Measurement Science in Forensics, and *Metrologia*

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Director of the BIPM Chemistry Department
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Executive Secretary of the CCQM (Chemistry and Biology)

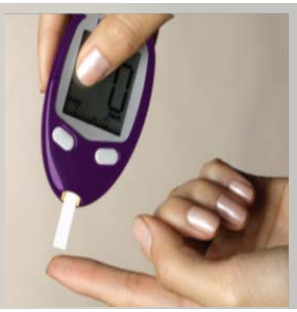
With thanks to Dr Janet Miles (BIPM, Metrologia Editor)

Bureau
International des
Poids et
Mesures

The BIPM

"The BIPM is an intergovernmental organization established by the Metre Convention, through which Member States act together on matters related to measurement science and measurement standards".

- **Founded in Paris in 1875 by 17 Member States and based at the *Pavillon de Breteuil* in Parc St Cloud, Sèvres, France**
- **Now involving about 100 states and economies as Members or Associates.**



The Metre Convention

THE METRE CONVENTION
established in 1875 by 17 States, now with 57 Member States in 2016.

CGPM – Conférence Générale des Poids et Mesures

Composed of Member State representatives.
Typically meets every 4 years to decide on matters relating to the Metre Convention and the SI

CIPM – Comité International des Poids et Mesures

18 individuals of different nationalities appointed by CGPM.

BIPM – Bureau International des Poids and Mesures

International Coordination:
- Infrastructure for committees
- Technical coordination

104th meeting of the CIPM (March 2015)

Consultative Committees (CCs)

CCAUV – Acoustics, US & Vibration
CCEM – Electricity & Magnetism
CCL – Length
CCM – Mass and related
CCPR – Photometry & Radiometry
CCQM – Amount of substance
CCRI – Ionizing Radiation
CCT – Thermometry
CCTF – Time & Frequency
CCU - Units

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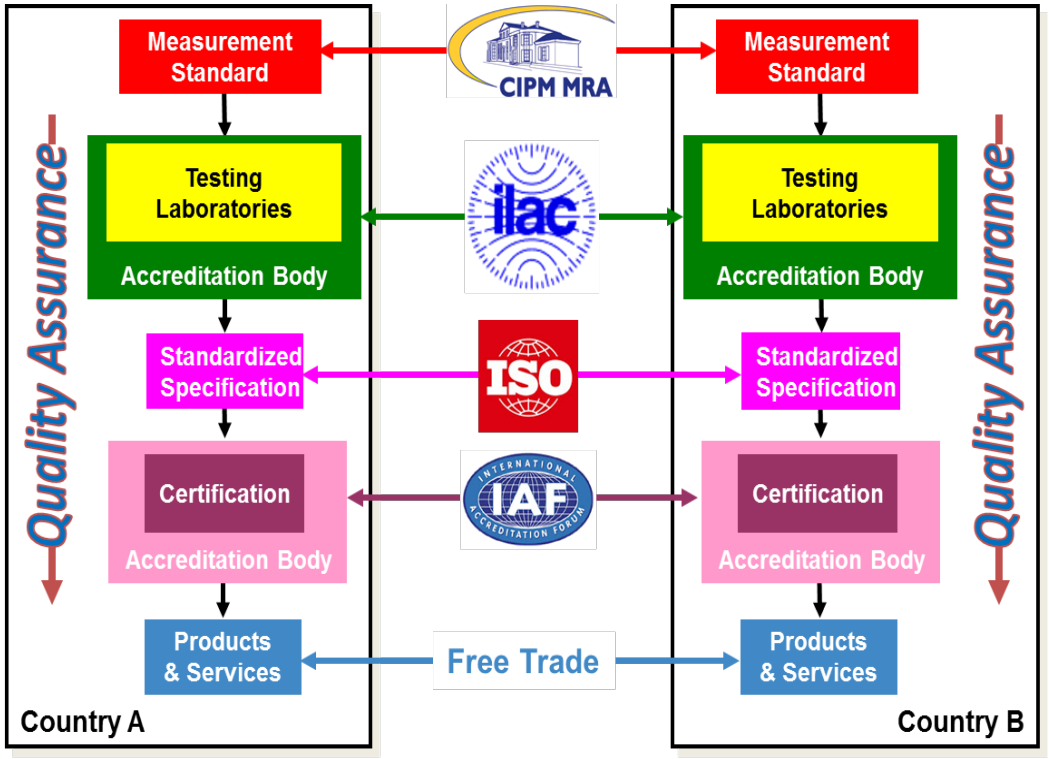
The CIPM Mutual Recognition Arrangement

- Metrology is a key part of the global "quality infrastructure" that underpins world trade.
- The work of the NMIs is made visible and transparent through the CIPM-MRA signed in 1999.
- The aim of the MRA is to provide the technical basis for the **worldwide acceptance** of national measurement standards and calibration and measurement certificates from NMIs.
- The work of the CIPM-MRA now goes far beyond matters of trade to cover climate change, healthcare etc.



