COLLEGE OF PHARMACY
PHARMACEUTICAL SCIENCES
UNIVERSITY OF MICHIGAN

## Pharmaceutical Sciences Seminar Series

Wednesday, March 15, 2023
4:00pm
NCRC Building 10 Research Auditorium
Zoom

# "Streamlining functional and structural characterization methods for originator and biosimilar monoclonal antibody therapeutics"

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. Industry, regulatory bodies and pharmaceutical standard organizations are all interested in validating protein characterization methods and developing guidances to help streamline the biologics approval process.

Therefore, to aid in developing best-practice methods, we have studied the Fab binding affinity, Fc binding affinity, cellular cytotoxic activity, and glycosylation patterns of competing anti-TNFa mAb originators, namely Humira®, Remicade®, and Simponi Aria®. From these studies, 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. By performing a range of structural and bioactivity assays on approved protein therapeutics, we aim to aid in the development of more guidances and validation of characterization methods for new biologics and biosimilars.