



INTERNATIONAL COUNCIL FOR
STANDARDIZATION IN HAEMATOLOGY



UNIVERSITY OF
BIRMINGHAM

Overview and update of ICSH activities in haematology standardization

**JCTLM meeting, Paris
2nd December 2019**

**Dr. Paul Harrison, University of Birmingham
ICSH Board Member & JCTLM representative**

What is the ICSH?

<https://icsh.org/>

- The International Council for Standardization in Haematology (ICSH) was initiated as a standardization committee by the European Society of Haematology (ESH) in 1963 and officially constituted by the International Society of Hematology (ISH) and the ESH in Stockholm in 1964.
- The ICSH is recognised as a Non-Governmental Organisation with official relations to the World Health Organisation (WHO).
- The ICSH is a not-for-profit organisation that aims to achieve reliable and reproducible results in laboratory analysis in the field of diagnostic haematology.
- The ICSH coordinates Working Groups of experts to examine laboratory methods and instruments for haematological analyses, to deliberate on issues of standardization and to stimulate and coordinate scientific work as necessary towards the development of international standardization materials and guidelines.
- The ICSH has published 25 Publications and guidelines since reforming in 2007 – seven more in draft form



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Current ICSH Management Board

Chair	Samuel J. Machin	UK	Chair
Vice-Chair	Szu-Hee Lee	Australia	Website & Haematology
Vice-Chair	Steve Kitchen	UK	Haemostasis Chair
Scientific Secretary	Gina Zini	Italy	Haematology
Treasurer	Alexander Kratz	USA	Finances & Haematology
Member	Paul Harrison	UK	Platelets and Flow cytometry
Member	Wendy Erber	Australia	Haematology & Molecular
Member	Kees Hartevelt	Netherlands	Haemoglobinopathies
Member	Bob Gosselin	USA	Haemostasis
Member	Richard McCafferty	Ireland	Haematology
Administrator	Terry Fawcett	Australia	Administration

ICSH General Assembly Meetings

- 2007 – Amsterdam Netherlands
- 2008 – Sydney Australia
- 2009 – Rome Italy
- 2010 – Bangor USA
- 2011 – Montpellier France
- 2012 – Chicago USA
- 2013 – Gerrards Cross UK
- 2014 – San Francisco USA
- 2015 – Shenzhen China
- 2016 – Lucerne Switzerland
- 2017 – Kobe Japan
- 2018 – Miami USA
- 2019 – Lund Sweden
- 2020 - Singapore



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AFFILIATE ORGANIZATIONS

NCCL CHINA
SCCL CHINA

UK NEQAS
International Quality Expertise



IEQAS
Irish External Quality Assessment Scheme



HSANZ NZ BRANCH



SEQC^{ML}
Sociedad Española de Medicina de Laboratorio



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Corporate Members



[Ventana](#)

ICSH Recent Publications (2016 - 2019)

<http://icsh.org/archives/>

ICSH GUIDELINES & RECOMMENDATIONS

2019 - Digital morphology analyzers in Hematology Review: ICSH review and recommendations

Kratz A, Lee SH, Zini G, Reidl J, Hur M, Machin S Int J Lab Hematol. 2019;1–11.

<https://onlinelibrary.wiley.com/doi/epdf/10.1111/ijlh.13042>

2018 - Laboratory Measurement of Direct Oral Anticoagulants (DOACS)

Gosselin RC, Adcock DM, Bates SM, Douxfils J, Favaloro EJ, Gouin-Thibault I, Guillermo C, Kawai Y, Lindhoff-Last E, Kitchen S. International Council for Standardization in Haematology (ICSH) Recommendations for Laboratory Measurement of Direct Oral Anticoagulants. Thromb Haemost. 2018 Mar;118(3):437-450

<https://www.thieme-connect.com/products/ejournals/pdf/10.1055/s-0038-1627480.pdf>

2017 – ESR Methods Guideline

Kratz A, Plebani M, Peng M, Lee YK, McCafferty R, Machin SJ and on behalf of the International Council for Standardization in Haematology (ICSH). ICSH recommendations for modified and alternate methods measuring the erythrocyte sedimentation rate. Int J Lab Hematol. 2017 Oct;39(5):448-57.

