Isabel Lea, Ph.D.

DIRECTOR, HEALTH SCIENCES
MANAGING SCIENTIST

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PROFESSIONAL PROFILE

Dr. Isabel Lea is a toxicologist in ToxStrategies' Health Sciences practice. She has more than 20 years of experience, focusing on evaluating and assessing data for environmental chemicals with the potential to cause health effects. Dr. Lea has broad experience, ranging from conducting primary research and performing systematic literature reviews to translating large bodies of evidence in scientific databases. Having conducted more than 50 literature reviews, she routinely develops search strategies and inclusion/exclusion criteria, extracts evidence from heterogeneous study types, conducts critical appraisals for study quality, and synthesizes evidence to develop qualitative conclusions. Dr. Lea has used this expertise to developing documents regarding risk-based toxicity assessment for regulatory agencies. She was involved in the preparation of OSRI (Other Significantly Relevant Information) reports identified for Endocrine Disruptor Screening Program Tier 1 screening, for use in their weight-of-evidence assessments for Tier 2 testing.

Dr. Lea has specific expertise in performing literature reviews to collect and synthesize data describing genetic alterations associated with the development of cancerous lesions, highlighted by a review of point mutations, insertions, deletions, and loss of heterozygosity, which documented the acquisition of alterations in tumor suppressor genes and oncogenes that could induce or promote the development of malignancy. This work was then used as the basis to design a structured query language (SQL) database and a public website platform (Genetic Alterations in Cancer knowledge system) that allowed users to query, search, and download data. Dr. Lea's role covered all aspects of the project—in addition to conducting the literature reviews, she also led an evaluation team and developed project-specific instructions, data dictionaries, and quality control criteria that led to the development of a genetic alterations database and website. In addition, Dr. Lea has significant experience evaluating *in vivo* and *in vitro* data, including genetic toxicology (Comet, micronucleus, and Ames assays), toxicogenomics, and high-throughput screening (Tox21) and high-content screening data. This work was conducted in support of toxicology projects for the National Toxicology Program (NTP) and the NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM).

Dr. Lea has extensive experience with toxicology data management for the Chemical Effects in Biological Systems (CEBS) and Integrated Chemical Environment (ICE) platforms. For CEBS, she played key roles, as lead data scientist and Program Manager. The CEBS database contains data from the NTP Toxicology Testing Program. In this capacity, Dr. Lea developed standard processes for data input to the CEBS system, created verification and validation processes to ensure that public data accurately represented the data delivered to the system. She was instrumental in promoting standard terminology in CEBS and oversaw the addition of CEBS terms to the Ontology for Biomedical Investigation. Promoting the FAIR guiding principles, she also was instrumental in making CEBS data available through Healthdata.gov. Regarding her role with ICE, which provides curated data sets and tools designed to facilitate the safety assessment of chemicals, Dr. Lea played a key role in updating data sets to include cancer endpoints.

Dr. Lea has published academic and professional work in peer-reviewed journals, has reviewed submissions for scientific journals, and regularly attends and presents at professional conferences and colloquia. Dr. Lea is a Program Manager Professional (PMP), which has provided her with the knowledge, expertise, and skill needed to lead a large team of scientists and manage simultaneous projects while delivering on time, within budget, and with excellent client satisfaction ratings.

EDUCATION, DEGREES, AND CERTIFICATIONS

Ph.D. Molecular and Cell Biology
London University and the Zoological Society of London, UK

B.S. Microbiology
London University, London, UK

P.M.P. Project Management Professional (2019)
Project Management Institute

SELECTED PROFESSIONAL EXPERIENCE

Toxicology

Performed systematic reviews of the cancer literature to collect and synthesize data describing genetic alterations, such as point mutations, insertions, deletions, and loss of heterozygosity in tumor suppressor genes and oncogenes.

Described site- and exposure-specific patterns in genetic pathways and mutation profiles for human respiratory-tract cancers associated with tobacco use.

Described genetic alterations in 9000 colorectal tumors, showing that point mutations in codon 248 of the TP53 gene occurred approximately three times more frequently in carcinomas than adenomas.

Composed chapter on Electrolytes, Blood Gases and Acid-Base Balance for Clinical Chemistry of the Laboratory Animal (https://doi.org/10.1201/9781315155807).

