Spring 5-11-2016

Establishing a pH measurement reference method for site/process transfer purposes

Meg Tung
Genentech, megtung@gene.com

Jacob Mauger
Genentech

Christian Klinger
Genentech

Detlef Eisenkratzer
Genentech

ESTABLISHING A PH MEASUREMENT REFERENCE METHOD FOR SITE/PROCESS TRANSFER PURPOSES

Meg Tung, Late Stage Cell Culture, Pharma Technical Development, Genentech
megtung@gene.com
Jacob Mauger, Early Stage Cell Culture, Pharma Technical Development, Genentech
Christian Klinger, Pharma Technical Development, Roche
Detlef Eisenkrätzer, Pharma Technical Development, Roche

Key Words: pH Measurement, Site/Process Transfers, Reference Method

pH is an important cell culture process parameter that must be carefully monitored and controlled to ensure optimal culture growth, productivity, and product quality. In mammalian cell culture processes, online bioreactor pH sensors are periodically recalibrated against an offline pH value generated by a reference instrument to allow true culture pH to be maintained at or near the target pH setpoint.

Within the Roche R&D and manufacturing network a variety of instrumentation are used to obtain offline pH measurements. While internal guidance exists for pH monitoring, differences in offline pH measurements – due to site-specific instrumentation and procedural differences – still resulted in a shift in the process operating target when offline pH was used as point of reference for calibrations in several instances of process transfer. The shifts in true culture pH experienced by the cells manifested in variable process performance between the process transfer sites, and pH as the root cause was identified in subsequent troubleshooting investigations.

To ensure consistency in true culture pH between the originating and receiving sites for any given cell culture process transfer, a simple, easy-to-implement offline pH reference method is necessary. This work summarizes the cross-site effort to establish a globally applicable reference method for offline pH measurement in mammalian cell cultures. Factors such as analytical device, sensor, calibration buffer, temperature, volume, sampling assembly, and hold time were evaluated to formulate the recommended reference method. pH values measured via this reference method should reduce measurement variability from instrumentation and sample handling, allowing for a reliable means to 1) monitor true culture pH across all sites, and 2) define offsets in offline pH from existing pH methods at each respective site/plant to facilitate translation of pH setpoints, thereby achieving more consistent process performance across sites.