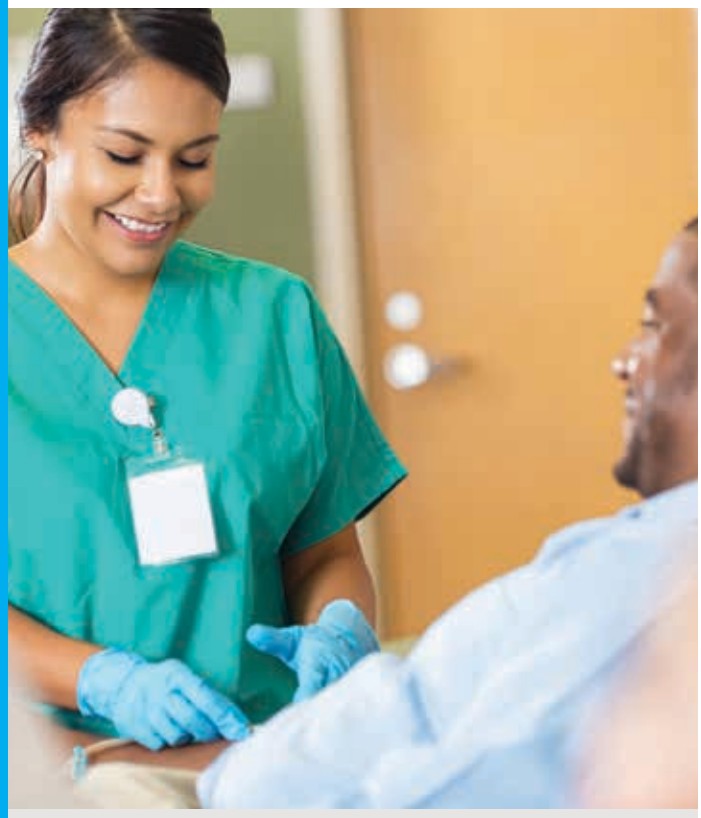
WCCT GLOBAL
AN ALTASCIENCES COMPANY

CASE STUDY:
FIRST-IN-HUMAN TRIAL IN A SPECIAL POPULATION

A First-in-Human (FIH) trial evaluates the safety, side effects, route of administration, optimal dosing, and dosing interval of a new treatment. Beyond this, it serves as the first opportunity for drug developers to take the observations produced during preclinical testing and translate them to meaningful information in human research participants.

When executed correctly, a FIH trial can provide a development team valuable information regarding the safety and exposure at several dose levels of a drug in a short period of time (6 to 12 months). Furthermore, the results from FIH trials can serve to inform every stakeholder at a Sponsor organization, including discovery scientists, formulation scientists, regulatory affairs personnel, marketing, and of course, the clinical operations team. Opportunities to accelerate or enhance a compound's chances of development may also be identified from a FIH project as well.

Over the past several years, the diversity of new therapeutic entities requiring FIH trials has resulted in increased complexity of trial design, often including multiple objectives beyond safety, tolerability, and pharmacokinetics/pharmacodynamics.



The below case study, performed at WCCT's clinical pharmacology unit, highlights a FIH trial which necessitated the identification of subjects from specialty populations in order to achieve the trial's endpoints.

STUDY OVERVIEW

In this FIH study, the Sponsor needed to evaluate how their product might affect the following:

- **Postprandial triglycerides (TG)** [in response to meal tolerance testing]
- **Fasting lipids:** TG, total, cholesterol, LDL-C, and HDL-C.

Therefore, the Sponsor decided to conduct the study in three parts, each with a different population:

- **Part IA:** Healthy volunteers ages 18 to 65, weighing at least 50kg with BMI 18-30kg/m2
- **Part IB:** Healthy volunteers weighing at least 70kg (females) or 79kg (males), with BMI 30-40 kg/m2
- **Part IC:** Healthy volunteers weighing at least 50kg with elevated TG in the range of 200-500 mg/dL

However, the volunteers in Part 1C were not in the original protocol—the protocol was amended when study conduct had already begun. In order to ensure full enrollment of this population as quickly as possible, the Sponsor initiated two sites in addition to WCCT.

