Minutes of the NGSP/IFCC Manufacturer Forum

Monday July 28, 2025 3:30—5:00 PM
Fairmont Chicago Millenium Park, Chicago, IL

Presenters:
Curt Rohlfing—NGSP Network Coordinator
David Sacks —Chair, NGSP Steering Committee
Carla Siebelder—IFCC HbA1c Network Coordinator
Emma English—Chair, IFCC C-EUBD

Present were members of the NGSP Steering Committee and representatives from various manufacturers and laboratories.

1. **Welcome and Introduction— David Sacks, Chair, NGSP Steering Committee**
   D. Sacks welcomed those in attendance on behalf of the NGSP and IFCC. He acknowledged the retirement of Randie Little, who co-founded the NGSP and served as the NGSP Network Coordinator since its beginning.

2. **NGSP Update—Curt Rohlfing, NGSP Network Coordinator**
   - The laboratory network consists of the Central Primary Reference Lab (CPRL), which runs the original DCCT HbA1c method, one backup PRL and 10 Secondary Reference Laboratories (SRLs) located in the U.S., the Netherlands, Japan and China.
   - The NGSP has three processes
     - Calibration: Informal process where samples are exchanged to assist manufacturers/labs with calibration of their methods.
     - Certification: Formal process where manufacturer or lab certifies against a SRL and must pass specific criteria.
     - Proficiency testing: CAP whole blood survey shows how well routine laboratories are performing.
   - NGSP network mean between-lab CVs by month were all <1.5% from May 2024 to May 2025.
   - Number of certified methods and laboratories
     - The numbers of certified methods and laboratories have increased over the years; currently there are over 400 certified methods and ~130 certified laboratories.
     - The number of certified methods continues to increase while the number of certified labs has leveled off.
     - Certified laboratories are mostly Level I and outside of the U.S., and are distributed throughout the world.
   - Current Limits for NGSP and CAP
     - Beginning January 2019: NGSP Manufacturer and Level II Lab Certification Criteria: 36/40 results must be within ±5% (37/40 for Level I labs)
     - CAP Accreditation Survey Grading for HbA1c is ±6%
   - There has been much improvement in the comparability of HbA1c results since 1993 when the results of the DCCT were reported. Improvement in between-method variability has been subtle over the past several years.
   - Latest CAP survey (2025 GH5A)
     - Pass Rates (±6%)

Specimen	NGSP Target (% HbA1c)	Acceptable Range (±6%)	Pass rate % (Low/High)	Cumulative Pass Rate % (±6%)
GH-01	9.84	9.2 - 10.5	88.5/100	96.8
GH-02	5.60	5.2 - 6.0	94.5/100	98.8
GH-03	7.97	7.4 - 8.5	92.2/100	98.4
GH-04	8.45	7.9 - 9.0	93.2/100	98.2
GH-05	6.00	5.6 - 6.4	92.3/100	98.1

  - The all-method CVs have shown an overall downward trend since 2000.
  - Method-specific, between-laboratory CVs ranged from 0.4% to 4.0%.
  - Overall, only 60% of laboratories are using methods with CVs ≤2.5% at all five HbA1c levels.
  - All-method CVs for the most recent survey ranged from 2.5-2.8%.
  - Overall Pass rates are between 96.8 and 98.8% for the current 6% accreditation limits.
- Conclusions
  - The NGSP network is still doing well with very low CVs.
  - CAP survey results show that the all-method CVs (including all laboratory & methods' results) have been <3% since the 2020C survey. We would like to see this get to <2.5%.
  - Measurement of HbA1c continues to improve but there are still a few methods with between lab CVs >3%.

3. CAP PT Update—David Sacks, Chair, NGSP Steering Committee

- Proficiency Testing (PT)
  - In US all labs that measure patient samples are required by law to perform PT
  - Regulated by CMS (Centers for Medicare & Medicaid Services) through CLIA
  - CAP is largest provider of PT material in the world
- CAP Grading
  - Initially, CAP used peer group grading for PT for HbA1c
  - Subsequently, introduced whole blood PT, but maintained peer group grading
  - In 2007 changed to accuracy-based grading
  - Target values assigned by NGSP network
  - ±15% acceptable
  - 99% of laboratories passed
- PT Criteria Tightened
  - In 2008 acceptability reduced to 12%
  - 2009 - 10%
  - 2010 - 8%
  - 2011 - 7%
  - 2014 - 6%
- Proposed CAP PT Criterion 2020: ±5%
- Pass Rates for CAP 2020 GH5-C: ±6% vs. ±5%

Sample ID	Target (%)	±6%	±5%
GH-11	5.5	97.9	**95.2**
GH-12	8.3	97.7	**95.4**
GH-13	5.1	97.6	**97.6**
GH-14	10.1	96.9	**95.1**
GH-15	6.0	97.6	**96.6**

- CLIA Proposed PT Rule 2019 (CLIA 88 update)

- Hemoglobin HbA1c would become a regulated analyte
- Criterion for acceptable performance: Target ±10%

