

CURRICULUM VITAE

Barry S. Levine, D.Sc.

Diplomate, American Board of Toxicology

www.levinetoxconsulting.com

1101 W. Armitage Ave.
Suite 210
Chicago, IL 60614
773-697-4846 (tel)
312-546-6334 (fax)
312-550-0100 (cell)
bslevine@levinetoxconsulting.com

SUMMARY

- Toxicology Consultant
- Expert Witness - 15+ years of experience regarding the toxicity of drugs, alcohol (blood alcohol levels), and environmental chemicals
- Former Medical School Professor of Pharmacology (tenured)
- Experience in the pharmaceutical industry and contract research organizations

AREAS OF EXPERTISE

- Toxicology of Drugs and Environmental Chemicals
- Forensic Toxicology/Drug Intoxication
- Product Liability
- Medical Malpractice
- Nonclinical Drug Development
- Regulatory Toxicology (FDA, EMEA, Health Canada)
- Pharmacology
- Expert Witness Testimony
- Blood Alcohol Levels
- Pharmacokinetics
- Clinical Pathology of Laboratory Animals
- Toxicology of Anticancer Drugs

EDUCATION

Diplomate, American Board of Toxicology (DABT), 1980
D.Sc., Toxicology, Harvard School of Public Health, 1976
M.Sc., Toxicology, Harvard School of Public Health, 1974
M.S., Medicinal Chemistry, University of Illinois, 1972
B.S., Pharmacy, University of Illinois, 1971

CURRENT POSITION

Principal, Levine Tox Consulting, LLC, Chicago, IL, 2008 – present.

Consultation services are provided in the following areas:

- Forensic Toxicology (Drugs, Pesticides, Ethyl Alcohol, etc.)
- Product Liability
- Medical Malpractice
- Toxicology/Safety Assessment.
- Nonclinical Drug Development
- New Drug Applications (FDA, EMEA, Health Canada)

PREVIOUS POSITIONS

Director, Preclinical Development, Hospira, Inc., 275 N. Field Dr., Lake Forest, IL, 2004 – 2008

Hospira, Inc. is the former Hospital Products Division of Abbott Laboratories, and develops proprietary and generic pharmaceutical products and medical devices.

Responsibilities:

- Direct activities of the Preclinical Development Dept. in support of products under development. This includes management of the 1) Toxicology & Bioanalytical Sciences and 2) Pharmacology & Clinical Services sections which include six Ph.D. scientists who plan, coordinate and monitor preclinical development studies of small molecules and biosimilar products.
- Provide preclinical expertise and consultation for products and medical devices throughout all phases of preclinical and clinical development.
- Represent preclinical issues to worldwide regulatory agencies, i.e., FDA, EMEA, etc.
- Preclinical representative on drug development project teams.
- Member of several business development, biogenerics venture, and due diligence teams.
- Oversee Hospira's Bioethics Program related to animal research.
- Mentor Preclinical Development senior staff.
- Prepare and/or oversee the preparation of non-clinical sections of regulatory filings (such as INDs and NDAs in CTD format), Investigator's Brochures, etc.

Examples of accomplishments:

- Established/organized the Preclinical Development Department, and the preclinical testing program for biosimilars and small molecules.
- Established toxicology requirements for drug substance and drug product impurities in accordance with ICH Guidelines.
- Established procedures to comply with Hospira's bioethics policies related to animal research.

Director, Toxicology Division, PharmaMar USA, Inc., Cambridge, MA, 2003 – 2004

PharmaMar USA is a Madrid-based oncology company with a preclinical research facility in Cambridge, MA.

Responsibilities:

- Leadership/management for the Toxicology Division, which included two senior scientists and several technical support personnel.
- Directed toxicology studies in-house.
- Planned, coordinated and monitored global toxicology and safety pharmacology studies.
- Represented preclinical issues to US and EU regulatory agencies.
- Study Sponsor for preclinical contracts with CROs.
- Preclinical representative on drug development project teams.
- Prepared non-clinical sections of INDs and NDAs.
- Interacted with FDA reviewing pharmacologists.

Associate Director, Dept. of Toxicology, Vertex Pharmaceuticals, Cambridge, MA, 2002-2003

Responsibilities:

- Co-managed the Toxicology Department.
- Provided toxicologic expertise to support the development of drug candidates.
- Study Sponsor for non-clinical contracts with CROs.
- Toxicology department representative and preclinical subteam leader on several drug development project teams.
- Prepared position papers and non-clinical sections of INDs and NDAs.

Examples of accomplishments:

- Standardized toxicology protocols.
- Coordinated/integrated toxicology and pharmacokinetics tracking systems.
- Headed the CRO site selection team.
- Established procedures for drug vehicle selection.

Associate Professor of Pharmacology (tenured) and Director, Toxicology Research Laboratory, University of Illinois at Chicago, Chicago, IL, 1987-2002

The Toxicology Research Laboratory (a Contract Research Organization which I established in 1987) conducts research programs focusing on the non-clinical development of drugs for government agencies and the pharmaceutical industry. These projects included research programs in toxicology, pharmacology, and pharmacokinetics.

I also participated in departmental teaching programs in pharmacology and toxicology for medical, dental, and graduate students. Lectures included the toxicity of drugs, pesticides, toxic gases, and ethyl alcohol.

Responsibilities:

- Administration and conduct of regulatory toxicology studies for industry and government clients in accordance with FDA GLP regulations.
- Principal Investigator on government contracts for the National Cancer Institute, the National Institute on Drug Abuse, the Dept. of Defense/US Army (Walter Reed Army Institute of Research) and the World Health Organization.
- Developed preclinical toxicology programs for industrial clients.
- Managed two Ph.D. senior scientists and 12 technical and administrative personnel.
- Budget preparation, fiscal accountability, and new business development.
- Assisted Sponsors in preparation of IND and NDA toxicology sections.
- Presented lectures to medical and graduate students, including Course Director for "Principles of Toxicology."

Typical studies:

- Subchronic and chronic toxicity studies in rodents, rabbits, dogs and monkeys.
- Reproductive and developmental toxicity studies in rats and rabbits.
- Pharmacokinetics, absorption, distribution, and excretion studies in rats, dogs and monkeys.