Prepared four OSRI (Other Significantly Relevant Information) reports for four chemicals identified for Endocrine Disruptor Screening Program Tier 1 screening for use in their weight-of-evidence assessments for determination of Tier 2 testing.

Data Science

Managed NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) Integrated Chemical Environment (ICE) database in support of the development of alternative test methods. Integrated *in vivo*, *in vitro*, and *in silico* data from quantitative structure-activity relationship (QSAR) and *in vitro*–to–*in vivo* extrapolation (IVIVE) modeling. Established the use of controlled vocabularies to facilitate data selection and improve the user experience for ICE users.

Led team and performed a key role in the redesign and management of NTP's toxicological testing database (CEBS), working with NTP to develop standard data import procedures, perform statistical analysis of data, and develop standardized reports for *in vivo* and *in vitro* data, single- and multigenerational studies, and multiple endpoints. Developed workflows to analyze multi-well plate data and a website to allow users to interact with the data.

Collected, cleansed, and provided depositor feedback for structured and unstructured toxicological testing data. Work included managing the development process and reporting progress to the client and recommending design strategies based on knowledge of the data and the development environment. Monitored the functionality and performance of client products.

Developed the NTP's Genetic Alterations in Cancer (GAC) database, collating genetic mutations in malignant lesions.

Project Management

Managed, expanded, and delivered a program handling a portfolio of up to 10 projects and developing services simultaneously. Allocated and scheduled resources while leading a multidisciplinary team comprising direct employees and subcontractors.

Monitored staff and provided comprehensive oversight of scientific team efforts, and guided development of reports and other written work products, including manuscripts for publication, CMMI level 3 documentation and processes, and software performance quality documents.

MANUSCRIPTS

Borghoff SJ, Rivera B, Fitch S, Buerger AN, Choksi N, Franzen A, Vincent MJ, Covington T, Bus J, Rushton E, **Lea IA**. 2025. Systematic evaluation of the evidence base on methyl tert-butyl ether supporting a lack of concern for carcinogenic hazard in human based on animal cancer studies and mechanistic data. Curr Res Toxicol 8:100224; doi: 10.1016/j.crtox.2025.100224.

Lea IA, Buerger AN, Feifarek D, Mihalchik A, Heintz MM, Haws LC, Nyambego H, Goyak K, Palermo C, Borghoff SJ. 2025. Evaluation of the endocrine disrupting potential of Di-isononyl phthalate. Curr Res Toxicol 8:100220; doi: 10.1016/j.crtox.2025.100220.

Lea IA, Feifarek D, Mihalchik A, Heintz M, Haws L, Nyambego H, Goyak K, Palermo C, Borghoff SJ. 2025. Evaluation of the endocrine disrupting potential of Di-isodecyl phthalate. Curr Res Toxicol 8:1002221; doi: 10.1016/j.crtox.2025.100221.

Rogers JM, Buerger AN, Heintz MM, Palermo CM, Haws LC, **Lea IA**. 2025. Evaluation of a hypothesized Sertoli cell-based adverse outcome pathway for effects of diisononyl phthalate on the developing testis. Curr Res Toxicol 8:100219; doi: 10.1016/j.crtox.2025.100219.

Borghoff SJ, Cohen SS, Jiang X, **Lea IA**, Klaren WD, Chappell GA, Britt JK, Rivera BN, Choksi NY, Wikoff DS. 2023. Updated systematic assessment of human, animal and mechanistic evidence demonstrates lack of human carcinogenicity with consumption of aspartame. Food Chem Toxicol 172:113549, online ahead of print.

Lea IA, Pham LL, Antonijevic T, Thompson C, Borghoff SJ. 2022. Assessment of the applicability of the threshold of toxicological concern for per- and polyfluoroalkyl substances. Regul Toxicol Pharmacol 133:105190, open access.

Lea IA, Chappell GA, Wikoff DS. 2021. Overall lack of genotoxic activity among five common low- and no-calorie sweeteners: A contemporary review of the collective evidence. Mutat Res Genet Toxicol Environ Mutagen 868–869:503389. doi: 10.1016/j.mrgentox.2021.503389. PMID: 34454695.

