

Douglas A. Keller, Ph.D., DABT

SENIOR CONSULTANT

CONTACT INFORMATION

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PROFESSIONAL PROFILE

Dr. Doug Keller is a Senior Consultant in ToxStrategies' Pharmaceuticals Practice. He has more than three decades of experience in the pharmaceutical and laboratory sectors, serving as a researcher, study director, senior advisor, director, and global head in a leading pharmaceutical development/manufacturing firm. Most recently, he led a global team of 20 toxicologists conducting projects for development and marketing within the pharmaceutical industry. In this role, his responsibilities included approving project strategy and reviewing and approving regulatory compliance documents. He also represented the company on trade organization scientific committees and collaborative consortia.

Dr. Keller has also managed a team of scientific advisors and advisory groups in areas of nonclinical safety evaluation and supported preclinical safety scientists charged with implementing the science and standards on pharmaceutical development projects. In this role, he directly handled agency presentations and addressed critical issues as needed, managing innovation and implementation of new predictive assays in preclinical safety. He has been involved at a senior management level in the development of best possible scientific practices and standards in the area of drug safety, providing scientific and regulatory advice on non-clinical strategy, data interpretation, and study design to small-molecule and biotherapeutic development projects in all therapeutic areas. He has reviewed and approved regulatory submissions and served on committees (hepatotoxicity, structure-activity relationships) internally and within the greater industry (PhRMA, IQ, HESI, ECVAM) to study safety assessment issues. Several of his publications outline best practices for development and use of microphysiological systems, safety biomarkers, and animal models of disease.

Dr. Keller has been a Diplomate of the American College of Toxicology (DABT) since 1990 and a member of the Society of Toxicology since 1986. He is widely published in the scientific literature, has two book chapters to his credit, and regularly attends and presents at scientific conferences and symposia.

EDUCATION AND DEGREES EARNED

- 1986–1988 Postdoctoral Fellow
Chemical Industry Institute of Toxicology, Research Triangle Park, NC
- 1986 Doctor of Philosophy (Ph.D.) in Pharmacology
Duke University, Durham, NC
- 1980 Advanced Baccalaureate (AB) in Chemistry
Duke University, Durham, NC

CERTIFICATIONS

- 1990–2025 Diplomate, American College of Toxicology

PROFESSIONAL ASSOCIATIONS

- 1986–Present Society of Toxicology

SELECTED SCIENTIFIC COMMITTEE SERVICE

- ICH S11 Expert Working Group (2015–2020, Rapporteur, 2015–2018)
- IQ Consortium
 - DruSafe Leadership Group (2010–2020)
 - Microphysiological Systems Affiliate (2018–2020)
 - Drug-Induced Liver Injury Affiliate (2016–2020)
- PhRMA Preclinical Development Committee (2008–2020)
- HESI Adverse versus Adaptive Committee (Chair, 2008–2013)
- HESI Alternatives to Carcinogenicity Testing (1999–2002)
- Critical Path Institute Predictive Safety Testing Consortium, Hepatotoxicity Committee (2008–2020) and Advisory Committee (2014–2020)
- Society of Toxicology
 - Board of Publications (2012–2015, Chair 2015)
 - Associate Editor, *Toxicological Sciences* (2004–2011)
 - Awards Committee (2009–2011)
 - Career Resource and Development Committee (2006–2008)
 - Continuing Education Committee (2003–2005)
- Chemical Manufacturers Association Butadiene Technical Committee (1990–1998)

SCIENTIFIC MEETING ORGANIZER / INVITED SPEAKER

Organizer and co-chair, **The Use of Cardiomyocytes for the Assessment of Proarrhythmic Risk**, a Society of Toxicology Contemporary Concepts in Toxicology workshop, October 2016

Organizing committee, **FutureTox III**, a Society of Toxicology Contemporary Concepts in Toxicology workshop, November 2015

Organizer and co-chair, **FutureTox II**, a Society of Toxicology Contemporary Concepts in Toxicology workshop, January 2014