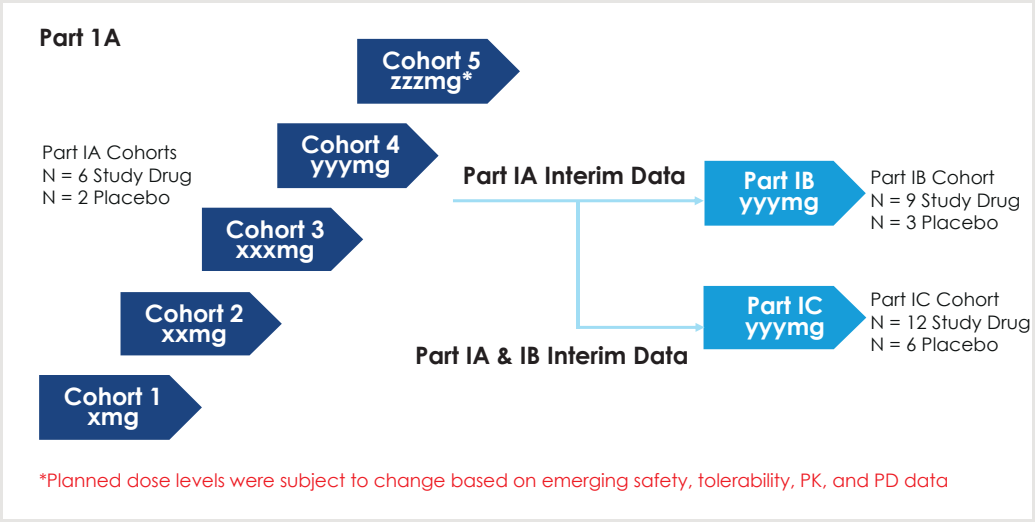
STUDY DESIGN

Subject-Blinded, placebo-controlled, randomized, dose escalation

- Five dose-escalation cohorts, two single-dose cohorts
- Cohort size:
  - Part IA: 5 Cohorts, 6 IP: 2 Placebo (N=40)
  - Part IB: 1 Cohort, 9 IP: 3 Placebo (N=12)
  - Part IC: 1 Cohort, 12 IP: 6 Placebo (N=18*)
    *Sponsor later reduced enrollment to target 12 in this group
- Study Periods
  - Screening: Day -28 to Day -1
  - Confinement: Day -1 to Day 8
  - Follow-up: Day 8 to Day 141
  - End of Study: Day 141

TO DISCUSS YOUR UPCOMING CLINICAL DEVELOPMENT PROGRAM, CALL US AT (714) 252-0770 OR E-MAIL US AT MGR@WCCT.COM

Address: 5630 Cerritos Ave, Cypress, CA 90630



*Planned dose levels were subject to change based on emerging safety, tolerability, PK, and PD data

MEETING THE CHALLENGE

In order to successfully enroll the newly added volunteer cohort, WCCT implemented the following measures:

1. Prescreening strategy to identify subjects with elevated TG. By using this approach, the cost and effort that would have been needed to identify eligible subjects through full screening procedures was significantly reduced.

Pre-Screening Metrics	
Total Subjects within BMI Range	2,287
Subjects Contacted	300
Pre-screening Visits Scheduled	78
Pre-screening Appointments	50
Subjects Meeting Pre-Screen Eligibility Criteria	29

2. Full review of triglyceride levels for any person screening for a study

3. Collaborated with the Sponsor to revise stipends to be more appealing for subjects—the study began enrolling in 2017 but the elevated TG group was added in 2019 and needed to reflect updated stipend rates

4. Advised Sponsor to allow subjects whose TG level met the criteria at pre-screening to be randomized to the study, even if TG levels dropped pre-dose

5. Opened a flexible enrollment period instead of enrolling in a cohort, to accommodate subjects' schedules and facilitate participation

RESULTS AND CONCLUSION

As a result of the sponsor-approved pre-screening strategy which was implemented, WCCT enrolled 9 of the 12 subjects needed in Part IC (as one of three study locations). These efforts allowed WCCT to quickly test a much larger population for TG levels, which proved to be a more cost-effective method overall, thus saving time and money for the Sponsor. All subjects who were cleared for this cohort were identified through the pre-screening effort and randomized into the study. There were no challenges enrolling subjects for Parts IA or IB and we enrolled the entirety of the 6 cohorts.

Due to the performance on this project, and after implementing a subsequent pre-screening strategy which demonstrated the ability to identify subjects in a similar population, WCCT was awarded another FIH trial for the same Sponsor.

COMPANY
OVERVIEW

WCCT is a full-service, early phase contract research organization (CRO) for the pharmaceutical, biotechnology, and medical device industries.
We are specialized regulatory and clinical development professionals who offer an innovative, agile and collaborative approach to every program we deliver.

. 180+ FTEs
. 180 bed Clinical Pharmacology Unit in Cypress, CA
. Participated in over 1,000 trials
. Over 600 Phase I studies
. Strong history of First-In-Human and Pivotal BA/BE trials

Areas of Focus:
. Ethnobridging
. Phase 1 Healthy Volunteer
. Infectious Disease & Vaccines
. Ophthalmology
. Women's Health
. Nicotine/Tobacco

Address:
5630 Cerritos Ave,
Cypress, CA 90630