JCTLM Database Report

2 December 2019

R.I. Wielgosz (BIPM)

S. Maniguet (BIPM)

Bureau International des Poids et Mesures

Overview: JCTLM Database Activities in 2019

Drivers for a Database

Nomination/Review/Approval Process

Update on database content

Review process Changes

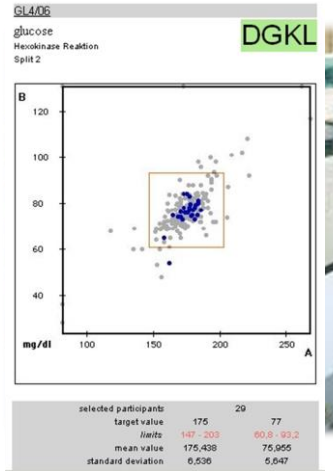
External Communication

Visits

JCTLM
Accurate results for patient care

Accurate Results for Patient Care:
Metrological Traceability in Laboratory Medicine

Physician requesting laboratory test



Medical Laboratory (Hospital)

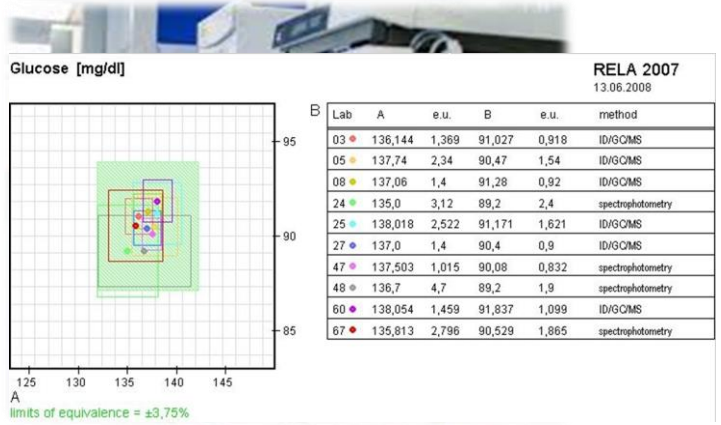
ISO 15189

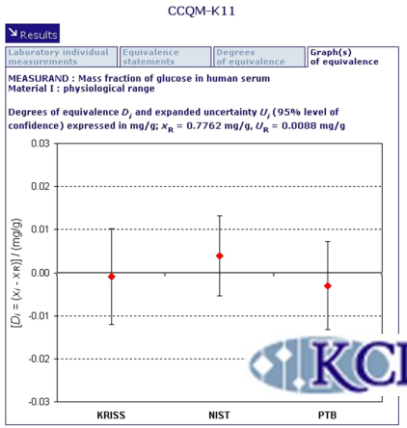
ISO 17511

IVD Manufacturers

Calibration (Reference) Laboratory

ISO 17025
ISO 15195
ISO 15193





ISO 15194

National Metrology Institutes
Certified Reference Materials

An important driver:
Essential Requirements of the IVD Directive

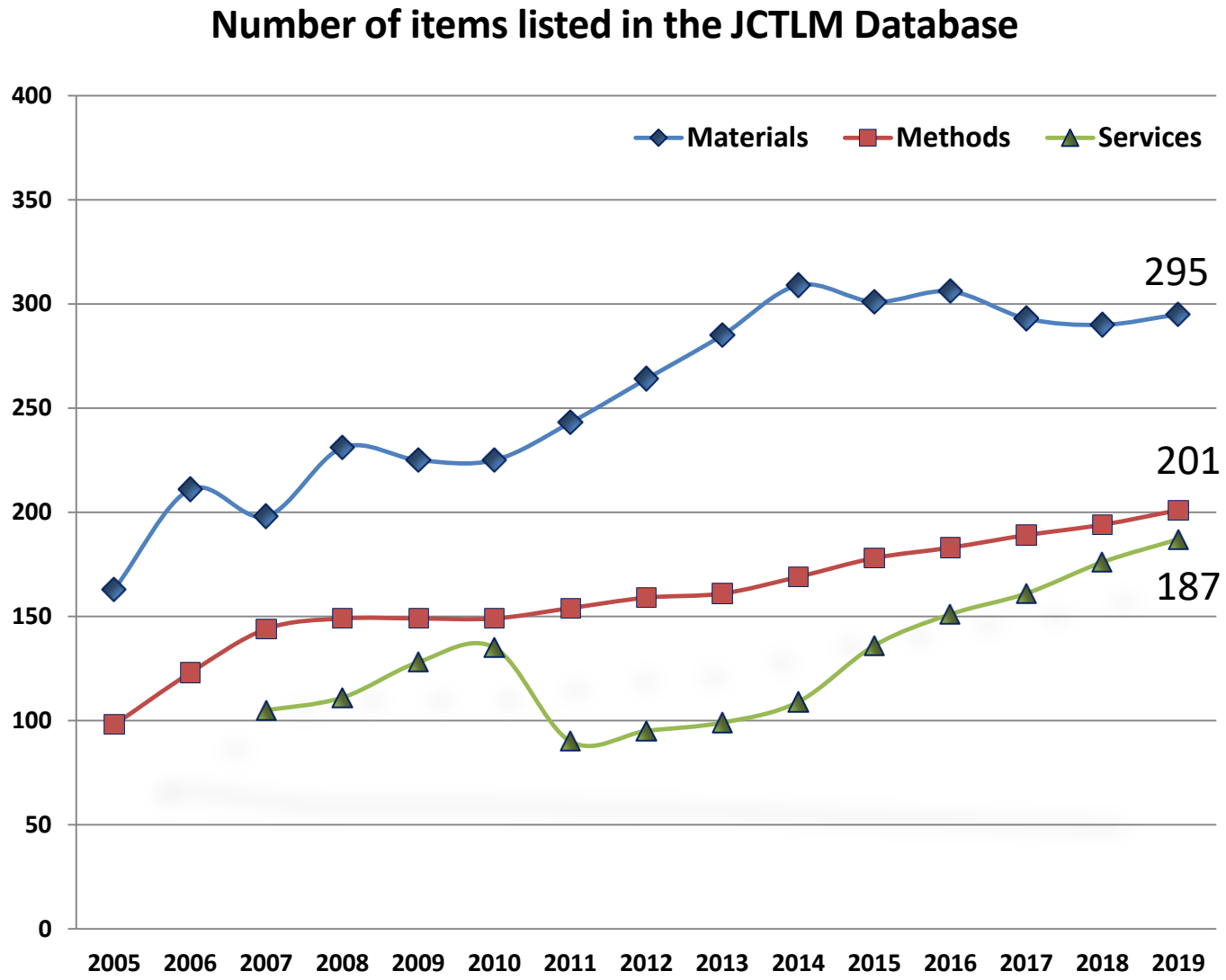
98/79/EC of 27 October 1998 on in vitro diagnostic medical devices

"The traceability of values assigned to calibrators and/or control materials must be assured through available reference measurement procedures and/or available reference materials of a higher order.. "

