Marvin A. Schneiderman, Ph.D., of Bethesda, Maryland, is a statistician and epidemiologist who is the former Chief of Statistics and Epidemiology and the former Director for Science Policy of the National Cancer Institute and is currently a consultant. His curriculum vitae is attached.

Dr. Schneiderman will testify concerning mathematical models, statistics, and epidemiology in the area of cancer. He will first discuss the epidemiology of dioxins and their contaminants to human cancer insofar as it relates to soft tissue sarcomas, and particularly the EPA peer review group conclusions in regard thereto, stomach cancers and lymphomas. In that regard, he will discuss the relationship of exposure to the time the disease appears, the so-called latency period. He will also discuss the multiplication of base rates in the production of such cancer.

Next, Dr. Schneiderman will present a multi-stage model of cancer induction. He will discuss age relationships and the stage of cancer development as they are affected by dioxins and their contaiminants or other materials. He will also present certain pertinent animal data and discuss it as a predictor for human experience. He will also testify that TCDD is more toxic than many other carcinogens, including being more carcinogenic by a factor of 4 or 5 than benzene, for example. He will also explain the concept of risk assessment and how judgments as to such are capable of being made with regard to humans. This will include discussion of a mathematical model for association of the multi-faceted presentation of symptoms and signs in the same veteran to exposure to Agent Orange as a causative factor.

He will also discuss the population incidences of these rare cancers, presenting a comparison of the onset ages for them in the general population with the ages of onset for the cancers observed in the Vietnam veterans.

He will also discuss the relationship of cancer induction to immune deficiencies or deficits. He will place special emphasis upon lymphomas and soft tissue sarcomas and explain how the experience with transplant patients validates his opinions in this regard.

Finally, he will discuss the question of a threshold in the induction of cancer. This will include testimony to the effect that there is no "safe" dose for a carcinogen and that a single exposure may cause cancer. He will also discuss the disease-producing behavior of generalized carcinogens, i.e., the chance of a single carcinogen leading to cancer at multiple sites.

MARVIN A. SCHNEIDERMAN

Dr. Schneiderman is a Clement Associates Senior Science Advisor with principal responsibilities in biostatistics, epidemiology, risk assessment, and health surveillance. He has more than 30 years of experience in cancer research and related subjects, and he is the author of more than 130 scientific papers in areas of biostatistics, epidemiology, risk assessment, and science and regulatory policy. During his career with the National Cancer Institute (NCI), he was, successively, Associate Chief of the Biometry Branch, Associate Director for Field Studies (Epidemiology) and Statistics, and Associate Director for Science Policy. In this last position, he was one of the principal advisors to the Director of the Institute. Dr. Schneiderman is a member of the adjunct faculty of the Georgetown University Graduate School, and Professor of Biostatistics at the Uniformed Services University of the Health Sciences. He has held teaching positions at the University of Pittsburgh Graduate School of Public Health and the University of Miami (Florida), as well as at the Georgetown University Medical School. He was also a Rockefeller Public Service Fellow at the London School of Hygiene and Tropical Medicine. He has served on a number of expert advisory committees and is or has been an associate editor of Cancer Research, Blood, Journal of the National Cancer Institute, Biometrics, Statistics in Medicine, American Journal of Industrial Medicine, and a number of other scientific journals.

DEGREES

Ph.D., Statistics, American University, Washington, D.C., 1961

M.S., Statistics, American University, Washington, D.C., 1953

B.S., Mathematics and Statistics, City College of New York, 1939

NON-DEGREE EDUCATION

Harvard University Graduate School of Business, 1945
Management sciences, economics, statistics

Ohio State University Graduate School, 1946-1947
Economics

London School of Hygiene and Tropical Medicine, 1959-1960
Epidemiology, medical research involving humans, controlled trials, biostatistics

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EMPLOYMENT HISTORY

1983-present	Senior Fellow, Environmental Law Institute, Washington, D.C.
1981-present	Professor (Division of Biometrics), Department of Preventive Medicine, USUHS, Bethesda, Md.
1980-present	Senior Science Advisor, Clement Associates
1975-present	Associate Professor, Graduate Faculty, Georgetown University
1980	Expert Consultant, Office of the Director, National Cancer Institute (NCI), National Institutes of Health (NIH)
1978-1980	Associate Director for Science Policy, Office of the Director, NCI
1970-1978	Associate Director NCI, Field Studies and Statistic Program, Division of Cancer Cause and Prevention, NCI
1967-1978	Adjunct Professor, Biostatistics, Graduate School of Public Health, University of Pittsburgh
1966-1975	Clinical Associate Professor, Medical Statistics, Georgetown University Medical School
1960-1970	Associate Chief, Biometry Branch, NCI
1960-1965	Professorial Lecturer, Georgetown University Medical School
1959-1960	Rockfeller Public Service Fellow, Statistical Research Unit of the British Medical Research Council, London School of Hygiene and Tropical Medicine
1955-1959	Mathematical Statistician and Acting Chief, Therapeutic Trials Section, NCI
1948-1955	Mathematical Statistician, Biometrics Section, NCI
1939-1948	Private Industry, Military Service (USAF), Other Federal government agencies

HONORS

Distinguished Lecturer, Lawrence Livermore Laboratories, University of California, 1982

American Conference of Government Industrial Hygienists, Symposium Speaker Award, June, 1982

Samuel Wilkes Public Lectureship, Princeton University, 1980

Keynote Lecturer, Society of Occupational and Environmental Health, 1979, North Carolina Public Health Association, 1980

Environmental Defense Fund, Public Interest Science Award, 1977

Distinguished Service Award, Department of Health, Education and Welfare (DHEW), 1974

Superior Service Award, DHEW, 1968

Rockefeller Public Service Fellow, London School of Hygiene and Tropical Medicine, 1959-1960

Phi Beta Kappa, 1939

SELECTED ADVISORY COMMITTEES

Committee on Toxicity Data Elements, National Academy of Sciences, 1981-present

Subcommittee on the Geochemical Environment in Relation to Health and Disease, NAS/NRC, 1980-present

Science Evaluation Board, National Health and Medical Research Council of Australia, 1980-present

American Cancer Society, Analysis and Projections Committee, 1976-1978, Institutional Grants Committee, 1980-present

Science Advisory Board, Howard University Cancer Center, 1979-present (External Review Committee)

Center for Science in the Public Interest, Board of Directors, 1983-present

Food Safety Council, Board of Directors, 1978-1982

Advisory Committee, Biomedical and Environmental Assessment Division, Brookhaven National Laboratory, 1978-present

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Advisory Committee, International Cancer Research Data Bank (CIDAC), Franklin Institute, Philadelphia, 1981-present

Task Force on Heart Disease Epidemiology, National Heart, Lung, and Blood Institute, 1979-1980

Science Advisory Board, National Center for Toxicological Research, 1974-1979

Ad Hoc Subcommittee on Asbestos-Related Health Problems, Armed Forces Epidemiology Board, 1978-1979

International (American) Chairman, U.S./U.S.S.R. Working Group on the Epidemiology of Cancer, 1973-1979

Committee on Maritime Hazardous Materials, National Academy of Sciences, 1978

Committee to Coordinate Toxicology and Related Programs, DHEW, 1978

President's Biomedical Panel, 1975-1976

Consultative Panel on Hazards of Chemical Pesticides, National Academy of Sciences, 1974-1976

Chairman and Executive Secretary, Committee of Presidents of Statistical Societies, 1973-1976

Board of Directors, American Statistical Association, 1972-1974

International Council, International Biometric Society, 1971-1973

Immunology-Epidemiology Segment, Special Virus Cancer Program, NCI, 1969-1971

Advisory Panel on Carcinogenicity of Pesticides, Secretary's Commission on Pesticides and Their Relationship to Environmental Health, 1969-1970

Chairman, Subcommittee on Medical Biostatistics, American Therapeutic Society, 1967-1968

Subcommittee on Biologic Effects of Atomic Radiation, NAS/NRC, 1964-1965

SELECTED SOCIETIES

American Association for Cancer Research
American Society for Preventive Oncology (Founding Member)
American Statistical Association (Fellow)
Biometric Society (International)
International Epidemiological Association
Royal Statistical Society (Fellow)
Washington Statistical Society
American Association for the Advancement of Science (Fellow)
International Statistical Institute (Fellow)
Society for Occupational and Environmental Health

SELECTED PUBLICATIONS

Schneiderman, M.A. Standard setting: Implications of sensitivity, and a search for an ethical base. In: Protection of the Sensitive Individual, Annals of the American Conference of Government Industrial Hygienists, 3:133-138 (1982)

Schneiderman, M.A. A personal reminiscence (Austin Bradford Hill). Statistics in Medicine 1:307-308 (1982)

Schneiderman, M.A. Discussion of "Some Aspects of Cancer Epidemiology" by Abraham Lilienfeld. Biometrics (Supplement) 38:161-165 (1982)

Davis, D.L., Bridbord, K., and Schneiderman, M.A. Cancer prevention: Assessing cause, exposure, and recent trends in mortality for U.S. males, 1968-1978. Teratogenesis, Carcinogenesis and Mutagenesis. Pp. 105-135 (June 1982)

Schneiderman, M.A. Trends in cancer mortality and incidence in the United States: Is the future clear or clouded? In Miké, V., ed. Statistics in Medical Research. John Wiley and Sons, New York. Pp. 71-107 (1982)

Schneiderman, M.A. Description and reliability of trends in cancer incidence. In Magnus, K. Trends in Cancer Incidence. Hemisphere Publishing Corp., Washington, D.C. Pp. 1-2 (1982)

Schneiderman, M.A. Cost-benefit, social values and the setting of occupational health standards. In Lee, J.S., and Rom, W.N. eds. Legal and Ethical Dilemmas in Occupational Health. Ann Arbor Science, Ann Arbor, Michigan. pp. 191-205 (1982)

Peto, R., and Schneiderman, M., eds. Quantification of Occupational Cancer: Banbury Report No. 9. Cold Spring Harbor Laboratory, Cold Spring Harbor, New York (1981)

Davis, D.L., Bridbord, K., and Schneiderman, M.A. Estimating cancer risks: Problems in methodology production trends. In Peto, R., and Schneiderman, M., eds. Quantification of Occupational Cancer: Banbury Report No. 9. Cold Spring Harbor Laboratory, Cold Spring Harbor, New York. Pp. 285-315 (1981)

Schneiderman, M.A. Summary comments. In Crandall, R.W., and Lave, R., eds. The Scientific Basis of Health and Safety Regulation. The Brookings Institution, Washington, D.C. Pp. 297-299 (1981)

Schneiderman, M.A. Regulation of carcinogens in an imprecise world. Ann. N.Y. Acad. Sci. 363:217-232 (1981)

Schneiderman, M.A. Extrapolation from incomplete data to total or lifetime risks at low doses. Environ. Health Perspect. V. 42, Pp. 33-38 (December 1981)

Schneiderman, M.A. Toxic Substances in Our Environment-Can we manage them so that they don't manage to harm us? Health Forum 81, The Coalition for Health and the Environment, Washington, D.C. (1981)

Schneiderman, M.A. Epidemiology: What Can it Tell Us? Proceedings of the Conference on Environmental Risk, New Orleans, Louisiana, December 10, 1980. The Electric Power Research Institute, Palo Alto, California, EPRI EA-2064, Project 1316-6. Pp. 369 - 3-89 (October 1981)

Schneiderman, M.A., Nisbet, I., and Brett, S.M. Assessment of Risks Posed by Low Levels of Asbestos in the General Environment. Berichte: Bundesgesundheitsamt. No. 4, 1981. Dietrich Reimer Verlag, Berlin. Pp. 3/1-3/28 (1981)

Schneiderman, M.A., and Levin, D.L. Needs, problems and prospects in cancer epidemiology. In Levin. D.L., ed. Cancer Epidemiology in the U.S.A. and U.S.S.R. U.S. Department of Health and Human Services, PHS, Bethesda, Maryland. NIH Publication No. 80-2044 (1980)

Schneiderman, M.A. The Relationship Between Diet, Occupation, the Environment and Cancer. Proceedings: US/Egypt Symposium on the Biomedical Effects of Technology Transfer, Cairo, Egypt (February 9-13, 1980) (In Press: Environmental Health Perspectives)

Schneiderman, M.A. Scientific Issues in a National Cancer Policy. Proceedings of the 4th Toxic Control Conference. Government Institutes, Inc., Washington, D.C. Pp. 95-107 (1980)

Schneiderman, M.A. The uncertain risks we run: Hazardous materials. In Schwin, R.C., and Albers, W.A., Jr., eds. Societal Risk Assessment. Plenum Press, New York. Pp. 19-41 (1980)

Schneiderman, M.A. What's Happening to Cancer in our Advanced Industrial Society? Have the Risks been Overstated? Keynote Address: Society for Occupational and Environmental Health, Washington, D.C. (In Press: Proceedings) (December 3-5, 1979)

Blokhin, N.N., and Schneiderman, M.A., eds. Epidemiology of Cancer in the USSR and USA. Meditsina, Moscow (Russian) (1979)

Schneiderman, M.A., DeCouflé, P., and Brown, C.C. Thresholds for environmental cancer: Biologic and statistical considerations. Ann. N.Y. Acad. Sci. 329:92-130 (1979)

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Schneiderman, M.A. The Links Between the Environment and Health. Proceedings: National Conference on the Environment and Health Care Costs, U.S. House of Representatives (August 15, 1978)

Biersteker, K., and Schneiderman, M.A. Epidemiologic Aspects of Drinking Water-Health Relationship. Proceedings of the Health Effects Committee of the NATO committee on challenges of Modern Society. Bonn, W. Germany (April 23-27, 1978)

Schneiderman, M.A., Mason, T.J., and Hoover, R. Cancer, geography, and geology--a problem for interdisciplinary cross-fertilization. In Geochemistry and the Environment. Vol. 3. National Academy of Sciences, Washington, D.C. (1978)

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Schneiderman, M.A. Environmental Factors and Cancer Prevention. Marcel Dekker, New York (1978). (Third National Symposium on Detection and Prevention of Cancer, New York (April 26-30, 1976)

Schneiderman, M.A. Risk assessment of the health effects of water chlorination. In Jolley, R.L., Gorchev, H., and Hamilton, D.H., eds. Water Chlorination--Environmental Impact and Health Effects. Ann Arbor Science Publications, Ann Arbor, Mich. Vol. 2, pp. 509-515 (1978)

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Schneiderman, M.A. Health effects--a scientific and statistical analysis. In Miller, M.L., ed. Proceedings of the First Toxic Substances Law Seminar. Washington, D.C. (1977)

Levin, D.L., and Schneiderman, M.A. Cancer. In Miller, S.S., ed. Symptoms. Thomas Y. Crowell, New York (1976)

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Scotto, J., and Schneiderman, M.A. Predicting survival in terminal cancer. Br. Med. J. 4:50 (1972)

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Schneiderman, M.A., and Scotto, J. Computer-Investigator Interactions in Small-Scale Clinical Trials. Proceedings of the Fifth Scientific Meeting of the International Epidemiology Association, Primosten, Yugoslavia. Pp. 449-467 (1970)

Gold, G.L., Shnider, B.I., Salvin, L.G., Schneiderman, M.A., Colsky, J., Owens, A.H., Krant, M.J., Miller, S.P., Frei, E., III, Hall, T.C., Spurr, C.L., McIntyre, O.R., Hoogstraten, B. and Holland, J.F. The use of mechlorethamine, cyclophosphamide, and uracil mustard in neoplastic disease: A cooperative study. J. Clin. Pharmacol. 10:110-120 (1970)

Schneiderman, M.A. How to read the drug literature--or any other organized collection of numbers from experiments. Mod. Med. 37:92-96 (1969)

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Schneiderman, M.A. Quantitative thinking in medicine--biostatistics. (Using numbers to mark the route from cause to effect and back.) In Cantor, P., ed. Traumatic Medicine and Surgery for the Attorney. Matthew Bender, New York. Pp. 419-477 (1969)

Givelber, H., DiPaolo, J.A., and Schneiderman, M.A. The influence of actinomycin D on survival of x-radiated RF mice. Cancer Res. 28:2484-2488 (1968)

Pipberger, H.V., Schneiderman, M.A., and Klingeman, J.D. The love-at-first-sight effect in research. Circulation 38:822-825 (1968)

Carbone, P.P., Spurr, C., Schneiderman, M.A., Scotto, J., Holland, J.F., and Shnider, B. Management of patients with malignant lymphoma: A comparative study with cyclophosphamide and vinca alkaloids. Cancer Res. 28:811-822 (1968)

Hall, T.C., Nevinny, H.B., Holland, J.F., Maldia, G., Schneiderman, M.A., Salvin, L., Shnider, B.I., Gold, G.L., Frei, E., III, Carbone, P.P., Colsky, J., Franzino, A., Grob, D., Matiasevic, D., Olson, K.B., Horton, J., Owens, A., Santos, G.W., Chalmers, T.C., and Krant, M.J. Comparison of antimetabolites in the treatment of breast and colon cancer. JAMA 200:770-778 (1967)

Schneiderman, M.A. The Shin Tokaido to developing new treatments in medicine: Unbiasedness. In Harris, R.J.C., ed. Proceedings of the 9th International Cancer Congress. Springer-Verlag, Heidelberg. Pp. 194-198 (1967)

Bull, B.S., Schneiderman, M.A., and Brecher, G. Semi-automatic dilution system for the hematology laboratory. Am. J. Clin. Pathol. 47:549-553 (1967)

Schneiderman, M.A. Mouse to man: Statistical problems in bringing a drug to clinical trial. In LeCam, L., and Neyman, J., eds. Biology and Problems of Health. University of California Press, Berkeley. Vol. 4, pp. 855-866 (1967)

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Spurr, C.L., Carbone, P.P., and Schneiderman, M.A. Comparative evaluation of cyclophosphamide and vinca alkaloids in lymphomas. Proceedings of the 57th Annual Meeting of the American Association of Cancer Research 7:67 (1966)

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Schneiderman, M.A. Experimental design considerations in multiclinic trials. In Radouco-Thomas, C., exec. ed. International Encyclopedia of Pharmacology and Therapeutics. Pergamon Press, Oxford. Vol. 2, pp. 617-636 (1966)

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Schneiderman, M.A. Looking backward: Is it worth the crick in the neck? Or: Pitfalls in using retrospective data. AJR 96:230-235 (1966)

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Plum, C.M., Clemmesen, J., and Schneiderman, M.A. In vitro study of bone marrow v. erythropoiesis of bone marrow from cases of pernicious anemia and leukosis. Acta Med. Scand. 143:237-248 (1952)

Dr. Ellen Silbergeld, Ph.D., is an environmental scientist and toxicologist who is the Chief Toxicologist for the Environmental Defense Fund and a Research Scientist in the Reproductive Toxicology Laboratory of the National Institutes of Health in Bethesda, Maryland. Her curriculum vitae is attached.

Dr. Silbergeld will testify as to the scientific models for TCDD toxicity. She will emphasize the receptor model, its role in physiology, how to detect receptors and how to link receptors to function. She will discuss how receptors recognize TCDD by virtue of structural "fine-tuning". She will testify as to the existence of receptors in humans and in their various organs, together with the implications of their presence for TCDD potency. She will also discuss the extrapolations which are possible between animals and humans. She will further testify as to the mechanisms of toxicity including the sensitivity of the reproductive system, both endocrine and gonadal, to the receptor-mediated effects of TCDD. Finally, she will discuss the consequences of receptor interaction with TCDD insofar as that interaction produces results involving RNA-DNA, AHH induction, and heme synthesis regulation, among others.