Speaker, **Metabolites in Safety Testing**, American College of Toxicology Continuing Education Course, November 2014

PEER REVIEWER

Toxicological Sciences, Associate Editor (2004–2011)

Toxicology and Applied Pharmacology

Drug and Chemical Toxicology

MANUSCRIPTS

Peters MF, Choy AL, Pin C, Leishman DJ, Moisan A, Ewart L, Guzzie-Peck PJ, Sura R, **Keller DA**, Scott CW, Kolaja KL. 2020. Developing in vitro assays to transform gastrointestinal safety assessment: Potential for microphysiological systems. *Lab Chip* 20(7):1177–1190, doi: 10.1039/c9lc01107b.

Phillips JA, Grandhi TSP, Davis M, Gautier J-C, Hariparsad N, **Keller D**, Sura R, Van Vleet TR. 2020. A pharmaceutical industry perspective on microphysiological kidney systems for evaluation of safety for new therapies. *Lab Chip* 20(3):468–476, doi: 10.1039/c9lc00925f.

Roth SE, Avigan MI, Bourdet D, Brott D, Church R, Dash A, **Keller D**, Sherratt P, Watkins PB, Westcott-Baker L, Lentini S, Merz M, Ramaiah L, Ramaiah SK, Stanley AM, Marcinak J. 2020. Next-generation DILI biomarkers: Prioritization of biomarkers for qualification and best practices for biospecimen collection in drug development. *Clin Pharmacol Ther* 107(2):333–346, doi: 10.1002/cpt.1571.

Baudy AR, Otieno MA, Hewitt P, Gan J, Roth A, **Keller D**, Sura R, Van Vleet TR, Proctor WR. 2020. Liver microphysiological systems development guidelines for safety risk assessment in the pharmaceutical industry. *Lab Chip* 20(2):215–225, doi: 10.1039/c9lc00768g.

Corliss BA, Delalio LJ, Stevenson Keller TC 4th, Keller AS, **Keller DA**, Corliss BH, Beers JM, Peirce SM, Isakson BE. 2019. Vascular expression of hemoglobin alpha in Antarctic icefish supports iron limitation as novel evolutionary driver. *Front Physiol* 10:1389, doi: 10.3389/fphys.2019.01389.

Monticello TM, Jones TW, Dambach DM, Potter DM, Bolt MW, Liu M, **Keller DA**, Hart TK, Kadambi VJ. 2017. Current nonclinical testing paradigm enables safe entry to first-in-human clinical trials: The IQ consortium nonclinical to clinical translational database. *Toxicol Appl Pharmacol* 334:100–109, doi: 10.1016/j.taap.2017.09.006.

Ewart L, Fabre K, Chakilam A, Dragan Y, Duignan DB, Eswaraka J, Gan J, Guzzie-Peck P, Otieno M, Jeong CG, **Keller DA**, de Morais SM, Phillips JA, Proctor W, Sura R, Van Vleet T, Watson D, Will Y, Tagle D, Berridge B. 2017. Navigating tissue chips from development to dissemination: A pharmaceutical industry perspective. *Exp Biol Med* (Maywood) 242(16):1579–1585, doi: 10.1177/1535370217715441.

Prescott JS, Andrews PA, Baker RW, Bogdanffy MS, Fields FO, **Keller DA**, Lapadula DM, Mahoney NM, Paul DE, Platz SJ, Reese DM, Stoch SA, DeGeorge JJ. 2017. Evaluation of therapeutics for advanced-stage heart failure and other severely-debilitating or life-threatening diseases. *Clin Pharmacol Ther* 102(2):219–227, doi: 10.1002/cpt.730.

Morgan SJ, Couch J, Guzzie-Peck P, **Keller DA**, Kemper R, Otieno MA, Schulingkamp RJ, Jones TW. 2017. Regulatory forum opinion piece: Use and utility of animal models of disease for nonclinical safety assessment: A pharmaceutical industry survey. *Toxicol Pathol* 45(3):372–380, doi: 10.1177/0192623317701004.