- Implications of New CLIA Proposal
  - HbA1c would become, for the first time, a regulated analyte
  - CAP is not permitted to fail a lab if it meets CLIA criteria
  - If CLIA accepts ±10%, CAP will have to loosen acceptability from ±6% to ±10%
- Response to CMS 2019 Proposal
  - Multiple organizations (clinical and lab) and individuals sent comments to CMS
  - Almost all the 107 comments received by CMS protested loosening HbA1c criteria
  - Delegation from ADA went to speak to CMS
  - An editorial was published in 2019 in a clinical diabetes journal criticizing the proposal (Klonoff et. al, J Diabetes Sci Technol 2019 May;13(3):424-427).
- CMS Response
  - Not persuaded by comments
  - Acknowledge improvement in accuracy
  - Concerned that "tighter criteria will limit access to testing…"
- Final CLIA Rule
  - Acceptance limits for HbA1c are 8%
  - Effective January 1, 2025
- CAP Conundrum
  - CAP has 2 separate programs
    - PT
    - Accreditation
  - Grading of regulated analytes by PT providers must follow rules in Federal Register
  - Accrediting agency can require better accuracy for lab to remain accredited, but PT provider must grade HbA1c at 8%
  - Formal grading will have to change to 8%
- CAP PT 2025: CAP has three HbA1c PT surveys
  - GH5 Accuracy-based: Main survey, >2500 labs (5 samples, 3X/year)
  - GH2 Accuracy-based: Waived assays, ~400 labs (3 samples, 2X/year)
  - GH5I Not accuracy-based: >425 labs, lyophilized material, mainly international labs (5 samples, 3X/year). Provided due to logistical issues with international shipping.
- CAP Solution—2 sets of criteria (dual grading)
  - Labs not using accuracy-based PT OR not accredited by CAP graded by +/- 8%
  - Labs using accuracy-based PT and accredited by CAP are graded by +/- 6%
  - Reports sent to participating labs show pass/fail for both criteria
- GH5-A 2025 Overall Pass Rate

Specimen	NGSP Target (% HbA1c)	Acceptable Range (+/- 8%)	Cumulative Pass Rate % for 8%	Acceptable Range (+/- 6%)	Cumulative Pass Rate % for 6%
GH-01	9.84	9.0 - 10.7	98.8	9.2 - 10.5	96.8
GH-02	5.60	5.1 - 6.1	99.4	5.2 - 6.0	98.8
GH-03	7.97	7.3 - 8.7	99.2	7.4 - 8.5	98.4
GH-04	8.45	7.7 - 9.2	99.1	7.9 - 9.0	98.2
GH-05	6.00	5.5 - 6.5	99.0	5.6 - 6.4	98.1

- Summary
  - Acceptable performance for HbA1c PT in USA changed to 8%
  - Change effective January 1st, 2025
  - Labs accredited by CAP that use accuracy-based PT will have to meet 6% criterion

Discussion:

D. Sacks noted that he was surprised that CAP did not receive any calls from laboratories concerning the survey changes.

4. Update: IFCC HbA1c Network—Carla Siebelder

- IFCC Roadmap and Optimum Performance HbA1c
  - IFCC Working Group
    - Reference Method
    - Global Network
    - Services Manufacturers
  - IFCC Task Force: Model Quality Targets
  - IFCC C-EUBD: Monitoring Quality
- Reference Method
  - National "Standardisation' Iinititives
    - Sweden: Mono-S
    - Japan: JDS/JSCC (KO500)
    - US: NGSP (Bio-Rex 70 HPLC)
    - Arbitrarily chosen
    - Different results!!
    - Not specific
    - Traceability required EUR law
  - To come to worldwide standardisation and worldwide comparability of HbA1c results. the IFCC WG developed a scientific sound Reference Measurement System within the concept of Metrological Traceability
  - Approved in 2001(published 2002), progress report was published in Clin Chem in 2008.
  - IFCC Reference Method x National Initiatives
    - Master equations established between IFCC RM and National Initiatives
    - Although significant differences in results, linear and reproducible relationship
    - We can transfer all old clinical studies to IFCC RM
    - Published in 2004: (NGSP=0.0915xIFCC) +2.15
- Global network of reference laboratories remains in place and continues to perform well. Currently there are 15 approved laboratories and one candidate laboratory.
- Services to Manufacturers
  - Calibrators to achieve Traceability
  - Controls to check Traceability
  - Certification Programme to prove Traceability
  - Variant Samples (FDA Approval)
  - Value Assignment Specimens
  - Monitoring Master Equation IFCC – NGSP
  - Calibrators: Specifications
    - Eight level frozen whole blood panel
    - Units provided: HbA1c: IFCC (mmol/mol) and NGSP (%) Units, mmol/L, g/dL
    - Total Hb: mmol/L, g/dL
  - Controls: Specifications
    - Low, medium and high levels
    - Medium provided with low, medium and high hemoglobin concentrations
  - Sustainability of calibrators: CBS test (Commutability, Batch-to-batch variability, Stability)
    - 6 methods calibrated with the respective calibrator batches of the last 4 yrs
    - The mean as measured in 10 fresh whole blood patient samples is reported
    - Results across (C) and within (B/S) methods are identical demonstrating sustainability
  - Certification Programme
    - 24 samples
    - Certificate is provided showing how the method performed compared to quality targets.
    - There are 4 levels of acceptable method performance: Gold, silver, bronze, standard (minimum).
    - TAE of 5 mmol/mol
    - In 2024, the number of manufacturer methods that fell into each category were:

a. Gold: 0 (0%)
b. Silver: 100 (41%)
c. Bronze: 98 (40%)
d. Standard: 43 (18%)
e. IFCC criteria not met: 2 (1%)
f. Lab Instruments:

