



IN STAND_{e.V.}

40 years EQA experience – on the road to harmonisation?

Prof. Dr.med.Michael Spannagl

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Munich- Heart of ?



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„O'zapft is“ - Oktoberfest 2015



Key facts

- Date: September - October (15 days)
- Location: Munich - Theresenwiese
- 6,3 Mio. Visitors
- 7,4 Mio. Liter beer = 7,4 Mio. Maß sold...

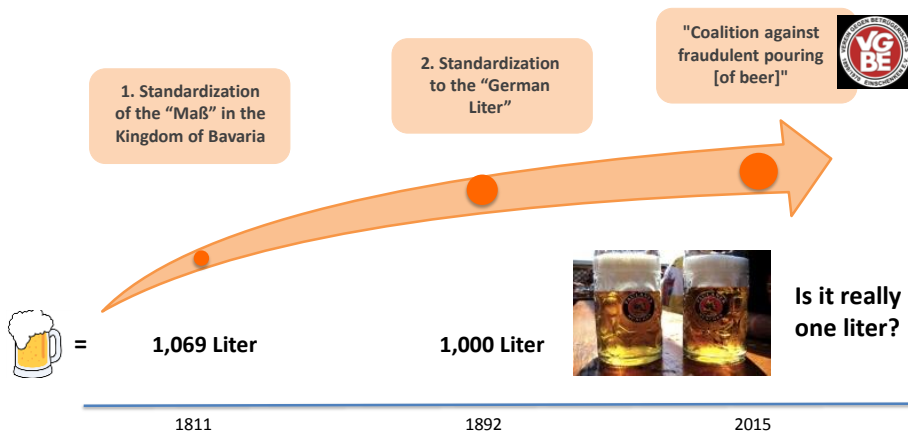
Exactly 7,4 Mio Liter?

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How to standardize the „Maß“?





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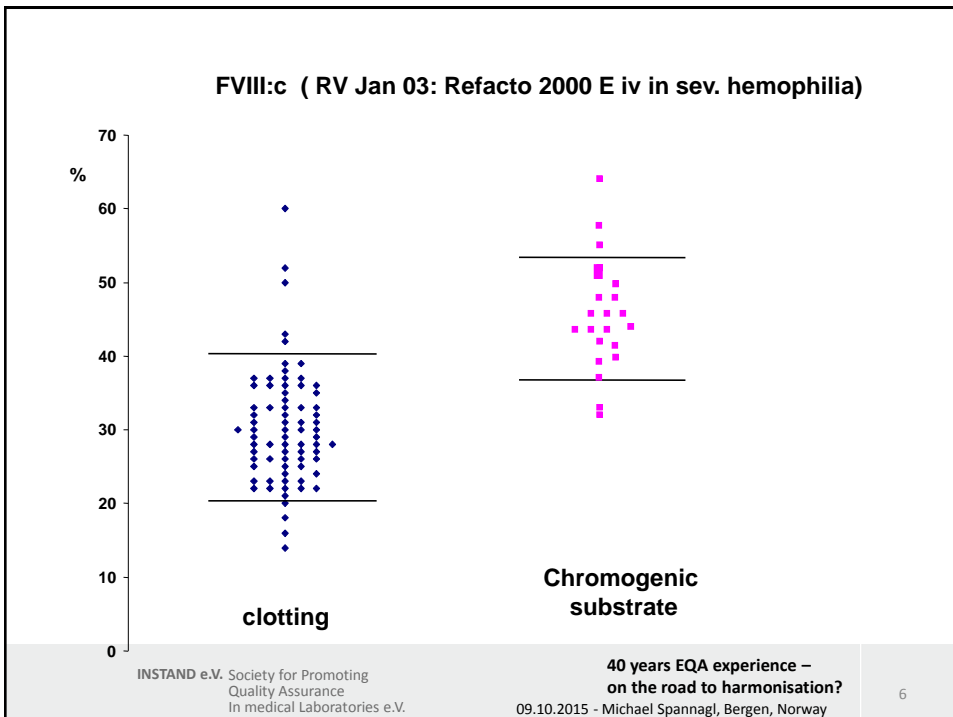
Potency Labeling


→


How to declare F VIII content ??

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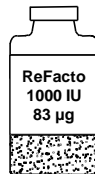
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ReFacto AF vs. Xyntha