Gentry R, Greene T, Chappell G, **Lea I**, Borghoff S, Yang C, Rathman J, Ribeiro JV, Hobocienski B, Mostrag A, Rodricks J, Clewell H. 2021. Integration of evidence to evaluate the potential for neurobehavioral effects following exposure to USFDA-approved food colors. Food Chem Toxicol 151:112097. doi: 10.1016/j.fct.2021.112097. Epub 2021 Mar 4. PMID: 33677041.

Gentry R, Rodricks J, Clewell H, Greene T, Chappell G, **Lea I**, Borghoff S, Yang C, Rathman J, Ribeiro JV, Hobocienski B, Mostrag A. 2021. RE: Response to the Office of Environmental Health Hazard Assessment on comments related to Gentry et al. (2021). Food Chem Toxicol 152:112202. doi: 10.1016/j.fct.2021.112202. Epub 2021 Apr 17. PMID: 33872725.

Palermo CM, Foreman JE, Wikoff DS, **Lea I**. 2021. Development of a putative adverse outcome pathway network for male rat reproductive tract abnormalities with specific considerations for the androgen sensitive window of development. Curr Res Toxicol 22:2:254–271. doi: 10.1016/j.crtox.2021.07.002. PMID: 34401750; PMCID: PMC8350458.

Bell S, Abedini J, Ceger P, Chang X, Cook B, Karmaus AL, **Lea I**, Mansouri K, Phillips J, McAfee E, Rai R, Rooney J, Sprankle C, Tandon A, Allen D, Casey W, Kleinstreuer N. 2020. An integrated chemical environment with tools for chemical safety testing. Toxicol in Vitro 67:104916. https://doi.org/10.1016/j.tiv.2020.104916.

Lea IA, Borghoff S, Travlos GS. 2018. Electrolytes, blood gases and acid-base balance. In: Kurtz DM, Travlos GS (eds): The Clinical Chemistry of Laboratory Animals (3rd edition). CRC Press, Boca Raton, FL.

Jackson MA, Yang L, **Lea I**, Rashid A, Kuo B, Williams A, Lyn Yauk C, Fostel J. 2017. The TGx-28 65 biomarker online application for analysis of transcriptomics data to identify DNA damage-inducing chemicals in human cell cultures. Environ Mol Mutagen 58(7):529–535.

Lea IA, Gong H, Paleja A, Rashid, A, Foster J. 2017. CEBS: A comprehensive annotated database of toxicological data. Nucleic Acids Res 45(D1):D964–D971.

Bhusari S, Malarkey DE, Hong HH, Wang Y, Masinde T, Nolan M, Hooth NJ, **Lea IA**, Vasconcelos D, Sills RC, Hoenerhoff MJ. 2014. Mutation spectra of Kras and Tp53 in urethral and lung neoplasms in B6C3F1 mice treated with 3,3′,4,4′-tetrachloroazobenzene. Toxicol Pathol 42(3):555–564.

Waters MD, Jackson MA, **Lea IA**. 2010. Characterizing and predicting carcinogenicity and mode-of-action using conventional and toxicogenomics methods. Mutat Res 705(3):184–200.

Lea IA, Jackson MA, Dunnick JK. 2009. Genetic pathways to colorectal cancer. Mutat Res 670(1–2):96–98.

Lea IA, Jackson MA, Li X, Bailey S, Peddada SD, Dunnick JK. 2007. Genetic pathways and mutation profiles of human cancers: Site- and exposure-specific patterns. Carcinogenesis 28:1851–1858.

Jackson MA, **Lea I**, Rashid A, Peddada SD, Dunnick JK. 2006. Genetic alterations in cancer knowledge system: Analysis of gene mutations in mouse and human liver and lung tumors. Toxicol Sci 90:400–418.

Lea IA, Widgren EE, O'Rand MG. 2004. Association of sperm protein 17 with A-kinase anchoring protein 3 in flagella. Reprod Biol Endocrinol 2:57.

Lea IA, Widgren EE, O'Rand MG. 2002. Analysis of recombinant mouse zona pellucida protein 2 (ZP2) constructs for immunocontraception. Vaccine 20(11–12):1515–1523.

Lea IA, Sivashanmugam P, O'Rand MG. 2001. Zonadhesin: characterization, localization, and zona pellucida binding. Biol Reprod 65(6):1691–700.

