Worldwide Clinical Trials

Guide

Managing AME Studies: Selecting the Right CRO for Success

AME Studies Are Highly Specialized — Is Your CRO?

Despite the large market for absorption, metabolism, and excretion (AME) studies, also known as human mass balance studies, why are so few CROs in the U.S. able to perform them? It can be hard to find an AME partner because, for CROs, the necessary setup is time consuming, labor intensive, and expensive.

To conduct AME studies, a CRO must have a radiation safety officer (RSO) experienced in clinical research trial activities and processes. It must also secure and maintain the appropriate license to handle radioactive materials. This licensure generally involves one or more federal, state, and local governmental agencies. CROs are also required to have the proper standard operating procedures (SOPs) and training procedures in place, which are reviewed by the relevant authorities for approval in specific radioisotopes, such as carbon-14 and/or tritium.

Many clinical pharmacology units (CPUs) — and their associated laboratories — either don't have the space to devote to a separate radioactive area (dedicated space for dose preparation, dose administration, subject confinement, and sample collection) or prefer not to undertake the rigorous training necessary for handling radioactive materials safely. Finding a partner to perform your AME studies in a reasonable time frame, let alone one with an excellent track record, can be a challenge.

Worldwide's Experience With and Capabilities for Performing AME Studies

For more than 20 years, we have been conducting AME studies, working with up to 150 uCi of carbon-14/IP dose to assist in the determination of drug absorption, metabolism, and excretion of parent compounds and metabolites.

Over the past three years, our dedicated, controlled-access CPU in San Antonio, Texas, has conducted has conducted, on average, four mass balance studies per year, as studies may not overlap to avoid radioactive contamination. or as simultaneous studies are not permitted to avoid radioactive contamination. Routine matrices for radioactive recovery include blood, urine, and fecal matter collected over extended time periods (five days or longer). Procedures have occasionally also included collection of expired air for 14CO2. Without exception, these studies have achieved excellent recovery rates as seen in Figure 1 despite some challenging compounds that demonstrated unexpected pharmacokinetic characteristics.

Radioactive materials licenses are held at both our CPU and our bioanalytical laboratory in nearby Austin, Texas. All necessary SOPs and training documents are in place at both locations. In addition, Worldwide has a strong working relationship with our central institutional review board (IRB), which allows for greater flexibility and significant time savings throughout the review process.

Worldwide's CPU goes to great lengths to properly handle AME study samples, including establishing specific procedures for collection, processing, labeling, and shipping. We work with well-established ground couriers that are licensed the for transport of radioactive materials. Sample shipments are made daily to our local laboratory, where they are analyzed immediately. This process allows Worldwide to carefully track radiation levels and make informed decisions around radioactive recovery and participant release from our studies.

Key Lessons and Best Practices

1 Ensure effective patient and site management

When managing patients and sites, our top priorities include participant comfort and compliance alongside high-quality data. We make every effort using traditional and novel approaches to recruit and retain the right participants for our studies. AME studies are more challenging in this regard and special considerations apply.

From screening with a careful assessment of medical history and daily bowel habits through informed consent and the instructional and dosing phases, our staff ensures patients fully understand and feel comfortable with the intimate details and importance of total radioactive recovery during these studies.

Subjects must be flexible with their time and provide us with the samples we need. Proactive management of subject expectations includes information regarding:

- No definitive stopping date
- Dry restrooms
- Dietary requirements: High-fiber diet for bowel motility
- 24/7 collection of all urine, fecal matter, and blood sample collection

2 Prioritize excellence in total radioactive dose recovery rates

As shown in Figure 1, Worldwide has an outstanding track record of 98.9% radioactivity collection. To attain this level of radioactivity recovery requires careful attention to both dosing and sample collection.

Dosing

It is vital for subjects to take the entire dose, down to the last drop, for liquid doses, and administering the liquids in wide-mouth containers for easy and efficient delivery is best practice. To ensure full dosing, protocols should include steps where trialists rinse bottles with water for the subjects to consume, then follow with more water. Finally, scan the bottles for residual radioactivity.

> Worldwide has an outstanding track record of 98.9% radioactivity collection.

At Worldwide, a pharmacist with radiolabel product preparation and administration oversees all dosing and is also available to deliver pre- and post-dose instructions and answer questions to ensure uniform, complete dosing across subjects.

Biological sample collection

Reminders are strategically placed around the CPU radiolabel confinement area, especially near the shower, to reinforce the need for collection of all urine and fecal samples. Diet is modified if needed to promote bowel movements. Collection time is typically five to seven days and subjects, cannot miss a collection. Once collections are made each day, they are sent to the lab for measurement of radioactive recovery.

