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

Selected Research Topic number: **SRT-h20**
Version: 1.0

Title: Metrological characterisation of micro-vesicles from body fluids as non-invasive diagnostic biomarkers

Abstract

Micro-vesicles are released by cells and occur in all body fluids (e.g. saliva, blood and urine). They are potential biomarkers for the diagnosis of life threatening diseases and their number, size and composition is disease-state dependent. Progression in the use of micro-vesicles as biomarkers is hampered by the lack of accurate measurement techniques, sample techniques and standard methods, for the accurate detection and characterisation of micro-vesicles.

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 page 22 and 41.

Keywords

Micro-vesicles, biomarkers, AFM, ellipsometry, Raman spectroscopy, mass spectrometry, reference standards

Background to the Metrological Challenges

The use of body fluid micro-vesicles biomarker tests in early diagnosis and treatment of life threatening diseases is hampered by the absence of accurate methods for their detection and characterisation. Further to this, a lack of standard measurement methodology also leads to discrepancies between micro-vesicle biomarker tests.

Currently, classical ellipsometers are used for the characterisation of biomolecules. However, in recent years, several techniques have been developed for the characterisation of nano-sized biological systems. Atomic Force Microscopy (AFM) can detect several orders of magnitude more micro-vesicles than the standard health care test, flow cytometry. Label free and fluorescently labelled optical imaging techniques (e.g. Raman spectroscopy) have been progressed and photo-activated localisation microscopy (PALM) has reported a spatial resolution of several nanometres using a model system. The detection of unlabeled compounds using mass spectrometry techniques is very powerful for applications in medical research, methods such as plasma assisted desorption ionisation (PADI), MALDI and DESI.

However, being able to really use any of these biomarker tests depends on the development of methods and standards for traceable, repeatable, quantitative measurements.

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 traceable measurement and characterisation of techniques to enable the detection and characterisation of micro-vesicles as biomarkers.

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The specific objectives are:

1. To develop methodologies for traceable dimensional characterisation of micro-vesicles.
2. To develop methodologies for characterising concentration, surface structure and chemical composition of micro-vesicles. The developed methods should be able to:
    - distinguish micro-vesicles from other biomaterials in body fluids,
    - identify the concentration of micro-vesicles in body fluids,
    - identify the presence of specific proteins or enzymes on the surfaces of micro-vesicles or internally,
    - identify the topography of the micro-vesicles in liquid medium at sub-nanometre resolution,
    - provide biochemical information on the micro-vesicles,
    - identify the micro-vesicles species and quantify their composition.
3. To develop micro-vesicle reference standards. Reference standards should be stable, provide repeatable measurements and have similar properties (e.g. size and morphology) to micro-vesicles.
4. To generate reliable micro-vesicle sample procedures. The sample procedures should encompass controlled body fluid collection as well as the isolation and purification of micro-vesicle from collected body fluids. The deposition of micro-vesicles on substrates should also be addressed.

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.

Proposers should establish the current state of the art, and explain how their proposed project goes beyond this, including the currently funded EMRP project T3 J1.1. Nanoparticles; 'Traceable characterisation of Nanoparticles'.

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.