

## ICON Laboratory Services Customised Flow Cytometry Solutions

Given the cost, time and expertise needed to develop and qualify robust internal capabilities in flow cytometry, a partner with the scientific expertise, global resources and mission commitment can help sponsors effectively develop and uniformly execute flow cytometric assays.

ICON Laboratory Services has distinguished itself within the clinical trials industry through its specialised Flow Cytometry Solutions. Our mission is to cultivate a partnership with sponsors to provide scientific expertise and full-service assay development to drive successful clinical trials forward.

### Full-Service Assay Development

ICON's full-service offering begins with early collaboration with the sponsor's scientific team to gain a thorough understanding of the testing methods and parameters required. ICON provides industry-recognised research and development services to support technology transfers, assay development and validation via an extensive biomarker test menu and standardised analyses to monitor key molecules, targets and receptors. Our innovative and interconnected global flow cytometry network provides a central data repository and facilitates consistent result interpretation.

ICON works with sponsors to:

- Develop and/or optimise flow cytometry methodology to meet the required specifications for monitoring therapeutics
- Provide the sponsor with validation data for approval
- Rollout flow cytometric assays globally as required

- Develop a customised standard operating procedure (SOP) for performing assays globally
- Collaborate with the sponsor regarding special requirements, including secure transfer of listmode and data analysis files
- Utilise mature operational processes that optimise the sponsor's requirements
- Precisely define the specifications for result reporting

Additionally, ICON has expertise using the following instrumentation platforms:

- BD FACSymphony A3 flow cytometers (RUO; ≤ 25 fluorescent colours)
- BD FACSCanto II flow cytometers (RUO and IVD; ≤ 8 fluorescent colours)
- Veridex CellSearch CTC

## Development of Customised Flow Cytometric Assays

ICON's R&D and Operational teams have the resources and scientific expertise to implement a broad range of custom flow cytometric assays in clinical trials. Types of flow cytometric assays that are developed/validated at ICON include:

- Receptor occupancy assays, customised per drug
- Antibody-dependent cell-mediated cytotoxicity assays
- Rare event enumeration (myeloid-derived suppressor cells, dendritic cell subpopulations, blasts)
- Ultra-rare event enumeration (circulating tumor cells, tetramer assays for antigen-specific T lymphocytes)
- T cell maturation phases (naïve, central memory, effector memory)
- B cell maturation phases (naïve, switched memory, unswitched memory, double negative)
- In vitro stimulation and quantification of intracellular cytokines (IL-2, -4, -5, 13, -17,  $\gamma$ -IFN)
- Intracellular small molecule measurement (antibody-drug-conjugate) correlating to relative amount of drug delivered per cell
- Phosphorylation assays (NF- $\kappa$ B, p38)
- Microbead-based enrichment of T lymphocytes, B lymphocytes, granulocytes, monocytes and disease-state immune cells
- Basophil, eosinophil assays
- Custom research use only flow cytometric assay approved by New York State Department of Health for use as a clinical diagnostic assay to support patient enrolment
- Flow cytometric assays to support companion diagnostics

Custom flow cytometric assays are validated using a fit-for-purpose approach with the level of assay characterisation consistent with the intended use of the assay results.

Moreover, an experienced R&D scientific team develops and validates complex flow cytometric assays and trains dedicated Operational staff to perform ongoing clinical trial sample processing and analysis using standardised SOPs and data analysis strategies.



## Rigorous Quality Control

ICON's quality control program includes:

- Lot-to-lot verification of antibody reagents to maintain consistency of data
- Thorough training of all laboratory personnel performing the test to ensure strict compliance with the SOP
- Documentation of analyst training on method procedures and data analysis
- Use of the same lot number of calibration beads for flow cytometers across all locations
- Stringent processes for harmonising fluorescence output of instrumentation across global laboratories
- Standardised data analysis procedures to ensure harmonized interpretation of global clinical trial samples
- Two levels of data analysis review and confirmation prior to releasing test results
- Secure transfer of raw data and test results to allow for sponsor review while maintaining stringent levels of data protection

## Global Flow Cytometry Network

Our global flow cytometry network has laboratory locations in New York, Dublin and Singapore, and all instruments are connected to a central flow cytometry server. Having a central server allows us to utilise fully harmonised and standardised processes and instrumentation for even the most complex assays. Moreover, joint technical meetings with global teams ensure open communication to implement best practices and resolve queries in a timely manner.

This network enables mature processes for developing, validating and implementing complex flow cytometric assays globally. Other benefits of this network include:

- Ability to obtain appropriate material from a reputable supplier of disease-specific specimens for split sample comparisons globally
- Centralised data analysis and validated reporting processes. Secondary review of data analysis is employed to assure quality results
- Data monitoring and technical expertise provided throughout the clinical trial
- Ongoing scientist-to-scientist communications to ensure project objectives and timelines are met
- Active partnerships to provide the most optimised flow cytometric assay for implementation in clinical trials
- Comprehensive documentation processes

Further information on ICON Flow Cytometry Solutions, or any of our central laboratory services, is available at [iconplc.com/services/laboratories](http://iconplc.com/services/laboratories)