CIPM MRA

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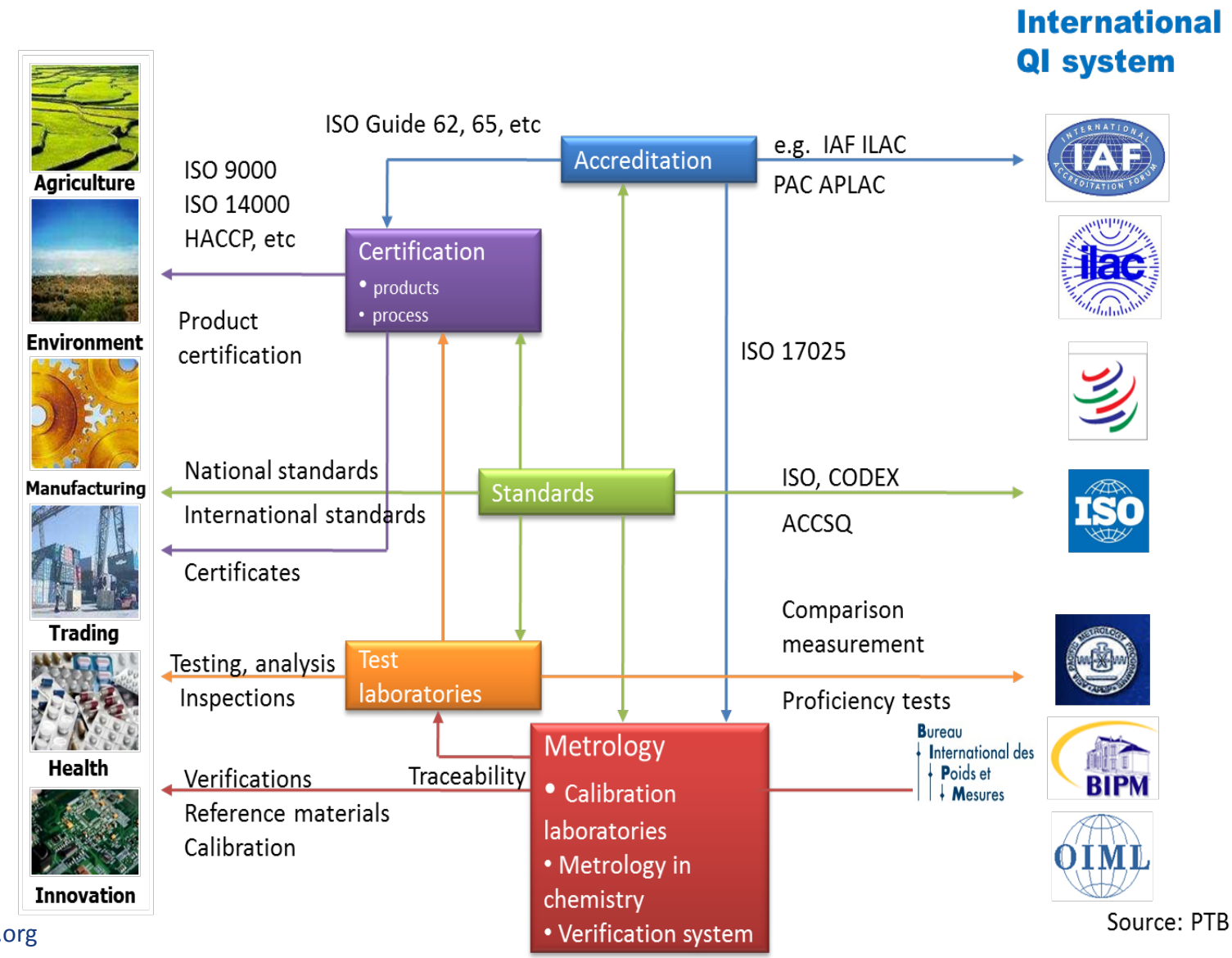
The Role of Metrology in National Quality Infrastructure



Source: PTB

metrologia

www.iopscience.org/met

Bureau International
des Poids et Measures

IOP Publishing

Major topics of this presentation about *Metrologia*

- Introduction to Metrologia: Scope and audience
- Key statistics (including impact factor)
- Appropriate articles for *Metrologia*
- Focus Issues: Measurement Science in Forensics
- *Reference Method Example from Chemical Analysis*
- Benefits to authors

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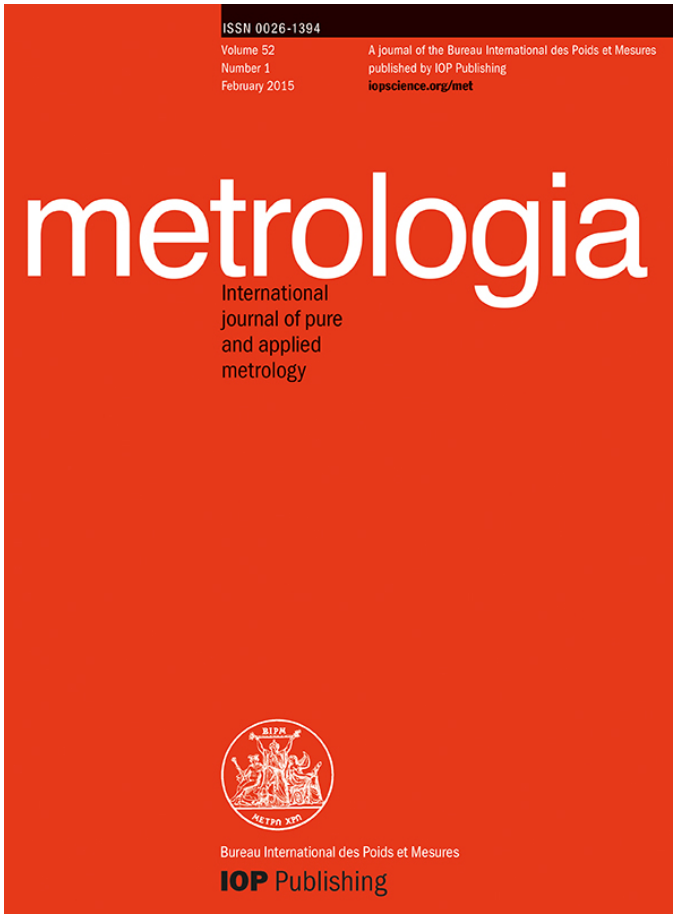
Basic information

THE JOURNAL

- *Metrologia* is an international journal dealing with pure and applied metrology (measurement science)
- First volume published in 1965
- Owned by the ***Bureau International des Poids et Mesures*** (BIPM) in Sèvres
- Published by IOP Publishing, a not-for-profit publisher owned by the Institute of Physics (IOP), since 2003
- 6 issues per year



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www.iopscience.org/met

Suitable articles for *Metrologia*

JOURNAL SCOPE

Metrologia covers the fundamentals of measurements, particularly those dealing with the seven base units of the International System of Units (metre, kilogram, second, ampere, kelvin, candela, mole) or proposals to replace them.