<http://onlinelibrary.wiley.com/doi/10.1111/ijlh.12693/full>

2016 - Haematology Reporting

Brereton M, McCafferty R, Marsden K, Kawai Y, Etzell J, Ermens A; International council for standardization in haematology. Recommendation for standardization of haematology reporting units used in the extended blood count. Int J Lab Hematol. 2016 Oct;38(5):472-82.

<http://onlinelibrary.wiley.com/doi/10.1111/ijlh.12563/full>

ICSH List of Current Haematology Projects

Project	Project Lead	Status	Completion
JCTLM Traceability	Dr Paul Harrison	Ongoing	Ongoing
Immunoplatelet - JCTLM	Dr Paul Harrison	Ongoing	Ongoing
Digital Morphology	Dr Alexander Kratz	Paper accepted	May 2019
Immunodifferential	Dr Brent Wood	Multi-centre trial	September 2019
Internal QC for analyzers	Mr Richard McCafferty	First Draft done	September 2019
MPV Standardization	Dr Paul Harrison	Retesting new material	May 2020
IRF Standardization	Dr Amrom Obstfeld	Retesting new material	May 2020
CD34 IHC Standardization	Dr Emina Torlakovic	First draft	September 2019
HbA2 Standard	Dr Kees Hartveld	In conjunction with IFCC	Uncertain
HbA Standard	Mr. Terry Fawcett	Need to retest old Eurotrol standard	December 2019
WCC Standardization by flow cytometry**	Mr. Vuong Nguyen	Evaluation of candidate methods	September 2019
WHO Liaison	Dr Gina Zini	Ongoing	Ongoing

ICSH List of Current Haemostasis Projects

Project	Project Lead	Status	Completion
Preanalytical Variables Guideline	Dr Steve Kitchen	Draft near completion	December 2109
FVIII/FIX Inhibitors Guideline	Dr Piet Meijer	Draft near completion	December 2019
Mixing Studies Guideline	Dr Dot Adcock	Draft near completion	December 2019
POC Guideline	Dr Dave Fitzmaurice	Draft near completion	May 2020
ADAMST13 guideline	Dr Ian Mackie	Draft near completion	September 2019
DOACS guideline update	Mr Bob Gosselin	Draft near completion	January 2020
Critical Results in Haemostasis	Mr Bob Gosselin	Just published	September 2019
Coagulation Analyzers Evaluation Guideline	Dr Chris Gardiner	Project has started	October 2020
Coagulation Reagents Evaluation Guideline	Mr Bob Gosselin	Project approved	October 2020

ICSH and JCTLM (Joint Committee for Traceability in Laboratory Medicine)



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Accurate results
for patient care

- Important Collaboration
- Very few Laboratory Haematology entries in JCTLM Database
- Both organizations have identified the need to collaborate

