Food Effect Study Best Practices

Food can alter systemic drug exposure, which can negatively affect safety and efficacy. A meal can either increase or decrease drug exposure through several mechanisms. For instance, food increases gastric pH, delays gastric emptying, increases residence time in the stomach and impacts bile salt levels that sequester drug molecules. For the development of drugs that are to be administered orally, it is recommended to assess the impact of a meal in a food effect (FE) study. Regulators suggest to assess FE early during drug development in a small pilot study, often incorporated in a single ascending dose (SAD). A pivotal, dedicated, study may be recommended in the later stage of development if the formulation has changed since the SAD study and/or a FE was initially identified.

Meal Type

In a typical FE study, a high-fat meal consisting of 800-1000 Kcal (≥50% fat) is consumed, as it has the greatest chance to induce an effect. A low-fat meal should be considered as the test meal if results from a high-fat FE study revealed a significant increase in drug exposure, toxicity or loss of efficacy, or if a high-fat meal cannot be tolerated in the indicated patient population. A low-fat meal consists of 400-500 Kcal (25% fat). In some cases, a high-carbohydrate or moderate-fat meal is consumed to evaluate their impact on drug absorption.

Celerion Differentiators:

Experience:

– Over 100 FE studies in the past decade

Expertise:

– Dedicated team of expert PK Scientists and Biostatisticians

Efficiencies:

– FE studies can be combined with multi-part bioavailability or acid reducing agent studies

– On-site kitchen and Registered Dietician to help customize meals as necessary

Study Design Characteristics

Study Design Characteristics	Pilot FE Study	Pivotal FE Study
Study Purpose	To evaluate the impact of a high-fat meal on drug PK early in drug development	To confirm the impact of a meal on drug PK, especially if: • To-Be-Marketed formulation differs from pilot drug formulation, unless a biowaiver is accepted • Efficacy or safety is adversely impacted by fed/fasting conditions
Study Design	Incorporated in a first-in-human study, typically a SAD study	Randomized, single-dose, two-way or three-way crossover
Drug Intake & Meal Regimen	• Fasting: Drug administered following overnight fast (10 hours) • Fed Condition: Following an overnight fast (10 hours), meal consumed 30 min prior to dose administration and eaten within 30 min • Meal Type: High-fat and/or Low-fat	
Participants	Healthy volunteers, participants with lactose deficiency or on a keto diet are excluded	
Sample Size	6 active / 2 placebo	Powered study (n= 24-48)
Key PK Parameters	AUC, C_{max}, T_{max}	

AUC, area-under-the curve; **C_{max}**, maximal concentration; **FE**, food effect; **PK**, pharmacokinetic; **SAD**, single ascending dose; **T_{max}**, time to maximal concentration


Example of Meal Compositions
Low-Fat Meal
400-500 Kcal (25% fat)
✓ Eight ounces milk (1% fat)
✓ One boiled egg
✓ One packet instant oatmeal
High-Fat Meal
800-1000 Kcal (50% <fat)
✓ Eight ounces of whole milk
✓ Two eggs fried in butter
✓ Two strips of bacon
✓ Two slices of toast with butter
✓ Four ounces of hash brown potatoes