

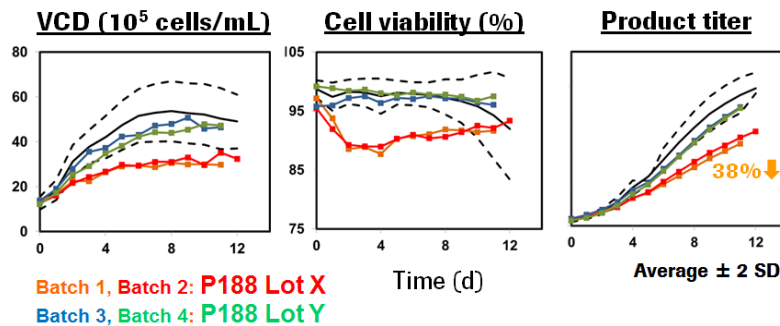
TECHNICAL ASSESSMENT APPROACH FOR VENDOR INITIATED CHANGES OF DIRECT MATERIALS

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Key Words: Direct materials, Vendor initiated changes, Lot-to-lot variation

Hundreds of direct materials are used for each biologic production process. Vendor initiated changes (VIC) to the production process, packaging, raw material sources, and other aspects of these direct materials can and will happen. Each change could have the potential for both process and product impact not only to one product, but to every product that uses it across a manufacturing network. In order to ensure these changes are assessed appropriately and in a timely manner, procedures and processes need to be in place both from the customer and supplier. In addition, if changes are complex, communication between both parties is often necessary. Complex changes may also require a deeper level of collaboration between multiple functional groups from the customer and supplier. This poster will describe Roche/Genentech's approach for technical assessments of VICs to ensure they are evaluated properly by the necessary subject matter experts (SMEs). It will highlight case studies such as a complex VIC pertaining to Poloxamer 188 (P188) and the effective collaboration between Roche/Genentech and its supplier.

Poloxamer 188 is a complex nonionic tri-block co-polymer composed of a central hydrophobic chain of polyoxypropylene (PPO) flanked by two hydrophilic chains of polyoxyethylene (PEO) which is used in biopharmaceutical manufacturing for the cultivation of mammalian cells. The supplier informed Roche/Genentech of a production site change of P188 through the VIC business process. The complexity associated with the site change VIC was further compounded by an ongoing investigation based on observed low cell growth and product yield for some large-scale biomanufacturing processes at Roche/Genentech. Lot-to-lot variability in P188 was identified as the primary source of the observed low growth and yield even though all release specifications were met (Figure below).



Coupled with this investigation and the supplier initiated site change, it provided the opportunity for a collaboration to understand the causal elements of P188 lot variability and to ensure that measures and controls were identified and implemented for consistent P188 production.