



VNIIMS

**Biennial activity report (2020-2021)
from JCTLM Member – VNIIMS,
Moscow, Russia**

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Organization: VNIIMS (All - Russian Research Institute for Metrological Service), Moscow, Russia

JCTLM Member status: JCTLM National & Regional Member

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Period covered: 2020 – 2021

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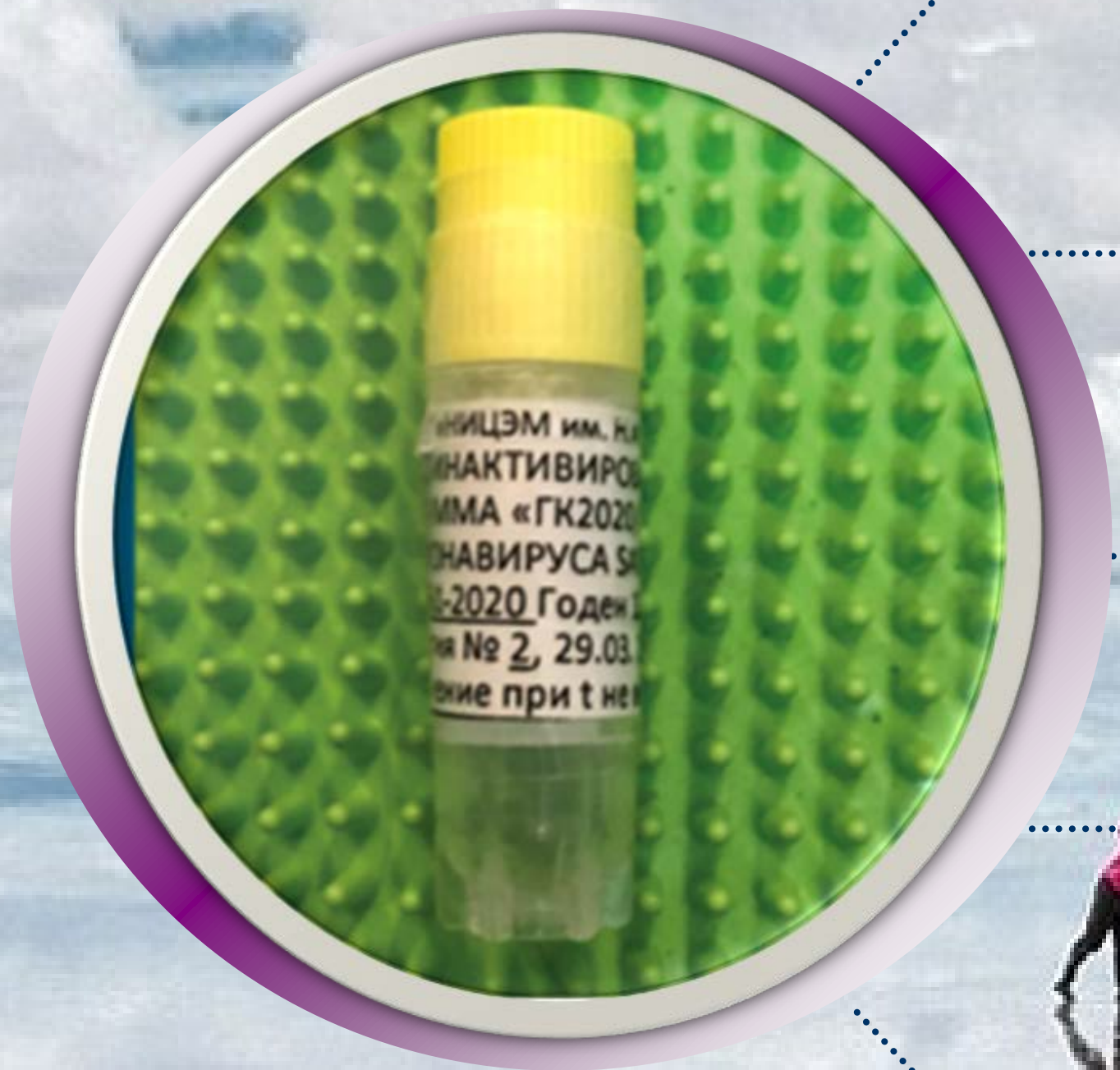
1. Major achievement(s) in support of standardization in laboratory medicine

