Clinical Impact of EQA

16. October 2024
EQALM
Prof. Dr. Michael Spannagl

LMU KLINIKUM

INSTAND

Standardization

1809:
bayerische Mass:
1,069 Liter

CLINICAL IMPACT OF EQA

BIERKRUG-BETRUG?

Ein Drittel der Oktoberfest-Maßkrüge enthielt zu wenig Bier

In rund 31 Prozent der Krüge wurde ein sogenannter Unterschank festgestellt – deutlich mehr als in den Jahren zuvor

20. Oktober 2022, 17:55

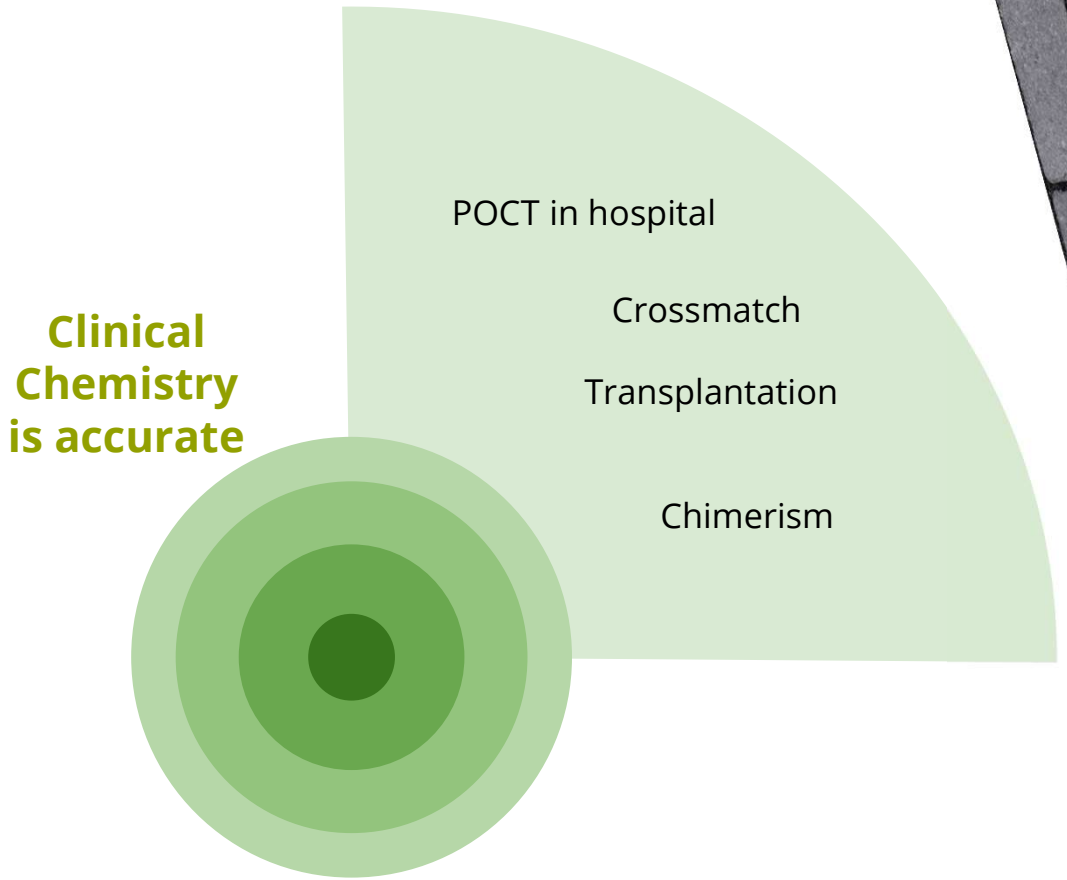
226 Postings | Später lesen

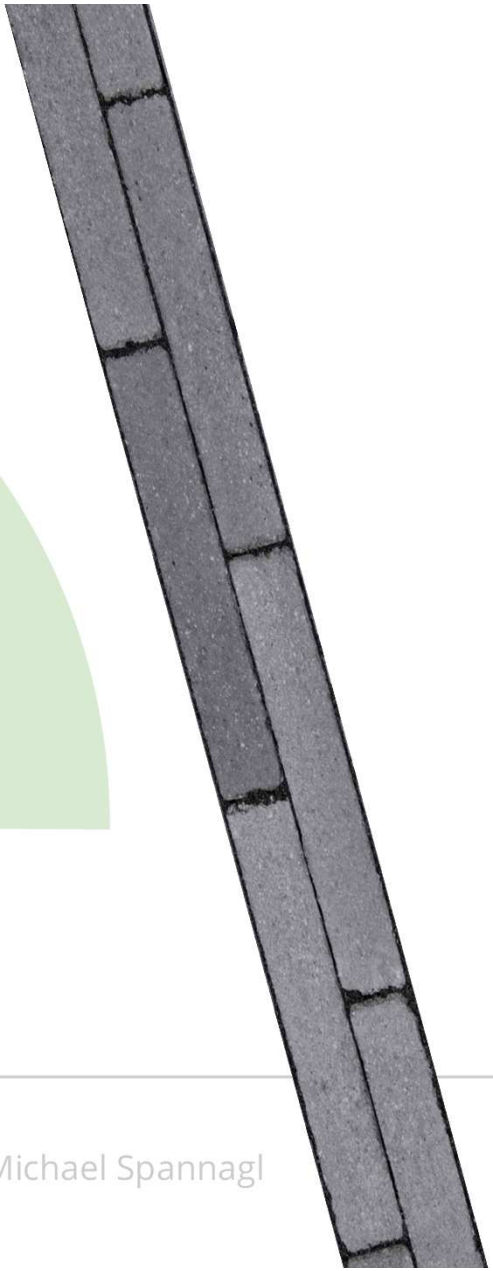
Ein Liter ist am Oktoberfest nicht immer ein Liter.

Foto: APA / dpa / Sven Hoppe

DERSTANDARD

International | Deutschland | Österreich | Web | Wirtschaft | Wissen und Gesellschaft | Sport | Lifestyle | Kultur





POCT

Pharmacy

GP

Emergency

Nursing home

Table 1: Interval of potential results for a theoretical result due to the use of different APS in national EQA schemes.

Measurand	EPA Result	CLIA´19 (USA)	RILIBÄK (Germany)	UK-NEQAS (United Kingdom)	SKML (Netherlands)	NOKLUS (Norwey)	RCPAQAP (Australia)	ASQUALAB (France)	SEQC^{ML} (Spain)
Sodium	EPA	4 mmol/L	3%	2%	0.73%	2%	3 mmol/L (2%)	2.5%	1.1%
	133 mmol/L	129–**137**	130–**137**	130–**136**	132–134	130–**136**	130–**136**	130–**136**	132–134
TSH	EPA	20%	13.5%	12.5%	23.7%	12%	0.6 mU/L (15%)	20%	11.9%
	4.1 UI/L	3.28–**4.92**	3.5–4.7	3.6–4.6	3.1–**5.1**	3.6–4.6	3.5–4.7	3.28–**4.92**	3.6–4.6
aPTT	EPA	15%	10.5%	15%	4.5%	5%	–	20%	6.7%
	1.4	**1.19**–1.61	1.25–1.55	**1.19**–1.61	1.34–1.46	1.34–1.46	–	**1.18**–1.65	1.31–1.49

Values in bold indicate the accepted values that could lead to a poor clinical indication.

RILIBAEK

Guideline of the German Medical Association on Quality Assurance in Medical Laboratory Examinations

In accordance with a resolution passed by the Executive Board of the German Medical Association at its meeting on 18 October 2019, last amended through a resolution by the Executive Board of the German Medical Association on 14 April 2023.

