Organization Name: D.I. Mendeleyev Institute for Metrology (VNIIM)

JCTLM Member status: National and Regional Member

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Period covered: 2020 – 2021

1. **Major achievement(s) in support of standardization in laboratory medicine**

In the period of 2020 – 2021 VNIIM produced and supplied certified reference materials for laboratory medicine in Russian Federation to be used for instrumentation calibration and validation:

- GSO 10669-2015- CRM of blood cell composition - hematological control.
- GSO 9913-2011 - CRM of the cholesterol molar concentration in blood.
- GSO 10023-2011 - CRM of the artificial urine composition.
- GSO 10238-2013 - CRM of the hemiglobin cyanide solution composition.
- GSO 10390-2013 - CRM of the testosterone molar concentration in blood serum.
- GSO 11192-2018 - CRM of low molecular weight nitrogenous substances in blood.
- GSO 9866-2011 - CRM of the soybean DNA composition (GM-soy-VNIIM kit).
- GSO 11291-2019 - CRM of the inorganic substances molar concentration in the blood.
- GSO 11312-2019 – CRM of composition of biochemical analysts in blood.
- GSO 7969-2006 – CRM of the of ethanol aqueous solution composition.
- GSO 9531-2010 … 9534-2010 - a set of CRMs of the gas mixture (anesthetic and respiratory mixtures) composition.

Technical characteristics of VNIIM produced CRMs are available at https://www.vniim.ru/files/catalog-ss2021.pdf

On routine level VNIIM conducted trials of medical devices in order to approve the type of measuring instrument. In the period of 2020 – 2021 we conducted trials and confirmed metrological characteristics for a number of biochemical and hematological analyzers, like Evidence Investigator automatic analysers, BioChem automatic biochemical analysers (types FC-120, FC-200, FC-360), Y-15 and Y-25 biochemical analysers ("Biosystems S.A.), coagulometers KC-1, KC-4 and other.

VNIIM participate in CCQM NAWG and CAWG working group activities directed to establishing global comparability in nucleic acid and cellular measurements. In 2020 -2021 period VNIIM participated in CCQM-K176 key comparison, CCQM-P199, CCQM-P199b pilot comparisons with laboratory medicine important measurands.

In 2020-2021 period VNIIM became a member of the ISO TC212 “Clinical laboratory testing and in vitro diagnostic test systems” and TC48 “Laboratory equipment”, of the GOST R TC380 (a GOST R mirror committee of ISO TK212) and performed technical translation to Russian of following ISO standarts:

- ISO 17511:2020 “In vitro diagnostic medical devices — Requirements for establishing metrological traceability of values assigned to calibrators, trueness control materials and human samples”
- ISO 21151:2020 “In vitro diagnostic medical devices — Requirements for international harmonisation protocols establishing metrological traceability of values assigned to calibrators and human samples”
- ISO/TS 20914:2019 “Medical laboratories — Practical guidance for the estimation of measurement uncertainty”
- ISO 15195:2018 “Laboratory medicine — Requirements for the competence of calibration laboratories using reference measurement procedures”.
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Relevant technical/scientific publications include

1. Milavec M., Cleveland M.H., Bae Y.K., Wielgosz R.I., Vonsky M. & Huggett J.F. Metrological framework to support accurate, reliable, and reproducible nucleic acid measurements. Analytical and Bioanalytical Chemistry (2021) https://doi.org/10.1007/s00216-021-03712-x
2. Mester Z., Corbisier P., Ellison S.L.R., Gao Y., Niu C., Tang V., Lee F., Pérez-Urquiza M., Suárez A.R., Burns M., Milavec M., Wiangnon K., Griffiths K.R., McLaughlin J.L.H., Shibayama S., Takatsu A., Akgoz M., Vonsky M., Runov A., Guerrero J.E.L. Final report of CCQM-K86.c. Relative quantification of genomic DNA fragments extracted from a biological tissue. Metrologia, 57(1A): 0804 (2020) doi: 10.1088/0026-1394/57/1A/08004
3. Faruqui N., Kummrow A, Fu B., Divieto C., Rojas F., Kisulu F., Cavalcante J.J.V., Wang J., Campbell J., Martins J.L., Choi J.-H., Sassi M.P., Zucco M., Vonsky M., Vessillier S., Zou S., Fujii S.-I., Ryadnov M.G. Cellular Metrology: Scoping for a Value Proposition in Extra- and Intracellular Measurements. Front. Bioeng. Biotechnol. 7:456 (2020). doi: 10.3389/fbioe.2019.00456

2. Planned activity(ies) in support of standardization in laboratory medicine

1) In the period of 2021 – 2023 period State primary standard of DNA sequence copy number quantity unit will be created. This standard will be used for provision of metrological traceability for nucleic acid measurements in laboratory medicine on the national level.
2) Human DNA reference material with integrated part of human papillomavirus sequence HPV18 will be developed and approved.
3) In cooperation with IVD medical device manufacturer's reference material for viral load determination by NAT certified by virus-specific sequences copy number concentration will be developed. Our primary targets includes HBV, HCV and HIV.

3. Promoting traceability in laboratory medicine

Publications:

Emanuel V.L., Pronin A.N., Vonsky M.S., Chunovkina A.G., Kustova V.N., Martynova T.S., Ivanov I.V. Towards the concept of ensuring the uniformity of measurements in laboratory medicine. Measurements World. 2021. №2. p.22-26 (in Russian)

Vonsky M.S., Krylov A.I. National metrological institutes and measurements traceability provision in laboratory medicine. Laboratory Service. 2020; 9(3):41-48. https://doi.org/10.17116/labs2020903141 (in Russian)

By permission of authors was translated to Russian and published with the introduction of Beastall G.H. an article: Beastall G.H., Brouwer N., Quiroga S., Myers G.L. Traceability in laboratory medicine: a global driver for accurate results for patient care. Laboratory Service. 2020;9(3):54-64. https://doi.org/10.17116/labs2020903154 (in Russian)

Oral Presentations:

V Russian Congress with international participation "Molecular bases of clinical medicine - possible and real" (St.-Petersburg, March 21-23, 2020.)

