Summary

Pharmaceutical manufacturing operates within a uniquely complex environment characterized by stringent regulatory requirements, globalized operations. While Industry 4.0 promises transformative improvements in efficiency, quality, and decision-making through digital technologies, the sector faces substantial challenges in adopting these solutions due to validation demands, legacy systems, and fragmented planning data. Consequently, there is a pressing need for research that not only examines the barriers to Industry 4.0 adoption but also demonstrates how advanced analytics, machine learning, and simulation can be applied within regulated pharmaceutical contexts to deliver measurable operational impact.

This thesis addresses this need through four interrelated studies conducted primarily at a global biopharmaceutical Contract Development and Manufacturing Organization (CDMO), with one study including a chemical manufacturer for broader validation. The research is guided by three questions: (1) What factors impede progress toward higher Industry 4.0 maturity in pharmaceutical manufacturing? (2) How can Industry 4.0–oriented, data-driven approaches improve operational decision-making? (3) What role can Industry 4.0 play in addressing inaccuracies in enterprise resource planning (ERP) and production planning and control (PPC) systems?

The first study investigates barriers to Industry 4.0 maturity in a pharmaceutical CDMO through a mixed-method design combining a structured maturity assessment with 20 cross-functional interviews. It identifies strategic alignment, technological integration, and financial prioritization as primary barriers, reframing regulation as a constraint that amplifies other challenges rather than standing as the dominant blocker.

The second study explores machine learning–based optimization for upstream monoclonal antibody production, testing multiple regression and optimization algorithms on five years of industrial batch records. The results demonstrate strong predictive performance but also highlight the need for interpretability and constraint-aware modeling for adoption in Good Manufacturing Practice (GMP) environments.

The third study addresses planning and data governance by theorizing a “negative spiral” of ERP/PPC inaccuracies. Drawing from cases in both pharmaceutical and chemical manufacturing, it illustrates how infrequent updates, shadow systems, and data distrust undermine planning accuracy and proposes real-time telemetry, predictive analytics, and governance mechanisms to restore data fidelity.

The fourth study applies discrete-event simulation (DES) to packaging-line operations, complementing Overall Equipment Effectiveness (OEE) metrics with scenario-based capacity planning. The study demonstrates how simulation models, developed and validated

collaboratively with practitioners, can support decision-making around staffing, throughput, and investment planning.

Together, these studies form an integrative framework that links organizational and technical enablers of Industry 4.0 maturity to decision-grade analytics and simulation capabilities, which in turn support data fidelity in planning systems. The thesis contributes theoretically by clarifying Industry 4.0 adoption barriers in regulated environments, modeling systemic feedback loops that drive planning inaccuracies, and extending the literature on simulation and analytics under GMP constraints. Practically, it offers actionable frameworks, models, and methods for pharmaceutical manufacturers to prioritize digital initiatives, deploy interpretable analytics, and leverage simulation for improved decision-making.