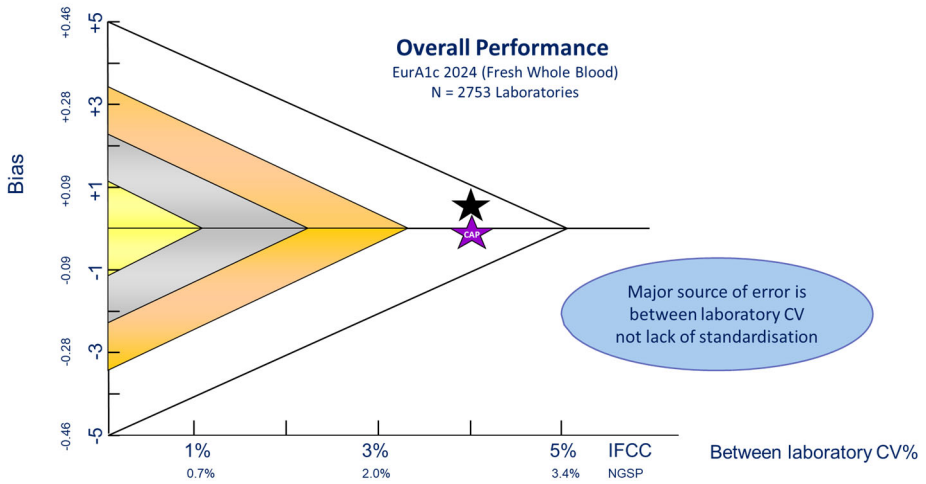
	Lab Instr %	POCT %
Ion-exchange HPLC	28	0
Immuno Assay	13	31
Affinity	1	14
Cap Electroph	1	<1
Enzymatic	9	2

- Variant samples: Collection of AS, AE, AC, AD samples in stock along with limited quantities of A2, elevated HbF and rare variants.
- Monitoring Master Equation IFCC – NGSP
  - Master Equation: NGSP = 0.0915 x IFCC + 2.15
  - The ME is monitored over time and has been shown to be stable over time since 2004

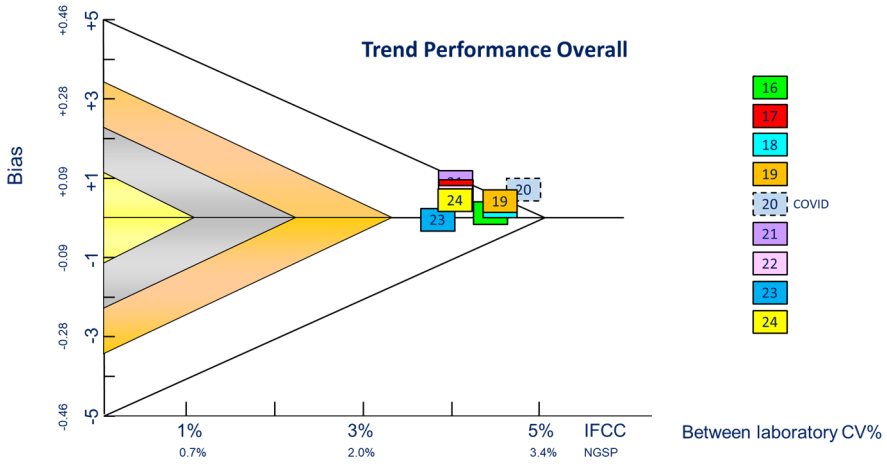
- IFCC Model Quality Targets
  - A small error has high impact on interpretation
  - Quality test is important
  - How good is good enough?
  - IFCC Task Force, published in 2015 (Clin Chem. 2015 May;61(5):752-9).
  - Concept of TE
    - 2 sources: Bias & Imprecision
    - Criterion: TEa 5 mmol/mol Risk 2 σ
  - Certificate shows the bias and imprecision (CV%) compared to targets
  - Impact of bias (Clinica Chimica Acta 548 (2023), 117495 https://doi.org/10.1016/j.cca.2023.117495)
    - Bias has a more significant impact (on the risk of misinterpretation) than imprecision when using HbA1c for diagnosis of diabetes.
    - It is suggested that the IFCC MQT is revised
    - Being considered by the IFCC C-EUBD
- Monitoring Quality— EurA1c: A Project of the IFCC C-EUBD and EQA/PT organisers
  - Ultimate check performance in the field
  - International Cooperation: Once a year EQA Organisers use the same 2 samples
  - Data are combined to get a global overview of the performance of HbA1c
  - EurA1c samples
    - Fresh Whole Blood
      a. Advantage: commutable and suitable all methods
      b. Disadvantage: limited stability
    - Lyophilised Hemolysate
      a. Advantage: stable
      b. Disadvantage: not commutable for all methods; note suitable for some POC instruments
    - Choice: National EQA organisers: logistics in the country
  - Number of Laboratories