- Vonsky M. "Development of a metrological traceability system for the results of genetic studies based on reference materials"

VII International Conference "Modern Biotechnology for science and practical applications" (St.-Petersurg, April 23-24, 2020):

- Vonsky M. "Modern trends in molecular diagnostics of HIV infection"

IV International Scientific Conference "Reference Materials for Measurements and Technologies" (St.-Petersurg, December 01-03, 2020):

- Runov A., Shevchenko N., Goryachaja T., Kurchakova E., Vonsky M. "Actual problems of reference materials development for cellular analysis"
- Vonsky M., Runov A., Kustikov Y. "Metrological support of nucleic acids measurements"
- Runov A., Kurchakova E., Vonsky M. "DNA reference materials as a way of metrological traceability of nucleic acids measuremens provision"

- Studenok V., Medvedevskih M., Sergeeva A. “Metrological support of ELISA measurements. State and development prospects”

SMSI 2021 “Sensor and Measurement Science International” (Nuremberg, Germany, May 03-06 2021,).

- Chunovkina A., Tumilovich A., Martynova T. Evaluation of precision of measurement results in medical laboratory

I All-Russian congress with international participation on fundamental problems of laboratory diagnostics “Academy of Laboratory Medicine” (Moscow, May 25 – 27, 2021):

- Vonsky M. “Clinical and metrological consensus: standardization and harmonization based on traceability of measurements”

I All-Russian Conference of Participants of the State Service of Reference Materials (Moscow, May 27, 2021):

- Vonsky M. “Reference Materials - a tool for ensuring metrological traceability of measurement results in laboratory medicine”

Conference QX ddPCR 2021 (St.-Petersburg, June 02, 2021):

- Vonsky M. “Metrological support of nucleic acid measurements - problems and solutions on the example of SARS-CoV-2”

Russian-Chinese Interenet Seminar “Metrology in Medicine and Healthcare” (July 7, 2021):

- Krylov A.I. “Development of organic component reference materials in biological matrixes for laboratory medicine”
- Chubchenko Y. “Metrological support for the diagnosis of diseases caused by *Helicobacter pylori* infection, based on the determination of carbon and oxygen isotopes in the exhaled air”

31st International Scientific Symposium “Metrology and metrology assurance 2021” (Sozopol, Bulgaria, September 07-11 2021,).

- Chunovkina A., Tumilovich A. “Analysis and evaluation of data available in a medical laboratory at estimating measurement uncertainty”,

V International Scientific and Technical Conference "Metrology of Physical and Chemical Measurements" (Moscow, September 14-16, 2021):

- Sakharova S. “Metrological support of medical measuring instruments using reference materials of physical and chemical properties”
- Runov A. “Metrology of cellular analysis – problems and solutions”
- Vonsky M. “Development of metrological support for measurements of nucleic acids”

X All-Russian scientific and technical conference "Problems of metrological support in healthcare and production of medical equipment" (Sochi, September 21–24 2021):

- Vonsky M. “Problems of the development of metrological support for measurements performed by DNA-diagnostics methods in laboratory medicine”
- Runov A. “Metrology of cell analysis - existing approaches and promising solutions”
- Kustova V. “Metrological support of clinical measurements through traceability of control materials and calibrators”
- Tumilovich A. “Measurement uncertainty calculations in laboratory diagnostics in medical decision making”

X anniversary international scientific and practical conference “Molecular diagnostics 2021” (Moscow, November 09-11 2021)

- Vonsky M. “Provision of metrological traceability for nucleic acids measurements”

During the World Metrology Day 2021 VNIIM took part in organization of the International public discussion “Measurements for Health” (May 19, 2021) – Zoom conference with Internet broadcast on Rosstandart YouTube channel. Invited foreign lecturers list includes Dr. W. Louw (CIPM); Dr R. Wielgosz (CCQM); Dr. C. Swart (PTB); Dr. M. Clievland, (NIST), Dr. L. Wu (NIMC); Dr. E.Theodorsson (JCTLM); Dr A. Bota (NMISA) Dr J. Morrow (MSU, USA); Dr M.Milavec (NIB). From Russian Federation in discussion participated specialists from Gamaleya National Center of Epidemiology and Microbiology, Pirogov Russian National Research Medical

University, Smorodintsev Research Institute of Influenza, Scientific and Methodological Center for Molecular Medicine of the Ministry of Health of the Russian Federation, VNIIFTRI, VNIIMS, VNIIM, representatives of MD IVD manufacturers.

May 20, 2021 on the public Internet discussion organized by Kazahstan NMI and devoted to the World Metrology Day 2021 a presentation "Provision of metrological traceability for measurements in laboratory medicine. Russian experience" was presented by M. Vonsky.

4. **Reference laboratory networks /collaborations focusing on developing /implementing reference measurement systems**
   VNIIM participates in activity of JCTLM TEP working group, taking part in preparation of manual on traceability in laboratory medicine.

   In 2021 VNIIM became a member of TC for standardization of the Federation of Laboratory Medicine (https://fedlab.ru/) – largest professional organization for laboratory medicine specialists in Russia.

5. **Open questions and suggestions to be addressed by JCTLM**
   Part 5 of the report not to be rendered public.