In the field of neurotoxicity, she will discuss the experimental and clinical studies with particular emphasis upon dose-response mechanisms, acute versus chronic exposures and early versus long latency effects. She will also discuss the

Schneiderman, M.A., Mantel, N., and Brecher, G. The effect of rejection procedures on the accuracy of blood counts. Am. J. Clin. Pathol. 21:973-978 (1951)

Schneiderman, M.A., and Brecher, G. The relative frequency of sparse cell elements--an application to reticulocyte blood counts. Biometrics 6:390-394 (1950)

Brecher, G., and Schneiderman, M.A. A time saving device for the counting of reticulocytes. Am. J. Clin. Pathol. 20:1074-1083 (1950)

Williamson, C.R., and Schneiderman, M.A. The use of mass x-ray survey films for heart disease case finding. Mass. Health J 30:7-14 (1950)

biochemical and morphological effects of TCDD, the electrophysiology involved and the effects of TCDD on such things as cognition, mood, and affect.

She will also emphasize the basic mechanisms of toxicity on both the central and peripheral nervous systems, specifically dealing with the role of altered porphyrin synthesis on the nervous system. Three aspects of this problem will be discussed: First, the effects of decreased cellular energy supply on neuronal activity and viability; second, the effects of decreased heme systhesis on the integrity of myelin; and third, the neuroactive properties of certain porphyrin precursors.

CURRICULUM VITAE

Name: - -Ellen Kovner Silbergeld

Date and Place of Birth: July 29, 1945, Washington, DC

Education:

1967 - A.B.	Vassar College
1972 - Ph.D.	Johns Hopkins University

Chronology of Employment:

1967	Instructor, California International Summer Program, Uppsala Sweden
1968-70	Secretary and Program Officer, National Academy of Sciences, National Research Council, Washington, DC
1969-71	"Nader's Raiders", Center for the Study of Responsive Law, Washington, DC
1972-75	Postdoctoral Fellow in Environmental Medicine and Neurosciences, Johns Hopkins University, Baltimore, Maryland
1975	Assistant Professor, Department of Environmental Medicine, School of Hygiene and Public Health, Johns Hopkins University
1975-79	Staff Fellow and Head, Unit on Behavioral Neuropharmacology, Experimental Therapeutics Branch, NINCDS,NIH
1979-81	Chief, Section on Neurotoxicology, NINCDS,NIH
1982	Chief Toxics Scientist, Environmental Defense Fund, Washington, DC
	Guest Scientist, Reproductive Toxicology Section, Pregnancy Research Branch, NICHD,NIH

Other Professional Appointments:

Consultant, NSF Energy Program, 1974-1975

Member,	Nutrition Foundation National Committee on Food Additives and Hyperkinesis, 1975-1980
Member,	USDHEW-FDA Committee to Coordinate Toxicology and Related Programs, 1977-1981
Member,	US Delegation of the Joint US-USSR Health Agreement on Environmental Health, 1977-78
Member,	Society for Neuroscience Committee on Social Issues, 1978 -
Member,	OECD Chemicals Program Ad Hoc Expert Review Committees on Reproductive Toxicity and Neurotoxicity, 1982 -

Member, US Delegation to OECD Expert Meetings on Existing Chemicals, 1983 -
Member, Hazardous Waste Task Force and Hazardous Waste Facilities Siting Board, State of Maryland, 1983
Member, Govenor's Blue Ribbon Panel on Binghamton, NY, State Office Building, 1982 -
Member, Executive Committee, Science Advisory Board, US EPA, 1983 -
Member, Board on Toxicology and Environmental Health Hazards, National Academy of Sciences, 1983 -
Member, Public Policy Committee, American Society for Neurochemistry, 1983 -

Professional Society Memberships:

American Public Health Association
Society for Occupational and Environmental Health
Society for Neuroscience
Association of Women in Science
American Association for the Advancement of Science
International Brain Research Organization
American Society for Neurochemistry
American Society for Pharmacology and Experimental Therapeutics
Engineering Society of Baltimore

Other Activities

Secretary-Treasurer, Society for Occupational & Environmental Health, 1983-
Editorial Board: Neurobehavioral Toxicology, 1979-
American Journal of Industrial Medicine, 1980-
Neurotoxicology, 1981-
Environmental Research, 1983-
Hazardous Waste, 1983 -
Participant, NIH Consensus conferences, 1979 and 1982
Expert consultant on lead poisoning, U.S. Secret Service, 1979-81
Chairperson, Society for Occupational and Environmental Health Special Committee on El Paso Lead Poisoning, 1977-1979
Preceptor, NIGMS Pharmacology-Toxicology Research Associateship Program, 1977-1981
Graduate board examiner, University of Pittsburgh and University of Toronto
Lecturer, continuing medical education courses in environmental medicine (Johns Hopkins) and occupational medicine (NIOSH)

13003

Elected councillor, NIMH-NINCDS Assembly of Scientists, 1979-1981
Elected representative, NINCDS EEO Committee, 1977-1980
Co-organizer, Women in Neuroscience
Member, Solowey Lectureship selection committee, NIH, 1980-1981
Environmental Health Consultant, Oil, Chemical and Atomic Workers Union, AFL-CIO, Washington, D.C., 1970
Reviewer, EPA documents on lead, manganese, mercury, dioxin, risk assessment, and exposure, 1981-
Ad Hoc Member, Occupational Safety and Health Study Section, NIOSH, 1983-
Member, NIMH Committee on Frontiers of Neuroscience, 1983-
Grants reviewer, National Foundation - March of Dimes; National Science Foundation; Nutrition Foundation; Thrasher Foundation; Hereditary Diseases Foundation, NIH
Manuscript reviewer, Life Sciences, Biochemical Pharmacology, Environmental Journal Pharmacology, Science, Neurotoxicology, Neurobehavioral Toxicology Teratology, Pharmacology Biochemical Behavior, Procs. Society Experimental Biological Medicine, Experimental Neurology, etc.

Honors and Awards:

Graduated summa cum laude, 1967
elected to Phi Beta Kappa, 1967
undergraduate academic scholarship, 1963-1965
Woodrow Wilson National Foundation Fellow, 1967-1968
Leverhulme and Fulbright Fellowships to University of London, 1967
National Science Foundation Graduate Traineeship, 1968-1972
Public Health Service Research Fellowship to Woods Hole, 1970
Rockefeller Foundation predoctoral research fellowship, 1971-1972
NIH postdoctoral fellowship in environmental health sciences, 1972-1972
Joseph P. Kennedy, Jr. Fellowship in neurosciences, 1974-1975
Pharmaceutical Manufacturers Association Foundation Research Starter Award, 1974-1975
National Academy of Sciences Exchange Fellow to Yugoslavia, 1976
George Miller lectureship in environmental studies, University of Illinois, 1984

Professional Interests:

Neuropharmacology & Toxicology
Environmental Risk Assessment

13004

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ELLEN KOVNER SILBERGELD

A. SCIENTIFIC PUBLICATIONS

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2. Silbergeld, E. K.: and Goldberg, A.M.: A lead-induced behavior disorder. Life Sci. 13(9):1275-1283, 1973.

3. Silbergeld, E. K.: Blood glucose: A sensitive indicator of environmental stress in fish. Bull. Environ. Contam. Toxicol 11(1):20-25, 1974.

4. Silbergeld, E. K., Fales, J. T. and Goldberg, A.M.: Lead: Evidence for a prejunctional effect on neuromuscular function. Nature 247:49-50, 1974.

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6. Silbergeld, E. K. and Goldberg, A.M.: Lead induced behavioral dysfunction: An animal model of hyperactivity. Exp. Neurol. 42:146-157, 1974.

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Silbergeld, E.K.: Neurotoxicity of lead. In Manzo, L. and Blum, J. (eds) Neurotoxicology, Dekker.

Fowler, B.F., and Silbergeld, E.K.: Mechanisms of metal toxicity. In Nriagu, J., and Hornig, D.F. (eds) Changing Geochemical Cycles of Metals and Implications for Human Health, Berlin, Springer Verlag.

Mattison, D.R., and Silbergeld, E.K.: Occupational risks to reproduction. In Osofsky, H. (ed) Advances in Gynecology and Obstetrics, Baltimore, Williams & Wilkins.

Silbergeld, E.K.: Mitochondrial mechanisms of lead neurotoxicity. In Narahashi, T. (ed) Cellular and Molecular Mechanisms of Environmental Neurotoxins, Raven Press, NY, in press.

Silbergeld, E.K.: Review of occupational health studies on PCBs. In Kuiper, H. (ed) PCBs, Marcel Dekker, in press.

Silbergeld, E.K.: Effects of PCBs in Occupational Populations. In Visser, R. (ed) PCBs, Amsterdam, Elsevier.

Mattison, D.R., and Silbergeld, E.K.: Reproductive toxicity of TCDD. In Lowrance, W. (ed) Dioxins, Rockefeller University Press.

IN PREPARATION:

Silbergeld, E.K., and Mattison, D.R.: Effects of three polycyclic aromatic hydrocarbons on fertility in female mice: A lifetime study of the effects of single-dose treatment.

Silbergeld, E.K.: A Textbook in Neurotoxicology.

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B. ABSTRACTS

1. Silbergeld, E. K.: Effects of lead on neuromuscular functions: In vitro evidence for site of action at the presynaptic level. Fed. Proc. 32:275, 1973.

2. Silbergeld, E. K. and Goldberg, A. M.: Lead poisoning: an animal model of hyperactivity. Pharmacologist 15:143, 1973.

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REVIEWS -

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Silbergeld, E.K.: "Hazardous Waste in American" for Quarterly Review of Biology, in press

Silbergeld, E.K.: "Nutrition and Brain Function" for Trends in Neurosciences, in press

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Silbergeld, E.K.: "US Lead Program Vital" (editorial) Clin. Chem. News, February, 1983, page 4

Silbergeld, E.K.: "Where do we go from here?", in Legator, M.S. (ed) Community Health STudies: A Guide for Citizens, Johns Hopkins Press, Baltimore, MD, in press

Silbergeld, E.K.: "Health Effects" in Environmetal Defense Fund, Dumpsite Cleanups: A Guide to the Superfund Program, Washington, DC, 1983

Silbergeld, E.K., and Highland, J.: "Ghost Dumps" (letter) Science, 216:462, 1982

Silbergeld, E.K.: "Cancer Policy: Has the Dust Settled?" Environmental Forum, 2:25-29, 1983

Hall, K.L., and Silbergeld, E.K.: "Reappraising Epidemiology" Harvard Environmental Law Review, 7:441-448, 1983

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Dr. Raymond Singer, Ph.D., is a neurotoxicologist and neuropsychologist practicing at Occupational Health Consulting, Inc., of New York, New York. Dr. Singer's curriculum vitae is attached.

Dr. Singer will prepare reports concerning each of the veteran plaintiffs. These reports will be based upon personal interviews and review of appropriate test findings performed by himself and/or by others. The personal interview will consist of a thorough account of the veteran's background and current and historic symptoms. It will also detail the educational and occupational background of each veteran. Various neuropsychologic tests will be given and discussed with particular reference to whether any deficits or changes noted are due to the results of any toxic chemical exposures. Neurophysiologic tests will also be given or reviewed and interpreted, with particular emphasis placed upon nerve conduction velocity findings, and the results will be set out and discussed, with particular reference to whether the findings are related to toxic chemical exposures. To the extent warranted, Dr. Singer will relate any findings to Agent Orange exposure.

Dr. Singer will also testify to the effects of toxic chemical exposures as they have been studied in a number of research efforts in both animals and humans. He will discuss the findings reported in various populations exposed to toxic chemicals

and particularly to TCDD through the mechanism of industrial accidents. He will also discuss the findings concerning demyelination of the fatty sheaths surrounding the nerves and the "dying-back" neuropathy which has been associated with toxic chemical exposures.

Dr. Singer will also discuss the results of his own work in relation to occupational exposures to TCDD, and will explain how his results are consistent with those obtained from tests performed on the veterans here, and how those results are consistent with causation by phenoxy herbicides and their contaminants.

RESUME

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EDUCATION AND DEGREES

Ph.D.	Washington State University	1978	Psychology
M.S.	Washington State University	1975	Psychology
B.A.	University of Rochester	1972	Psychology

PROFESSIONAL ORGANIZATIONS

Certified Psychologist, New York State Board of Psychology
Member, American Psychological Association
Member, National Academy of Neuropsychologists
Member, Society for Occupational and Enviromental Health
Member, American Public Health Association
Associate Member, College of Toxicology

PROFESSIONAL EXPERIENCE

1983 -	Adjunct Instructor, Mount Sinai School of Medicine Department of Community Medicine, New York City
1983 -	Consultant, New York State Department of Social Services, Office of Disability Determinations
1982 -	President, Occupational Health Consulting, Inc.
1982 -	Clinical Psychologist, Private Practice, New York City
1982 -	Reviewer, The American Journal of Industrial Medicine
1981 - 1982	Fellow, Mount Sinai School of Medicine, Department Community Medicine, Enviromental Sciences Laboratories, New York City
1979 - 1981	NIH Post-Doctoral Fellow in Environmental Epidemiology, Mount Sinai Medical School of Medicine, New York City
1978 - 1979	NIH Post-Doctoral Fellow in Biological Psychiatry, Millhauser Laboratories, New York University Medical Center, New York City
1978 - 1979	Clinical Psychology Intern, Park East Psychological Associates, New York City

Dr. Raymond Singer December 5, 1983

1972 - 1978 Teaching and Research Assistant, Department of Psychology, Washington State University, Pullman, Washington

PUBLICATION AND PAPERS

Singer, Raymond. Peripheral nervous system assessment in the evaluation of toxic chemical exposure. Paper to be presented at the 12th Annual Meeting of the International Neuropsychological Society, Houston, February, 1984.

Singer, Raymond. Neural indicators of phenoxy herbicide exposure. Paper presented at the 1983 Annual Meeting of The Society for Occupational and Environmental Health, Washington (D.C.), December, 1983.

Singer, R., Valciukas, J., and Lilis, R. Lead exposure and nerve conduction velocity: The differential time course of sensory and motor nerve effects. Neurotoxicology, 4, 2, 193-202, 1983. Presented at the XI Triennial World Congress of Pathology, Jerusalem (Israel), September, 1981.

Singer, R., Moses, M., Valciukas, J., Lilis, R., and Selikoff, I.J. Nerve conduction velocity studies of workers employed in the manufacture of phenoxy herbicides. Environmental Research, 29, 297-311, 1982. Presented at the XX International Congress of Occupational Health, Cairo (Egypt), September, 1981.

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Singer, R. The Neuropsychological Evaluation of Patients Affected by Occupational Neurotoxic Agents. Invited address, New York State Psychological Association Convention, New York City, May, 1980.

Valciukas, J., Lilis, R., Singer, R., et al. Neurobehavioral studies of painters. Presented at the International Symposium on Occupational Health Hazards Encountered in Surface Coating, Handling of Paints in the Construction Industry, Stockholm (Sweden), October, 1979. Manuscript submitted, Archives of Environmental Health.

Singer, R. The role of the psychologist in the prevention of myopia. Paper presented at the annual meeting of the American Psychological Association, New York, New York, September, 1979.

Singer, R. The Camphill approach to the education of the retarded person. Symposium presented at the annual meeting of the American Psychological Association, New York, New York, September, 1979.

Singer, R. The behavioral etiology of myopia. Paper presented at the annual meeting of the Eastern Psychological Association, Philadelphia, Pennsylvania, May, 1979.

Singer, R. The relationship between visual refractive error and interests, values, personality, academic performance, and reading. Doctoral dissertation, Washington State University, 1978.

Singer, R., Young, F., and Rokeach, M. Values as predictors of visual refractive error (in Barrow Eskimos). Paper presented at the Western Psychological Association Convention, Seattle, Washington, April, 1977.

Singer, R. Can myopia be prevented? Invited address - Presented to the Washington State University Chapter of Sigma XI, February, 1976.

Singer, R. The association of personality and myopia. Papers presented at the Western Psychological Association Convention, Sacramento, California, April, 1975.

Young, F., Singer, R., and Foster, D. The psychological differentiation of male myopes and non-myopes. American Journal of Optometry, October, 52, 10, 679-686, 1975.

THEODOR D. STERLING, Ph.D.

Dr. Sterling is Professor in the Facility of Interdisciplinary Studies and Department of Computing Science, Simon Fraser University, Vancouver, British Columbia, Canada. His Curriculum Vitae is attached.

Dr. Sterling is a mathematician, statistician, and epidemiologist; as well, Dr. Sterling is intimately familiar with existing data and analyses concerning the effects of phenoxy herbicides and impurities, e.g. 2,3,7,8-TCDD, contained therein. Dr. Sterling has devoted much of his teaching and research to the collection and analysis of data and their use for scientific inference.

Dr. Sterling will testify that there exists a considerable body of medical and scientific evidence which demonstrates that the preparations of 2,4,5-T and 2,4-D are toxic, teratogenic, and carcinogenic. Further, there is no credible scientific evidence of a no effect level; said another way, as a carcinogen, there is no safe level and therefore a single exposure years ago may be responsible for human cancer which develops today.

In addition, Dr. Sterling will testify that there is ample evidence that exposure to 2,4,5-T is teratogenic in humans when the mother is exposed, and convincing evidence is now extant that the outcome of pregnancy is influenced by exposure to the father alone.

Most especially, Dr. Sterling will testify of the incidence of subjective symptoms and/or medical records documenting such symptoms. These symptoms are those which have been compiled by the National Center for Health Statistics, and will be compared, to the extent available, to those symptoms of the Vietnam veterans, particularly those of the representative plaintiffs.

The purpose will be to ascertain the incidence of such symptoms in the general population so as to analyze statistically the symptoms of the plaintiffs. The product of such overall incidence will be calculated to examine the possibility or likelihood of such a constellation of Agent Orange/dioxin related symptom complex to occur in a random fashion.

The bases or grounds for the facts and opinions of Dr. Sterling's testimony are: educational and professional background; publications regarding the subject phenoxy herbicides; review of the applicable medical and scientific literature; attendance and participation in various symposia dealing with the scientific issues in question; training as a mathematician, statistician, and epidemiologist; and training and experience in the computer sciences.

CURRICULUM VITAE

Theodor D.Sterling

EDUCATION

B.A. (CUM LAUDE), 1949, M.A., 1952, University of Chicago; Ph.D., 1955, Tulane University.

PROFESSIONAL AFFILIATIONS

Present: Professor, The Faculty of Interdisciplinary Studies and Department of Computing Science, Simon Fraser University.

Previous: Visiting Professor, Department of Statistics, Princeton University, (78). Chairman, Department of Computing Science, Simon Fraser University, (72-77). Professor in the Department of Applied Mathematics and Computer Science, Washington University, St. Louis, Missouri (66-72). Also Joint appointment as Professor in the Department of Sociology (66-68), and Visiting Professor in Computers and Humanities, Hebrew Union College, Cincinnati, Ohio (68-70). Professor of Biostatistics and Director of the Computing Center, College of Medicine, University of Cincinnati, Ohio (58-66). Previously instructed in the Department of Statistics, Michigan State University and Department of Mathematics, University of Alabama.