Year	Total	Fresh Whole Blood	Lyophilised Hemolysate
2016	2166	1517	649
2017	2647	1809	838
2018	3980	2875	1105
2019	4575	3038	1537
2020	5120	3286	1834
2021	4077	2524	1553
2022	4325	2788	1537
2023	4082	2546	1536
2024	4284	2753	1531

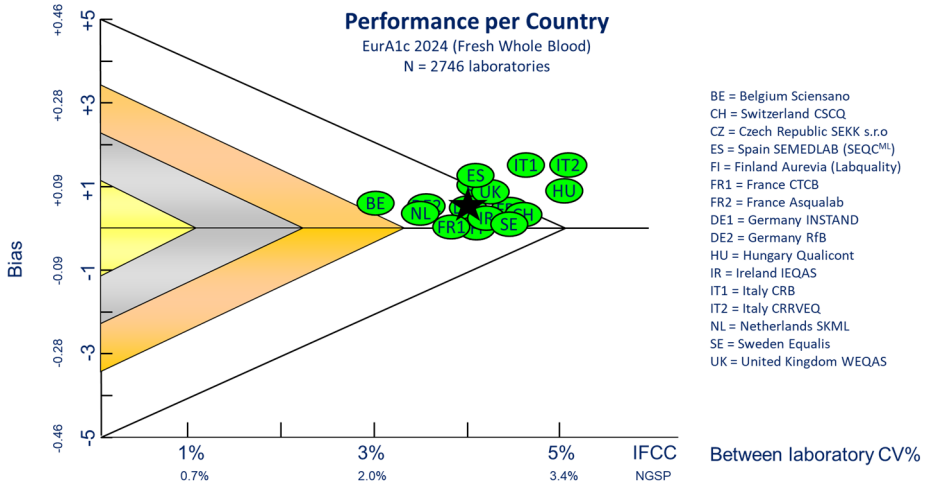
- First survey performed in 2016 (published 2018)
- Review paper (20116-2024) in progress
- 2024 report will be available end of September on the www.ifcchba1c.org
- EurA1c 2024: 9th Trial, 23 countries - 27 EQA (5 of the countries from outside of Europe: Mexico, South Africa, South Korea, Vietnam, Thailand)
- Evaluation of results: QT Model applicable for multiple use.
  - Performance of a single lab (within-lab CV)
  - Group of labs/manufacturer (between-lab CV)
  - Country (between-lab CV)
- EurA1c 2024 Results (preliminary)
  - Overall Performance