JCTLM & ICSH History

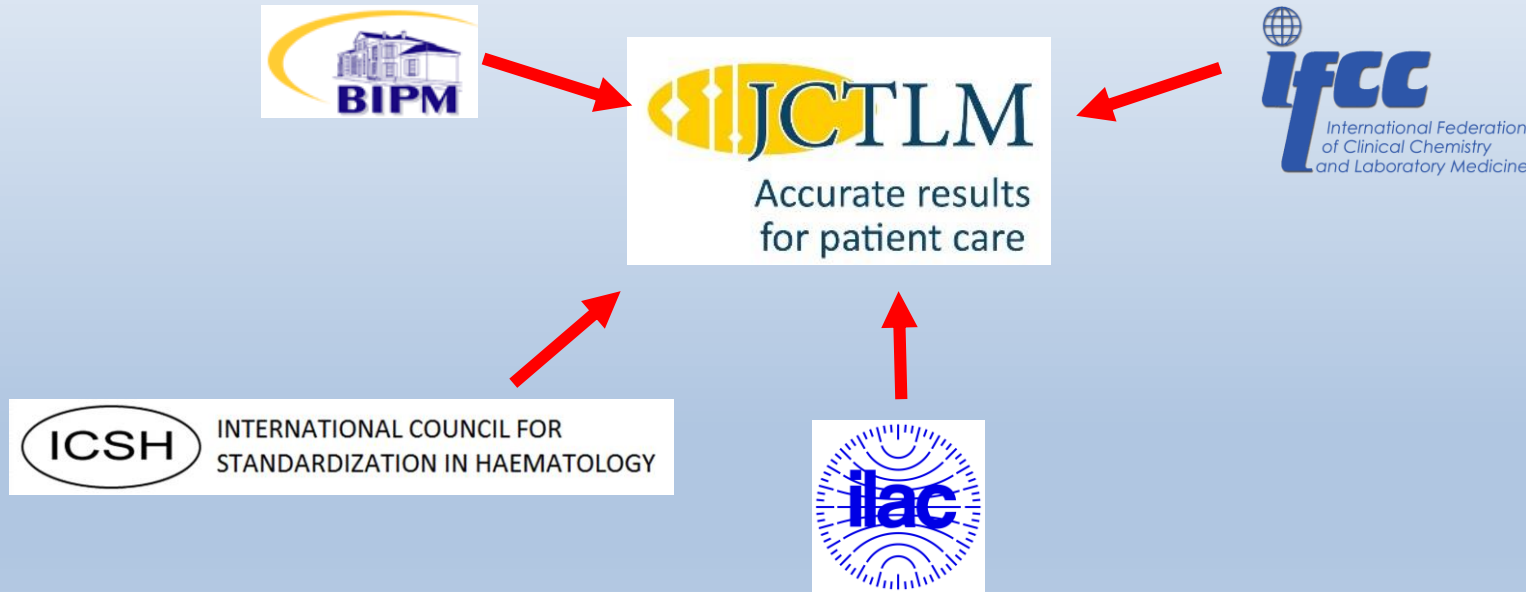
- Expand JCTLM Executive Member organizations to include other disciplines in laboratory medicine
- Outreach to ICSH as peer Lab Haem organization
 - Reps from JCTLM and ICSH met 22 June 2015 @ EuroMedLab Paris
 - Sam Machin gave a Webex presentation @ 2015 JCTLM Members & Stakeholders Meeting
 - Graham Beastall attended ICSH General Assembly, 26 October 2016 Lucerne
 - Bruce Davis & George Cembrowski attended 2017 JCTLM Members & Stakeholders Meeting, BIPM
 - JCTLM and ICSH convened a meeting 14-15 May 2018, BIPM
 - Gary Myers attended 2018 ICSH General Assembly, Miami USA
 - ICSH Submitted Reference Method for Platelet Counting in 2018
 - ICSH accepted as Executive Member in January 2019
 - Ian Young attended 2019 ICSH General Assembly, Lund, Sweden
 - Dr Paul Harrison, UK, appointed ICSH Board Member liaising with JCTLM



