Product Labeling Studies

Celerion collaborates with pharmaceutical companies seeking market approval for new drugs. Based on the regulatory requirements highlighted in the table below, product labeling studies are a key component of drug development.

We proactively create efficient and cost-effective packages of product labeling studies that form the basis for specific labeling claims in your drug applications. Most importantly:

– For speed and accuracy of your data, Celerion's global clinics and bioanalytical laboratories share SOPs, data capture and analysis systems

– Expert scientists support the design and execution of labeling studies for your drug during early clinical development

– Celerion has the capacity to manage multiple studies simultaneously to accelerate your timelines toward submission

Table. Types and Features of Product Labeling Clinical Pharmacology Studies

Study Type	Regulatory Requirement	Study Design Elements	Study Population & Sample Size	Duration of Clinical Conduct	Comments
Drug-Drug Interactions	To evaluate if drug concentration and PK profile are altered upon co-administration of other medications	• 1-way or 2-way crossover • 2,3,4 arm parallel • Fixed sequence	• Healthy participants • N=14-16	• 1-3 months	• Common co-administered drugs • Warfarin, Digoxin – low TI • Drugs that reflect activity of certain drug metabolizing enzymes of transport proteins where in vitro studies suggest that the new drug candidate may interact • Strong inhibitors or inducers of key elimination pathways for a new drug candidate
Hepatic Insufficiency	To determine if drug dose should be adjusted or if the drug is contraindicated for patients with hepatic disease	• 2,3,4 arm parallel • Adaptive (staged)	• Patients with hepatic impairment and healthy matched controls • N=6-8 per group	• 6-12 months	• Mild, moderate and severely impaired as measured by Child-Pugh score
Renal Insufficiency	To determine if drug dose should be adjusted or if the drug is contraindicated for patients with renal disease	• 2,3,4 arm parallel • Adaptive (staged)	• Patients with renal impairment and healthy matched controls • N= 10-14* per group *Sample size calculation highly recommended	• 6-12 months	• Mild, moderate and severely impaired as measured by estimated GFR or creatinine clearance • During and between hemodialysis
Absorption, Distribution, Metabolism, Excretion (ADME)	A critical PK study to understand how the drug is metabolized	• Single dose of radiolabeled drug (traditional dose ~100 microCuries; microtracer dose <500 nanoCuries)	• Healthy young male participants • N=6	• 2 weeks conduct • 1-4 months sample analysis	• At times, it can only be done in patient populations (e.g. oncology) which might require microtracer approach in hospital setting with conduct covering 1-2 patients at a time

Table. Types and Features of Product Labeling Clinical Pharmacology Studies (cont'd)

Study Type	Regulatory Requirement	Study Design Elements	Study Population & Sample Size	Duration of Clinical Conduct	Comments
Thorough QT (TQT)	To evaluate the proarrhythmic risk of a drug in development	• 3,4-way crossover • 3,4 arm parallel • Parallel with nested crossover	• Healthy participants • N=48-180	• 2-6 months	• QT interval of ECG is a biomarker for proarrhythmic risk • Moxifloxacin is the usual positive control • Highly automated digital ECG analysis
Market-Image Bioequivalence	To evaluate the market ready drug batch	• 2-way crossover • Parallel (rare)	• Healthy participants • N=14 (not powered)	• 1-2 months	• Compare bioavailability of product from commercial production batch versus product used in pivotal clinical trials
Definitive Food Effect	To determine how a meal impacts a drug's PK profile	• 2,3-way crossover (fasting, low-fat and/or high-fat meal)	• Healthy participants • N=14 (not powered)	• 1-2 months	• For orally delivered drugs where earlier studies indicated a potentially clinically significant food effect
Ethnic Bridging PK Studies	To explore how genetic and polymorphic differences affect drug PK	• Parallel need to relate clinical data collected in one population to use in another defined population	• First and second generation descendants of an ethnic group and matched controls • N=14 per cohort (not powered)	• 1-4 months (depends on availability of suitable participants)	• Justified by known polymorphic differences among different ethnic or genetic populations in expression of proteins involved in metabolism, transport or effect
PK in Special and Subpopulations	To determine if dose adjustment or contraindication is required for special populations	• Single dose or repeated dose as justified by intended clinical use	• Older adults, obese cohorts, post-menopausal women • N=14 per cohort (not powered)	• 1-12 months (depends on availability of suitable participants)	• Other special populations include pediatrics and pregnant/lactating women
Population PK or PK/PD Analysis	To determine if dose adjustment or contraindication is required for special populations	• Sparse sampling from patients enrolled in pivotal efficacy and safety studies	• Target population	• Duration of phase III program	• Effect of disease, age, BMI, gender, genetics, ethnicity on intersubject variability PK parameters • Population PK model is often set up from Phase I and II PK studies

BMI, body mass index; ECG, electrocardiogram; GFR, glomerular filtration rate; PD, pharmacodynamic; PK, pharmacokinetic; TI, therapeutic index