The journal also publishes papers that contribute to the solution of difficult measurement problems and improve the accuracy of derived units and constants that are of fundamental importance.

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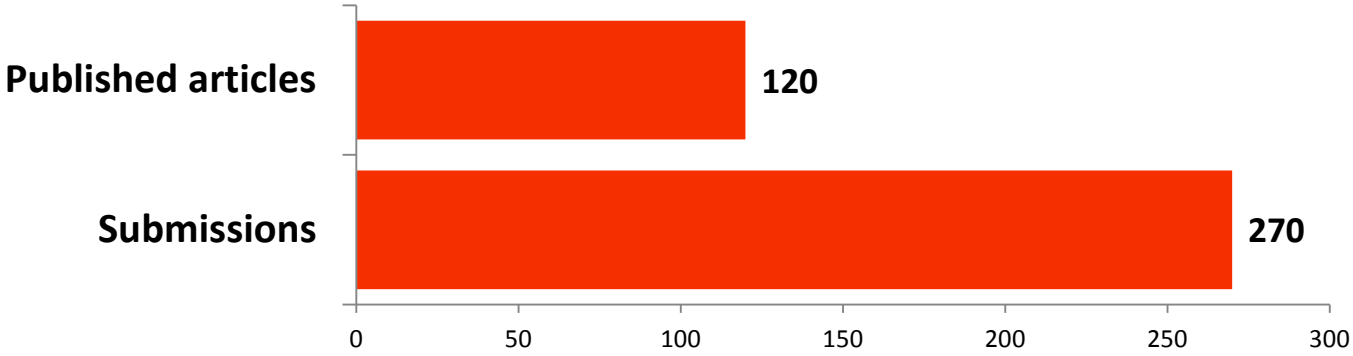
Statistics about *Metrologia*

- Submissions received and articles published in 2014



- Over **150 000** article downloads in 2015
- Over **2850** institutions have access
- Official 2015 JCR Impact Factor of **2.500**
    - Highest Impact Factor measurement journal, in the **top 15** journals in *Instruments and Instrumentation* JCR category
- Total citations to *Metrologia* articles topped **2700** in 2014

Metrologia publishes several kinds of articles

ARTICLE TYPES

In addition to regular papers, the journal also publishes;

- Review Articles, Letters to the Editor and Short Communications
- A Technical Supplement is published each year as an additional issue (outside the main 6 issues)
- Special Issues which have now been replaced with **Focus Issues**
  - **Devoted to single topics of timely interest and sometimes to conference proceedings**
  - **Current Focus Issue: Metrology for Dynamic Measurements**

Metrologia

Focus on Metrology for Dynamic Measurements

Guest Editors

Takashi Usuda, *National Metrology Institute of Japan/AIST, Japan*
Thomas Bruns, *Physikalisch-Technische Bundesanstalt, Germany.*

Figure. One of the low intensity shock acceleration exciter used to calibrate accelerometer dynamic sensitivity by measuring the transient motion of the accelerometer employing a laser interferometer. Image provided by the National Metrology Institute of Japan, Japan.

Scope

Today, traceability from NMI level to calibration laboratory level is usually established under static conditions. However, there are some notable exceptions, such as for shock and impact mechanical quantities (measured at a few NMIs), where experimental approaches to primary dynamic calibration are developed. Verification of dynamic measurement capabilities via key comparisons remains a long way off, due to a lack of validated methods and widely accepted procedures. Consequently, dynamic calibrations of measurement equipment at calibration laboratories and dynamic measurements at testing laboratories are rarely performed, or are performed without validation of the method's traceability and uncertainty.

There are, however, many demands from industry for dynamic measurements, with the aim of improving efficiency, safety, and reliability as well as encouraging innovation. There are also many implicit demands for traceable dynamic measurements from the regulatory and legislative sectors, such as energy efficiency or environmental requirements.

Recognizing the importance of the emerging area of dynamic measurements, an issue on dynamic measurements is planned to focus on the following subjects:

- Mechanical Quantities (Force, Torque, Vibration, etc.)
- Fluid and Flowmetry (Pressure, temperature, and volume of fluid)
- Thermo Physical Quantities (material properties, etc.)
- Electrical Quantities (AC Josephson, etc)
- System Identification and Calibration (Numerical analysis, GUM etc.)

Focus Issues: Several advantages…

- Each Focus Issue highlights advances made in an exciting area of research with articles authored by the leading researchers in these specific fields.
- The articles are commissioned together by an **expert** in the field, who acts as **Guest Editor**.
- The articles can be published across numerous issues of the journal and are brought together in online collections.
- For **Measurement Science in Forensics** (a new field) this provides an ideal way of introducing the subject to the journal.

Focus on Measurement Science in Forensics

Guest Editor(s): XXX

Agreed submissions:

-
-
-

Are you interested in submitting a paper?

Please contact XXX!