Juberg DR, Knudsen TB, Sander M, Beck NB, Faustman EM, Mendrick DL, Fowle JR 3rd, Hartung T, Tice RR, Lemazurier E, Becker RA, Fitzpatrick SC, Daston GP, Harrill A, Hines RN, **Keller DA**, Lipscomb JC, Watson D, Bahadori T, Crofton KM. 2017. FutureTox III: Bridges for translation. *Toxicol Sci* 155(1):22–31, doi: 10.1093/toxsci/kfw194.

Andrews PA, **Keller DA**. 2016. On the use of juvenile animal studies to support oncology medicine development in children. *Reprod Toxicol* 66:128–130, doi: 10.1016/j.reprotox.2016.05.012.

Knudsen TB, **Keller DA**, Sander M, Carney EW, Doerrer NG, Eaton DL, Fitzpatrick SC, Hastings KL, Mendrick DL, Tice RR, Watkins PB, Whelan M. 2015. FutureTox II: In vitro data and in silico models for predictive toxicology. *Toxicol Sci* 143(2):256–267, DOI: 10.1093/toxsci/kfu234.

Keller DA, Juberg DR, Catlin N, Farland WH, Hess FG, Wolf DC, Doerrer NG. 2012. Identification and characterization of adverse effects in 21st century toxicology. *Toxicol Sci* 126(2):291–297, doi: 10.1093/toxsci/kfr350.

Sistare FD, Morton D, Alden C, Christensen J, **Keller D**, Jonghe SD, et al. 2011. An analysis of pharmaceutical experience with decades of rat carcinogenicity testing: Support for a proposal to modify current regulatory guidelines. *Toxicol Pathol* 39(4):716–744, doi: 10.1177/0192623311406935.

Xue C-B, Chen L, Cao G, ... **Keller D**, et al. 2010. Discovery of INCB9471, a potent, selective, and orally bioavailable CCR5 antagonist with potent anti-HIV-1 activity. *ACS Med Chem Lett* 1(9):483–487, doi: 10.1021/ml1001536.

MacDonald J, French JE, Gerson RJ, Goodman J, Inoue T, Jacobs A, Kasper P, **Keller D**, Lavin A, Long G, McCullough B, Sistare FD, Storer R, van der Laan JW. 2004. The utility of genetically modified mouse assays for identifying human carcinogens: a basic understanding and path forward. *Toxicol Sci* 77(2):188–194, doi: 10.1093/toxsci/kfh037.

Cappon GD, **Keller DA**, Brock WJ, Slauter RW, Hurtt ME. 2002. Effects of HCFC-123 exposure to maternal and infant Rhesus monkeys on hepatic biochemistry, lactational parameters and postnatal growth. *Drug Chem Toxicol* 25(4):481–496, doi: 10.1081/DCT-120014798.

McClain RM, **Keller D**, Casciano D, Fu P, MacDonald J, Popp J, Sagartz J. 2001. Neonatal mouse model: review of methods and results. *Toxicol Pathol* 29 (SUPPL.):128–137, doi: 10.1080/019262301753178537.

Bevan C, **Keller DA**, Panepinto AS, Bentley KS. 2001. Effect of 4-vinylcyclohexene on micronucleus formation in the bone marrow of rats and mice. *Drug Chem Toxicol* 24(3):273–285, doi: 10.1081/DCT-100103724.

Keller DA, Kennedy Jr. GL, Ross PE, Kelly DP, Elliott GS. 2000. Toxicity of tetrafluoroethylene and S-(1,1,2,2-tetrafluoroethyl)-L- cysteine in rats and mice. *Toxicol Sci* 56(2):414–423, doi: 10.1093/toxsci/56.2.414.

Uttamsing V, **Keller DA**, Anders MW. 1998. Acylase I-catalyzed deacetylation of N-acetyl-L-cysteine and S-alkyl-N-acetyl-L-cysteines. *Chem Res Toxicol* 11(7):800–809, doi: 10.1021/tx980018b.

