WORLDWIDE CLINICAL TRIALS

CASE STUDY: PROACTIVE STRATEGIES FOR MEETING NDA TIMELINES DESPITE LAST-MINUTE SUPPLEMENTAL STUDY REQUESTS

THE CASE

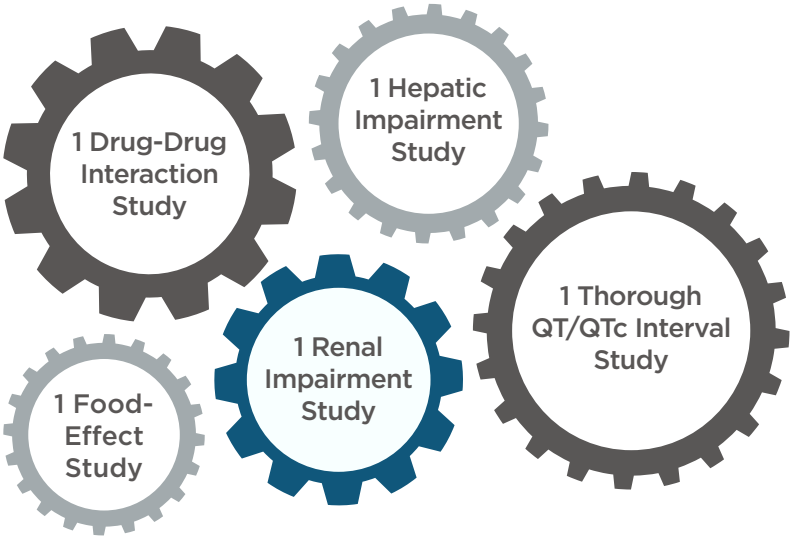
With just months left until planned submission of a new drug application (NDA), the Food and Drug Administration mandated a series of unexpected supplemental studies for a new oncology drug.

THE FACTS

Sponsor: Midsize pharmaceutical company

Study Location: Worldwide's Clinical Pharmacology Unit (CPU) in San Antonio, Texas, and partner sites in the United States.

5 LAST-MINUTE STUDIES REQUESTED:



Document the effect of a low-fat diet on the study drug pharmacokinetics, drug-drug interactions, impact on QT interval, and liver and kidney metabolism.

These last-minute studies were completed on an expedited timeline to achieve the required NDA filing date.

THE RESULT:

Worldwide Clinical Trials engaged sites to dramatically boost recruitment and improve data entry, allowing the sponsor to hit recruitment targets and database lock on schedule.

The NDA was submitted on schedule, and the drug received approval.

THE SPONSOR'S CHALLENGES

TIMELINE

The last-minute FDA requirements had the potential to significantly delay NDA submission for a program that was already near completion.

LOGISTICS

With five unexpected studies to execute, operations had to align seamlessly to enable time-saving multitasking on clinical logistics and reporting requirements.

Without a comprehensive, organized plan and a flexible research partner, execution of five supplemental studies could have derailed the sponsor's chances of submitting its NDA on schedule.

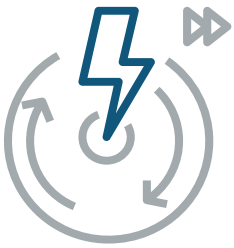
- **The sponsor selected Worldwide to manage all five studies.**

WORLDWIDE'S SOLUTIONS

Having a CRO that is experienced in the common FDA-required studies for NDA submission can make or break the submission timeline. Nimble responses and expert logistics setups can make all the difference.

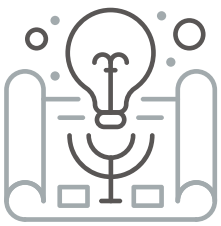
SOLUTION 1

Regular communication with the FDA revealed the request early enough in the timeline to accommodate the requirements without sacrificing the targeted NDA submission date.



SOLUTION 2

Rapid start-up processes and utilization of our own experienced clinical pharmacology unit and multi-site network allowed the design and launch of the first of the 5 required studies in less than 1 month.



SOLUTION 3

Parallel clinical, project management, and regulatory work processes on the studies resulted in fast protocol and CSR writing, rapid recruitment, prompt test results, and the successful execution of multiple studies simultaneously.

THE RESULT: On-Time NDA Submission

Five last-minute studies were accommodated, executed, analyzed, and properly documented for the FDA and EMA in just 8 months.

AUGUST 2017

- FDA requests five supplemental studies
- Hepatic impairment and renal impairment protocols complete

SEPTEMBER 2017

- First hepatic and renal subjects dosed
- DDI protocol complete
- Thorough QT/QTc interval protocol complete

OCTOBER 2017

- First DDI subject dosed
- First thorough QT/QTc interval subject dosed

FEBRUARY 2018

- Food-effect study protocol complete
- First food-effect subject dosed

MARCH 2018

- Food-effect study complete

APRIL 2018

- Last CSR for food-effect study delivered

The sponsor submitted the NDA as planned – on schedule.