Consultant (part-time), Chicago, IL, 1988-2002

Consultation services were provided in the following areas:

- Preclinical Drug Development including pharmacology and toxicology testing programs for pharmaceutical and biotechnology clients.
- Forensic Aspects of Drug and Chemical Intoxication
- Medical Malpractice
- Product Liability
- Clinical Pathology of Laboratory Animals

Director, General Toxicology Department and Head, Clinical Pathology Division, Microbiological Associates, Inc. (currently BioReliance Corp.), Bethesda, MD, 1985-87.

Responsibilities:

- Scientific direction, e.g., Study director, protocol development, report writing, etc.
- Supervision and training of 13 technical and administrative support personnel.
- Establishment and maintenance of standard operating procedures.
- Budget preparation and fiscal accountability.
- Proposal preparation.

Experience:

- Acute toxicology studies in rats, mice, rabbits and guinea pigs.
- Subchronic and chronic toxicology studies in rats and mice.
- Generation and interpretation of clinical pathology data to support toxicology studies.
- Functioned as Toxicologist and Clinical Pathologist for the National Toxicology Program, NIH.

Senior Toxicologist and Head, Clinical Pathology Laboratory, Life Sciences Department, IIT Research Institute, Chicago, IL, 1982-85. **Research Toxicologist**, 1976-81.

Responsibilities:

- Design, implementation, conduct and reporting of toxicology studies for government and industry-sponsored research programs.
- Supervision of one research scientist and 10 technical support personnel.

Experience:

- Acute and subchronic toxicology studies in rats, mice, dogs and monkeys.
- Chronic toxicology studies in rats and mice.
- Supervision of clinical pathology laboratory.
- *In vivo* cytogenetic assays in rats.

Toxicology Group Leader, Drug Safety Evaluation Division, Ortho Pharmaceuticals, Raritan, NJ, 1981-82.

Responsibilities:

- Scientific and administrative supervision of two senior scientists and 15 technical support personnel
- Monitoring of outside toxicology contracts.

PROFESSIONAL ACTIVITIES

Diplomate, American Board of Toxicology
Society of Toxicology
Midwest Regional Chapter, Society of Toxicology
American Association for the Advancement of Science
American College of Toxicology
Society of Toxicologic Pathologists
Society of Forensic Toxicologists

APPOINTMENTS

Liaison to the Amer. Assoc. for Cancer Research, American College of Toxicology, 1999 - 2002.
Awards Committee, American College of Toxicology, 1998-1999.
Nominating Committee, Society of Toxicology, Midwest Regional Chapter, 1992-1993.
Chair, Educational Committee, Society of Toxicology, Midwest Regional Chapter, 1992-1993.
Regulatory Affairs Committee, Animal Clinical Chemistry Division of the American Association for Clinical Chemistry (AACC), 1991-1995.
National Meeting Committee, Animal Clinical Chemistry Division of AACC, 1991- 1994.
President, Society of Toxicology, Midwest Regional Chapter, 1991-1992.
Chair, Program Committee, Society of Toxicology, Midwest Regional Chapter, 1990-1991.
Educational Committee, Society of Toxicology, Midwest Regional Chapter, 1989-1990.
Chair, Animal Clinical Chemistry Division of AACC, 1984-1986.
Nominating Committee, Society of Toxicology, Midwest Regional Chapter, 1984-1985.
Executive Committee, Animal Clinical Chemistry Division of AACC, 1982-1983.
Chair, Nominating Committee, Society of Toxicology, Midwest Regional Chapter, 1982-1983.
Society of Toxicology Liaison to AACC, 1982-1986.
AACC Liaison to National Society for Medical Research, 1982-1986.
Executive Council, Society of Toxicology, Midwest Regional Chapter, 1981-1983.

REVIEWER

Reviewer, National Cancer Institute, Cancer Chemoprevention Grant Applications, 2002.
Ad Hoc Reviewer, *Cancer Chemotherapy and Pharmacology*, 2002.
Ad Hoc Reviewer, *Pharmaceutical Biology*, 1999 - 2001.
Annual Meeting Abstracts Reviewer, American Association for Clinical Chemistry, 1998.
Ad Hoc Reviewer, National Institutes of Health, Grant Application, 1997.
Editorial Board, *Toxicology Mechanisms and Methods*, 1996 - 2003.
Ad Hoc Reviewer, *Phytomedicine*, 1996 - 1998.
Peer Review Panel, Toxicological Profile of RDX, U.S. Dept. Health and Human Services, 1995.
Ad Hoc Reviewer, *Pharmacology and Toxicology*, 1994 - 1996.
Ad Hoc Reviewer, World Health Organization, 1992 - 1997.
Ad Hoc Reviewer, *International Journal of Pharmacognosy*, 1990 - 1995.
Technical Review Panel, Great Lakes Protection Fund, 1990 - 2000.

INVITED PRESENTATIONS

Invited speaker, Relationship Between Dosing Vehicles, Dose Volume, and Stress, The Humane Society of the United States Workshop entitled "Refinement in Toxicology Testing," New Orleans, LA, March 1999.

Invited speaker, "Good Laboratory Practices," Biologic Resources Laboratory, University of Illinois at Chicago, Chicago, IL, Nov. 1997.

Course Co-director and speaker, "Conduct of GLP Toxicology Studies," National Institute of Military Medical Sciences, Beijing, China, Oct. 1993.

Invited speaker, "Good Laboratory Practices," Biologic Resources Laboratory, University of Illinois at Chicago, Chicago, IL, Oct. 1993.

Invited speaker, "Preclinical Toxicology Studies for New Drugs and Vaccines," U.S. Army Medical Research and Development Command Core Drug Development Symposium, Aug. 1993.

Invited speaker, "Toxic Interactions between Piperonyl Butoxide and Organophosphorus Insecticides," Dept. of Medicinal Chemistry, University of Illinois at Chicago, Chicago, IL, Oct. 1988.

Invited speaker, "Principles of Toxicology," American Industrial Hygiene Association Refresher Course, Berkeley, CA, Oct. 1987.

BOOK CHAPTERS

1. Levine, B.S. Animal Clinical Pathology. In: *CRC Handbook of Toxicology* (M.A. Hollinger and M.J. Derelanko, eds.), CRC Press, Inc., Boca Raton, FL, second edition, 2001.

