COLLEGE OF PHARMACY
PHARMACEUTICAL SCIENCES
UNIVERSITY OF MICHIGAN

Department of Pharmaceutical Sciences
Ph.D. Dissertation Defense Seminar

Thursday, July 20th at 9:30AM
NCRC Building 32 Auditorium
Zoom: https://umich.zoom.us/j/95371709279 Passcode: 938778

"Biologics *In Vitro* Characterization Advancements to Streamline Development and Approval Timelines"

Presented by:

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Abstract: Many of the top-selling drug products on the market, with sales in the billions annually, are monoclonal antibodies (mAbs). Due to the success of originator mAb products, it is unsurprising that the overall biologics market is saturated with competition in the form of other originator products approved for similar indications, or, as products lose their exclusivity, in the form of biosimilars. Despite being approved for similar indications, competitor products can have differences in their structure and function. To determine the extent of these differences and the efficacy and safety implications they might provoke, numerous in vitro and in vivo assays have to be conducted and validated prior to drug approval. Yet, often the methods performed by each company for their drug's approval are disparate.

Therefore, to aid in developing universally performed, best-practice methods for biologics development, we have studied characteristics including Fab binding affinity, Fc binding affinity, antibody dependent cellular cytotoxic activity, disulfide shuffling, degradation patterns, and glycosylation profiles of numerous competing originators and originator/biosimilar pairs. From our initial studies with three anti-TNFα mAbs, we sought to not only determine any correlation between higher binding affinity, glycosylation patterns and efficacy, but also to look into the feasibility of repeating these assays with additional lots and drug products for future validation. Similarly, we monitored structural similarities and differences, including disulfide bonds and glycans, for originator and biosimilar mAbs. The results from these experiments were used to identify indicators (i.e. mannosylated glycans, shuffled disulfide bonds) of potentially reduced therapeutic efficacy and/or safety concerns. We also were interested in seeing the extent of variability between originators and biosimilars and between multiple biosimilars of the same reference, as that could have implications for drug interchangeability. By performing a range of structural and bioactivity assays on approved protein therapeutics, we aim to aid in the development and validation of characterization methods for new biologics and biosimilars.