PROFESSIONAL ACTIVITIES

ACM Committee on Scientific Freedom and Human Rights; President of the Computer Science Association of Canada (75-80); Chairman, Ombudsman Committee, Canadian Information Processing Society (73-80); Chairman, President of Biological Information Processing Organization (64-65); Chairman, CIPS Special Interest Groups, Humanization of Information Systems (73-80); Chairman, SIGCAS Committee of Information and Public Policy (72-); President of Missouri Chapter, American Association of Workers for the Blind (70-72); Member of the Panel for Biology, Management, and Social Sciences of the Mathematics Association of America (62-67); Chairman, Committee on Professional Activities of the Blind of the Association for Computing Machinery (63-71); Chairman, Ad Hoc Committee on Accreditation, Association for Computing Machinery (66-67); Committee on Radiation Dosimetry, American Association of Physicists in Medicine (66-69); National Lecturer for Association for Computing Machinery (72-3, 75-6).

EDITORIAL ACTIVITIES:

Associate Editor - Canadian Journal of Statistics (73-78); Editorial Board - International Journal of Biomedical Computing (69-); Computers and Applied Mathematics (73-), Humanist in Canada (73-).

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GOVERNMENT AND OTHER SERVICES:

(Consultant/adviser, now and previous): (In Canada) - Canadian Standards Board; Environment Canada, The Royal Commission (B.C.); Consumers Association of Canada; Society for Professional and Environmental Control. (In U.S.) - NIH; PHS; EPA; FTC; SRA; U.S. National Academy of Science, National Research Council; American Lung Association; Natural Resource Board (Wisconsin); Environmental Defense Fund, MECCA (Minnesota); Citizens Against Toxic Sprays (Oregon). (In Kuwait) - Ministry of Health.

PROFESSIONAL SOCIETIES:

Can. Inf. Proc. Soc.; Can. Comp. Sci. Assoc.; Assoc. Comp. Machinery; Amer. Math. Assoc.; Math. Soc.; Inst. Math. Stat.; Amer. Stat. Assoc.; Biometric Soc.; N.Y. Acad. Sci.; Amer. Assoc. Phys. Med.; Assoc. Res. Opthamology.

HONORS AND AWARDS:

Fellow, Amer. Assoc. for Advancement of Science; Fellow, Amer. College of Epidemiology; Fellow, Amer. Stat. Assoc.; Fellow, Can. Com. of Scientists and Scholars; Sigma Xi; Pi Nu Epsilon, Morrison Cressy Award in National Science; University Research Professor (1980-1981).

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Theodor D. Sterling

Books

A Guide to PL/1 and Structured Programming. Holt, Rinehart and Winston, February, 1969. Second edition - 1976. Third Edition - 1980.

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Articles

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Trap. In A. Ralston and E. Reilly, Jr., (ed.) Encyclopedia of Computer Science and Engineering (second edition). Van Nostrand Reinhold Company, New York. pp. 1534-1535.

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Natural Language Compilers and Interpreters in Radiation Treatment Planning or Nous Parlons Anglais Better Than Dece Andere Sprache. In V. Rosenow (ed), Computers in Radiation Therapy: Proceedings of the Sixth International Congress on the Use of Computers in Radiation Therapy, University of Goettingen, Goettingen, FRG.

1977

Computers in Developing Nations: A Cautionary Tale. Communications of the ACM. December, 20(12): 971-972.

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13043

Bio-Statistician/Mathematician-

This witness will be identified in the near future. At that time a curriculum vitae will be supplied.

This witness will describe the mathematical/statistical model which will be used in the presentation of the figures to which the witness will testify. The theory subserving the testimony is that the multi-faceted presentation of symptoms and signs and test results in the same veteran makes a random composition of such an array extremely unlikely in view of the relative in-frequency of each facet of the array. As such, this testimony will be used in the generic and specific proximate causation areas.

HENDERSON & GOLDBERG, P.C.
1612 Frick Building
Pittsburgh, PA 15219

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February 27, 1984

Thomas W. Henderson
Theodore Goldberg
Robert L. Jennings, Jr.
Joel Persky
Antonio D. Pyle
Thomas W. White

Ms. Nancy Petrilla
U.S. District Clerk
U.S. District Courthouse
225 Cadman Plaza
Brooklyn, New York 11201

Re: MDL No. #381, Agent Orange Product Liability Litigation

Dear Ms. Petrilla:

Please find enclosed for the Court file, Plaintiffs' Compliance with Guideline No. 34 on Plaintiffs' Government Causation witnesses which are to begin being deposed on March 1, 1984 in Washington, D.C.

Also please find enclosed an additional copy of Plaintiffs' Expanded Summaries on the following Plaintiffs' Causation Experts which I promised Magistrate Shindlin she would receive before Wednesday, February 29, 1984. Apparently, the original court copies were missing some pages. I apologize for this inconvenience.

Please be advised that by copy of this letter and the enclosed documents I have notified all parties on the attached service list of the filing of said documents with the Court and I have served the U.S. Department of Justice, Ms. Gretched Witt, on or before noon, February 27, 1984, with the enclosed documents as per our agreement.

Thank you in advance for your kindness and cooperation in this matter.

Very truly yours,

Alison Pettiette

13045

cc: Enclosures
Ms. Gretchen Witt
See attached Service List Hand Delivery

1939

PLAINTIFF'S GOVERNMENT CAUSATION WITNESSES

I. Vernon M. Houk

A. Center for Disease Control (CDC) Atlanta, GA

B. Both factual and expert testimony is sought.

C. General Events

Pre-1961: Any factual knowledge of the history of herbicide spraying in U.S. and abroad; including, but not limited to, (1) industrial exposures and explosions; (2) registration of 2,4-D, 2,4,5-T with the Department of Agriculture and any other government agencies by any and/or all of the Defendants;

1961-present: Any factual knowledge of the history of herbicide spraying in the U.S. and abroad; including, but not limited to, (1) U.S. military use of Agent Orange and other phenoxy herbicides in Vietnam, (2) changes in the registration requirements of herbicides with the U.S. government and its agencies including knowledge of FIFRA, FDA, EPA, and OSHA; and (3) any knowledge of industrial and other human exposures to 2,4-D, 2,4,5-T in the U.S. and abroad;

See Answer and Supplemental Answer of Plaintiffs' to Defendants' Interrogatory No. 19 attached hereto and incorporated herein for all purposes re: events or occurrences which these causation witnesses may be expected to give any factual information they may have regarding the subjects outlined in said Answer.

Human Risk Assessment of Exposure to 2,4-D, 2,4,5-T and dioxins and any factual knowledge in support thereof.

D. Expert Testimony

1) Testimony is sought in witness' personal and official capacity.

2) Subject Matter
2,4-D, 2,4,5-T, TCDD's and dioxins; Agent Orange I/II (also White, Blue, Pink, Green, and Purple

received 2/27/84

and related chlorophenols and human risk assessment regarding exposure, including, but not limited to, one or more of the following subject areas:

a) Chemistry/Biochemistry

b) Manufacture and/or Production

c) Toxicity

d) Modes of Human Exposure

e) Fate in the Environment (Humans, Plants, Animals)

f) State of Art/State of Medical and Scientific Literature

1) Plant Physiology/Studies
2) Animal Physiology/Studies
3) Human Studies

g) Epidemiology/Biostatistics

1) Plants, animals, humans
2) Cancer Epidemiology
3) Reproductive Epidemiology

h) Adverse Health Effects

3) Yes, witness will be asked opinions about both published and/or on-going studies.

4) Yes, witness will be asked opinions about any studies or research witness has personally performed or actually participated in.

5) Yes, witness will be asked opinions about other governmental studies.

6) Yes, witness is expected to review the following documents prior to giving testimony:

See, EPA, Research and Development, Health Assessment Document on Dioxin for the Offices of Air Quality, Planning and Standards, prepared by the Environmental Criteria and Assessment Office, Cincinnati, Ohio 45268 (July 1

EPA, Research and Development, Health and Environmental Effects Profile for; Tetra Penta, and Hexachlorodibenzo-p-dioxins, for the Office of Solid Waste and Emergency Response, by the Environmental Criteria and Assessment Office, Cincinnat Ohio 45268 (June 1983).

EPA, Research and Development, Ambient Water Quality Criteria for 2,3,7,8 TCDD, prepared for Office of Water Regulations and Standards, by the Environmental Criteria and Assessment Office, Cincinnat Ohio 45268 (July 1983).

EPA, Research and Development, Dioxins, Industrial Environmental Research Cincinnati, Ohio (1979).

A copy of these documents is attached.

k. Major Alvin Young
l. Dr. Rodney Bovey
m. Kenneth V. Themein
n. David T. Buzzelli
o. Dr. Michael Gross
p. Dr. Renee Stringham
q. Dr. Van Miller

SUPPLEMENTAL ANSWER TO INTERROGATORY NO. 19

Plaintiffs note preliminarily that the court's Order on producing fact witnesses states that fact witnesses are not due until March 2, 1984. However, Plaintiffs may call one or more of the following persons (or those from various categories listed below) at time of trial to testify as to factual knowledge they may have including:

1. Ranch Hand Personnel: These persons will testify to their knowledge of the Ranch Hand Operation, Ranch Handers' exposure to Agent Orange, and/or knowledge relating to the spraying, testing, and effects of Agent Orange on humans.

2. Members of the U. S. Armed Forces: These persons may testify to the circumstances and conditions surrounding the spraying of Agent Orange.

3. Persons present in Vietnam during the exposure period in question 1961-1972, including, but not limited to, military and paramilitary personnel of the U. S., New Zealand and Australia, who have knowledge of the spraying operations of the herbicides, the exposure of the Plaintiffs' class, the hazards accompanying any such exposure, the Plaintiffs' themselves, and the Defendant company representatives present in Vietnam to oversee the deliveries and spraying operations of the herbicides they manufactured.

4. Persons together with their demonstrative and documentary evidence who gave testimony (which will form the substance of their testimony herein) at the EPA Cancellation Hearings of 2,4,5-T (1979-1980) under FIFRA, including but not limited to:

a. Dr. Roy Albert
Dr. K. Diane Courtney
Robert G. Baughman, Ph.D.

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10. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has factual knowledge of how dioxins work upon plants, animals, and/or humans.

11. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has factual knowledge of any statistics concerning the effects of dioxins upon plants, animals, and/or humans.

12. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person including, but not limited to, members of EPA and other governmental agencies, who has factual knowledge of the following incidents:

a. Love Canal
b. Times Beach, Missouri
c. Seveso, Italy
d. BASF (1953, 1954 - Badische in Germany)
e. Production mishaps and/or explosions since 1943 at any of the plants of any of the Defendants manufacturing, TCP, 2,4-D, 2,4,5-T phenol, chlorine, acetic acid, benzene, sodium hydroxide, potassium hydroxide, and/or Agent Orange, including mishaps in the packaging, and transporting of the Defendants' products to the U.S. Armed Forces bases for eventual shipment to Vietnam.
f. Spraying of Vietnam from 1961-1972.

13. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has factual knowledge of any surveys, tests, epidemiological studies of any kind relating to the effects of exposure to Agent Orange, 2,4-D, 2,4,5-T or any constituent thereof including the secondary by-product known as dioxins.

14. Any person with factual knowledge of how decisions are made within the United States government, particularly the decision to use and to continue to use phenoxy herbicides in Vietnam, particularly Agent Orange; any person with factual knowledge of government procurement contracts and the invitation to bidders, particularly those persons who negotiated the government contracts for all phenoxy herbicides (agents white, blue, purple, pink, green, orange I and II) with the individual defendants' representatives between 1961-1972.

15. Any person with factual knowledge through any surveys, tests, epidemiological studies or otherwise undertaken by any state government, any private public or foreign corporation, the U. S. Congress or the government of any nation concerning the chemical compounds, 2,5-D, 2,4,5-T, dioxins, or related chlorophenols relating to the creation of dioxins, the detection of dioxins, the dangers of dioxins' exposure, and/or the toxicity, carcinogenicity, fetotoxicity, teratogenicity, acute and/or chronic effects on plants, animals and the human population

16. Any and all persons listed in The Chemical Scythe by Alastair Hay as having factual knowledge regarding 2,4,5-T, 2,4-D, and its contaminant dioxins.

17. All worker compensation carriers for the Defendants and documentation on all occupational exposures filed since 1928 which evidence industrial injuries or diseases at the TCP, 2,4,5-T, 2,4-D, Phenol, packaging, and/or transportation plants of the Defendants.

18. Any and all current or prior workers compensation claimants of the Defendants who claimed relevant occupational exposures and/or relevant occupational injuries and/or diseases and/or symptoms at the relevant plant listed in Answer to No. 19 (sub 17) above.

19. Any and all members of the U. S. House of Representatives Committee on Ways and Means Review of the EPA actions (1983) and/or any person together with their documentary and demonstrative evidence giving testimony at said hearing (which will form the substance of their testimony herein) on the failure of the EPA to take prompt and effective action to ban the production of 2,4-D, 2,4,5-T, and its contaminant dioxins.

20. Any and all persons having knowledge of relevant facts regarding the financial status of the Defendants and their ability to respond in punitive damages, including, but not limited to, their past, present, and future profits and earnings in the United States and abroad since 1928 through and including the present from the sale of the products made the basis of this lawsuit, i.e., 2,4-D, 2,4,5-T, phenoxy herbicides and the relevant herbicide market.

21. Any and all persons having knowledge of relevant facts regarding the ownership interests of the Defendants and their ability to respond in punitive damages, including, but not limited to, defendants' domestic and foreign subsidiaries, joint venturers, licensing agreements, and/or other public or private corporations in the U. S. and abroad, in which those defendants own a substantial financial interest since 1928 through and including the present.

22. Any and all persons listed by Plaintiffs' in both original and amended witness lists, as expert witness (medical, scientific or causation), government witness, government causation witness, defendants' employees and/or related personnel and/or any witnesses listed by all Defendants, may be called at time of trial to present factual information as to any issue involved in this case.

23. Any and all members of the scientific and/or medical community who have knowledge of relevant facts, including information on any of the previously listed subjects in this Answer, including, but not limited to:

a. David Kotlebel, Ph.D.
b. Dr. Alan Poland
c. Dr. [illegible], BAL
d. Dr. G. Pappa
e. Dr. Caudell, EAGF
f. Dr. E. T. McDonnell
g. Dr. H. G. Ohlsen
h. Alvin Alm
i. Marilyn Klingenhut

24. Any and all persons who have factual knowledge concerning the individual representative Plaintiff's damages, including, but not limited to, the following:

a. Any and all medical persons who have examined, observed, treated and/or tested the Plaintiffs' for injuries diseases and/or related physical and emotional conditions which resulted from Plaintiffs' exposure to Agent Orange, and/or phenoxy herbicides, their constituents, secondary by-products, wastes, residuals and contaminants.

b. Any and all hospital personnel where Plaintiffs have been confined for treatment relating to their exposure to Defendants' products in Vietnam.

c. Any and all persons with knowledge of the economic losses, psychological and/or intangible damages sustained by your Plaintiffs as a result of their injuries and diseases resulting from their exposure to Defendants' products in Vietnam.

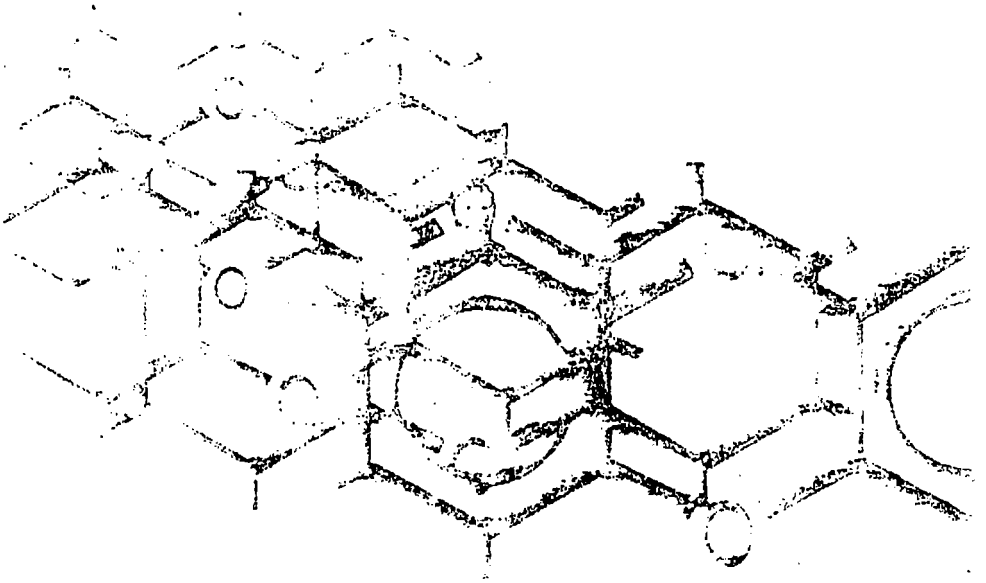
d. Any and all persons with knowledge of the past, present and/or future economic losses your Plaintiffs have or will sustain in the future as a result of their loss of wage earnings and/or wages earning capacity resulting from the injuries and diseases made the basis of this lawsuit which were caused by Plaintiffs exposure to Defendants' products in Vietnam.

United States
Environmental Protection
Agency

Environmental
Laboratory
Cincinnati OH 45268

Research & Development

EPA Dioxins



13051

PLAINTIFF'S GOVERNMENT CAUSATION WITNESSES

1. Debdas Mukerjee

A. EPA, Washington, D.C.

B. Both factual and expert testimony is sought.

C. General Events

Pre-1961: Any factual knowledge of the history of herbicide spraying in U.S. and abroad; including, but not limited to, (1) industri exposures and explosions; (2) registration 2,4-D, 2,4,5-T with the Department of Agriculture and any other government agencies by any and/or all of the Defendants;

1961-present: Any factual knowledge of the history of herbicide spraying in the U.S. and abroad; including, but not limited to, (1) U.S. military use of Agent Orange and other pher herbicides in Vietnam; (2) changes in the istration requirements of herbicides wit U.S. government and its agencies includin knowled of FIFRA, FDA, EPA, and OSHA; and any knowledge of industrial and other human exposures to 2,4-D, 2,4,5-T in the U.S. and abroad;

See Answer and Supplemental Answer of Plaintiffs' to Defendants' Interrogatory No. 19 attached hereto and incorporated herein for all purposes re: events or occurrences which these causation witnesses may be expected to give any factual information they may have regardi the subjects outlined in said Answer.

Human Risk Assessment of Exposure to 2,4-D, 2,4,5-T and dioxins and any factual knowledge in support thereof.

D. Expert Testimony

1) Testimony is sought in witness' personal and officia capacity.

2) Subject Matter
2,4-D, 2,4,5-T, TCDD's and dioxins; Agent Oran I/II (also White, Blue, Pink, Green, and Purp

and related chlorophenols and human risk assessment regarding exposure, including, but not limited to, one or more of the following subject areas:

a) Chemistry/Biochemistry

b) Manufacture and/or Production

c) Toxicity

d) Modes of Human Exposure

e) Fate in the Environment (Humans, Plants, Animals)

f) State of Art/State of Medical and Scientific Literature

1) Plant Physiology/Studies
2) Animal Physiology/Studies
3) Human Studies

g) Epidemiology/Biostatistics

1) Plants, animals, humans
2) Cancer Epidemiology
3) Reproductive Epidemiology

h) Adverse Health Effects

3) Yes, witness will be asked opinions about both published and/or on-going studies.

4) Yes, witness will be asked opinions about any studies or research witness has personally performed or actually participated in.

5) Yes, witness will be asked opinions about other governmental studies.