Annex I - Essential Requirements
Part A. General Requirements, Clause 3

2019 JCTLM Database Content

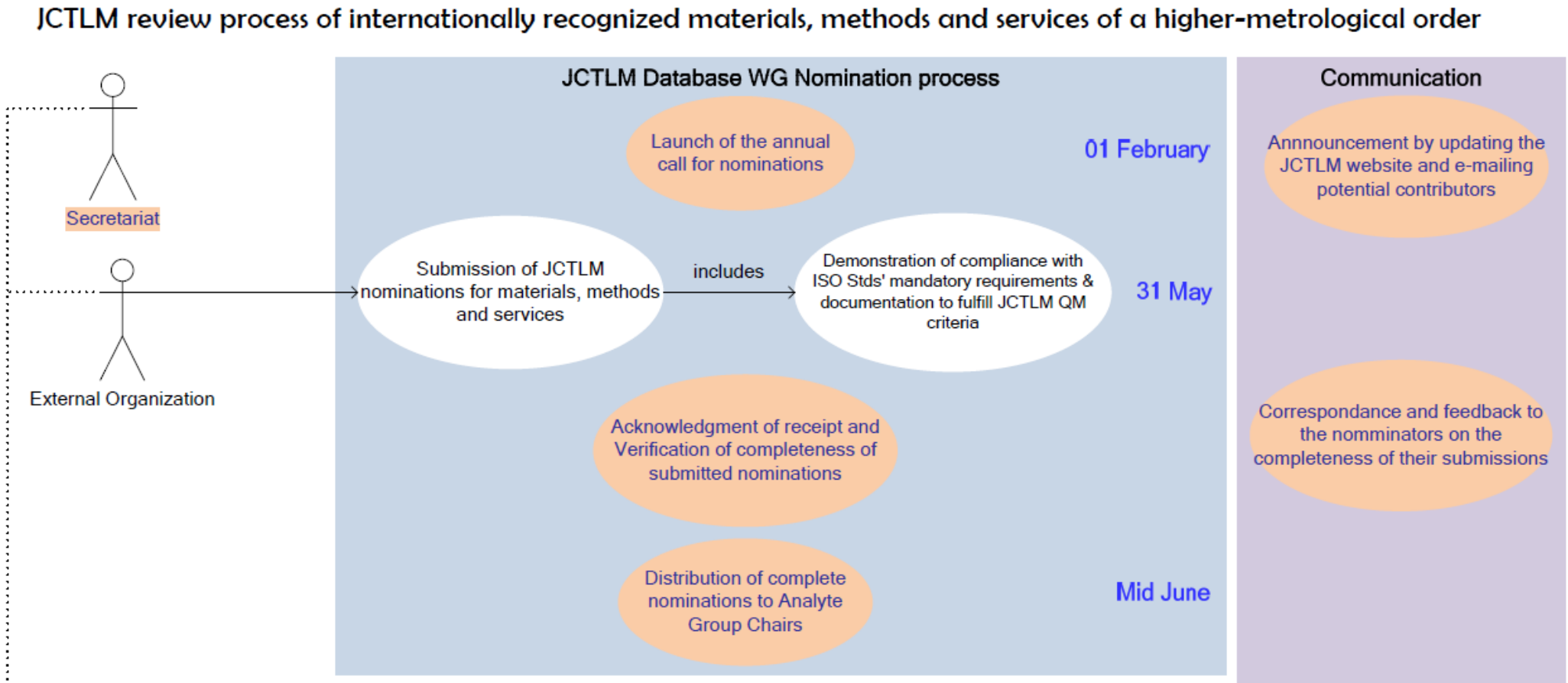
JCTLM
Accurate results for patient care



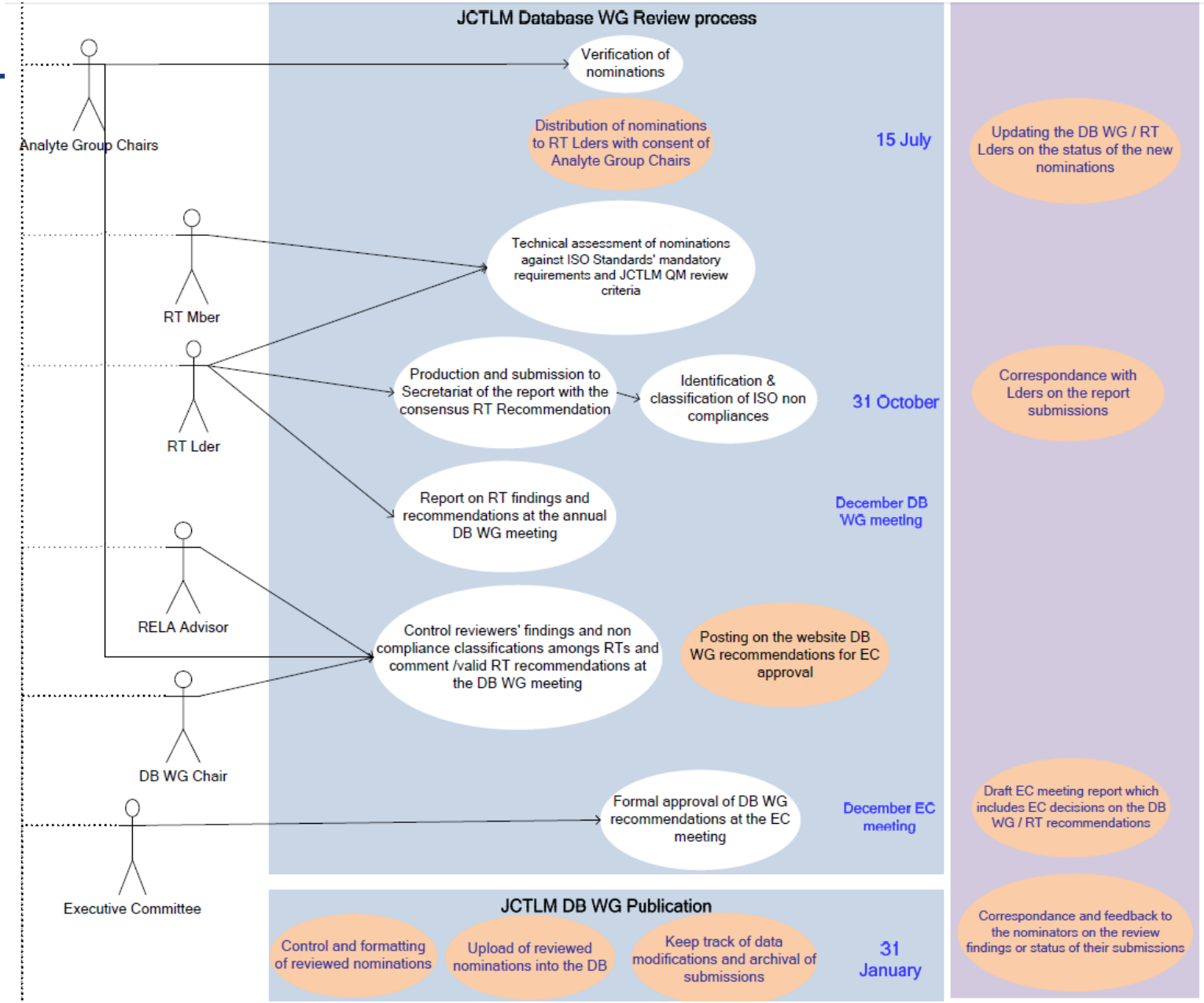
683 entries for 150 analytes

JCTLM Review process

JCTLM
Accurate results
for patient care



JCTLM Review process



BIPM activities in support of JCTLM

Activities:

- BIPM provides the Secretariat for JCTLM
- Maintains the **JCTLM IVD Reference Measurement Systems Database**
  - **JCTLM Database Coordinator: S. Maniguet (BIPM)**
- Coordinates the nomination and review process for database entries
- Organizes and hosts annual meetings of the JCTLM Executive, Database and TEP WGs
- Organizes and hosts biennial Stakeholder meeting at the BIPM

Supported Financially by: BIPM and IFCC

Expert Participation in JCTLM

- Experts can participate in JCTLM Review Teams

Proteins Review Team

Mission | Team Members | Procedures | Working area | JCTLM Review Teams | JCTLM

Leader:

- Dr Milena Quaglia (LGC)

Members:

- Dr Chris Burns [National Institute for Biological Standards and Control, NIBSC]
- Prof. Baorong Chen [Medicine Laboratory of Kingmed Diagonostics]
- Dr Tomoya Kinumi [NMIJ/AIST]
- Dr Mark Lowenthal [NIST]
- Prof. Mauro Panteghini [Univeristy of Milan]
- Dr Alexander Semenov [HyTest Ltd.]
- Dr Dewei Song [NIM]
- Dr Claudia Swart [PTB]
- Dr Toshiyuki Yamada [Jichi Medical University; Japan Society of Clinical Chemistry]
- Dr Katsuhiko Yamamoto [Fujirebio Inc]
- Dr Jessica Yu [Beckman Coulter]

See also:

- Procedure: Application, nomination and approval for membership of JCTLM DBWG Review Teams (DBWG-P-06)
- DBWG Review Team membership application/nomination form

