

Ralph I. Freudenthal, Ph.D.

Consultant in Toxicology and Regulatory Affairs
8737 Estate Drive
West Palm Beach, Florida 33411-6594
Phone (561) 791-3234
Fax (561) 791-3334

PROFILE

Senior consultant with 30 years experience in the broad area of occupational health, toxicology, product safety assessment, and regulatory affairs. Provides guidance to corporate executives and industry scientists in product development, product safety assessment, and regulatory compliance. Provides technical support and toxicology expertise to law firms in product liability litigations.

- Assists corporations and law firms on issues relating to chemicals (products) and their impact on human health and the environment.
- Provides corporate officers an independent assessment of in-house capabilities in areas of product safety assessment, environmental and regulatory compliance, and risk assessment.
- Testifies before Congress, EPA, Consumer Product Safety Commission, and other federal regulators.
Provides technical guidance to law firms and testifies as an expert witness in cases involving alleged adverse health effects from exposure to hazardous chemicals

PROFESSIONAL EXPERIENCE

1988 - Present

Senior Consultant in Product Safety, Toxicology, and Regulatory Affairs. Provides guidance to corporate management and industry scientists, government agencies, research institutes, and attorneys, on issues relating to chemicals and their impact on human and environmental health.

1984 - 1988

Director of Health, Safety, and Regulatory Affairs for Stauffer Chemical Company, Westport, Connecticut. Directed Occupational Medicine, Industrial Hygiene, Toxicology, and Regulatory Affairs Departments. Operational responsibility for 4 locations, 2 laboratories, a staff of 210, and an annual budget of \$18 million.

1977 - 1984

Director of Toxicology for Stauffer Chemical Company. Managed worldwide corporate toxicology programs and laboratories. Designed, staffed, and operated Stauffer's well-known state-of-the-art \$12 million research laboratory in Farmington, Connecticut. Managed and coordinated product safety assessments, operated 2

toxicology laboratories (Conn. and Calif.), directed a staff of 165, conducted risk assessments on company products, devised successful strategies for product defense, negotiated favorable regulatory compliance requirements, and provided risk analyses in support of environmental projects.

1973 - 1977

Associate Manager, Pharmacology, Toxicology and Pathology Section, Battelle Memorial Institute, Columbus, Ohio. Responsible for contract research programs in toxicology and pathology, including major NTP, NCI, and EPA contracts.

1969 - 1973

Biochemical Pharmacology Section Head, Research Triangle Institute, Research Triangle Park, North Carolina.

EDUCATION

Ph.D. - June 1969
State University of New York, Buffalo, New York
Major: Biochemical Pharmacology

B.S. - January 1963
New York University, New York, New York
Major: Biology

PROFESSIONAL AFFILIATIONS

Society of Toxicology
European Society of Toxicology
American Society for Pharmacology and Experimental Therapeutics
American Association for Cancer Research
American Board of Forensic Examiners
American Board of Forensic Medicine
American College of Toxicology
Society of Environmental Toxicology and Chemistry
International Society for the Study of Xenobiotics
Connecticut Academy of Science and Engineering
American Chemical Society

PROFESSIONAL SERVICE

Editorial Board, several professional journals
Board of Directors, Psychiatric Diagnostic Laboratories
Board of Directors, Chemical Industry Institute of Toxicology
Board of Directors, Earth BioScience, Inc.
Steering Committee, Rene Dubos Center for Human Environments
Research Professor, Toxicology Program, University of Connecticut

Clinical Associate, Department of Laboratory Medicine, School of Medicine, University of Connecticut

PUBLICATIONS - BOOKS

Polynuclear Aromatic Hydrocarbons: Chemistry, Metabolism, and Carcinogenicity. R.I. Freudenthal and P.W. Jones, eds. Raven Press, New York, 1976.

Polynuclear Aromatic Hydrocarbons: Second International Symposium on Analysis, Chemistry, and Biology. P.W. Jones and R. I. Freudenthal, eds. Raven Press, New York, 1978.