6) Yes, witness is expected to review the following documents prior to giving testimony:

See, EPA, Research and Development, Health Assessment Document on Dioxins for the Offices of Air Quality, Planning and Standards, prepared by the Environmental Criteria and Assessment Office, Cincinnati, Ohio 45268 (July 19

EPA, Research and Development, Health and Environmental Effects Profile for; Tet Penta, and Hexachlorodibenzo-p-dioxins for the Office of Solid Waste and Emergency Response, by the Environmental Criteria and Assessment Office, Cincin Ohio 45248 (June 1983).

EPA, Research and Development, Ambient Water Quality Criteria for 2,3,7,8 TCDD, prepared for Office of Water Regulations and Standards, by the Environmental Criteria and Assessment Office, Cincin Ohio 45243 (July 1983).

EPA, Research and Development, Dioxins, Industrial Environmental Research Cincinnati, Ohio (1978).

A copy of these documents is attached.

SUPPLEMENTAL ANSWER TO INTERROGATORY NO. 19

Plaintiffs note preliminarily that the extent Order on producing fact witnesses states that fact witnesses are not due until March 1984. However, Plaintiffs may call one or more of the following persons (or those from various categories listed below) at time of trial to testify as to factual knowledge they may have, including:

1. Ranch Hand Personnel: These persons will testify to their knowledge of the Ranch Hand Operation, Ranch Handers exposure to Agent Orange, and/or knowledge relating to the spraying, testing, and effects of Agent Orange on humans.

2. Members of the U.S. Armed Forces: These persons may testify to the circumstances and conditions surrounding the spraying of Agent Orange.

3. Persons present in Vietnam during the exposure period in question 1961-1972, including, but not limited to, military and paramilitary personnel of the U. S., New Zealand and Australia, who have knowledge of the spraying operations of the herbicides, the exposure of the Plaintiffs' class, the hazards accompanying any such exposure, the Plaintiffs' themselves, and the Defendant company representatives present in Vietnam to oversee the deliveries and spraying operations of the herbicides they manufactured.

4. Persons together with their demonstrative and documentary evidence who gave testimony (which will form the substance of their testimony herein) at the EPA Cancellation Hearings of 2,4,5-T (1979-1980) under FIFRA, including but not limited to:

   a. Dr. Roy Albert
   b. Dr. K. Diane Courtney
   c. Robert K. Baughman, Ph.D.
   d. Dr. Olav Axelson
   e. Dr. Renate Kimbrough
   f. Dr. Dawn G. Goodman
   g. Dr. Kirk T. Kitchin
   h. Dr. Ronald Thomas
   i. Dr. Rainer Frentzel-Beyme
   j. Dr. Matthew Meselson, Harvard

13053

k. Major Alvin Young
l. Dr. Rodney Bovey
m. Kenneth V. Thamein
n. David T. Buzzelli
o. Dr. Michael Gross
p. Dr. Renee Stringham
r. Dr. Van Miller

5. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has knowledge of the manufacturing processes, chemistry, occupational exposure and/or toxicity of 2,4-D and/or 2,4,5-T or related chlorophenols; including, but not limited to, laborers; operators; supervisors; contract administrators; quality control personnel; engineers (process, chemical, mechanical and/or safety).

6. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has knowledge of the possible means of prophylactic protection from the hazards of dioxins' exposure; including, but not limited to, laborers, operators, supervisors, contract administrators, quality control personnel, engineers (process, chemical, mechanical and/or safety).

7. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has knowledge of the means to warn those who might be exposed to use of the herbicides in question, particularly Agent Orange, including, but not limited to, laborers, operators, supervisors, contract administrators, quality control personnel, engineers (process, chemical, mechanical and/or safety).

8. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has factual knowledge of any other manufacturing processes which could reduce the risks of exposure to Agent Orange and/or other phenoxy herbicides being contaminated with dioxins and further reduce the risk and hazard to human health of any such exposure.

9. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has factual knowledge of conspiratorial conduct of the Defendants, individually and/or duplicative efforts (acts which are parallel in nature) which tended to or did in fact result in misleading the public and the United States government from gaining knowledge of the dangers attendant from exposure to Agent Orange and other phenoxy herbicides.

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10. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has factual knowledge of how dioxin work upon plants, animals, and/or humans.

11. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has factual knowledge of any statistics concerning the effects of dioxins upon plants, animals and/or humans.

12. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person including, but not limited to, members of EPA and other governmental agencies, who has factual knowledge of the following incidents:

a. Love Canal
b. Times Beach, Missouri
c. Seveso, Italy
d. BASF (1953, 1954 -- Badische in Germany)
e. Production mishaps and/or explosions since 1925 at any of the plants of any of the Defendants manufacturing, T, 2,4-D, 2,4,5-T phenol, chlorine, acetic acid, benzene, sodium hydroxide, potassium hydroxide, and/or Agent Orange, including mishaps in the packaging, and transporting of the Defendants' products to the U. S. Armed Forces bases for eventual shipment to Vietnam.
f. Spraying of Vietnam from 1961-1972.

13. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has factual knowledge of any surveys, tests, epidemiological studies of any kind relating to the effects of exposure to Agent Orange, 2,4-D, 2,4,5-T or any constituent thereof including the secondary by-product known as dioxins.

14. Any person with factual knowledge of how decisions are made within the United States government, particularly the decision to use and to continue to use phenoxy herbicides in Vietnam, particularly Agent Orange; any person with factual knowledge of government procurement contracts and the invitation to bidders, particularly those persons who negotiated the government contracts for all phenoxy herbicides (agents white, blue, purple, pink, green, orange I and II) with the individual defendants representatives between 1961-1972.

13060

15. Any person with factual knowledge through any surv s, tests, epidemiological studies or otherwise undertaken by ny state government, any private public or foreign corporat on, the U. S. Congress or the government of any nation concernin the chemical compounds, 2,5-D, 2,4,5-T, dioxins, or related chl ophenols relating to the creation of dioxins, the detection of dioxins, the dangers of dioxins' exposure, and/or the toxicity, arcinogenicity, fetotoxicity, teratogenicity, acute and/or chronic ffects on plants, animals and the human population.

16. Any and all persons listed in The Chemical Scyche Alastair Hay, as having factual knowledge regarding 2,4,5-T 2,4-D, and its contaminant dioxins.

17. All worker compensation carriers for the Defendant and documentation of all occupational exposures filed sinc 1925 which evidence industrial injuries or diseases at the TC 2,4,5-T, 2,4-D, Phenol, packaging, and/or transporatio pla s of the Defendants.

18. Any and all current or prior workers compensation c imants of the Defendants who claimed relevant occupational e sures and/o relevant occupational injuries and/or diseases and symptoms a the relevant dates listed in answer to No. 19 (sub) above.

19. Any and all members of the U. S. House of Represent ives Committee on Oversight's Review of the EPA actions 983) and/or any person together with their documentary and demo trative evidence giving testimony at said hearing (which wi form th substance of their testimony herein) on the failure the EP to take prompt and effective action to ban the prod tion of 2,4-D, 2,4,5-T, and its contaminant dioxins.

20. Any and all persons having knowledge of relevant fac s regarding the financial status of the Defendants and their ab ity to respond in punitive damages, including, but not limi ed to, their past, present, and future profits and earnings in t United States and abroad since 192 through and including the pres nt from the sale of the products made the basis of this lawsuit, i.e., 2,4-D, 2,4,5-T, phenoxy herbicides and the relevant rbicide market.

21. Any and all persons having knowledge of relevant fac s regarding the ownership interests of the Defendants and their bility to respond in punitive damages, including, but not limi d to, defendants' domestic and foreign subsidiaries, joint ventures, licensing agreements, and/or other public or private corporations in the U. S. and abroad, in which these defendants own a substantial financial interest since 192 through and including the present.

13061

e. Any and all persons with knowledge of past, pre
and/or future reasonable and necessary costs of
doctors, hospitals, nursery care, medical equip
drugs, and any other related medical services r ed
or to be rendered in the future to Plaintiffs a
result of their injuries and disease resulting
their exposure to Defendants' products in Vietn

f. Any and all persons with knowledge of the physi
disfigurement (past and present), physical and al
impairment (past and present), physical pain (pa and
present) and mental anguish (past and present) v h
Plaintiffs have sustained as a result of their e osure
to Defendants' products in Vietnam and which in
reasonable probability Plaintiffs will continue
sustain for an indefinite time into the future
beyond the date of this trial.

Respectfully sub tted,

Thomas W. Hender n, Esquire
Allison Pettiett Esquire

CERTIFICATE OF SERVICE

I hereby certify that a true and correct copy of the oregoing Supplement to Plaintiff's Interrogatories were mailed Federal Express to Mr. William Krohley, Kelley, Drye & Warren, Mr. Gene Locks, Plaintiffs' Management Committee Agent Orange Office, with copies to personally serve the remaining Defendants at the Tuesday depositions and Ms. Nancy Petrilla, U.S. District Clerk, U.S. Courthouse, 225 Cadman Plaza, Brooklyn, New York 11201 this 20th day of February, 1984.

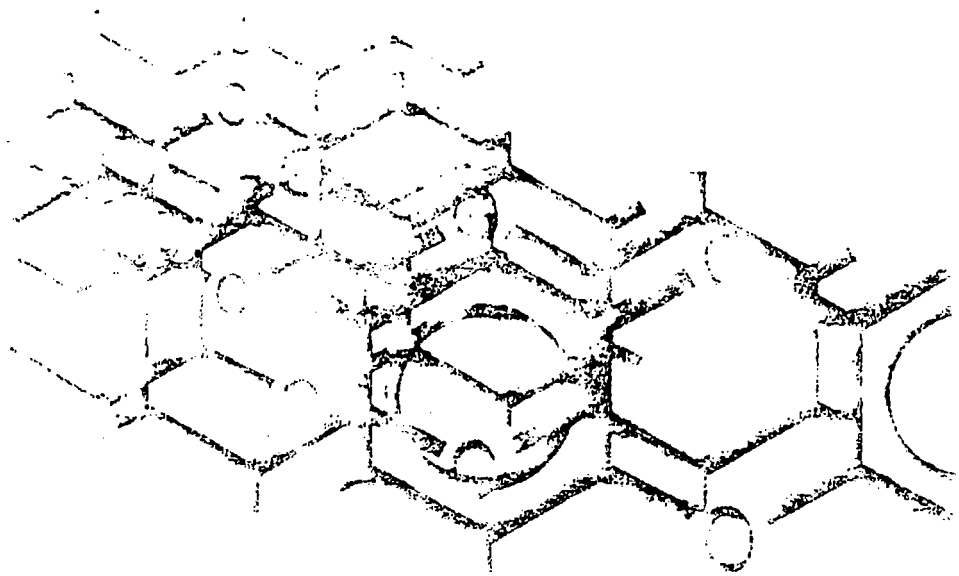
Allison Pettiette

United States
Environmental Protection
Agency

Industrial Environmental
Laboratory
Cincinnati OH 45268

Research & Development

EPA Dioxin:



13063

PLAINTIFF'S GOVERNMENT CAUSATION WITNESSES

I. Janet Springer

A. EPA, Washington, D.C.

B. Both factual and expert testimony is sough

C. General Events

Pre-1961: Any factual knowledge of the h ry of herbicide spraying in U.S. and road; including, but not limited to,) industrial exposures and explosions; (2) istration of 2,4-D, 2,4,5-T with the Departt t of Agriculture and any other governme agencies by any and/or all of the Defendant

1961-present: Any factual knowledge of th istory of herbicide spraying in the U.S. l abroad; including, but not limited to,) U.S. military use of Agent Orange an other phen herbicides in Vietnam; (2) chan in the gistration requirements of herb ides with the U.S. government and its agencie including knowledge of NIFRA, FDA, EPA, an OSHA; and (3) any knowledge of industrial and ther human exposures to 2,4-D, 2,4,5-T in U.S. and abroad

See Answer and Supplemental Answer of Plai ffs' t Defendants' Interrogatory No. 1 ttached hereto and incorporated herein all pur- poses re events or occurrences which these causation witnesses may be expec ed to give any factual information they may have regarding the subjects outlined in said An ver.

Human Risk Assessment of Exposure to 2,4-D, ,4,5-T and ioxins and any factual knowledg in support thereof.

D. Expert Testimony

1) Testimony is sought in witness' persona and official capacity.

2) Subject Matter
2,4-D, 2,4,5-T, TCDD's and dioxi Agent Orang I/II (also White, Blue, Pink, Gre and Purple

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and related chlorophenols and human risk assessment regarding exposure, including, but not limited to, one or more of the following subject areas:

a) Chemistry/Biochemistry

b) Manufacture and/or Production

c) Toxicity

d) Modes of Human Exposure

e) Fate in the Environment (Humans, Plants, Animals)

f) State of Art/State of Medical and Scientific Literature

1) Plant Physiology/Studies
2) Animal Physiology/Studies
3) Human Studies

g) Epidemiology/Biostatistics

1) Plants, animals, humans
2) Cancer Epidemiology
3) Reproductive Epidemiology

h) Adverse Health Effects

3) Yes, witness will be asked opinions about both published and/or on-going studies.

4) Yes, witness will be asked opinions about any studies or research witness has personally performed or actually participated in.

5) Yes, witness will be asked opinions about other governmental studies.

6) Yes, witness is expected to review the following documents prior to giving testimony:

See, EPA, Research and Development, Health Assessment Document on Dioxins for the Offices of Air Quality, Planning and Standards, prepared by the Environmental Criteria and Assessment Office, Cincinnati, Ohio 45248 (July 19

EPA, Research and Development, Health and Environmental Effects Profile for; Te Penta, and Hexachlorodibenzo-p-dioxin for the Office of Solid Waste and Eme gency Response, by the Environmental Criteria and Assessment Office, Cinci Ohio 45268 (June 1983).

EPA, Research and Development, Ambient Water Quality Criteria for 2,3,7,8 TCDD, pr pared for Office of Water Regulations and Standards, by the Environmental Criteria and Assessment Office, Cinci Ohio 45268 (July 1983).

EPA, Research and Development, Dioxins, [illegible] Environmental Research Lab. Cincinnati, Ohio (1978).

A copy of these documents is attached.

SUPPLEMENTAL ANSWER TO INTERROGATORY NO. 19

Plaintiffs note preliminarily that the extant Order on producing fact witnesses states that fact witnesses are not due until March 2, 1984. However, Plaintiffs may call one or more of the following persons (or those from various categories listed below) at time of trial to testify as to factual knowledge they may have, including:

1. Ranch Hand Personnel: These persons will testify to their knowledge of the Ranch Hand Operation, Ranch Handers' exposure to Agent Orange, and/or knowledge relating to the spraying, testing, and effects of Agent Orange on humans.

2. Members of the U. S. Armed Forces: These persons may testify to the circumstances and conditions surrounding the spraying of Agent Orange.

3. Persons present in Vietnam during the exposure period in question 1961-1972, including, but not limited to, military and paramilitary personnel of the U. S., New Zealand and Australia, who have knowledge of the spraying operations of the herbicides, the exposure of the Plaintiffs' class, the hazards accompanying any such exposure, the Plaintiffs' themselves, and the Defendant company representatives present in Vietnam to oversee the deliveries and spraying operations of the herbicides they manufactured.

4. Persons together with their demonstrative and documentary evidence who gave testimony (which will form the substance of their testimony herein) at the EPA Cancellation Hearings of 2,4,5-T (1979-1980) under FIFRA, including but not limited to:

   a. Dr. Roy Albert:
   b. Dr. K. Diane Courtney
   c. Robert K. Baughman, Ph.D.
   d. Dr. Olav Axelson
   e. Dr. Renate Kimbrough
   f. Dr. Dawn G. Goodrich
   g. Dr. Kirk T. Kitchin
   h. Dr. Ronald Thomas
   i. Dr. Rainer Frentzel-Beyme
   j. Dr. Matthew Meselson, Harvard

k. Major Alvin Young
l. Dr. Rodney Povey
m. Kenneth V. Themein
n. David F. Buzzelli
o. Dr. Michael Gross
p. Dr. Renea Stringham
r. Dr. Van Miller

5. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has knowledge of the manufacturing processes, chemistry, occupational exposure and/or toxicity of 2,4-D and/or 2,4,5-T or related chlorophenols; including, but not limited to, laborers; operators; supervisors; contract administrators; quality control personnel; engineers (process, chemical, mechanical and/or safety).

6. Any current or previous employee, contractor, subcontractor in-house or private consultant of each of the Defendants or any other person who has knowledge of the possible means of prophlactic protection from the hazards of dioxins' exposure; including, but not limited to, laborers, operators, supervisors; contract administrators, quality control personnel, engineers (process, chemical, mechanical and/or safety).

7. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has knowledge of the means to warn those who might be exposed to use of the herbicides in question, particularly Agent Orange, including, but not limited to, laborers, operators, supervisors, contract administrators, quality control personnel, engineers (process, chemical, mechanical and/or safety).

8. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has factual knowledge of any other manufacturing processes which could reduce the risks of exposure to Agent Orange and/or other phenoxy herbicides being contaminated with dioxins and further reduce the risk and hazard to human health of any such exposure.

9. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has factual knowledge of conspiratorial conduct of the Defendants, individually and/or duplicative efforts (acts which are parallel in nature) which tended to or did in fact result in misleading the public and the United States government from gaining knowledge of the dangers attendant from exposure to Agent Orange and other phenoxy herbicides.

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10. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has factual knowledge of how dioxins work upon plants, animals, and/or humans.

11. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has factual knowledge of any statistics concerning the effects of dioxins upon plants, animals, and/or humans.

12. Any current or previous employee, contractor, subcontactor, in-house or private consultant of each of the Defendants or any other person including, but not limited to, members of EPA and other governmental agencies who has factual knowledge of the following incidents:

a. Love Canal
b. Times Beach, Missouri
c. Seveso, Italy
d. BASF (1953, 1964 - Badische in Germany)
e. Production mishaps and/or explosions since 1935 at any of the plants of any of the Defendants manufacturing, TCP, 2,4-D, 2,4,5-T phenol, chlorine, acetic acid, benzene, sodium hydroxide, potassium hydroxide, and/or Agent Orange, including mishaps in the packaging, and transporting of the Defendants' products to the U. S. Armed Forces bases for eventual shipment to Vietnam.
f. Spraying of Vietnam from 1961-1972.

13. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has factual knowledge of any surveys, tests, epidemiological studies of any kind relating to the effects of exposure to Agent Orange, 2,4-D, 2,4,5-T or any constituent thereof including the secondary by-product known as dioxins.

14. Any person with factual knowledge of how decisions are made within the United States government, particularly the decision to use and to continue to use phenoxy herbicides in Vietnam, particularly Agent Orange; any person with factual knowledge of government procurement contracts and the invitation to bidders, particularly those persons who negotiated the government contracts for all phenoxy herbicides (agents white, blue, purple, pink, green, orange I and II) with the individual defendants representatives between 1961-1972.

15. Any person with factual knowledge through any surveys, tests, epidemiological studies or otherwise undertaken by any state government, any private public or foreign corporation, the U. S. Congress or the government of any nation concerning the chemical compounds, 2,5-D, 2,4,5-T, dioxins, or related chlorophenols relating to the creation of dioxins, the detection of dioxins, the dangers of dioxins' exposure, and/or the toxicity, carcinogenicity, fetotoxicity, teratogenicity, acute and/or chronic effects on plants, animals and the human population.

16. Any and all persons listed in The Chemical Scythe / Alastair Hay, as having factual knowledge regarding 2,4,5-T 2,4-D, and its contaminant dioxins.