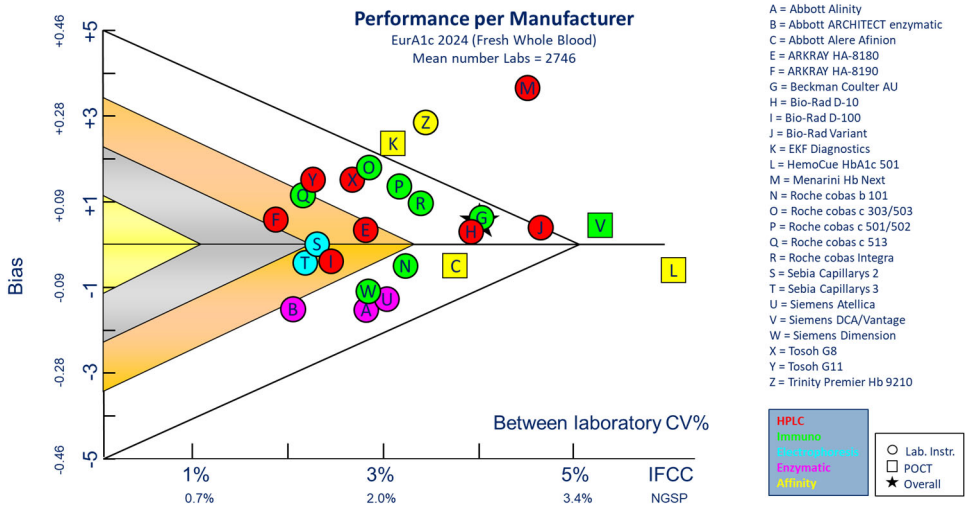
  - Trend performance overall



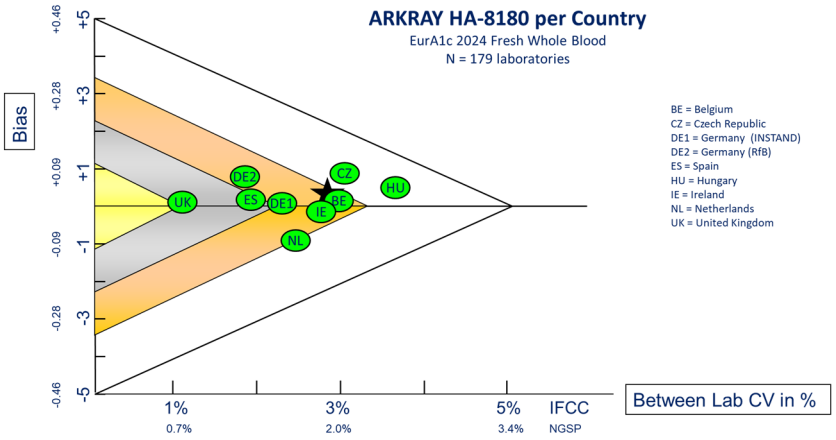
- Performance Per Country

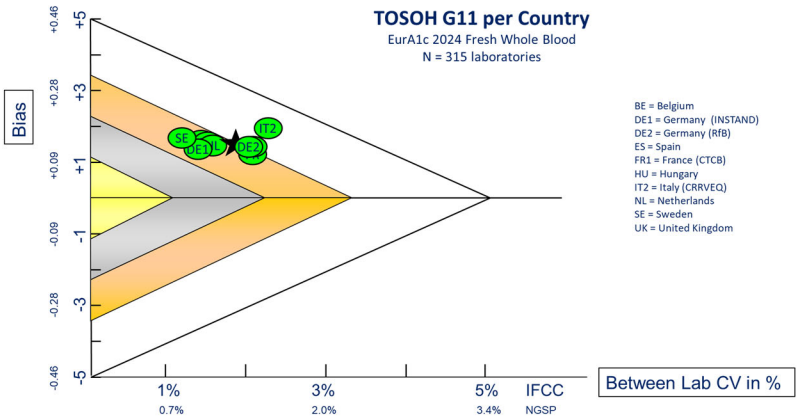


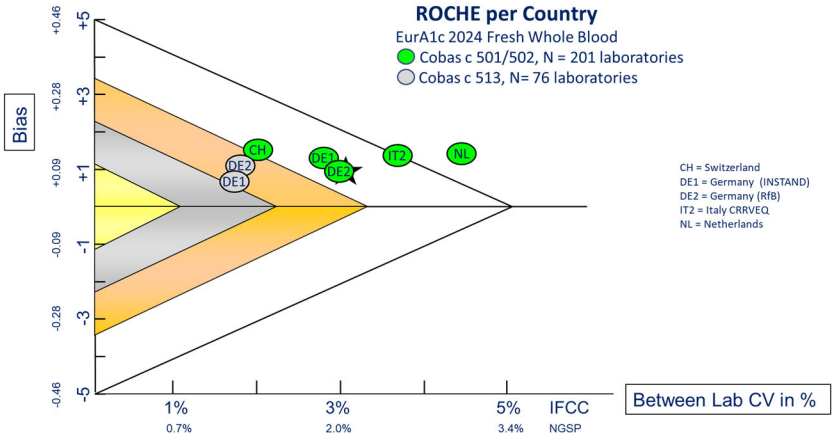
- Performance per Manufacturer

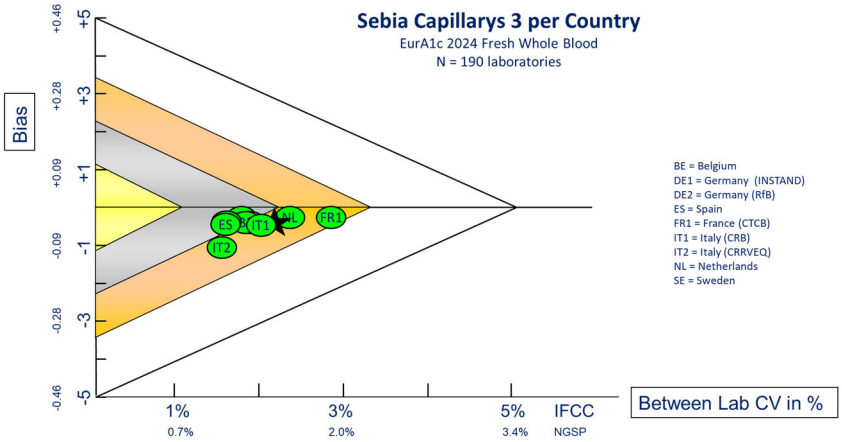


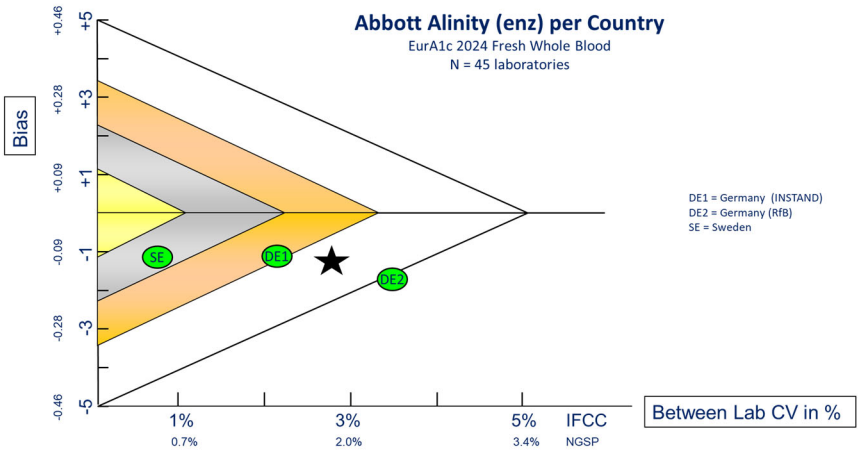
- Performance per Manufacturer per Country

