



TAUBER INSTITUTE  
FOR GLOBAL OPERATIONS  
UNIVERSITY OF MICHIGAN

## Pfizer Clinical Manufacturing: Accelerating Molecule to Market Timelines by Maximizing Resource Utilization



Founded in 1849 in New York City, Pfizer Inc. is an American multinational pharmaceutical corporation and one of the world's largest pharmaceutical companies. A leader in the biopharmaceutical industry, Pfizer has grown by mergers with such pharmaceutical companies as Warner–Lambert, Pharmacia, and Wyeth to a reported 2019 revenue of \$51.8 billion and has 67,671 employees.

Pfizer develops and produces medicines and vaccines for a wide range of medical disciplines including immunology, oncology, cardiology, endocrinology and neurology. Its products include Lipitor (atorvastatin), used to lower LDL blood cholesterol; Lyrica (pregabalin) for neuropathic pain and fibromyalgia; Diflucan (fluconazole), an oral antifungal medication; Zithromax (azithromycin), an antibiotic; Viagra (sildenafil) for erectile dysfunction; and Celebrex (celecoxib), an anti-inflammatory drug.

Pfizer is currently addressing two industry-wide disruptions: an increasing difficulty to deliver blockbuster drugs and a shift towards precision medicines for cancers and rare diseases.

These shifts led to two initiatives by CEO Albert Bourla. The first initiative focuses on accelerated delivery of medicines to market by reducing operational cycle times across product development. The second initiative focuses on portfolio diversification, with a goal of bringing 25 new drugs to market by 2025 and an emphasis on delivering breakthrough therapies to satisfy unmet patient needs globally.

In order to support the accelerated delivery of a diversified portfolio, Pfizer identified an opportunity to review working practices and enhance capacity in clinical manufacturing at its Sandwich, UK research and development facility.

The project's goal was to increase batch throughput with reduced cycle times by maximizing resource utilization, thus delivering an expanded portfolio on expedited timelines.

To help achieve this goal, Pfizer brought in a student team from the Tauber Institute for Global Operations at the University of Michigan consisting of **Andrés Fuentes-Afflick**, who is earning a Master of Business Administration degree; and **Jason Ji**, a member of the Engineering Global Leadership (EGL) Honors Program who is earning a BSE in Chemical Engineering and an MSE in Industrial and Operations Engineering.

Above, L to R: Andrés Fuentes-Afflick and Jason Ji

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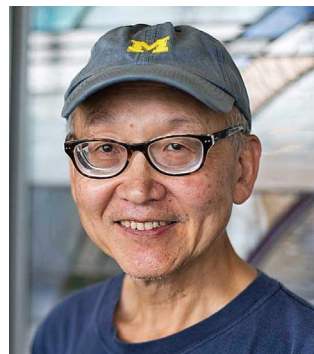
“The students’ professionalism, well roundedness, dedication, general intelligence, and ability to deliver astounded me. Way above my expectations!”

*Chris Turnbull, Pfizer*

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“Given that our project was focused on the clinical pharmaceutical industry, there are many unique industry challenges before drugs can be brought to market for patients,” said Ji. “The primary challenges are the time, money, and resources required for the end-to-end regulatory process, from discovery through patient testing to approval, which represents 12 years total, with over 1,000 patients tested and roughly \$2.6 billion for research and development per drug.

“Focusing on the operation of manufacturing clinical medicines that are tested on patients, a key aspect to highlight is the lead time of seven years for the three phases of trials to confirm the safety and efficacy of the product. This represents a unique difficulty to quickly and effectively deliver medicines to patients. Sandwich primarily produces the medicines for Phase II and III trials, which constitute the longest time frame and biggest barrier to bringing



**Henry Wang**  
College of Engineering



**Brian Talbot**  
Ross School of Business

medicines to market. Thus, to quickly and effectively deliver medicines to market, it is vital to have effective and efficient operations within the Sandwich facility.