Attributes of a ‘Measurement Science’ article in the Focus Issue (agreed by Metrologia Editor and Guest Editor)

- Metrological evaluation of measurement methods used for forensic applications
- Looking at the science behind the method… and evaluating the probability of getting the right result!
- A careful description of the method, including the various measurements involved , and its validation
- An estimate of the component uncertainties and the overall uncertainty of the results obtained [“GUM”]

Example of 'Measurement Science' Articles from other fields: Insulin and C-peptide measurement

Review

Drug Testing and Analysis

Received: 25 March 2009 Revised: 29 April 2009 Accepted: 6 May 2009 Published online in Wiley Interscience:

(www.drugtestinganalysis.com) DOI 10.1002/dta.38

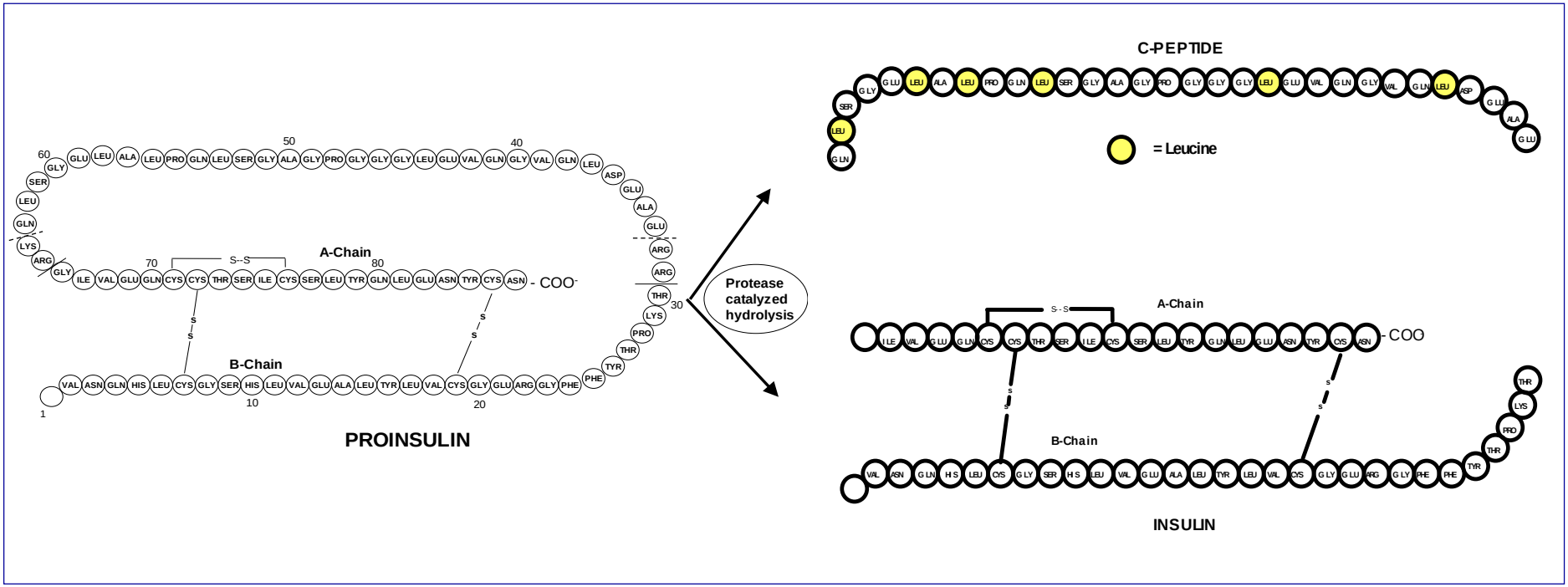
Murder by insulin: suspected, purported and proven – a review

Vincent Marks*

Murder by insulin – whether attempted, suspected or proven – is rare. Only 66 cases worldwide could be found for this review. A conviction was secured in 31 cases and additional weapon was employed in 11. Differentiation of attempted homicide from Munchausen syndrome by proxy in the young and from 'mercy killing' in the elderly was not attempted. Most perpetrators were close relatives and most victims were alive when discovered and responded to treatment. Hypoglycaemia is the first clue to homicidal insulin use in living subjects and requires the demonstration of a plasma insulin concentration of generally more than 1000 pmol/L and undetectable plasma C-peptide concentration to establish the diagnosis. Serum glucose measurements are valueless in victims found dead. The presence near the body of insulin vials, syringes or needles, loose talk by the suspected perpetrator or their ready access to insulin may be the only clue. The demonstration of insulin in tissue around an injection site by immunohistopathology or by measuring it in an extract clinches the diagnosis. Immunoassays suitable for clinical use to detect and measure insulin and C-peptide are subject to random errors and cannot be relied upon unless special precautions including separation by gel filtration or HPLC are undertaken prior to analysis. They do not detect or measure accurately a new generation of synthetic insulin analogues. Mass spectrometry will be required to do this and to validate clinical immunoassays, upon which convictions have always had to rely in the past.