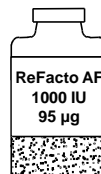
previous ReFacto

Worldwide
CS Assay WHO 6. IS

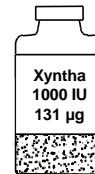


Xyntha/ReFacto AF

Europe
CS Assay WHO 7. IS



USA/Canada
OS Assay WHO 7. IS



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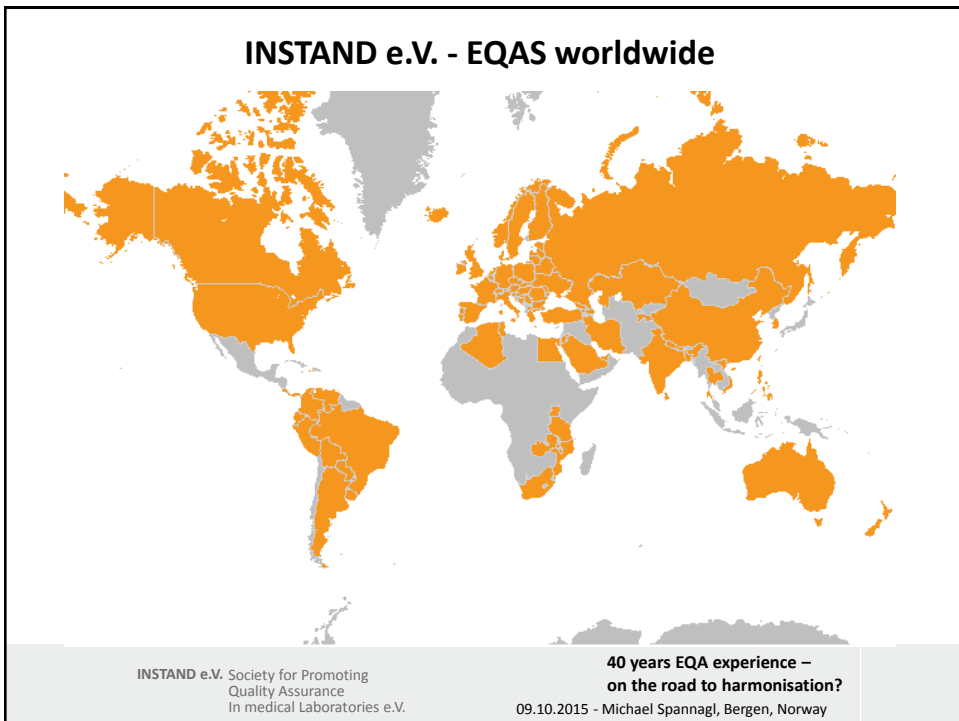
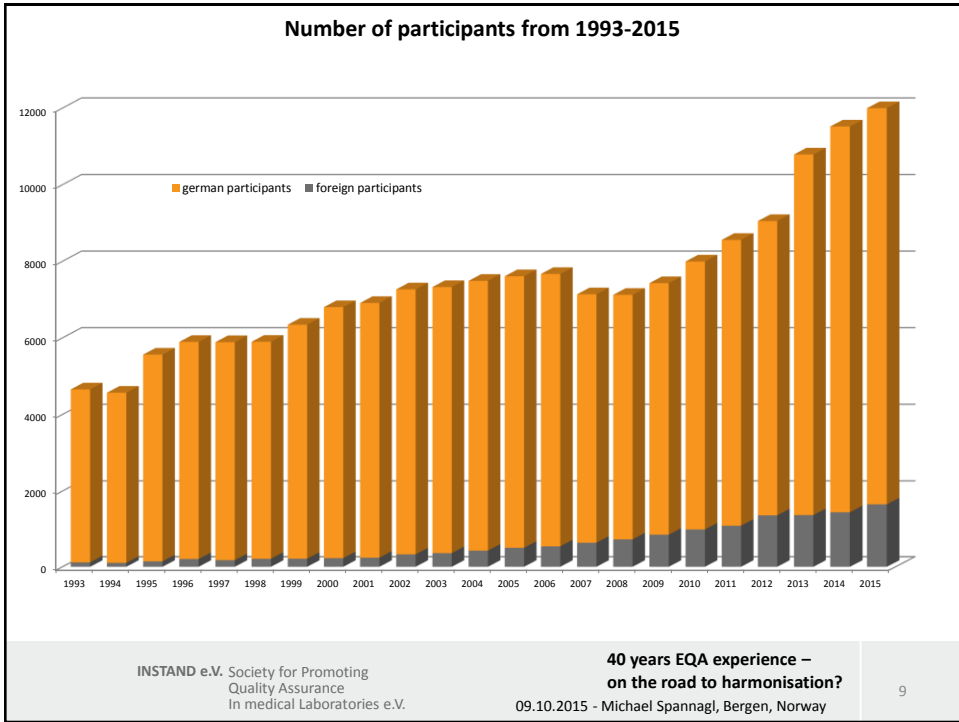


