Drug Metabolism and Pharmacokinetics (DMPK)

RTI International is a leader in metabolism, disposition, and pharmacokinetic studies of pharmaceuticals and other xenobiotics in mammalian systems. With more than 25 years of experience conducting DMPK studies, our highly trained scientific staff members offer innovative approaches to unique development issues. From protocol development through data interpretation, all studies are directed by senior DMPK scientists.

In Vivo Capabilities

RTI uses Lablogic Systems' Debra, a validated, industry-standard data collection system, ensuring accuracy and speed in reporting GLP-compliant ADME studies. Our capabilities in whole-animal studies include the following:

- Pharmacokinetic studies in standard biological models
- Experience with a variety of dose routes
- Radiolabeled studies (absorption, distribution, mass balance, excretion)
- Discovery pharmacokinetics screening
- Pharmacokinetic models (classical and physiologically based)
- Oral and percutaneous bioavailability
- Drug interactions (induction and inhibition)
- Metabolic profiles, metabolite identification
- Biomarkers of exposure (hemoglobin and DNA adducts)
- Disposition of nanomaterials

In Vitro Capabilities

- CYP inhibition (competitive and mechanism-based)
- CYP induction in HepRG cells and hepatocytes
- CYP reaction phenotyping (HLM or rhCYPs)
- Metabolic stability, clearance, and metabolite identification in hepatocytes or microsomes
- Protein binding (equilibrium dialysis)
- Permeability in Caco-2 and MDCK cells; PAMPA
- hERG

Analytical Capabilities

- HPLC with UV, fluorescent, electrochemical, and radiometric detection
- UPLC
- LC/MS/MS (API 4000, API 5000)
- Thermo Finnigan LTQ Orbitrap Velos ETD
- Synapt G2 Q-TOF with Acquity UPLC
- GC/MS/MS (Triple Quadrapole) with SPME/HS/Liquid Injection; also FID, EC detection
- 300- and 500-MHz nuclear magnetic resonance spectrometers

Additional Resources

- AAALAC-accredited animal research facility
- Quality Assurance Unit
- DEA Schedule 1 certificate
- Radiolabel synthesis

Working Closely with Our Clients

RTI's technical, research, and development services meet the highest standards of professional performance. We work closely with our clients to identify their requirements and clarify their expectations, including cost and time constraints.

RTI extends its excellence in research and technical services to its business systems and processes, making it easy to partner with us. We have the contractual, legal, and business structures to serve any client with projects of all sizes. RTI is a 501(c)(3) nonprofit corporation.

Recent Publications

Quinnies, K. M., Harris, E. P., Snyder, R. W., Sumner, S. S., and Rissman, E. F. (2017). Direct and transgenerational effects of low doses of perinatal di-(2-ethylhexyl) phthalate (DEHP) on social behaviors in mice. *PloS one* 12, e0171977, 10.1371/journal.pone.0171977.

Fennell, T. R., Mortensen, N. P., Black, S. R., Snyder, R. W., Levine, K. E., Poitras, E., Harrington, J. M., Wingard, C. J., Holland, N. A., Pathmasiri, W., and Sumner, S. C. (2016). Disposition of intravenously or orally administered silver nanoparticles in pregnant rats and the effect on the biochemical profile in urine. *J Appl Toxicol*, 10.1002/jat.3387.

Owens, S. M., Pollard, G. T., Howard, J. L., Fennell, T. R., Snyder, R. W., and Carroll, F. I. (2016). Pharmacodynamic relationships between duration of action of JDTic-like Kappa-Opioid receptor antagonists and their brain and plasma pharmacokinetics in rats. *ACS Chemical Neuroscience* 7, 1737–1745.

Roberts, G. K., Waidyanatha, S., Kissling, G. E., Fletcher, B. L., Silinski, M. A. R., Fennell, T. R., Cunny, H. C., Robinson, V. G., and Blystone, C. R. (2016). Exposure to butyl paraben during gestation and lactation in Hsd:Sprague dawley SD rats via dosed feed. *Toxicology Reports* 3, 774–783, http://dx.doi.org/10.1016/j.toxrep.2016.09.004.

Waidyanatha, S., Mathews, J. M., Patel, P. R., Black, S. R., Snyder, R. W., and Fennell, T. R. (2015). Disposition of bisphenol AF, a bisphenol A analogue, in hepatocytes in vitro and in male and female Harlan Sprague-Dawley rats and B6C3F1/N mice following oral and intravenous administration. *Xenobiotica* 45, 811–819.

Sumner, S. C., Snyder, R. W., Wingard, C., Mortensen, N. P., Holland, N. A., Shannahan, J. H., Dhungana, S., Pathmasiri, W., Han, L., Lewin, A. H., and Fennell, T. R. (2015). Distribution and biomarkers of carbon-14-labeled fullerene C60 ([14C(U)]C60) in female rats and mice for up to 30 days after intravenous exposure. *J Appl Toxicol* 35, 1452–1464.

Snyder, R. W., Fennell, T. R., Wingard, C. J., Mortensen, N. P., Holland, N. A., Shannahan, J. H., Pathmasiri, W., Lewin, A. H., and Sumner, S. C. (2015). Distribution and biomarker of carbon-14 labeled fullerene C60 ([14C(U)]C60) in pregnant and lactating rats and their offspring after maternal intravenous exposure. *J Appl Toxicol* 35, 1438–1451.

Fennell, T. R., Snyder, R., Hansen, B., and Friedman, M. (2015). Dosimetry of Acrylamide and Glycidamide over the lifespan in a 2-year bioassay of Acrylamide in wistar han rats. *Toxicol Sci* 146, 386–394.

Fennell, T. R., Morgan, D. L., Watson, S. L., Dhungana, S., and Waidyanatha, S. (2015). Systemic uptake, albumin and hemoglobin binding of [14C]2,3-butanedione administered by intratracheal instillation in male Harlan Sprague Dawley rats and oropharyngeal aspiration in male B6C3F1/N mice. *Chem Biol Interact* 227, 112–119.

Waidyanatha, S., Gaudette, N. F., Hong, Y., and Fennell, T. R. (2014). Formation of epichlorohydrin, a known rodent carcinogen, following oral administration of 1,3-dichloro-2-propanol in rats. *Chem Res Toxicol* 27, 1787–1795.

Hassler, C., Zhang, Y., Gilmour, B., Graf, T., Fennell, T., Snyder, R., Deschamps, J. R., Reinscheid, R. K., Garau, C., and Runyon, S. P. (2014). Identification of neuropeptide S antagonists: structure-activity relationship studies, X-ray crystallography, and in vivo evaluation. *ACS Chem Neurosci* 5, 731–744.

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