A Basic requirements for quality assurance in medical laboratory examinations

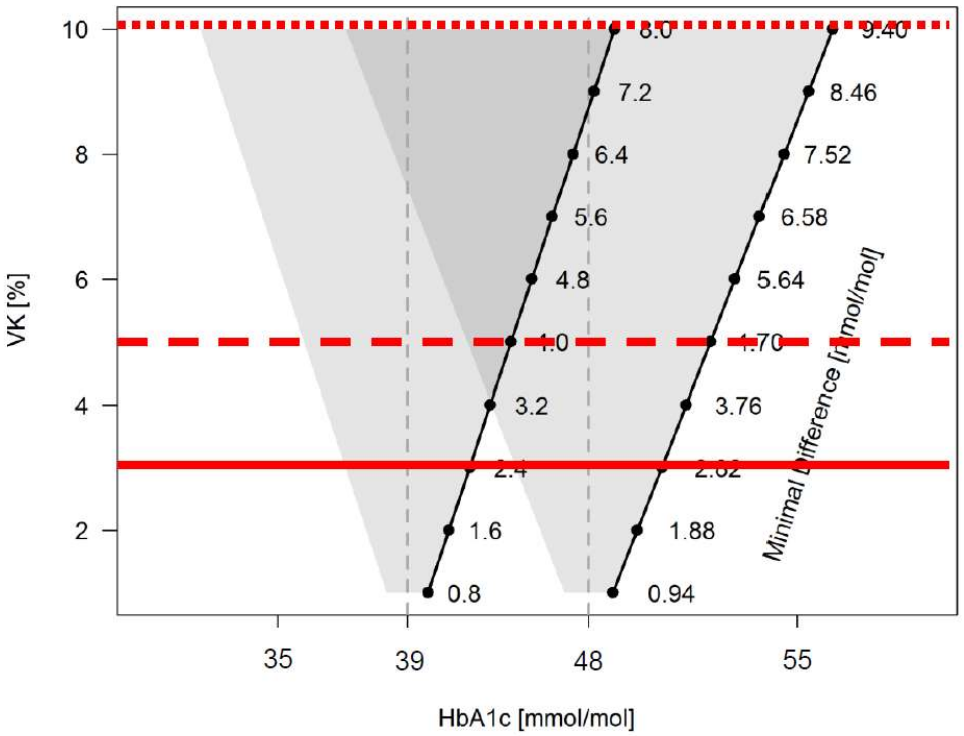
1 Scope

This guideline sets out the basic requirements for quality management and quality assurance for medical laboratory examinations in the field of medicine.
Part A of the guideline specifies the basic requirements for structural and process quality which apply to all medical laboratory examinations. The sections in Part B contain the specific requirements pertaining to the quality of the results.

2 Objective

The objective of this guideline is to ensure, and constantly improve the quality of medical laboratory examinations, and to keep risks for patients and users to a minimum. It aims to

HbA1c



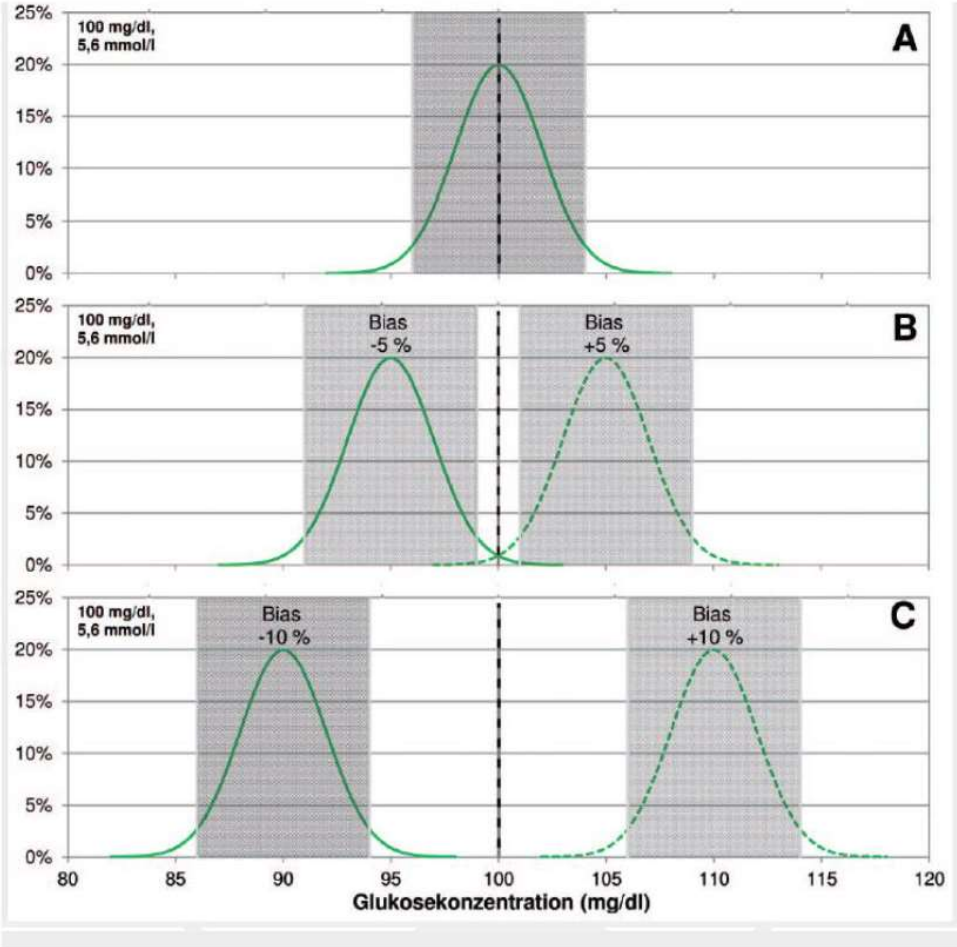
Rili-BAEK 2014

Rili-BAEK 2019

Rili-BAEK 2019*

Minimal difference for HbA1c at a threshold of 39 mmol/mol Hb related to CV %:
+ 4.0 mmol/mol Hb at a CV of + 5%
+ 2.4 mmol/mol Hb at a CV of + 3%

Glucose: bias



Freckmann, et al. Deutsch Med Wochenschr 2022;147:407-13.

Measurand Glucose and HbA1c

– according to Rili-BAEK **Table B 1-2a – Measurands in plasma/serum/whole blood**

1 No.	2 Measurand	3 Permissible relative deviation of the single measurement of the control sample or the relative root mean square of the deviation of measurement	4 Rili-BAEK applicable concentration intervals for columns 3 and 5 From	To	Unit	5 Permissible relative deviation in the EQA	6 Type of EQA target value
43	Glucose	±5,0%*	40 2,2	400 22	mg/dl mmol/l	±8,0%*	RMV
46	Haemoglobin A 1c (HbA1c)	±3,0%	30	140	mmol/mol Hb	±8,0%	RMV

* To be complied with no later than three years after the publication in Deutsches Ärzteblatt

Measurand Glucose – Adjustments to the permissible deviations according to Rili-BAEK

1 **Version**	2 **Measurand** (in plasma/ serum/ whole blood)	3 **Permissible relative deviation of the single measurement of the control sample or the relative root mean square of the deviation of measurement**	4 **Applicable concentration intervals for columns 3 and 5**			5 **Permissible relative deviation in the EQA**	6 **Type of EQA target value**
			From	**To**	**Unit**		
Deutsches Ärzteblatt | Jg. 98 | Heft 42 | **October 19, 2001**	Glucose	±4% (imprecision) ±7% (inaccuracy)		≥60	mg/dl	±15%	RMV
		±2,4 mg/dl (imprecision) ±4,2 mg/dl (inaccuracy)		<60	mg/dl	±9 mg/dl	
Deutsches Ärzteblatt | Jg. 105 | Heft 7 | **February 15, 2008**	Glucose	±11,0%	40 2,2	400 22	mg/dl mmol/l	±15,0%	RMV
Deutsches Ärzteblatt | Jg. 111 | Heft 38 | **September 19, 2014**	Glucose	±11,0%	40 2,2	400 22	mg/dl mmol/l	±15,0%	RMV
Deutsches Ärzteblatt | Jg. 116 | Heft 51-52 | **December 23, 2019**	Glucose	±11,0%	40 2,2	400 22	mg/dl mmol/l	±15,0%	RMV
Deutsches Ärzteblatt | DOI: 10.3238/arztebl.2023.rili_baek_QS_Labor | **May 30, 2023**	Glucose	±5,0%*	40 2,2	400 22	mg/dl mmol/l	±8,0%*	RMV

Measurand Glucose – Adjustments to the permissible deviations according to Rili-BAEK