The FDA approved the drug, which is now on the market for cancer patients.

FORWARD DEVELOPMENT PROGRESS: The FDA requested another post-approval hepatic impairment study, which the sponsor has awarded to Worldwide.

4 STRATEGIES TO AVOID NDA SUBMISSION HICCUPS

This case study highlights 4 takeaways for other contract research organizations (CROs) and sponsors hoping to avoid – or at least successfully accommodate – last-minute requests for supplemental studies from the FDA or other regulatory bodies.

1

TALK WITH THE FDA EARLY AND OFTEN.

Communicate on a regular basis in the year or two leading up to submission about current clinical trial findings and drug metabolism data. This helps avoid last-minute surprises in the weeks leading up to a scheduled NDA submission date.

2

TRY TO ANTICIPATE LIKELY REQUESTS FOR SUPPLEMENTAL STUDIES.

Many studies struggle with compliance either among patients or study staff. In this case, patients were not sufficiently reporting symptoms – required as part of the primary end point – in the electronic diary. This disrupted the timeline and jeopardized data integrity.

3

BUILD IN TIME TO INVESTIGATE ISSUES DISCOVERED DURING STANDARD TRIALS.

Leave room for extra studies to examine effects of the drug on special populations, metabolic concerns, or DDI issues discovered during the planned course of clinical research. This gives your program wiggle room to accommodate supplemental studies or unexpected timeline shifts (from any cause).

4

GET CREATIVE, NIMBLE, EFFICIENT ASSISTANCE.

Adapt to last-minute requests by optimizing processes and timelines, operating as much in parallel as possible. Coordinate with all key parties to gain commitments to rapid turnaround, and leverage network-wide resources to cut time from sample processing, recruitment, data analysis, and regulatory documentation.

A WORD FROM THE PROJECT MANAGER

Worldwide Clinical Trials was selected to manage a suite of last-minute NDA-enabling studies required for FDA submission of an oncology product. The sponsor selected Worldwide because of its historical experience working with our Phase I clinical pharmacology unit and our full-spectrum CRO services.

The FDA's supplemental requests included hepatic impairment, renal impairment, pharmacokinetics and food effect, DDI, and thorough QT/QTc studies. Work on the first project began in fall 2017, and the last study was completed in March 2018.

Worldwide Clinical Trials was able to overlap the studies to achieve completion in an expedited fashion. This included collaboration with multiple partner sites to reach the hepatic impaired and renal impaired populations quickly and effectively.

By running some of the studies in parallel, Worldwide was able to deliver the final clinical study report in April 2018. The expedited timeline allowed the sponsor to meet its NDA submission date. The FDA subsequently approved the product, and it is now on the market to treat patients.

The number of requested studies – and the sponsor's ideal NDA submission deadline – made it a challenge to adapt logistics and processes while maintaining quality. Our strategic collaboration with all involved parties helped us achieve rapid progress and a successful, timely outcome for the sponsor.

Charles Adam Spencer, M.Adm.
Director, Project Management
Worldwide Clinical Trials

THERE'S NO SUBSTITUTE FOR UNCOMMON EXPERTISE **MEET YOUR PARTNERS**

Sherilyn Adcock, Ph.D., R.Ph.

Executive Vice President, Scientific Solutions

Dr. Adcock has been a top expert in early phase research and Phase 1 cGMP pharmacy manufacturing since 1990. Prior to joining Worldwide in 2001, Dr. Adcock had served in senior-level positions in major contract research organizations. Dr. Adcock's experience in operations and research methods offers valuable expertise from protocol concept and preclinical through transition to Phase II and beyond.

She began her career as a Pharmacist and Clinical Instructor in Pharmacy and was the Pharmacy Services Supervisor at Mother Frances Hospital in Tyler, Texas. In addition to her licensure by the Texas State Board of Pharmacy, Dr. Adcock is certified in basic cardiac life support and sterile products preparation. She is a Member of the American Association of HealthCare Pharmacists, the Drug Information Association (DIA), and the American Association of Pharmaceutical Scientists (AAPS). Dr. Adcock earned her B.S. in pharmacy, a M.S. in health science, and a Ph.D. specializing in community health research, all from the University of Texas at Austin.

Lona Sheeran

Senior Vice President, Clinical Operations Early Phase

Lona serves as the Senior Vice President of Early Phase Clinical Operations at Worldwide Clinical Trials. With over 20 years operating in the early phase environment, Lona has a track record of driving organizational and financial excellence through risk and benefit oversight and Lean Six Sigma techniques. She holds a B.S. degree from Concordia University in Wisconsin.