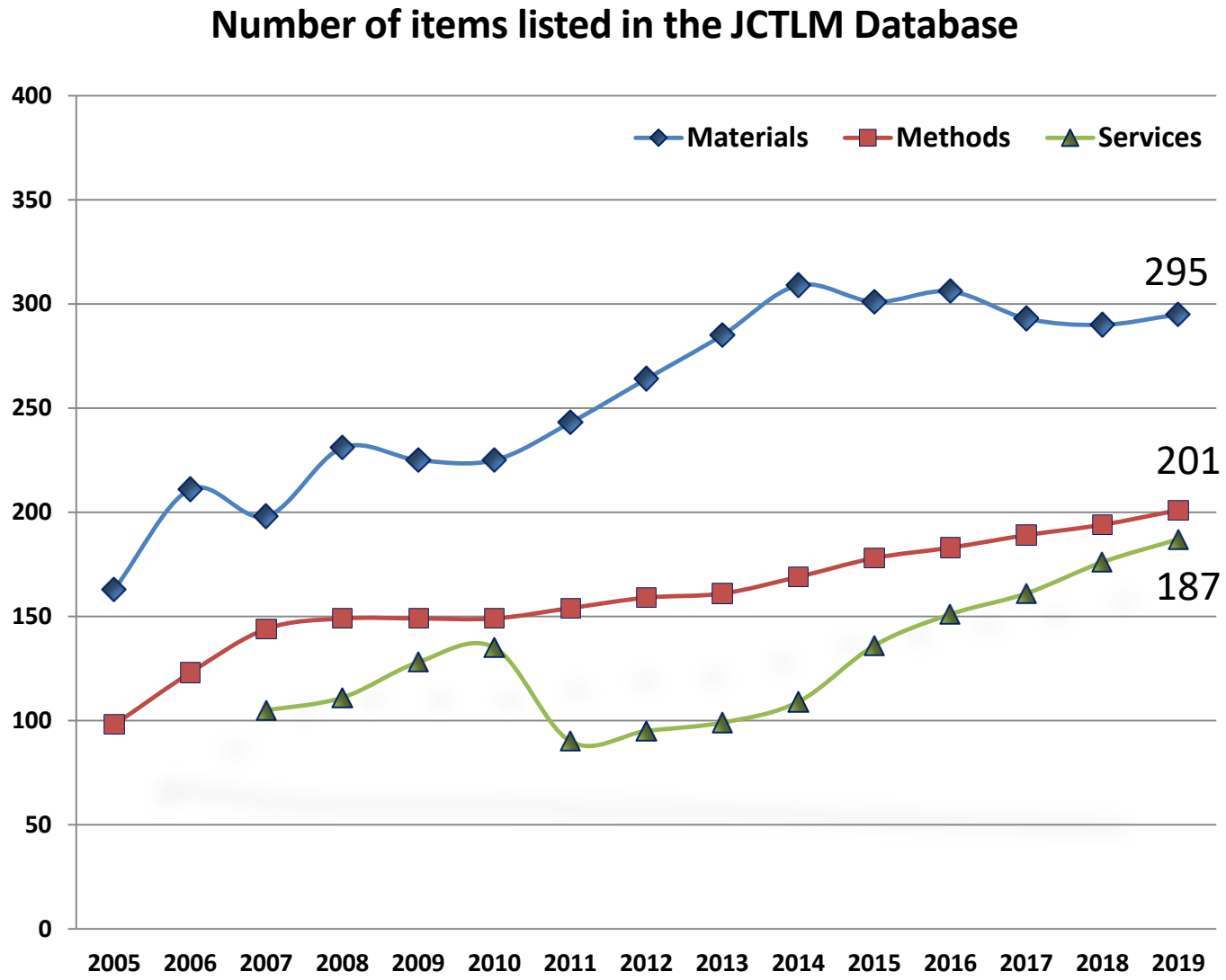
JCTLM RT Membership
15 New Appointments in 2019

JCTLM
Accurate results for patient care

Dr. Alison Devonshire (LGC) – Nucleic Acids
Mr. Wayne Dimech (NRL, Australia) – Nucleic Acids
Dr. Young-Kyung Bae (KRISS) – Nucleic Acids
Dr. Tomoya Kinumi (NMIJ AIST, Japan) – Proteins
Dr Alexander Semenov (HyTest Ltd, Finland) - Proteins
Dr Dewei Song (NIM, China) - Proteins
Dr. Mark Lowenthal (NIST) – Proteins
Prof. Chen Baorong (Kingmed Diagonostics , China) – Enzymes, Meta & Subst , Non-Peptide Hormones and Proteins
Prof. Xianzhang Huang (Guangdong Provincial Hospital of Chinese Medicine) – Meta & Subs,Non-peptide Hormones
Dr Tianjiao Zhang (NCCL, China) – Metabolites & Substrates, Non Peptide Hormones, and Vitamins
Dr Joanne Adaway (Manchester University NHS Foundation Trust) – Metabolites & Substrates
Dr Marie Christine Bene (University of Nantes, France) – Blood cell counting
Dr. Jeannine Holden (Beckman Coulter Diagnostics & Beckman Coulter Life Sciences) – Blood cell counting
Dr. Virginia Litwin (Caprion Biosciences, Inc) – Blood cell counting
Dr. Yutaka Nagai (Nihon Kohden Corp) – Blood cell counting
Mr. Joffrey Feriel (Diagnostica Stago) – Blood cell counting

2019 JCTLM Database Content

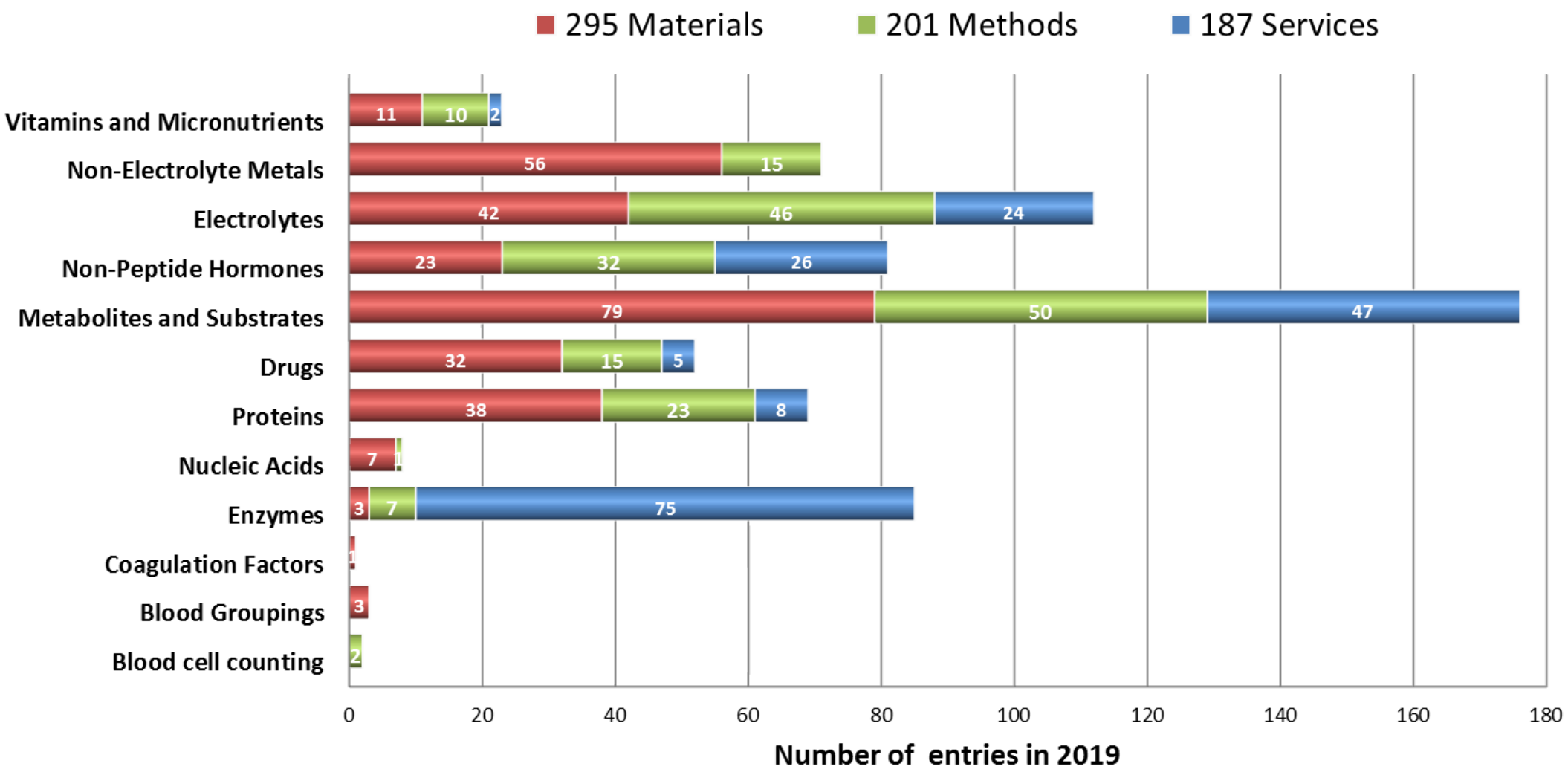
JCTLM
Accurate results for patient care



683 entries for 150 analytes

JCTLM Database
Content status in 2019

JCTLM
Accurate results for patient care



2019 JCTLM Database Publication

JCTLM
Accurate results for patient care

New materials listed (12 CRMs)

