EVALUATING THE QUALITY OF CELL COUNTING MEASUREMENTS USING EXPERIMENTAL DESIGN AND STATISTICAL ANALYSIS

Sumona Sarkar, National Institute of Standards and Technology (NIST)
sumona.sarkar@nist.gov
Steven Lund, NIST
Anne Plant, NIST
Sheng Lin-Gibson, NIST

Key Words: Measurement Assurance, Cell Counting, Experimental Design, Quality Attributes, Analytical Methods

Cell counting measurements are critical in the research, development, and manufacturing of cell therapy products where they support decision-making in product testing and release. Evaluating cell quantity with accuracy and precision has remained a challenge for many specific applications or purposes. While new measurement platforms have been developed with increased measurement throughput and improved precision, discrepancies between cell counts acquired via various measurement processes are still pervasive. In addition, the industry as a whole has recognized that complex biological properties, as well as operator, equipment, and procedure variations can greatly affect the measurement quality, and the development of a single reference material or reference measurement is impractical to address broad counting needs.

Here, we describe an experimental design and statistical analysis approach to evaluate the quality of a given cell counting measurement process. The experimental design uses a dilution series study with replicate samples as well as procedures to reduce pipetting error, and operator and temporal bias. The statistical analysis methods generate a set of metrics for evaluating measurement quality in terms of accuracy and precision, where accuracy is based on deviation from proportionality. In this design, a proportional response to dilution fraction serves as an internal control, where deviation from a proportional response is indicative of a systematic or non-systematic bias in the measurement process. The utility of this approach was demonstrated in the counting of human mesenchymal stem cells (hMSC) via automated or manual counting methods, where the automated method performed better in terms of both precision and proportionality. These results enabled a transition from the labor intensive and often imprecise manual counting method to the automated counting method.

The experimental design and statistical method presented here is agnostic to the cell type and analytical platform, thus suitable as a horizontal approach to evaluate the quality of cell counting measurements with respect to method selection, optimization, and validation, thereby facilitating subsequent decision making. We are also working closely with industry partners and Standards Development Organizations (SDOs) to develop cell counting standards using this and other strategies.