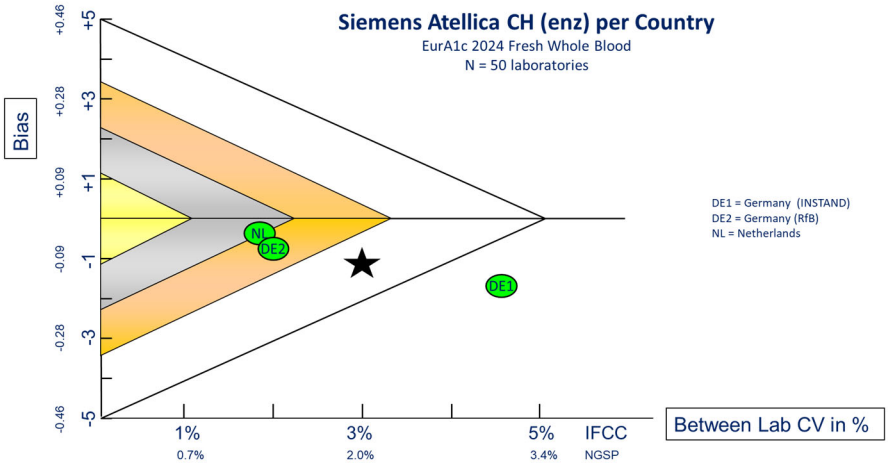


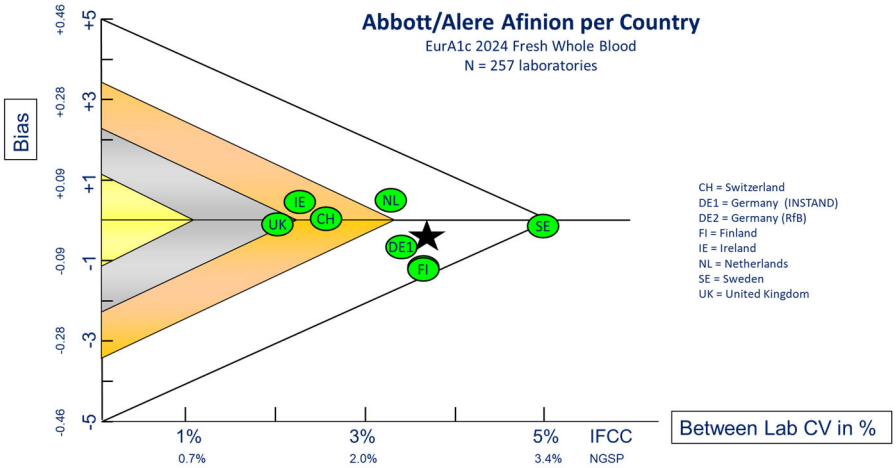

TOSOH G11 per Country
EurA1c 2024 Fresh Whole Blood
N = 315 laboratories
Bias
+0.46
+0.28
+0.09
-0.09
-0.28
-0.46
+5
+3
+1
-1
-3
-5
SE
DE1
NL
DE2
IT2
BE = Belgium
DE1 = Germany (INSTAND)
DE2 = Germany (RfB)
ES = Spain
FR1 = France (CTCB)
HU = Hungary
IT2 = Italy (CRRVEQ)
NL = Netherlands
SE = Sweden
UK = United Kingdom
1%
0.7%
3%
2.0%
5%
3.4%
IFCC
NGSP
Between Lab CV in %