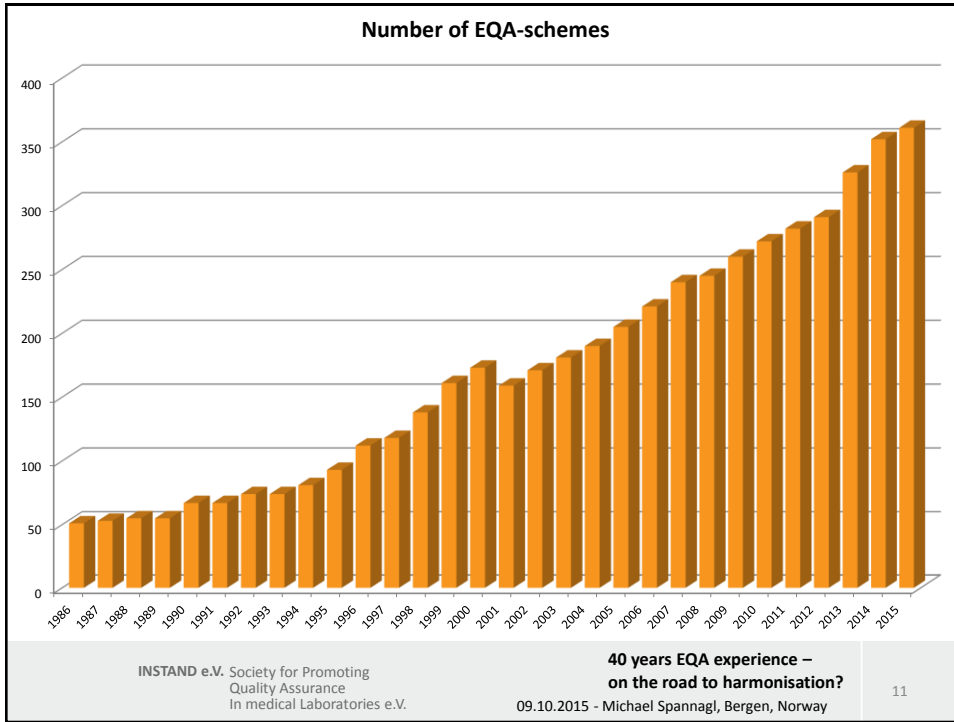
- 28 Employees in Düsseldorf
- 104 Experts
- 360 EQA-programs
- Participants in 93 countries

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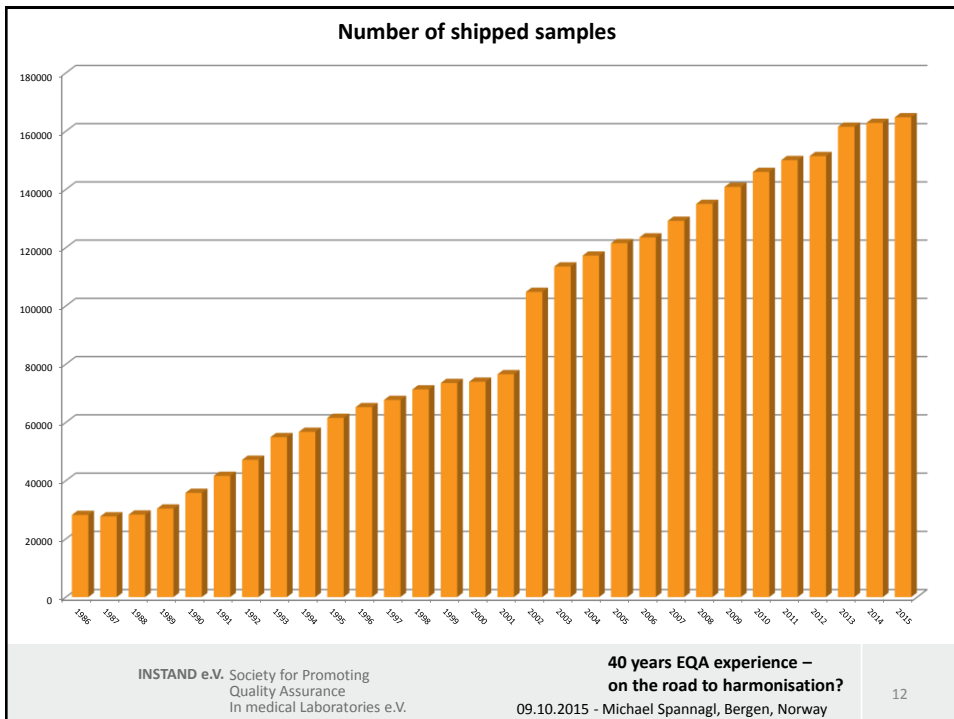
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RiliBÄK - Guidelines of the German Medical Association on Quality Assurance in Medical Laboratory Testing



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New Guideline for Quality Assurance of the German Medical Association (RiliBÄK)

-> mandatory for all medical laboratories in Germany

Section A Fundamental requirements for quality assurance	Effective since 1 April 2008
Specific Section B 1 Quantitative analyses in laboratory medicine <i>- internal QA - external QA</i>	Effective since 1 April 2008
Specific Section B 2 Qualitative analyses in laboratory medicine <i>- internal QA - external QA</i>	Effective since 1 July 2011
Specific Section B 3 Direct detection and characterization of pathogens <i>- internal QA - external QA</i>	Effective: 1 June 2015
Specific Section B 4 Analyses of ejaculate <i>- internal QA - external QA</i>	Effective since 1 July 2011
Specific Section B 5 Molecular- and cytogenetic analyses <i>- internal QA - external QA</i>	Effective since 1 October 2011

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**Guideline of the German Medical Association on Quality Assurance
in Medical Laboratory Examinations (RiliBAEK)**
(extract from annex B1)