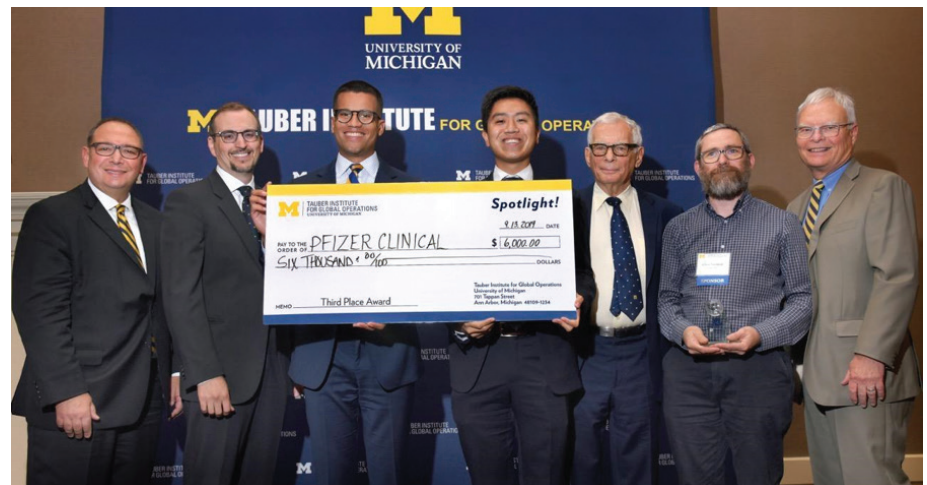
“The Tauber team focused its solution in two primary areas: operational revamp and data utilization. In addressing the operational revamp the team developed a series of new work processes to minimize cycle time and maximize resource utilization. The revised system enables several improvement levers such as continuous manufacturing, optimized technician allocation, and expedited changeover times.”

The main recommendations included two technician teams for manufacturing, continuous manufacturing enablement, and a structured approach to fulfilling non-manufacturing tasks. The team also recommended several manufacturing cubicle design changes and technician training program enhancements.

“To improve data utilization, the Tauber team developed a simulation tool that incorporates the facility’s process flows, resource constraints, and capabilities.” said Ji. “The data utilization imperative was especially challenging, as all of Sandwich’s data sources were paper driven rather than Excel driven due to the strict regulations of clinical manufacturing.

“To overcome the lack of data availability, we utilized a three-pronged approach to paint a full picture of the operation: reviewing batch cards (which are detailed logs of the manufacture process step-by-step), interviewing the manufacturing leadership and technicians, and visualizing the operation with ground-floor analysis. Through this detailed and targeted approach, we developed useful proxies for the lack of cycle time and process data, which could then be leveraged to simulate scenarios to amplify data availability.”

Ji explains, “The simulation tool can analyze major site changes such as changing product mixes and new product



*L to R: Ray Muscat, Damian Beil, Andres Fuentes-Afflick, Jason Ji, Joel Tauber, Chris Turnbull, and Larry Seiford*

capabilities, enabling data-driven decisions on potential cost-benefit changes.

“In developing the simulation tool, we designed the model to output data in metrics directly vital to capacity analysis such as throughput, utilization, and cycle times. For swift analysis, we designed the simulation model to incorporate quick changes in product mix, technician training, and work process. We also ensured various scenarios could be simulated at once to directly compare output data between different changes to the operation, allowing for direct analysis of the impact of different scenarios.

“The finalized simulation tool effectively enabled data-informed decisions for the best short-term operational changes to meet increased demand. Following detailed demonstrations and discussion with leadership regarding the tool and its capabilities, the site director immediately gave his overwhelming support for direct integration with stakeholder leadership to enable further analysis for operational changes to increase long-term capacity.”

To improve performance visibility, the team developed 10 key performance indicators and a visual dashboard to encourage continuous improvement.

“The greatest roadblocks we ran into were the strict regulatory requirements for a manufacturing site that produces medicines that are tested on patients.” said Ji. “These regulatory requirements, known as Good Manufacturing Practices (GMP), greatly constrain process flows and limit flexibility in modifying the operational structure to enable process improvements.”

“Our team had to be very creative in designing solutions that maintained GMP regulatory compliance and did not compromise the quality of clinical pharmaceutical manufacturing while still enabling significant improvements in operational structure to achieve success for ambitious goals in batch throughput increase and cycle time reduction.”