1 Version	2 Measurand (in plasma/ serum/ whole blood)	3 Permissible relative deviation of the sin measurement of th sample or the relati mean square of the deviation of measu	4	5	6
Deutsches Ärzteblatt | Jg. 98 | Heft 42 | **October 19, 2001**	Glucose	±4% (imprecision) ±7% (inaccuracy) ±2,4 mg/dl (imprecisi ±4,2 mg/dl (inaccura			
Deutsches Ärzteblatt | Jg. 105 | Heft 7 | **February 15, 2008**	Glucose	±11,0%			
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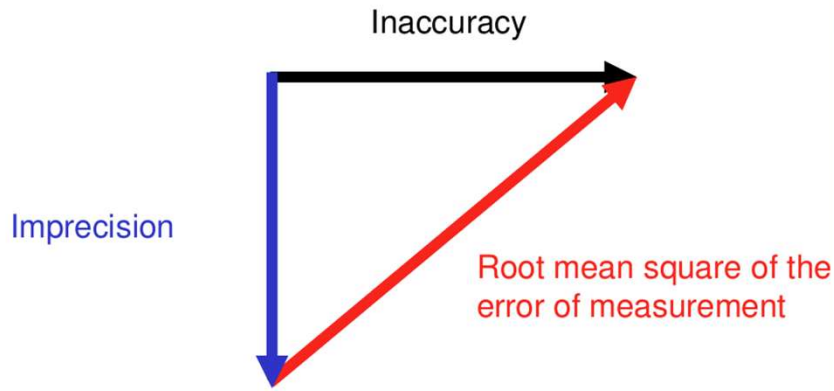
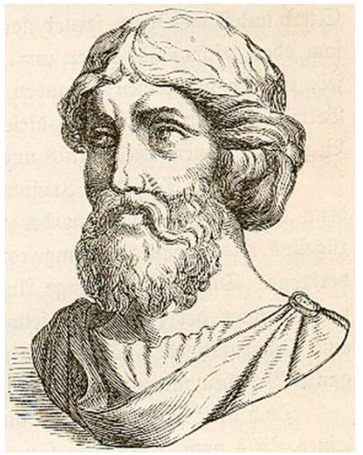
Deutsches Ärzteblatt | Jg. 116 | Heft 51-52 | **December 23, 2019**	Glucose	±11,0%			
Deutsches Ärzteblatt | DOI: 10.3238/arztebl.2023.rili_baek_QS_Labor | **May 30, 2023**	Glucose	±5,0%*	2,2	22	mmol/l ±8,0%*

root mean square of the error of measurement



$$a^2 + b^2 = c^2$$



Pythagoras von Samos

(570 v. Chr. – 510 v. Chr.)

RMV

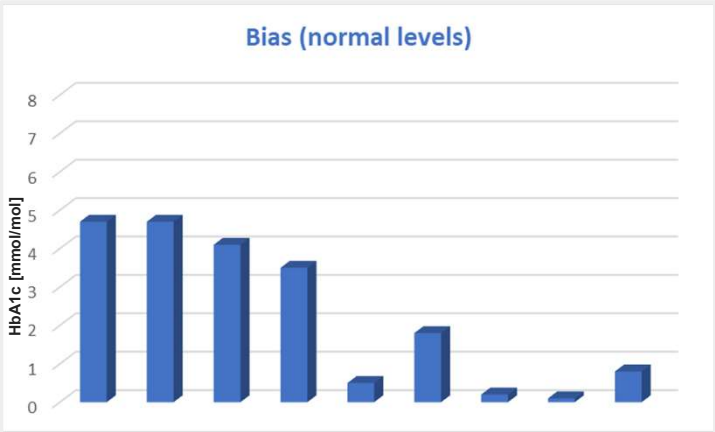
Measurand HbA_{1c} – Adjustments to the permissible deviations according to Rili-BAEK

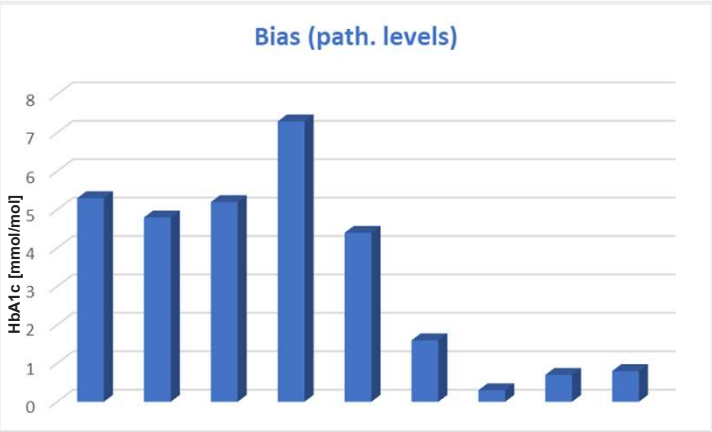
1 **Version**	2 **Measurand** (in whole blood)	3 **Permissible relative deviation of the single measurement of the control sample or the relative root mean square of the deviation of measurement**	4 **Applicable concentration intervals for columns 3 and 5**			5 **Permissible relative deviation in the EQA**	6 **Type of EQA target value**
			From	**To**	**Unit**		
Deutsches Ärzteblatt | Jg. 98 | Heft 42 | **October 19, 2001**	HbA1c	±6% (imprecision) ±12% (inaccuracy)	-	-	-	±24%	RMV
Deutsches Ärzteblatt | Jg. 105 | Heft 7 | **February 15, 2008**	HbA1c	±10,0%	30	140	mmol/mol Hb	±18,0%	RMV
Deutsches Ärzteblatt | Jg. 111 | Heft 38 | **September 19, 2014**	HbA1c	±10,0%	30	140	mmol/mol Hb	±18,0%	RMV
Deutsches Ärzteblatt | Jg. 116 | Heft 51-52 | **December 23, 2019**	HbA1c	±5,0% ±3,0%*	30	140	mmol/mol Hb	±8,0%	RMV
Deutsches Ärzteblatt | DOI: 10.3238/arztebl.2023.rili_baek_QS_Labor | **May 30, 2023**	HbA1c	±5,0% ±3,0%*	30	140	mmol/mol Hb	±8,0%	RMV

* To be complied with from 22 December 2023 at the latest

EQAS HbA1c

from 2010 to 2018





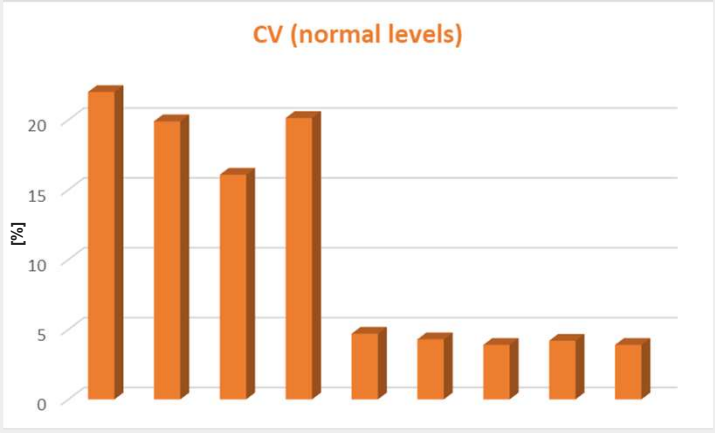


Tabelle B 1-1: Vorgaben auf zu verwendende Untersuchungsmaterialien*

1 lfd. Nr	2 Messgröße	3 zu verwendende Untersuchungsmaterialien	4 Vorgaben zur Präanalytik	5 Erläuterung
1	Glucose	Plasma oder Vollblut	Wenn Plasmaseparation oder Messung nicht innerhalb von 15 min erfolgt, sind Blutentnahmeröhrchen mit geeigneter Glykolyseinhibition zu verwenden. Die Verwendung von Serum ist ungeeignet.	Ohne Glykolyseinhibition werden zu niedrige Glucosewerte ermittelt.
2	Kalium	Heparin-Plasma oder Vollblut (ggf. mit geeigneten Antikoagulanzien)	Die Verwendung von Serum ist ungeeignet.	Bei Verwendung von Serum sind die Kalium-Werte falsch hoch.

