



ONCOLOGY HUMAN MASS BALANCE IN PHASE 1 PATIENT STUDIES

**INCLUDE A MICROTRACER IN YOUR PHASE 1 EXPANSION COHORT TO
OBTAIN REGULATORY REQUIRED HUMAN ADME DATA EARLY ON**

Oncology is special:

- Oncology drugs are often cytotoxic or genotoxic, which is ethically not acceptable for studies with healthy participants
- Dosing up to MTD is related to increased likelihood of saturation of transporters and metabolic enzymes.
- Phase 1 often tested as monotherapy, while in Phase 2/3 co-medication and combination therapy is common. DDI prediction is therefore essential for a successful Phase 2/3 design.

- Comorbidities like renal or hepatic impairment are common in cancer patients.

Microtracer studies use 100-fold less radioactivity than conventional studies

- ICRP Ethical Class 1: No QWBA dosimetry study needed
- Low radiation burden gives more flexibility in choice for clinics.

**EARLY INSIGHTS ON HUMAN ABSORPTION, METABOLISM AND
EXCRETION IN CANCER PATIENTS SUPPORT THE OPTIMAL DESIGN OF
YOUR LATE-STAGE DEVELOPMENT PROGRAM**

- Data on human metabolism and excretion routes supports the design of your later DDI and hepatic/renal impairment studies.
- Details on absolute bioavailability and fraction absorbed helps you decide if an optimized formulation will improve exposure levels.

TAILWIND SUPPORTIVE FOR MICROTRACER ENABLED EARLY HUMAN MASS BALANCE STUDIES

FDA guidance

- ✓ Conduct human *in vivo* metabolic evaluation as early as feasible
 - 📄 Clinical Pharmacology Considerations for Human Radiolabeled Mass Balance Studies Guidance, July 2024
 - 📄 Safety Testing of Drug Metabolites Guidance for Industry, March 2020
- ✓ Project Optimus aims to prioritize cancer patient safety and therapeutic precision with a revamped dose optimization framework, including the use of PK data to make informed dosing decisions
 - 📄 www.fda.gov/about-fda/oncology-center-excellence/project-optimus

Ethical considerations

- ✓ FDA: moving away from animal testing
 - 📄 General Considerations for the Use of New Approach Methodologies in Drug Development Guidance for Industry, March 2026
- ✓ Neonatal studies: microdosing studies to provide preliminary pharmacokinetic information
 - 📄 General Clinical Pharmacology Considerations for Neonatal Studies for Drugs and Biological Products, Guidance for Industry, July 2022
- ✓ Women's health
 - 📄 Progress and opportunities for women in clinical trials: A look at recent data and initiatives from the U.S. FDA, 2021
- ✓ Low dose over high dose RA labelling (ALARA)

Complex formulation

- ✓ Indication of increasing number of complex formulations
 - 📄 BCS class IV drugs: Highly notorious candidates for formulation, 2017

Examples of microtracer studies in cancer patients:

A Phase 1, two-period, study for berzosertib Bolleddula *et al.* (2025)
Merck KGaA, DOI:10.1002/cpdd.1554

A notable metabolite was identified in circulation, with clearly higher plasma exposure than the parent drug.

A Phase 1, single arm, study for vemurafenib Zhang *et al.* (2020)
Roche, DOI: 10.1002/cpdd.773

The majority of radioactivity was recovered in feces.



Contact us for more information via info@peregrion.com or the contact page on the website



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