Keywords: insulin; murder; homicide; C-peptide; immunoassay

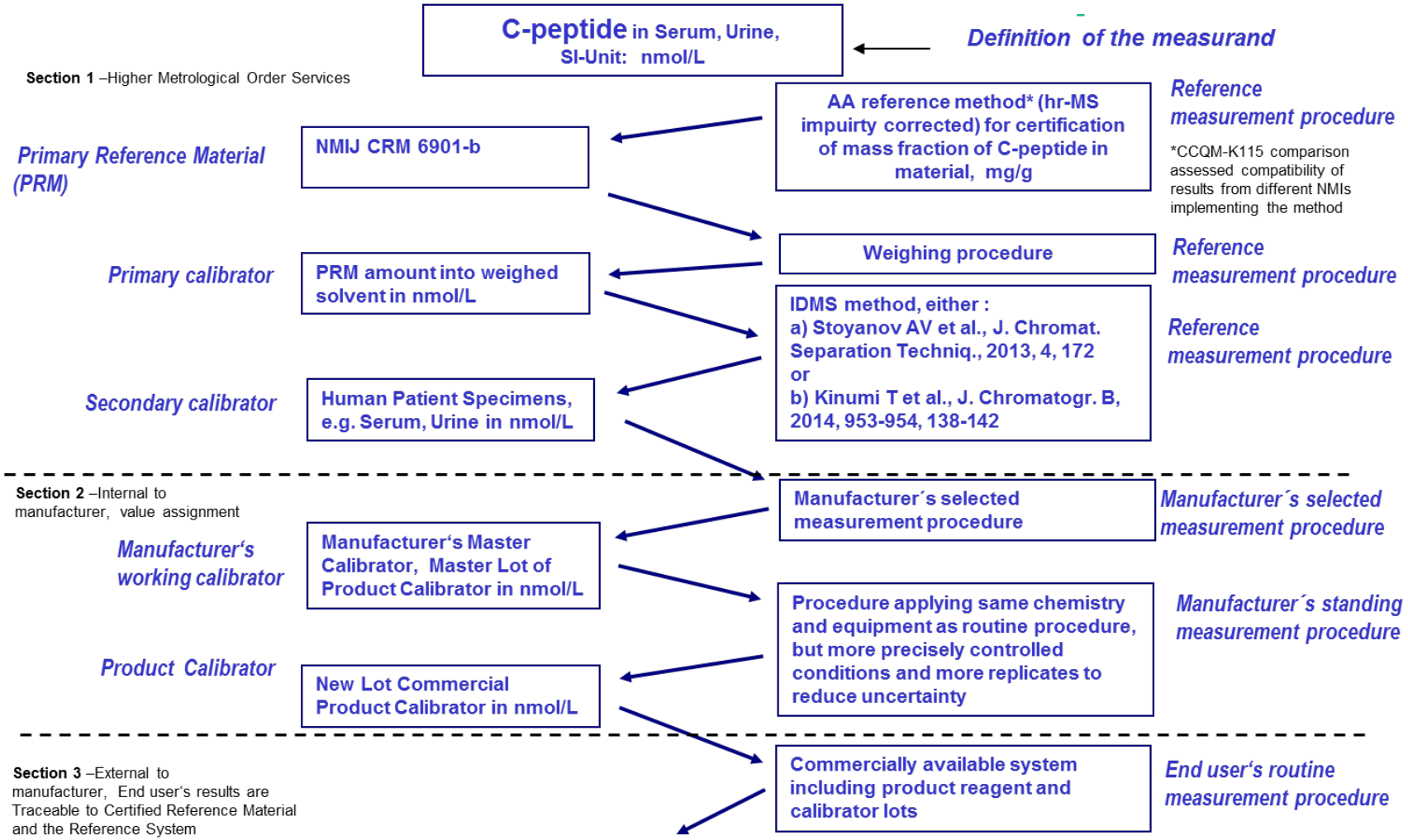
Example of ‘Measurement Science’ Articles from other fields: Laboratory Medicine – C-peptide



- Pro-insulin is synthesized in the pancreatic beta cells
- Pro-insulin is packaged into granules and cleaved to insulin and C-peptide.
- Insulin and C-peptide are secreted in a 1:1 molar ratio.
- Insulin (but not C-peptide) is cleared by the liver; C-peptide remains in the circulation longer than insulin
- C-peptide is the best marker of insulin secretion

Courtesy of R.Little UMC DDL

Example of 'Measurement Science' Articles from other fields: Laboratory Medicine – C-peptide



Calibration hierarchy for C-peptide measurements as per ISO 17511

Bureau International des Poids et Mesures

Example of 'Measurement Science' Articles from other fields: Laboratory Medicine – C-peptide

J Chromatogr A. 2011 Dec 23;1218(51):9244-9. doi: 10.1016/j.chroma.2011.10.080. Epub 2011 Nov 2.

Use of cation exchange chromatography for human C-peptide isotope dilution - mass spectrometric assay.

Stoyanov AV[1], Rohlfing CL, Connolly S, Roberts ML, Nauser CL, Little RR.

⊕ **Author information**

Abstract

An application of ion exchange chromatography for C-peptide analysis is described here. At the stage of C-peptide isolation, a strong cation exchanger (SP HP or MonoS) was used to purify the analyte from ballast proteins and peptides. The conditions of ion-exchange chromatographic separations were optimized using theoretical modeling of the net surface electric charge of the peptide as a function of pH. The purified and concentrated sample was further subjected to LC-MS/MS. In order to improve the reliability of analysis, two fragment ions were monitored simultaneously both for native C-peptide and internal standard, isotopically labeled C-peptides analogues (fragments with m/z of 927.7 and 147.2). Using ion-exchange chromatography, it became possible to process larger sample volumes, important for testing patients with very low C peptide levels, compared to currently used solid phase extraction methods.

PMID: 22098929 DOI: 10.1016/j.chroma.2011.10.080

Compliance Requirements for Reference Methods and Reference Materials

ISO 17511 In vitro diagnostic medical devices - Measurement of quantities in biological samples - Metrological traceability of values assigned to calibrators and control materials (under revision)

ISO 15193:2009 Requirements for content and presentation of reference measurement procedures

ISO 15194:2009 Requirements for certified reference materials and the content of supporting documentation

ISO 18153 Metrological traceability of values for catalytic concentration of enzymes assigned to calibrators and control materials