- **Heated debate concerning :**

- Glycolyse inhibitors in collection tubes

- Potassium only in plasma or whole blood

Members of the Advisory Board according to Rili-BAEK Section C

Representatives from these institutions

(1) representatives of the competent **scientific medical societies**

(2) the chairs of the **Expert Groups listed in each Part B** of the Rili-BÄK

(3) a representative from the **German Medical Association**

(4) a representative from the **National Association of Statutory Health Insurance Physicians**

(5) a representative from the **German Hospital Federation**

(6) a representative from **the German Association of Medical Technologists and Analysts**

(7) a representative from **a competent industrial association**

(8) three **state representatives**

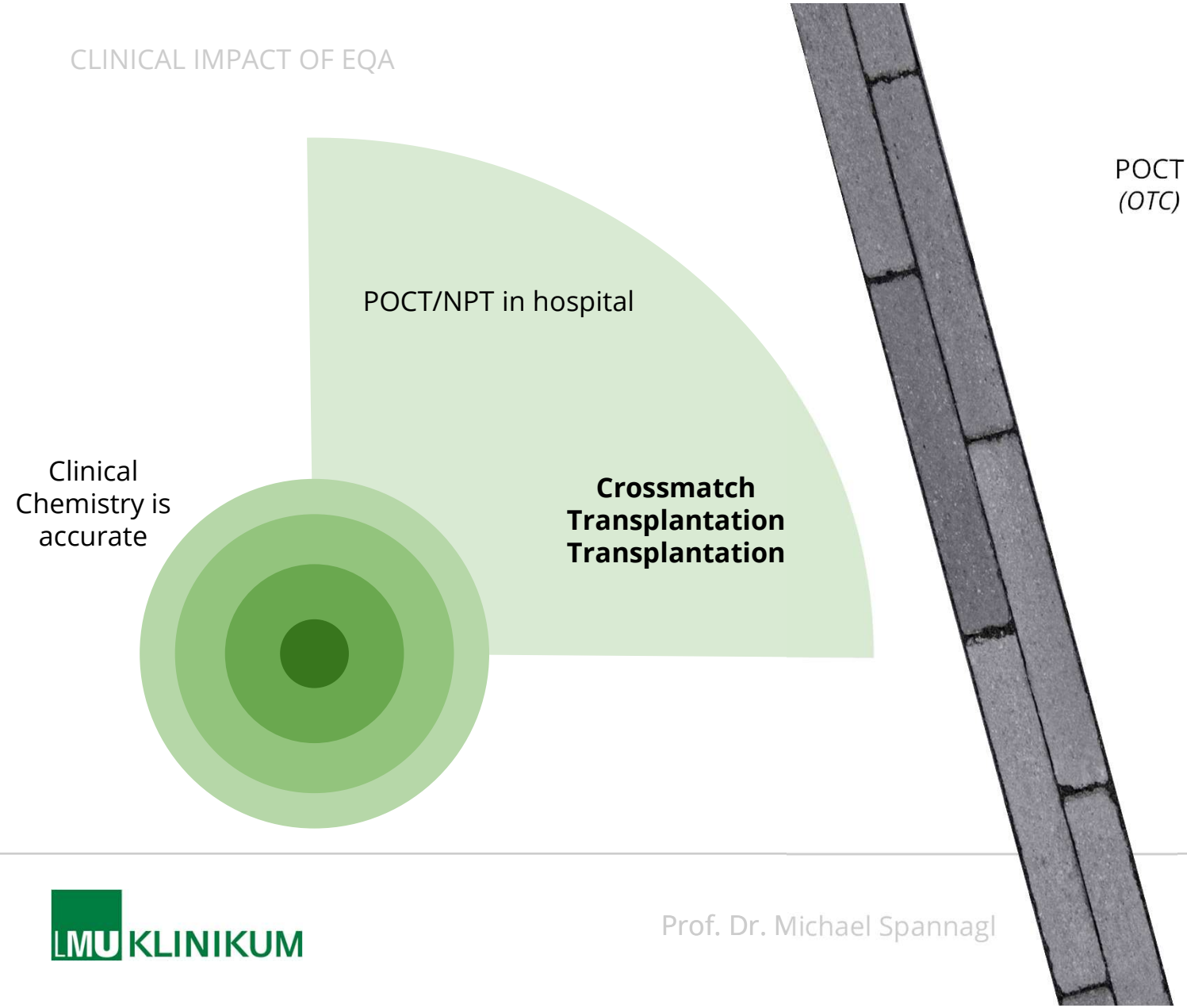
(9) representative from the **German Federal Ministry for Health**

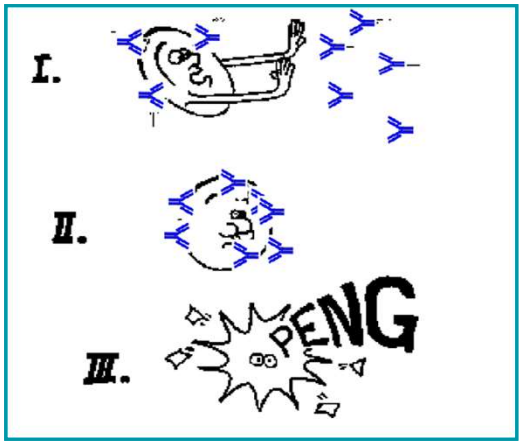
(10) a representative from the **Federal Institute for Drugs and Medical Devices (BfArM)**

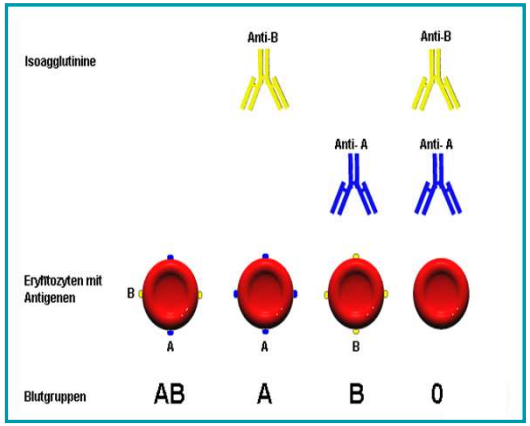
(11) representative from **the Physikalisch-Technische Bundesanstalt** (PTB)

Permanent guest

(1) One representative from **each of the reference institutions**


POCT
(OTC)
POCT/NPT in hospital
Pharmacy
Clinical
Chemistry is
accurate
Crossmatch
Transplantation
Transplantation
GP
Emergency





Assay reflects a complex biology ..

→ Proficiency testing mandatory !

Eurotransplant

COUNTRIES AND NUMBER OF ACTIVE TRANSPLANT CENTERS IN 2023

SERVICES ACCORDING TO THE BASIC MANDATE

We distinguish the following services to the member states:

Allocation services

- 24/7 duty desk organ allocation services.
- 24/7 immunological support to the allocation office and transplant centers by ETRL.

