UTILISATION OF DIELECTRIC SPECTROSCOPY TO MEASURE LIVE BIOMASS AS A PAT TOOL FOR CONTINUOUS MANUFACTURING AND OTHER APPLICATIONS

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Following FDA's PAT initiative, it is imperative that critical process parameters (CPP) that significantly impact critical quality attributes (CQA's) of a process need to be monitored and controlled strictly. It is also well known that viable biomass is one such CPP, which can impact CQA's in a biopharmaceutical process. In addition, for reasons already established, the present drive is to move towards process intensification and continuous biomanufacturing. The need for controlling biomass at a specific high cell concentration at high viability also spells the need for a technology that allows implementation of automatic cell bleeding strategies. Dielectric spectroscopy, often referred to as capacitance measurement, has been used for monitoring biomass in bioprocesses in real time routinely over the past two decades. Based on the ability of cells to get polarised under the influence of an infinitesimal electric field, it is only sensitive to the presence of live cells. This presentation will not only cover the need and benefit of this technology as well as the detailed theory behind it, but it will also cover the various applications it has been successfully used for. Applications surrounding monitoring biomass in suspension, microcarrier and 3D tissue cultures will be presented. Controlling complex nutrient feed and cell concentration automatically based on capacitance measurement will be discussed in detail. In this section, the strategy of automatic cell bleeding in perfusion cultures will be explained in detail. Other applications involving the use of capacitance measurement for identification and optimisation of feed timing, harvest point detection, scale up success and outlier detection will be looked into. Finally the concept of frequency scanning with dielectric spectroscopy and its application and perceived benefits will be explored.