2. Levine, B.S. Single and Repeat Dose Toxicity. In: *International Pharmaceutical Product Registration* (Cartwright, A.C. and Matthews, B.), Informa Healthcare USA, Inc., New York, NY, second edition, 2009.

PUBLICATIONS

1. Gearien, J.E., Bauer, L., Klein, M. and Levine, B.S. (1975). Structure of Lupeol and its 19 α -H-isomer. *J. Pharm. Sci.* 649, 152-154.

2. Mirer, F.E., Levine, B.S. and Murphy, S.D. (1977). Parathion and methyl parathion toxicity and metabolism in piperonyl butoxide and diethyl maleate pretreated mice. *Chem-Biol. Interactions* 17, 99-112.

3. Levine, B.S. and Murphy, S.D. (1977). Esterase inhibition and reactivation in relation to piperonyl butoxide-phosphorothionate insecticide interactions. *Toxicol. Appl. Pharmacol.* 40, 379-391.

4. Levine, B.S., Henry, M.C., Port, C.D. and Rosen, E. (1979). Effect of particle size distribution on hexamethylmelamine toxicity in rats. *Drug Chem. Toxicol.* 2, 269-281.

5. Levine, B.S., Henry, M.C., Port, C.D. and Rosen, E. (1980). Toxicologic evaluation of streptozotocin (NSC 85998) in mice, dogs and monkeys. *Drug. Chem. Toxicol.* 3, 201-212.

6. Levine, B.S., Preache, M.M. and Pergament, E. (1980). Mutagenic potential of cis-dichlorodiamine platinum II in rodents. *Toxicol.* 17, 57-65.

7. Henry, M.C., Port, C.D. and Levine, B.S. (1980). Preclinical toxicologic evaluation of 4'(9-acridinylamino) methane-sulphon-m-anisidide monochloride (NSC 24992) in mice, dogs and monkeys. *Cancer Treatment Reports* 64, 855-860.

8. Henry, M.C., Rosen, E., Port, C.D. and Levine, B.S. (1980). Toxicity of spirogermanium (NSC 192965) in mice and dogs after intravenous or intramuscular administration. *Cancer Treatment Reports* 64, 1207-1210.
9. Levine, B.S., Henry, M.C., Port, C.D. and Rosen, E. (1980). Preclinical toxicologic evaluation of ICRF 187 (NSC 169780) in dogs. *Cancer Treatment Reports* 64, 1211-1215.
10. Henry, M.C., Port, C.D., Rosen, E. and Levine, B.S. (1980). Preclinical toxicologic study of 2,3-dihydro-1-H-imidazo [1,2-b] [pyrazole (NSC 51143) in mice, dogs and monkeys. *Cancer Treatment Reports* 64, 1031-1038.
11. Levine, B.S., Henry, M.C., Port, C.D., Richter, W.R. and Urbanek, M. (1981). Nephrotoxic potential of cis-dichlorodiamine platinum II and four analogs in rats. *J. Natl. Cancer Inst.* 67, 201-206.
12. Levine, B.S., Furedi, E.M., Gordon, D.E., Burns, J.M. and Lish, P.M. (1981). Thirteen-week toxicity study of hexahydro-1,3,5-trinitro-1,3,5-triazine in Fischer 344 rats. *Toxicol. Letters* 8, 241-245.
13. Levine, B.S., Pergament, E. and Driscoll, K. (1982). Dose- and time-response relationships of triethylenemelamine-induced chromosomal aberrations in rat bone marrow cells. *Toxicol. Letters* 10, 281-285.
14. Levine, B.S. (1982). Clinical chemistry measurements in drug safety assessment studies: Toxicologic Implications. *Lab Animal* 11, 37-39.
15. Levine, B.S., Furedi, E.M., Gordon, D.E., Lish, P.M. and Barkley, J.J. (1984). Subchronic toxicity of trinitrotoluene in Fischer 344 rats. *Toxicol.* 32, 253-265.
16. Levine, B.S., Furedi, E.M., Gordon, D.E., Barkley, J.J. and Lish, P.M. (1990). Toxic interactions of the munitions compounds TNT and RDX in F344 rats. *Fundam. Appl. Toxicol.* 15, 373-38.
17. Levine, B.S., Rust, J.H., Barkley, J.J. and Lish, P.M. (1990). Six month oral toxicity study of trinitrotoluene in dogs. *Toxicology* 16, 233-244.
18. Gaworski, C.L., Aranyi, C., Vana, S., Rajendran, N., Abdo, K., Levine, B.S. and Hall III, A. (1991). Prechronic inhalation toxicity studies of 2-mercaptobenzimidazole (2-MBI) in F344/N rats. *Fundam. Appl. Toxicol.* 16, 161-171.
19. Levine, B.S., Long, R.E. and Chung, H. (1991). Subchronic oral toxicity of pyridostigmine bromide in rats. *Biomed. and Environ. Sci.* 4, 59-65.
20. Dietz, D.D., Leininger, J.R., Rauckman, E.J., Thompson, M.B., Chapin, R.E., Morrissey, R.L. and Levine, B.S. (1991). Toxicity studies of acetone administered in the drinking water of rodents. *Fundam. Appl. Toxicol.* 17, 347-360.
21. Levine, B.S. and Parker, R.M. (1991). Reproductive and developmental toxicity studies of pyridostigmine bromide in rats. *Toxicology* 69, 291-300.
22. Gaworski, C.L., Aranyi, C., Hall, A., III, Levine, B.S., Jackson, C.D. and Abdo, K.M. (1992). Prechronic inhalation toxicity studies of isobutyl nitrite. *Fundam. Appl. Toxicol.* 19, 169-175.

