



Schweizerische Eidgenossenschaft
Confédération suisse
Confederazione Svizzera
Confederaziun svizra

Federal Institute of Metrology METAS



Nucleic Acid Metrology

Kai N. Stölting

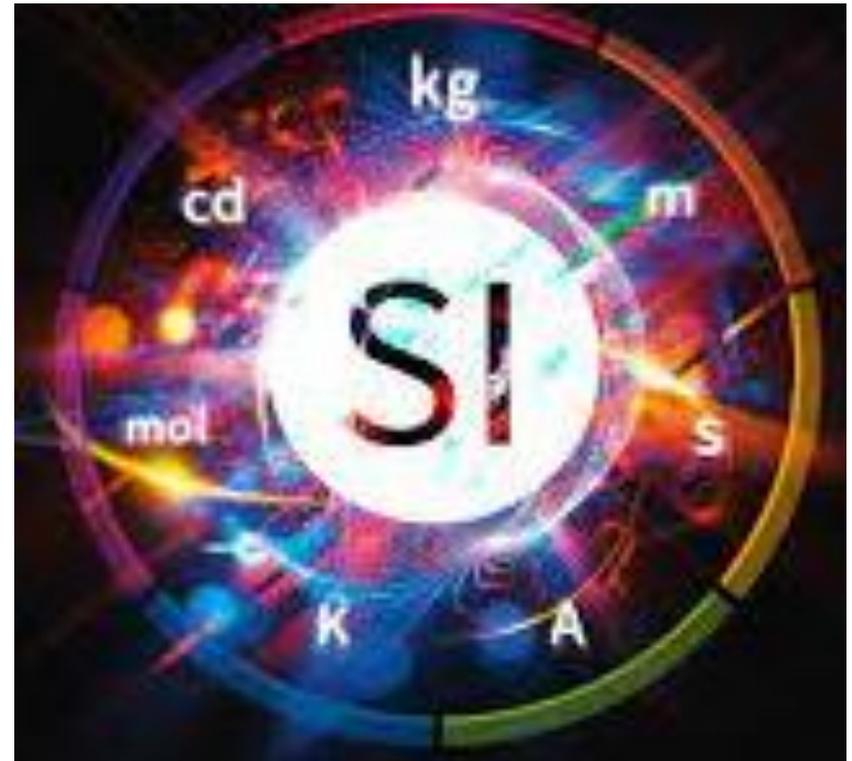
Karin Stettler, Fabian Wiestner, Tanja Hetke, and Gisela Umbricht

Agenda

- What
- Why
- How
- Thank you

Health-related metrological activities

1. Dosimetry
2. Audiometry
3. Nanoparticles
4. Aerosols
5. CT Measurements
6. Microflow
7. → Laboratory medicine



Laboratory medicine

- Measurements are used in ~70% of all medical decisions
- CH: ~8'000 measuring medical laboratories, ~98% part in EQA
- 1.75 Mrd. reimbursement for measurements p/a
- «Culture» of dealing with uncertain measurement results
 - Metrological traceability is little known
- Risks:
 - Limited comparability
 - Repetition of measurements
 - Erroneous medical decisions



Vision nucleic acid metrology

METAS:

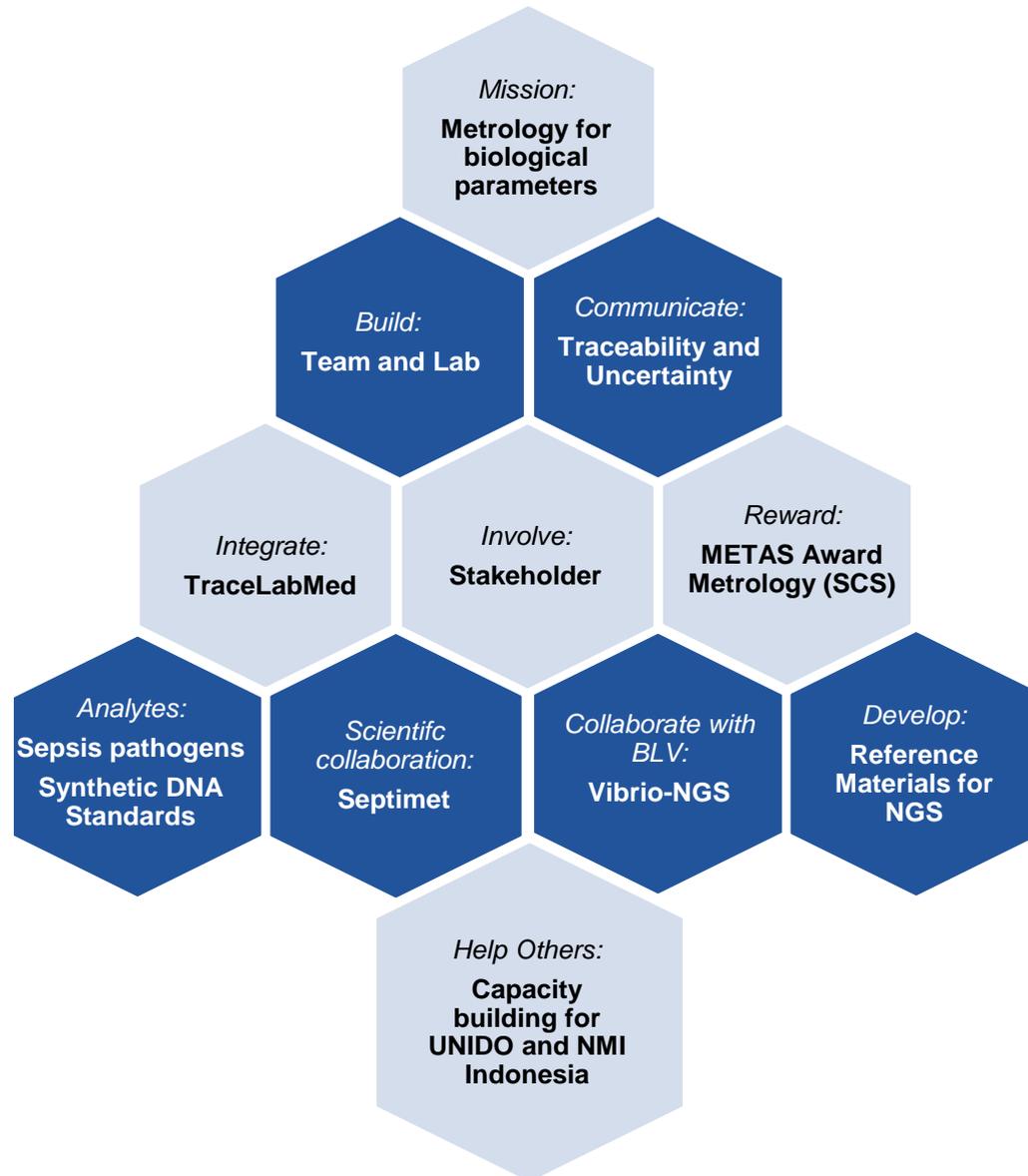
- 
- ✓ is a reliable contact and **service provider** for questions re. metrological traceability
 - ✓ ... wants to help shape developments in **nucleic acid analysis** in the long term
 - ✓ is neither an inspector nor a diagnostics provider
 - ✓ provides its **metrological experience** within the framework of the legal mandate and in the interest of the Swiss health care system.

Nucleic Acid Metrology at METAS:

- 
- ✓ arises in response to changing **regulatory** and **scientific** framework conditions in CH and abroad
 - ✓ is part of intensive **European** efforts to improve comparability, measurement accuracy and traceability in medical laboratory measurements



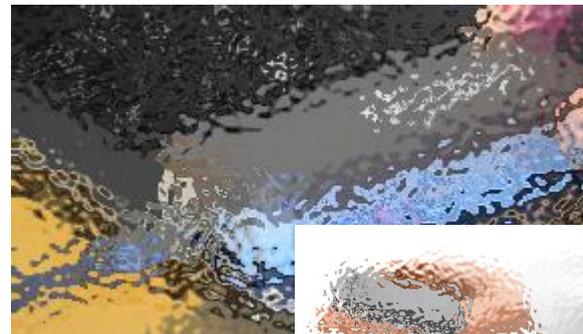
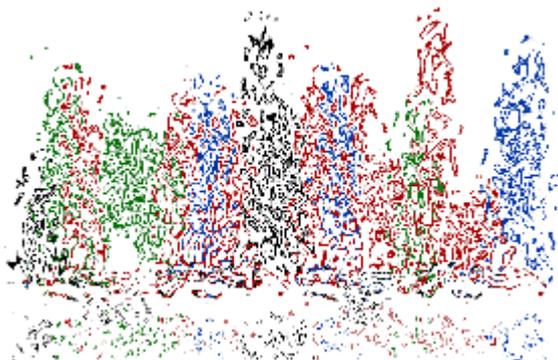
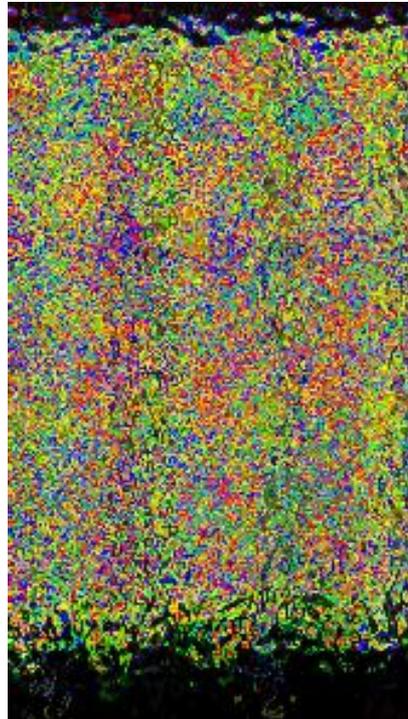
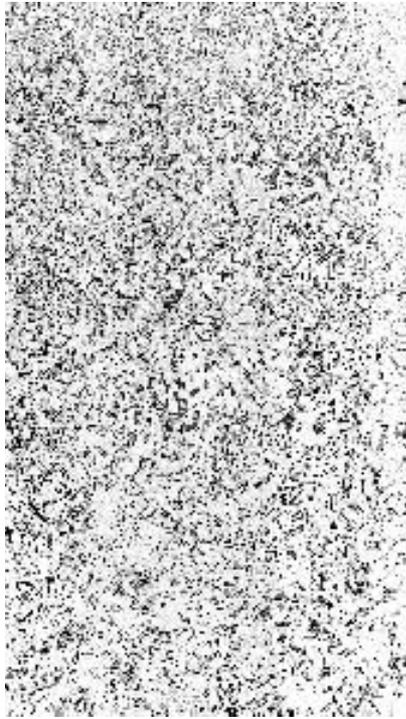
Nucleic acid metrology: implementation