What You Need to Know to Live With Chemicals, Ralph I. Freudenthal and Susan L. Freudenthal. Hill and Garnett Publishing, Inc., Greens Farms, Connecticut, 1989.
Japanese translation, Japan Plant Protection Association, Tokyo, 1993.

Directory of Contract Laboratories Offering Contract Services, Ralph I. Freudenthal, ed. Hill and Garnett Publishing, Inc., Greens Farms, Connecticut, 1990.

Food: Facts and Fictions, Ralph I. Freudenthal and Susan L. Freudenthal. Hill and Garnett Publishing, Inc., Greens Farms, Connecticut, 1991.
Japanese translation, Japan Plant Protection Association, Tokyo, 1993.

1992 Directory of Contract Laboratories Offering Contract Services, Ralph I. Freudenthal, ed. Hill and Garnett Publishing, Inc., Boca Raton, Florida, 1992.

Material Safety Data Sheets: The Writer's Desk Reference, Richard P. Molinelli, Michael J. Reale, and Ralph I. Freudenthal, eds. Hill and Garnett Publishing, Inc., Boca Raton, Florida, 1992.

1995 Directory of Contract Laboratories Offering Contract Services, Ralph I. Freudenthal. Aribet Books, West Palm Beach, Florida, 1995.

1997 Directory of Contract Laboratories Offering Contract Services, Ralph I. Freudenthal. Aribet Books, West Palm Beach, Florida, 1997.

PUBLICATIONS - BOOK CHAPTERS

The Preparation of Stereospecific Tritium-Labeled Reduced Nicotinamide Adenine Dinucleotide Phosphate. R.I. Freudenthal. Chapter in: *Methods in Enzymology*, Vol. LXVI. Academic Press, New York, 1980.

Use of Toxicology Studies. Ralph I. Freudenthal. Chapter in: *Material Safety Data Sheets: The Writer's Desk Reference*, Richard P. Molinelli, Michael J. Reale, and Ralph I. Freudenthal, eds., Hill and Garnett Publishing, Inc., Boca Raton, Florida, 1992.