17. All worker compensation carriers for the Defendants and documentation of all occupational exposures filed since 1925 which evidence industrial injuries or diseases at the TCP, 2,4,5-T, 2,4-D, Phenol, packaging, and/or transporation plants of the Defendants.

18. Any and all current or prior workers compensation claimants of the Defendants who claimed relevant occupational exposures and/or relevant occupational injuries and/or diseases and/or symptoms at the relevant plants listed in Answer to No. 19 (sub 1) above.

19. Any and all members of the U. S. House of Representatives Committee on Oversights Review of the EPA actions (1983) and/or any person together with their documentary and demonstrative evidence giving testimony at said hearing (which will form the substance of their testimony herein) on the failure of the E.P.A. to take prompt and effective action to ban the production of 2,4-D, 2,4,5-T, and its contaminant dioxins.

20. Any and all persons having knowledge of relevant facts regarding the financial status of the Defendants and their ability to respond in punitive damages, including, but not limited to, their past, present, and future profits and earnings in the United States and abroad since 1925 through and including the present from the sale of the products made the basis of this lawsuit, i.e., 2,4-D, 2,4,5-T, phenoxy herbicides and the relevant herbicide market.

21. Any and all persons having knowledge of relevant facts regarding the ownership interests of the Defendants and their ability to respond in punitive damages, including, but not limited to, defendants' domestic and foreign subsidiaries, joint venturers, licensing agreements, and/or other public or private corporations in the U. S. and abroad, in which these defendants own a substantial financial interest since 1925 through and including the present.

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e. Any and all persons with knowledge of past, present and/or future reasonable and necessary costs of doctors, hospitals, nursery care, medical equipment, drugs, and any other related medical services rendered or to be rendered in the future to Plaintiffs as a result of their injuries and disease resulting from their exposure to Defendants' products in Vietnam.

f. Any and all persons with knowledge of the physical disfigurement (past and present), physical and mental impairment (past and present), physical pain (past and present) and mental anguish (past and present) which Plaintiffs have sustained as a result of their exposure to Defendants' products in Vietnam and which in reasonable probability Plaintiffs will continue to sustain for an indefinite time into the future far beyond the date of this trial.

Respectfully submitted,

[illegible] W. Henderson, Esquire
Allison Pettiet Esquire

CERTIFICATE OF SERVICE

I hereby certify that a true and correct copy of the foregoing Supplement to Plaintiff's Interrogatories were mailed Federal Express to Mr. William Krohley, Kelley, Drye & Warren, Mr. Gene Locks, Plaintiffs' Management Committee Agent Orange Office, with copies to personally serve the remaining Defendants at [illegible] Tuesday depositions and Mr. Nancy Petrilla, U.S. District Clerk, U.S. Courthouse, 225 Cadman Plaza, Brooklyn, New York 11201 this 20th day of February, 1984.

Allison Pettiette

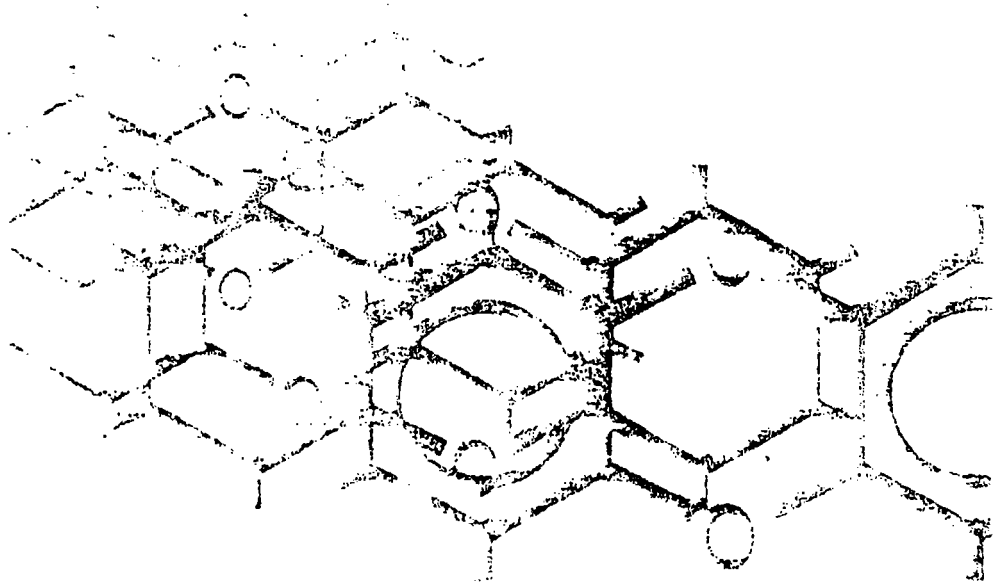
13071

United States
Environmental Protection
Agency

Industrial Environmental
Laboratory
Cincinnati OH 45268

Research & Development

EPA Dioxins



13072

PLAINTIFF'S GOVERNMENT CAUSATION WITNESSES

I. Peter Infante

A. National Institute for Occupational Safety & Health, Wash.

B. Both factual and expert testimony is sought.

C. General Events

Pre-1961: Any factual knowledge of the history of herbicide spraying in U.S. and abroad; including, but not limited to, (1) industrial exposures and explosions; (2) registration of 2,4-D, 2,4,5-T with the Department of Agriculture and any other government agencies by any and/or all of the Defendants;

1961-present: Any factual knowledge of the history of herbicide spraying in the U.S. and abroad; including, but not limited to, (1) U.S. military use of Agent Orange and other herbicides in Vietnam; (2) changes in the registration requirements of herbicides with the U.S. government and its agencies including knowledge of FIFRA, FDA, EPA, and OSHA; and (3) any knowledge of industrial and other human exposures to 2,4-D, 2,4,5-T in the U.S. and abroad

See Answer and Supplemental Answer of Plaintiffs' to Defendants' Interrogatory No. 19 attached hereto and incorporated herein for all purposes re. events or occurrences which these causation witnesses may be expected to give any factual information they may have regarding the subjects outlined in said Answer.

Human Risk Assessment of Exposure to 2,4-D, 2,4,5-T and dioxins and any factual knowledge in support thereof.

D. Expert Testimony

1) Testimony is sought in witness' personal and official capacity.

2) Subject Matter
2,4-D, 2,4,5-T, TCDD's and dioxins; Agent Orange I/II (also White, Blue, Pink, Green, and Purple

and related chlorophenols and human risk assessment regarding exposure, including, but not limited to, one or more of the following subject areas:

a) Chemistry/Biochemistry

b) Manufacture and/or Production

c) Toxicity

d) Modes of Human Exposure

e) Fate in the Environment (Humans, Plants, Animals)

f) State of Art/State of Medical and Scient Literature

1) Plant Physiology/Studies
2) Animal Physiology/Studies
3) Human Studies

g) Epidemiology/Biostatistics

1) Plants, animals, humans
2) Cancer Epidemiology
3) Reproductive Epidemiology

h) Adverse Health Effects

3) Yes, witness will be asked opinions about both published and/or on-going studies.

4) Yes, witness will be asked opinions about any studie or research witness has personally performed or actually participated in.

5) Yes, witness will be asked opinions about other governmental studies.

6) Yes, witness is expected to review the following documents prior to giving testimony:

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EPA, Research and Development, Health and Environmental Effects Profile for; Tetra Penta, and Hexachlorodibenzo-p-dioxins, for the Office of Solid ste and Emergency Response, by the Environmental Criteria and Assessment fice, Cincinnat Ohio 45248 (June 1983).

EPA, Research and Development, bient Water Quality Criteria for 2,3 ,8 TCDD, prepared for Office of Wate Regulations and Standards, by the Environmental Criteria and Assessment fice, Cincinnat Ohio 45248 (July 1983).

EPA, Research and Development, dins, Industrial Environmental Research Cincinnati, Ohio (1978).

A copy of these documents is attached.

SUPPLEMENTAL ANSWER TO INTERROGATORY NO. 19

Plaintiffs note preliminarily that the extant Order on producing fact witnesses states that fact witnesses are not due until March 2 1984. However, Plaintiffs may call one or more of the following persons (or those from various categories listed below) at time of trial to testify as to factual knowledge they may have, including:

1. Ranch Hand Personnel: These persons will testify to their knowledge of the Ranch Hand Operation, Ranch Handers' exposure to Agent Orange, and/or knowledge relating to the spraying, testing, and effects of Agent Orange on humans.

2. Members of the U. S. Armed Forces: These persons may testify to the circumstances and conditions surrounding the spraying of Agent Orange.

3. Persons present in Vietnam during the exposure period in question 1961-1972, including, but not limited to, military and paramilitary personnel of the U. S., New Zealand and Australia, who have knowledge of the spraying operations of the herbicides, the exposure of the Plaintiffs' class, the hazards accompanying any such exposure, the Plaintiffs themselves, and the Defendant company representatives present in Vietnam to oversee the deliveries and spraying operations of the herbicides they manufactured.

4. Persons together with their demonstrative and documentary evidence who gave testimony (which will form the substance of their testimony herein) at the EPA Cancellation Hearings of 2,4,5-T (1979-1980) under FIFRA, including but not limited to:

   a. Dr. Roy Albert;
   b. Dr. K. Diane Courtney
   c. Robert K. Baughman, Ph.D.
   d. Dr. Olav Axelson
   e. Dr. Renate Kimbrough
   f. Dr. Dawn G. Goodman
   g. Dr. Kirk T. Kitchin
   h. Dr. Ronald Tarman
   i. Dr. Rainer Frentzel-Beyme
   j. Dr. Matthew Meselson, Harvard

13076

k. Major Alvin Young
l. Dr. Rodney Bovey
m. Kenneth V. Thermin
n. David T. Buzzelli
o. Dr. Michael Gross
p. Dr. Renee Stringham
r. Dr. Van Miller

5. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has knowledge of the manufacturing processes, chemistry, occupational exposure and/or toxicity of 2,4-D and/or 2,4,5-T or related chlorophenols; including, but not limited to, laborers; operators; supervisors; contract administrators; quality control personnel; engineers (process, chemical, mechanical and/or safety).

6. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has knowledge of the possible means of prophylactic protection from the hazards of dioxins' exposure; including, but not limited to, laborers, operators, supervisors, contract administrators, quality control personnel, engineers (process, chemical, mechanical and/or safety).

7. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has knowledge of the means to warn those who might be exposed to use of the herbicides in question, particularly Agent Orange, including, but not limited to, laborers, operators, supervisors, contract administrators, quality control personnel, engineers (process, chemical, mechanical and/or safety).

8. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has factual knowledge of any other manufacturing processes which could reduce the risks of exposure to Agent Orange and/or other phenoxy herbicides being contaminated with dioxins and further reduce the risk and hazard to human health of any such exposure.

9. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has factual knowledge of conspiratorial conduct of the Defendants, individually and/or duplicative efforts (acts which are parallel in nature) which tended to or did in fact result in misleading the public and the United States government from gaining knowledge of the dangers attendant from exposure to Agent Orange and other phenoxy herbicides.

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10. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has factual knowledge of how dioxin work upon plants, animals, and/or humans.

11. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendant or any other person who has factual knowledge of any statistics concerning the effects of dioxins upon plants, animals, and/or humans.

12. Any current or previous employee, contractor, subcontactor, in-house or private consultant of each of the Defendant or any other person including, but not limited to, members of EPA and other governmental agencies, who has factual knowledge of the following incidents:

a. Love Canal
b. Times Beach, Missouri
c. Seveso, Italy
d. BASF (1953, 1954 - Badische in Germany)
e. Production mishaps and/or explosions since 1925 at any of the plants of any of the Defendants manufacturing, 2,4,5-T, 2,4-D, 2,4,5-T phenol, chlorine, acetic acid, benzene, sodium hydroxide, potassium hydroxide, and/or Agent Orange, including mishaps in the packaging, and transporting of the Defendants' products to the U. S. Armed Forces bases for eventual shipment to Vietnam.
f. Spraying of Vietnam from 1961-1972.

13. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has factual knowledge of any surveys, tests, epidemiological studies of any kind relating to the effects of exposure to Agent Orange, 2,4-D, 2,4,5-T or any constituent thereof including the secondary by-product known as dioxins.

14. Any person with factual knowledge of how decisions are made within the United States government, particularly the decision to use and to continue to use phenoxy herbicides in Vietnam, particularly Agent Orange; any person with factual knowledge of government procurement contracts and the invitation to bidders, particularly those persons who negotiated the government contracts for all phenoxy herbicides (agents white, blue, purple, pink, green, orange I and II) with the individual defendants representatives between 1961-1971.

13078

15. Any person with factual knowledge through any surveys, tests, epidemiological studies or otherwise undertaken by any state government, any private public or foreign corporation, the U. S. Congress or the government of any nation concerning the chemical compounds, 2,5-D, 2,4,5-T, dioxins, or related chlorophenols relating to the creation of dioxins, the detection of dioxins, the dangers of dioxins' exposure, and/or the toxicity, carcinogenicity, fetotoxicity, teratogenicity, acute and/or chronic effects on plants, animals and the human population.

16. Any and all persons listed in The Chemical Scythe by Plastaras Hay, as having factual knowledge regarding 2,4,5-T, 2,4-D, and its contaminant dioxins.

17. All worker compensation carriers for the Defendants and documentation of all occupational exposures filed since 1925 which evidence industrial injuries or diseases at the TCP, 2,4,5-T, 2,4-D, Phenol, packaging, and/or transporation plants of the Defendants.

18. Any and all current or prior worker compensation claimants on the Defendants who claim relevant occupational exposures and/or relevant occupational injuries and/or diseases and/or symptoms at the relevant plants listed in Answer to No. 19 (sub 17) above.

19. Any and all members of the U. S. House of Representatives Committee on Oversights Review of the EPA Actions (1983) and/or any person together with their documentary and demonstrative evidence giving testimony at said hearing (which will form the substance of their testimony herein) on the failure of the EPA to take prompt and effective action to ban the production of 2,4-D, 2,4,5-T, and its contaminant dioxins.

20. Any and all persons having knowledge of relevant facts regarding the financial status of the Defendants and their ability to respond in punitive damages, including, but not limited to, their past, present, and future profits and earnings in the United States and abroad since 1921 through and including the present from the sale of the products made the basis of this lawsuit, i.e., 2,4-D, 2,4,5-T, phenoxy herbicides and the relevant herbicide market.

21. Any and all persons having knowledge of relevant facts regarding the ownership interests of the Defendants and their ability to respond in punitive damages, including, but not limited to, Defendants' domestic and foreign subsidiaries, joint venturers, licensing agreements, and/or other public or private corporations in the U. S. and abroad, in which these defendants own a substantial financial interest since 1925 through and including the present.

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22. Any and all persons listed by Plaintiffs' in both original and amended witness lists, as expert witness (medical, scientific or causation), government witness, government causation witness, defendants' employees and/or related personnel and/or any witnesses listed by all Defendants, may be called at time of trial to present factual information as to any issue involved in this case.

23. Any and all members of the scientific and/or medical community who have knowledge of relevant facts, including information on any of the previously listed subjects in this Answer, including, but not limited to:

a. David Kriebel, Ph.D.
b. Dr. Alan Poland
c. Dr. Paul Goldman, BASF
d. Dr. C. Pappe
e. Dr. Cottel, BASF
f. Dr. E. E. McDermall
g. Dr. K. S. Kelly
h. Alvin Alm
i. Marilyn Fingerhut

24. Any and all persons who have factual knowledge concerning the individual representations Plaintiffs' damages, including, but not limited to, the following:

a. Any and all medical persons who have examined, observed, treated and/or tested the Plaintiffs' for injuries, diseases and/or related physical and emotional conditions which resulted from Plaintiffs' exposure to Agent Orange, and/or phenoxy herbicides, their constituents, secondary by-products, wastes, residuals and contaminants.

b. Any and all hospital personnel where Plaintiffs have been confined for treatment relating to their exposure to Defendants' products in Vietnam.

c. Any and all persons with knowledge of the economic losses, psychological and/or intangible damages sustained by your Plaintiffs as a result of their injuries and diseases resulting from their exposure to Defendants' products in Vietnam.

d. Any and all persons with knowledge of the past, present and/or future economic losses your Plaintiffs have or will sustain in the future as a result of their loss of wage earnings and/or wages earning capacity resulting from the injuries and diseases made the basis of this lawsuit which were caused by Plaintiffs exposure to Defendants' products in Vietnam.

13080

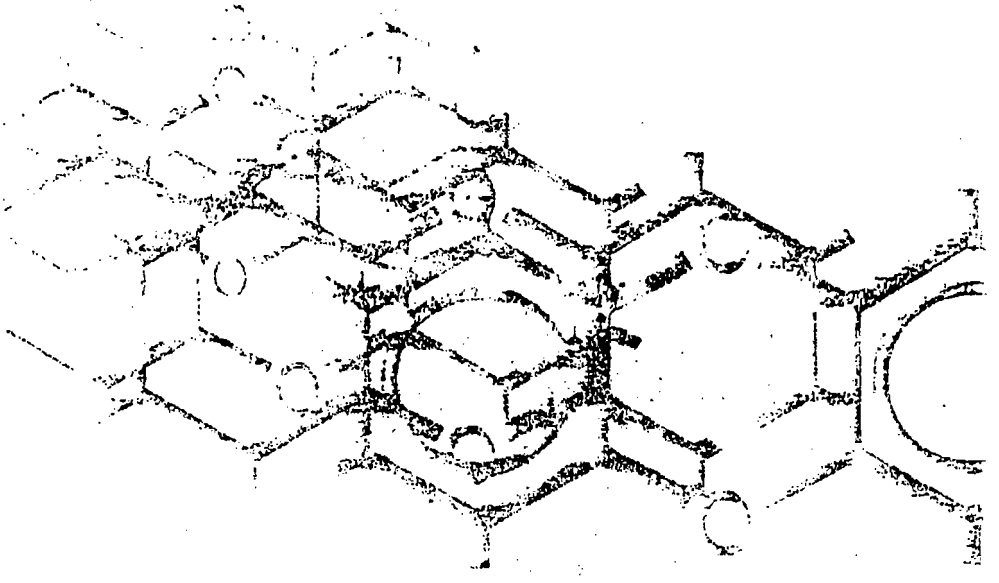
United States
Environmental Protection
Agency

Industrial Environmental Re
Laboratory
Cincinnati OH 45268

Research & Development

EPA

Dioxins



19051

PLAINTIFF'S GOVERNMENT CAUSATION WITNESSES

I. D. Diane Courtney

A. EPA, Washington, D.C.

B. Both factual and expert testimony is sought.

C. General Events

Pre-1961: Any factual knowledge of the history of herbicide spraying in U.S. and abroad; including, but not limited to, (1) industrial exposures and explosions; (2) registration of 2,4-D, 2,4,5-T with the Department of Agriculture and any other government agencies by any and/or all of the Defendants;

1961-present: Any factual knowledge of the history of herbicide spraying in the U.S. and abroad; including, but not limited to, (1) U.S. military use of Agent Orange and other phenoxy herbicides in Vietnam; (2) changes in the registration requirements of herbicides with U.S. government and its agencies including knowledge of FIFRA, FDA, EPA, and OSHA; and (3) any knowledge of industrial and other human exposures to 2,4-D, 2,4,5-T in the U.S. and abroad;

See Answer and Supplemental Answer of Plaintiffs' to Defendants' Interrogatory No. 19 attached hereto and incorporated herein for all purposes re: events or occurrences which these causation witnesses may be expected to give any factual information they may have regarding the subjects outlined in said Answer.