Why focus on metrology for laboratory medicine?

- Technological
- Demographic
- Scientific
- Legal
- Regulatory
- Financial
- Personal

Technological – DNA

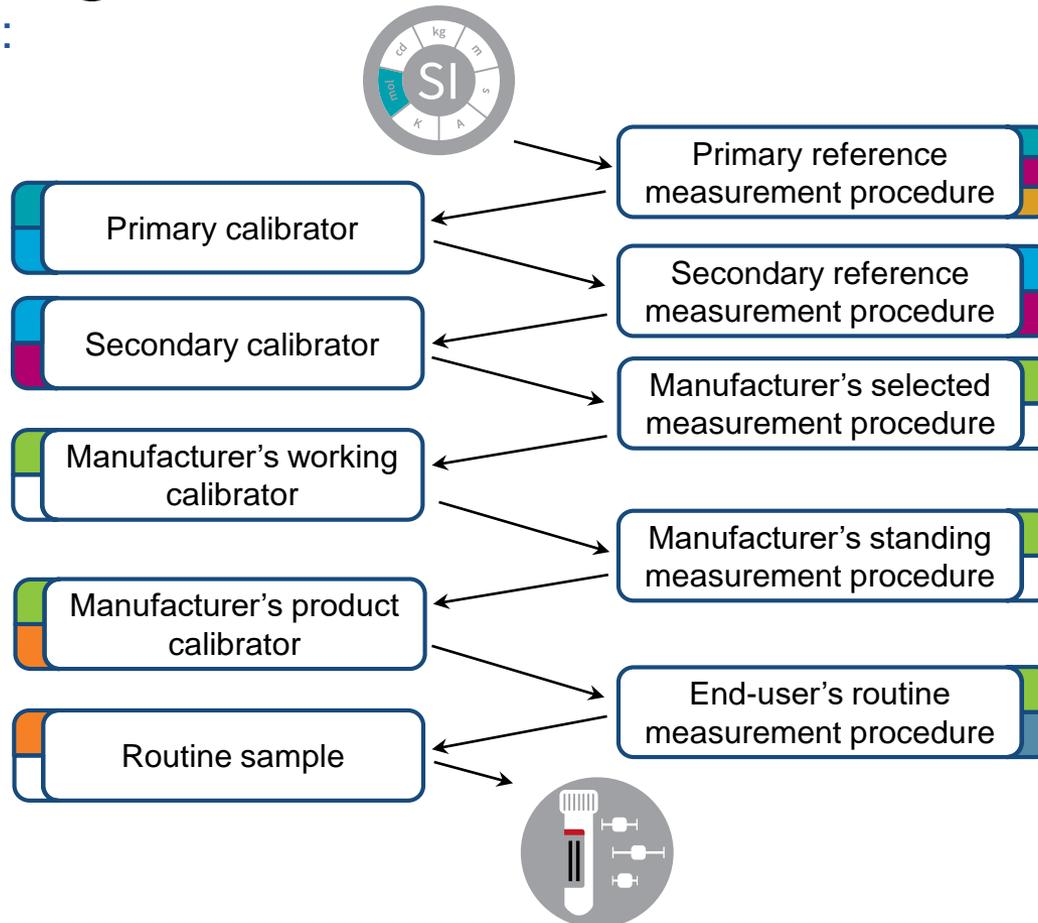


Scientific

Calibrating the calibrator: the traceability chain

Implementation:

- BIPM
- NMIs
- Ref. Labs
- Manufacturer
- End-user



Legal Framework – Federal law

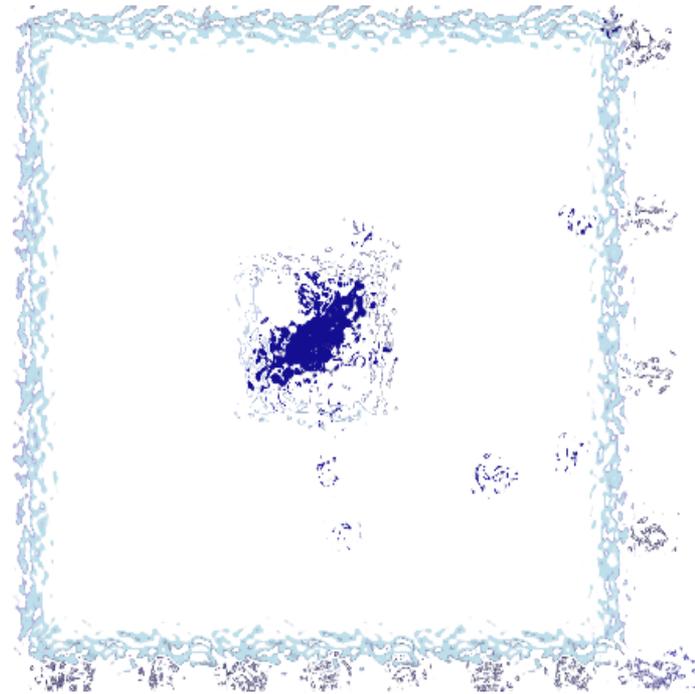
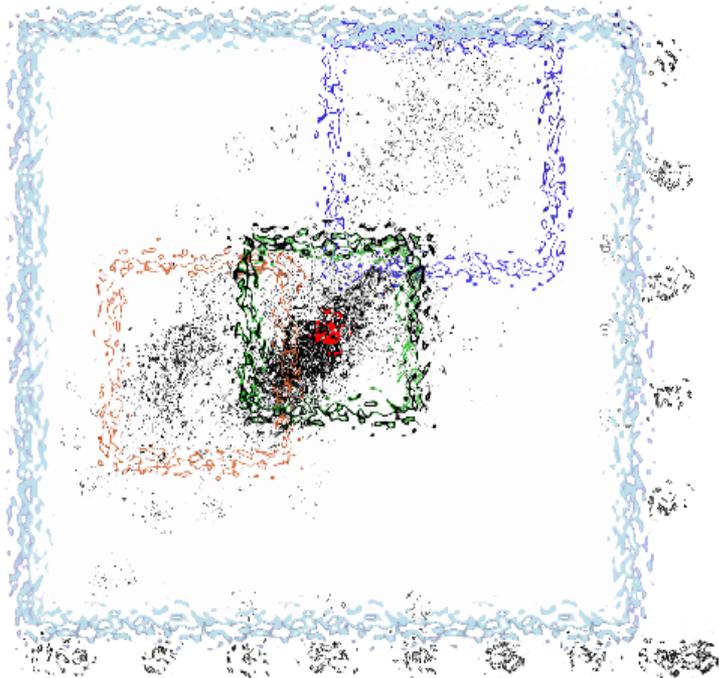
Landesrecht	Bundesgesetz über das Eidgenössische Institut für Metrologie	Dieser Text ist in Kraft.
1 Staat – Volk – Behörden	(EIMG) vom 17. Juni 2011 (Stand am 1. Januar 2012) <i>Die Bundesversammlung der Schweizerischen Eidgenossenschaft, gestützt auf Artikel 125 der Bundesverfassung¹, nach Einsicht in die Botschaft des Bundesrates vom 27. Oktober 2010²,</i> <i>beschliesst:</i>	Abkürzung EIMG Beschluss 17. Juni 2011 Inkrafttreten 1. Januar 2012 Quelle AS 2011 6515 Chronologie Chronologie Zitate Zitate
2 Privatrecht – Zivilrechtspflege – Vollstreckung	– Art. 1 Rechtsform und Organisation	Werkzeug Sprachenvergleich
3 Strafrecht – Strafrechtspflege – Strafvollzug	¹ Das Eidgenössische Institut für Metrologie (Institut) ist eine öffentlich-rechtliche Anstalt des Bundes mit eigener Rechtspersönlichkeit. Es wird im Handelsregister eingetragen.	Alle Fassungen
4 Schule – Wissenschaft – Kultur	² Es ist in seiner Organisation und Betriebsführung selbstständig und führt eine eigene Rechnung. Es wird nach betriebswirtschaftlichen Grundsätzen geführt.	• 01.01.2013 PDF DOC • 01.01.2012 PDF DOC
5 Landesverteidigung	³ Der Bundesrat legt die Firma und den Sitz des Instituts fest.	Revisionen
6 Finanzen	– Art. 2 Ziele	01.01.2012 Bundesgesetz vom 17. Juni 2011 über das Eidgenössische Institut für Metrologie (EIMG)
7 Öffentliche Werke – Energie – Verkehr	¹ Der Bund strebt mit dem Institut folgende Ziele an:	
8 Gesundheit – Arbeit – Soziale Sicherheit	a. Sicherstellung richtiger und gesetzeskonformer Messungen zum Schutz von Mensch und Umwelt;	
9 Wirtschaft – Technische Zusammenarbeit	b. Bereitstellung und Vermittlung der für die Schweizer Wirtschaft, Forschung und Verwaltung nötigen metrologischen Infrastruktur und Kompetenz.	
	² Das Institut erfüllt zu diesem Zweck die Aufgaben nach Artikel 3 und kann nachwirkliche Leistungen nach Artikel 35 erheben.	

