

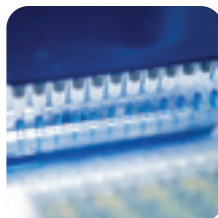
A flexible approach to
DMPK

QPS DMPK PROVIDES A DEDICATED TEAM OF SENIOR SCIENTISTS TO HELP SELECT, DESIGN AND CONDUCT THE APPROPRIATE ADME STUDIES FOR YOUR SPECIFIC COMPOUNDS AND THERAPEUTIC TARGETS.

Working with QPS DMPK is a collaborative and consultative endeavor that also incorporates our operational effectiveness and dedication to customer service.

**TIME IS OF THE ESSENCE IN DRUG DEVELOPMENT.
CONTACT THE QPS BUSINESS DEVELOPMENT TEAM TODAY!**

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Macro & Micro Autoradiography

One of QPS' main services in DMPK is the combined mass balance, biliary excretion, PK, and QWBA studies.

- ▶ Increased efficiency by using a single study protocol
- ▶ Better study oversight with an integrated study report
- ▶ Elimination of the possibility of radiolabel degrading over an extended period of time between the two studies
- ▶ Metabolite profiling and identification can be done using the samples from the same study
- ▶ Micro-autoradiography provides insight into sub-cellular tissue distribution

Biotransformation

QPS biotransformation studies determine how a molecule may be altered by the action of enzymes. These study types include:

- ▶ *In vitro* metabolic stability in hepatic subcellular fractions to determine intrinsic clearance
- ▶ *In vitro* comparison of metabolite formation in animal and human hepatic preparations, using non-labeled and radio-labeled test articles
- ▶ *In vivo* metabolite profiling, identification and quantification using samples collected from animal PK, mass balance excretion studies, and human AME studies to satisfy Metabolites in Safety Testing (MIST)

Protein Binding

QPS protein binding studies determine the extent of protein binding in various plasma species and tissues.

- ▶ Methods: equilibrium dialysis (RED, Harvard device, 96-well HTD), ultrafiltration, and ultracentrifugation
- ▶ Discovery screening, *in vitro* protein binding for IND, and *ex vivo* studies in clinical phases
- ▶ Experience in compounds with very high binding, stability issues, or non-specific issues

Drug-Drug Interaction

QPS drug interaction studies determine the potential of a substance to alter cytochrome P450 activity. Studies conducted to assess inhibition and induction potential to support discovery and development of new drug candidates are:

- ▶ *In vitro* inhibition characterization in human liver microsomes or hepatocytes to determine reversible or time dependent IC50
- ▶ *In vitro* mechanistic characterization of reversible inhibitory rate constants K_i
- ▶ Identification of the reversible mechanism of inhibition as competitive, non-competitive or uncompetitive
- ▶ *In vitro* mechanistic characterization of time dependent inhibition K_{inact} and K_I
- ▶ Identification of the mechanism of time dependent inhibition as metabolite mediated via covalent modification or due to tight binding effect of substrate
- ▶ *In vitro* characterization of CYP1A2, CYP2B6, and CYP3A4 induction potential in human hepatocytes based on mRNA and/or CYP activity using isoform selective probe substrates

QPS is a Global CRO with locations around the world