Keller DA, Lieder PH, Brock WJ, Cook JC. 1998. 1,1,1-Trifluoro-2,2-dichloroethane (HCFC-123) and 1,1,1-trifluoro-2-bromo-2-chloroethane (halothane) cause similar biochemical effects in rats exposed by inhalation for five days. *Drug Chem Toxicol* 21(4):405–415, doi: 10.3109/01480549809002214.

Cantoreggi S, **Keller DA**. 1997. Pharmacokinetics and metabolism of vinyl fluoride in vivo and in vitro. *Toxicol Appl Pharmacol* 143(1):130–139, doi: 10.1006/taap.1996.8041.

Keller DA, Marshall CE, Lee KP. 1997. Subchronic nasal toxicity of hexamethylphosphoramide administered to rats orally for 90 days. *Fundam Appl Toxicol* 40(1):15–29, doi: 10.1006/faat.1997.2375.

Keller DA, Carpenter SC, Cagen SZ, Reitman FA. 1997. In vitro metabolism of 4-vinylcyclohexene in rat and mouse liver, lung, and ovary. *Toxicol Appl Pharmacol* 144(1):36–44, doi: 10.1006/taap.1996.8098.

Birnbaum LS, **Keller DA**. 1996. Metabolism and pharmacokinetics of 1,3-butadiene. *Toxicology* 113(1-3):14–16, doi: 10.1016/0300-483X(96)03421-X.

Keller DA, Christopher Roe D, Lieder PH. 1996. Fluoroacetate-mediated toxicity of fluorinated ethanes. *Fundam Appl Toxicol* 30(2):213–219, doi: 10.1006/faat.1996.0058.

Lieder PH, **Keller DA**. 1992. Toxic fluoroethanes [1]. *Chem Eng News* 70(19):2.

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Leung KH, **Keller DA**, Menzel DB. 1989. Effect of sulfite on the covalent reaction of benzo(a)pyrene metabolites with DNA. *Carcinogenesis* 10(2):259–264, doi: 10.1093/carcin/10.2.259.

Keller DA, Menzel DB. 1989. Effects of sulfite on glutathione S-sulfonate and the glutathione status of lung cells. *Chem Biol Interact* 70(1-2):145–156, doi: 10.1016/0009-2797(89)90069-0.

Heck d'A H, **Keller DA**. 1988. Toxicology of formaldehyde. *ISI Atlas of Science: Pharmacology* 2(1):5–9.

Keller DA, Heck H d'A. 1988. Mechanistic studies on chloral toxicity: Relationship to trichloroethylene carcinogenesis. *Toxicol Lett* 42(2):183–191, doi: 10.1016/0378-4274(88)90076-8.

Menzel DB, **Keller DA**, Leung KH. 1986. Covalent reactions in the toxicity of SO₂ and sulfite. *Adv Exp Med Biol* 197:477–492, doi: 10.1007/978-1-4684-5134-4_46.

Keller DA, Menzel DB. 1985. Picomole analysis of glutathione, glutathione disulfide, glutathione S-sulfonate, and cysteine S-sulfonate by high-performance liquid chromatography. *Anal Biochem* 151(2):418–423, doi: 10.1016/0003-2697(85)90197-6.

Post GB, **Keller DA**, Connor KA, Menzel DB. 1983. Effect of culture conditions on glutathione content in A549 cells. *Biochem Biophys Res Commun* 114(2):737–742, doi: 10.1016/0006-291X(83)90842.

BOOK CHAPTERS

Keller DA, Brennan RJ, Leach KL. 2015. Clinical and nonclinical adverse effects of kinase inhibitors. In: Urban L, Patel V, Vaz RJ (eds), *Antitargets and Drug Safety*, pp. 365–400. Wiley, doi: 10.1002/9783527673643.ch16.

Bogdanffy MS, **Keller DA**. 1999. Metabolism of xenobiotics by the respiratory tract. In: Gardener, DE (ed), *Toxicology of the Lung*, 3rd ed., pp. 85–124. Taylor and Francis, Philadelphia, PA.