

# Mass Balance

## AMS study design considerations



Purpose Mass balance studies investigate the absorption, distribution, metabolism and excretion (ADME) of a drug following a single administration to humans. The drug is often radiolabeled to allow determination of drug disposition and assessment of major metabolic pathways, as well as exposure to the parent drug and its metabolites, and the rate and route of elimination. The mass balance study generates the following PK parameters based on urine and feces total radioactivity:

	Urine	Feces
Amount of drug excreted over the sampling interval ( $A_{eu}$ )	√	√
Renal clearance (CLR)	√	
% Excreted	√	√

Accium has successfully delivered on a wide range of AMS-based mass balance studies. Each study was customized to address particular challenges that were specific to each program. In particular, we provide real-time processing and analysis of fecal samples and submit QC'd results to the clinic to support discharge decisions. An outline of the various approaches we have employed in the design and conduct of these studies is shown below:

### Clinical Design

1. Six to eight subjects.
2. Single dose at, or near, pharmacologic dose.
3. Radiolabel dose around 100-nCi if agent is well absorbed.
4. Radiolabel dose up to 10 uCi if agent is poorly absorbed (fecal samples analyzed by scintillation not at Accium!).
5. Collect 1-2 mL plasma and all urine and fecal samples for analysis.
6. Clinic may ship urine and fecal samples to Accium each day to receive AMS results as early as five days after collection.

### Bioanalytical Design

#### Pre-study Phase

1. No activity required.

#### Study Phase

1. Blend and process fecal samples for measurement by AMS.
2. Process urine samples for measurement by AMS.
3. Measure total carbon concentration in each urine and fecal sample for accurate reporting of  $^{14}\text{C}$  recovery.
4. Report ng-eq drug product recovered in each urine and feces collection period.
5. Report % dose recovered and % cumulative dose recovered in each urine and feces collection period.

### Advantages

- Radiolabeling permits recovery of isotope in urine and fecal collections without method development.
- Reduction of isotope to nCi range eliminates dosimetry requirements.
- Eliminates radiolysis for certain drug products administered at high-specific-activity.
- Samples are often treated as non-radioactive during shipment and processing.
- These studies can often be coupled with metabolite profiling studies.

### Disadvantages

- Requires  $^{14}\text{C}$ -labeled drug product.
- AMS analysis can be more costly than traditional methods.
- Reporting of results can take longer than traditional methods.