PUBLICATIONS - JOURNAL ARTICLES

- Freudenthal, R.I. and Hebborn, P. Studies on Dihydrofolate Reductases from Normal and Neoplastic Mouse Tissue. I. A Comparison of the Biochemical Parameters. *Int. J. Biochem.* 1 :21-130, 1970.
- Freudenthal, R.I. and Hebborn, P. Studies on Dihydrofolate Reductase from Normal and Neoplastic Mouse Tissue. II. Effects of Some Organic Solvents on the Enzyme. *Int. J. Biochem.* 1 :150-159, 1970.
- Wall, M., Brine, D., Pitt, C., Freudenthal, R., and Christensen, H. Isolation, Structure, and Biological Activity of Several Metabolites of Δ^9 -Tetrahydrocannabinol. *Comm. Ed. J. Amer. Chem. Soc.* 92 :3466-3468, 1970.
- Freudenthal, R.I. Graphic Methods for Determination of K_M and K_i Values for Dihydrofolate Reductase. *Anal. Biochem.* 35 :346-352, 1970.
- Freudenthal, R.I., Lowe, J., and Hebborn, P. NADPH Requirements for the Binding of Competitive Inhibitors to Dihydrofolate Reductase. *Molec. Pharmacol.* 6 :617-620, 1970.
- Freudenthal, R.I., Cook, C.E., Wall, M., and Rosenfeld, R. The Effects of Different Incubation Systems on the *In Vitro* Metabolism of Norethynodrel. *J. Steroid Biochem.* 2 :77-82, 1971.
- Freudenthal, R., Cook, C., Twine, M., Rosenfeld, R., and Wall, M. The Metabolism of Norethynodrel by Rat Liver. *Biochem. Pharmacol.* 20 :1507-1512, 1971.
- Freudenthal, R.I., Cook, C.E., Forth, J., Rosenfeld, R., and Wall, M. The Metabolism of Ethynodiol Diacetate by Rat and Human Liver. *J. Pharmacol. Exp. Ther.* 177 :468-473, 1971.
- Freudenthal, R.I., Rosenfeld, R., Cook, C.E., and Wall, M. The Epimerization of an Intermediary Metabolite of Norethynodrel by a 3β -Hydroxy- $\Delta^{5(10)}$ Steroid Epimerase. *Biochem. Pharmacol.* 20 :2349-2354, 1971.
- Christensen, H., Freudenthal, R., Gidley, J., Rosenfeld, R., Boegli, G., Pitts, C., and Wall, M. Activity of THC and Related Compounds on the Mouse. *Science* 172 :165-167, 1971.
- Freudenthal, R.I., Rosenfeld, R., and Wall, M. Species and Strain Differences in the Epimerization of 3β , 17β -Dihydroxy- 17α -Ethynyl- $\Delta^{5(10)}$ -Estrone to the 3α -Hydroxy Epimer. *Biochem. Pharmacol.* 20 :2930-2933, 1971.
- Freudenthal, R., Rosenfeld, R., and Wall, M. Epimerization of an Intermediary Metabolite of Norethynodrel by a Steroid Epimerase from Rat Liver. *Fed. Proc.* 30 :266, 1971.
- Freudenthal, R.I., Martin, J., and Wall, M. The Distribution of Δ^9 -Tetrahydrocannabinol in the Mouse. *Brit. J. Pharmacol.* 44 :244-249, 1972.
- Freudenthal, R.I., Martin, J., and Wall, M. The Whole Body Distribution of Norethindrone, Ethynodiol Diacetate, and Progesterone in the Pregnant Mouse. *J. Pharmacol. Exp. Ther* 182 :328-334, 1972.
- Freudenthal, R.I., Martin, J., Cook C., and Wall, M. The Metabolism and Distribution of Norethynodrel in Mice. *Toxicol. Appl. Pharmacol.* 24 :125-132, 1973.
- Freudenthal, R.I., Kepler, J., and Cook, C.E. The Preparation of Steriospecific Tritium-Labeled Reduced Nicotinamide Adenine Dinucleotide Phosphate. *Anal. Biochem.* 51 :632-636, 1973.

Freudenthal, R.I., Amerson, E., Martin, J., and Wall, M. The Effect of Noethynodrel, Norethindrone, and Ethynodiol Diacetate on Hepatic Microsomal Drug Metabolism. *Pharmacol. Res. Commun.* 6 :457-468, 1974.

Freudenthal, R.I., and Amerson, E., The Effect of Synthetic Estrogens and Estrogen-Progestin Combinations on the Hepatic Microsomal Enzyme System. *Biochem. Pharmacol.* 23 :2651-2656, 1974.

Freudenthal, R.I., and Carroll, F. Metabolism of Certain Commonly Used Barbiturates. *Drug Metab. Rev.* 2 :265-289, 1975.

Freudenthal, R.I., and Martin, J. Correlation of Brain Levels of Barbiturate Enantiomers with Reported Differences in Duration of Sleep. *J. Pharmacol. Exp. Ther.* 193 :664-668, 1975.

Freudenthal, R.I., Leber, P., and Emmerling, D. Partial Characterization of Hepatic Microsomes from Tupaia Glis. *Res. Commun. Chem. Path. Pharmacol.* 10 :117-125, 1975.

Freudenthal, R.I., Leber, P., and Emmerling, D. The Use of High Pressure Liquid Chromatography to Study Chemically Induced Alterations in Pattern of Benzopyrene Metabolism. *Chemico-Biological Interactions* 11 :449-458, 1975.

