EMPIR Call 2015 – Health, SI, Normative and Research Potential

Selected Research Topic number: **SRT-h17**
Version: 1.0

Title: Metrology support for improved surveillance of safety of blood products

Abstract

Reliable surveillance of blood products, regulated by European directives, is highly relevant for patients and the health system, since critical incidents may result in fatal outcomes. Provision of metrological support will allow high accuracy measurements of therapeutically active ingredients like platelet or stem cell concentrations as well as accompanying disturbing ingredients, e.g. residual leucocytes. Viral and bacterial contaminations need to be addressed and their detection limit quantified. In particular, metrological traceability of end-users' need to be achieved by releasing standards for validated methods with short turnaround times and applicable in a clinical environment and which enable testing of 100 % of the product before application.

Keywords

Transfusion medicine, stem cell transplantation, reference measurement procedures, viral contamination, bacterial contamination, rare cell detection, residual leucocytes, free haemoglobin, cell function, blood cell concentration, stem cell counting, external quality assurance, metrological traceability, pre-analytic, control material

Background to the Metrological Challenges

Transfusion of blood products and (stem) cell transplantation are a therapeutic strategy which is of vital importance in the medical treatment of patients in intensive care, during surgery and suffering from cancer. To avoid critical incidents, which may result in fatal outcome, a stringent monitoring of blood products from the donor to the final application is mandatory as stated in the Directive 2002/98/EC. Such stringent monitoring, which warrants safety for donors and patients, includes the requirements of traceability of the product to the donor and the determination of cell concentrations, e.g. platelet concentrations at the transfusion limit and haemoglobin concentrations to characterise the efficacy of the medicinal product. Besides the therapeutically active ingredients, it is mandatory to detect accompanying products, which may induce unwanted immune response, e.g. the concentration of residual leucocytes in erythrocyte and platelet concentrates.

A relevant part of blood safety is the proof of sterility, i.e. the negative testing against viral and bacterial contaminations is required. In future, detection of new and emerging pathogens influencing blood products will become more and more important as the number of air-passenger journeys increase.

The present situation to ensure functionality and sterility of blood products is not based on reference measurement procedures. External quality assurance schemes, e.g. for viral contamination, are exclusively based on consensus values since reference measurement values are not available so far. By using reference measurements values as target values, tests and test kits not adequate with respect to accuracy and sensitivity are easier identified and could be rejected to avoid hazardous complications for patients and additional costs for health care.

Objectives

The overall objective of the project is the development of high accuracy measurement procedures for the comprehensive and reliable characterisation of blood products as well as measurement protocols and instrumentation for *on-site* analysis of blood products just before transfusion or transplantation.

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The specific objectives are

1. To develop high accuracy reference measurement procedures for therapeutically active components to allow concentration measurements of platelets in platelet concentrates ($u(C) \leq 5$ %), CD34 positive stem cells in stem cell products ($u(C) \leq 5$ %), and intra-erythrocyte haemoglobin ($u(C) \leq 1$ %), i.e. drug content in erythrocyte concentrates
2. To develop high accuracy reference measurement procedures for the quantification of accompanying perturbing ingredients, like residual leucocytes in concentrates of erythrocytes, platelets and in blood plasma, residual erythrocytes in platelet concentrates and blood plasma, residual platelets in erythrocyte concentrates, CD34 negative nucleated cells in stem cell products, CD3 positive cells in stem cell products, and concentrations of free, extra-erythrocyte haemoglobin in erythrocyte concentrates
3. To develop high sensitivity methods including characterisation of limit of detection (well below 10 IU per mL) in different products to detect contamination by viruses (i.e. HIV, HBV, HCV and CMV) and bacteria
4. To develop procedures and instrumentation suited for on-site analysis of blood products, characterised by short turnaround times (2 min – 5 min) and easy handling in a sterile environment. Validation of *on-site* protocols by comparison experiments with the reference measurement procedures developed and verification in clinical laboratories in cooperation with scientific medical associations and manufacturers to optimise test kits.
5. To develop standardisation and reference measurement procedures applicable in clinical laboratories, to control routine protocols for the specific target cell populations given in objectives 1 and 2 and to validate these procedures by inter-laboratory comparisons, To work closely with the European and International Standards Developing Organisations, and the users of the Standards they develop, to ensure that the outputs of the project are aligned with their needs, communicated quickly to those developing the standards, and in a form that can be incorporated into Standards at the earliest opportunity.

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, medical (academic) hospitals 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.

EURAMET expects the average EU Contribution for the selected JRPs in this TP to be 1.8 M€, and has defined an upper limit of 2.1 M€ for this project.

EURAMET also expects the EU Contribution to the external funded partners to not exceed 35 % of the total EU Contribution to the project. Any deviation from this must be justified.

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 e.g. CEN/TC140,
- Transfer knowledge to the health sector.

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

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.