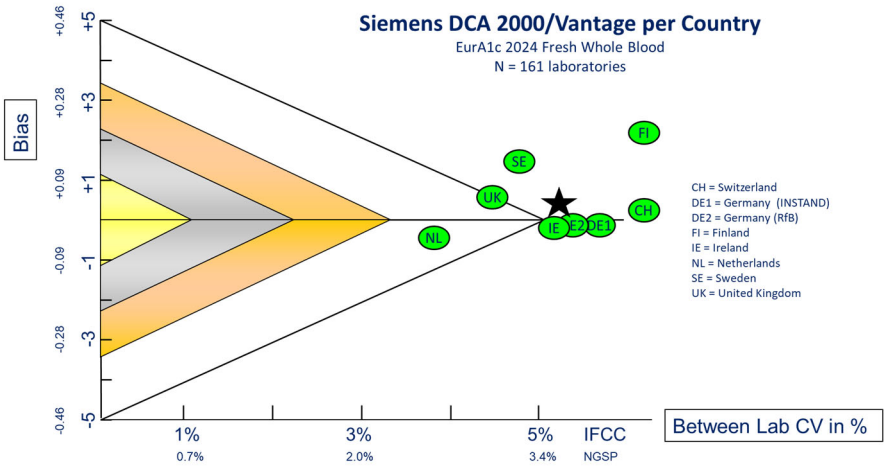

ROCHE per Country
EurA1c 2024 Fresh Whole Blood
Cobas c 501/502, N = 201 laboratories
Cobas c 513, N= 76 laboratories
Bias
+0.46
+0.28
+0.09
-0.09
-0.28
-0.46
+5
+3
+1
-1
-3
-5
CH
DE2
DE1
DE1
DE2
IT2
NL
CH = Switzerland
DE1 = Germany (INSTAND)
DE2 = Germany (RfB)
IT2 = Italy CRRVEQ
NL = Netherlands
1%
0.7%
3%
2.0%
5%
3.4%
IFCC
NGSP
Between Lab CV in %


Sebia Capillarys 3 per Country
EurA1c 2024 Fresh Whole Blood
N = 190 laboratories
Bias
+0.46
+0.28
+0.09
-0.09
-0.28
-0.46
+5
+3
+1
-1
-3
-5
ES
IT1
NL
FR1
IT2
BE = Belgium
DE1 = Germany (INSTAND)
DE2 = Germany (RfB)
ES = Spain
FR1 = France (CTCB)
IT1 = Italy (CRB)
IT2 = Italy (CRRVEQ)
NL = Netherlands
SE = Sweden
1%
0.7%
3%
2.0%
5%
3.4%
IFCC
NGSP
Between Lab CV in %


Abbott Alinity (enz) per Country
EurA1c 2024 Fresh Whole Blood
N = 45 laboratories
Bias
+0.46
+0.28
+0.09
-0.09
-0.28
-0.46
+5
+3
+1
-1
-3
-5
SE
DE1
DE2
DE1 = Germany (INSTAND)
DE2 = Germany (RfB)
SE = Sweden
1%
0.7%
3%
2.0%
5%
3.4%
IFCC
NGSP
Between Lab CV in %


Siemens Atellica CH (enz) per Country
EurA1c 2024 Fresh Whole Blood
N = 50 laboratories
Bias
+0.46
+0.28
+0.09
-0.09
-0.28
-0.46
+5
+3
+1
-1
-3
-5
NL
DE2
DE1
DE1 = Germany (INSTAND)
DE2 = Germany (RfB)
NL = Netherlands
1%
0.7%
3%
2.0%
5%
3.4%
IFCC
NGSP
Between Lab CV in %


Abbott/Alere Afinion per Country
EurA1c 2024 Fresh Whole Blood
N = 257 laboratories
Bias
+0.46
+0.28
+0.09
-0.09
-0.28
-0.46
+5
+3
+1
-1
-3
-5
IE
NL
UK
CH
SE
DE1
FI
CH = Switzerland
DE1 = Germany (INSTAND)
DE2 = Germany (RfB)
FI = Finland
IE = Ireland
NL = Netherlands
SE = Sweden
UK = United Kingdom
1%
0.7%
3%
2.0%
5%
3.4%
IFCC
NGSP
Between Lab CV in %



- EurA1c: Lot of information about the performance of many HbA1c tests
  - Pressure to improve the quality
  - Optimum Performance of HbA1c

Discussion:

None of the manufacturer methods, even the most precise ones, achieved the gold level in the certification program.
C. Siebelder acknowledged this, stating that gold is extremely difficult to achieve, especially given that 24 samples covering a range of HbA1c values are included.

Are there criteria for lot-to-lot variation?
C. Siebelder said lot-to-lot variations are the responsibility of the manufacturers.

There were a large number of labs that dropped their participation in EurA1c during Covid and did not come back, did they close or just chose not to participate?
C. Siebelder said it is difficult to know. Logistics were especially difficult during Covid, because of this one QA organizer chose not to participate any more. It is possible that some labs chose not to as well.

5. IFCC EUBD Update—Emma English

- Who are the IFCC – EUBD?
  - Chair—Emma English
  - Full members – J. Skrha, E. Kilpatrick, K.Lee, L. Kunz
  - Consultant members – D. Sacks, E. Lenters-Westra, C. Siebelder, A. Zemlin
  - Corresponding members – 16 members nominated by national associations
  - Corresponding members – 7 members nominated by corporate organisations
- Continue to have oversight of IFCC HbA1c Standardisation Network--This is facilitated through the partnerships between the C-EUBD, C-TLM and the network meetings.
- WHO Pre-qualification of Medical Products
  - The aim of WHO prequalification of in vitro diagnostics (IVDs) is to promote and facilitate access to safe, appropriate and affordable in vitro diagnostics of good quality in an equitable manner. The focus is on IVDs for priority diseases that are appropriate for use in resource-limited settings.
  - Steps to achieve pre-qualification: WHO IVD prequalification incorporates comprehensive assessment of individual IVDs through a standardized procedure, to determine whether the product meets WHO prequalification requirements. Assessment has three components:
    - Review of a product dossier
    - Laboratory evaluation of performance and operational characteristics
    - Manufacturing site(s) inspection