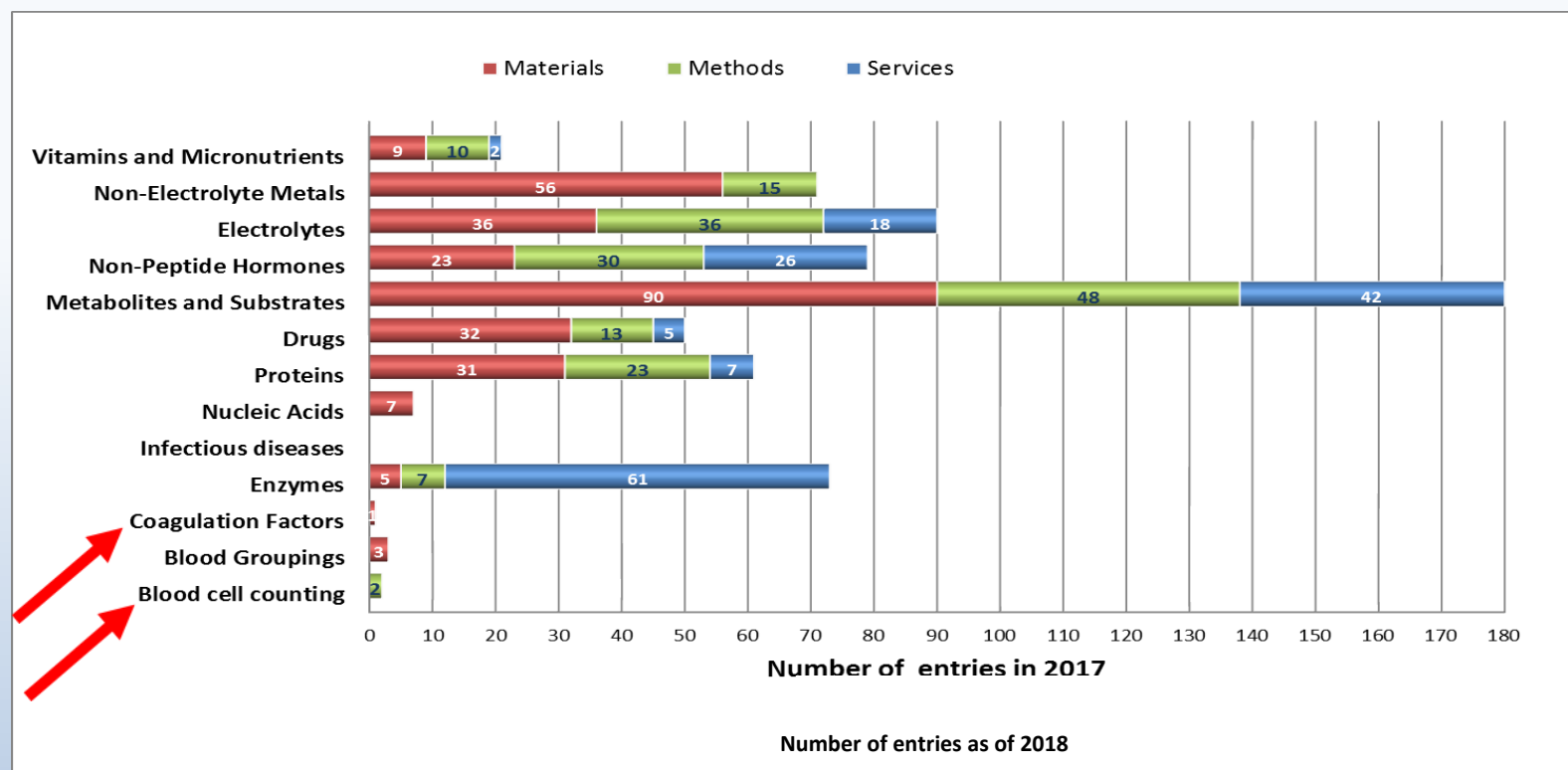
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JCTLM Structure - 2019

In 2019, the Joint Committee for Traceability in Laboratory Medicine accepted ICSH as an executive member of JCTLM. ICSH will assist with Haematology and Haemostasis traceability. This will encompass the sciences of metrology, laboratory medicine and laboratory quality management to help the IVD industry meet traceability requirements of the EC IVD Directive



JCTLM Database: Entries as of March 2018



26 measurands with complete reference systems
293 Certified Reference Materials
184 RMPs that represent 83 different measurands
in 9 categories
161 reference measurement services delivered by
17 reference labs

**NOTE – VERY SMALL NUMBER OF BLOOD CELL COUNTING AND HAEMOSTASIS
ENTRIES – HENCE NEED FOR ICSH LIAISON WITH JCTLM**

Immuno-platelet counting

ICSH/ISLH (Late 1990's) - proposed that the immunocount derived from the platelet:RBC ratio should become the new reference method

- Requirements of Platelet:RBC ratio method

- Optimal resolution of platelets from noise and other cells

- Antibody must specifically recognise all platelets

- Elimination of Coincidence events (platelet:RBC or RBC:RBC) by optimisation of dilution

