Reliably Assessing Comparability in Autologous Cell Therapy Change Protocols: A Compliance Perspective

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A Change Protocol (CP) is a prospective plan to evaluate the impact of proposed bioprocess changes post-approval on the identity, strength, quality, purity, and potency of a drug product or biological product. This assessment is crucial for ensuring product quality in compliance with regulatory requirements.

Autologous cell therapy, involving the processing of an individual's cells or tissues outside the body and their subsequent reintroduction, poses unique challenges when changes are introduced to the bioprocess. Given the personalized nature of autologous therapy, the comparison between processes before and after changes, but within donors, becomes imperative. Current regulations primarily assume uniformity across batches and do not specifically address the intricacies of within-donor variability.

In a draft guidance (July 2023), FDA suggest that the cells of a single donor are divided into two equal pools of cells (split-source design), where each portion is subjected to either the pre-change or post-change manufacturing process. Two One-Sided Test (TOST) is proposed to analyze data.

Demonstrating the comparability between two versions of the manufacturing process is calculating the capability of the post-change process to be within the range of the pre-change process. Our presentation will show how a criteria on a TOST can obtained to ensure process capability. This involves a comprehensive study design and addresses the fundamental question of predefining acceptance limits. Current regulations lack specific provisions for this scenario, and our approach fills this void.

Our presentation will demonstrate the application of Bayesian statistics in deriving and justifying acceptance limits, taking into account within-donor evaluations. By integrating historical data and leveraging Bayesian statistics, our approach offers a robust framework for reliably assessing comparability in autologous cell therapy change protocols, ensuring compliance with regulatory standards.

Short bio

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Jean-François Michiels has been working as a statistical consultant in Cencora Pharmalex since 2013 and he is mostly involved in CMC projects. He has a bioengineering degree from the Université Catholique de Louvain (Belgium-2003). He has a PhD degree in animal cell culture (2004-2011-UCL-Belgium). He accumulates more than 10 years of experience in several areas of pharmaceutical research and industry including bioassay and process development/validation,

drug and vaccine discovery and manufacturing, with the usage various statistical tools such as design of experiments and advanced statistical models (e.g. nonlinear and mixed models). Drawing upon his extensive background and experience, he adeptly communicates statistical concepts to individuals with limited statistical knowledge and skillfully establishes appropriate analytical frameworks.