TOOLS AND METHODS FOR PROVIDING ASSURANCE OF CLONALITY FOR LEGACY CELL LINES

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Over the last several years demonstration of cell line clonality has been a topic of many industry and regulatory presentations and papers. Guidance has been provided by the regulatory authorities, especially the FDA, on a path forward for providing evidence of clonality with high probability. It has been recommended that two-rounds of limiting dilution cloning (LDC) at sufficiently low seeding densities (≤0.5 cells/well) provides sufficient evidence that a cell line is clonal. Furthermore, one-round of LDC may also suffice if supplemental data from a characterized FACS or plate-imaging workflow are also included in the package.

Cell lines generated by methods that do not demonstrate high probability of clonal derivation, including legacy cell lines, may require additional studies to provide assurance and/or process control strategies to satisfy regulatory expectations.

Within the Biologics function of the IQ Consortium the “Clonality” Working Group is focusing on methods and tools which could be utilized to provide a high assurance of clonality for legacy cell lines.

The presentation will outline a three tier approach to address legacy cell line clonality assurance: standard practices already used in industry to support limit of in vitro cell age studies, enhanced control strategies to ensure process consistency, and emerging technologies that could be used to further support cell line clonality.