ISO 15195: 2003 Reference Measurement Laboratories

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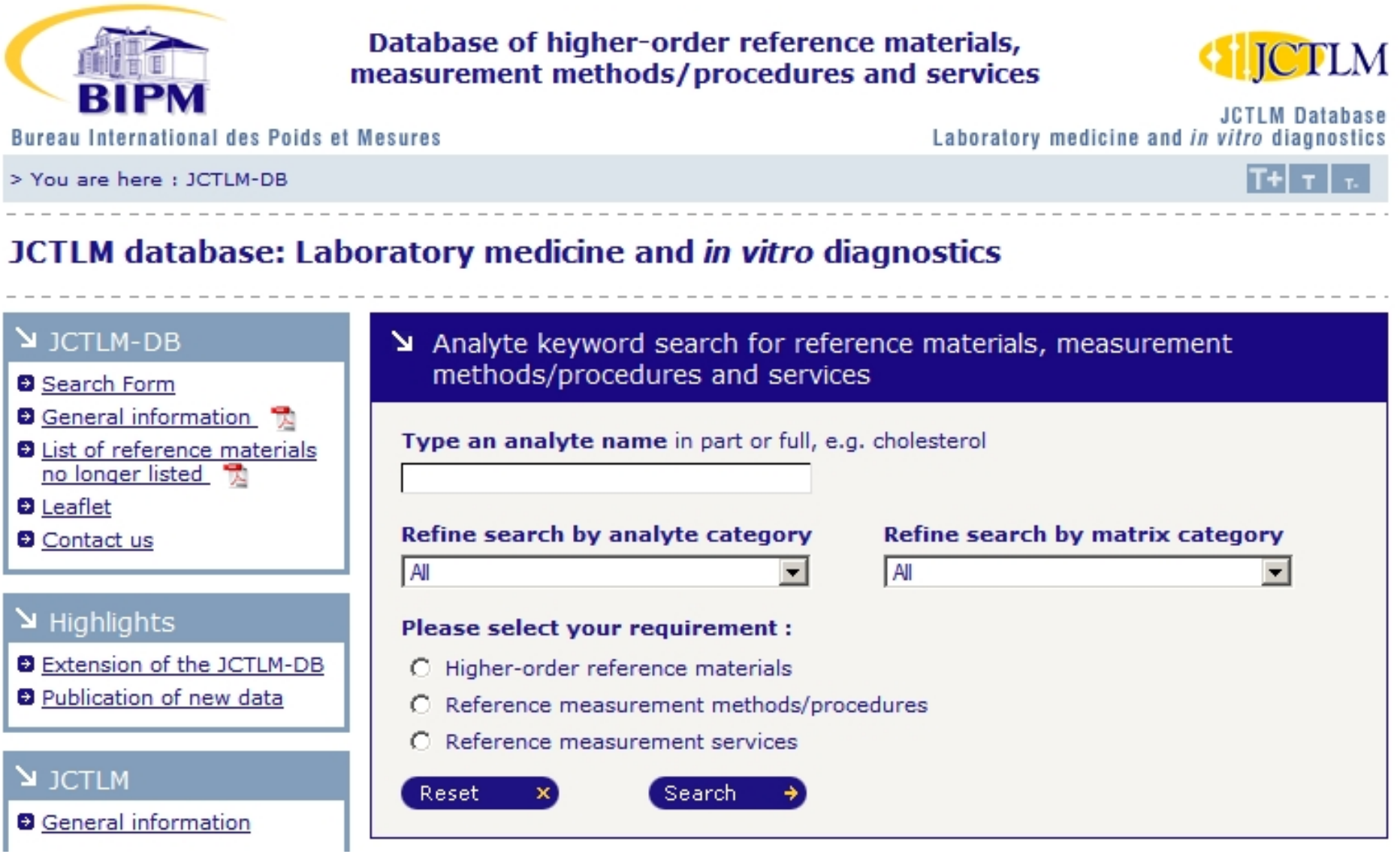
Independent review of compliance by Experts

Review Team Leaders and Members of Working Group 1 and 2 of JCTLM

JCTLM-WG1: Reference Materials and Measurement Methods/Procedures		
Analyte Category	**Review Team Leader**	**Review Team Members**
Blood cell counting	**Lili Wang**, National Institute of Standards and Technology (NIST)	**Mingting Peng**, National Center for Clinical Laboratories **Yohko Kawai**, International University of Health and Welfare **Joerg Neukammer**, Physikalisch-Technische Bundesanstalt (PTB) **Johannes J. Hoffmann**, Abbott Diagnostics Division **Giuseppe d'Onofrio**, Catholic University of Rome **Alexander von Ruecker**, University of Bonn
Blood Groupings	**Susan Thorpe**, National Institute for Biological Standards and Control (NIBSC), Division Haematology	**John Allan**, Alba Bioscience **Kathleen Reis**, Ortho-Clinical Diagnostics
Coagulation Factor	**Elaine Gray**, National Institute for Biological Standards and Control (NIBSC)	**Craig Jackson**, The Hartwell Foundation **Barry Woodhams**, Stag **Steve Kitchen**, Royal H **Steffen Rosen**, Rossix
Drugs	**Andre Henrion**, Physikalisch-Technische Bundesanstalt (PTB)	**Lothar Siekmann**, Univ **Christoph Seger**, Institu Hospital Innsbruck **Zhu Zhu**, Beckman Coul
Electrolytes and Blood Gases	**Brigitte Toussaint**, Institute for Reference Materials and Measurements (IRMM)	**Chandra Jain** **Stephen Long**, National **Christoph Ritter**, Roche **Samuel Wunderli**, Fede
Enzymes	**Mauro Panteghini**, University of Milan	**Ferruccio Ceriotti**, Diagnostica e Ricerca San Raffaele S.p.A. **Wenxiang Chen**, National Center for Clinical Laboratories, Ministry of Health **Gerhard Schumann**, Medizinische Hochschule Hannover **Steve Wolf**, Beckman Coulter, Inc. **David Armbruster**, Abbott Laboratories **Craig Jackson**, The Hartwell Foundation **Shigeru Ueda**, Hasahi Kasei Pharma Corporation
Metabolites and Substrates	**Xu Bei**, National Institute of Metrology (NIM)	**Steve Wolf**, Beckman Coulter, Inc. **David Armbruster**, Abbott Laboratories **Wenxiang Chen**, National Center for Clinical Laboratories, Ministry of Health **Lothar Siekmann**, University Hospital Bonn, DGKL Reference Laboratory **Hanspeter Andres**, Federal Office of Metrology (METAS) **Qinde Liu**, Health Science Authority, Singapore (HSA)