23. Johnson, C.W., Nachman, J.P., Cimprich, R.E., Moon, H.L., Mills, S.E., Beckendorf, J., Levine, B.S., Long, R.E., Fuller, G.B., Losos, G., Provencher, A. and Stoll, R. (1993). Clinical and histopathological effects of M-CSF in laboratory animals. *Int. Rev. Exp. Path.* 34A, 189-204.
24. Levine, B.S. and Tomlinson, M.J.(1993). Subacute intramuscular toxicity of the acetylcholinesterase reactivating agent HI-6 in rats and dogs. *J. Amer. Coll. Tox.* 12, 185-193.
25. Weingand, K., Bloom, J., Carakostas, M., Helfrich M., Latimer, K., Levine, B.S., Neptun, D., Rebar, A., Stitzel, K. and Troup, C. (1993). Clinical pathology testing recommendations for nonclinical safety studies. *Tox. Pathol.* 20, 539-543.
26. Levine, B.S., Tomlinson, M.J., and Parker, R.M. (1994). Onset and reversibility of ribavirin-induced testicular toxicity in mice. *Tox. Subst. J.* 13, 173-188.
27. Levine, B.S. and Tebbett, I. (1994). Cocaine pharmacokinetics in ethanol-pretreated rats. *Drug. Met. Disp.* 22, 498-500.
28. Brewer, T.G., Peggins, J.O., Grate, S.J., Petras, J.M., Levine, B.S., Weina, P.J., Swearngen, J., Heiffer, M.H. and Schuster, B.G. (1994). Neurotoxicity in animals due to arteether and artemether. *Trans. Roy. Soc. Trop. Med. Hyg.* 88, 33-36.
29. Brewer, T.G., Grate, S.J., Peggins, J.M., Weina, P.J., Petras, J.O., Levine, B.S., Heiffer, M.H. and Schuster, B.G. (1994). Fatal neurotoxicity of arteether and artemether. *Amer. J. Trop. Med. Hyg.* 51, 251-259.
30. Hodge, J.W., Schlom, J., Donohue, S.J., Tomaszewski, J., Wheeler, C.W., Levine, B.S., Gritz, L., Panicali, D. and Kantor, J.A. (1995). A recombinant vaccinia virus expressing human prostate-specific antigen (PSA). Safety and immunogenicity in a nonhuman primate. *Intl. J. Cancer* 63, 231-237.
31. Matamoros, R.A. and Levine, B.S. (1996). Stress response and drug metabolism in mice. *Fundam. Appl. Tox.* 30, 255-263.
32. Tolhurst, T.A., Negrusz, A., Liebelt, B., Woods, E.F., and Levine, B.S. (1996). Determination of ampicillin in New Zealand White rabbit plasma using a column switching technique and HPLC. *Chromatog.* 42, 223-226.
33. Putman, D., San, R., Bigger, A., Levine, B.S. and Jacobson-Kram, D. (1996). Genetic Toxicology Assessment of HI-6 Dichloride. *Env. Mol. Mutagen.* 27, 152-161.
34. Levine, B.S., Furedi-Machacek, E.M., Brown, A.P., and Tomlinson, M.J. (1997). Subchronic toxicity and reversibility of the antileishmanial drug WR6026 Dihydrochloride in rats and dogs. *Drug Development Research*, 40, 75-87.
35. Negrusz, A., Tolhurst, T.A., Buehler, P.W., Woods, E.F., Levine, B.S., and Crowell, J.A. (1997). High-performance liquid chromatographic determination of fumaric acid in rat plasma, urine, and fecal samples. *J. Liq. Chromatog. & Rel. Technol.*, 20, 3365-3376.
36. Mousa, S.A., Bozarth, J., Youssef, A., and Levine, B.S. (1998). Oral antiplatelet efficacy of the platelet GPIIb/IIIa antagonist DMP 754 in non-human primates. *Thromb. Res.* 89, 217-225.
37. Negrusz, A., Moore, C., McDonagh, N., Woods, E.F., Crowell, J.A. and Levine, B.S. (1998).

- Determination of phenethylamine, a phenethyl isothiocyanate marker, in dog plasma using solid phase extraction and GC-MS with chemical ionization. *J. Chromatog. B*, 718, 193-198.
38. Brown, A.P., Morrissey, R.L., Crowell, J.A., and Levine, B.S. (1999). Thirteen week oral toxicity study of difluoromethylornithine in combination with tamoxifen citrate in female dogs. *Cancer Chemother. Pharmacol.* 43, 479-488.
 39. Kirchner, D.L., Levine, B.S., Mercieca, M., and Crowell, J.A. (1999). Developmental toxicity studies of the chemopreventive agent DFMO in rats and rabbits. *Toxicol. Sci.* 50, 127-135.
 40. Levine, B.S., Youssef, A.Y., Kirchner, D.L., and Merceica, M. (1999). Retinol palmitate (RP) as a positive control agent in rat and rabbit developmental toxicity studies. *Tox. Methods* 9, 229-243.
 41. Brown, A.P., Morrissey, R.L., Crowell, J.A., and Levine, B.S. (1999). Thirteen week oral toxicity study of difluoromethylornithine in combination with tamoxifen citrate in female rats. *Cancer Chemother. Pharmacol.* 44, 475-483.
 42. Brown, A.P., Dinger, N., and Levine, B.S. (2000). Stress produced by gavage administration in the rat. *Contemporary Topics in Laboratory Animal Science* 39, 17-21.
 43. Brown, A.P., Morrissey, R., Tolhurst, T., Crowell, J.A., and Levine, B.S. (2000). Oral toxicity of 1,2-dithiole-3-thione, a potential cancer chemopreventive agent, in the rat. *Inter. J. Toxicol.* 19, 375-381.
 44. Brown, A.P., Morrissey, R.L., Faircloth, G.T., and Levine, B.S. (2002). Intravenous toxicity of Kahalalide F, a new anticancer agent, in the rat. *Cancer Chemo. & Pharmacol.* 50, 333-340.
 45. Brown, A.P., Kirchner, DL, Morrissey, R.L., Das, S.R., Fitzgerald, R.L., Crowell, J.A., and Levine, B.S. (2003). Endocrine effects of dehydroepiandrosterone (DHEA) and a fluorinated analogue, fluasterone, in rats. *Drug Development Res.* 58, 169-178.
 46. Stokvis, E., Nan-Offeringa, L., Rosing, H., Lopez-Lazaro, L., Acena, J.L., Miranda, E., Lyubimov, A., Levine, B.S., D'Aleo, C.D., Sxhellens, J.H.M., and Beijnen, J.H. (2003). Quantitative analysis of ES-285, an investigational marine anticancer drug, in human, mouse, rat, and dog plasma using coupled liquid chromatography and tandem mass spectrometry. *J. Mass Spectrom.* 38, 548-554.
 47. Cheng, X., Shin, Y.G., Levine, B.S., Smith, A.C., Tomaszewski, J.E., and van Breemen, R.B. (2003). Quantitative analysis of betulonic acid in mouse, rat, and dog plasma using electrospray liquid chromatography/mass spectrometry. *Rapid Commun. Mass Spectrom.* 17, 2089-2092.
 48. Korytko, P.J., Rodvold, K.A., Crowell, J.A., Stacewicz-Sapuntzakis, M., Diwadkar-Navsariwala, V., Bowen, P.E., Schalch, W., and Levine, B.S. (2003). Pharmacokinetics and tissue distribution of orally dosed lycopene in male dogs. *J. Nutrition* 133, 2788-2792.
 49. Lyubimov A.V., Smith, J.A., Rousselle, S.D., Merceica, M.D., Tomaszewski, J.E., Smith, A.C. and Levine, B.S. (2004). The effects of Tetrathiomolybdate (TTM, NSC-714598) and copper supplementation on fertility and early embryonic development in rats. *Repro. Tox.* 19, 223-233.
 50. Crowell, V., Shen, G., Hu, R., Kim, B.R., Chen, C., Korytko, P.J., Crowell, J.A., Levine, B.S., Kong, A.N. (2005). Toxicogenomics of resveratrol in rat liver. *Life Sci.* 76, 2299-2314.
 51. Glaze, E. R., Lambert, A. L., Smith, A. C., Page, J. G., Johnson, W. D., McCormick, D. L., Brown, A. P., Levine, B. S., Covey J. M., Egorin, M. J., Eiseman, J. L., Holleran J. L., Sausville, E.A. and

