

QUALIFICATION OF LOW DRIFT SINGLE-USE PH SENSORS FOR USE IN SINGLE USE BIOREACTOR PLATFORMS

Alexander J. Hodge, Thermo Fisher Scientific
Alex.hodge@thermofisher.com
Nephi Jones, Thermo Fisher Scientific

Key Words: Single-use, bioreactor, PAT.

The biopharmaceutical industry is currently limited by access to low drift, gamma stable, easy-to-integrate single-use pH sensors for application in single-use bioreactors (S.U.B.). Hamilton Company has developed the OneFerm VP 70 sensor, a unique single-use glass electrode, which provides an additional option for customers wishing to implement reliable single-use pH sensing capabilities in the S.U.B. platform. In order to demonstrate the efficacy of these devices, a series of qualification experiments were carried out using a Thermo Fisher Scientific 50L bioprocess container (BPC) custom-fitted with Hamilton OneFerm sensors. BPCs were manufactured in a cGMP facility and allowed to age for a pre-established period (either 30 or 180 days). A 14 day fed-batch cell run was executed using an in-house CHO-S cell line (mAb producing clone) and standard operating conditions. Online pH was controlled with a Hamilton EasyFerm pH sensor; reactor pH was controlled using CO₂ without acid or base. Each BPC was built with 6 OneFerm sensors (containing 2 each from 3 different production lots), which were monitored using stand-alone transmitters. Offline samples were evaluated every 24 hours using an Oakton pH sensor.

The results from the initial 30 day aged BPC evaluation demonstrate functional activity of the OneFerm sensors over a 14 day fed-batch cell run using a TruBio DeltaV S.U.B. controller. Functional stability of these sensors was demonstrated by maintaining the devices in sterile culture conditions for a period of 60 days; 5 out of 6 sensors met all manufacturers' specifications during this hold period. To determine if BPC storage time contributes to loss in sensor functionality, a 14 day fed-batch cell run was repeated using a 180 day aged BPC. All 6 OneFerm sensors met manufacturer's specifications after the cell run with no sensor exhibiting a gross pH drift greater than 0.11 during the entire 14 day period. Additionally, all 6 sensors also met manufacturer's specifications during the 60 day hold period with no sensor exhibiting an average gross pH drift greater than 0.15 during this extended time. Furthermore, all sensors demonstrated an average response time of less than 10 seconds following the 60 day hold period.

The results of these experiments demonstrate the effectiveness of Hamilton OneFerm sensors in the Thermo Fisher Scientific HyPerforma S.U.B. platform. Thermo Fisher Scientific has since developed a custom polycarbonate probe port adapter to robustly integrate the OneFerm sensor in a S.U.B. BPC. Future work will continue to evaluate the performance of sensors aged in BPCs for 24 to 36 months. We are excited to share this growing body of data with the bioprocess industry as probe drift, ionic strength sensitivity, and shelf life have greatly limited implementation of SU pH over the past decade. These results appear to indicate a viable technology is now available and is suitable for cGMP bio manufacturing.