COLLEGE OF PHARMACY
PHARMACEUTICAL SCIENCES
UNIVERSITY OF MICHIGAN

Pharmaceutical Sciences Seminar Series

Wednesday, March 1, 2023
4:00pm
NCRC Building 10 Research Auditorium
Zoom

"Understanding of the critical quality attributes of Doxil®/Caelyx™ performance *in vitro* and *in vivo*"

Presented by:

Adaeze Eneli
PhD Candidate, Pharmaceutical Sciences
University of Michigan

Abstract: Doxil®, a PEGylated liposomal formulation of doxorubicin hydrochloride, was the first liposome drug product to be approved by the FDA in 1995. Although off patent, limited generic products have been approved due to challenges in achieving bioequivalence which are compounded by the complexity of the manufacturing process. Regulatory agencies require that generic drug products be bioequivalent to the reference listed drug. As defined by the FDA, the term bioequivalence refers to the qualitative and quantitative sameness of the generic drug product and its physicochemical similarity to its reference listed drug. Therefore, the purpose of this research is to understand the critical quality attributes of Doxil® that are relevant for bioequivalence. We developed a series of analytical methods to analyze the critical quality attributes of Doxil® including liposome size distribution, zeta potential, doxorubicin and lipid content, purity, free versus encapsulated doxorubicin, morphology and *in vitro* drug release.

Lot-to-lot variability of concentration and purity was evaluated. Minor differences exist for particle size and zeta potential across different lots. Cryo-TEM imaging reveals the distinct shape and morphology of the Doxil® liposome. Eighty percent cumulative release was achieved using a previously established USP-4 dissolution assay. Our work in characterizing the critical quality parameters of Doxil® can provide a baseline for the characterization and analytical comparison of approved generics. Subsequent work will result in the development of specification ranges for each parameter relevant to guide generic companies to produce their bioequivalent generic versions. This research supports the generic development of Doxil® and can provide a framework for the development of other similar, complex liposomal generics.