- Tomaszewski, J. E. (2005). Preclinical toxicity of a geldanamycin analog, 17-(Dimethylaminoethylamino)-17-demethoxygeldanamycin (17-DMAG), in rats and dogs: potential clinical relevance. *Cancer Chemother. Pharmacol.* 56, 637-647.
52. Lyubimov, A.V., Carr, S.N., Brown, A.P., Art, J.J., Crowell, J.A., and Levine, B.S. (2005). Evaluation of hydrogen ion concentrations in prostates from rats and dogs using fluorescent confocal microscopy. *J. Photochem. Photobiol. B: Biology* 80, 225-234.
53. Crowell, J.A., Page, J.G., Levine, B.S., and Hebert, C.D. (2006). Indole-3-carbinol, but not its major digestive product 3,3'-diindolylmethane, induces reversible hepatocyte hypertrophy and cytochromes P450. *Toxicol. Appl. Pharmacol.* 211, 115-123.
54. Holovics, H.J., Anderson, C.R., Levine, B.S., Ho-Wah, H., and Lunte, C.E. (2008). Investigation of drug delivery by iontophoresis in a surgical wound utilizing microdialysis. *Pharm. Res.* 25, 1762-1770.
55. McGinley, C.M., Zhul, Z.J., Levine, B.S., and Bigwarfe, Jr., P.M. (2008). Managing Impurities and Degradation Products in Drug Products and Drug Substances. *Pharmaceutical Canada*, 9, 6-10.

ABSTRACTS

1. Mirer, F.E., Levine, B.S. and Murphy, S.D. (1975). Effect of piperonyl butoxide and diethyl maleate on the toxicity and metabolism of parathion and methyl parathion. *Toxicol. Appl. Pharmacol.* 33, 181.
2. Levine, B.S. and Murphy, S.D. (1976). Toxic interactions of piperonyl butoxide with dimethyl and diethyl phosphorothionate insecticides in mice. *Toxicol. Appl. Pharmacol.* 37, 166.
3. Levine, B.S., Furedi, E.M., Gordon, D.E. and Lish, P.M. (1981). Subchronic toxicity of trinitrotoluene (TNT), cyclotrimethylene trinitramine (RDX) and TNT/RDX mixtures in F344 rats. *The Toxicol.* 1, 8-59.
4. Levine, B.S., Furedi, E.M., Gordon, D.E., Burns, J.M., Rust, J.H., Lish, P.M. and Barkley, J.J. (1982). Comparative toxicity of trinitrotoluene in rats, dogs and mice. *The Toxicol.* 2, 34.
5. Levine, B.S., Furedi, E.M., Gordon, D.E., Burns, J.M. and Lish, P.M. (1982). Strain differences in the response of mice to TNT. *The Pharmacol.* 24.
6. Levine, B.S., Furedi, E.M., Gordon, D.E., Sagartz, J.W., Rac, V.S., Lish, P.M. and Barkley, J.J. (1984). Two year chronic toxicity/carcinogenicity studies on the munitions compound hexahydro-1,3,5-trinitro-1,3,5-triazine (RDX) in rats and mice. *The Toxicol.* 4, 52.
7. Levine, B.S., Furedi, E.M., Gordon, D.E., Rac, V.S., Barkley, J.J. and Lish, P.M. (1985). Two year chronic oral toxicity/carcinogenicity studies on the munitions compound trinitrotoluene (TNT) in rats. *The Toxicol.* 5, 175.
8. Levine, B.S., Dietz, D.D., Sonawane, R.B., Rubenstein, R. and DeRosa, C. (1987). Subchronic toxicity of methyl isobutyl ketone in Sprague-Dawley rats. *The Toxicol.* 7, 247.
9. Dietz, D.D., Levine, B.S., Sonawane, R.B., Rubenstein, R. and DeRosa, C. (1987). Comparative toxicity of cresol isomers. *The Toxicol.* 7, 246.