Human Risk Assessment of Exposure to 2,4-D, 2,4,5-T and dioxins and any factual knowledge in support thereof.

D. Expert Testimony

1) Testimony is sought in witness' personal and official capacity.

2) Subject Matter

2,4-D, 2,4,5-T, TCDD's and dioxins; Agent Orange (also White, Blue, Pink, Green and Purple

and related chlorophenols and human risk assessment, regarding exposure, including, but not limited to, one or more of the following subject areas:

a) Chemistry/Biochemistry

b) Manufacture and/or Production

c) Toxicity

d) Modes of Human Exposure

e) Fate in the Environment (Humans, Plants, Animals)

f) State of Art/State of Medical and Scientific Literature

1. Plant Physiology/Studies
2. Animal Physiology/Studies
3. Human Studies

g) Epidemiology/Biostatistics

1) Plants, animals, humans
2) Cancer Epidemiology
3) Reproductive Epidemiology

h) Adverse Health Effects

3) Yes, witness will be asked opinions about both published and/or on-going studies.

4) Yes, witness will be asked opinions about any studies or research witness has personally performed or actually participated in.

5) Yes, witness will be asked opinions about other governmental studies.

6) Yes, witness is expected to review the following documents prior to giving testimony:

See, EPA, Research and Development, Health Assessment Document on Dioxins for the Offices of Air Quality, Planning and Standards, prepared by the Environmental Criteria and Assessment Office, Cincinnati, Ohio 45248 (July 198

SUPPLEMENTAL ANSWER TO INTERROGATORY NO. 19

Plaintiffs note preliminarily that the extant Order on producing fact witnesses states that fact witnesses are not due until March 2, 1984. However, Plaintiffs may call one or more of the following persons (or those from various categories listed below) at time of trial to testify as to factual knowledge they may have, including:

1. Ranch Hand Personnel: These persons will testify to their knowledge of the Ranch Hand Operation, Ranch Handers' exposure to Agent Orange, and/or knowledge relating to the spraying, testing, and effects of Agent Orange on humans.

2. Members of the U. S. Armed Forces: These persons may identify to the circumstances and conditions surrounding the spraying of Agent Orange.

3. Persons present in Vietnam during the exposure period in question 1961-1972, including, but not limited to, military and paramilitary personnel of the U. S., New Zealand and Australia, who have knowledge of the spraying operations of the herbicides, the exposure of the Plaintiffs' class, the hazards accompanying any such exposure, the Plaintiffs themselves, and the Defendant company representatives present in Vietnam to oversee the deliveries and spraying operations of the herbicides they manufactured.

4. Persons together with their demonstrative and documentary evidence who gave testimony (which will form the substance of their testimony herein) at the EPA Cancellation Hearings of 2,4,5-T (1979-1980) under FIFRA, including but not limited to:

   a. Dr. Roy Albert
   b. Dr. K. Diane Courtney
   c. Robert K. Baughman, Ph.D.
   d. Dr. Olav Axelson
   e. Renate Kimbrough
   f. Dr. Dawn G. Goodman
   g. Dr. Kirk T. Kitchin
   h. Dr. Ronald Thomas
   i. Dr. Rainer Prentzel-Thyme
   j. Dr. Matthew Meselson, Harvard

k. Major Alvin Young
l. Dr. Rodney Bovey
m. Kenneth V. Themein
n. David T. Buzzelli
o. Dr. Michael Gross
p. Dr. Renee Stringham
r. Dr. Van Miller

5. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has knowledge of the manufacturing processes, chemistry, occupational exposure and/or toxicity of 2,4-D and/or 2,4,5-T or related chlorophenols; including, but not limited to, laborers; operators; supervisors; contract administrators; quality control personnel; engineers (process, chemical, mechanical and/or safety).

6. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has knowledge of the possible means of [illegible] protection from the hazards of dioxins' exposure; including, but not limited to, laborers, operators, supervisors, contract administrators, quality control personnel, engineers (process, chemical, mechanical and/or safety).

7. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has knowledge of the means to warn those who might be exposed to use of the herbicides in question, particularly Agent Orange, including, but not limited to, laborers, operators, supervisors, contract administrators, quality control personnel, engineers (process, chemical, mechanical and/or safety).

8. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has factual knowledge of any other manufacturing processes which could reduce the risks of exposure to Agent Orange and/or other phenoxy herbicides being contaminated with dioxins and further reduce the risk and hazard to human health of any such exposure.

9. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has factual knowledge of conspiratorial conduct of the Defendants, individually and/or duplicative efforts (acts which are parallel in nature) which tended to or did in fact result in misleading the public and the United States government from gaining knowledge of the dangers attendant from exposure to Agent Orange and other phenoxy herbicides.

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10. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has factual knowledge of how dioxins work upon plants, animals, and/or humans.

11. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has factual knowledge of any statistics concerning the effects of dioxins upon plants, animals, and/or humans.

12. Any current or previous employee, contractor, subcontactor, in-house or private consultant of each of the Defendants or any other person including, but not limited to, members of EPA and other governmental agencies, who has factual knowledge of the following incidents:

    a. Love Canal
    b. Times Beach, Missouri
    c. Seveso, Italy
    d. BASF (1953, 1954 - Badische in Germany)
    e. Production mishaps and/or explosions since 1925 at any of the plants of any of the Defendants manufacturing, TCP, 2,4-D, 2,4,5-T phenol, chlorine, acetic acid, benzene, sodium hydroxide, potassium hydroxide, and/or Agent Orange, including mishaps in the packaging, and transporting of the Defendants' products to the U. S. Armed Forces bases for eventual shipment to Vietnam.
    f. Spraying of Vietnam from 1961-1972.

13. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has factual knowledge of any surveys, tests, epidemiological studies of any kind relating to the effects of exposure to Agent Orange, 2,4-D, 2,4,5-T or any constituent thereof including the secondary by-product known as dioxins.

14. Any person with factual knowledge of how decisions are made within the United States government, particularly the decision to use and to continue to use phenoxy herbicides in Vietnam, particularly Agent Orange; any person with factual knowledge of government procurement contracts and the invitation to bidders, particularly those persons who negotiated the government contracts for all phenoxy herbicides (agents white, blue, purple, pink, green, orange I and II) with the individual defendants representatives between 1961-1972.

15. Any person with factual knowledge through any surveys, tests, epidemiological studies or otherwise undertaken by any state government, any private public or foreign corporation, the U. S. Congress or the government of any nation concerning the chemical compounds, 2,5-D, 2,4,5-T, dioxins, or related chlorophenols relating to the creation of dioxins, the detection of dioxins, the dangers of dioxins' exposure, and/or the toxicity, carcinogenicity, fetotoxicity, teratogenicity, acute and/or chronic effects on plants, animals and the human population.

16. Any and all persons listed in The Chemical Scythe by Alastair Hay, as having factual knowledge regarding 2,4,5-T, 2,4-D, and its contaminant dioxins.

17. All worker compensation carriers for the Defendants and documentation of all occupational exposures filed since 1925 which evidence industrial injuries or diseases at the TCP, 2,4,5-T, 2,4-D, Phenol, packaging, and/or transporation plants of the Defendants.

18. Any and all current or prior workers compensation claimants of the Defendants who claimed relevant occupational exposures and/or relevant occupational injuries and/or diseases and/or symptoms the relevant plants listed in Answer to No. 19 (sub 17) above.

19. Any and all members of the U. S. House of Representatives Committee on Oversights Review of the EPA actions (1983) and/or any person together with their documentary and demonstrative evidence giving testimony at said hearing (which will form the substance of their testimony herein) on the failure of the EPA to take prompt and effective action to ban the production of 2,4-D, 2,4,5-T, and its contaminant dioxins.

20. Any and all persons having knowledge of relevant facts regarding the financial status of the Defendants and their ability to respond in punitive damages, including, but not limited to, their past, present, and future profits and earnings in the United States and abroad since 1925 through and including the present from the sale of the products made the basis of this lawsuit, i.e., 2,4-D, 2,4,5-T, phenoxy herbicides and the relevant herbicide market.

21. Any and all persons having knowledge of relevant facts regarding the ownership interests of the Defendants and their ability to respond in punitive damages, including, but not limited to, defendants' domestic and foreign subsidiaries, joint venturers, licensing agreements, and/or other public or private corporations in the U. S. and abroad, in which these defendants own a substantial financial interest since 1925 through and including the present.

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15. Any person with factual knowledge through any surveys, tests, epidemiological studies or otherwise undertaken by any state government, any private public or foreign corporation, the U. S. Congress or the government of any nation concerning the chemical compounds, 2,5-D, 2,4,5-T, dioxins, or related chlorophenols relating to the creation of dioxins, the detection of dioxins, the dangers of dioxins' exposure, and/or the toxicity, carcinogenicity, fetotoxicity, teratogenicity, acute and/or chronic effects on plants, animals and the human population.

16. Any and all persons listed in The Chemical Scythe by Alastair Hay, as having factual knowledge regarding 2,4,5-T, 2,4-D, and its contaminant dioxins.

17. All worker compensation carriers for the Defendants and documentation of all occupational exposures filed since 1925 which evidence industrial injuries or diseases at the TCP, 2,4,5-T, 2,4-D, Phenol, packaging, and/or transporation plants of the Defendants.

18. Any and all current or prior workers compensation claimants of the Defendants who claimed relevant occupational exposures and/or relevant occupational injuries and/or diseases and/or symptoms at the relevant plants listed in Answer to No. 19 (sub 17) above.

19. Any and all members of the U. S. House of Representatives Committee on Oversights Review of the EPA actions (1983) and/or any person together with their documentary and demonstrative evidence giving testimony at said hearing (which will form the substance of their testimony herein) on the failure of the EPA to take prompt and effective action to ban the production of 2,4-D, 2,4,5-T, and its contaminant dioxins.

20. Any and all persons having knowledge of relevant facts regarding the financial status of the Defendants and their ability to respond in punitive damages, including, but not limited to, their past, present, and future profits and earnings in the United States and abroad since 1925 through and including the present from the sale of the products made the basis of this lawsuit, i.e., 2,4-D, 2,4,5-T, phenoxy herbicides and the relevant herbicide market.

21. Any and all persons having knowledge of relevant facts regarding the ownership interests of the Defendants and their ability to respond in punitive damages, including, but not limited to, defendants' domestic and foreign subsidiaries, joint venturers, licensing agreements, and/or other public or private corporations in the U. S. and abroad, in which these defendants own a substantial financial interest since 1925 through and including the present.

22. Any and all persons listed by Plaintiffs' in both original and amended witness lists, as expert witness (medical, scientific or causation), government witness, government causation witness, defendants' employees and/or related personnel and/or any witnesses listed by all Defendants, may be called at time of trial to present factual information as to any issue involved in this case.

23. Any and all members of the scientific and/or medical community who have knowledge of relevant facts, including information on any of the previously listed subjects in this Answer, including, but not limited to:

a. David Kriebel, Ph.D.
b. Dr. Alan Poland
c. Dr. Paul Goldmann, BASF
d. Dr. C. Rappe
e. Dr. Oettel, BASF
f. Dr. E. E. McDonnell
g. Dr. K. S. Khiera
h. Alvin Aim
i. Marilyn Fingerhut

24. Any and all persons who have factual knowledge concerning the individual representative Plaintiff's damages, including, but not limited to, the following:

a. Any and all medical persons who have examined, observed, treated and/or tested the Plaintiffs' for injuries, diseases and/or related physical and emotional conditions which resulted from Plaintiffs' exposure to Agent Orange, and/or phenoxy herbicides, their constituents, secondary by-products, wastes, residuals and contaminants.

b. Any and all hospital personnel where Plaintiffs have been confined for treatment relating to their exposure to Defendants' products in Vietnam.

c. Any and all persons with knowledge of the economic losses, psychological and/or intangible damages sustained by your Plaintiffs as a result of their injuries and diseases resulting from their exposure to Defendants' products in Vietnam.

d. Any and all persons with knowledge of the past, present and/or future economic losses your Plaintiffs have or will sustain in the future as a result of their loss of wage earnings and/or wages earning capacity resulting from the injuries and diseases made the basis of this lawsuit which were caused by Plaintiffs exposure to Defendants' products in Vietnam.

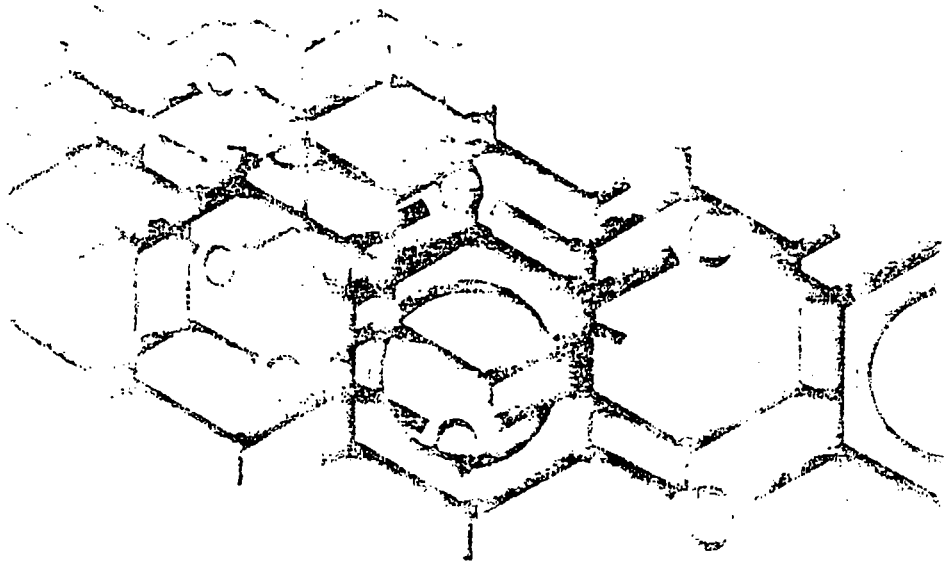
18389

United States
Environmental Protection
Agency

Industrial Environmental
Laboratory
Cincinnati OH 45268

Research & Development

EPA Dioxins



13090

PLAINTIFF'S GOVERNMENT CAUSATION WITNESSES

1. Phillip J. Landrigan

A. Center for Disease Control (CDC), Nat'l Inst. Occupat Safety and Health, Cincinnati, Ohio

B. Both factual and expert testimony is sought.

C. General Events

Pre-1961: Any factual knowledge of the history of herbicide spraying in U.S. and abroad; including, but not limited to, (1) industr exposures and explosions; (2) registration 2,4-D, 2,4,5-T with the Department of Agri culture and any other government agencies any and/or all of the Defendants;

1961-present: Any factual knowledge of the history of herbicide spraying in the U.S. and abroad; including, but not limited to, (1) U.S. military use of Agent Orange and other phe noxy herbicides in Vietnam; (2) changes in the registration requirements of herbicides with U.S. government and its agencies including knowledge of FIFRA, FDA, EPA, and OSHA; and any knowledge of industrial and other human exposures to 2,4-D, 2,4,5-T in the U.S. and abroad;

See Answer and Supplemental Answer of Plaintiffs' to Defendants' Interrogatory No. 19 attached hereto and incorporated herein for all pur-poses as: events or occurrences which this causation witnesses may be expected to give any factual information they may have regar ding subjects outlined in said Answer.

Human Risk Assessment of Exposure to 2,4-D, 2,4,5-T and dioxins and any factual knowledge in support thereof.

B. Expert Testimony

1) Testimony is sought in witness' personal and offici capacity.

2) Subject Matter
2,4-D, 2,4,5-T, TCDD's and dioxins; Agent Or I/II (also White, Blue, Pink, Green, and Pur

13092

EPA, Research and Development, Health and Environmental Effects Profile for; Te Penta, and Hexachlorodibenzo-p-dioxin for the Office of Solid Waste and Eme gency Respcrse, by the Environmental Criteria and Assessment Office, Cinci Ohio 45248 (June 1983).

EPA, Research and Development, Ambient Water Quality Criteria for 2,3,7,8 TCDD pr pared for Office of Water Regulations and Standards, by the Environmental Criteria and Assessment Office, Cinci Ohio 45248 (July 1983).

EPA, Research and Development, Dioxins, Industrial Environmental Research Cincinnati, Ohio (1978).

A copy of these documents is attached.

13093

SUPPLEMENTAL ANSWER TO INTERROGATORY No. 10

Plaintiffs note preliminarily that the extant Order on producing fact witnesses states that fact witnesses are not due until March 2, 1984. However, Plaintiffs may call one or more of the following persons (or those from various categories listed below) at time of trial to testify as to factual knowledge they may have, including:

1. Ranch Hand Personnel: These persons will testify to their knowledge of the Ranch Hand Operation, Ranch Handers' exposure to Agent Orange, and/or knowledge relating to the spraying, testing, and effects of Agent Orange on humans.

2. Members of the U. S. Armed Forces: These persons may testify to the circumstances and conditions surrounding the spraying of Agent Orange.

3. Persons present in Vietnam during the exposure period in question 1961-1971, including, but not limited to, military and paramilitary personnel of the U. S., New Zealand and Australia, who have knowledge of the spraying operations of the herbicides, the exposure of the Plaintiffs' class, the hazards accompanying any such exposure, the Plaintiffs' themselves, and the Defendant company representatives present in Vietnam to oversee the deliveries and spraying operations of the herbicides they manufactured.

4. Persons together with their demonstrative and documentary evidence who gave testimony (which will form the substance of their testimony herein) at the EPA Cancellation Hearings of 2,4,5-T (1978-1980) under FIFRA, including but not limited to:

   a. Dr. Roy Albert:
   b. Dr. K. Diane Courtney
   c. Robert K. Baughman, Ph.D.
   d. Dr. Olav Axelson
   e. Dr. Renate Kimbrough
   f. Dr. Dawn G. Goodman
   g. Dr. Kirk T. Kitchin
   h. Dr. Ronald Thomas
   i. Dr. Rainer Frentzel-Beyme
   j. Dr. Matthew Meselson, Harvard

13094

10. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has factual knowledge of how dioxins work upon plants, animals, and/or humans.

11. Any current or previous employee, contractor, subcontractor,

[redacted]

6. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has knowledge of the possible means of prophlactic protection from the hazards of dioxins' exposure; including, but not limited to, laborers, operators, supervisors, contract administrators, quality control personnel, engineers (process, chemical, mechanical and/or safety).

7. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has knowledge of the means to warn those who might be exposed to use of the herbicides in question, particularly Agent Orange, including, but not limited to, laborers, operators, supervisors, contract administrators, quality control personnel, engineers (process, chemical, mechanical and/or safety).

8. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has factual knowledge of any other manufacturing processes which could reduce the risks of exposure to Agent Orange and/or other phenoxy herbicides being contaminated with dioxins and further reduce the risk and hazard to human health of any such exposure.

13095

9. Any current or previous employee

15. Any person with factual knowledge through any surveys, tests, epidemiological studies or otherwise undertaken by any state government, any private public or foreign corporation, the U. S. Congress or the government of any nation concerning the chemical compounds, 2,5-D, 2,4,5-T, dioxins, or related chlorophenols relating to the creation of dioxins, the detection of dioxins, the dangers of dioxins' exposure, and/or the toxicity carcinogenicity, fetotoxicity, teratogenicity, acute and/or chronic effects on plants, animals and the human population.