- **JRC (EU)** Amyloid beta peptide (1-42) in liquid frozen human CSF
- **LNE (FR)** HbA1c in lyophilized human blood hemolysates
- **NCCL (CN)** Glycated Hemoglobin in Human Hemolysate buffer
- **NIM (CN)** Electrolytes (6) in Frozen Human Serum

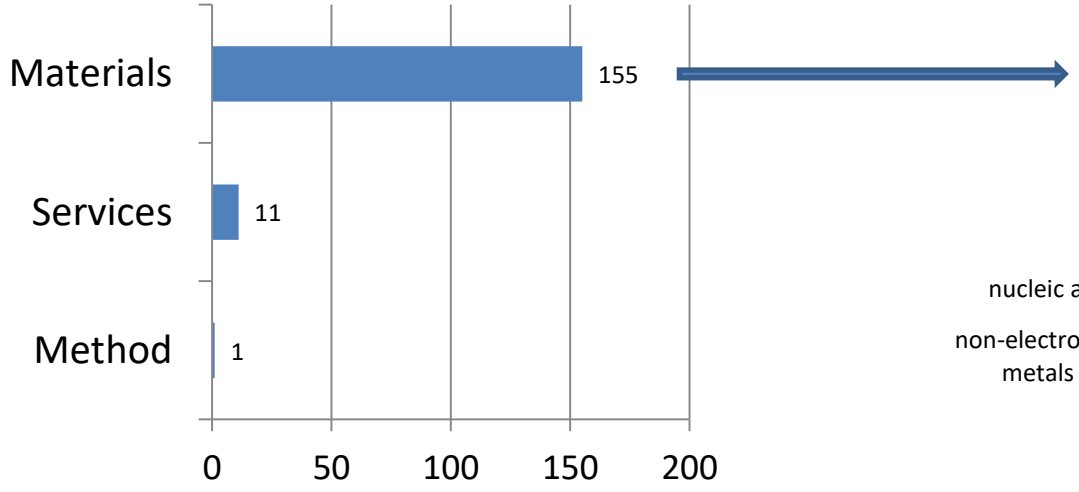
Materials delisted (6 CRMs)

- **HSA (SG)** HRM-3002A:
  Creatinine, Glucose, Total Cholesterol, Urea, and Uric Acid in Frozen Human Serum
- **ReCCS (JP)** JDS HbA1c Lot 2
- **NIST (US)** SRM 909b: human serum
  SRM 1955: Homocysteine and folate in frozen human serum
- **JRC (EU)** **IRMM/IFCC-456**: alpha-amylase purified from human pancreas
  BCR-405: HbA1c in human haemolysate

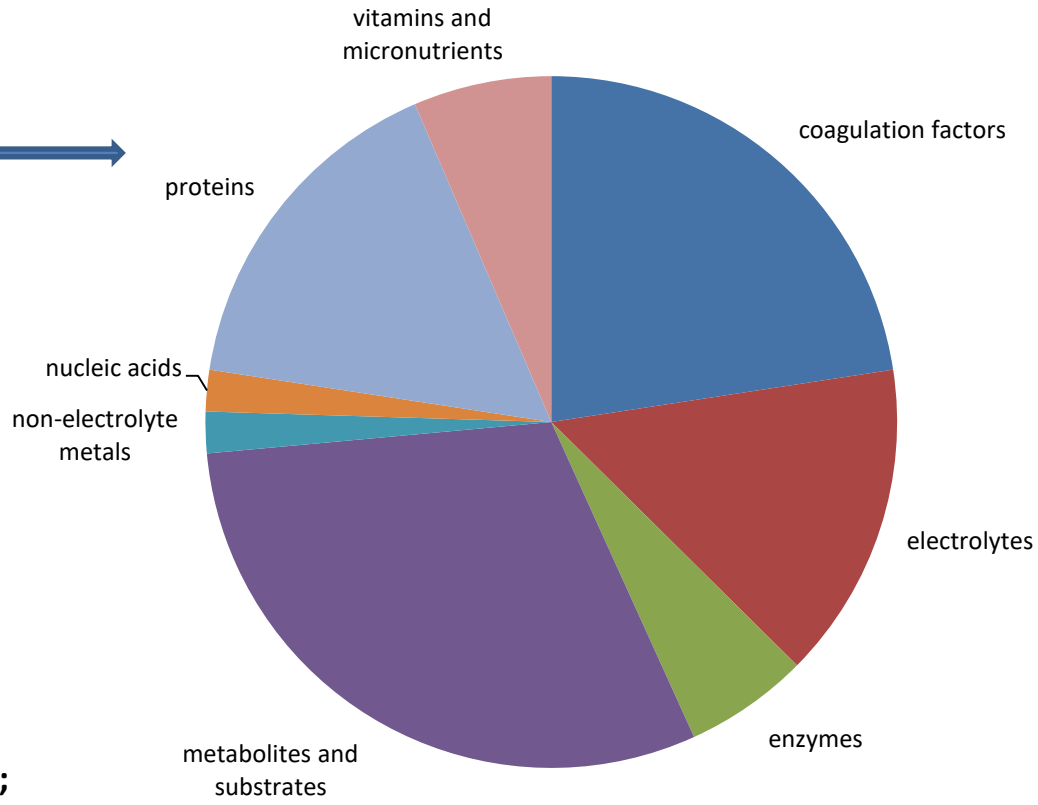
Entries no longer in the JCTLM Database

Database entries delisted

Number of items delisted



Distribution of materials entries per Analyte group



Reason for delisting DB entries:

Materials no longer available , 46 CRMs

Services no longer delivered by the lab or improved/replaced ;