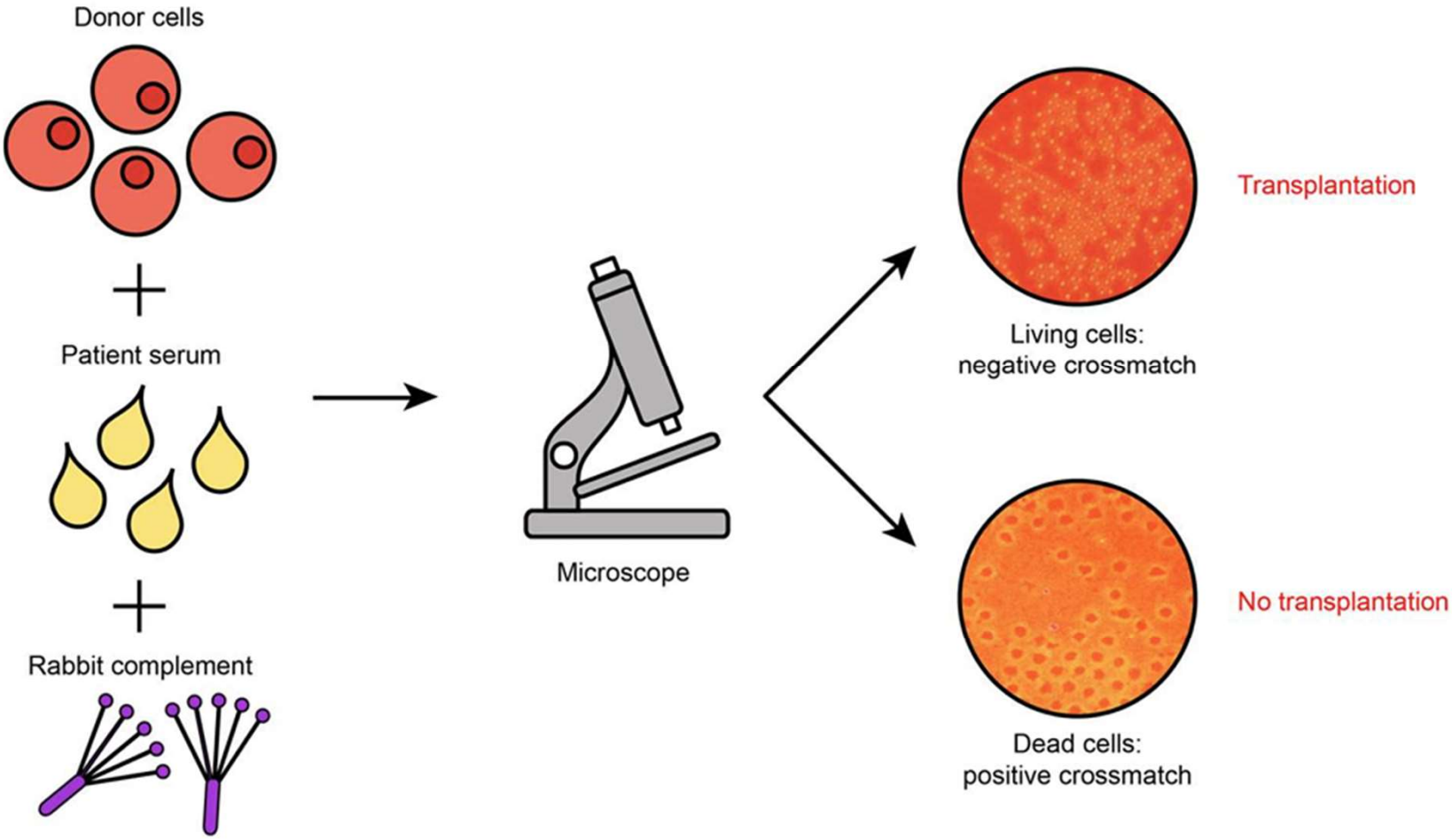
Eurotransplant reference laboratory

Proficieny testing

Spannagl

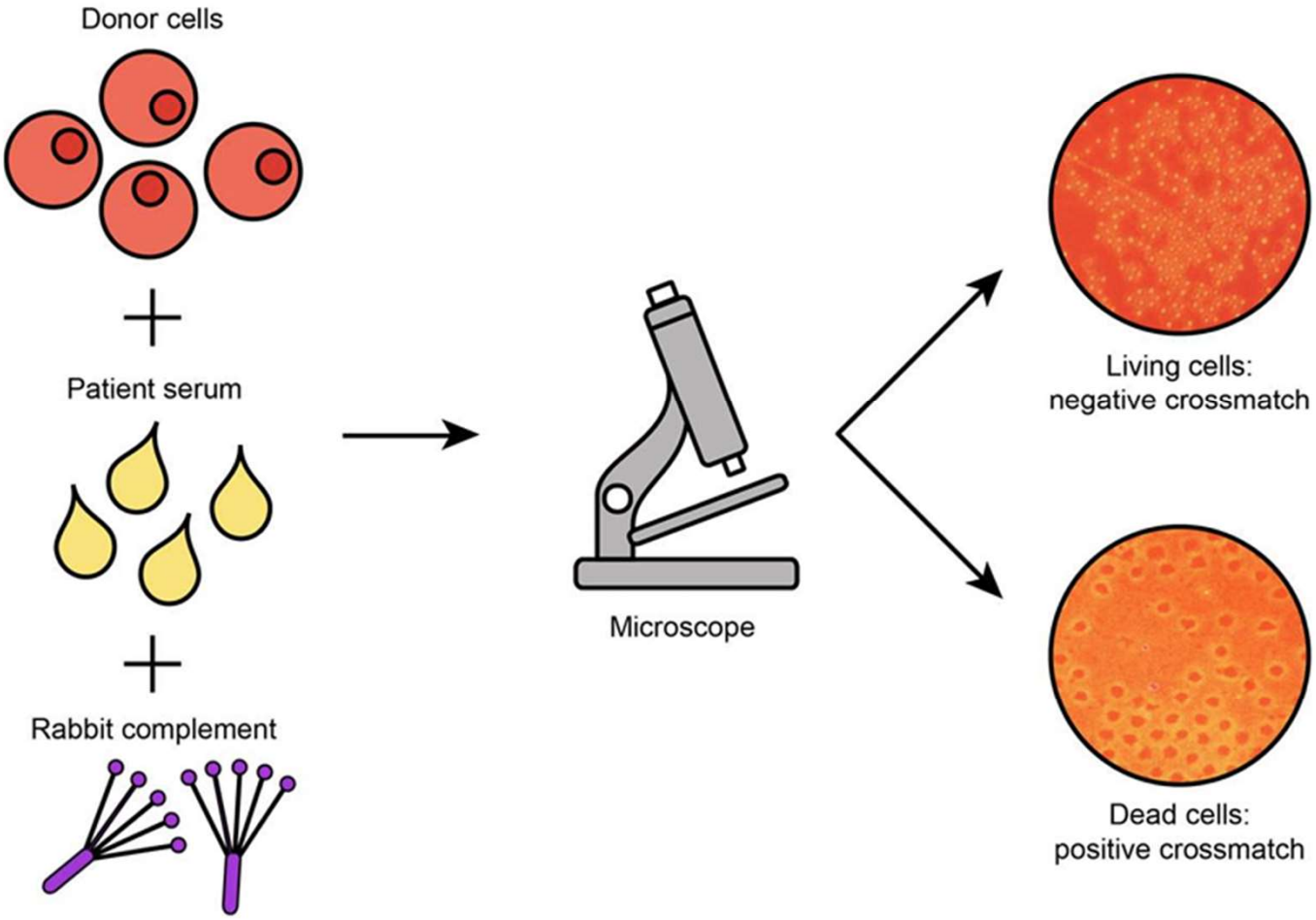
INSTAND

The complement dependent cytotoxicity (CDC) test and crossmatch



Please note that the principle of this test is also used in screening for HLA antibodies and for HLA typing

The complement dependent cytotoxicity (CDC) test and crossmatch



HLA-Diagnostik 06 - HLA-Antikörper-Nachweis und -

Proben:	5 Proben
Probeneigenschaften:	humanes Serum á 1 ml

Please note that the principle of this test is also used in screening for HLA antibodies and for HLA typing

Newsletter

ISSUE #18 SPRING 2022

Dear colleagues,

Eurotransplant is heading towards the introduction of virtual crossmatching to replace the physical donor center crossmatch. This will significantly reduce cold ischemia time, increase specificity, and make the serum exchange redundant The introduction of the virtual crossmatch requires several conditions to be met and multiple steps to be taken. These will be discussed in the current newsletter.

Extension of vPRA panel

To be able to perform a crossmatch virtually, all unacceptable antigens for a given patient must be reported. This includes those at HLA-DQA, -DPB and -DPA, since antibodies directed against antigens encoded on these loci can result in a positive physical crossmatch. To make sure that the vPRA is representative of HLA immunisation including these loci, a new panel for vPRA calculation is required. Such panel on 11-loci unambiguous 2nd field HLA typing is not readily available for the Euotransplant geographic area. Therefore, the ETRL is making an inventory through the individual TTAC representatives to determine how many actual ET donors have been typed at unambiguous 2nd field resolution at 11 loci (for example in case of DSA, or in study context). An additional source may be donors for living transplant procedures. Please contact your national TTAC representative in case your laboratory has donor HLA typing data that fulfills these requirements.

Unacceptable antigen definition

The virtual crossmatch will necessitate a more detailed listing of unacceptable antigens. The unacceptable antigen definition will be extended to include also HLA-DQA, -DPB and -DPA. Furthermore, the possibility to register unacceptable alleles will also be implemented, to solve the problem of registering transplant-relevant allele-specific antibodies.

donors for immunized patients. Eurotransplant will col lect second field, ambiguous donor HLA typing data for all 11 loci. The complexity of these data will be re duced by filtering for European CIWD alleles (Hurley e al, HLA 2020). If any of the remaining alleles is listed as an unacceptable antigen, this will be regarded as a positive virtual crossmatch.
The second step in the allocation process is matching which in principle remains unchanged, meaning broad serological antigen matching for HLA-A and -B, and split serological antigen matching for HLA-DR (match determinants). Within the Eurotransplant system match determinants will automatically be assigned based on the CIWD filtered allele list.

Donor HLA reporting

The ETRL, together with the Eurotransplant office, and in close collaboration with Matchis and the DSO, is working hard to integrate Histoimmunogenetics Mark up Language (HML) as the future HLA typing data standard within Eurotransplant. This development is necessary to transfer 11-loci ambiguous 2nd field HLA typing data to Eurotransplant in order to perform the virtual crossmatch. More detailed information on HML can be found here: https://bioinformatics.bethematch clinical.org/hla-resources/hml/.