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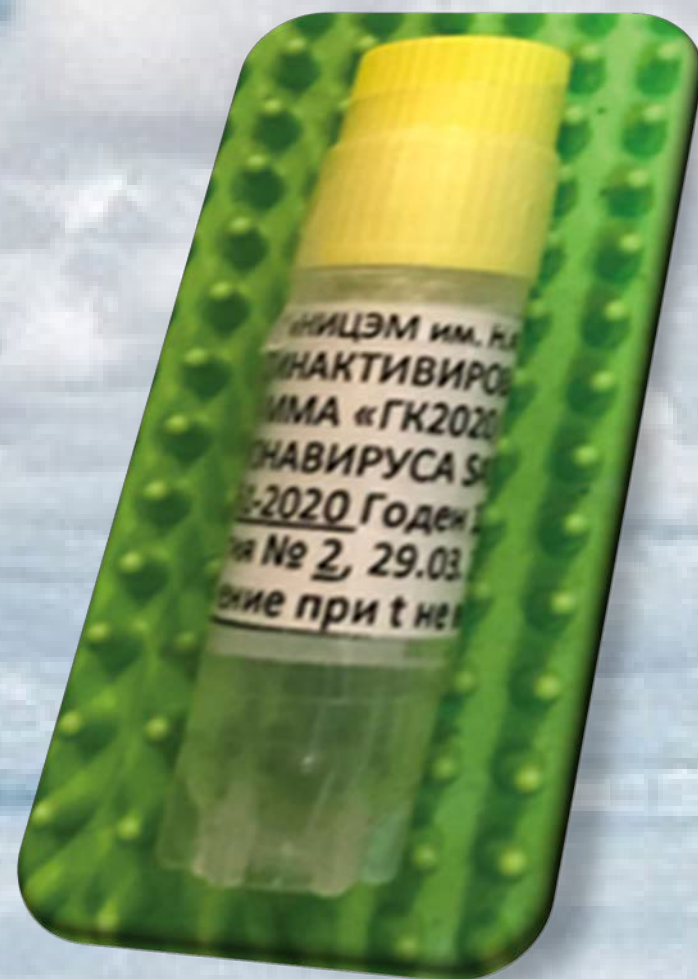
3. Promoting traceability in laboratory medicine

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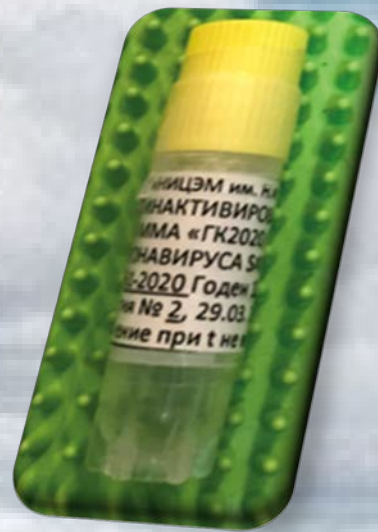
1. Major achievement(s) in support of standardization in laboratory medicine



Information on:

- the tested and approved of certified reference materials:
were tested and approved certified reference materials:
 - the reference material of inactivated strain "GK2020/1" coronavirus SARS-CoV-2;
- the development of measurement procedures:
 - measurement procedure for measurement of the reference material values for purpose of approval reference material;
- participated in testing and certified measurement procedures:
 - measurement procedure for measuring the nucleotide sequence of a section of the control region of mitochondrial DNA of fish of the families of sturgeons and copepods by Sanger sequencing using fluorescently labeled reaction terminators and using capillary electrophoresis;
- or the establishment of calibration (reference) measurement services - not.

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



The National Research Center for Epidemiology and Microbiology named after Honorary Academician N.F. Gamaleya of the Ministry of Health of the Russian Federation produced a **standard sample of inactivated strain "GK2020 / 1" coronavirus SARS-CoV-2.**

VNIIMS tested and approval reference material and developed measurement procedure of the reference material values for purpose of approval reference material.

The characteristics of the reference material were determined:

- The number of nucleotides in the genome region of the coding RNA of the SARS-CoV-2 coronavirus is 8629.
- Nucleotide sequence of a specific region of the genome of single-stranded RNA of the coronavirus SARS-CoV-2. The sequence is presented in the GISAID database (EPI_ISL_421275).
- The number of RNA copies in 1 dm³ of the standard sample material - 10⁹ - 10¹¹ copies/dm³.



ФНИЦ эпидемиологии
и микробиологии
имени Н.Ф. Гамалеи

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



VNIIMS developed measurement procedure of the reference material values for purpose of approval reference material.

