Sistema Interamericano de Metrología

DEVELOPMENT OF BASIC METROLOGY INFRASTRUCTURE TO SUPPORT MEDICAL TESTING EQUIPMENT (VENTILATORS)

with support from

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February 18th, 2021

Activity N°4: **Virtual Workshops: Technical exchange and knowledge transfer**

SIM Technical Exchange, 2nd Workshop

Wednesday February 24th, 2021. 14:00 to 16:30 (UTC time)

Introduction:

The Covid-19 pandemic demonstrates that health systems in most Latin America and the Caribbean are not well prepared for such a crisis. One of the most important bottlenecks to date are the lack of respiratory equipment, intensive care units, sufficient and sure oxygen supply and enough qualified medical personnel for handling this equipment. The demand for mechanical ventilators increased dramatically but could not be satisfied by the existing producers. Some Latin American countries made a lot of efforts to overcome this situation and to promote the development of low cost ventilators and testing facilities.

SIM and PTB have agreed to execute a project that should help to overcome the bottleneck mechanical ventilators. That is not only important in times of the CoVID-19 pandemic but also in a long-term perspective for all diseases that need artificial ventilation, and to ensure the quality of these equipments, controlling that all the functioning parameters (with focus in flow and volume) fulfill the established requirements.

An important component of the project consists in some virtual workshops that have as objectives:

- Facilitate the exchange of experiences of the initiatives that different NMIs have developed in the field of mechanical ventilators,
- Disseminate the lessons learnt,
- Improve the technical knowledge of the participants and enable the technology transfer,
- Exchange the experiences in the accuracy of the measurement methods,
- Strengthen the relationship between NMIs, research laboratories and industry,

Create awareness in the Latin American and Caribbean health sector for the importance of a functioning metrological infrastructure.

During this workshop metrologist and experts from América will share experiences in the fight against worldwide historical pandemic crisis, presenting the following topics:

Presentation 1: Ventilators for Panama Initiative-VPP. CENAMEP AIP - INDICASAT AIP, Panamá.

Presentation 2: Importance and impact of microvolume measurements in clinical assay. INN - ISP, Chile.

Presentation 3: Implementation of INACAL gas flow measurement systems for calibration of flow patterns (of mechanical Ventilators). INACAL, Perú.

Presentation 4: Development of basic metrology infrastructure to support medical testing equipment (ventilators), SIM-PTB Project. Activities 1, 2 and 3. INMERO, Brasil / CENAM, Mexico / INEN, Ecuador.

Presentations info:

Presentation 1

Title: **Ventilators for Panama Initiative-VPP**

NMI: **CENAMEP AIP** - **INDICASAT AIP** (Panamá)

Presenter: **Rolando A. Gittens, PhD**. Center for Biodiversity & Drug Discovery, Instituto de Investigaciones Científicas y Servicios de Alta Tecnología (INDICASAT AIP)

Abstract: In Panama, the mathematical models developed at the beginning of the COVID-19 pandemic, in March 2020, projected a collapse of the health system at the end of April, with tens of thousands of infected, thousands in intensive care, and hundreds of deaths, mainly due to lack of human resources, supplies and equipment such as mechanical ventilators. This catastrophe was avoided through drastic mitigation and quarantine measures for an extended period of time. However, the global shortage of these equipment due to the export bans of the manufacturing countries that are also in need of them, among other problems such as price volatility and the asymmetry of negotiating power of small countries like Panama, put the focus of attention on the local capacity to manufacture these devices.

With this scenario in mind, since the end of March the initiative "Ventiladores por Panamá" was organically created to support the development of emergency mechanical ventilators manufactured locally by teams of engineers from universities, research centers and private companies. The objective is to support the Ministry of Health (MINSA) with the health crisis and global shortage of equipment faced by COVID-19, with a strategic local inventory of emergency mechanical ventilators that serve as a containment plan in case that the intensive care resources of our public health system are saturated. One of the most important roles of the Ventiladores por Panamá initiative was to establish a structure to validate the functioning of the devices, which had three phases:1) functional tests with medical simulation mannequins; 2) preclinical trials with healthy animals; and 3) preclinical trials in a lung injury model that simulates COVID-19 respiratory distress. After eight months of exemplary interdisciplinary and interinstitutional work focused on the single goal of saving lives, we now have two locally designed and manufactured emergency mechanical ventilator devices that have been validated through the three evaluation phases. In this presentation we will provide details on the validation tests and some design criteria that were implemented so that the teams could move forward in the most efficient way.