There is close contact with the vendors of intermediate resolution HLA typing kits to implement HML reporting

LMU KLINIKUM

and accurate

AND

The Virtual Crossmatch project was the most important project delivered.
This project was delivered according to plan in January 2023. In the first three months it operated in shadow mode, with a physical crossmatch being done next to the virtual crossmatch. Since the virtual crossmatch worked successfully, the physical crossmatch could be stopped in April 2023.

With the Virtual Crossmatch project, Eurotransplant has provided a significant improvement in the organ allocation process. The Virtual Crossmatch project has several benefits:

1 It leads to a higher quality in the allocation process.
2 It saves money and effort (since sending serum of all immunized patients to all Donor Centers every three months is no longer necessary).
3 The allocation process will go faster (allocation crossmatch takes 3 to 4 hours, virtual crossmatch takes a few minutes).
4 Manual input of Donor HLA is no longer necessary (this saves time and reduces the risk of errors).

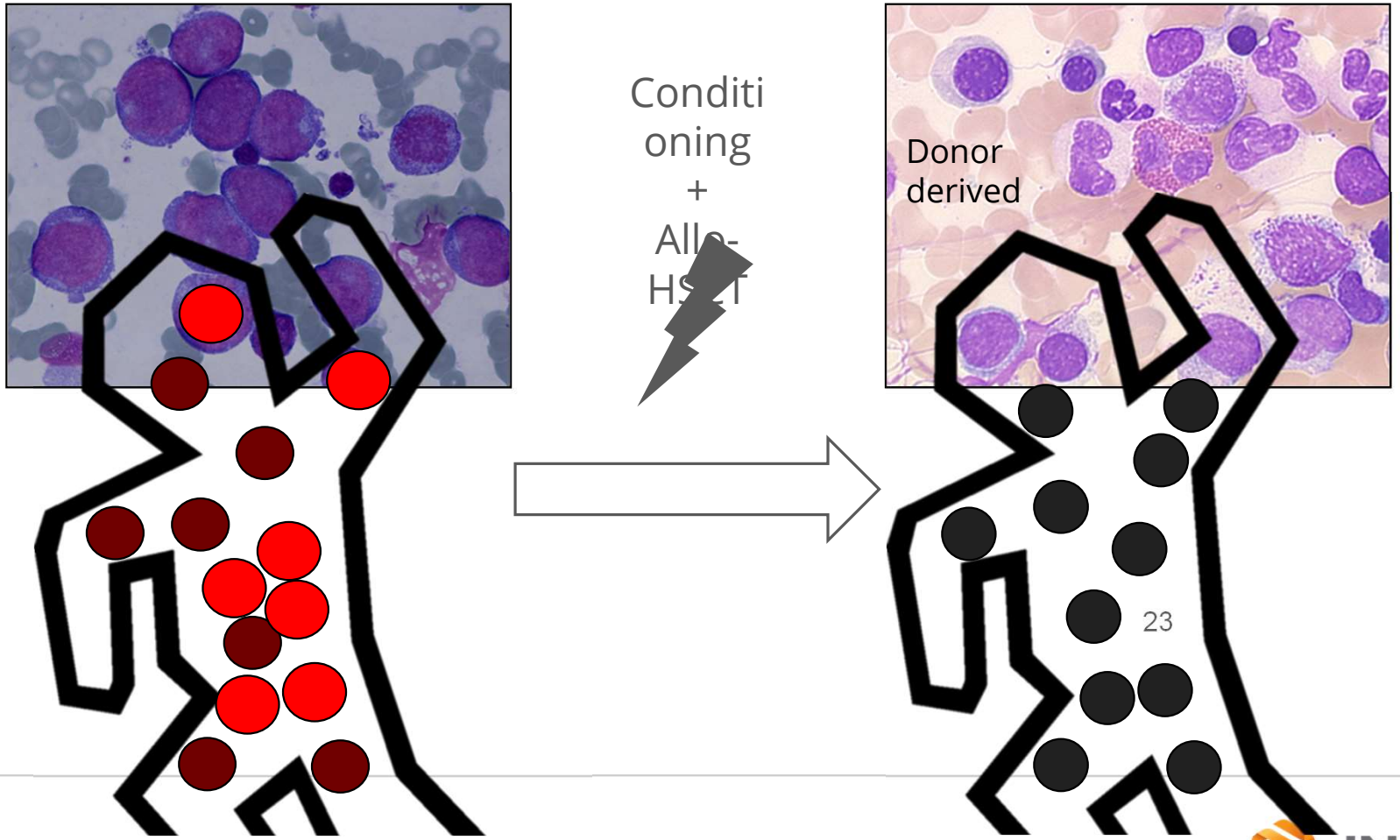
The Eurotransplant Reference Laboratory has been carefully studying the results of the Virtual Crossmatch project since its implementation, and the conclusions are that virtual crossmatch is very successful, as Cynthia

Prerequisites:

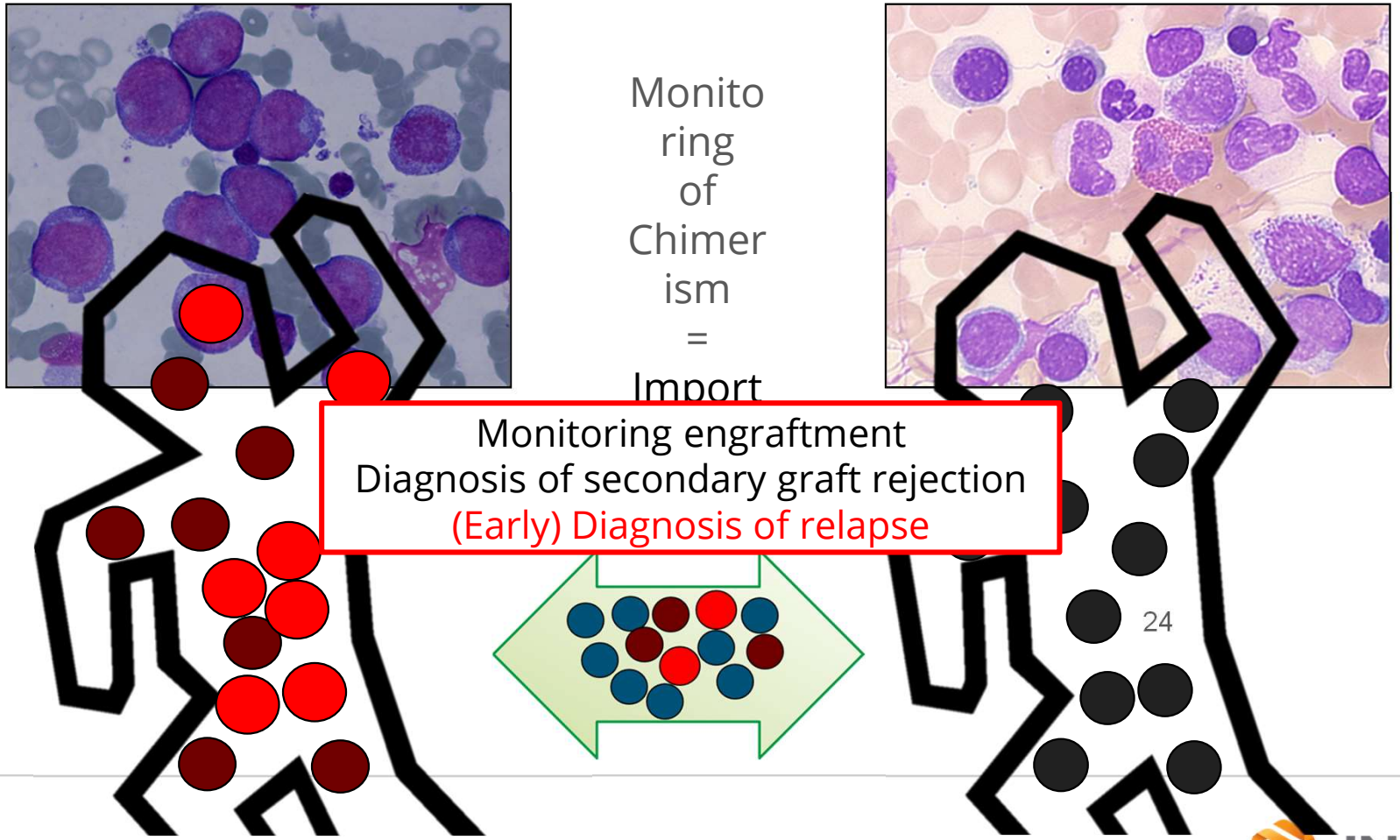
Precise and equivalent typing and antibody characterisation
In ALL participating laboratories