Art 2 Der Bund strebt mit dem Institut folgende **Ziele** an:

- a. Sicherstellung richtiger und gesetzeskonformer Messungen zum **Schutz von Mensch und Umwelt**;
- b. **Bereitstellung** und Vermittlung der für die Schweizer Wirtschaft, Forschung und Verwaltung **nötigen metrologischen Infrastruktur** und Kompetenz.

Art 3 d) Es führt die **nötigen wissenschaftlich-technischen Untersuchungen und Entwicklungsarbeiten** durch, erforscht namentlich die Auswirkungen neuer Techniken und entwickelt praktisch anwendbare Messmethoden, die dem Stand der wissenschaftlichen Erkenntnisse entsprechen.

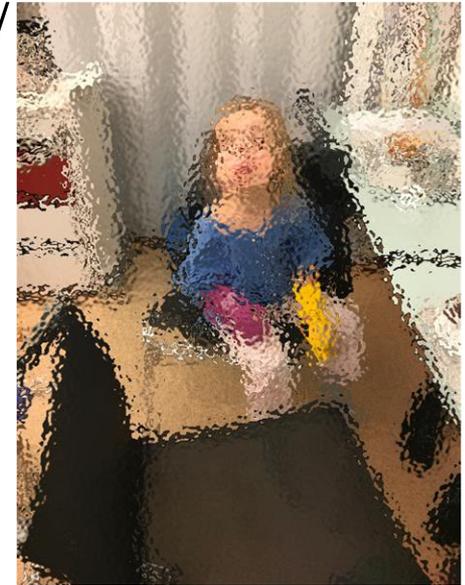
Financial and analytical benefits of using traceable calibrants



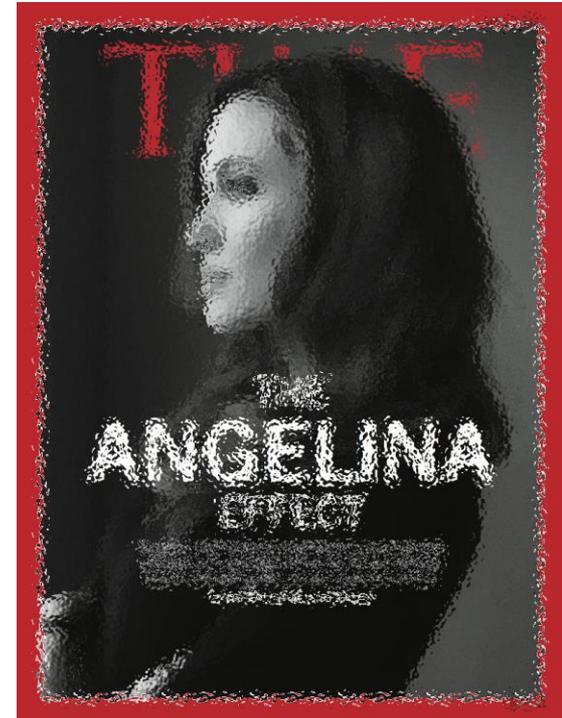
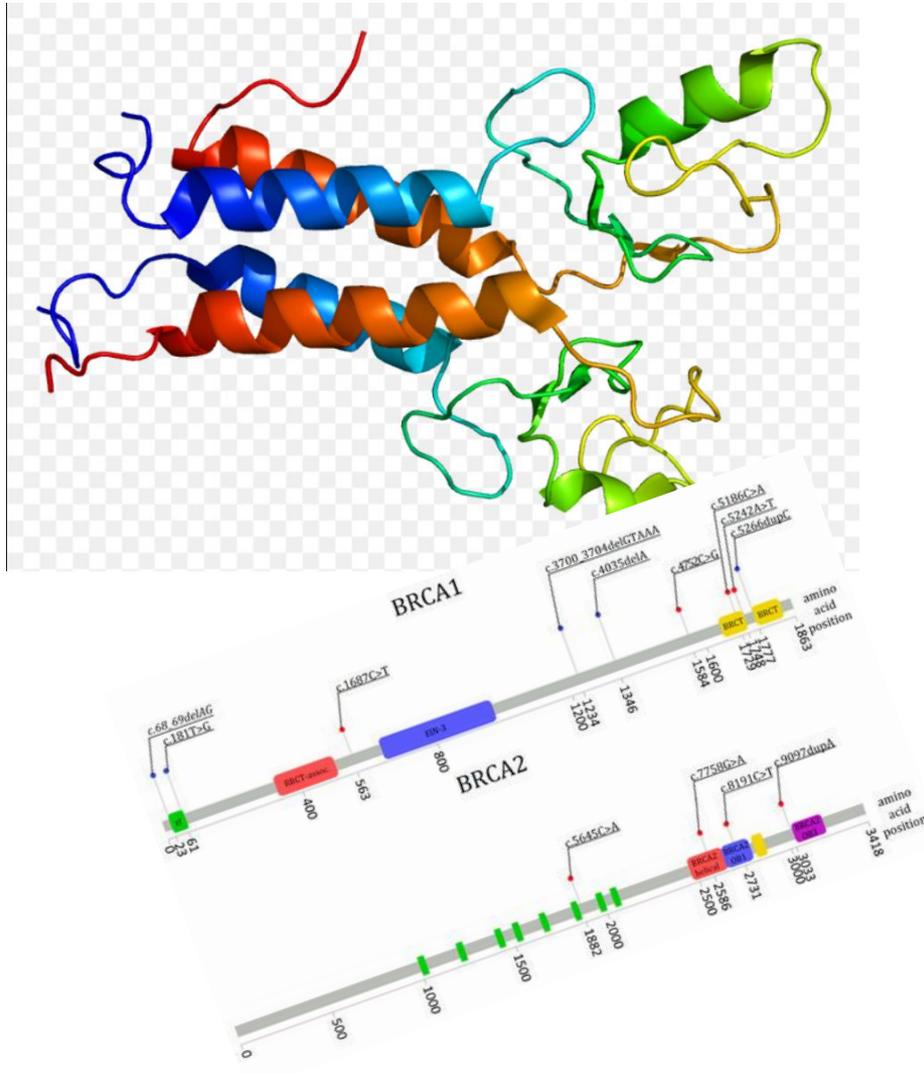
Significant reduction in measurement uncertainty and elimination of inaccurate analytical measurement procedures before (left) and after (right) implementation of metrologically traceable measurement procedures for cholesterol