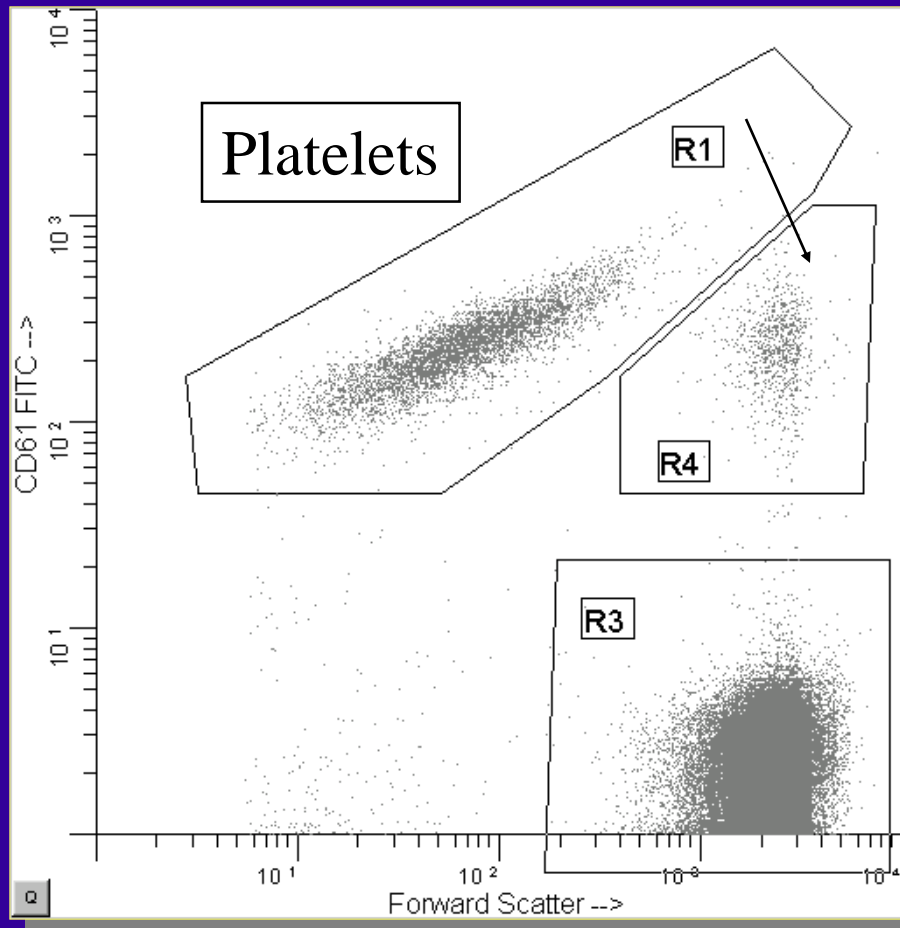
- Sufficient platelets must be counted for accuracy

- Main Advantage

- Independent of pipetting and dilution artefacts

PLATELET/RBC RATIO

For full method see Harrison et al, 2001, AJCP, 115, 448-59
& ICSH/ISLH, 2001, AJCP, 115, 460-4



Plt/RBC Coincidence

RBC

INTERNATIONAL STANDARD

ISO
15193

Second edition
2009-05-01

***In vitro* diagnostic medical devices — Measurement of quantities in samples of biological origin — Requirements for content and presentation of reference measurement procedures**

*Dispositifs médicaux de diagnostic in vitro — Mesurage des grandeurs
dans des échantillons d'origine biologique — Exigences relatives au
contenu et à la présentation des procédures de mesure de référence*

Reference measurement procedures for the accurate determination of cell concentrations: present status and future developments

Referenzmessverfahren für die genaue Bestimmung von Zellkonzentrationen: Status und zukünftige Entwicklungen

Martin Kammel, Andreas Kummrow
and Jörg Neukammer*

Physikalisch-Technische Bundesanstalt, Braunschweig
and Berlin, Germany

Abstract

Accurate determination of cell concentrations serves as a valuable tool to support medical diagnosis and therapy control, e.g., in haematology, immunology and transfusion medicine. Intra- and inter-laboratory comparability of measurement results is essential for patient safety. To derive the so-called “conventional quantity value” of a measurand as target value for intra- or inter-laboratory quality assurance and to establish a traceability chain to the international System of Units (SI), a primary reference measurement procedure is needed, defined as a procedure which includes a complete analysis of influence quantities and perturbing factors and a complete description of measurement uncertainties. We describe a primary reference measurement procedure for the determination of erythrocyte concentration, based on flow cytometric cell counting by impedance measurements. To correct for instrument- and sample-dependent counting loss due to random coincidences, dilution series are prepared. The reference quantity value of the cell concentration is derived by extrapolation to vanishing volume fraction of the sample in the measurement suspension. Typically, for erythrocyte and leucocyte concentrations respective uncertainties of approximately 0.75% and 2% are reached. Future developments concern the extension of the procedures validated for erythrocyte and leucocyte counting by including immunological staining and microscopic techniques.