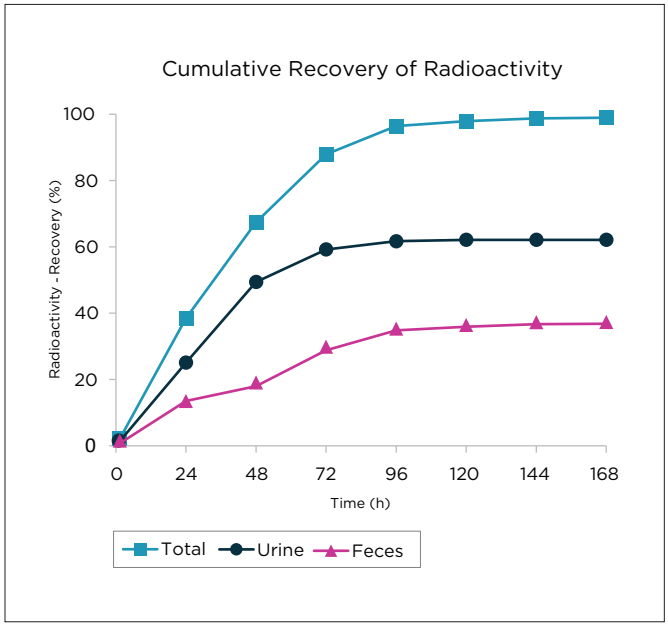

Figure 1. Total radioactivity recovered in sponsor radiolabeled AME studies at Worldwide — 98.9%.

3 Build a specialized team for radiolabeled drug research

The prospective CRO must have a highly trained specialized team to guide the study's safe conduct. Ours includes:

- **Radiation safety officer (RSO):** The RSO engages in staff training, reviews SOPs, oversees contamination and sample collection testing, and reviews dose calculation, preparation, and administration by the pharmacy.
- **Radiologist/Sub-investigator:** A board-certified radiologist is available in addition to the primary physician investigator for protocol review, comments, consultation on study design, and to sign off on dose/dosimetry calculations.
- **Pharmacists:** Full-time, specially trained pharmacists handle and prepare the radiolabeled materials. A CPU pharmacist oversees all the dosing.
- **Health physicist:** A health physicist consultant reviews the data from preclinical studies and assists in preparation of dosimetry and radiation exposure reports as needed.

> "Don't wait until you receive a letter from the FDA requesting AME data. Act early to accelerate your approval journey."

Just-in-time, medic and technical staff training is performed to ensure facility staff is up-to-date on their understanding of SOPs, processes, and protocol-specific requirements. The RSO covers both the lab and the CPU and is involved in training at both facilities.

4 The onsite cGMP Phase I pharmacy must have significant radiolabel drug preparation experience

A CPU used for AME studies must be licensed and experienced in handling radioactive investigational drugs. Our CPU's radiolabel pharmacy is licensed and capable of hot and cold compounding to achieve target investigational product (IP) dose and radioactivity.

We utilize on-site scintillation counting to test investigational drug preparations to see that they conform with the target radioactivity and to confirm full-dose administration.

5 Prioritize custom services suited to the study needs

Due to the complexity and expertise required for successful AME studies, selecting a partner that provides custom-tailored solutions for your IP and study goals, with open, bidirectional communication and flexibility throughout, becomes essential. Worldwide offers true partnerships for early phase development, with professionals dedicated to fulfilling the needs of sponsors' unique development programs. Our bioanalytical laboratory sets the bar for efficiency and will ensure sponsors receive the AME insights and evaluations they need to make the best possible decisions.

Our bioanalytical lab is flexible in productivity and can accommodate analysis based on your study's requirements. State-of-the-art instrumentation and more than 2,400 validated assays make Worldwide an industry leader in bioanalytical method development and validation.

6 Select a CRO that has a streamlined patient-to-lab procedure

A rapid turnaround with accelerated decision-making is vital, as it allows for immediate identification of individual subjects who have met study objectives, saving costs and maintaining the predetermined study time course. The close proximity of Worldwide's bioanalytical lab to our CPU enables streamlined daily ground transport and rapid radioanalysis of AME samples, supporting efficient and informed decision-making..

Our full-service CPU contains 200 beds with flexible procedure space, a cGMP Phase I compounding pharmacy, and a CLIA safety lab. At the bioanalytical lab, in-house bioanalytical scientists engage in LC-MS method development and bioanalysis. In addition, our Pharmacokinetics team performs a comprehensive analysis and final study report of radioactive recovery and PK analysis.

The state of Texas defers to federal regulations for licensing and there are no additional state rules with which to comply. Scintillation counting can be conducted daily to provide timely monitoring of cumulative radioactive output.

Collect AME data early to guide development — and satisfy the FDA

All NCEs require an AME study. Whether, the FDA is calling for AME data early or not, plan for AME studies proactively. Since only a limited number of CROs can perform them in the United States, reserve ahead. AME data can add valuable insight at the start of a clinical trial journey and can help anticipate later trial expectations, helping sponsors save time and costs.

Worldwide Clinical Trials is the ideal partner for AME research. We have significant success and experience conducting AME clinical trials. Sponsors benefit from a highly qualified project team of AME experts. Our integrated lab and clinic facilitate prompt analysis of radioactive samples, allowing for efficient subject dismissal.

At Worldwide, our team can assist throughout your AME clinical trial, from protocol writing to the final study report.

Worldwide Clinical Trials

About Worldwide Clinical Trials

Worldwide Clinical Trials (Worldwide) is a leading full-service global contract research organization (CRO) that works in partnership with biotechnology and pharmaceutical companies to create customized solutions that advance new medications – from discovery to reality.

Anchored in our company's scientific heritage, we are therapeutically focused on cardiovascular, metabolic, neuroscience, oncology, and rare diseases. Our deep therapeutic knowledge enables us to develop flexible plans and quickly solve problems for our customers.

For more information on Worldwide, visit www.worldwide.com or connect with us on LinkedIn.

Last Update:01292025