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Lea IA, Kurth B, O'Rand MG. 1998. Immune response to immunization with sperm antigens in the macaque oviduct. Biol Reprod 58(3):794–800.

O'Rand MG, **Lea IA**. 1997. Designing an effective immunocontraceptive. J Reprod Immunol 36(1–2):51–59; Review.

Adoyo PA, **Lea IA**, Richardson RT, Widgren EE, O'Rand MG. 1997. Sequence and characterization of the sperm protein Sp17 from the baboon. Mol Reprod Dev 47(1):66–71.

Lea IA, Adoyo P, O'Rand MG. 1997. Autoimmunogenicity of the human sperm protein Sp17 in vasectomized men and identification of linear B cell epitopes. Fertil Steril 67(2):355–361.

Lea IA, Richardson RT, Widgren EE, O'Rand MG. 1996. Cloning and sequencing of cDNAs encoding the human sperm protein, Sp17. Biochim Biophys Acta 1307(3):263–266.

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ABSTRACTS AND PRESENTATIONS

Borghoff SJ, Rivera BN, Fitch S, Buerger A, Choksi N, Franzen A, Bus J, Rushton EK, **Lea I**. Systematic evaluation of the evidence base on methyl tert-butyl ether for carcinogenic potential in humans; Low concern based on animal cancer studies and mechanistic data. Abstract 4702, Society of Toxicology 64th Annual Meeting, Orlando, FL, March 2025.

Lea IA, Holt J, Bunnage E, Long M, Chew R, Bell S, Edwards S, Sayre R, Vliet SM, Lynn SG, Kristan MJ. Integrated computational approaches in systematic evidence mapping: Bridging human expertise and machine learning for advanced toxicological assessments. Abstract 3409, Society of Toxicology 64th Annual Meeting, Orlando, FL, March 2025.

Rivera BN, **Lea IA**, Fitch S, Choksi N, Franzen A, Bus J, Rushton EK, Borghoff SJ. Systematic evaluation of the evidence base on ethyl tert-butyl ether and tert-butyl alcohol for carcinogenic potential in humans: Low concern based on animal cancer studies and mechanistic data. Abstract 4697, Society of Toxicology 64th Annual Meeting, Orlando, FL, March 2025.

Holt JR, Chew RF, Bunnage E, **Lea I**, Borghoff SJ, Sayer R, et al. Categorizing articles for environmental health systematic evidence mapping: A zero-shot machine learning approach using large language models. American Society of Cellular and Computational Toxicology Annual Meeting, Research Triangle Park, NC, October 2024.

Lea IA, Borghoff SJ, Chew R, Bell S, Edwards S, Vasko J, et al. Leveraging computational tools for enhanced human-in-the-loop systematic literature reviews. American Society of Cellular and Computational Toxicology Annual Meeting, Research Triangle Park, NC, October 2024.

Lea IA, Feifarek D, Mihalchik A, Heintz M, Haws L, Nyambego H, Goyak K, Borghoff SJ. Evaluation of the endocrine disrupting potential of di-isodecyl phthalate. Abstract 3930, Society of Toxicology 63rd Annual Meeting, Salt Lake City, UT, March 2024.

Borghoff SJ, Feifarek D, Mihalchik A, Heintz M, Haws L, Nyambego H, Goyak K, Lea IA. Evaluation of the endocrine disrupting potential of di-isodecyl phthalate. Abstract 3931, Society of Toxicology 63rd Annual Meeting, Salt Lake City, UT, March 2024.

Lynn SG, Lea IA, Urban J, Borghoff SJ, Wikoff D, Fitch S, Perry C, Choksi N, Britt J, Heintz M, Klaren W, et al. Development and application of systematic approach to inventory and interrogate thyroid hormone network information. Abstract 4357, Society of Toxicology 63rd Annual Meeting, Salt Lake City, UT, March 2024.

Lea IA, Heintz MM, Feifarek D, Haws LC, Borghoff SJ. Weight-of-evidence evaluation of endocrine activity for di-isodecyl phthalate (DIDP) and di-isononyl phthalate (DINP). Poster presented at Society of Toxicology 62nd Annual Meeting, Nashville, TN, March 2023.