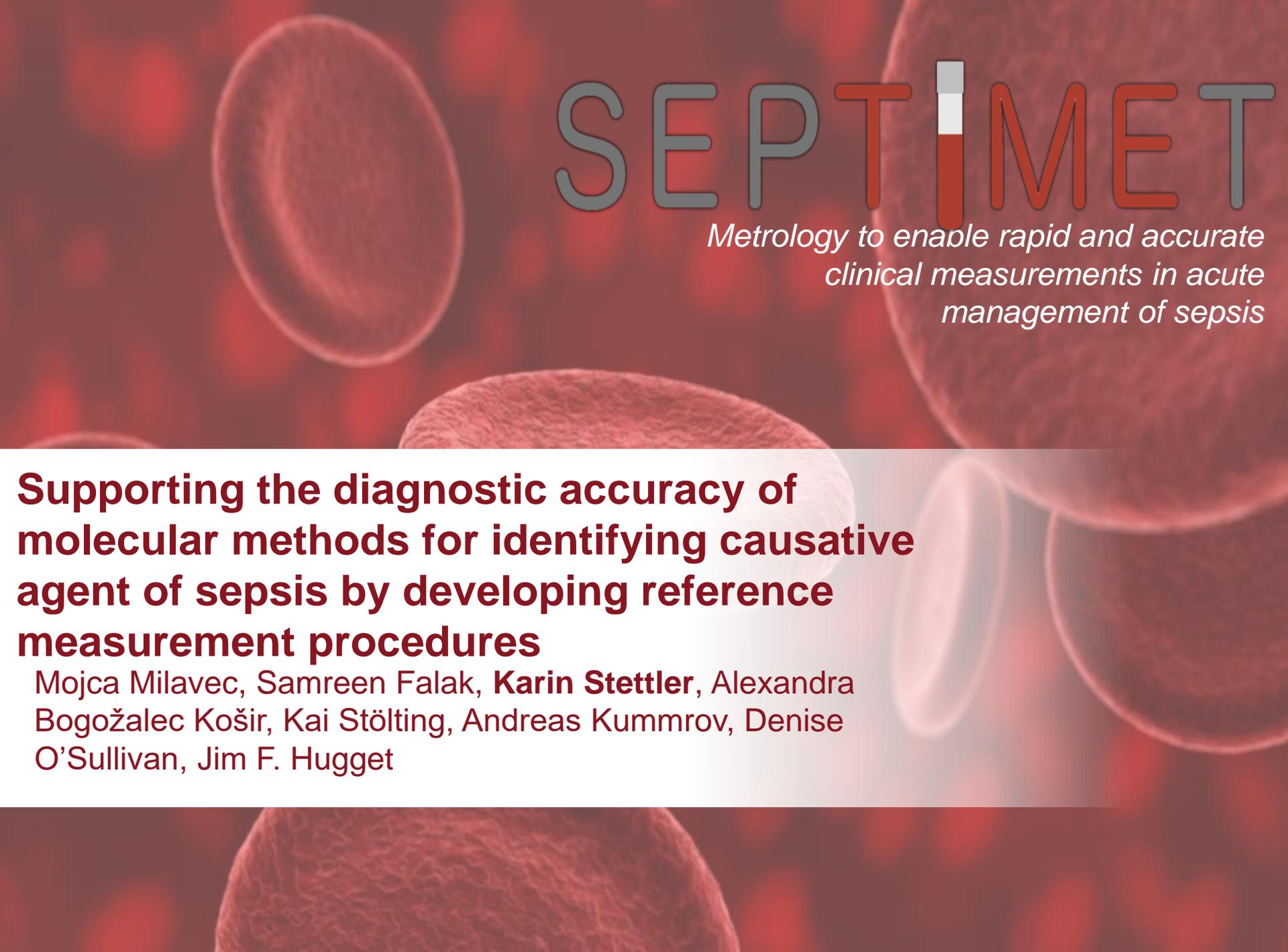
Personal - A Case Report

- How many measurements during initial diagnosis / hospitalization / therapy?
 - 316 measurements
- How many analytes?
 - 65
- How many were from POCT?
 - 242 → 76%
- How many were immediately detected wrong?
 - 27/28 (POC) → 9% (lipemic samples, elev., turbidity hemolytic sample)
- How many measurements outside reference range?
 - 111 → 35%
- Currently HbA1c every 3mo
- ~12 DGM daily + capillary, >4'500 p/a