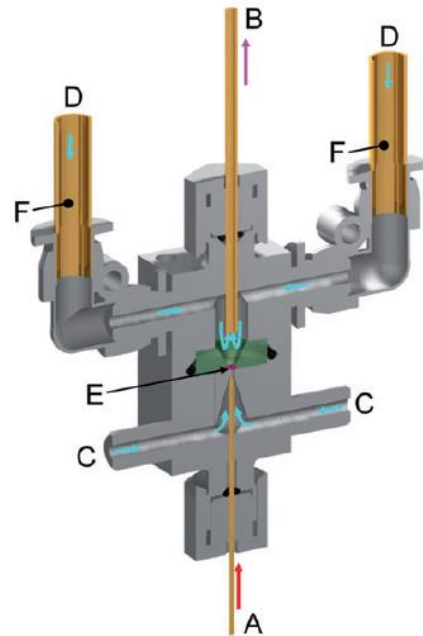


Figure 1 Schematic view of the measuring cell for impedance counting used in the PTB reference particle counter. (A) Sample inlet, (B) outlet to waste container, (C) front sheath flow, (D) rear sheath flow, (E) measuring orifice (\varnothing 40 μ m or 60 μ m), (F) electrodes.

List of reference measurement methods/procedures

This file was created on 27 April 2018 from the JCTLM-DB website (<https://www.bipm.org/jctlm/>)

Your search criteria: Reference measurement methods/procedures; Analyte: thrombocyte; Analyte category: -; Matrix category: -

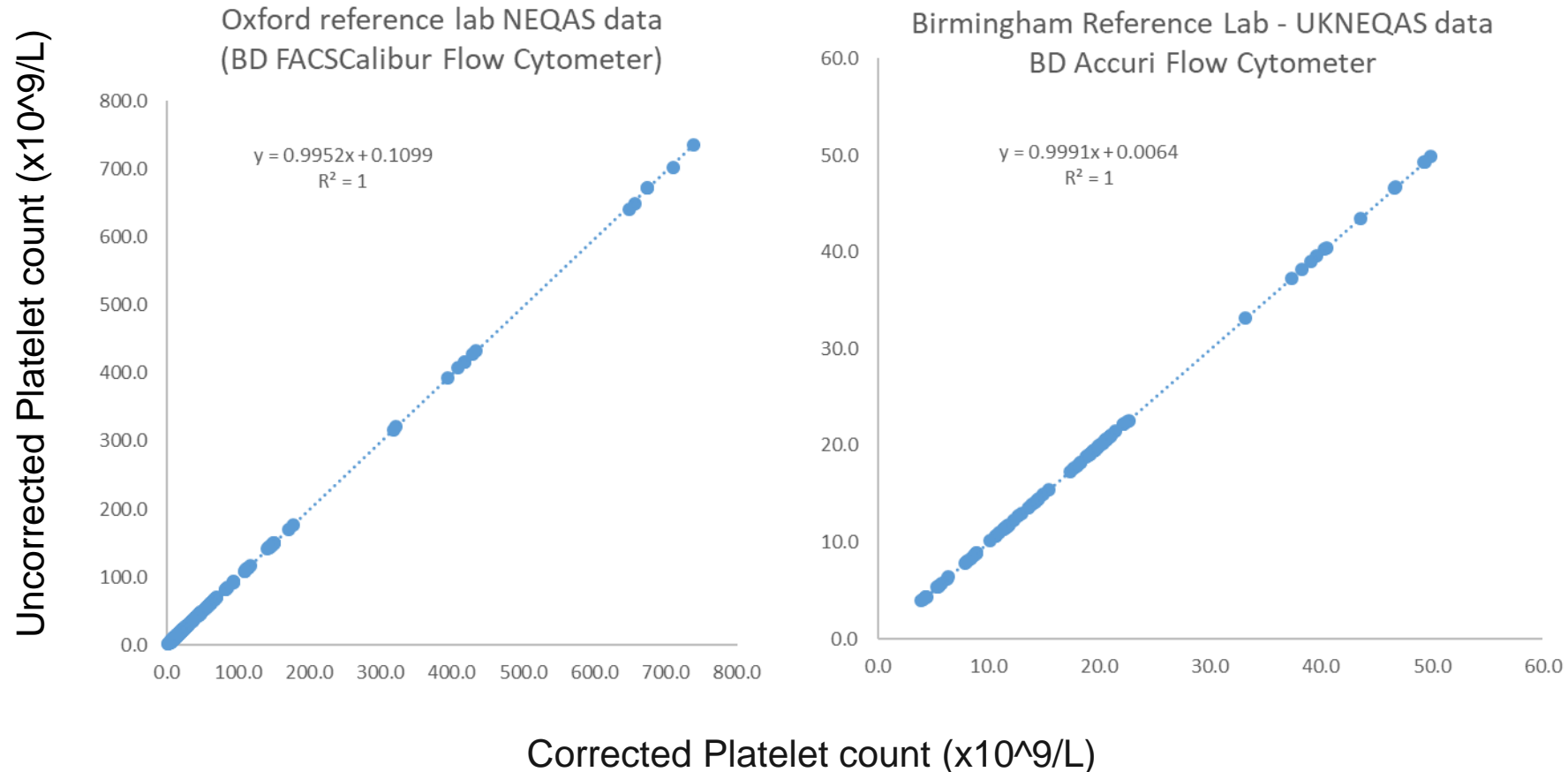
Flow cytometry methods for thrombocyte in whole blood	
▸ PTB reference method for blood cell counting	
Applicable matrice(s)	fresh whole blood
Full description of technique(s)	Flow cytometry, cell differentiation by fluorescence detection of antibody stained platelets and light scattering, coincidence correction by dilution series
Quantity	Particle concentration
Applicable range	30 nl ⁻¹ to 1500 nl ⁻¹
Expected uncertainty (level of confidence 95%)	10 % relative
Reference(s)	J. Lab. Med., 2012, 36(1), 25-35 German National Standard DIN 58932-5
Comment(s)	Validation of the reference method described in DIN 58932-5 is presently accomplished. Procedures used to derive the thrombocyte concentration by determining the platelet / erythrocyte ratio (<i>Am. J. Clin. Pathol.</i> , 2001, 115, 480-484 and references therein) are not suited as primary reference procedure, since coincidence correction has not been proved to yield correct results for particle subpopulations exhibiting dramatically different concentrations (e.g. 10 platelets / nl compared to 4000 erythrocytes / nl)
JCTLM DB identification number	C3RMMP32
▸ PTB reference method for blood cell counting (for lower particle concentration)	
Applicable matrice(s)	fresh whole blood
Full description of technique(s)	Flow cytometry, cell differentiation by fluorescence detection of antibody stained platelets and light scattering, coincidence correction by dilution series