10. Abdo, K.J., Elwell, M., Levine, B.S., Mulligan, L.T., and Kovatch, R. (1988). Thirteen-week dosed feed toxicity studies of m-nitrobenzoic acid in F344 rats and B6C3F1 mice. *The Toxicol.* 8, 83.
11. Levine, B.S., Abdo, K.M., Kovatch, R., Elwell, M., and Mulligan, L.T. (1988). Prechronic toxicity of p-nitrobenzoic acid in rats and mice. *The Toxicol.* 8, 250.
12. Dietz, D.D., Leininger, J.R., Thompson, M.B., Mulligan, M.B., Morrissey, R.L. and Levine, B.S. (1989). Prechronic toxicity studies of acetone administered in the drinking water of rodents. *The Toxicol.* 7, 990.
13. Levine, B.S., Waller, D.P., Long, R., Parker, R., Denny, K. and Chung, H. (1989). Subchronic and reproductive toxicity studies on pyridostigmine bromide. *J. Amer. Coll. Toxicol.* 8, 1209.
14. Levine, B.S., Long, R., Fischer, J.H. and Chung, H. (1990). Subchronic oral toxicity of the antimalarial drug WR 238605 in dogs. *The Toxicol.* 10, 44.
15. Aranyi, C., Gaworski, C.L., Senese, P.B., Long, R.C., Levine, B.S., Abdo, K.M. and Yang, R.S.H. (1990). Subchronic inhalation toxicity study of ethylbenzene in F344/N rats and B6C3F1 mice. *The Toxicol.* 10, 121.
16. Levine, B.S., Tomlinson, M.J. and Schieferstein, G. (1991). Subacute intramuscular toxicity studies in rats and dogs on the acetylcholinesterase reactivating drug HI-6. *The Toxicol.* 11, 152.
17. Johnson, C.W., Nachman, J.P., Cimprich, R.E., Moon, H.L., Mills, S.E., Beckendorf, J., Levine, B.S., Long, R.C., Fuller, G.B., Losos, G., Provencher, A. and Stoll, R. (1991). Clinical and histopathological effects of M-CSF in laboratory animals. *Workshop on Cytokines and Growth Factor Pathology*, Basil, Switzerland, August.
18. Levine, B.S., Tomlinson, M.J. and Parker, R.M. (1992). Onset and reversibility of ribavirin-induced testicular toxicity in mice. *The Toxicol.* 12, 434.
19. Aranyi, C., Rajendran, N., Vana, S., Bradof, J., Drummond, J., Sherwood, R., Tomlinson, M., Tepper, J., Levine, B., Gibbons, R. and Dacre, J. (1992). Inhalation exposure of laboratory rats to aerosol mixtures of fog oil and graphite for use as military obscurants. US Army Smoke and Obscurants Symposium.
20. Levine, B.S. and Tomlinson, M.J. (1992). Subchronic intramuscular toxicity studies in rats and dogs on the antimalarial drug arteether. *Tox. Letters Suppl.* 246.
21. Weingand, K., Bloom, J., Carakostas, M., Hall, R., Helfrich M., Latimer, K., Levine, B.S., Neptun, D., Rebar, A., Stitzel, K. and Troup, C. (1992). Recommendations for hematology testing in nonclinical safety studies. Society of Toxicologic Pathologists Symposium.
22. Weingand, K., Bloom, J., Carakostas, M., Hall, R., Helfrich M., Latimer, K., Levine, B.S., Neptun, D., Rebar, A., Stitzel, K. and Troup, C. (1992). Recommendations for clinical chemistry testing in nonclinical safety studies. International Society for Animal Clinical Biochemistry Symposium.
23. Brewer, T.G., Grate, S.J., Peggins, J.O., Weina, P.J., Petras, J.M., Levine, B.S., Heiffer, M.H. and Schuster, B.G. (1992). Fatal neurotoxicity due to arteether (AE) and artemether (AM). American Society of Tropical Medicine and Hygiene Conference.
24. Weingand, K., Bloom, J., Carakostas, M., Hall, R., Helfrich, M., Latimer, K., Levine, B.S., Neptun,

- D., Rebar, A., Stitzel, K., and Troup, C. (1992). Recommendations for clinical pathology testing in nonclinical toxicity and safety studies. American Society for Veterinary Clinical Pathology Symposium.
25. Aranyi, C., Rajendran, N., Vana, S., Bradof, J., Drummond, J., Sherwood, R., Tomlinson, M., Tepper, J., Levine, B.S., Gibbons, R., and Dacre, J. (1992). Subchronic inhalation exposure of rats to aerosol mixtures of fog oil and graphite used as military obscurants. American College of Toxicol. Symposium.
 26. Brewer, T.G., Peggins, J.O., Petras, J.M., Levine, B.S., Weina, P.J., Swearengen, J., Heiffer, M.H. and Schuster, B.G. (1992). Fatal neurotoxicity in animals due to arteether (AE) and artemether (AM). Welcome Trust Meeting on Artemisinin.
 27. Levine, B.S., Furedi-Machacek, E.M. and Tomlinson, M.J. (1994). Subchronic toxicity and reversibility of the antileishmanial drug WR6026 in rats and dogs. *The Toxicol.* 14, 395.
 28. Santi, B.W., Levine, B.S. and Youssef, A.F. (1994). Simple neurobehavioral functional observational battery (FOB) and objective gait analysis validation by the use of acrylamide (i.p.) and methanol (p.o.) with built-in recovery periods. Fifth International Symposium on Neurobehavioral Methods and Effects in Occupational and Environmental Health, Cairo, Egypt.
 29. Wheeler, C.W., Levine, B.S., Furedi-Machacek, E.M. and Tomlinson, M.J. (1995). Subchronic toxicity and reversibility of the antimalarial drug WR238605 succinate in rats and dogs. *The Toxicol.* 15, 74.
 30. Youssef, A.F., Levine, B.S., Tomlinson, M.J. and Crowell, J. (1995). Thirteen week oral toxicity studies of the chemopreventive agent indole-3-carbinol in rats and dogs. *The Toxicol.* 15, 292.
 31. Levine, B.S. and Matamoros, R.A. (1995). Influence of stress on the toxicity and metabolism of organophosphorus insecticides. *The Toxicol.* 15, 208.
 32. Matamoros, R.A. and Levine, B.S. (1995). Stress response and drug metabolism in mice. *The Toxicol.* 15, 267.
 33. Wheeler, C.W., Levine, B.S., Kantor, J., Tomaszewski, J.E. and Donohue, S.J. (1995). Safety and immunogenicity of a recombinant vaccinia virus vaccine expressing a 70kDa fragment of the human carcinoembryonic antigen in a nonhuman primate. *Proc. Amer. Assoc. Cancer Res.* 35, 366.
 34. Matamoros, R.A. and Levine, B.S. (1996). Modulation of drug metabolism during stress. *The Toxicol.* 16, 317.
 35. Levine, B.S., Wheeler, C.W. and Tomlinson, M.J. (1996). Acute and subchronic oral toxicity of the anticyanide drug WR242511 Tartrate. *The Toxicol.* 16, 106.
 36. Youssef, A.Y., Mercieca, M. and Levine, B.S. (1996). Retinol palmitate (RP) as a positive control agent in rat and rabbit developmental toxicity studies. *The Toxicol.* 16, 196.
 37. Putman, D.L., San, R.H.C., Bigger, C.A., Levine, B.S. and Jacobson-Kram, D. (1996). Genetic toxicology assessment of HI-6 dichloride. *The Toxicol.* 16, 46.
 38. Levine, B.S., Wheeler, C.W., Tomaszewski, J.E., Morrissey, R.L., Schweikart, K.M., Tosca, P.J., Singer, A.J. and Donohue, S.J. (1996). Preclinical toxicology studies of SarCNU. *Proc. Amer.*