Presenter Bio data: Dr. Rolando A. Gittens received his Bachelor in Electrical and Electronics Engineering from the Technological University of Panama (2006), and his Master in Materials Science & Engineering (2011) and PhD in Bioengineering (2012) from the Georgia Institute of Technology. His research focuses on the role of nanostructural and electrical properties of biomaterials in cell differentiation processes for tissue regeneration. His work has resulted in one patent and another active application for surface nanomodificación of titanium implants, more than 20 publications in high impact journals, co-authorship in a book chapter and prestigious awards such as the TWAS-ROLAC Affiliated Member recognition in 2017, being named one of Central America Innovators Under 35 by the MIT Tech Review, obtaining several Young Investigator Awards in recognized international conferences, and being appointed as a Distinguished Member of the National Research System (SNI) in Panama. Currently, Dr. Gittens is a Research Engineer at the Institute for Scientific Research and High Technology Services (INDICASAT AIP) in Panama, where he continues to study biomaterials and stem cells for regenerative engineering, as well as applications of mass spectrometry for innovations in public health. Finally, he actively applies his soft skills in intellectual property and scientific diplomacy for scientific lobbying to enact laws that support the Science, Technology and Innovation system. Dr. Gittens also works as a consultant for business innovation through R&D and the formulation of new ventures.

Presentation 2

Title: **Importance and impact of microvolume measurements in clinical assay**

NMI: **INN** - **ISP** (Chile)

Presenter: **QF., Mgtr. Soraya Sandoval Riquelme.** Head of the Designated Laboratory and Candidate of Metrology of the Institute of Public Health of Chile (ISP). Head of the Sub-department of Metrology and Technological Development of the Department of Environmental Health of the ISP. soraya@ispch.cl

Abstract: The Public Health Institute (ISP), within the framework of the Health Authority law, is responsible for the "Inspection of Compliance with Quality Standards and Accreditation of Clinical Laboratories and Blood Banks". The accreditation of clinical laboratories is carried out under the ISO 15189: 2012 standard "Medical laboratories - Quality and competence requirements". This standard establishes within the requirements of "Calibration and metrological traceability of equipment" that there must be a documented procedure for the calibration of equipment that directly or indirectly affects the results of the tests, thus ensuring the adequate precision of the measurement.

Among the equipment that the laboratory must verify to evaluate adequate performance during the assay process, are automatic pipettes that are widely used by clinical laboratories. This makes us wonder: What is the national need to ensure metrological traceability of micro-volume measurements? What is the impact it will have on the accuracy of the results? How does the volume measurement influence the uncertainty of the results? To answer these questions, it is necessary to know what types of automatic pipettes laboratories use, in what stages of the test they are used, and thus establish the volume measurement range and thus identify the calibration needs.

Due to the global pandemic of COVID-19, Chile, like all countries, had to expand its diagnostic capacity by RT-PCR, for which the Ministry of Health (MINSAL) created the COVID-19 Laboratory Network. The national analytical capacity in February 2020 was a single laboratory (ISP) with a capacity of 550 samples per day for the analysis of SARS-CoV-2. As of november of the same year, the capacity was increased to 54,400 daily samples through 145 laboratories nationwide.

The reliability of the results for the purpose of an adequate diagnosis of the patient is fundamental, the sources of random variation that affect the results of the analyte measured in the patient sample are: Pre-analytical (preparation, sample taking, sample preparation and sample management), analytical (imprecision and bias) and biological (patient-specific). During the preanalytical and analytical stage of PCR, a series of microvolume measurements are performed for the extraction of RNA from the sample and the preparation of the reagents involved in the amplification and visualization of the result. In this regard, volume measurement contributes significantly to the measurement uncertainty of the PCR test for COVID 19, as in other clinical assay.

In order to collect information on the pipettes used in Chile in clinical laboratories, the antecedents of the National Laboratory and Department of Biomedical Reference of the ISP were collected, and in this way to be able to have a projection at the country level of the types of pipettes and ranges of measurement volumes. The clinical laboratories of this Department have around 530 pipettes, of which 87% correspond to simple pipettes of variable volume, the volume measurement ranges from 2 μL to 10 mL, a total of 33% of the pipettes used have a capacity less than 20 μL. For the ISP, the cost of calibrating automatic pipettes (clinical laboratory only) to an accredited external calibration laboratory would be around US $ 89,143 (per year).

