

# MADISON

## COVANCE CLINICAL RESEARCH UNIT

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### Site Features

- ▶ Total capacity – 72 beds
- ▶ Safety monitoring – 16 beds
- ▶ Participant database – 23,434
- ▶ Longest continuous in-house stay – 72 days
- ▶ cGMP pharmacy, including two sterile and three non-sterile manufacturing suites
- ▶ Emergency response time – < 5 minutes
- ▶ On-site Nuclear Pharmacists, Radiation Safety Officer, Radiation Safety Committee and physician-authorized users
- ▶ Medical Director is an MD. We have conducted 330 AME studies over the past 20 years.

The Clinical Research Center (CRU) in Madison, Wisconsin, is a state-of-the-art, 72-bed purpose-built clinic co-located with Covance Laboratories. The Madison team has 40 years of experience conducting Phase I trials in healthy volunteers, including AME, FIH and complex study design. Studies requiring real-time cell identification with flow cytometry are also a focus for the Madison clinic. Our staff includes three physicians, three board-certified pharmacists and more than 50 full-time medical and technical personnel. The clinic also has close relationships with academia and physicians at the University of Wisconsin and Unity Point Meriter Hospitals due to their close proximity.

The Madison clinic is the global leader in the conduct of radiolabeled clinical studies with three board-certified pharmacists (two are authorized nuclear pharmacists) and a Radiation Safety Officer to ensure consistent compliance with FDA, NRC/Agreement state and DOT regulations across all Covance sites. Real-time radioanalysis (for recovery) is performed on-site to determine exact day of discharge.

The cGMP pharmacy includes two sterile and three non-sterile manufacturing suites, which can manage and handle high-potency and hazardous drugs. In addition, the cGMP dose analysis group provides on-site, real-time quality assessments of clinic-formulated doses. On-campus, Covance Laboratories provides services from bioanalytical to metabolite ID and profiling.

# REAL-TIME DATA. EXPERT ANALYSIS. HIGH RECOVERY.

## A RADIOANALYSIS CASE STUDY

A leading biotechnology client contracted with Covance for a human absorption, metabolism and excretion (AME) study using  $^{14}\text{C}$  to determine the excretory pathway and metabolite identification and potential enterohepatic recycling. The Covance CRU team in Madison, Wisconsin, gave subjects doses of the radiolabeled drug, then collected samples, analyzed data and reported results each day of the trial – with a target threshold of 90 percent recovery. The sponsor would compare the clinical study results to the preclinical data to make decisions regarding the drug's further development.

### Understanding the Challenge

- ▶ Accurate and timely collection of samples and data
- ▶ Same-day analysis and interpretation of results
- ▶ Daily reporting against target of 90 percent recovery
- ▶ Scientific expertise to aid decision-making

### On-Campus Clinic and Radioanalysis Deliver Real-Time Data and Analysis

A dedicated Covance team administered doses of the radiolabeled drug to subjects at the CRU. The staff then collected blood samples plus urine and feces during the two-week study. Rigorous collection techniques allowed for correct assessment of drug metabolites, drug excretion and potential enterohepatic recycling. The clinic immediately delivered samples to the on-campus radioanalysis lab for same-day processing. Data were electronically captured for fast, reliable analysis.

**Having the CRU and radioanalysis lab on one campus allowed for virtual real-time data and analysis, supporting every effort to achieve 90 percent recovery.**

Analysis revealed longer-than-expected circulating levels of the drug in the subjects' blood and plasma, with an increased blood-to-plasma level over time and preferential binding to plasma. Usually, the team sees a recovery rate of 91-92 percent for radiolabeled drugs, but this compound presented a lower rate of 88 percent. The lagging recovery of  $^{14}\text{C}$  suggested that the compound was reappearing in the blood and, as a result, being slowly excreted over a longer time than the sponsor anticipated. Because these results did not match the sponsor's preclinical data, Covance experts consulted daily with the client to review results.

With virtually real-time data, the sponsor could draw conclusions quickly, meeting objectives, timelines and budgets. In this case, the client determined that further analysis and development of the drug were needed to complete the puzzle regarding its circulation pattern. Subsequently, Covance was able to offer its hAME service – collecting bile samples from the  $^{14}\text{C}$ -drug-dosed human subjects – to assess quantitatively both the importance and extent of the drug's metabolism via the biliary route.

Covance helps sponsors determine the best use of radiation for trials, based on our extensive experience. U.S. regulations allow a higher radiation level than other countries, with 60 percent of U.S. studies using 100  $\mu\text{Ci}$  and about 20 percent using doses between 150 and 600  $\mu\text{Ci}$ . This allows us to detect even the subtle presence of a  $^{14}\text{C}$ -compound systemically to evaluate enterohepatic recycling in humans.

Covance Inc., headquartered in Princeton, NJ, USA is the drug development business of Laboratory Corporation of America Holdings (LabCorp). COVANCE is a registered trademark and the marketing name for Covance Inc. and its subsidiaries around the world.

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