Method publication no longer maintained by CLSI

CRMs listed in the JCTLM Database

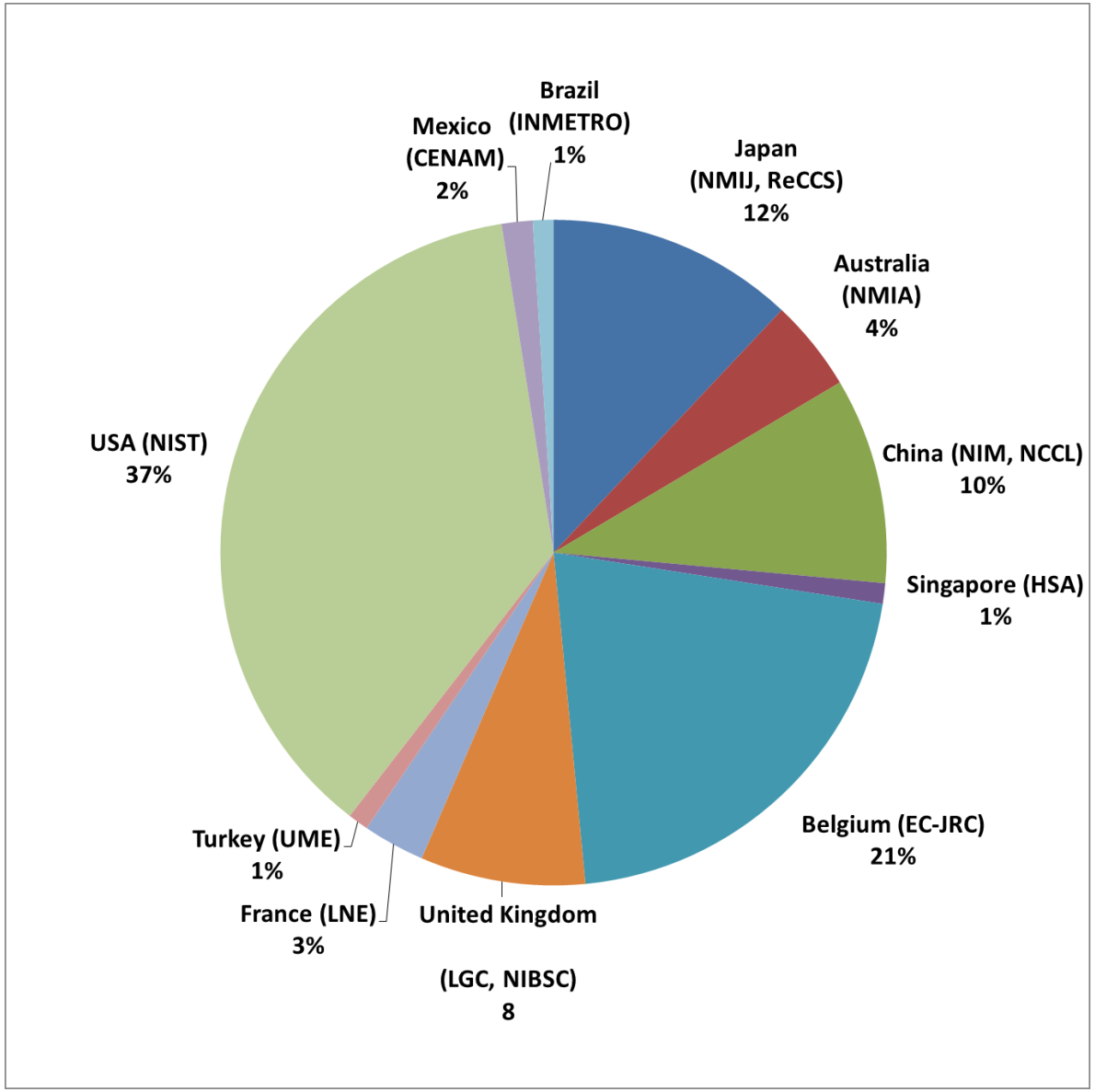
JCTLM
Accurate results for patient care

295 materials entries in the database

131 CRMs

14 producers including 12 NMIs/DIs

95 % CRMs listed from NMIs/DIs



New methods published in the JCTLM Database in 2019

JCTLM
Accurate results for patient care

Review Cycle 15 (2018) methods

+ 7 methods

RfB, Germany

ICP-OES based reference measurement procedure for the determination of **Lithium,Calcium, Potassium, Magnesium, and Sodium** in human blood

National Center for Clinical laboratories (NCCL), China

ID LC-MS/MS based reference measurement procedure for **glucose** in blood serum

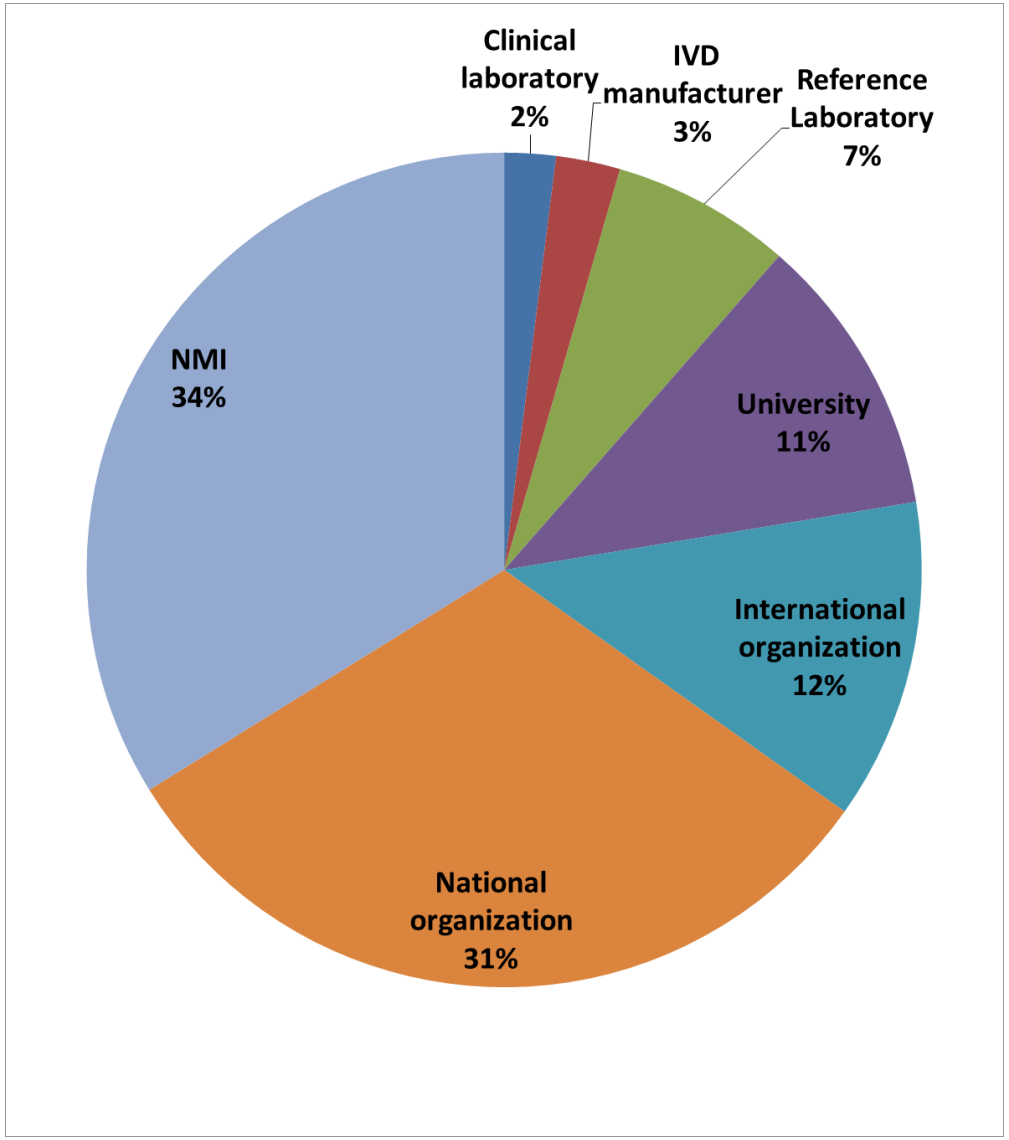
LGC, UK

Digital PCR based reference measurement method for **KRAS G12D/WT** in solution

Distribution of methods by organizations

JCTLM
Accurate results for patient care

201 RMMs in the database



Reference Measurement Services added to the JCTLM DB in 2019

JCTLM
Accurate results for patient care

Review Cycle 13 (2018) Services

+ 15 reference measurement services

Analyte Category	Analyte	Location of Laboratory
Electrolytes	Lithium, Sodium, Potassium, Magnesium and Calcium	Germany China
Enzymes	Alanine aminotransferase (ALT) Aspartate aminotransferase (AST) Creatine kinase (CK) Lactate dehydrogenase (LDH) Gamma-glutamyltransferase (GGT) Alpha-amylase Alkaline phosphatase (ALP)	China
Metabolites and substrates	Urea	China
Proteins	HbA1c	Japan