Freudenthal, R.I., Leber, P., Emmerling, D., and Kerchner, G. The Characterization of the Hepatic Microsomal Mixed Function Oxidase Enzyme System in Miniature Pigs. *Drug Metab. Dispos.* 4 :25-27, 1976.

Litterst, G., Gram, T., Mimnaugh, E., Leber, P., Emmerling, D., and Freudenthal, R.I. A Comprehensive Study of *In Vitro* Drug Metabolism in Several Laboratory Species. *Drug Metab. Dispos.* 4 :203-207, 1976.

Leber, P., Kerchner, G., and Freudenthal, R.I. A Comparison of Benzo(a)pyrene Metabolism by Primates, Rats, and Miniature Swine. *Polynuclear Aromatic Hydrocarbons: Chemistry, Metabolism, and Carcinogenesis*, R.I. Freudenthal and P. Jones, eds. Raven Press, New York, 1976, pp. 35-43.

Freudenthal, R.I., Leber, P., Emmerling, D., and Kerchner, G. Comparison of the Drug Metabolizing Enzymes in the Liver and Kidneys from Homozygous Nude Swiss, Heterozygous Normal Swiss, Homozygous Normal Swiss, and DBA/2 Mice. *Res. Commun. Chem. Pathol. Pharmacol.* 15 :267-278, 1976.

Freudenthal, R.I., Kerchner, G., Persing, R., Baumel, I., and Baron, R. Subacute Toxicity of Ethylenebisisothiocyanate Sulfide in the Laboratory Rat. *J. Toxicol. Environ. Health* 2 :1067-1078, 1977.

Hundley, S., and Freudenthal, R.I. High Pressure Liquid Chromatographic Analysis of Benzo(a)pyrene Metabolism by Microsomal Enzymes from Rhesus Liver and Lung. *Cancer Res.* 37 :244-249, 1977.

Freudenthal, R.I. and Emmerling D. Separation of Rotenoids by High-Pressure Liquid Chromatography. *J. Chromatography* 134 :207-209, 1977.

Freudenthal, R.I. and Emmerling D. The Disposition of Ftorafur in the Rhesus Monkey and Beagle Dog. *Xenobiotica* 7 :757-764, 1977.

Freudenthal, R.I., Kerchner, G., Persing, R., and Baron, R. Dietary Subacute Toxicity of Ethylene Thiourea in the Laboratory Rat. *J. Environ. Pathol. Toxicol.* 1 :147-161, 1977.

Hundley, S. and Freudenthal, R.I. A Comparison of Benzo(a)pyrene Metabolism by Liver and Lung Microsomal Enzymes from 3-Methylcholanthrene-Treated Rhesus Monkeys and Rats. *Cancer Res.* 37 :3120-3125, 1977.

Freudenthal, R.I., Hundley, S.G., and Cattaneo, S.M. A Comparison of the Metabolites of Benzopyrene by Lung Mixed Function Oxidase from Rat, Rhesus, and Human. *Polynuclear Aromatic Hydrocarbons: Second International Symposium on Analysis, Chemistry, and Biology*, P.W. Jones and R.I. Freudenthal, eds. Raven Press, New York, 1978, pp. 313-323.

Freudenthal, R.I. Present-day Knowledge and a Rational Cancer Policy. *Chemical Times and Trends* 1 :24-30, 1978. (A summary of Dr. Freudenthal's testimony to the U.S. Congress)

Katz, A.C., Frank, D.W., Sauerhoff, M.W., Zwicker, G., and Freudenthal, R.I. A 6-Month Dietary Toxicity Study of Acidic Sodium Aluminum Phosphate in Beagle Dogs. *Food Chem. Toxicol.* 22 :7-9, 1984.

Cohen, S.D., Williams, R.A., Killinger, J.M., and Freudenthal, R.I. Comparative Sensitivity of Bovine and Rodent Acetylcholinesterase to *In Vitro* Inhibition by Organophosphate Insecticides. *Toxicol. Appl. Pharmacol.* 81 :452-458, 1985.