16. Any and all persons listed in The Chemical Scythe by Alastair Hay, as having factual knowledge regarding 2,4,5-T, 2,4-D, and its contaminant dioxins.

17. All workers compensation claimants for the Defendants and documentation of all occupational exposures filed since 1925 which evidence industrial injuries or diseases at the T[illegible], 2,4,5-T, 2,4-D, Phenol, packaging, and/or transportation plants of the Defendants.

18. Any and all current or prior workers compensation claimants of the Defendants who claimed relevant occupational exposures and/or relevant occupational injuries and/or diseases and/or symptoms the relevant plaintiffs listed in Answer to No. 19 (sic 17) above.

19. Any and all members of the U. S. House of Representatives Committee on Oversights Review of the EPA actions (1983) and/or any person together with their documentary and demonstrative evidence giving testimony at said hearing (which will form the substance of their testimony herein) on the failure of the EPA to take prompt and effective action to ban the production of 2,4-D, 2,4,5-T, and its contaminant dioxins.

20. Any and all persons having knowledge of relevant facts regarding the financial status of the Defendants and their ability to respond in punitive damages, including, but not limited to, their past, present, and future profits and earnings in the United States and abroad since 1925 through and including the present from the sale of the products made the basis of this lawsuit, i.e., 2,4-D, 2,4,5-T, phenoxy herbicides and the relevant herbicide market.

21. Any and all persons having knowledge of relevant facts regarding the ownership interests of the Defendants and their ability to respond in punitive damages, including, but not limited to, defendants' domestic and foreign subsidiaries, joint ventures, licensing agreements, and/or other public or private corporations in the U. S. and abroad, in which these defendants own a substantial financial interest since 1925 through and including the present.

13096

22. Any and all persons listed by Plaintiffs' in both original and amended witness lists, as expert witness (medical, scientific or causation), government witness, government causation witness, defendants' employees and/or related personnel and/or any witnesses listed by all Defendants, may be called at time of trial to present factual information as to any issue involved in this case.

23. Any and all members of the scientific and/or medical community who have knowledge of relevant facts, including information on any of the previously listed subjects in this Answer, including, but not limited to:

a. David Kriebel, Ph.D.
b. Dr. Alan Poland
c. Dr. Paul Goldmann, RAS
d. Dr. C. Rappe
e. Dr. Oettel, FASE
f. Dr. E. E. McConnell
g. Dr. K. S. Thiera
h. Alvin Al
i. Morilyn Fingerhut

24. Any and all persons who have factual knowledge concerning the individual representative Plaintiff's damages, including, but not limited to, the following:

a. Any and all medical persons who have examined, observed, treated and/or tested the Plaintiffs' for injuries, diseases and/or related physical and emotional conditions which resulted from Plaintiffs' exposure to Agent Orange, and/or phenoxy herbicides, their constituents, secondary by-products, wastes, residuals and contaminants.

b. Any and all hospital personnel where Plaintiffs have been confined for treatment relating to their exposure to Defendants' products in Vietnam.

c. Any and all persons with knowledge of the economic losses, psychological and/or intangible damages sustained by your Plaintiffs as a result of their injuries and diseases resulting from their exposure to Defendants' products in Vietnam.

d. Any and all persons with knowledge of the past, present and/or future economic losses your Plaintiffs have or will sustain in the future as a result of their loss of wage earnings and or wages earning capacity resulting from the injuries and diseases made the basis of this lawsuit which were caused by Plaintiffs exposure to Defendants' products in Vietnam.

13097

e. Any and all persons with knowledge of past, present and/or future reasonable and necessary costs of doctors, hospitals, nursery care, medical equipment, drugs, and any other related medical services rendered or to be rendered in the future to Plaintiffs as a result of their injuries and disease resulting from their exposure to Defendants' products in Vietnam.

f. Any and all persons with knowledge of the physical disfigurement (past and present), physical and mental impairment (past and present), physical pain (past and present) and mental anguish (past and present) which Plaintiffs have sustained as a result of their exposure to Defendants' products in Vietnam and which in reasonable probability Plaintiffs will continue to sustain for an indefinite time into the future far beyond the date of this trial.

Respectfully submitted,

Thomas F. Henderson, Esquire
Allison Pettiette, Esquire

CERTIFICATE OF SERVICE

I hereby certify that a true and correct copy of the foregoing Supplement to Plaintiff's Interrogatories were mailed Federal Express to Mr. William Knibley, Kelley, Drye & Warren, Mr. Gene Locks, Plaintiffs' Management Committee Agent Orange Office, with copies to personally serve the remaining Defendants at the Tuesday depositions and Ms. Nancy Petrillo, U.S. District Clerk, U.S. Courthouse, 225 Cadman Plaza, Brooklyn, New York 11201 this 20th day of February, 1984.

Allison Pettiette

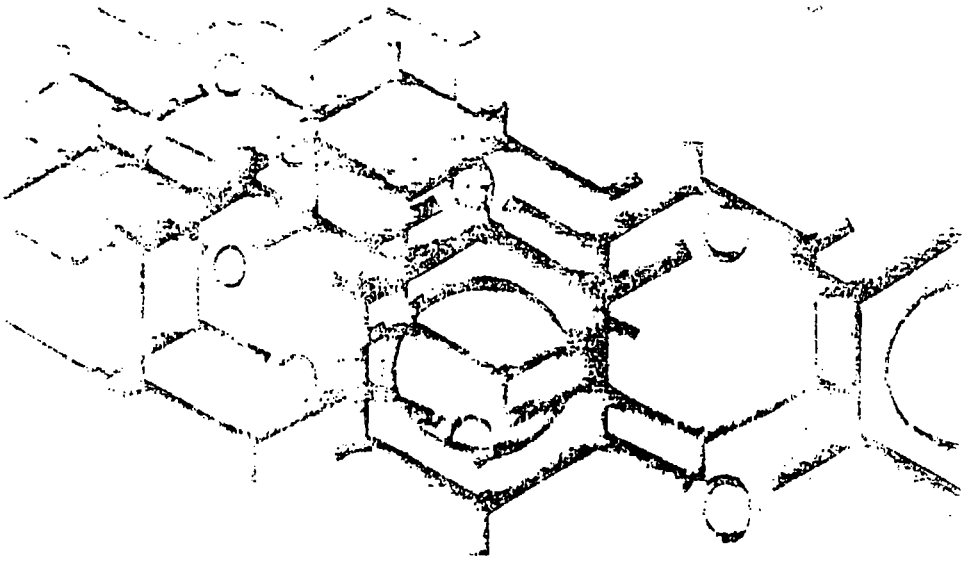
13098

United States
Environmental Protection
Agency

Industrial Environmental
Laboratory
Cincinnati OH 45268

Research and Development

EPA Dioxins



13099

PLAINTIFF'S GOVERNMENT CAUSATION WITNESSES

I. Donald Barnes

A. EPA, Washington, D.C.

B. Both factual and expert testimony is sought.

C. General Events

Pre-1961: Any factual knowledge of the history of herbicide spraying in U.S. and abroad; including, but not limited to, (1) industry exposures and explosions; (2) registration 2,4-D, 2,4,5-T with the Department of Agriculture and any other government agencies any and/or all of the Defendants;

1961-present: Any factual knowledge of the history of herbicide spraying in the U.S. and abroad; including, but not limited to, (1) U.S. military use of Agent Orange and other phenoxy herbicides in Vietnam; (2) changes in the registration requirements of herbicides with U.S. government and its agencies including knowledge of FIFRA, FDA, EPA, and OSHA; and any knowledge of industrial and other human exposures to 2,4-D, 2,4,5-T in the U.S. and abroad;

See Answer and Supplemental Answer of Plaintiffs' to Defendants' Interrogatory No. 19 attached hereto and incorporated herein for all purposes re: events or occurrences which these causation witnesses may be expected to give any factual information they may have regarding the subjects outlined in said Answer.

Human Risk Assessment of Exposure to 2,4-D, 2,4,5-T and dioxins and any factual knowledge in support thereof.

D. Expert Testimony

1) Testimony is sought in witness' personal and official capacity.

2) Subject Matter
2,4-D, 2,4,5-T, TCDD's and dioxins; Agent Orange I/II (also White, Blue, Pink, Green, and Purple

and related chlorophenols and human risk assessment regarding exposure, including, but not limited to, one or more of the following subject areas:

a) Chemistry, Biochemistry

b) Manufacture and/or Production

c) Toxicity

d) Modes of Human Exposure

e) Fate in the Environment (Humans, Plants, Animals)

f) State of Art/State of Medical and Scienti Literature

1) Plant Physiology/Studies
2) Animal Physiology/Studies
3) Human Studies

g) Epidemiology/Biostatistics

1) Plants, animals, humans
2) Cancer Epidemiology
3) Reproductive Epidemiology

h) Adverse Health Effects

3) Yes, witness will be asked opinions about both published and/or on-going studies.

4) Yes, witness will be asked opinions about any studie or research witness has personally performed or actually participated in.

5) Yes, witness will be asked opinions about other governmental studies.

6) Yes, witness is expected to review the following documents prior to giving testimony:

See, EPA, Research and Development, Health Assessment Document on Dioxins for the Offices of Air Quality, Planning and Standards, prepared by the Environmental Criteria and Assessm Office, Cincinnati, Ohio 45248 (July 1

EPA, Research and Development, Health and Environmental Effects Profile for; Tet Penta, and Hexachlorodibenzo-p-dioxins for the Office of Solid Waste and Emergency Response, by the Environmental Criteria and Assessment Office, Cincin Ohio 45248 (June 1983).

EPA, Research and Development, Ambient Water Quality Criteria for 2,3 ,8 TCDD, pre pared for Office of Water Regulations and Standards, by the Environmental Criteria and Assessment Office, Cincin Ohio 45248 (July 1983).

EPA, Research and Development, Dioxins, Industrial Environmental Research Cincinnati, Ohio (1978).

A copy of these documents is attached.

SUPPLEMENTAL ANSWER TO INTERROGATORY NO. 19

Plaintiffs note preliminarily that the extant Order on ing fact witnesses states that fact witnesses are not due until March 984. However, Plaintiffs may call one or more of the following person those from various categories listed below) at time of trial to testify to factual knowledge they may have, including:

1. Ranch Hand Personnel: These persons will testify t eir knowledge of the Ranch Hand Operation, Ranch Hander xposure to Agent Orange, and/or knowledge relating to the s ing, testing, and effects of Agent Orange on humans.

2. Members of the U. S. Armed Forces: These persons m estify to the circumstances and conditions surrounding the aying of Agent Orange.

3. Persons present in Vietnam during the exposure peri n question 1961-1972, including, but not limited to, m ary and paramilitary personnel of the U. S., New Zealand l Australia, who have knowledge of the spraying operat s of the herbicides, the exposure of the Plaintiffs' clas the hazards accompanying any such exposure, the Plaintif themselves, and the Defendant company representative present in Vietnam to oversee the deliveries and spra g operations of the herbicides they manufactured.

4. Persons together with their demonstrative and docume y evidence who gave testimony (which will form the sub on of their testimony herein) at the EPA Cancellation H ngs of 2,4,5-T (1979-1980) under FIFRA, including but not mited to:

   a. Dr. Roy Albert
   b. Dr. K. Diane Courtney
   c. Robert K. Baughman, Ph.D.
   d. Dr. Olav Axelson
   e. Dr. Renate Kimbrough
   f. Dr. Dawn G. Goodman
   g. Dr. Kirk T. Kitchin
   h. Dr. Ronald Thomas
   i. Dr. Rainer Frentzel-Beyme
   j. Dr. Matthew Meselson, Harvard

13103

k. Major Alvin Young
l. Dr. Rodney Bovey
m. Kenneth V. Themein
n. David T. Buzzelli
o. Dr. Michael Gross
p. Dr. Renee Stringham
r. Dr. Van Miller

5. Any current or previous employee, contractor, sub ...actor, in-house or private consultant of each of the Def... ...s or any other person who has knowledge of the manufac... ...g processes, chemistry, occupational exposure and/o... ...icity of 2,4-D and/or 2,4,5-T or related chlorophenols; i... ...ing, but not limited to, laborers; operators; supervisors; ...tract administrators; quality control personnel; engine... ...process, chemical, mechanical and/or safety).

6. Any current or previous employee, contractor, sub... ...ractor, in-house or private consultant of each of the Def... ...nts or any other person who has knowledge of the possibl... ...ns of prophiactic protection from the hazards of dioxin... ...posure; including, but not limited to, laborers, operator... ...pervisors, contract administrators, quality control personne... ...gineers (process, chemical, mechanical and/or safety).

7. Any current or previous employee, contractor, subc... ...ractor, in-house or private consultant of each of the Defe... ...ts or any other person who has knowledge of the means to ... those who might be exposed to use of the herbicides in q... ...ion, particularly Agent Orange, including, but not limit... ...to, laborers, operators, supervisors, contract admini... ...ors, quality control personnel, engineers (process, che... ...l, mechanical and/or safety).

8. Any current or previous employee, contractor, subc... ...ac or, in-house or private consultant of each of the Defen... ...ts or any other person who has factual knowledge of any ... ...r manufacturing processes which could reduce the risk ...f exposure to Agent Orange and/or other phenoxy herbicides bei... ...contaminated with dioxins and further reduce the risk and hazard ...human health of any such exposure.

9. Any current or previous employee, contractor, subc... ...actor, in-house or private consultant of each of the Defen... ...ts or any other person who has factual knowledge of conspirat... ...al conduct of the Defendants, individually and/or duplicative ... ...orts (acts which are parallel in nature) which tended to or di... ...n fact result in misleading the public and the United Stat... ...government from gaining knowledge of the dangers attendant fro... ...posure to Agent Orange and other phenoxy herbicides.

13104

10. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has factual knowledge of how dioxins work upon plants, animals, and/or humans.

11. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has factual knowledge of any statistics concerning the effects of dioxins upon plants, animals, and/or humans.

12. Any current or previous employee, contractor, subcontactor, in-house or private consultant of each of the Defendants or any other person including, but not limited to, members of EPA and other governmental agencies, who has factual knowledge of the following incidents:

a. Love Canal
b. Times Beach, Missouri
c. Sevesco, Italy
d. BASF (1953, LD 1 - Dadische in Germany)
e. Production mishaps and/or explosions since 1925 at any of the plants of any of the Defendants manufacturing, TCP, 2,4-D, 2,4,5-T phenol, chlorine, acetic acid, benzene, sodium hydroxide, potassium hydroxide, and/or Agent Orange, including mishaps in the packaging, and transporting of the Defendants' products to the U. S. Armed Forces bases for eventual shipment to Vietnam.
f. Spraying of Vietnam from 1961-1972.

13. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has factual knowledge of any surveys, tests, epidemiological studies of any kind relating to the effects of exposure to Agent Orange, 2,4-D, 2,4,5-T or any constituent thereof including the secondary by-product known as dioxins.

14. Any person with factual knowledge of how decisions are made within the United States government, particularly the decision to use and to continue to use phenoxy herbicides in Vietnam, particularly Agent Orange; any person with factual knowledge of government procurement contracts and the invitation to bidders, particularly those persons who negotiated the government contracts for all phenoxy herbicides (agents white, blue, purple, pink, green, orange I and II) with the individual defendants' representatives between 1961-1972.

13105

22. Any and all persons listed by Plaintiffs' in both original and amended witness lists, as expert witness (medical, scientific or causation), government witness, government causation witness, defendants' employees and/or related persons and/or any witnesses listed by all Defendants, may be called at time of trial to present factual information as to any issue involved in this case.

23. Any and all members of the scientific and/or medical community who have knowledge of relevant facts, including information on any of the previously listed subjects in this Answer, including but not limited to:

a. David Kriebel, Ph.D.
b. Dr. Alan Poland
c. Dr. Paul Goldmann, BASF
d. Dr. C. Koppe
e. Oettel, BASF
f. Dr. E. E. McDonnell
g. Dr. K. C. Khiem
h. Alvin Ahn
i. Marilyn Fingerhut

24. Any and all persons who have factual knowledge concerning the individual representative Plaintiff's damages, including, but not limited to, the following:

a. Any and all medical persons who have examined, observed, treated and/or tested the Plaintiffs' for injuries, diseases and/or related physical and emotional conditions which resulted from Plaintiffs' exposure to Agent Orange, and/or phenoxy herbicides, their constituents, secondary by-products, wastes, residuals and contaminants.

b. Any and all hospital personnel where Plaintiffs have been confined for treatment relating to their exposure to Defendants products in Vietnam.

c. Any and all persons with knowledge of the economic losses, psychological and/or intangible damages sustained by your Plaintiffs as a result of their injuries and diseases resulting from their exposure to Defendants' products in Vietnam.

d. Any and all persons with knowledge of the past, present and/or future economic losses your Plaintiffs have or will sustain in the future as a result of their loss of wage earnings and/or wages earning capacity resulting from the injuries and diseases made the basis of this lawsuit which were caused by Plaintiffs exposure to Defendants' products in Vietnam.

13106

e. Any and all persons with knowledge of past pr
and/or future reasonable and necessary cos's o
doctors, hospitals, nursery care, medical qui
drugs, and any other related medical serv es red
or to be rendered in the future to Plaint ffs
result of their injuries and disease resulting
their exposure to Defendants' products in Viet

f. Any and all persons with knowledge of the phys
disfigurement (past and present), physical and al
impairment (past and present), physical p in and
present) and mental anguish (past and present) in
Plaintiffs have sustained as a result of their osure
to Defendants' products in Vietnam and which i
reasonable probability Plaintiffs will continu
sustain for an indefinite time into the future
beyond the date of this trial.

Respectfully su ted,

Thomas W. Hende n, Esquire
Allison Pettiett Esquire

CERTIFICATE OF SERVICE

I hereby certify that a true and correct copy of the re ding Supplement to Plaintiff's Interrogatories were mailed Federal E ess to Mr. William Krohley, Kelley, Drye & Warren, Mr. Geno Locks, Pla iff's Management Committee Agent Orange Office, with copies to persona y serve the remaining Defendants at the Tuesday depositions and Ms. Nanc Petrilla, U.S. District Clerk, U.S. Courthouse, 225 Cadman Plaza, Brooklyn New York 11201 this 20th day of February, 1984.