- Following prequalification post-market surveillance is undertaken
- Review of the product dossier: Publications:
  - TSS-18: Haemoglobin A1c point of care analyzers for professional use
  - TSS-19: In-vitro diagnostic medical devices for monitoring of blood glucose in capillary blood
- The independent evaluation
  - The aim of the performance evaluation is to independently verify the manufacturer's claim regarding product performance. In addition, if UN procurement criteria have been established, performance evaluation enables it to be determined whether these criteria have been met.
  - Manufacturers can choose between organization of performance evaluation coordinated and financed by WHO (option 1), or performance evaluation coordinated and paid for by themselves (option 2). But whichever option is chosen, the evaluation must be performed by a WHO prequalification laboratory according to the appropriate standardized evaluation protocol for the corresponding type of assay.
- However
  - The need to undertake a prequalification independent evaluation also follows risk-based principles.
  - In this context and as part of a broader effort to streamline assessment processes **WHO has taken the executive decision to waive prequalification performance evaluations for in vitro diagnostic medical devices for monitoring of blood glucose in capillary blood and HbA1c point-of-care assays.**
  - For such products the prequalification assessment will include the review of a product dossier, a site inspection and labelling review.
- Why am I still talking about this?
  - Joint study between FIND Dx and European Reference Laboratory
  - Evaluation of 19 different POCT IVDs for HbA1c
  - CLSI based protocols
  - Protocols mirror those of the proposed independent evaluation and protocols required for evidence dossier
  - Most devices purchased independently for the study
  - Data now published in Clin Chem (Clin Chem 71:7; 775-788 (2005)). Key findings
    a. Only 5 out of 19 devices managed to meet the IFCC and NGSP criteria with at least one SRL
    b. A further 5 only met IFCC certification criteria
    c. Some CVs were found to be as high as 15%
    d. Some devices suffered from interference from Hb variants, some could not be assessed

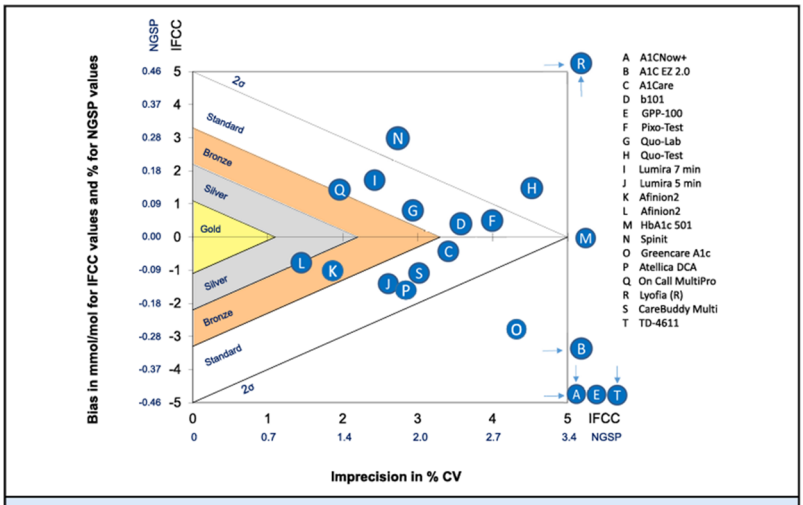


Fig. 1. Analytical performance at ±6.5% (48 mmol/mol) in sigma metrics of 20 Hb A_{1c} POCT instruments using EP-15-A3 and EP-9-A3 data. The devices are labeled A-T, with the Afinion 2 showing in duplicate. Color figure available at https://academic.oup.com/clinchem.

- Glycated albumin
  - Standardisation and analytical performance
  - As a clinical tool
  - Further develop our understanding of the analytical and clinical utility of glycated albumin (GA) measurement Task A: Lenters-Westra et al. Limitations of glycated albumin standardization when applied to the assessment of diabetes patients. Clin Chem Lab Med 2024 Jun 17. doi: 10.1515/cclm-2024-0591.
- Task B – create an educational output around the use of Glucose Management Indicator and HbA1c: Lenters-Westra et al. Managing discordance between HbA1c and glucose management indicator. Diabet Med 2025 Jun;42(6):e70023. doi: 10.1111/dme.70023. Epub 2025 Mar 23.
- What next?
  - EurA1c trial data will be published this year
  - Using this and other real world data we will review the current IFCC targets for performance
  - It is very likely that these targets will be tightened – the degree of change will be determined by the data sources available
- What do you need to do?
  - Keep moving forward with quality improvement processes
  - Keep an open dialogue with the IFCC we want to hear from you
- Thank you—please get in touch: emma.english@ice.cam.ac.uk

Discussion:

E. English noted that corporate organizations that would like to participate but are not currently represented on the EUBD can contact the IFCC if they wish to participate.

D. Sacks thanked everyone present for their attendance; the meeting was adjourned at 5:05 PM.

Minutes prepared by C. Rohlfing 10/16/2025.