The implementation of the Volume Laboratory of the Physical Metrology Unit (In the Designated Metrology Laboratory of the ISP) in 2012 for the purposes of internal verification of pipettes, has allowed a significant saving of institutional resources in the maintenance and calibration program of computers in the ISP. In order to be able to support the ISP's clinical laboratories, the definition of the personnel in charge of the pipette verification process had to be carried out and an annual verification frequency of pipettes was established, the ISP's Designated Metrology Laboratory ,

through the Physical Metrology Unit, used the definition of verification protocols, training of personnel responsible for the verification of pipettes, and the skills of analysts in terms of good laboratory practices in the use of pipettes were strengthened, balances, metrological traceability, use and interpretation of calibration certificates according to ISO / IEC 17025.

The role of National Metrology Institutes (NMIs) is essential in order to strengthen the competencies of professional analysts, as well as; ensure the metrological traceability of the measurements made by clinical laboratories, and thus support the assurance and reliability of the results for diagnostic purposes.

Key Words: micro-volume, pipettes, metrological traceability, COVID 19, Verification.

Presenter Bio data: Ms. Sandoval has a Bachelor's Degree in Pharmaceutical Chemistry from the Universidad de Concepción and a Master's degree in Health Institution Management from the Universidad Mayor.

In 1998, she began to work at the Institute of Public Health of Chile (ISP), the National Reference Laboratory of Chile, in charge of the Water Chemistry Laboratory. In 2007, he was entrusted with the development of the metrology area of the Department of Environmental Health, creating the Environmental Metrology and Food Section, focused on the development of food metrology at the national level, developing reference materials and proficiency testing, this under the international quality standards ISO 17043, ISO / IEC 17025 and ISO 17034. In 2012, the Section joined the National Metrology Network of Chile (RNM). She is the head of this section until 2016, when she assumes the Head of the Sub-department.

Through the ISP, it carries out technology transfer, audits, training and supervision of laboratories of the National Network of Environmental Laboratories of the Ministry of Health. She has directed various Degree Theses and has extensive participation in Congresses, giving conferences on his specialty. She has been a researcher in various Research Projects related to the subject of his specialty. She is the Lead Auditor of ISO / IEC 17025 and ISO 17043. Coordinator and Delegate of the National Subcommittee on Methods of Analysis and Sampling of the Codex Alimentarius (CCMAS), representative of the ISP in CAPCHICAL and member of SOCHITAL. It participates in the Consultative Committee of Chilean Standards of the National Institute of Standardization (INN) in matters of metrology, food and water, as well as in working groups of National Regulations of the MINSAL. During his professional practice she has acquired extensive experience in research in metrology, production of reference materials, metrological traceability, physical metrology, organization of aptitude tests, environmental and food regulations, application of analytical methods and quality control and food safety. Representative of Chile in the CCQM Working Group on Inorganic Analysis (CCQM-IAWG) of the International Bureau of Weights and Measures, BIPM.

Presentation 3

Title: **Implementation of INACAL gas flow measurement systems for calibration of flow standards (of mechanical Ventilators).**

NMI: **INACAL** (Perú)

Presenters: **Ing. Carlos Ochoa**

Abstract: INACAL's Gas Flow Laboratory has flow measurement systems used for the calibration / verification of natural gas meters and flow meters used in air quality monitoring activities, these systems have been adapted for the calibration of gas flow analyzers, standards used in the verification of mechanical ventilators.

For the calibration of the flow analyzers, a Bench of volumetric meters are used, consisting of a Rotary meter and a wet gas meter for the high range and a Bench with a Positive Displacement piston for the low range. The test benches reach a measurement uncertainty less than 0.3% which makes it possible to use them in the calibration of flow analyzers.

Presenter Bio data: Chemical engineer Carlos Ochoa is currently the head of the gas flow laboratory of the Metrology Directorate of the National Quality Institute, INACAL, with more than 10 years of experience in metrology in the magnitudes of gas flow, liquid flow, temperature and pressure. He participated in the implementation of the measurement systems and approval of the quality management system of the gas flow and liquid flow laboratories review by QSTF.

Carlos Ochoa participated in the development of the measurement systems for the gas and liquid flow laboratory used in the services that INACAL currently offers such as calibration and verification services of natural gas meters for residential, commercial, industrial and vehicular use, verification of gas meters. water, gas meter model evaluation, water meter model evaluation and calibration of gas and liquid flow meters.