Mihalchik AL, Choksi NY, Lea I, Wood ML. Modern strategies to evaluate drug impurities. Session presented at Society of Toxicology 62nd Annual Meeting, Nashville, TN, March 2023.

Wikoff D, Edwards S, Angrish M, Baumgartner, Bever R, Borghoff S, Chappell G, Chew R, Fitch S, Hench G, Hamernik K, Henderson D, Kirk A, Lea I, Mandel M, Payne L, Shapiro S, Urban J, Williams D, Markey K. Application of systematic methods to characterize thyroid adverse outcome pathways (AOPs). Presented at American Society for Cellular and Computational Toxicology 10th Annual Meeting, Virtual, October 2021.

Bell S, Mansouri K, Phillips J, Chang X, Abedini J, Karmaus AL, Lea I, Rai R, Allen DG, Casey W, Kleinstreuer NC. NCEATM computational tools and resources supporting alternative test method development and evaluation. Abstract #2976-P607, Society of Toxicology 59th Annual Meeting, Anaheim CA, March 2020.

Sheridan E, Moose J, Liu Y, Martini C, Lea I, Fostel J. NTP high-level summary data collections in the Chemical Effects in Biological Systems (CEBS) database. Poster PS01-0606, 15th International Congress of Toxicology, Honolulu, HI, July 2019.

Bhawana B, Lea I, Liu Y, Martini C, Fostel J. Access to National Toxicology Program histopathology lesion collection in Chemical Effects in Biological Systems (CEBS) database. Poster P040, 38th Annual Symposium of Society for Toxicologic Pathology, Raleigh, NC, June 2019.

Lea I, Liu Y, Sheridan E, Motti D, Martini C, Fostel J, Auerbach S. Hallmark gene set annotation for NTP toxicogenomic studies. Abstract #1743-P119, Society of Toxicology 58th Annual Meeting, Baltimore, MD, March 2019.

Martini C, Liu Y, Motti D, Johnson J, McCormick K, Lea I, Fostel F. Integrating assay datasets into Chemical Effects in Biological Systems (CEBS). Abstract #1749-P125, Society of Toxicology 58th Annual Meeting, Baltimore, MD, March 2019.

Sheridan ER, Jackson M, Paleja A, Martini C, Rashid A, Lea I, Fostel J. Improved searching in the Chemical Effects in Biological Systems (CEBS) database leads to greater utility of NTP data. Abstract 2525-P887, Society of Toxicology 57th Annual Meeting, San Antonio, TX, March 2018.

Sheridan E, Raghuraman A, Brown P, Jackson M, Martini C, Lea I, Smith-Roe S, Witt K, Fostel J. Genetic toxicology data in the Chemical Effects in Biological Systems (CEBS) database. Poster P3, Environmental Mutagenesis and Genomics Society 48th Annual Meeting, San Antonio, TX, September 2018.

Lea I, Yang L, Rashid A, Fostel JM. Chemical Effects in Biological Systems (CEBS) Database: Treatment-related findings. Abstract 2918-P412, Society of Toxicology 56th Annual Meeting, Baltimore, MD, March 2017.

Martini C, Rashid A, Paleja A, **Lea I**, Fostel JM. Chemical Effects in Biological Systems (CEBS) database: Treatment-related findings. Abstract 1381-P119, Society of Toxicology 56th Annual Meeting, Baltimore, MD, March 2017.

Sheridan E, Martini C, Shaw M, Shockley K, Brix A, Rashid A, **Lea I**, Fostel J. Using the Chemical Effects in Biological Systems (CEBS) database to answer pathology questions. Poster P035, Society for Toxicologic Pathology 36th Annual Symposium, Montreal, Quebec, Canada, June 2017.

Jackson M, Yang L, Yauk CL, **Lea I**, Kuo B, Williams A, Rashid A, Fostel J. The TGx-28.65 biomarker — A web-based application using transcriptomics to identify DNA damage-inducing chemicals. Abstract 1224, Environmental Mutagenesis and Genomics Society 48th Annual Meeting, Raleigh, NC, September 2017.

Lea I, Rashid A, Favaro C, Fostel J. Chemical Effects in Biological Systems (CEBS) database: Advanced histopathology search applications. Abstract 2195-P410, Society of Toxicology 54th Annual Meeting, San Diego, CA, March 2015.