1 No.	2 Analyte	3 Acceptable relative deviation of the single value or the relative root mean square	4 Range of validity of columns 3 to 5			5 Acceptable relative deviation in a round robin test	6 Type of target value in a round robin test
			From	To	Unit		
19	Uric acid	14.0% 17.5%	≤ 1	≥	μg/l	30.0%	RMV
20	Erythrocytes	4.0%	1.5	7	10 ¹² /l	8.0%	RMV
21	Estradiol 17-beta	22.0%	10 37	500 1835	ng/l pmol/l	35.0%	RMV
22	Ethanol (clinical toxicology)	9.0%	> 0.6	5	g/l	12.0%	SV
		15.0%	0.2	≤ 0.6	g/l	21.0%	
23	Ferritin	13.5%	10	600	μg/l	25.0%	SV
24	FSH	14%	4	70	U/l	21.0%	
25	Gamma glutamyl transferase (γ-GT) EC 2.3.2.2	11.5%	20 0.33	300 5	U/l μkat/l	21.0%	RMV
			40 2.2	400 22	mg/dl mmol/l	15.0%	
26	Glucose	11.0%	10 0.1	60 0.6	% l/l	9.0%	SV
27	Haematocrit	5.0%	2 1.2	20 12.4	g/dl mmol/l	6.0%	RMV
28	Haemoglobin	4.0%	30	140	mmol/mol Hb	18.0%	RMV
29	Haemoglobin A 1 c (HbA1 c)	10.0%	2	13	mmol/l	13.0%	RMV
30	Uric acid	7.0%	2	13	mg/dl	13.0%	RMV

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INSTAND Reference Laboratory



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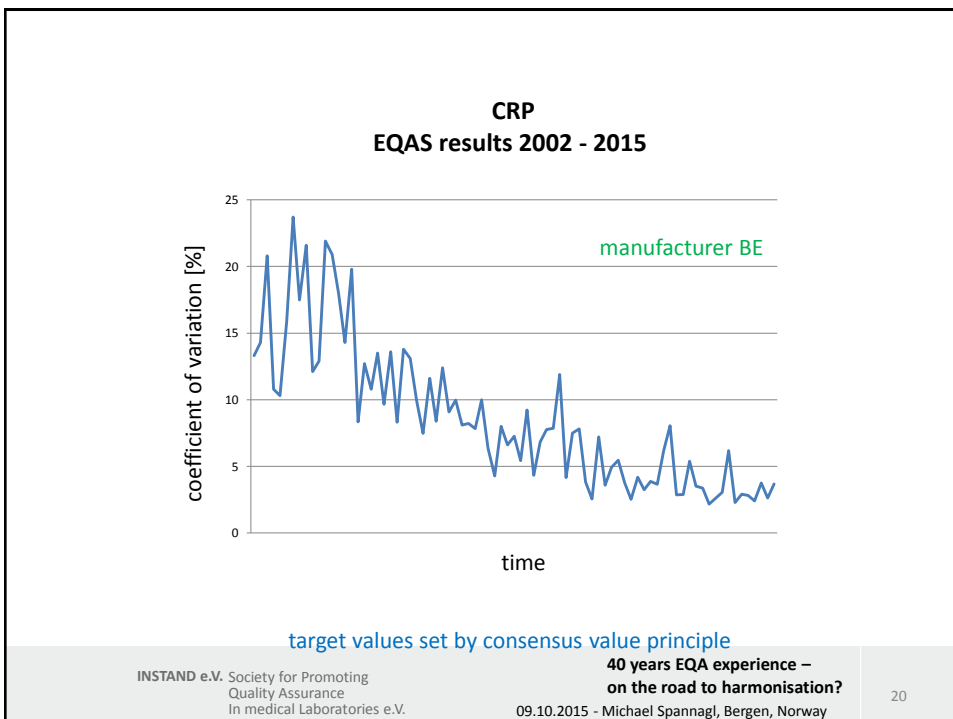
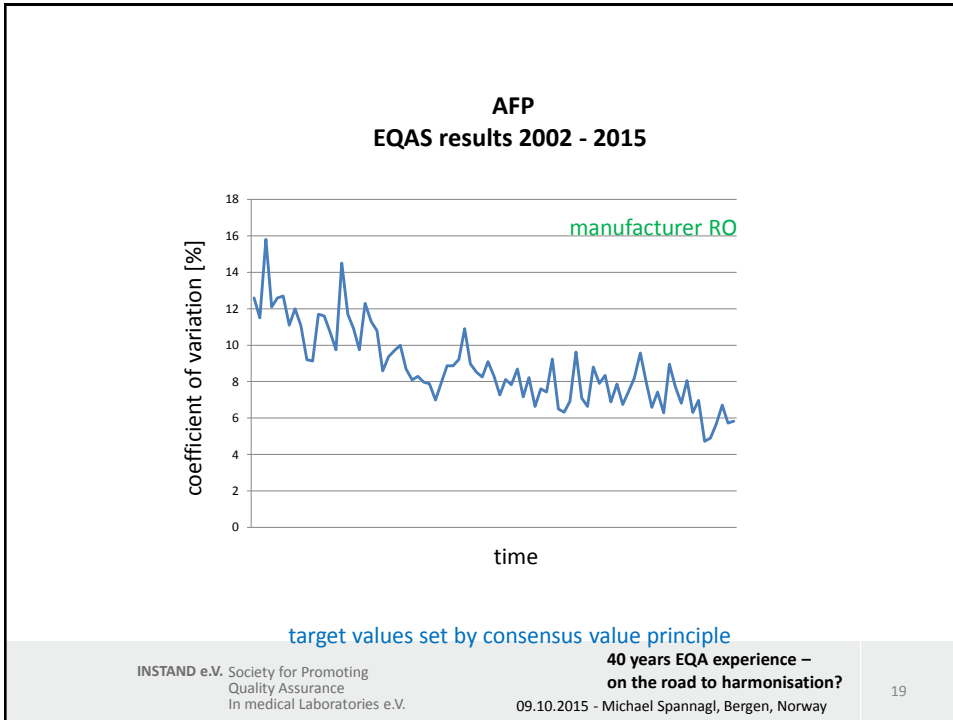
Reference laboratory