Quantity	Particle concentration
Applicable range	0 nl ⁻¹ to 30 nl ⁻¹
Expected uncertainty (level of confidence 95%)	3 nl ⁻¹
Reference(s)	J. Lab. Med., 2012, 36(1), 25-35 German National Standard DIN 58932-5
Comment(s)	Validation of the reference method described in DIN 58932-5 is presently accomplished. Procedures used to derive the thrombocyte concentration by determining the platelet / erythrocyte ratio (<i>Am. J. Clin. Pathol.</i> , 2001, 115, 480-484 and references therein) are not suited as primary reference procedure, since coincidence correction has not been proved to yield correct results for particle subpopulations exhibiting dramatically different concentrations (e.g. 10 platelets / nl compared to 4000 erythrocytes / nl)
JCTLM DB identification number	C3RMMP34

UKNEQAS PH Reference Lab Data (2001 – 2019)

With and Without Coincidence Correction at 1:1000 final dilution

N = 480 (160 in triplicate)
Platelet counts 1.4 – 738 x 10⁹/L
RBC counts 1.83-5.75 x 10¹²/L

N = 90 (30 in triplicate)
Platelet counts 4 – 50 x 10⁹/L
RBC counts 2.04-3.98 x 10¹²/L



ICSH Platelet Counting Reference Method – Ongoing work

- **Reference Method papers sent to JCTLM for feedback/approval?**
- **Update ICSH method to be compliant with new ISO standard and after JCTLM feedback**
- **Attend JCTLM meeting in Paris in December**
- **Possible comparison with the PTB method?**

ICSH & JCTLM – In Summary

- Traceability in laboratory medicine is a requirement of the IVD Regulation
- JCTLM has been established to provide global support to IVD manufacturers and regulators on traceability in lab medicine
- Currently there are very few haematology entries in the JCTLM database
- ICSH is the organization producing standards and guidelines in Laboratory Haematology
- ICSH and JCTLM are collaborating on Haematology Projects
- ICSH has been accepted as an Executive Member of JCTLM
- Dr Paul Harrison is the ICSH Liaison Officer to JCTLM



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