Personal - BRCA



The background of the slide features a close-up, slightly blurred view of several red blood cells. The cells are spherical with a textured surface, and their colors range from a deep red to a lighter, almost pinkish hue. In the upper right quadrant, a small, vertical test tube is visible, containing a red liquid and a white cap. The overall lighting is soft and focused on the cells, creating a sense of depth and biological detail.

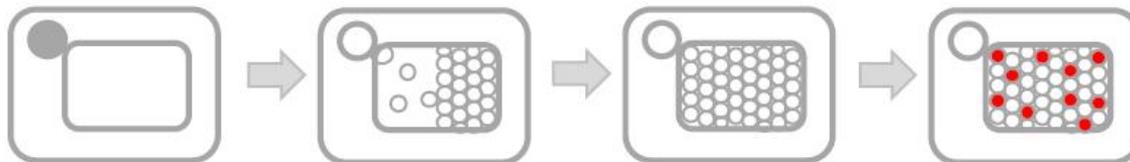
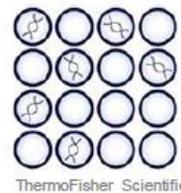
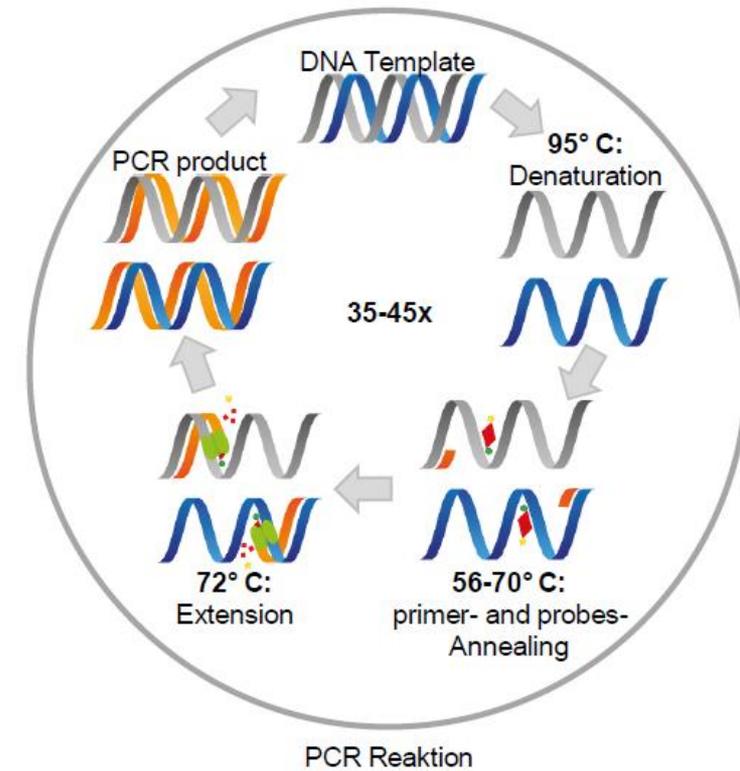
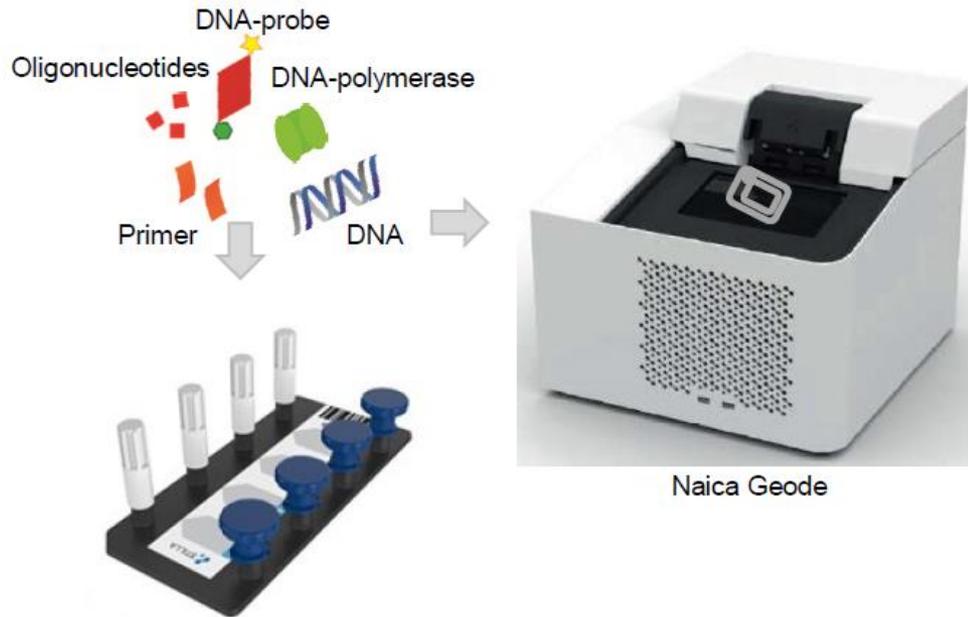
SEPTIMET