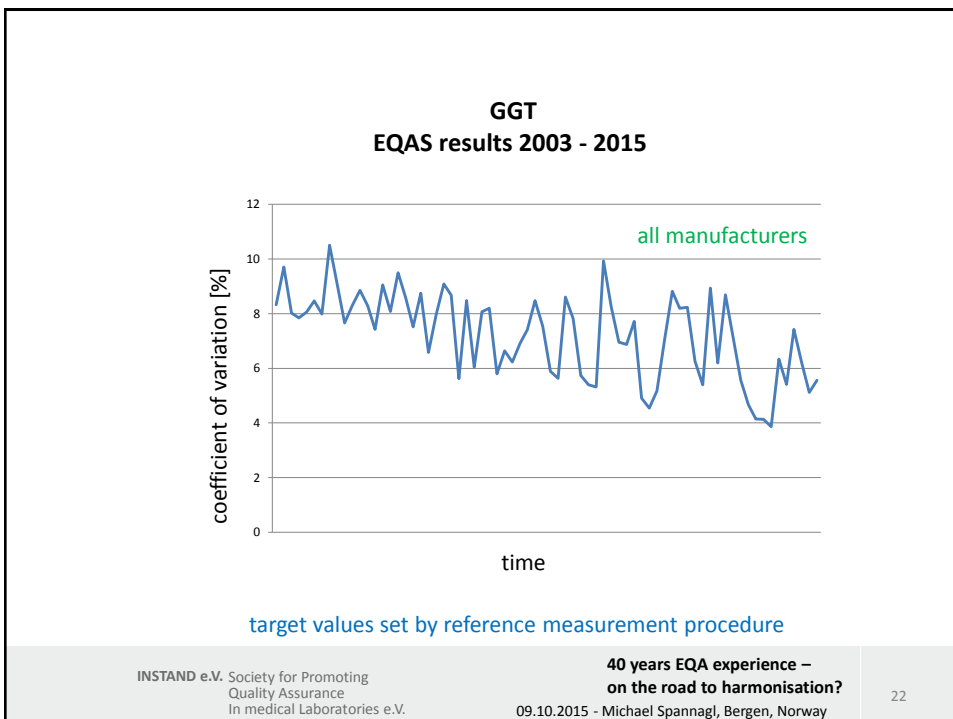
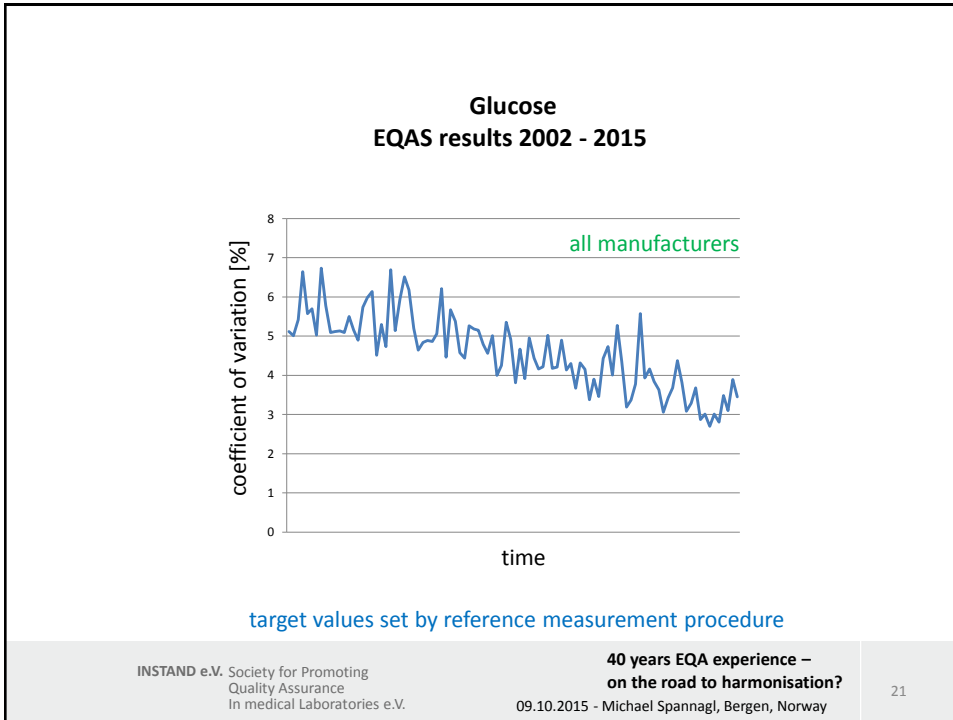
Accreditation according to ISO 17025 and ISO 15195