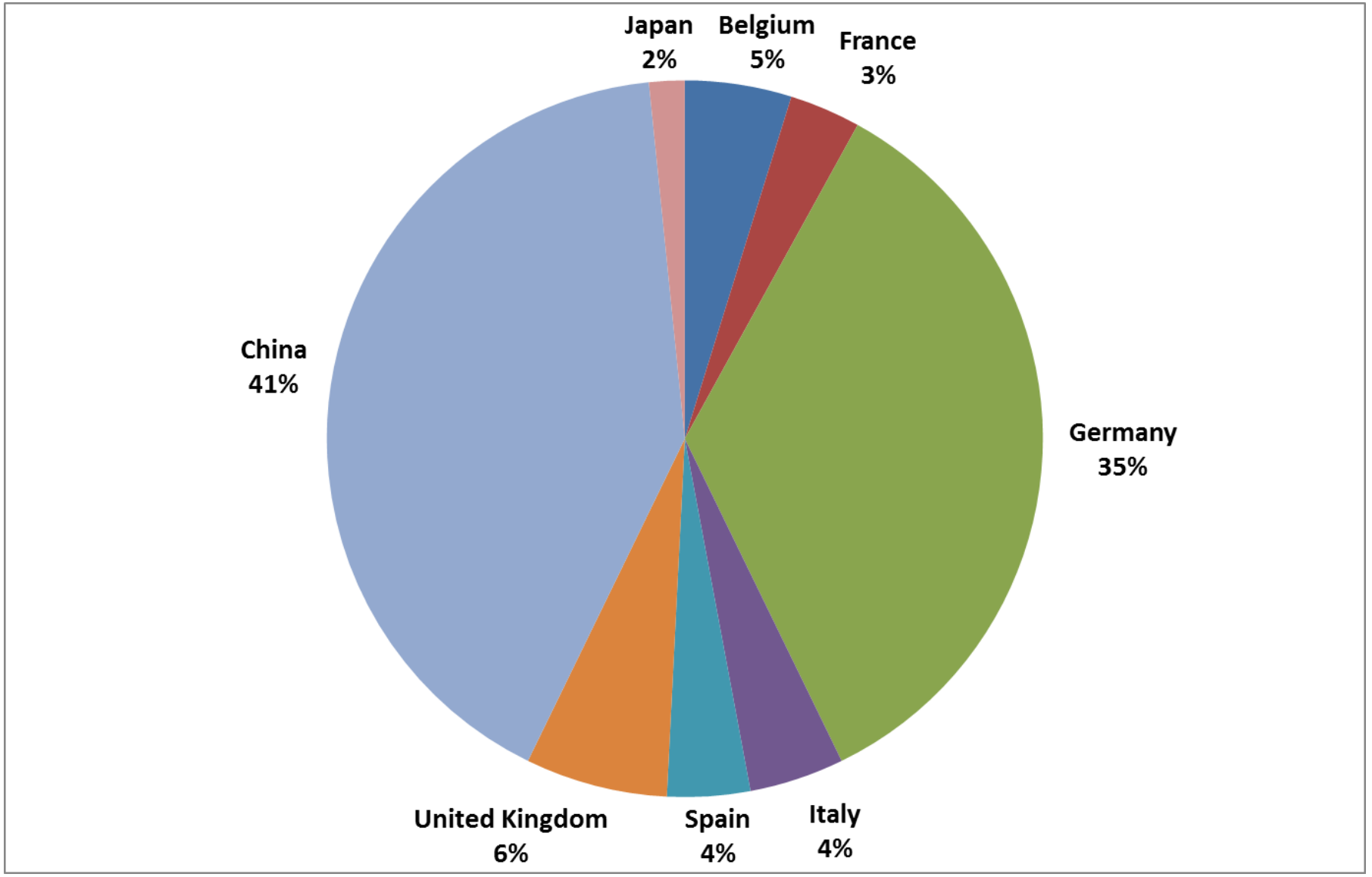
Distribution RMS providers by country of origin

JCTLM
Accurate results for patient care

187 reference measurement services in the database

18 services providers including

2 NMIs



Review Process Changes (Reference Method Comparisons)

JCTLM
Accurate results for patient care

Comparison Data for Methods for which Reference Measurement Services are not yet in operation

DBWG-P04B: Demonstrating the extent-of-equivalence of reference measurement methods/procedures (RMM/Ps) for the same measurand

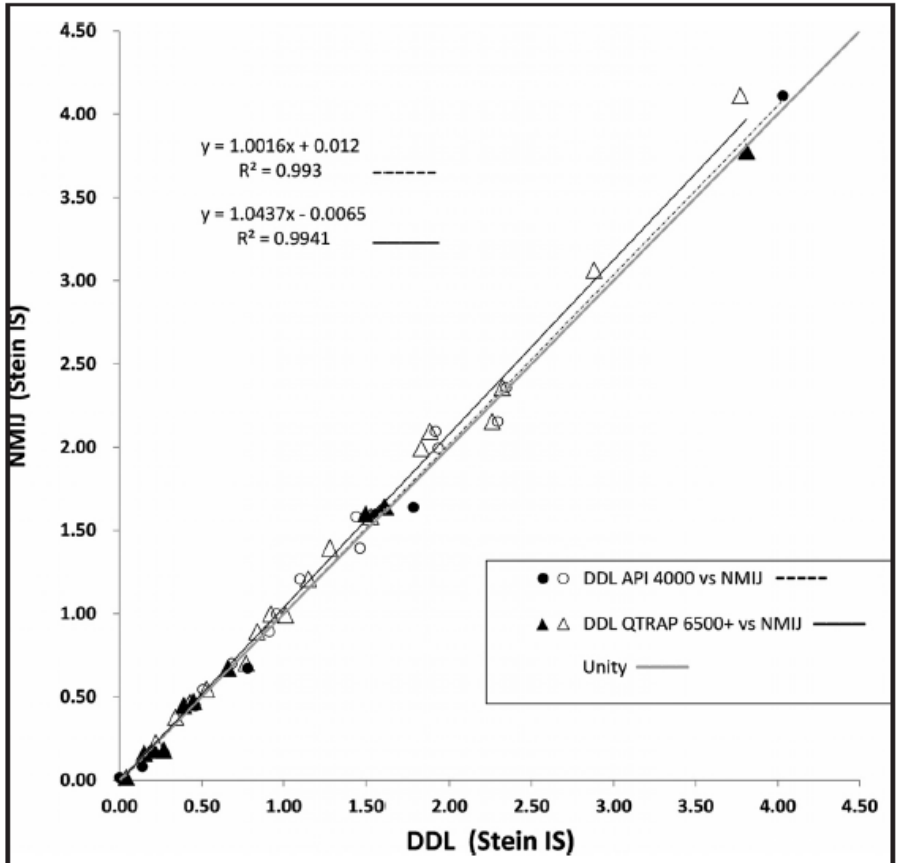


Fig. 1. The relationship between NMIJ and DDL when both laboratories used the same internal standard (IS).
Circles indicate analyses by DDL API 4000 and triangles indicate analyses by DDL QTRAP 6500+. Closed symbols and open symbols correspond to pooled and single-donor samples, respectively.

Little, Randie R., Robert I. Wielgosz, et al. "Implementing a Reference Measurement System for C-peptide: Successes and Lessons Learned." Clinical Chemistry (2016): clinchem-2016.

JCTLM Database: Web application

JCTLM
Accurate results for patient care

Main developments of the web based application

2006 : 1st version of the application implemented for Materials and Methods
2007 : 2nd version of the application implement for Services
2010 : 3rd version of the application extended to implement ISO 15194:2009 requirements for Materials

Current functionalities

Front interface : Web search form using specific criteria
Display information on reference measurement systems items

Administration interface: Management of data reviewed by JCTLM (archiving & publication)
Management of review documents issued by RTs

Going forward:

Since 2010: there were no major improvements on functionalities and technical matters

Functional issues

- Web interface not designed for new supports, e.g. tablets & mobiles
- No free search text engine

Technical issues

- Application is based on old Java Framework
- Changes on the web platform without changing the Framework will be costly and not reliable for future improvements

JCTLM Newsletter Issue 6 – April 2019

HIGHLIGHTS

- **JCTLM Governance update**
- **New JCTLM Task Force focusing on the implementation of reference measurement systems**
- **Activity of the WG-TEP - Working Group for Traceability, Education and Promotion**
- **JCTLM database content update**
- **JCTLM Membership**
- **Future Meetings**
- **SPECIAL REPORT on the Importance of metrological traceability for EQA**

Reference Materials, Measurement Methods and Services for *In Vitro* Diagnostics

JCTLM Accurate results for patient care

Database Newsletter

http://www.bipm.org/jctlm/ Issue 6 | April 2019

We are pleased to present the sixth issue of the Newsletter which reports on the activities of: JCTLM Working Groups and new Task Force; new entries in the database; the 2019 call for materials, methods and service nominations; and plans for 2019 JCTLM Meetings and events. We also welcome the new JCTLM Chair and new representatives to the JCTLM Executive Committee.

