



DEPARTMENT OF COMMERCE

National Institute of Standards and Technology

Flow Cytometry Standards Consortium

AGENCY: National Institute of Standards and Technology, Department of Commerce.

ACTION: Notice of research consortium.

SUMMARY: The National Institute of Standards and Technology (NIST), an agency of the United States Department of Commerce, in support of efforts to develop standards for regenerative medicine and advanced therapies, is establishing the Flow Cytometry Standards Consortium (“Consortium”). The Consortium will bring together stakeholders to identify and address measurement and standards needs related to flow cytometry used in the characterization and testing of cell and gene therapies. The Consortium efforts are intended to develop measurement solutions and standards to improve measurement confidence, establish measurement traceability, and enable comparability in flow cytometry measurements. Participation fees will be at least \$25,000 annually or in-kind contributions of equivalent value. Participants will be required to sign a Cooperative Research and Development Agreement (CRADA).

DATES: The Consortium's activities will commence on December 1, 2020 (“Commencement Date”). NIST will accept letters of interest to participate in this Consortium on an ongoing basis.

ADDRESSES: Completed letters of interest or requests for additional information about the Consortium can be directed via mail to the Consortium Manager, Dr. Lili Wang, Biosystems and Biomaterials Division of NIST's Material Measurement Laboratory, 100 Bureau Drive, Mail

Stop 8312, Gaithersburg, Maryland 20899, or via electronic mail to flowcytometry@nist.gov, or by telephone at (301) 975-2447.

FOR FURTHER INFORMATION CONTACT: Jaime Maynard, CRADA Administrator, National Institute of Standards and Technology's Technology Partnerships Office, by mail to 100 Bureau Drive, Mail Stop 2200, Gaithersburg, Maryland 20899, by electronic mail to Jaime.maynard@nist.gov, or by telephone at (301) 975-8408.

SUPPLEMENTARY INFORMATION:

Advances in cell and gene-based therapeutics as well as other regenerative medicine products have increased the need for high quality, robust, and validated measurements for cell characterization. Flow cytometry, including imaging cytometry, has emerged as an important platform due to its ability to rapidly and simultaneously characterize heterogeneous cell populations and subcellular analytes. For example, flow cytometry has been critical for establishing identity, purity, and potency for Chimeric Antigen Receptor (CAR)-T cell manufacturing; and associated data to support the approval of Biological License Applications (BLA) by the U.S. Food and Drug Administration (FDA) and the approval by the European Medicines Agency (EMA). In addition, multiparameter flow cytometric measurements are routinely carried out in vaccine, drug and cancer research, clinical diagnosis, and immunotherapies. However, challenges remain with respect to measurement confidence and comparability of measurement results from different instrument platforms, locations, and over time, hindering critical decision-making based on flow cytometry data in research and clinical settings.

NIST has extensively engaged with stakeholders to identify measurement needs. These include hosting joint workshops with the U.S. FDA and with the International Society for Advancement of Cytometry (ISAC) that brought together experts and stakeholders from industry, academia and government to discuss unique challenges for cell and gene therapy. The workshops identified three common, pre-competitive measurement needs: 1) high-quality reference materials, 2) confidence in the procedures from standardization/inter-laboratory studies, and 3) uncertainty associated with specimen quality and/or pre-analytical processes.

This Consortium aims to develop measurement solutions and standards for flow cytometry, including improving measurement confidence by establishing traceability and assisting measurement comparability. Measurement applications to be addressed may include the use of flow cytometry for the characterization and testing for cell identity, purity, count, activity, potency, and biomarker expression. The working cell types will be determined based on the collective input of the Consortium members and can start with common immunotherapy cell types, e.g., T cells, iPSCs, and NK cells. To fulfill the objectives of the Consortium, associated critical reagents, such as antibodies, plasmids, and viral vectors pertaining to the development of the high-quality measurements and reference materials, will be characterized using orthogonal measurement capabilities, e.g., ddPCR, qPCR, NGS, Flow-FISH, nanoflow cytometry, and mass spectrometry, most of which are available at NIST as a part of the NIST Advanced Therapy Program. NIST may also leverage current capabilities such as the state-of-the-art flow cytometry and automation capabilities and expertise, ERF measurement service, blood cell characterization, cell counting expertise, as well as existing collaborations with calibration bead and cytometer

manufacturers, international metrological institutions, and Standards Development Organizations (SDOs) such as CLSI to advance the goals of this Consortium.

The Consortium is expected to form several Working Groups to continuously identify and address needs and gaps in quantitative cytometry through workshops, public meetings, and other collaborative efforts. The scope of Working Groups can include:

(1) Equivalent Number of Reference Fluorophores (ERF) Measurement Service:

- a. Develop reference standards including reference materials, reference data, reference methods, and measurement service for assigning the ERF to calibration microspheres and assessing the associated uncertainties and utilities. This is the first step towards reliable quantitative measurements in flow cytometry.

(2) Reference Material Selection and Design:

- a. Develop candidate reference standards including biological reference materials, reference data, reference methods;
- b. Evaluate common reagents and control materials including various types of compensation controls;
- c. Design and carry out interlaboratory testing to characterize and evaluate the reference materials using multiple methods, including orthogonal methods.

(3) Assay and Protocol Selection and Design:

- a. Establish an inventory of existing protocols, shared data, existing standards;

- b. Generate standard operating procedures/methods for cross platform assay standardization and data analysis;
- c. Test the robustness of assays and associated uncertainties.

No proprietary information will be shared as part of the Consortium.

Participation Process:

Interested parties with relevant flow cytometry associated capabilities (see below), products, and/or technical expertise to support this Consortium should contact NIST using the information provided in the ADDRESSES section of this notice. NIST will then provide each interested party with a letter of interest template, which the party must complete, and submit to NIST. NIST will contact interested parties if there are questions regarding the responsiveness of the letters. NIST will determine the eligibility to participate in the Consortium based on the requirements listed below. NIST will select participants based on information provided by interested organizations in their letter of interest and upon the availability of necessary resources to NIST.

Requirements: Each letter of interest should provide the following information:

(1) A description of the experience in flow cytometry/imaging cytometry, production and characterization of microparticles, antibodies, biological cells, other critical reagents of cytometric applications, and analysis of large data sets and related expertise to contribute to the Consortium.

(2) Subgroups or topic areas of interest for participation.

(3) List of interested party's anticipated participants.

Letters of interest must not include business proprietary information. NIST will not treat any information provided in response to this Notice as proprietary information. NIST will notify each organization of its eligibility. In order to participate in this Consortium, each eligible organization must sign a CRADA for this Consortium. All participants to this Consortium will be bound by the same terms and conditions. Participants will be required to contribute at least \$25,000 annually as participation fees or in-kind resources of equivalent value, as determined by NIST. NIST does not guarantee participation in the Consortium to any organization submitting a Letter of interest.

Authority: 15 U.S.C. 272; 21 U.S.C. 356g.

Kevin Kimball,
Chief of Staff.

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