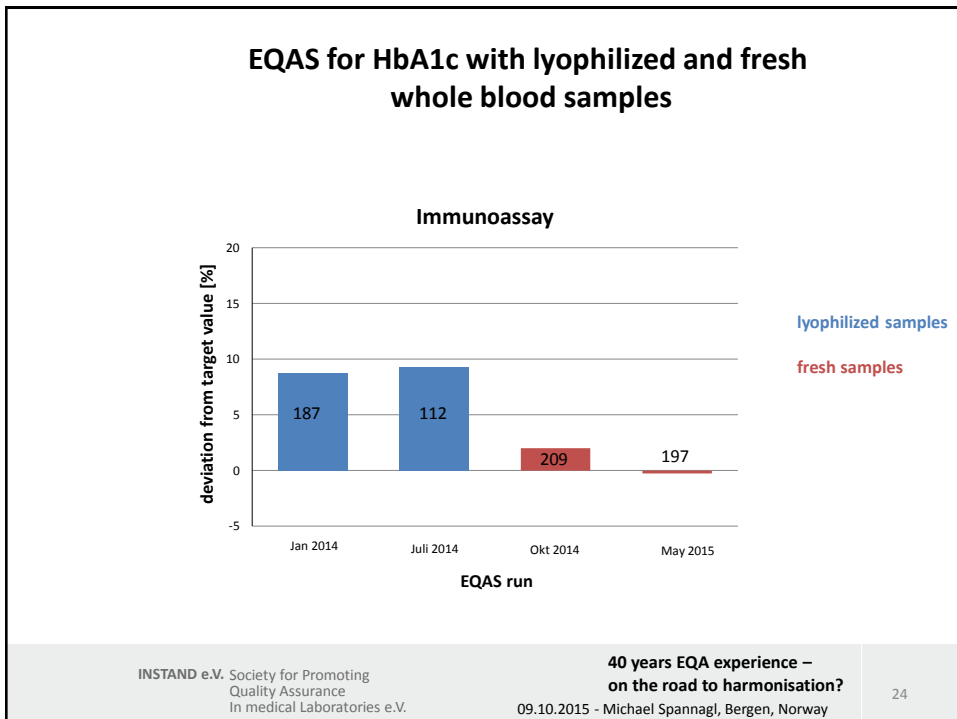
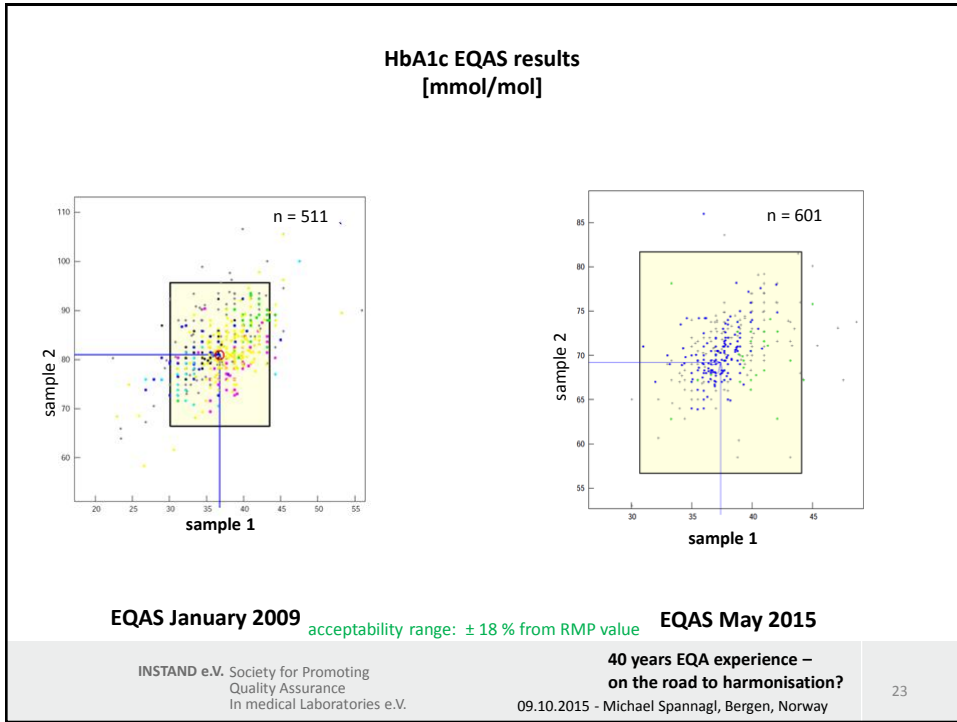
2006	Cholesterol
2009	Chloride, Potassium, Sodium, ALT, AST, GGT, CK, LDH Creatinine, Urea, Cortisol, Total Protein, HbA1c, Theophylline
2012	Calcium, Lithium, Magnesium, Uric Acid, Total Glycerides, Testosterone, Thyroxine
2015	Glucose, 17- β -Estradiol, Progesterone, Digoxin, Digitoxin

