Industry: Drug Development and Manufacturing

Evaluating Process Deviations

SAMPLE DELIVERABLE

Task 1: Summary of deviations and possible impacts on product quality.

Deviation 1: During an informal check, you discover that the incubator logbooks indicate that the cleaning cycle was not properly documented. You go to the incubator event log and see that "auto-zero" was not completed there, either. Additionally, the red CO2 cap had not been removed prior to use. Lacking control of the level of CO2 in the incubator could have negatively affected cell culture growth.

Deviation 2: Manufacturing scientists noticed that cell cultures were exhibiting varying degrees of growth profile and metabolic trend differences. The source of these variations couldn't be identified even after review of documentation, inspection of the gas expeller and a screen for the presence of contamination in the cultures. Inspection of the bioreactors indicated that the temperature transmitter was out of calibration. Further investigation revealed that the bioreactors had died after a power outage 9 months previous. When bringing the reactors back online, they had reverted to factory settings and the temperature during cell culturing was not maintained in line with key performance predictors (were running at 34.7°C outside of the acceptable range 35.7-37.3°C). This resulted in some cell culture lots produced with the bioreactor operating at a temperature that differed from approved specifications leading to the observed changes in cell culture performance.

Task 2: List indicators to assess cell culture performance and viability

growth curve
pH changes
viable cell density
metabolic profiles using metabolite concentrations

Task 3: Identify what corrective actions, if any, to address with personnel.

It was determined that neither deviation resulted in a severe product impact and product recall would not be necessary. However, in both deviations, corrective actions would be recommended to ensure proper training of personnel involved in the affected processes.
In Deviation 1, possible actions: The scientist notified of issues upon detection. The standard operating procedure (SOP) re-reviewed and verbal training of pertinent sections of SOP were emphasized to mitigate any future problems with incubator operations. An instructor-led training plan was put in place.
In Deviation 2, possible actions: It was determined that the root cause for the calibration failures of temperature transmitters was due to a procedural gap. Several facilitative corrective actions were made to prevent recurrences in the future including training of personnel and updates to facility procedures.