The characteristics of the measurement procedure:

● Measurement range of RNA copies number	$10^9 - 10^{11}$ copies/dm ³
● Standard uncertainty (u)	2.6 %
● Coverage factor (k)	2
● Relative expanded uncertainty (Rel U)	5.2 %



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



Outline the measurement area(s)/measurands covered, and, provide a listing of the relevant technical/scientific publications:

- the measurement area(s)/measurands:
 - measurements of the enzymes catalytic concentration for laboratory medicine;
 - measurements of the purity of initial pharmaceutical substances purity (composition);
 - measurements of the mass concentration of toxicants in biological objects;
 - measuring the nucleotide sequence;

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

- the relevant technical/scientific **Journal** publications:



1	Leonid A. Konopelko, Yuri A. Kustikov, Mikhail V. Okrepilov, Anna V. Kolobova, Pavel V. Migal, Anatoly I. Krylov, Maksim S. Vonskiy, Ian K. Chubchenko, Olga V. Efremova, Elena V. Kulyabina , Vladimir I. Dobrovolskiy, Alyena Yu. Mikheeva	Measurement Techniques 2021. v. 7, p. 65–72. https://doi.org/10.32446/0368-1025it.2021-7-65-72	Development of international key comparisons in the field of chemico-analytical measurements	2021
2	Aleksandr A. Volkov, Il'ya A. Volkov, Aleksandr G. Plugov, Elena V. Kulyabina , Olga N. Melkova , Georgii S. Lavrov, Dariya V. Bocharova, Yakov I. Alekseev	Measurement Techniques 2021, v.1, p. 60-65 https://doi.org/10.32446/0368-1025it.2021-1-60-65	Genetic Analyzer Nanophore 05 as a measuring instrument for DNA sequencing	2021
3	E. V. Kuliabina , A. N. Tevyashova, S. E. Solov'eva, O. N. Melkova , E. A. Guskova	Measurement Techniques, 2020, v. 63, p. 325–331 https://doi.org/10.32446/0368-1025it.2020-4-66-71	Reference Materials of Composition of Biologically Active Substances	2020
4	E. V. Kulyabina , T. V. Kulyabina, V. V. Morozova , O. N. Melkova , E. A. Guskova	Journal of Physics Conference Series 12/2019; 1420:012016., https://doi.org/10.1088/1742-6596/1420/1/012016	Questions of metrological support for bioanalysis. Catalytic activity of enzymes	2019
5	Oleg Kubryak, Nadezda Bagdasaryan, Marina Yu. Gerasimenko, Valeriy N. Krasnov, Elena Kulyabina , Denis G. Podvoyskiy, Sergey A. Trushchelev	Monitoring of Public Opinion: Economic and Social Changes. No. 6. 2019, P. 274—292. https://doi.org/10.14515/monitoring.2019.6.15	On doctor's criticism: an interdisciplinary approach	2019
6	E. V. Kulyabina , V. V. Morozova	Legal and Applied Metrology, 3 (165)/2020, pp. 27-30 https://www.elibrary.ru/item.asp?id=43084420	Metrological assurance for measurement of catalytic activity of biological and chemical substances part 2. Normative regulation	2020

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

- the relevant technical/scientific publications:



7	Chernyshev S.L., <u>Isaev L.K.</u>, <u>Kozlov A.D.</u>	Measurement Techniques. 2020. T. 63. № 8. C. 602-609 DOI: 10.1007/s11018-020-01829-6	Mendeleev's periodic system of elements: between past and future	2020
8	<u>Isaev L.K.</u>	Legal and Applied Metrology, 4 (166)/2020, pp. 7-12 https://www.elibrary.ru/item.asp?id=44047876	Legal metrology in the country: a retrospective look	2020
9	<u>Isaev L.K.</u>	Legal and Applied Metrology, 4 (166)/2020, p. 2	Behind the line of amendment	2020

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

- the relevant comparison:

CCQM NAWG P199b: SARS-CoV-2 RNA copy number quantification

2020

Our results:

MATERIAL	MEASURAND (UNIT)
STUDY MATERIAL 1	Measurand 1 (N gene) (copies/μL)
Value (x)	1480,9
Standard uncertainty (u)	126
Coverage factor (k)	2
Expanded uncertainty (U)	252
Relative expanded uncertainty (Rel U), %	17.0
	Measurand 2 (E gene) (copies/μL)
Value (x)	979
Standard uncertainty (u)	106
Coverage factor (k)	2
Expanded uncertainty (U)	212
Relative expanded uncertainty (Rel U)	21.6
STUDY MATERIAL 2	Measurand 1 (N gene) (copies/μL)
Value (x)	11,7
Standard uncertainty (u)	2.26
Coverage factor (k)	2
Expanded uncertainty (U)	4.5
Relative expanded uncertainty (Rel U), %	38.6
	Measurand 2 (E gene) (copies/μL)
Value (x)	13,6
Standard uncertainty (u)	2.35
Coverage factor (k)	2
Expanded uncertainty (U)	4.7
Relative expanded uncertainty (Rel U)	34.6
STUDY MATERIAL 3	Measurand 1 (N gene) (copies/μL)
Value (x)	1569,2
Standard uncertainty (u)	185,2
Coverage factor (k)	2
Expanded uncertainty (U)	370,3
Relative expanded uncertainty (Rel U)	23,6

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

- organized and led a “International public discussion “measurements for health” May 19, 2021:

	Speaker	Topic
1	Dr Wynand Louw, President International Committee for Weights and Measures (CIPM)	Addressing the panelists
2	Dr Robert I. Wielgosz, Executive Secretary Consultative Committee for Amount of Substance: Metrology in Chemistry and Biology (CCQM), Director of the Chemistry Department BIPM	Accurate measurements for laboratory medicine and patient care
3	Dr Claudia Swart, PTB	Comparability of Results in Laboratory Diagnostic
4	Dr Megan Cleveland, NIST	Measurement Infrastructure to Support Health and Bioscience
5	Dr Liqing WU, NIM, P.R. China	Metrological support for protein measurement in laboratory medicine
6	Dr Elvar Theodorsson, JCTLM, Chair, JCTLM Working Group for Traceability, Education & Promotion	What is special for measurements in Laboratory Medicine
7	Dr Angelique Botha, NMISA, Chair of ISO/TC 334 – Reference materials	Metrological traceability and the role of reference materials in measurements for health
8	Dr Jayne B. Morrow, Assistant Vice President for Research and Economic Development Montana State University	A cutting-edge response to COVID challenges and potential future challenges. Recommendations for the metrology community
9	Dr Mojca Milavec, NIB, Slovenia	Wastewater surveillance for SARS-CoV-2 in Slovenia
10	Dr Vladimir Gushchin, The Gamaleya National Center for Epidemiology and Microbiology	Competitiveness of Russian test systems and their components at the international level

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

- organized and led a “International public discussion “measurements for health” May 19, 2021:

	Speaker	Topic
11	Dr. Denis Rebrikov, professor RAS, Vice-rector for scientific work Pirogov Medical University	Metrological support of traceability of measurement results in DNA diagnostics
12	Dr Andrey Komissarov, Smorodintsev Research Institute of Influenza	Prospects for metrological support of genetic surveillance for SARS-CoV-2
13	Dr. Vladimir Emanuel, Director, Professor Scientific and Methodological Center of the Ministry of Health of Russia for Molecular Medicine on the basis of the Pavlov University	Improvement of the system for ensuring the uniformity of measurements in laboratory medicine
14	Dr. Yakov Alekseev, Science Director, Synthol LLC Dr. Vladimir Kurochkin, Institute for Analytical Instrumentation, RAS, Head of the direction of development of devices for genetic and immune analysis	Genetic analyzers of three generations as measuring instruments in DNA sequencing
15	Dr. Vladimir Dobrovolsky, VNIIFTRI	Metrological support for measuring the characteristics of filter materials for individual and collective respiratory protection
16	Dr Alexander Berlyand, VNIIFTRI	Metrological support for measuring the characteristics of ionizing radiation in radiation therapy
17	Dr Elena Kulyabina, VNIIMS, Moscow	Metrology for bioanalysis
18	Dr. Maxim Vonsky, D.I. Mendeleev Institute for Metrology (VNIIM)	Metrological traceability of nucleic acid measurements
19	Alexander Chubarov, D.I. Mendeleev Institute for Metrology (VNIIM)	Functional diagnostics. Significance and promising directions of development
20	Ilya Alekseev , D.I. Mendeleev Institute for Metrology (VNIIM)	Metrology of radionuclide activity in medicine: ensuring traceability of a unit of radionuclide activity in radiopharmaceuticals. Challenges and scientific and technical problems of ensuring the uniformity of measurements of the activity of radionuclides in radiopharmaceuticals
21	Dr Max Ryadnov, NPL, United Kingdom	Developing a toolbox of reference materials for healthcare

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



R&D project(s) and/or programme(s) planned by our institute in the next two years including information on: new measurement area(s)/measurands of interest for us:

1. R&D project – Development of reference procedure of the analytical sensitivity and risk assessment of false positives of diagnostic tests for the determination of SARS-CoV-2 coronavirus RNA *in vitro*, including getting false positive and false negative results.