- Assoc. Cancer Res.* 37, 374.
39. Negrusz, A., Moore, C.M., McDonagh, N.S., Woods, E.F., Levine, B.S., and Crowell, J.A. (1996). Determination of phenethylamine, a phenethyl isothiocyanate marker, in dog plasma using solid phase extraction and GC-MS with chemical ionization. *Clin. Chem.* S6, S254.
 40. Levine, B.S., Brown, A.P., and Morrissey, R.L. (1997). Subchronic toxicity of the anticyanide agent WR242511 tartrate in dogs. *The Toxicol.* 17, 275.
 41. Kirchner, D.L., Levine, B.S., Mercieca, D., and Crowell, J.A. (1997). Oral developmental toxicity studies of α -difluoromethylornithine in rats and rabbits. *The Toxicol.* 17, 259.
 42. Brown, A.P., Morrissey, R.L., Tomaszewski, J.E., Donohue, S.J., and Levine, B.S. (1997). Oral Toxicity of (2-chloroethyl)-3-sarcosinamide-1-nitrosourea (SarCNU) in the rat. *Proc. Amer. Assoc. Cancer Res.* 38, 2.
 43. Brown, A.P., Schultze, A.E., and Levine, B.S. (1997). An animal model of chemical-induced cholangiolitic hepatitis with progression to portal fibrosis. *Hepatology* 26, 150A.
 44. Kirchner, D.L., Mercieca, M., Youssef, A., and Levine, B.S. (1998). Evaluation of WR238605 Succinate, a candidate antimalarial agent, in reproductive toxicity studies. *The Toxicol.* 42, 105.
 45. Brown, A.P., Morrissey, R.L., Crowell, J.A., and Levine, B.S. (1998) Thirteen week oral toxicity study of difluoromethylornithine (DFMO) in combination with tamoxifen in female dogs. *The Toxicol.* 42, 104.
 46. Levine, B.S., Brown, A.P. and Morrissey, R.L. (1998). Six month oral toxicity study of the antimalarial agent WR238605 succinate in rats. *The Toxicol.* 42, 55.
 47. Brown, A.P., Rodvold, K.A., Tomaszewski, J.E., Donohue, S.J. and Levine, B.S. (1998). Oral bioavailability and plasma elimination of (2-chloroethyl)-3-sarcosinamide-1-nitrosourea (SarCNU) in the rat and dog. *Proc. Soc. Amer. Assoc. Cancer Res.* 39, 525.
 48. Tomaszewski, J.E., Donohue, S.J., Brown, A.P., Levine, B.S., Morrissey, R.L., Carter, C.A., Waud, W.R., and Alley, M.C. (1998). Preclinical efficacy and toxicity of (2-chloroethyl)-3-sarcosinamide-1-nitrosourea (SarCNU, NSC 36432). [Presented at the 10th Annual NCI-EORTC Symposium on New Drugs in Cancer Therapy, Amsterdam, The Netherlands]
 49. Kirchner, D.L., Mercieca, M.D., Crowell, J.A., and Levine, B.S. (1998). Developmental toxicity of dehydroepiandrosterone (DHEA) in rats and rabbits. *Teratology* 57, 243.
 50. Brown, A.P., Morrissey, R.L., Donohue, S.J., Vishnuvajjala, B.R., Tomaszewski, J.E., and Levine, B.S. (1999). 8-Chloro-cyclic AMP, but not 2-fluoro-8-chloro AMP, is nephrotoxic in mice. *The Toxicol.* 48, 29.
 51. Levine, B.S., Brown, A.P., Morrissey, R.L., and Crowell, J.A. (1999). Thirteen week oral toxicity study of difluoromethylornithine (DFMO) in combination with tamoxifen in female rats. *The Toxicol.* 48, 388.
 52. Brown, A.P., Morrissey, R.L., Rodvold, K.A., Tolhurst, T.A., Donohue, S.J., Tomaszewski, J.E., and Levine, B.S. (1999). Intravenous plasma elimination kinetics and toxicity of an aminoflavone in the dog. *Proc. Soc. Amer. Assoc. Cancer Res.* 40, 390.