“One of our working recommendations focused on continuous manufacture capability via break time realignment” said Ji. “One major difference between the UK and US is the tea break, in which all technicians took a 30-minute break at the same time every morning. As such, long machine runs could not be run continuously with the current shift and break schedule. The several starts and stops of machine runs throughout the day resulted in a large disparity between prescribed machine run time and actual manufacture time.

“Our solution, which was indeed a risky one and prone to major pushback, was to encourage two technician teams to use their discretion to stagger their breaks to enable continuous machine processing, reducing machine times required for long runs by reducing stoppages. This recommendation was successful for two reasons: the first was technicians showing openness and suggesting realigning breaks in our initial meetings, and the second was giving technician teams the responsibility to make these realignments rather than forcing technicians onto different break schedules.”

“The Sandwich facility had a general culture of risk-aversion due to the strict regulatory restrictions and high stakes nature of a manufacturing operation that produces drugs for patient testing” said Ji. “Thus, we ran into a roadblock in planning a working pilot. No one would want their batch to be ‘piloted’ because if something went wrong with the new work process, they would be held accountable for the delayed or low quality delivery of the batch. However, due to the collaboration and leadership we displayed throughout the project, we had some room to work with in terms of communicating with stakeholders and winning buy-in for the facility-wide pilot.

“Through my consistent check-ins with leadership and a general habit of confirming my analysis and solutions with stakeholders as we developed them, they were generally aware of my analysis and subsequent solutions. Thus, we first communicated with stakeholders and leadership that my recommendations were structured not around the manufacturing operation, but rather the various time sinks that occur during and around manufacturing steps that adds to significantly higher cycle times.

“Therefore, the pilot and the recommendations didn’t involve anything that would jeopardize the quality of manufacture, as the aspects that were getting changed were on all the events that occurred outside of manufacture. Following clear

communication of its nature, stakeholders bought into the three-week pilot.

“We saw great success in our pilot results with both operational improvements and technician feedback. In operational improvements, we confirmed a cycle time reduction of 45% for the batches and an increase in throughput of 66% from three batches to five batches, extrapolated to an annual capacity increase of 62%. Technicians also provided overwhelming positive feedback in a wide range of aspects, including smoother day-to-day workflow, continuous manufacturing capability, parallel processing benefits, training development capacity, and scheduling and planning ease.”

The Tauber team’s recommendations were fully implemented in August 2019.

“The team’s recommendations have enabled a 62% annual batch throughput increase, while reducing end-to-end batch cycle times by 45% and technician working time per batch by 23%” said Ji.

These projections were derived from the Sandwich facility’s forecasted 2020 clinical demand and product mix. The results were confirmed by the three-week facility-wide pilot with long-term impact validated by the simulation tool. These impacts will enable Sandwich to deliver clinical products at an accelerated pace, reducing the time to deliver new medicines to market.

This supports Pfizer’s industry leadership in both developing future blockbusters and satisfying unmet patient needs through the development of breakthrough therapies and precision medicines.

## Pfizer Project Team

### Student Team

Andrés Fuentes-Afflick—Master of Business Administration

Jason Ji—EGL BSE Chemical Engineering, MSE Industrial and Operations Engineering

### Project Sponsors

Ross MacRae—Senior Director, Drug Product Supply

Paul Stuart—VP, Drug Product Supply

Chris Turnbull—Informatics Lead, Drug Product Supply

### Faculty Advisors

Brian Talbot—Ross School of Business

Henry Wang—College of Engineering

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## About Tauber Team Projects

The 2019 Tauber Team Projects resulted in \$390.3 million in savings according to sponsoring company calculations, an average of \$30 million per project over 3 years. Each two to three person Tauber Team consists of graduate engineering and/or graduate business students. Along with receiving high-level corporate support from the sponsoring company, each team is advised by a College of Engineering and a Ross School of Business faculty member and overseen by a Tauber Institute Co-Director. The projects begin on-site in May and continue for 14 weeks. Students present the results of their projects and compete for over \$40,000 in scholarships at the U-M Tauber Institute’s annual Spotlight! event, held each September in Ann Arbor, Michigan. Spotlight! provides outstanding opportunities for students and corporate partners to establish relationships while exploring innovations in operations and manufacturing.

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