Central ref lab in Leiden

ALLOGENEIC HSCT FOR MALIGNANT DISEASES



IMPACT OF CHIMERISM AFTER ALLOGENEIC HSCT



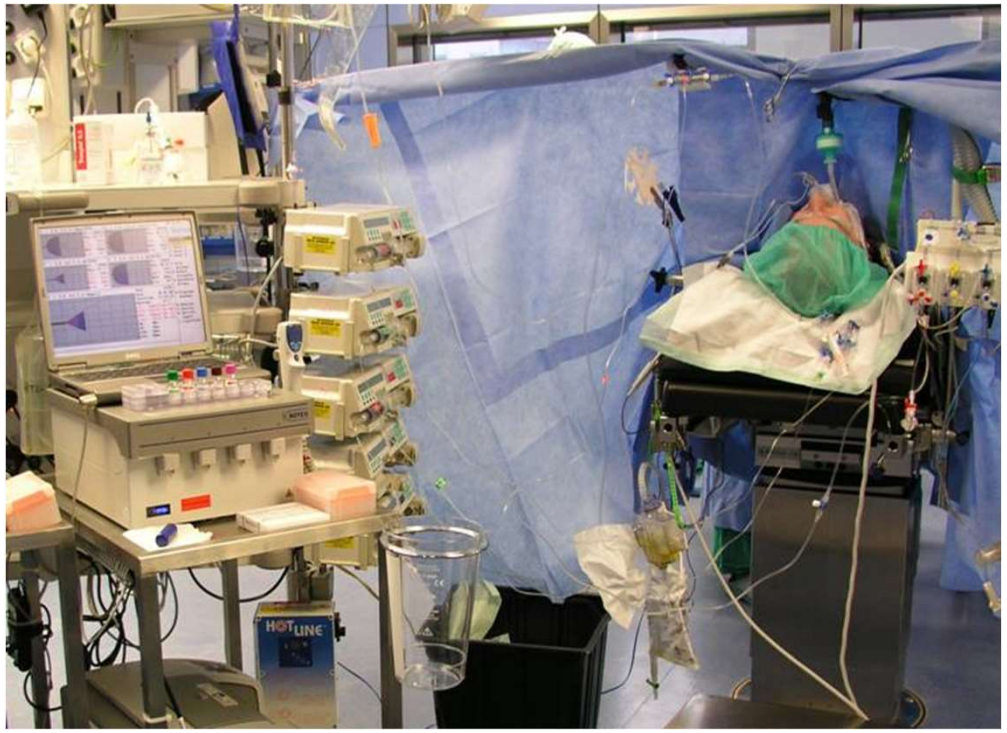
PILOT RINGVERSUCH
CHIMÄRISMUSDIAGNOSTIK

2012/2013

Different questions –
Different methods
applied by participants

Ery phenotype
Ig isotypes
cytogenetics

STR
FISH
qPCR
dPCR
NGS



OPERATION THEATER

SHOCK

CATH LAB

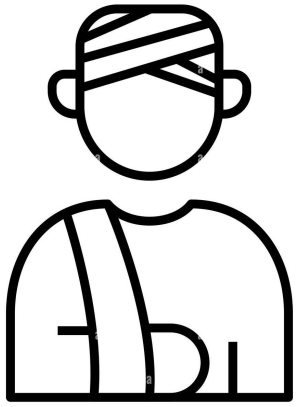
ANAESTHESIA – DELIVERY -

NEURORADIOLOGY

Whole blood

Less commutable

Less accurate



But faster

Near-patient

Process quality vs. analytical quality !
To the detriment of laboratories these 2 are not identical! ?

Whole blood

Less commutable

Less accurate

But faster

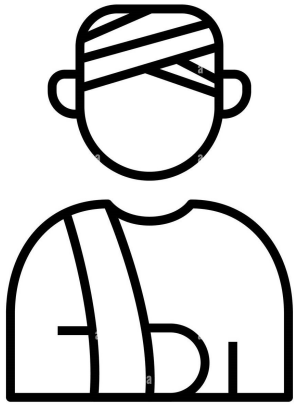
Near-patient

Plasma (frozen. lyophilized)

Reference system

Commutability

Accuracy



Process quality vs. analytical quality !
To the detriment of laboratories these 2 are not identical!?

Specialized assays such as TEG / ACT / Platelet function

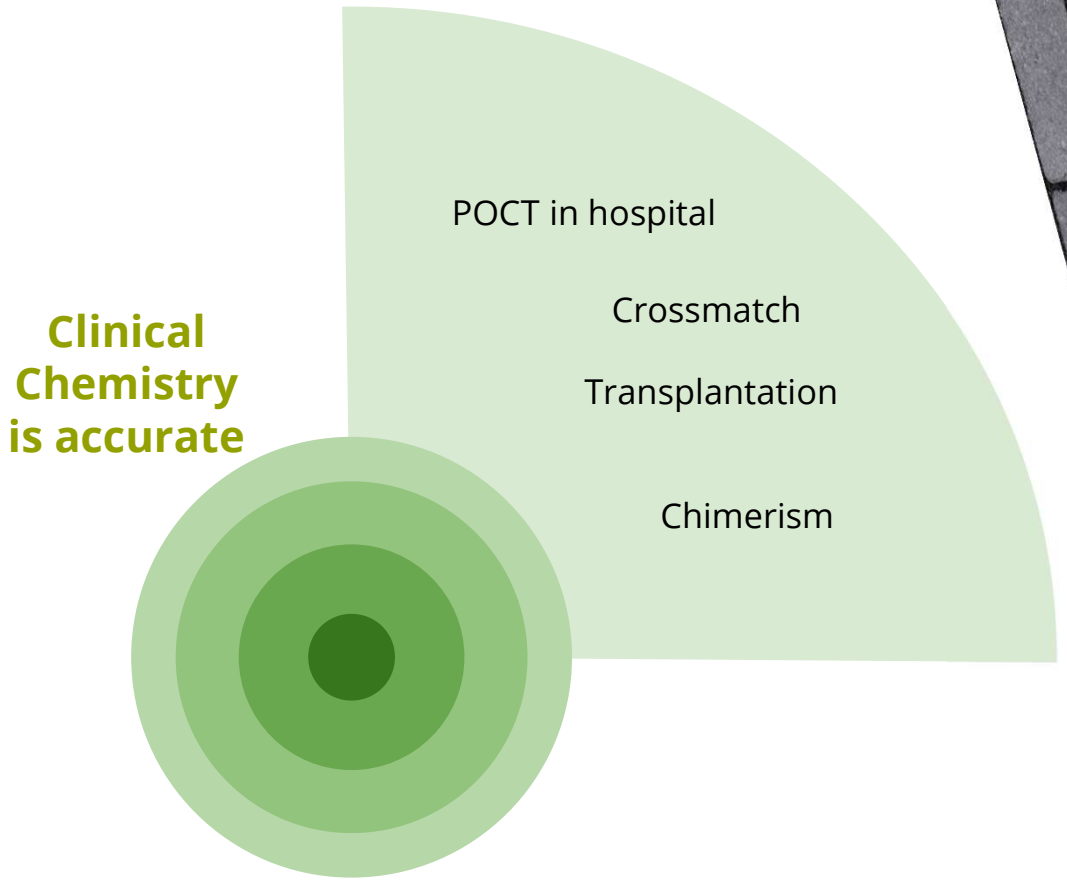
No international standards

→ Variability between different manufacturers and even instruments of the same manufacturer

Longitudinal stability relies on internal standardisation of the manufacturer

Consequences:

- assay results can only be compared to assay reference range (manufacturer-specific) or previous results using the same assay
- Standardisation relies on manufacturer quality system



POCT
OTC

Pharmacy

GP

Emergency

Nursing home

How does the ePA work?

Every statutory health insurance fund provides its insured persons with a mobile application (app), allowing them to view their own ePA at any time. With a mobile device (smartphone or tablet), it is then possible to access your own ePA and see all your medical documents.