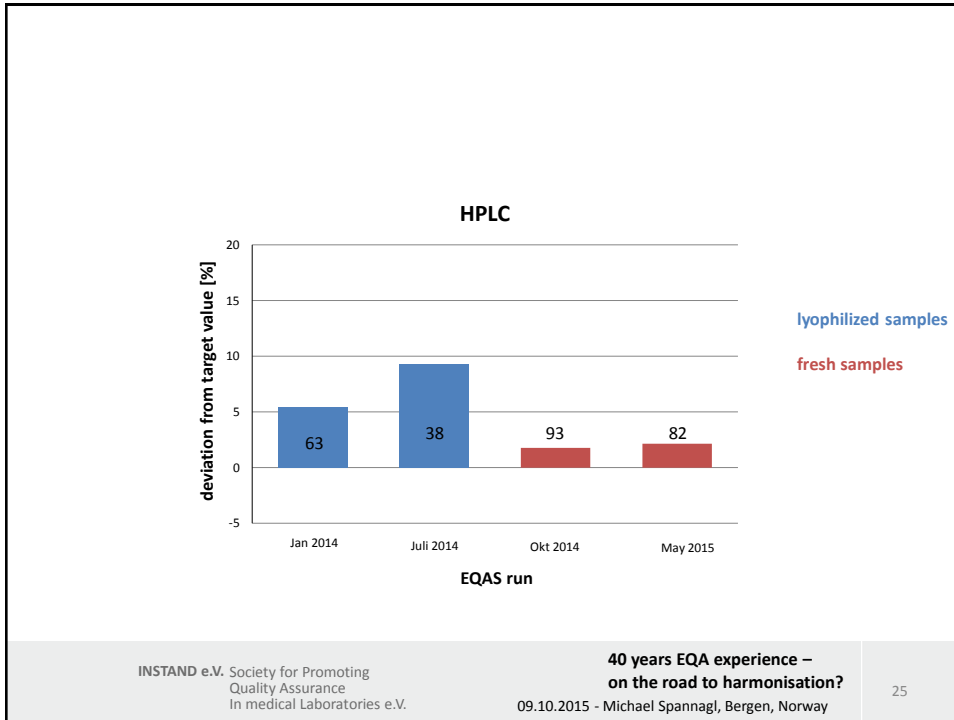
Reference measurement procedures established in the reference laboratory of INSTAND e.V.

Before 2002:	Cholesterol, Cortisol, Creatinine, 17 β -Estradiol, Glucose, Progesterone, Testosterone, Thyroxine, Total Glycerides, Uric Acid
2002:	Theophylline
2003:	ALT, AST, CK, GGT, LDH, Calcium, Chloride, Potassium, Lithium, Magnesium, Sodium, Digoxin, Digitoxin
2004:	HbA1c, Total Haemoglobin, Total Protein
2006:	Urea









RiliBÄK Specific Section B 3: Direct Detection and Characterization of Pathogens - Quantitative Detection of Nucleic Acid of HIV-1

Table B 3-2a
Evaluation thresholds for external quality assurance of nucleic acid detection of pathogens transmitted by blood/plasma/serum

1 No.	2 Analyte	3 Acceptable deviation of log ₁₀ value of participant from log ₁₀ target value of EQA scheme	4 Range of validity in respect to column 3			5 Target value of EQA scheme	6 Frequency of EQA scheme
			from	to	unit		
1	CMV DNA	-0,8 to+0,8	5 000	5 000 000	IU/mL	Target value	2x/year
2	HBV DNA	-0,6 to+0,6	500	5 000 000	IU/mL	Target value	2x/year
3	HCV RNA	-0,6 to +0,6	500	5 000 000	IU/mL	Target value	2x/year
4	HIV-1 RNA	-0,6 to +0,6	500	5 000 000	copies/mL	Target value	2x/year

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INSTAND-EQA schemes for quantitative HIV-1 genome detection for mimicing therapy monitoring

- quantitative genome determination
 - basis for therapy monitoring
- decrease of $\geq \log_{10}$ copies/ml within 1 month
 - indicator for antiviral efficacy
 - if not: antiviral resistance?
- target
 - get viral load below level of detection
- example for EQA scheme
dilution series of one and the same HIV stock:
 - 1 : 200×10^7
 - 1 : 50×10^7
 - 1 : $12,5 \times 10^7$
 - 1 : $3,125 \times 10^7$

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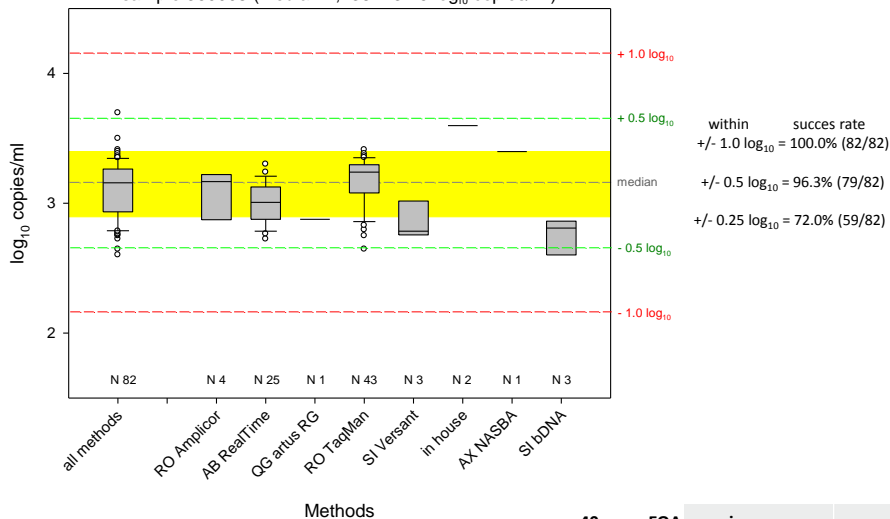
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INSTAND-EQAS for HIV-1: Sample Dilution Series