Presentation 4

Title: **Development of basic metrology infrastructure to support medical testing equipment (ventilators), SIM-PTB Project. Activities 1, 2 and 3**

Presentation 4.1

Title: **Activity 1. Design and development of a Low Cost Flowmeter for mechanical ventilators**

Duration: 10 min (max)

NMI: **INMERO** (Brasil)

Presenter: **Fábio Ouverney Costa**. Chefe Substituto da Divisão de Metrologia em Dinâmica de Fluidos (Dinam). Chefe do Laboratório de Vazão de Gás - Lagas. Instituto Nacional de Metrologia, Qualidade e Tecnologia (Inmetro). Diretoria de Metrologia Científica e Tecnologia (Dimci). Divisão de Metrologia em Dinâmica de Fluidos(Dinam)

Abstract: The aim of the project is to design a gas flow calibration bench and a low-cost portable multi-variable testing device for medical equipments, including mechanical ventilators, anaesthesia machines, flowmeters and pressure gauges. It will be able to reliably and accurately measure flow rate, gas volume and pressure values to compare it with setup values, based on ISO 80601-2-12 standard. All of the variables will be traceable to National Standards.

The calibration bench will be based on a Master Meter and is being designed to calibrate flowmeters up to 250 slpm with air. Other gases may be considered in the future as well. The testing device will be a two-port compact device, on which the tubes from the equipment under test will be hooked on the inlet port and a simulated lung on the outlet port. This way, all of the main parameters from ISO 80601-2-12 may be checked.

By the end of the project, we intend to make the technology avaiable for production and to have a intercomparison with other NMIs

Presenter Bio data: My technical background is in Control and Automation Engineering, with master degree in Instrumentation and Photonics. I'm the head of the Fluid Flow Laboratory, at the Fluid Dynamics Division, from The Brazilian National Institute of Metrology (Inmetro). Right after graduating, I was admitted at Inmetro where I started working with automation. In 2016 I started working with fluid speed standardization and in 2018, with liquid and gas flowmeters. Nowadays, most of my work is related to the oil industry, with projects about alternative calibration methods (transferable calibration), and to the development of primary standards.

Presentation 4.2

Title: **Activity 2. Design and build a Lung Simulator as a basic infrastructure for the testing of mechanical ventilators**

Duration: 10 min (max)

NMI: **CENAM** (Mexico)

Presenter: **Roberto Arias**

Abstract: The project is about the design and construction of a human lung simulator prototype that can be used not only to test mechanical ventilators but also to train physicians on the functioning of the respiratory system. The aim of the project is to create a simulation tool that is able to replicate different abnormal respiratory behaviors.

Presenter Bio data: Mechanical Engineer. Joined CENAM in 1993. Worked at the Gas Flow Laboratory. Member of the CENAM Uncertainty Working Group. Former Chairman of the SIM MWG 10 for Volume and Flow. Responsible of the 2003 and 2012 CIPM CCM.FF-K4 Key Comparisons for Volume of Liquids. Member of the CIPM WGFF and IMEKO TC-9

Presentation 4.3

Title: **Activity 3. Improve and strengthen the micro-volume calibration processes in LNM-INEN**

Duration: 10 min (max)

NMI: **LNM-INEN** (Ecuador)

Presenter: **Ing. Victor Guevara**

Abstract: The project presented by the National Metrology Laboratory aims to promote their participation at the international level and strengthen the activities carried out by the Volume Laboratory. In addition, increase its microvolume measurement range, by gravimetric method, maintaining its metrological traceability to the Units of the International System through the National Mass Standards.

The project arises internally due to the growing demand for a calibration services for instruments that measure volume lower than 20 µL and which is currently accentuated due to the global health crisis. The proposal aims to ensure measurements in the calibration processes of instruments to measure microvolume, in order to improve and increase the measurement and calibration capabilities, as well as the technical capacity and competence of the personnel. This requires the assistance of NMI's with greater knowledge and development on the area, participation in comparisons, in general, the support of the INM's in the region and those who wish to join.

Presenter Bio data: Currently, Head of the Fluids Division at the National Metrology Laboratory - INEN. Victor is from Ecuador, born in 1978. Bachelor of Science, Chemical-Biologist Specialist, from the National College "Juan de Salinas" (Sangolquí). Chemical Engineer graduated from the National Polytechnic School (Quito).

Between 2007 and 2014, collaborated in "Environmental Control" laboratories as a Project Technician performing measurements of combustion gases and particulate matter in fixed combustion sources, under Management Systems guidelines based on the ISO / IEC 17025 standard. In February 2014, started working in the Ecuadorian Institute for Standardization, in the area of technical regulation. As of July of the same year, he became part of the human talent at the National Metrology Laboratory.