WHICH FLOW CYTOMETRY GUIDELINES DOES YOUR LAB FOLLOW?

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Flow cytometry can deliver the sensitivity and accuracy needed to profile cells effectively, but its power to analyze multiple single cell characteristics rapidly comes with validation challenges. This may explain why, despite the technique being bound by the usual compliance requirements, regulatory bodies have issued no official guidelines on its validation. However, recommendations are available and an experienced partner can help ensure that you deliver compliant, consistent results to optimize your testing outcomes.

Understanding the Importance of Flow Cytometry Validation Can Protect Your Research Investment

Flow cytometry technology is advancing quickly, making it challenging to keep up with new applications. It involves conducting a wide variety of assays, usually in low volumes that do not justify developing them into in vitro diagnostic (IVD) tests. They therefore are performed as laboratory developed tests (LDTs), requiring adapting the level of validation. Being cell-based, these assays don't fit neatly within the usual chemistry-based testing paradigms and standard guidelines do not apply.

Ignoring or misinterpreting guidelines could lead to delays in product approval, increased costs and lost revenues, perhaps even jeopardizing patient safety. By leveraging expert insights, you can avoid pitfalls and reveal new opportunities to maximize your research.

Leveraging Expert Scientific Support to Overcome the Lack of Official Guidance

Having recognized the absence of official regulatory validation guidelines, stakeholders from the pharmaceutical industry and clinical laboratories decided to act.

In 2011, the AAPS Flow Cytometry Action Program Committee (APC) published recommendation papers applying to instrument and method validation in drug development. Experts from the International Council for Standardization in Haematology (ICSH) and the International Clinical Cytometry Society (ICCS) also formed a work group and in 2013 published draft guidelines for validating flow cytometry assays in clinical labs. These were submitted to the FDA for consideration as official guidance. The FDA subsequently initiated public dialogue, expressing regulatory interest in these LDTs and conducted several workshops. At this time, no definitive guidelines have materialized to help scientists develop assays.

Pending resolution, the 2013 recommendations remain the most widely followed. However, with expert assistance, you can navigate these waters and carry out productive validation.
Transforming Results Through Rigorous Validation of Instruments and Methods

Assay validation should be conducted only on a validated instrument. A cross-functional validation team should therefore develop and execute an instrument validation plan outlining deliverables and testing protocols for Installation Qualification (IQ), Operational Qualification (OQ) and Performance Qualification (PQ).

Method validation requires addressing parameters such as specificity. Developing a scientifically valid approach will enable you to demonstrate fitness for purpose. Because flow cytometry can achieve a wide variety of data outputs, identifying your assay category first will determine validation requirements. You must then consider your instruments’ capabilities, ensure component compatibility, select the right antibody combinations and use appropriate controls during assays to differentiate cell populations effectively.

Delivering Combinable Data is Possible When You Minimize Variability Through Standardization

When you run multi-center clinical trials using different instruments, methods and personnel, or carry out longitudinal studies involving ongoing data collation, you need to generate comparable and combinable data. Reducing variability is critical at all stages, from preserving sample integrity to final analysis. At Covance, we focus on consistency; our central labs feature standardized instruments, SOPs, training and also use the same reagents to ensure data combinability across labs. By introducing gating strategies at the final stages of flow cytometry analysis and having data analyzed by a small team, we can also minimize subjectivity, further reducing variability.

Despite regulatory ambiguity, we are committed to advancing science and actively pushing for universally recognized flow cytometry guidelines; we can also help you meet regulatory requirements and advance targeted drug development.

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Linsen Du received her PhD in Biological Sciences from National University of Singapore and specialized in using flow cytometry technology for supporting biomedical research and clinical trials. She has extensive experience in cytometry platform management and assay development. She joined Covance in 2012 as a Scientist to work with pharmaceutical companies to design and implement custom flow assays in drug development.

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