EQAS Sep 2010, PCR/NAT HIV-1 (360)

sample 360008 (median 1,438 = 3.16 \log_{10} copies/ml)



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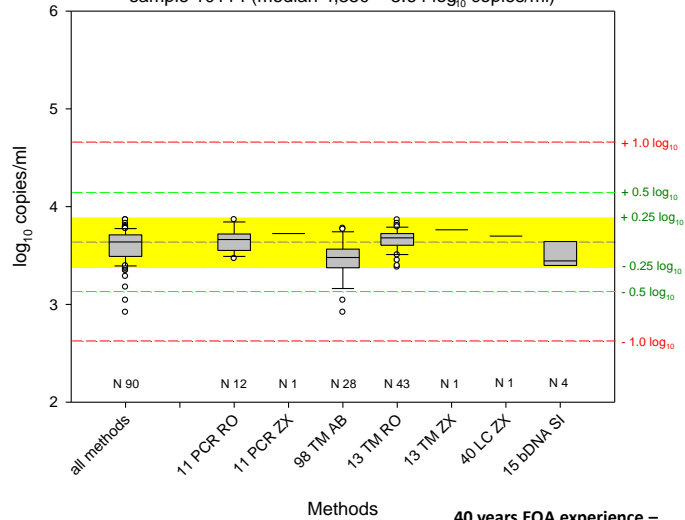
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INSTAND-EQAS for HIV-1: Test Performance

EQAS Nov 2008, HIV PCR/NAT (360)

sample 10114 (median 4,350 = 3.64 log₁₀ copies/ml)



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Methods

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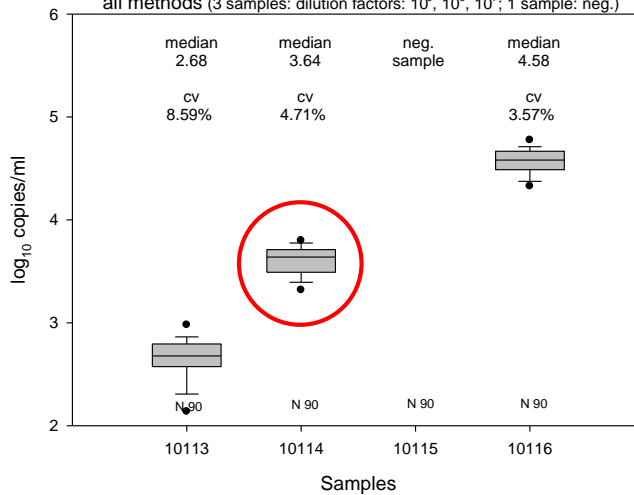
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INSTAND-EQAS for HIV-1: Sample Dilution Series

EQAS Nov 2008, HIV PCR/NAT (360)

all methods (3 samples: dilution factors: 10³, 10⁸, 10⁷; 1 sample: neg.)



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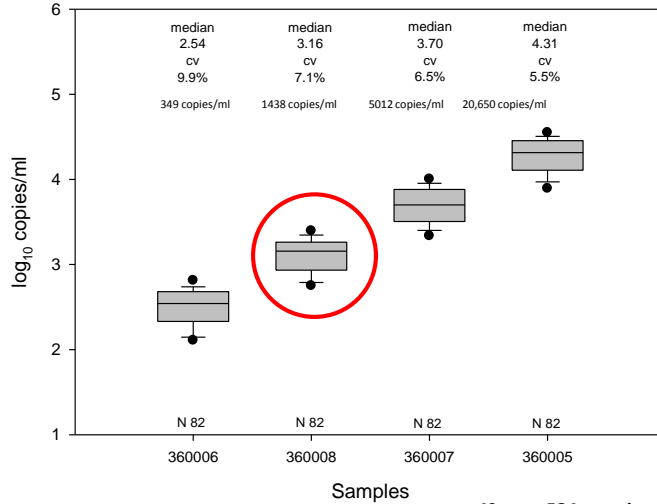
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INSTAND-EQAS for HIV-1: Sample Dilution Series

EQAS Sep 2010, PCR/NAT HIV-1 (360)

all methods (4 samples: dilution factors: $1:200 \times 10^7$, $1:50 \times 10^7$, $1:12.5 \times 10^7$, $1:3.125 \times 10^7$)



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The last problems

- The survey manager and EvidenceBasedM..
- No punishment
- Communication with manufacturers
- Harmonization of acceptance criteria



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TO...



Make RILIBAEK a success



Improve control material (like vs like, commutability...)



**Skip artificial surveys (not to test the control mat...)
Introduce new concepts (virtual..., educational..)**

Miles vs. Kilometer



Will this ever be standardized?

Thank you for attention

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