This measurement procedure involves the use of a reference material of inactivated strain "GK2020 / 1" coronavirus SARS-CoV-2.

This measurement procedure will be used to obtain:

- the results of measurements of analytical sensitivity and determine the risks of false positives of diagnostic tests used to determine the SARS-CoV-2 coronavirus *in vitro*, including obtaining false positive and false negative results,
- the copies number of the inactivated strain of the SARS-CoV-2 coronavirus,
- ensuring metrological traceability of copies number measurement results.

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



R&D project(s) and/or programme(s) planned by our institute in the next two years including information on: new measurement area(s)/measurands of interest for us:

2. R&D project – Development of reference procedure (maybe universal) for measuring the DNA / RNA sequence of infectious agents
3. R&D project – Development of reference procedure for measuring the human DNA sequence
4. R&D project – Development of reference procedure (maybe universal) for measuring any animals DNA sequence

3. Promoting traceability in laboratory medicine

Our institute activities - a listing of our publication(s), presentation(s) and other communication(s) on traceability at international and national conferences:



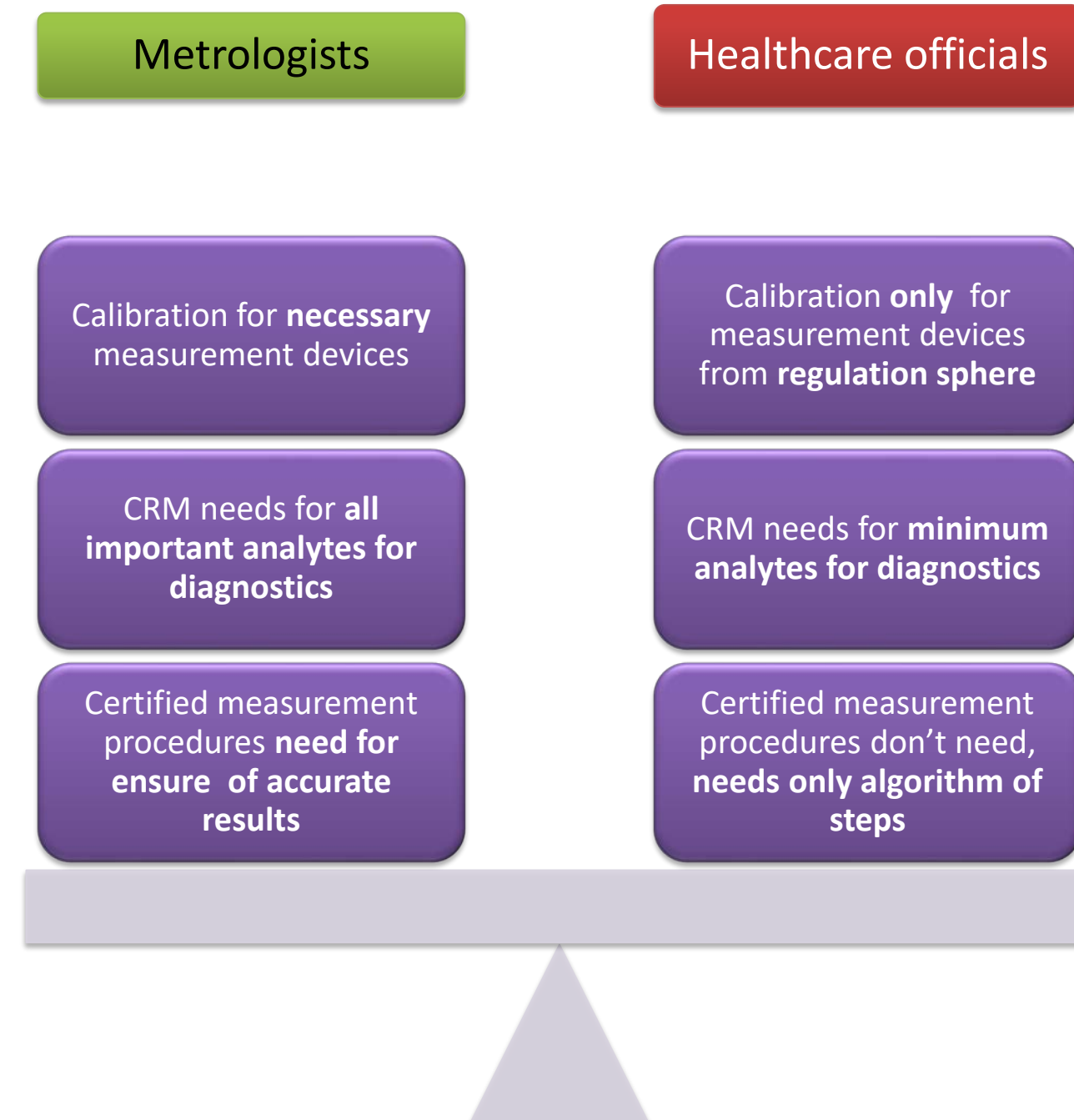
1	<u>E.V. Kulyabina, A.D. Kozlov, V.A. Kolobaev, O. N. Melkova, V.V. Morozova</u>	X All-Russian Scientific and Technical Conference “Problems of Metrological Support in Health Care and Production of Medical Equipment”. Abstracts, 09/2021, p.21-24 https://www.vniiofi.ru/news-list/news-20210930-1.html	Means of metrological support of measurements in laboratory medicine – reference materials, GSSSD data, calibrators	2021
2	<u>E.V. Kulyabina, O.N. Melkova, T.V. Kulyabina, Morozova V.V., Morozov V.U.:</u>	V International Scientific and Technical Conference "Metrology of Physical and Chemical Measurements". Abstracts, 09/2021, p.137-139 https://www.vniiftri.ru/press/news/nachala-svoyu-rabotu-v-mezhdunarodnaya-nauchno-tekhnicheskaya-konferentsiya-metrologiya-fiziko-khimi/	Issues of metrological assurance of measurements in areas of activity that contribute to improving the quality of human life	2021
3	<u>O.N. Melkova, E.V. Kulyabina, A.A. Volkov, S.U. Fomina</u>	V International Scientific and Technical Conference "Metrology of Physical and Chemical Measurements". Abstracts, 09/2021, p.150-154	Metrological support of molecular genetic expertise on the example of identification of fish products	2021
