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Changes in product quality – what is comparable "enough" and what is "similar enough?"

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Session II: Impact of Process Conditions on Product Quality

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Regulatory guidance documents clearly outline the requirements for demonstrating analytical comparability to support process changes and analytical similarity to support the approval of biosimilars. These include demonstration that process changes do not produce differences in product characteristics that might lead to an adverse impact on the safety or efficacy of the product[1]. For biosimilar products, a stepwise approach is required that starts with sponsors demonstrating that the product characteristics of the proposed biosimilar are either highly similar to that of the originator reference product or that any observed differences can be demonstrated to not impact the ability to leverage (or "conserve") the safety and efficacy profile previously demonstrated by the originator[2]. Some product characteristics are however uniquely sensitive to small changes in process conditions, including but not limited to isoform charge distribution and glycan profiles. Moreover, as analytical methods continue to evolve, the ability to quantitatively detect small changes in these characteristics continues to improve. As such, every biotechnologist is faced with the question of what is comparable enough and/or what is similar enough. The author will review twenty years of regulatory feedback on these questions and discuss how regulatory agencies in the major markets have answered these same questions.

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