53. Brown, A.P. and Levine, B.S. (1999). The relationship between dosing vehicles, dose volume, and stress. [Presented at the 1999 Annual Meeting of the ACLAM Foundation]
54. Crowell, J.A., Levine, B.S., Page, J.G., and Mirsalis, J.C. (2000). Preclinical safety studies of isoflavones. *J. Nutrition*. [Presented at the Third International Symposium on the Role of Soy in Preventing and Treating Chronic Disease, Washington, DC]
55. Brown, A.P., Morrissey, R.L., Das, S., Crowell, J.A., and Levine, B.S. (2000). Comparative endocrinology study of dehydroepiandrosterone (DHEA) and a fluorinated analogue in Beagle dogs. *The Toxicol.* 54, 258.
56. Levine, B.S., Brown, A.P., Morrissey, R.L., Das, S., and Crowell, J.A. (2000). Comparative endocrinology study of dehydroepiandrosterone (DHEA) and a fluorinated analogue in rats. *The Toxicol.* 54, 263.
57. Brown, A.P., Morrissey, R.L., Smith, A.C., Tomaszewski, J.E., and Levine, B.S. (2000). Comparison of 8-chloroadenosine (NSC-354258) and 8-chloro-cyclic-AMP (NSC-614491) toxicity in dogs. *Proc. Soc. Amer. Assoc. Cancer Res.* 41, 491.
58. Faircloth, G. Grant, W., Smith, B., Supko, J., Brown, A.P., Levine, B.S., Geldof, A., and Himeno, J. (2000). Preclinical development of Kahalalide F, a new marine compound selected for clinical studies. *Proc. Soc. Amer. Assoc. Cancer Res.* 41, 600.
59. Jiang, Z., Yang, B., Hebbar, V., Brown, A.P., Levine, B.S., Crowell, J., and Kong, A. (2000). Induction of phase II drug metabolizing enzymes by the chemopreventive agent 1,2-dithiole-3-thione in rat liver. Presented at the 2000 annual meeting of the *Amer. Assoc. Pharm. Sci.*, 10/29-11/02/00, Indianapolis, IN.
60. Donohue, S.J., Brown, A.P., Prezioso, J.A., Tosca, P.J., Stinson, S.F., Tomaszewski, J.E., Levine, B.S., and Turner, N.A. (2001). Toxicity findings and pharmacokinetics of benzothiazole (NSC 674495) and the lysyl prodrug of 5-F-benzothiazole (NSC 710305) in beagle dogs. *Proc. Soc. Amer. Assoc. Cancer Res.* 42, 933.
61. Shin, Y.G., Cheng, X., van Breemen, R.B., Smith, A.C., Tomaszewski, J.E., Levine, B.S. (2001). Quantitative analysis of betulinic acid in mouse, rat and dog plasma using electrospray LC-MS. Presented at the 49th ASMS Conference on Mass Spectrometry and Allied Topics, 5/27-31/01, Chicago, IL.
62. Levine, B.S., Korytko, P.J., Stacewicz-Sapuntzakis, M., Rodvold, K.A., Bowen, P.E., and Crowell, J.A. (2002). Pharmacokinetics and tissue distribution of the prostate cancer chemopreventive agent lycopene in beagle dogs. *The Toxicol.* 66, 323.
63. Korytko, P.J., Morrissey, R.L., Hebbar, V., Shen, G., Kong, T., Crowell, J.A., and Levine, B.S. (2002). Four week oral toxicity study of the cancer chemopreventive agent resveratrol in rats. *The Toxicol.* 66, 322.
64. Lyubimov, A.V., Smith, J.D., Rousselle, S., Merceica, M., Tomaszewski, J.E., Smith, A.C., and Levine, B.S. (2002). The effects of tetrathiomolybdate (TTM, NSC-714598) and copper supplementation on fertility and early embryonic development in rats. *The Toxicol.* 66, 375.
65. Lyubimov A.V., Merceica, M.D., Tomaszewski, J.E., Smith, A.C., and Levine, B.S. (2002). The

- developmental toxicity of tetrathiomolybdate (TTM, NSC-714598) and protective effects of copper in rats. *Teratology*, 65, 309.
66. Hebbar, V., Shen, G., Hu, R., Kim, B., Chen, C., Korytko, P.J., Crowell, J. A., Levine, B. S., and Kong, A.-N.T. (2002). cDNA microarray analysis of gene expression profiles elicited by resveratrol in rat liver. *Presented at the 2002 annual meeting of the American Assoc. of Pharmaceutical Scientists, 10/02, Toronto, Canada.*
 67. Lyubimov, A.V., Bartholomew, A.M., McIntosh, K.R., and Levine, B.S. (2003). Six month safety and immunology study in baboons of allogeneic baboon mesenchymal stem cells labeled with fluorescent dye. *The Toxicol.* 72, 383.
 68. Levine, B.S., Krishnaraj, R., Morrissey, R.L., Kapetanovic, I., Pezzuto, J.M., and Crowell, J.A. (2003). Twenty-eight day toxicity study of the cancer chemopreventive agent 4-bromoflavone in dogs. *The Toxicol.* 72, 210.
 69. Krishnaraj, R., Morrissey, R.L., Crowell, J.A., Pezzuto, J.M., and Levine, B.S. (2003). Twenty-eight day toxicity study of the cancer chemopreventive agent 4-bromoflavone in rats. *The Toxicol.* 72, 46.
 70. Levine, B.S., Lyubimov, A.V., Carr, S., Brown, A.P., ART, J. and Crowell, J.A. (2003). Evaluation of hydrogen ion concentrations in prostates from rats and dogs using fluorescent confocal microscopy. *Proc. Soc. Amer. Assoc. Cancer Res.* 44, 189.
 71. Glaze, E.R., Smith, A.C., Johnson, W.D., McCormick, D.L., Brown, A.P., Levine, B.S., Krishnaraj, R., Lyubimov, A., Egorin, M. J., and Tomaszewski, J.E. (2003). Dose range-finding toxicity studies of 17-DMAG. *Proc. Soc. Amer. Assoc. Cancer Res.* 44, 1046.
 72. Krishnaraj, R., Kapetanovic, I., Morrissey, R.L., Crowell, J.A., Kensler, T., and Levine, B.S. (2003). Pre-clinical toxicologic evaluation of 5,6-dihydro-4H-cyclopenta-1,2-dithiole-3-thione, a potential cancer chemopreventive drug, in rats. *Proc. Soc. Amer. Assoc. Cancer Res.* 44, 1266.
 73. Lyubimov, A. V., Mercieca, M.D., Tomaszewski, J.E., Smith, A.C., and Levine, B.S. (2003). Oral developmental toxicity study of ammonium tetrathiomolybdate (NSC-714598) in rabbits. *Develop. and Repro. Tox.* 68, 232.
 74. Krishnaraj, R, Morrissey, R.L., and Levine, B.S. (2004). A ninety day toxicological evaluation of GBR 12909 in dogs. *The Toxicol.* 78, 295-296.
 75. Levine, B.S., Sved, D., Harman, L., and Draganov, D. (2011). Pharmacokinetics, Excretion Balance, and Metabolite Profiling following a Single Intravenous or Oral Dose of [¹⁴C]-Forodesine in Cynomolgus Monkeys. *The Toxicol.* 2011.
 76. Draganov, D., Sved, D., Harman, L., and Levine, B.S. (2011). Pharmacokinetics, Tissue Distribution, Excretion Balance, and Metabolite Profiling following a Single Intravenous or Oral Dose of [¹⁴C]-Forodesine in Rats. *The Toxicol.* 2011.