1 Appointment of a new JCTLM Chair

Dr Gary Myers completed his second two-year term as JCTLM Chair in December 2018. During his term, the structure and operation of the JCTLM were revised in order to open member status to new organizations and the Working Group on Traceability: Education and Promotion was established. Under his leadership the number of JCTLM member organizations increased significantly (by 50 % in number) and the awareness of the importance of traceability in laboratory medicine and its impact for accurate results for patient care has continued to grow. The JCTLM Executive Committee expressed its sincere thanks to Dr Myers for his significant contributions over the last four years.

Dr Myers is currently the Chairman of the International Consortium for Harmonization of Clinical Laboratory Results (ICHCLR), which is an organization member of JCTLM. Therefore, Dr Myers will continue to work closely with JCTLM as he was also appointed as new IFCC representative to the JCTLM Executive Committee.

During its 19th meeting in December 2018, the JCTLM Executive Committee appointed Prof. Ian Young as new Chair of the JCTLM for a renewable two-year term starting in January 2019. Prof. Ian Young is Professor of Medicine at Queen's University Belfast, and Deputy Medical Director and Consultant Chemical Pathologist at Belfast Health and Social Care Trust. In addition, he is Chief Scientific Advisor to the Department of Health, Northern Ireland, and Director of Research for Health and Social Care. He is currently President of the Association for Clinical Biochemistry and Laboratory Medicine (UK), and a member of the IFCC SD Executive Committee. The JCTLM welcomed Prof. Young to the committee.

Handover of JCTLM Chairmanship from Dr Myers (right) to Prof. Young (left) at the BIPM in December 2018

2 New CIPM representatives to the JCTLM

At its March 2019 meeting the International Committee of Weights and Measures (CIPM) appointed two of its members as new representatives to the JCTLM Executive Committee: Dr Thomas. Liew (Singapore) and Dr Sang-Ryoul Park (Republic of Korea) as Deputy.

Dr Thomas Liew is the Executive Director of the National Metrology Center of NMC, A*STAR, Singapore. Dr Sang-Ryoul Park is President of the Korea Research Institute of Standards and Science (KRISS), Republic of Korea.

Dr Park was also appointed President of the Consultative Committee for Amount of Substance: Metrology in Chemistry and Biology (CCQM) for a four-year term at the March 2019 meeting of the CIPM.

Dr Thomas Liew

Dr Sang-Ryoul Park

Reference Materials, Measurement Methods and Services for *In Vitro* Diagnostics

JCTLM Accurate results for patient care

Database Newsletter

http://www.bipm.org/jctlm/ Special Report | April 2019

External Quality Assurance is mandatory for many laboratories but when used effectively it can provide many opportunities for improvement including the following:

- Characterize test bias and imprecision across multiple methods
- Identify interfering substances and quantify their effects across multiple methods
- Provide clinical laboratories with reliable information for replacing unsatisfactory methods
- Identify clinical laboratories that are at risk of poor performance
- Satisfy accreditation and regulatory requirements
- Assessment of method robustness to clinically relevant interference
- Assessment of individual laboratory performance
- Audit of wider aspects of analytical performance and educational activities.

However, because EQA schemes have access to large volumes of method specific data which can be used at a more global level they can assist in the harmonization of methods. This data can be used as a post market surveillance process. But EQA schemes are often tailored to and operate at local level rather than globally and this limits their ability to perform this key role. In this Newsletter's Special Report, Dr Tony Badrick shares his views on how EQA schemes can work together and provide much needed information on an aspect of traceability in laboratory medicine.

The role of EQA in monitoring metrological traceability – a personal view

Dr Tony Badrick
RCPA Quality Assurance Programs, St Leonards, Sydney, Australia
Email: Tony.Badrick @ rcpaqap.com.au

The primary role of EQA schemes are to identify poorly performing laboratories and poorly performing methods or a combination of these, for example a poorly performing method(s) in a laboratory with an otherwise history of good performance. Sometimes an EQA scheme will be structured to specifically target the identification of poorly performing laboratories as a component of a Regulatory programme. A categorization of different EQA schemes based on the presence of sample commutability, source of value assignment, and use of replicates has been published by Miller et al (1). Another significant difference between EQA schemes is how acceptable performance is assessed. Based on the primary aim of the EQA scheme both the EQA sample characteristics and the Acceptable Performance Specifications (2) differ, with programs that seek to identify (very) poorly performing laboratories generally having wider allowable limits and ranking at a higher category in Miller's table than schemes that aim to improve overall laboratory performance (aspirational schemes).

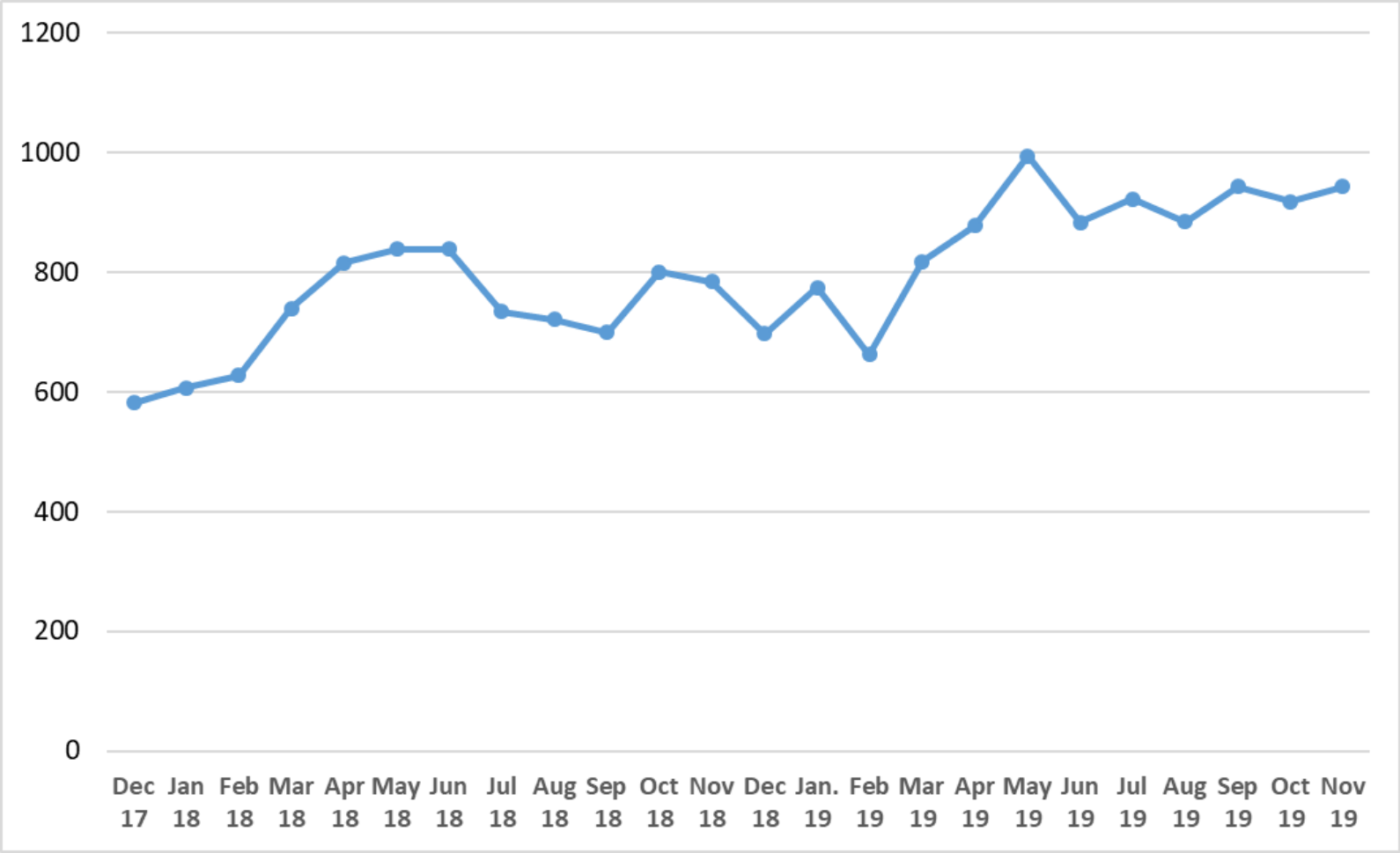
Traceability to what?