JCTLM review team members providing independent review of nominated reference materials and methods in compliance with ISO 15194 and ISO 15193

Independent review of compliance for Reference Methods and Reference Materials



Independent review of compliance for Reference Methods and Reference Materials: JCTLM Database

Liquid chromatography mass spectrometry method for C-peptide in blood serum	
▸ UMC DDL reference method for serum C-peptide	
Applicable matrice(s)	lyophilized, fresh, or frozen human serum or urine
Full description of technique(s)	Liquid chromatography mass spectrometry (LC/MS)
Quantity	Amount-of-substance concentration
Applicable range	0.01 nmol/L to unlimited after appropriate dilution
Expected uncertainty (level of confidence 95%)	0.036 nmol/L to 0.09 nmol/L
Reference(s)	Use of cation exchange chromatography for human C-peptide isotope dilution - Mass spectrometric assay, Stoyanov AV et al., *J. Chromatogr. A*, 2011, **1218**, 9244-9249;
Comparability assessment study(ies)	Human C-peptide Quantitation by LC-MS Isotope-Dilution Assay in Serum or Urine Samples, Stoyanov AV et al., *J. Chromat. Separation Techniq.*, 2013, **4**, 172
Comment(s)	University of Missouri-Columbia Diabetes Diagnostic Laboratory (UMC DDL)
JCTLM DB identification number	C10RMP12_C-Peptide

JCTLM database entry for a Reference Method for C-peptide in serum measurements reviewed to be compliant with ISO 15193 requirements

Independent review of compliance for Reference Methods and Reference Materials: JCTLM Database

Isotope dilution mass spectrometry method for C-peptide in blood serum	
▸ NMIJ Reference measurement method for serum C-peptide	
Applicable matrice(s)	blood serum, blood plasma
Full description of technique(s)	Isotope dilution mass spectrometry
Quantity	Mass concentration
Applicable range	0.01 ng/ml (0.003 ng on column) to 17.4 ng/ml (2.9 ng on column)
Expected uncertainty (level of confidence 95%)	9.1 % to 11.4 %
Reference(s)	Quantification of serum C-peptide by isotope-dilution liquid chromatography tandem-mass spectrometry: Enhanced detection using chemical modification and immunoaffinity purification, Kinumi T et al., *J. Chromatogr. B*, 2014, **953-954**, 138-142
JCTLM DB identification number	C11RMP1

JCTLM database entry for a Reference Method for C-peptide in serum measurements reviewed to be compliant with ISO 15193 requirements

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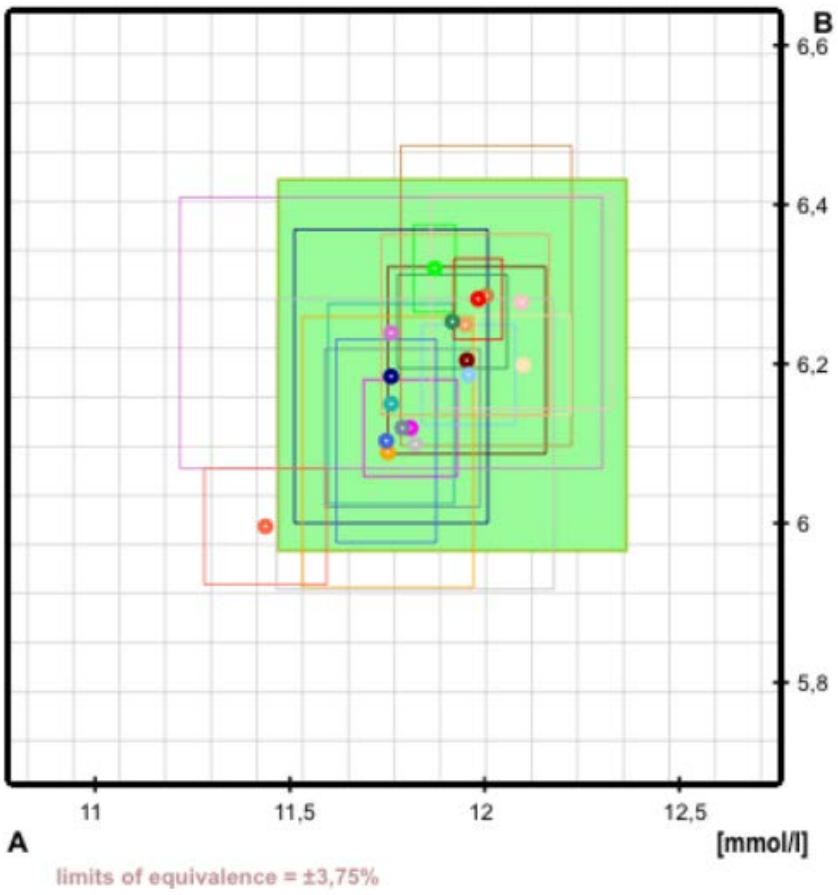
Compliance Requirements for Laboratories Providing Reference Measurement Services