*Metrology to enable rapid and accurate
clinical measurements in acute
management of sepsis*

Supporting the diagnostic accuracy of molecular methods for identifying causative agent of sepsis by developing reference measurement procedures

Mojca Milavec, Samreen Falak, **Karin Stettler**, Alexandra
Bogožalec Košir, Kai Stölting, Andreas Kummrov, Denise
O'Sullivan, Jim F. Hugget

dPCR analysis

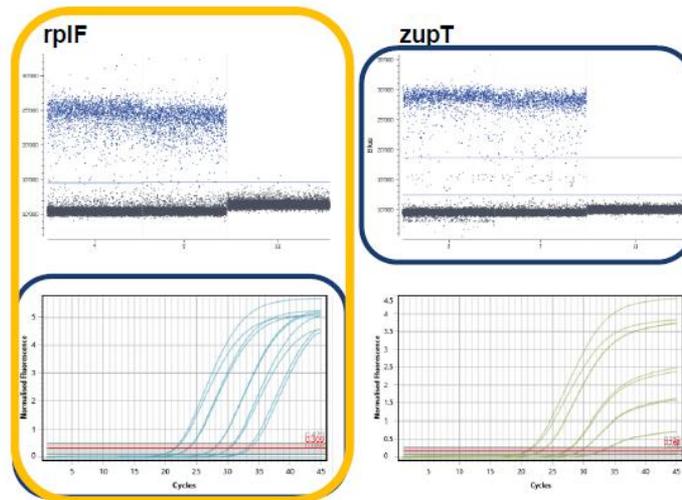


20'000-25'000 partitions

Design of synthetic DNA template

- Synthetic DNA fragment (genscript): 970 bp

PCR sequences of eight loci (870 bp)
 Flanking regions (20 bp)



Summary

		porA (LGC)		metaA (Diene et al., 2026)		rpIF		
	Estimated Dilution concentration (cp/rxn)	Measured concentration (cp/rxn)	Measurement uncertainty (%)	Measured concentration (cp/rxn)	Measurement uncertainty (%)	Measured concentration (cp/rxn)	Measurement uncertainty (%)	
	1	150440	221308	6.4	225504	3.5	218079	6.4
	2	30090	47537	2.3	46175	5.1	44470	4.9
	3	10030	15780	10.5	14480	9.3	14552	8.9
	4	2005	2996	5.5	2928	4.4	2916	5.4
	5	400	664	8.4	619	6.7	573	11.1
	6	135	207	16.1	207	11.3	198	11.0
LOQ	7	45	69	10.4	67	21.8	67	24.9
LOD	8	15	23	29.5	25	48.8	20	41.7
	11	7.5	15	<i>n.a.</i>	12	<i>n.a.</i>	20	<i>n.a.</i>
	9	5	9	<i>n.a.</i>	10	<i>n.a.</i>	9	<i>n.a.</i>
	12	2.5	6	<i>n.a.</i>	0	<i>n.a.</i>	10	<i>n.a.</i>

EURAMET's Research Programme



EURAMET's **European Metrology Networks (EMNs)** are aiming to ensure Europe has a world-leading metrology capability, based on high-quality scientific research and an effective and inclusive infrastructure, that meets the rapidly advancing needs of stakeholders.

EURAMET's research programme **EMPIR** enables the European metrology community and their stakeholders to collaborate on **Joint Network Projects (JNPs)** to support these EMNs in areas such as **health, energy** and the **environment**.

EMPIR follows on from the **EMRP** programme, which has now been successfully completed.



The EMPIR initiative is co-funded by the European Union's Horizon 2020 research and innovation programme and the EMPIR Participating States

See <https://www.euramet.org/> for more details.

EMN Trace Lab Med



13 NMIs/DIs
9 Countries

TRACE LAB MED



EU IVDR (2017/746):
Demand for **metrological Traceability**



International Standards for medical Laboratories:
Demand for **metrological Traceability**



EU citizens: Metrological traceability
for **patient safety & public confidence**



The EMPIR initiative is co-funded by the European Union's Horizon 2020 research and innovation programme and the EMPIR Participating States





Support for EU reference laboratories



Metrological traceability for *in vitro* diagnostics



Service-oriented European metrology infrastructure



Coordinated top-down research



Capacity building & knowledge transfer

Conclusion

- Metrological traceability
- Metrological principles → financially rewarding and substantially decrease measurement uncertainties
- METAS is active in a field of significant (international) developments
- International consortia
- International networks
- Stakeholders – This is for You



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Thank you very much for your attention