Thomas D. Steele, MS, PhD
Toxicologist

Summary. Critical and pragmatic scientific and regulatory expertise (20+ years) in the nonclinical safety evaluation and risk assessment of novel small molecule and biological therapeutics in multiple therapeutic areas across the entire pharmaceutical value chain. Specific areas of experience and expertise include:

- Toxicology, Pharmacology, ADME, PK
- Regulatory Strategy, IND and NDA Preparation and Filing
- FDA review, evaluation and approval process
- Troubleshooting toxicologic/safety concerns
- Negotiations with global health authorities
- Preparation of scientific arguments to reduce animal toxicity testing

Professional Experience

Nonclinical Safety Solutions
Independent Contractor/Consultant, 2014-Present

ARIAD Pharmaceuticals, Inc.
Director, Preclinical Safety: 2013-2014

ImClone Systems; a wholly-owned subsidiary of Eli Lilly & Co.
Associate Vice President, Nonclinical Safety: 2009–2013

Hoffmann-LaRoche, Inc.
Head, Science and Strategy Group: 2003-2008
Research Leader, Toxicology: 1998-2003

US Food and Drug Administration
Pharmacologist: 1995-1998

Interneuron Pharmaceuticals, Lexington, MA
Senior Research Neuroscientist: 1992-1994

Education and Training

1983 B.S., Biology, University of Lowell (MA)
1986 M.S., Pharmacology and Toxicology, Purdue University
1988 Ph.D., Pharmacology and Toxicology, Purdue University
1988-1990 Post-Doctoral Fellow, Physiology, University of Maryland at Baltimore
1990-1992 Post-Doctoral Fellow, Neurology, Johns Hopkins University
1991-1992 Guest Fellow, National Institute on Drug Abuse

Drug Development and Regulatory Experience

- Intimate knowledge of FDA review, evaluation and approval process based on experience as Pharm/Tox reviewer (Neuropharmacological Drug Products)
- Strategic and operational leadership of toxicology, pharmacokinetic and bioanalytical scientists, nonclinical safety groups, and nonclinical development project teams.

- Key contributor or ultimate preclinical authority for numerous successful “first in human” regulatory applications; Preclinical Expert for two initial marketed product approvals in US, EU and other global markets.
- Designed and implemented mechanistic and investigative studies to address specific safety concerns including peripheral neuropathy, immunosuppression, vascular and neurotoxicity.
- Due diligence, impurity/degradant/extractable/leachable assessments, PK comparability testing of biological therapeutics

Selected Publications

Steele, T.D., D.E. Nichols and G.K.W. Yim. Stereochemical Effects of 3,4-Methylenedioxymeth-amphetamine (MDMA) and Related Amphetamine Derivatives on Inhibition of Uptake of [3H]-Monoamines into Synaptosomes from Different Regions of Rat Brain. Biochem Pharmacol 36:2297-2303, 1987.

Steele, T.D., H.U. Bryant, P.V. Malven and G.K.W. Yim. Nocturnal Depletion of Hypothalamic Dynorphin in Anorexic Walker-256 Tumor-Bearing Rats. Pharmacol Biochem Behav 29:542-545, 1988.

Steele, T.D., D.E. Nichols and G.K.W. Yim. 3,4-Methylenedioxymethamphetamine Transiently Alters Mouse Brain and Cardiac Biogenic Amines. Pharmacol Biochem Behav 34:223-227, 1989.

Steele, T.D., W.K. Brewster, M.P. Johnson, D.E. Nichols and G.K.W. Yim. Assessment of the Role of α-Methylepinine in the Neurotoxicity of MDMA. Pharmacol Biochem Behav 38:345-351, 1991.

Blaustein, M.P., W.F. Goldman, G. Fontana, B.K. Krueger, E. Santiago, **T.D. Steele**, D.N. Weiss and P.J. Yarowsky. Physiology of the Sodium/Calcium Exchanger in Nerve and Muscle. Ann NY Acad Sci 639:254-274, 1991.

Zhao, Z., N. Castagnoli, Jr., G. Ricaurte, **T. Steele** and M. Martello. Synthesis and Neurotoxicological Evaluation of Putative Metabolites of the Serotonergic Neurotoxin 2-(Methylamino)-1-[3,4-(methylenedioxy)phenyl]propane [(Methylenedioxy)methamphetamine]. Chem Res Toxicol 5:89-92, 1992.

Steele, T.D., J.L. Katz and G.A. Ricaurte. Evaluation of the Neurotoxicity of N-Methyl-1-(4-methoxyphenyl)-2-aminopropane (Para-methoxymethamphetamine). Brain Res 589:349-352, 1992.

Steele, T.D., U.D. McCann and G.A. Ricaurte. 3,4-Methylenedioxymethamphetamine (MDMA, "Ecstasy"): Pharmacology and Toxicology in Animals and Humans. Addiction 89:539-551, 1994.

Witkin, J.M., **T.D. Steele** and L.G. Sharpe. Effects of Strychnine-Insensitive Glycine Receptor Ligands in Rats Discriminating Dizolcipine or Phencyclidine from Saline. J Pharmacol Exp Ther 280:46-52, 1997.

Fasciano, J., T. Steele, N. Castagnoli, J. Katz, G. Ricaurte. The Effect of N-Methylation on Fenfluramine's Neurotoxic and Pharmacologic Actions. Brain Res 763:182-190, 1997.

Steele, T.D., D.B. Hodges, Jr. and K.W. Locke. The D1 agonist Dihydrexidine Releases Acetylcholine and Improves Cognitive Performance in Rats. Pharmacol Biochem Behav 58:477-483, 1997.

Ruepp, S., F. Boess, L. Suter, MC de Vera, G. Steiner, T. **Steele, T**. Weiser, S. Albertini. Assessment of hepatotoxic liabilities by transcript profiling. Toxicol. Appl. Pharmacol. 207:S161-S170, 2005.

Sarabu R, Bizzaro FT, Corbett WL, Dvorozniak MT, Geng W, Grippo JF, Haynes NE, Hutchings S, Garofalo L, Guertin K, Hilliard DW, Kabat M, Kester RF, Wang Ka, Liang Z, Mahaney PE, Marcus L, Matschinsky F, Moore D, Racha J, Radinov R, Ren Y, Qi L, Pignatello M, Spence CL, **Steele T,** Tengi J, Grimsby J. Discovery of piragliatin - first glucokinase activator studied in type 2 diabetic patients. J Med Chem. 2012, 55(16):7021-36.

Steele, T., W. Geng, F. Burleson and G. Burleson. Enfuvirtide Does Not Impair Host Resistance to Infection in Rats. Abstract No. 872, Toxicologist, 84(S-1), March, 2005.

Steele, T.D., and J. Grimsby. Preclinical Safety Assessment: Understanding Mechanism-based Toxicities of Glucokinase Activators. 44th Annual Meeting of the Drug Information Association, Boston MA, June 2008.

Patent

"Dopamine D1 Agonists for the Treatment of Dementia", US Patent 5,744,476, issued 4/28/98, K.W. Locke and T.D. Steele.