Metrological traceability is important to laboratories. Primarily a laboratory wants to ensure that they get the same result on a sample as another laboratory using the same sample method and instrument. In this case it doesn't matter if the sample is commutable or not, however it must be stable, reflect the concentrations seen in practice and as patient-like as possible (3). The frequency of EQA samples is also important. The fewer EQA samples there are the greater the impact of blunders (incorrect preparation of the EQA sample, EQA sample mix up/swap, incorrect data entry) or collusion as EQA samples will always be treated differently from patient samples. The fewer the number of samples, then statistically the less accurate is any measure of imprecision or accuracy. The fewer samples, the less of an external monitor of the impact in a method of changes in reagent or calibrator lots and the decreased opportunity to detect error in instrument processes which deal with patient samples and not on-board QC samples (e.g. some auto-dilution steps).

Metrological traceability is also important to the community as we need to ensure that ultimately a (correct) result for any test is the same no matter where or how it is measured. For this to be achieved, commutable samples need to be used and certified reference material (CRM)/reference measurement procedure (RMP) targets assigned. The measurand needs to be identified because in many cases different methods for the same analyte measure different measurands, for example isoenzymes and immunoassays where different antibodies, reagents or calibrators will give a different result for the same patient (3).

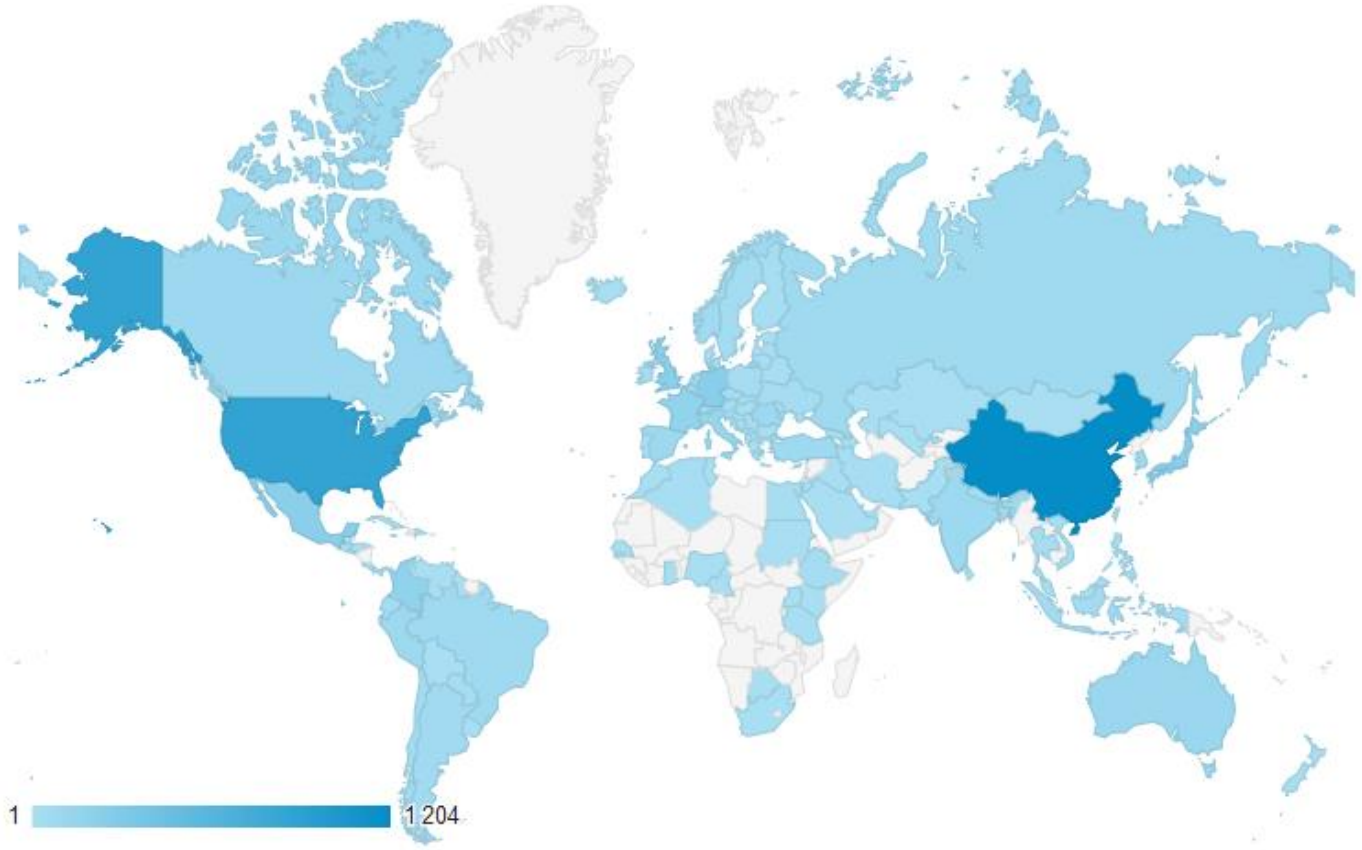
1

JCTLM Database: Visits in 2019

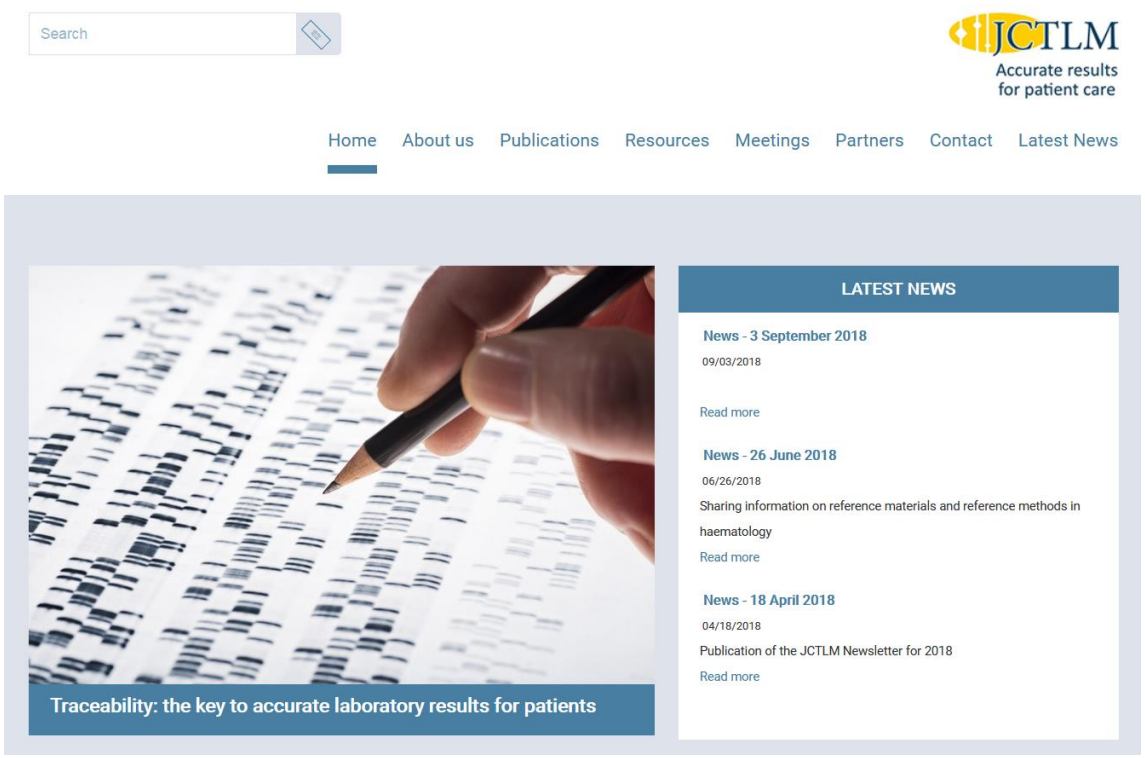


JCTLM Database: Visits in 2019

JCTLM
Accurate results for patient care



China	21,41 %
United States	15,63 %
Germany	4,29 %
Japan	4,09 %
Mexico	4,09 %
United Kingdom	3,89 %
Colombia	3,25 %
France	3,11 %
Italy	2,17 %
Australia	1,94 %



www.jctlm.org

THANK YOU