	1	100.00
Total		**16**	**1156**	**98.63**

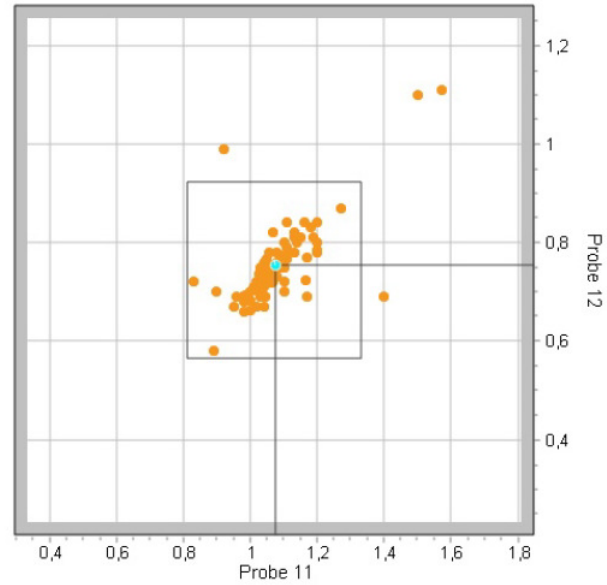
Kommentar U02

Der Urin stammte von einer gesunden Spenderin. Dem Urin wurde Natriumnitrit und HCG beigefügt.

Amiodaron (mg/l, N = 80)

Kollektiv	Probe	Zielwert	Bewertungs-bereich	Teilnehmerkollektiv MW	VK	Anz.	Quote (%) Probe	ges.
alle Methoden	11	1.07	0.813 - 1.33	1.07	7.29	80	96.3	95.0
	12	0.744	0.565 - 0.923	0.744	7.53	80	96.3	

Bestehensquote: 95%



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Take Home Message

- Medical Laboratories use a huge number of different analytical techniques
- They often operate at least partially during 24hrs and 365 days
- The sample materials are in most cases very complex and not standardized at all
- Since > 50 years internal and external quality controls are analysed
  - In the first decades as a voluntary measure to increase quality of the results, mainly in classical medical laboratories but shortly afterwards also in general practitioner's offices
  - In the 90ties the participation at an external quality control scheme became mandatory as well as the implementation of internal quality controls
  - Since 2022 all results of the external quality control schemes are collected centrally and each laboratory has to sign a statement that internal quality control samples are performed as demanded
- The reimbursement of the results produced is dependent on the successful performance of the internal and external quality control samples

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Thank you very much for your attention