In addition to the option to view their data in the ePA from anywhere in the world, the insured persons also assign all authorisations themselves. This means that they alone decide which doctor or which doctor's practice or hospital may view the ePA and enter new documents. Doctors only have access to view or add to the ePA when this access has been granted. Authorisation can only be granted for the entire ePA currently. More targeted authorisation management is expected to be introduced from 2022.

To the topic

Die elektronische Patientenakte

Personal Health Record (ePA)

Current blood counts, previous illnesses, medications or the specialist's most recent examination report -- with the electronic patient record (ePA), all health data can be accessed via an app anywhere in the world. Since 1 January, the ePA has been available on a voluntary basis. It is provided free of charge by the health insurers in order to further digitise the

Electronic Patient Record

Equivalence of Lab values ?

Potential misintepretation of therapy / disease course

Ring trials compare the performance of different diagnostic methods and of laboratories that use the same diagnostic method against each other

They do not test overall performance of laboratories and do not test for clinical process quality.

Case based EQA - major concerns

technicians , chemists, genetic- bioinformatic specialists…. get out of focus

artificial cases minor stimulus for clinincal management

would have to add pathologic imaging and some else

outcome may hamper accurate performance data of analytics

Electronical documentation eg electronic patient record is an ultimate challenge for the accuracy of results from the medical laboratory

Lab results as key elements in scientific documentation and guidelines

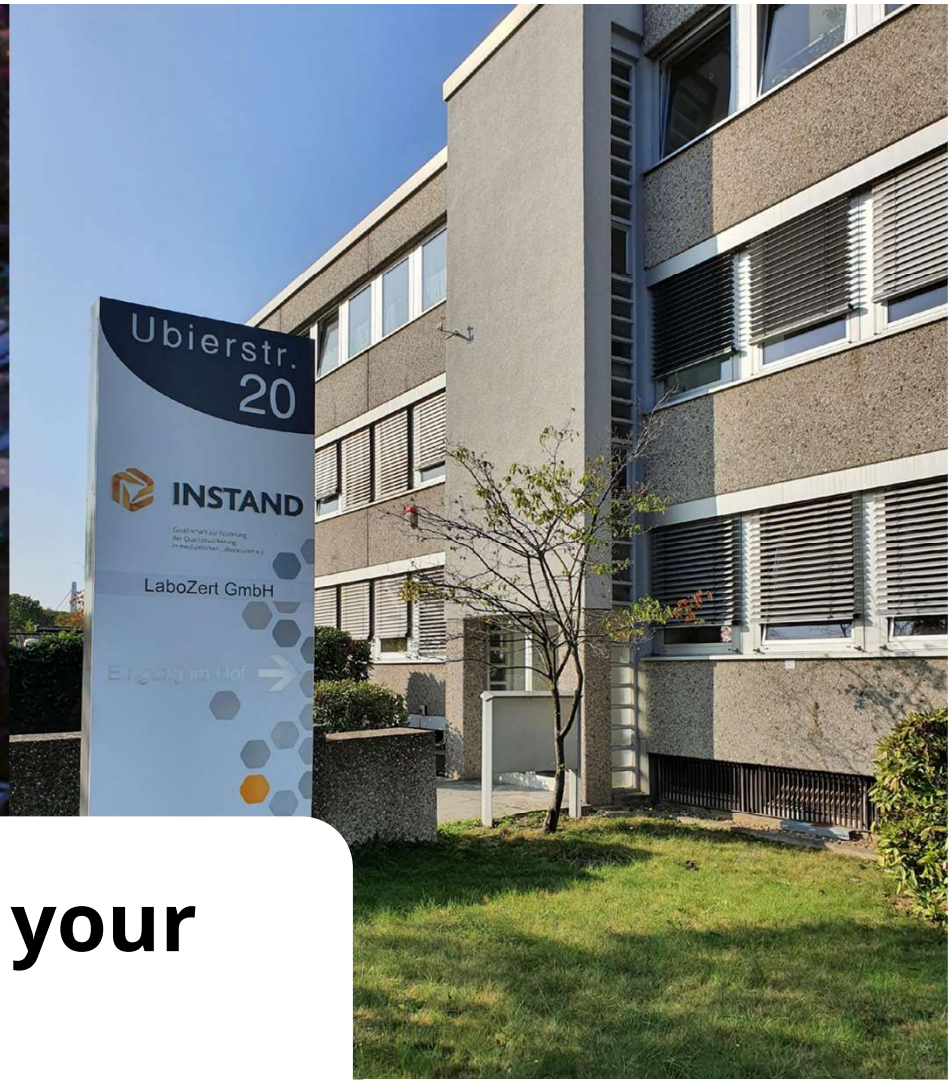
Precise single shot in preventive medicine screening

Comprehensive concept for EQA in clinical chemistry
Based on reference system,stability, homogeneity selectivity, commutability

Major concern of translantion into complex biological methods (Hematology, Coagulation, Cross Match... and POCT)
(what is the analyte?)

New concepts for near patient testing, new participants (outcome?case based?)

Respect the laboratory perspective – respect the clinical perspective



Thank you for your attention

Prof. Dr. Michael Spannagl

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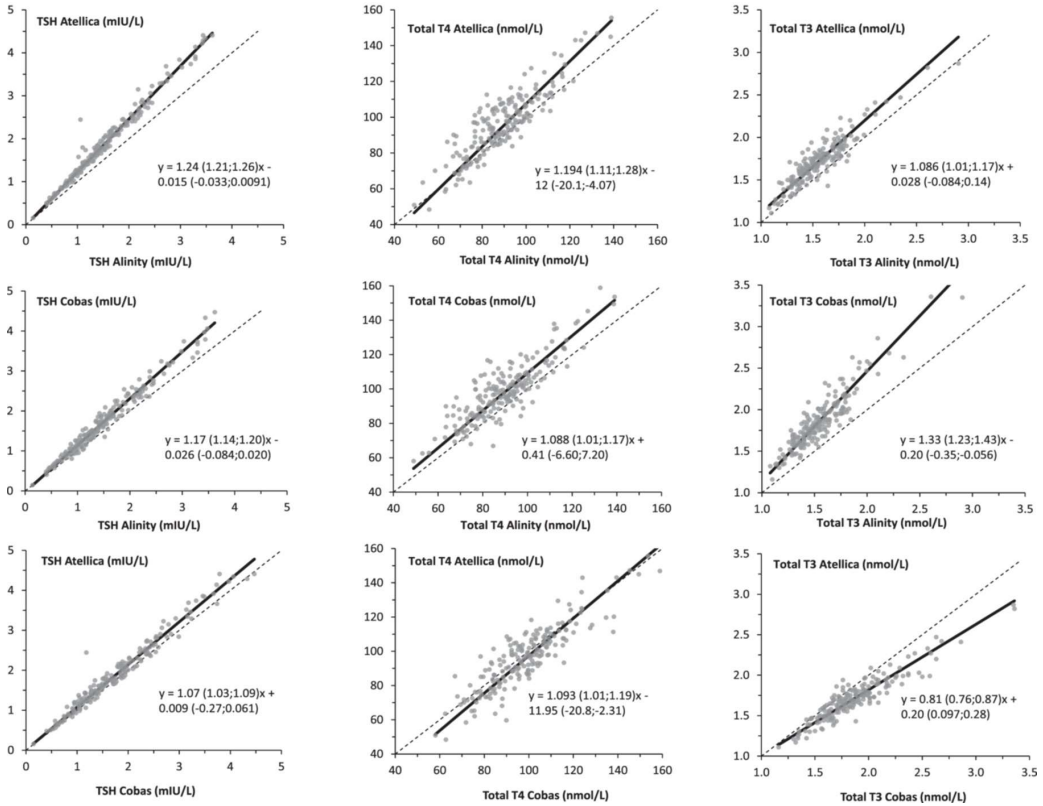
Case besed EQA maj concerns

technicians chemists genet. Bioinformatis get out of focus

artif cases minor stimulus for clin
would have to add pathol imaging

outcome may hamper accuraye performance data of analytics

Agreement between routinely used immunoassays for thyroid function testing in non-pregnant and pregnant adults



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CLINICAL IMPACT OF EQA

RILIBAEK HbA1c Gluc Pleus

The IT challenge
el patient el record automated diagnostic pathways

one shot one hit CDL Cut OFF (Range)

Trop DD PCT

CROSSMATCH

Transfusion Transplantation COAG?
What is the analyte, What ist traceability

Clin chem ist mother of labmed
complex boil methods need new perspectives for standard.

Persp High freq, POCT