Clement, R.P., Zwicker, G.M., Chin, T.Y., and Freudenthal, R.I. 1-(8-Methoxy-4, 8-dimethylnonyl)-4-(1-methylethyl)benzene (MV-678): A Reversible Inducer of Rat Hepatic Microsomal Drug Metabolism. *J. Toxicol. Environ. Health* 19 :111-117, 1986.

Freudenthal, R.I., Rausch, L., Gerhart, J., Barth, M., Mackerer, C., and Bisinger, E. Subchronic Neurotoxicity of Oil Formulations Containing Either Tricresyl Phosphate or Tri-orthocresyl Phosphate. *J. Amer. College Toxicology* 12 :409-416, 1993.

Freudenthal, R.I. and Anderson, D.P. A Re-examination of the Cause of Excess Bladder Cancers in Chemical Plant Workers. *J. Natl. Cancer Inst.* 86 :59-62, 1993.

Freudenthal, R.I. and Anderson, D.P. A Re-examination of Several Publications Suggesting o-Toluidine May Be a Human Bladder Carcinogen. *Reg. Tox. Pharmacol.* 21:199-202, 1995.

Freudenthal, R.I. and Anderson, D.P. Monitoring of Aromatic Amine Exposures in Workers at a Chemical Plant with Known Bladder Cancer Excess. *J. Natl. Cancer Inst.* 89:734-736, 1997.

Freudenthal, R.I. and Henrich, R.T. A Subchronic Toxicity Study of Fyrol PCF in Sprague-Dawley Rats. *18:173-176*, 1999.

Freudenthal, R.I., Stephens, E., and Anderson, D. Determining the Potential of Aromatic Amines to Induce Cancer of the Urinary Bladder. *Intl. J. Toxicol.* 18:353-359, 1999.

Freudenthal, R.I. and Henrich, R.T. The Chronic Toxicity and Carcinogenic Potential of tris-(1,3-dichloro-2-propyl) phosphate in the Sprague Dawley Rat. *Intl. J. Toxicol.* 19:119-125, 2000.

Freudenthal, R.I., McDonald, L.J., Johnson, J.V., McCormick, D.L., and Henrich, R.T. Comparative Metabolism and Toxicokinetics of ¹⁴C-Resorcinol bis-diphenylphosphate in the rat, mouse, and monkey. *Intl. J. Toxicol.* 19:233-242, 2000.

Sherwood, R.L., House, R.V., Freudenthal, R.I., and Henrich, R.T. Immunotoxicity Evaluation of Resorcinol Bis-Diphenylphosphate (Fyrolflex RDP) in B₆C₃F₁ Mice. *Intl. J. Toxicol.* 19:265-275, 2000.

Henrich, R., Ryan, B.M., Garthwaite, S., and Freudenthal, R.I., Two-Generation Oral (Diet) Reproductive Toxicity Study of Resorcinol Bis-Diphenylphosphate (Fyrolflex RDP) in Rats. *Intl. J. Toxicol.* 19:243-255, 2000.

Henrich, R.T., Johnson, W.D., Rajendran, N., Freudenthal, R.I. and Aranyi, C. Twenty-eight Day Nose-Only Inhalation Toxicity Study of Resorcinol bis-Diphenyl- phosphate (Fyrolflex RDP) in Rats. *Intl. J. Toxicol.* 19:223-231, 2000.

Ryan, B.M., Henrich, R.T., Mallett, E., and Freudenthal, R.I. Developmental Toxicity Study of Orally Administered Resorcinol bis-Diphenylphosphate in Rabbits. *Intl. J. Toxicol.* 19:257-264, 2000.

Freudenthal, R.I., Brandwene, D., and Clous, W. A Subchronic Toxicity Study of Phosflex 51B in Sprague-Dawley Rats. *Intl. J. Toxicol.* 20:269-274, 2001.