RELA - Homepage
External quality control for Reference Laboratories



Labcode	A	e.u. A	B	e.u. B	Method
3	**11,81**	**0,12**	**6,12**	**0,06**	**ID/GC/MS**
5	11,95	0,203	6,204	0,117	ID/GC/MS
6	**12**	**0,22**	**6,285**	**0,189**	**spectrophotometry**
					ctrophotometry
					D/LC/MS/MS
					ctrophotometry
					ID/GC/MS
					ctrophotometry
					ctrophotometry
51	**11,75**	**0,22**	**6,09**	**0,17**	**spectrophotometry**
54	11,76	0,54	6,24	0,17	ID/LC/MS/MS
61	12,09	0,233	6,276	0,134	spectrophotometry
65	11,44	0,157	5,996	0,072	spectrophotometry
87	11,75	0,13	6,104	0,128	spectrophotometry
104	11,98	0,062	6,282	0,05	spectrophotometry
119	**11,95**	**0,215**	**6,249**	**0,113**	**spectrophotometry**

Results from the IFCC RELA (an external quality assurance scheme) scheme for Calibration Laboratories showing results for glucose measurements from 2014

Metrologia: Author benefits

- No page charges
- Free hosting of supplementary data such as multimedia files
- Hybrid Open Access option
- Forward citing and reference linking of your paper, allowing the community to find your work with ease
- Abstracted in – ISI, Scopus, Inspec, etc
- Alerting services will deliver your research directly to the community via e-mail and RSS feeds
- Professional proof reading and typesetting

Short time from submission to publication

PEER REVIEW

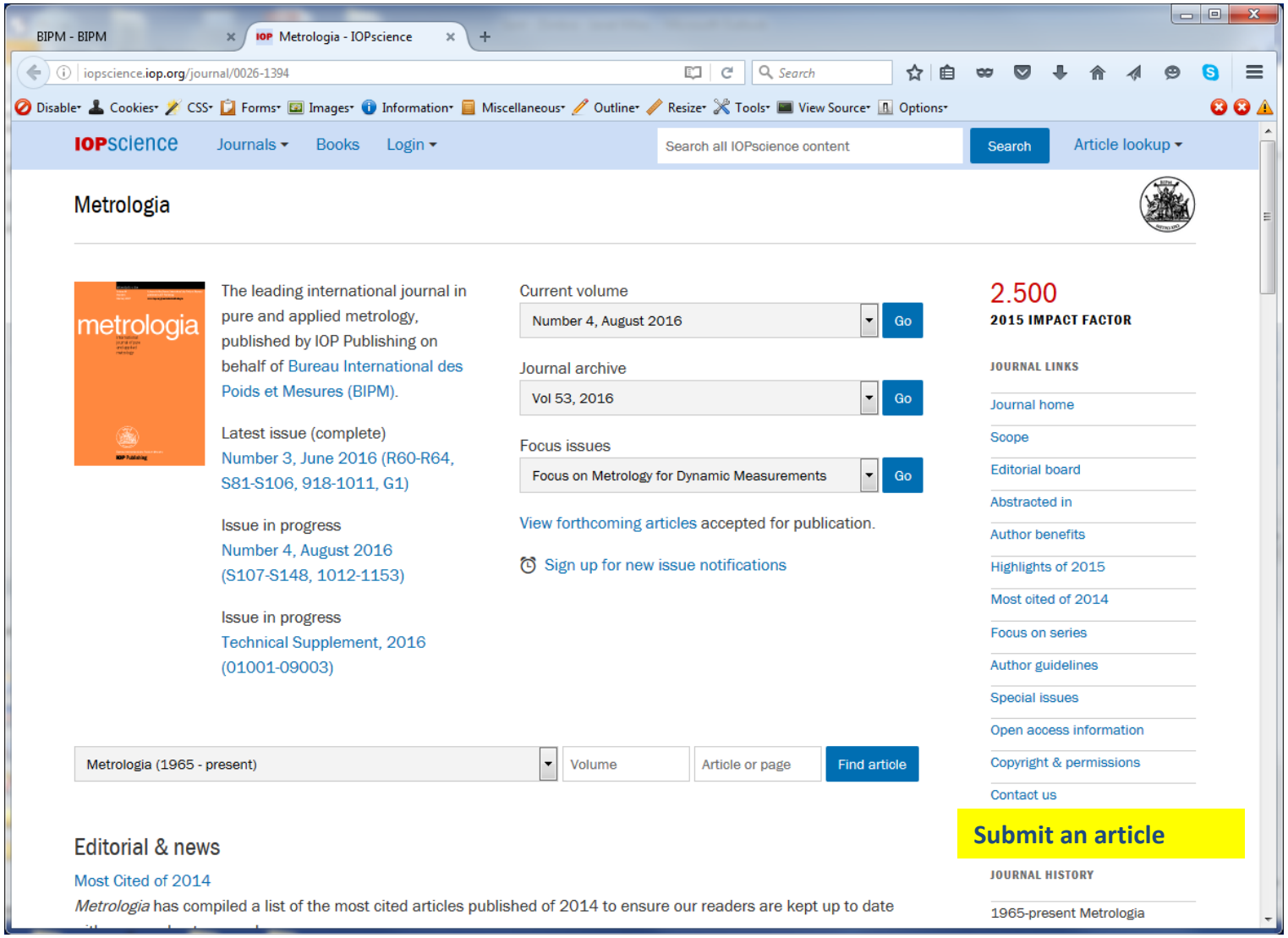
- Single blind peer review system managed by a professional Editor based at the BIPM
- Editor is supported by
  - IOP Editorial, Administration and Technical Staff
  - World leading scientific experts who sit on the Editorial Board
- Industry leading online submission and tracking system provided by ScholarOne

Efficient process:

- Average Receipt-To-First Decision time - **33 days**
- Average Receipt-to-Accept time - **58 days**
- Average Accept-to-Web Publication time – **32 days**

Where to find *Metrologia* from BIPM home page

Metrologia home page



Thanks for your attention

Any questions?