EMPIR Call 2020 – Fundamental, Industry and Normative

Selected Research Topic number: **SRT-n14**
Version: 1.0

Title: Establishing metrology standards in microfluidic devices

Abstract

Microfluidics is concerned with fluid-handling in the nano-to-millilitre scale and has major applications in biomedical and chemical analysis however global standards are lacking. ISO/TC48/WG3 has been set up to develop microfluidic standards covering metrology for the methodologies and fabrication processes that are essential to ensure measurement accuracy and traceability of devices. The goal of this project is to contribute to the development of globally accepted standards for microfluidics and disseminate them to end users in industry (health, pharmaceutical) and academia.

Keywords

Microfluidics, standards, protocols, microfabrication, lab-on-chip, organ-on-a-chip, flow control, testing methods, metrology, traceability.

Background to the Metrological Challenges

The increased technical capability required to miniaturise devices along with the growing need for faster, more accessible and cost-effective solutions for precision analytical tools has led to the rapid growth of microfluidics (study of fluid behaviour in micron-sized fluidic passages) in a diverse group of sectors (e.g. pharmaceutical and biomedical industries). However, due to this rapid growth, microfluidics and specifically the control of fluids in microfluidic devices still lacks universal solutions and standards. Stakeholders from industry, academia and government have recognised these needs and as a result ISO/TC48/WG3 has been set up to develop microfluidic standards covering metrology for the methodologies and fabrication processes that are essential to ensure measurement accuracy and traceability of devices.

Different types of equipment (e.g. syringe and capillary pumps) are used to generate and control flows in microfluidic systems however volumetric flow rate accuracy has not yet reached a satisfactory level. It is necessary to characterise components within a system in order to correctly model and predict the system level behaviour and to make decisions regarding component usability and interchangeability. As such, there is an immediate need to map and categorise components used for flow control in microfluidic systems. Standardisation of performance characteristics is needed for the different classes of components, including test conditions, measurement protocols and guidelines. The increasing demand for passive flow devices has already led NMIs to develop protocols and calibrations services for the small flow rates. Traceability to National Standards has been available since 2012 down to 0.1 µl/min but there is the need to transpose this information to the microfluidics technology, especially for flow control specifications.

The development of testing methods is fundamental in order to address different key measurement quantities in a variety of materials and production schemes for microfluidics to ensure measurement accuracy and traceability. Testing methods and procedures for microfluidics are usually user/manufacturer or device specific.

Interfaces, connectivity, modularity and sensor integration in microfluidic devices are becoming strong requisites as the market is gaining maturity and moving towards mass production. Currently, manufacturers offer individual solutions for their own dimensions and connecting procedures without any harmonisation and consequently a wide variety of materials and formats are required to interface with each other. There is clear demand for a standardised way in which these interchangeable components interoperate.

In 2016, a first step towards microfluidic standardisation was made with the development of ISO IWA23. The document was created to facilitate the uptake of microfluidic devices by making them easier to use, reducing the cost for assembling and enabling plug and play functionality. However, this standard lacks the metrological specifications required for accurate and reproducible manufacturing.

EURAMET EMPIR MSU
Phone: +44 20 8943 6666 Email: EMPIR.msu@euramet.org
msu.euramet.org

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Objectives

Proposers should address the objectives stated below, which are based on the PRT submissions. Proposers may identify amendments to the objectives or choose to address a subset of them in order to maximise the overall impact, or address budgetary or scientific / technical constraints, but the reasons for this should be clearly stated in the protocol.

The JRP shall focus on metrology research necessary to support standardisation for microfluids used in the health and pharmaceutical industry.

The specific objectives are

1. To investigate, evaluate and formulate consensus-based flow control specifications to enhance the manufacturing capability of the microfluidics industry supply chain through voluntary compliance.
2. To develop measurement protocols for different quantities (e.g. flow rate and liquid properties), in different microfluidics devices, to be used in pharmaceuticals, biomedical and mechanobiology applications. A EURAMET guide on these measurement protocols should be developed.
3. To define general standards and guidelines for interfaces and connectivity between fluidic passages and optical/electrical connections of microfluidics components and corresponding measurement standards, from micro to macro size scales.
4. To define guidelines for the standardisation of dimensions and accuracy for modularity (either module-to-module or module-to-world) and sensor integration (combination of sensing elements/materials with microfluidic modules).
5. To contribute to the standards development work of ISO/TC 48 and ISO IWA23 to ensure that the outputs of the project are aligned with their needs. The project outputs from objective 1-4 shall be communicated and disseminated quickly to those developing the standards and to those who will use them (health and pharmaceutical industry), and in a form (e.g. specifications and guidelines) that can be incorporated into the standards (e.g. new technical guides,ISO-10991 and ISO/AWI 22916) at the earliest opportunity.

The proposed research shall be justified by clear reference to the measurement needs within strategic documents published by the relevant Regulatory body or Standards Developing Organisation or by a letter signed by the convenor of the respective TC/WG. EURAMET encourages proposals that include representatives from industry, regulators and standardisation bodies actively participating in the projects. The proposal must name a “Chief Stakeholder”, not a member of the consortium, but a representative of the user community that will benefit from the proposed work. The “Chief Stakeholder” should write a letter of support explaining how their organisation will make use of the outcomes from the research, be consulted regularly by the consortium during the project to ensure that the planned outcomes are still relevant, and be prepared to report to EURAMET on the benefits they have gained from the project.

Proposers should establish the current state of the art, and explain how their proposed research goes beyond this.

In particular, proposers should outline the achievements of the EMRP project HLT07 MeDD and EMPIR projects 15SIP03 InfusionUptake and 18HLT08 MeDDII and how their proposal will build on those.

EURAMET expects the average EU Contribution for the selected JRPs in this TP to be 0.8 M€, and has defined an upper limit of 1.0 M€ for this project.

EURAMET also expects the EU Contribution to the external funded partners to not exceed 30 % of the total EU Contribution across all selected projects in this TP.

Any industrial partners that will receive significant benefit from the results of the proposed project are expected to be unfunded partners.

Potential Impact

Proposals must demonstrate adequate and appropriate participation/links to the “end user” community, describing how the project partners will engage with relevant communities during the project to facilitate knowledge transfer and accelerate the uptake of project outputs. Evidence of support from the “end user” community (e.g. letters of support) is also encouraged.

You should detail how your JRP results are going to:

- Address the SRT objectives and deliver solutions to the documented needs,
- Feed into the development of urgent documentary standards through appropriate standards bodies,

- Transfer knowledge to the heath and pharmaceutical sector.

You should detail other impacts of your proposed JRP as specified in the document “Guide 4: Writing Joint Research Projects (JRPs)”

You should also detail how your approach to realising the objectives will further the aim of EMPIR to develop a coherent approach at the European level in the field of metrology and include the best available contributions from across the metrology community. Specifically, the opportunities for:

- improvement of the efficiency of use of available resources to better meet metrological needs and to assure the traceability of national standards
- the metrology capacity of EURAMET Member States whose metrology programmes are at an early stage of development to be increased
- organisations other than NMIs and DIs to be involved in the work.

Time-scale

The project should be of up to 3 years duration.