EMRP Call 2011 - Health, SI Broader Scope & New Technologies

Selected Research Topic number: **SRT-h18**
Version: 1.0

Title: Metrology for drug delivery

Abstract

To improve the accuracy and efficiency of patient treatment, methods need to be developed for the reliable and accurate delivery of drugs to patients. In order to do this, the metrological infrastructure for pharmaceutical drug delivery needs improving; it requires a primary standard for flow rates from 150 μl/min to 1 nl/min, the characterisation of flow meters and flow generators and the validation of infusion pumps.

Conformity with the Work Programme

This Call for JRPs conforms to the EMRP Outline 2008, section on “Grand Challenges” related to Health on pages 7 and 8 and in the sections on pages 21 and 22.

Keywords

drug delivery, flow meters, flow generators, infusion pumps, flow sensors, pulsating flow

Background to the Metrological Challenges

During the last decades, developments in Micro-Electro-Mechanical Systems and Nano-Electro-Mechanical Systems have enabled the integration of multiple elements such as sensors and electronics on a common silicon substrate. The important health related applications of this include miniaturised flow sensors, medical diagnostics, pharmaceutical drug delivery and implanted infusion pumps.

Currently, implantable infusion pumps are predominantly used for pain-therapy. The pumps can deliver flow rates down to 300 nl/min, however they do not contain flow sensors and hence cannot measure the output of the drug. Further to this the development of new and more effective drugs means that a reduction in flow rate to 1 nl/min is required. However, flow rates of 1 nl/min cannot currently be measured by conventional sensors. Thermal flow sensors are the most promising candidates for measuring flows in the nl/min range, but they require fluid-specific calibration, as their performance is fluid-dependent. Therefore, new validated flow sensors that can measure 1 nl/min need to be produced and integrated into infusion pumps.

In addition to this, there is no reliable, primary standard for drug delivery at flow ranges down to 1 nl/min. The development of a primary standard for such flow rates is an urgent requirement for the calibration of flow sensors. Such a standard would support the use of flow sensors and would also help infusion pumps to meet current legislation (e.g. European Directive 93/42/EEC) [1] and standards (e.g. ISO 8536-1 to 12 - Infusion equipment for medical use [2] , ISO 28620:2010 - Medical devices, non-electrically driven portable infusion devices [3]).

Standard miniaturised connectors, to couple together flow sensors and generators are also required to support accurate drug delivery and calibration.

In terms of producing constant flow rates; gas-driven infusion pumps presently have the advantage over the pulsating flow of motorised peristaltic pumps. However, gas-driven pumps require an adjustable flow restrictor to do this. For infusion pumps such as rotation/stepper type pumps, flow rate is calibrated with a reference, however, installation effects can cause significant errors in flow rate.

Other parameters that affect infusion pump flow rate and hence drug delivery, include drug type (e.g. viscosity), (hydrostatic) pressure, temperature and pump usage pattern.

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EMRP
European Metrology Research Programme
Programme of EURAMET

The EMRP is jointly funded by the EMRP participating countries within EURAMET and the European Union

Scientific and Technological 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 JRP-Protocol.

The JRP shall focus on the measurement and characterisation of drug delivery flow meters and flow generators to provide traceability for infusion pumps and enable reliable, highly efficient drug delivery to patients.

The specific objectives are:

1. To develop and characterise a primary standard for drug delivery at liquid flow rates of 150 μl/min - 1 nl/min. The primary standard should have an uncertainty of < 0.5 % under atmospheric conditions.
2. To evaluate existing flow meters with focus on their behaviour for pulsating flow.
3. To perform quantitative and traceable analysis of infusion pumps (e.g. dispensing systems such as syringe pumps, peristaltic pumps, tubing pumps and gear pumps).
4. To develop new miniaturised connectors that can be used to couple flow sensors and flow generators

This JRP will require a close cooperation with experts and practitioners from the relevant medical areas.

These objectives will require large-scale approaches that are beyond the capabilities of single National Metrology Institutes and Designated Institutes, and it is expected that multidisciplinary teams will be required. To enhance the impact of the research, the involvement of the appropriate user community such as medical practitioners and industry is strongly recommended, both prior to and during methodology development..

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

The total eligible cost of any proposal received for this SRT is expected to be around the 2.7 M€ guideline for proposals in this call.

Potential Impact

Proposals must demonstrate adequate and appropriate participation/links to the “end user” community. This may be through the inclusion of unfunded JRP partners or collaborators, or by including links to industrial/policy advisory committees, standards committees or other bodies. Evidence of support from the “end user” community (eg letters of support) is encouraged.

You should detail other impacts of your proposed JRP as detailed in the document “Guide 4: Writing a Joint Research Project”

You should detail how your JRP results are going to:

- feed into the development of urgent documentary standards through appropriate standards bodies
- transfer knowledge to the medical community.

You should also detail how your approach to realising the objectives will further the aim of the EMRP to develop a coherent approach at the European level in the field of metrology. 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 Member States and countries associated with the Seventh Framework Programme whose metrology programmes are at an early stage of development to be increased
- outside researchers & research organisations other than NMIs and DIs to be involved in the work

Time-scale

The project should be of up to 3 years duration.

Additional information

The references were provided by the PRT submitters; proposers should therefore establish the relevance of any references.

[1] Medical Devices Directive 93/42/EEC

[2] ISO 8536-1 to 12 - Infusion equipment for medical use

[3] ISO 28620:2010 - Medical devices, non-electrically driven portable infusion devices