4	<u>Elena Kulyabina</u>	I All-Russian Conference of Participants of the State Service of Reference Materials of Composition and Properties of Substances and Materials (GSSO), 05/2021 https://www.vniim.ru/news.html	Issues of creating reference materials of composition, structure and properties of substances measured in "non-existent" units of physical quantities	2021
5	<u>Elena Kulyabina</u>	CCQM NAWG, BIPM, online-meeting, 13 Jan. 2021. Presentation	VNIIMS’ SARS-CoV-2 RNA related work	2021

4. Reference laboratory networks /collaborations focusing on developing /implementing reference measurement systems

We regularly organize and participate in meetings / discussions on the development of solutions to complex issues between physicians, manufacturers of measuring instruments, medical devices, reference materials, calibrators and consumers of metrological services, clinical diagnostic laboratories, hospitals, scientific institutions:

- according to a unified terminology both in metrology and in laboratory medicine,
- on the use of reference measurement procedures and reference materials in medical laboratories,
- on the convergence of the points of view of healthcare officials and metrologists,
- to ensure metrological traceability for in vitro diagnostic medical devices to the highest available level of the reference measuring system,
- on the development of new, more successful and simple methods for testing the functionality and metrological characteristics of medical devices, etc.

Several question between parties:



5. Open questions and suggestions to be addressed by JCTLM



Our Institute has suggestions:

As part of the work of JCTLM, carry out constant monitoring and forecasting of newly emerging dangerous pathogens.

As a perspective development within the JCTLM framework we offer the following works:

- a. development of CRM biomarkers of diseases (strains of coronavirus, bacteria, pathogenic biological agents ...);
- b. development of marker identification methods (measurement procedures);
- c. development of reference methods for measuring the composition of markers in a biological object (new);
- d. monitoring existing and emerging needs for DNA sequence decoding:
 - living organisms (endangered species);
 - raw materials for food production (origin of raw materials, impact on the quality of final products);
 - materials for transplantation of donor organs, synthetic materials...



Thank You for attention!
Health for everybody!