Allison Pettiette

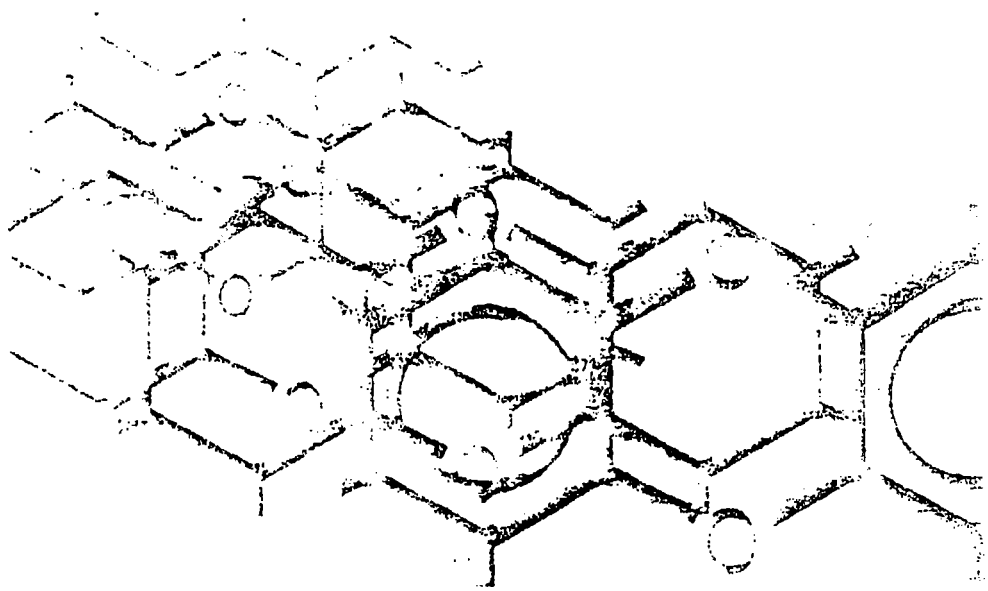
13107

United States
Environmental Protection
Agency

Industrial Environmental Re
ratory
innati OH 45268

Research & Development

EPA Dioxins



13103

PLAINTIFF'S GOVERNMENT CAUSATION WITNESSES

I. Umberto Saffiotti

A. National Cancer Institute, Washington, D.C.

B. Both factual and expert testimony is sought.

C. General Events

Pre-1961: Any factual knowledge of the history of herbicide spraying in U.S. and abroad; including, but not limited to, (1) industrial exposures and explosions; (2) registration of 2,4-D, 2,4,5-T with the Department of Agriculture and any other government agencies by any and/or all of the Defendants;

1961-present: Any factual knowledge of the history of herbicide spraying in the U.S. and abroad; including, but not limited to: (1) U.S. military use of Agent Orange and other phenoxy herbicides in Vietnam; (2) changes in the registration requirements of herbicides with the U.S. government and its agencies including knowledge of FIFRA, FDA, EPA, and OSHA; and (3) any knowledge of industrial and other human exposures to 2,4-D, 2,4,5-T in the U.S. and abroad;

See Answer and Supplemental Answer of Plaintiffs' to Defendants' Interrogatory No. 19 attached hereto and incorporated herein for all purposes re: events or occurrences which these causation witnesses may be expected to give any factual information they may have regarding the subjects outlined in said Answer.

Human Risk Assessment of Exposure to 2,4-D, 2,4,5-T and dioxins and any factual knowledge in support thereof.

D. Expert Testimony

1) Testimony is sought in witness' personal and official capacity.

2) Subject Matter:
2,4-D, 2,4,5-T, TCDD's and dioxins; Agent Orange I/II (also White, Blue, Pink, Green, and Purple

and related chlorophenols and human risk assessment regarding exposure, including, but not limited to, one or more of the following subject areas:

a) Chemistry/Biochemistry

b) Manufacture and/or Production

c) Toxicity

d) Modes of Human Exposure

e) Fate in the Environment (Humans, Plants, Animals)

f) State of Art/State of Medical and Scientific Literature

1) Plant Physiology/Studies
2) Animal Physiology/Studies
3) Human Studies

g) Epidemiology/Biostatistics

1) Plants, animals, humans
2) Cancer Epidemiology
3) Reproductive Epidemiology

h) Adverse Health Effects

3) Yes, witness will be asked opinions about both published and/or on-going studies.

4) Yes, witness will be asked opinions about any studies or research witness has personally performed or actually participated in.

5) Yes, witness will be asked opinions about other governmental studies.

6) Yes, witness is expected to review the following documents prior to giving testimony:

See, EPA, Research and Development, Health Assessment Document on Dioxins for the Offices of Air Quality, Planning and Standards, prepared by the Environmental Criteria and Assessment Office, Cincinnati, Ohio 45248 (July 1

EPA, Research and Development, Health and Environmental Effects Profile for; Tet Penta, and Hexach orodibenzo-p-dioxins for the Office of Solid Waste and Emergency Response, by the Environmental Criteria and Assessment Office, Cincin Ohio 45248 (June 1983).

EPA, Research and Development, Ambient Water Quality Criteria for 2,3,7,8 TCDD, prepared for Office of Water Regulations and Standards, by the Environmental Criteria and Assessment Office, Cincin Ohio 45248 (July 1983).

EPA, Research and Development, Dioxins, Industrial Environmental Research Cincinnati, Ohio (1978).

A copy of these documents is attached.

SUPPLEMENTAL ANSWER TO INTERROGATORY NO. 19

Plaintiffs note preliminarily that the extant Order on producing fact witnesses states that fact witnesses are not due until March 2, 1984. However, Plaintiffs may call one or more of the following persons (or those from various categories listed below) at time of trial to testify as to factual knowledge they may have, including:

1. Ranch Hand Personnel: These persons will testify to their knowledge of the Ranch Hand Operation, Ranch Handers' exposure to Agent Orange, and/or knowledge relating to the spraying, testing, and effects of Agent Orange on humans.

2. Members of the U. S. Armed Forces: These persons may testify to the circumstances and conditions surrounding the spraying of Agent Orange.

3. Persons present in Vietnam during the exposure period in question 1961-1972, including, but not limited to, military and paramilitary personnel of the U. S., New Zealand and Australia, who have knowledge of the spraying operations of the herbicides, the exposure of the Plaintiffs' class, the hazards accompanying any such exposure, the Plaintiffs' themselves, and the Defendant company representatives present in Vietnam to oversee the deliveries and spraying operations of the herbicides they manufactured.

4. Persons together with their demonstrative and documentary evidence who gave testimony (which will form the substance of their testimony herein) at the EPA Cancellation Hearings on 2,4,5-T (1979-1980) under FIFRA, including but not limited to:

   a. Dr. Roy Albert
   b. Dr. K. Diane Courtney
   c. Robert K. Baughman, Ph.D.
   d. Dr. Olav Axelson
   e. Dr. Renate Kimbrough
   f. Dr. Dawn G. Goodman
   g. Dr. Kirk T. Kitchin
   h. Dr. Ronald Thomas
   i. Dr. Rainer Frentzel-Beyme
   j. Dr. Matthew Meselson, Harvard

13112

k. Major Alvin Young
l. Dr. Rodney Bovey
m. Kenneth V. Themein
n. David T. Buzzelli
o. Dr. Michael Gross
p. Dr. Renee Stringham
r. Dr. Van Miller

5. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has knowledge of the manufacturing processes, chemistry, occupational exposure and/or toxicity of 2,4-D and/or 2,4,5-T or related chlorophenols; including, but not limited to, laborers; operators; supervisors; contract administrators; quality control personnel; engineers (process, chemical, mechanical and/or safety).

6. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has knowledge of the possible means of prophylactic protection from the hazards of dioxins' exposure; including, but not limited to, laborers, operators, supervisors, contract administrators, quality control personnel, engineers (process, chemical, mechanical and/or safety).

7. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has knowledge of the means to warn those who might be exposed to use of the herbicides in question, particularly Agent Orange, including, but not limited to, laborers, operators, supervisors, contract administrators, quality control personnel, engineers (process, chemical, mechanical and/or safety).

8. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has factual knowledge of any other manufacturing processes which could reduce the risks of exposure to Agent Orange and/or other phenoxy herbicides being contaminated with dioxins and further reduce the risk and hazard to human health of any such exposure.

9. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has factual knowledge of conspiratorial conduct of the Defendants, individually and/or duplicative efforts (acts which are parallel in nature) which tended to or did in fact result in misleading the public and the United States government from gaining knowledge of the dangers attendant from exposure to Agent Orange and other phenoxy herbicides.

13113

15. Any person with factual knowledge through any surveys, tests, epidemiological studies or otherwise undertaken by any state government, any private public or foreign corporation, the U. S. Congress or the government of any nation concerning the chemical compounds, 2,5-D, 2,4,5-T, dioxins, or related chlorophenols relating to the creation of dioxins, the detection of dioxins, the dangers of dioxins' exposure, and/or the toxicity, carcinogenicity, fetotoxicity, teratogenicity, acute and/or chronic effects on

10. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has factual knowledge of how dioxins work upon plants, animals, and/or humans.

11. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has factual knowledge of any statistics concerning the effects of dioxins upon plants, animals, and/or humans.

12. Any current or previous employee, contractor, subcontactor, in-house or private consultant of each of the Defendants or any other person including, but not limited to, members of EPA and other governmental agencies who has factual knowledge of the

a. Love Canal
b. Times Beach, Missouri
c. Seveseo, Italy
d. BASF (1953, 1954 -- Badische in German
e. Production mishaps and/or explosions since 1925 at any of the plants of any of the Defendants manufacturing, TCP, 2,4-D, 2,4,5-T phenol, chlorine, acetic acid, benzene, sodium hydroxide, potassium hydroxide, and/or Agent Orange, including mishaps in the packaging, and transporting of the Defendants' products to the U. S. Armed Forces bases for eventual shipment to Vietnam.
f. Spraying of Vietnam from 1961-1972.

13. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has factual knowledge of any surveys, tests, epidemiological studies of any kind relating to the effects of exposure to Agent Orange, 2,4-D, 2,4,5-T or any constituent thereof including the secondary by-product known as dioxins.

13114

14. Any person with factual knowledge of how decisions are made within the United States government, particularly the decision to use and to continue to use phenoxy herbicides in Vietnam.

22. Any and all persons listed by Plaintiffs' in both original and amended witness lists, as expert witness (medical, scientific or causation), government witness, government causation witness, defendants' employees and/or related personnel and/or any witnesses listed by all Defendants, may be called at time of trial to present factual information as to any issue involved in this case.

23. Any and all members of the scientific and/or medical community who have knowledge of relevant facts, including information on any of the previously listed subjects in this Answer, including, but not limited to:

a. David Kriebel, Ph.D.
b. Dr. Alan Poland
c. Dr. Paul Goldmann, BASF
d. Dr. C. Rappe
e. Dr. Oettel, BASF
f. Dr. E. E. McDonnell
g. Dr. K. S. Khiera
h. Alvin Alm
i. Marilyn Fingerhut

24. Any and all persons who have factual knowledge concerning the individual representative Plaintiff's damages, including, but not limited to, the following:

a. Any and all medical persons who have examined, observed, treated and/or tested the Plaintiffs' for injuries, diseases and/or related physical and emotional conditions which resulted from Plaintiffs' exposure to Agent Orange, and/or phenoxy herbicides, their constituents, secondary by-products, wastes, residuals and contaminants.

b. Any and all hospital personnel where Plaintiffs have been confined for treatment relating to their exposure to Defendants' products in Vietnam.

c. Any and all persons with knowledge of the economic losses, psychological and/or intangible damages sustained by your Plaintiffs as a result of their injuries and diseases resulting from their exposure to Defendants' products in Vietnam.

d. Any and all persons with knowledge of the past, present and/or future economic losses your Plaintiffs have or will sustain in the future as a result of their loss of wage earnings and/or wages earning capacity resulting from the injuries and diseases made the basis of this lawsuit which were caused by Plaintiffs exposure to Defendants' products in Vietnam.

13115

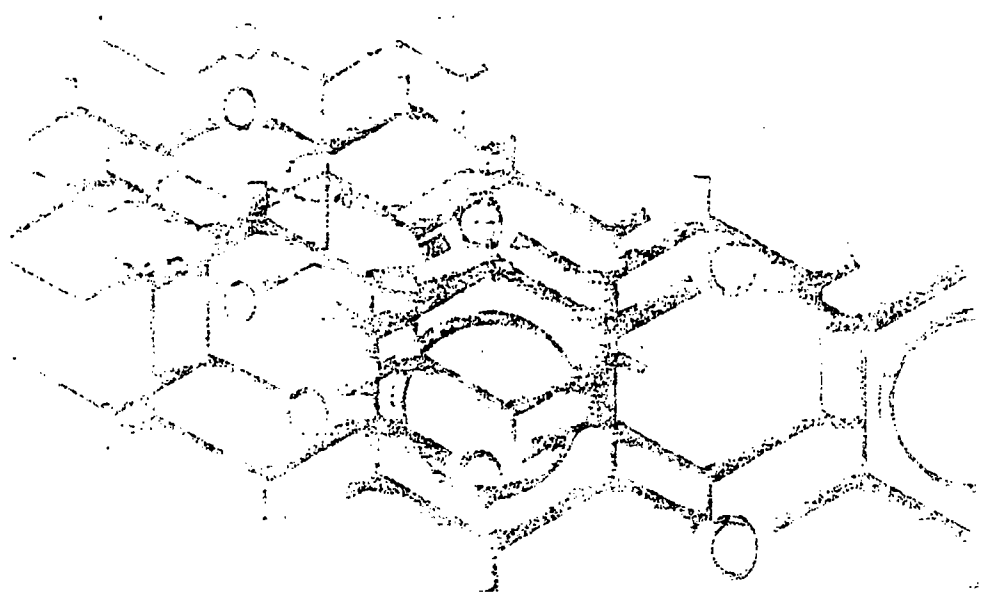
United States
Environmental Protection
Agency

Industrial Environmental
Laboratory
Cincinnati OH 45268

Research & Development

EPA

Dioxins



13116

and related chlorophenols and human risk assessment regarding exposure, including, but not limited to, one or more of the following subject areas:

a) Chemistry/Biochemistry

b) Manufacture and/or Production

c) Toxicity

d) Modes of Human Exposure

e) Fate in the Environment (Humans, Plants, Animals)

f) State of Art/State of Medical and Scientific Literature

1) Plant Physiology/Studies
2) Animal Physiology/Studies
3) Human Studies

g) Epidemiology/Biostatistics

1) Plants, animals, humans
2) Cancer Epidemiology
3) Use of in vivo Epidemiology

h) Adverse Health Effects

2) Yes, witness will be asked opinions about each published and/or on going studies

3) Yes, witness will be asked opinions about any study in which witness has personally performed or actively participated in.

4) Yes, witness will be asked opinions of the other governmental studies.

5) Yes, witness is expected to review the following documents prior to giving testimony:

Yes, EPA, Research and Development, Health Assessment Document on Dioxins for the Office of Air Quality, Planning and Standards, prepared by the Environmental Criteria and Assessment Office, Cincinnati, Ohio 45268 (Final

PLAINTIFF'S GOVERNMENT CAGNATION WITNESSES

I. James Mason

A. Center for Disease Control (CDC) Atlanta, GA

B. Both factual and expert testimony is sought.

C. General Areas

Dow Chemical: Any factual knowledge of the history of herbicide spraying in U.S. and abroad; including but not limited to, (1) industrial exposures and explosions; (2) registration of 2,4-D, 2,4,5-T with the Department of Agriculture and any other government agencies by any and/or all of the Defendants;

Monsanto: Any factual knowledge of the history of herbicide spraying in the U.S. and abroad; including, but not limited to, (1) U.S. efficacy use of Agent Orange and other phenoxy herbicides in Vietnam; (2) changes in the registration requirements of herbicides with the U.S. government and its agencies including knowledge of USDA, FDA, EPA, and OSHA; and (3) any knowledge of industrial and other human exposure to 2,4-D, 2,4,5-T in the U.S. and abroad;

See Answer and Supplemental Answer of Plaintiffs' to Defendants' Interrogatory No. 19 attached hereto and incorporated herein for all purposes re: events or occurrences which these cognation witnesses may be expected to give any factual information they may have regarding the subjects outlined in said Answer.

Human Risk Assessment of Exposure to 2,4-D, 2,4,5-T and dioxins and any factual knowledge in support thereof.

D. Expert Testimony

Testimony is sought in witness' personal and official capacity.

1) Subject Matter

2,4-D, 2,4,5-T, TCDD's and Dioxins; Agent Orange; Exhibits (same White, Blue, Pink, Green, and Purple

EPA, Research and Development, Health and Environmental Effects Profile for; Tetra-, Penta-, and Hexachlorodibenzo-p-dioxins, for the Office of Solid Waste and Emergency Response, by the Environmental Criteria and Assessment Office, Cincinnati Ohio 45268 (June 1983).

EPA, Research and Development, Ambient Water Quality Criteria for 2,3,7,8 TCDD, prepared for Office of Water Regulations and Standards, by the Environmental Criteria and Assessment Office, Cincinnati Ohio 45748 (July 1983).

EPA, Research and Development, Dioxins, Industrial Environmental Research Laboratory, Ohio (1979).

A copy of these documents is attached.

SUPPLEMENTAL ANSWER TO INTERROGATORY NO. 19

Plaintiffs note preliminarily that the extant Order on producing [illegible] witnesses states that fact witnesses are [illegible] until March 2, 1984. However, Plaintiffs may call one or more of the following persons (or those from various categories listed below) at time of trial to testify as to factual knowledge they may have, including:

1. Ranch Hand Personnel: These persons will testify to their knowledge of the Ranch Hand Operation, Ranch Hands' exposure to Agent Orange, and/or knowledge relating to the spraying, testing, and effects of Agent Orange on humans.

2. Members of the U. S. Armed Forces: These persons may testify to the circumstances and conditions surrounding the spraying of Agent Orange.

2. Persons present in Vietnam during the exposure period in question [illegible], including, but not limited to, military and paramilitary personnel of the U. S., New Zealand and Australia, the crews involved in the spraying operations of the herbicides, the spouse of the Plaintiffs' class, the husbands of any such spouse, the Plaintiffs' themselves, and the Defendant company representatives present in Vietnam to oversee the deliveries and spraying operations of the herbicides they manufactured.

3. Persons capable with their demonstrative and documentary evidence who prove testimony (which will form the substance of their testimony herein) at the Pre-Cancellation Hearing of 2/4/5-6 (1979-1980) under FIFRA, including but not limited to:

a. Dr. Jay Allred
b. Dr. K. Diann Courtney
c. Robert M. Faughman, [illegible]
d. Dr. Olav Axelson
e. Dr. Ronald Kilburn
f. Dr. [illegible] Meselson
g. Dr. Mark D. Mitchell
h. Dr. Ronald Thomas
i. Dr. Reimer de Haan-Beyer
j. Dr. Matthew M. Nelson, Harvard

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k. Major Alvin Young
l. Dr. Rodney Dovey
m. Kenneth V. Thomas
n. David T. Burnett
o. Dr. Michael Gross
p. Dr. Renee Stringham
q. Dr. Van Miller

5. Any current or previous employer, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has knowledge of the manufacturing processes, chemistry, occupational exposure and/or toxicity of 2,4-D and/or 2,4,5-T or correlated chlorophenols; including, but not limited to, laborers, operators, supervisors, contract administrators, quality control personnel, engineers (process, chemical, mechanical and/or safety).

6. Any current or previous employer, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has knowledge of the possible means of exposure; including, but not limited to, laborers, operators, supervisors, contract administrators, quality control personnel, engineers (process, chemical, mechanical and/or safety).

7. Any current or previous employer, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has knowledge of the means to warn those who might be exposed to use of the herbicides in question, particularly by light aircraft, including, but not limited to, laborers, operators, supervisors, contract administrators, quality control personnel, engineers (process, chemical, mechanical and/or safety).

8. Any current or previous employer, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has factual knowledge of any other manufacturing process which could reduce the risks of exposure to Agent Orange and/or other herbicides being contaminated with dioxin and further reduce the risk of hazard to human health of any such exposure.

9. Any current or previous employer, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has factual knowledge of conspiratorial conduct of the Defendants, individually or in the duplicative efforts (acts which are prohibited by statute which tended to or did in fact mislead or misdirect or prevent the United States government from gaining knowledge of the dangers attendant from exposure to Agent Orange and other phenoxy herbicides.

10. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has factual knowledge of how dioxins work upon plants, animals, and/or humans.

11. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has factual knowledge of any statistics concerning the effects of dioxins upon plants, animals, and/or humans.

12. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person, including, but not limited to, workers of EPA and other governmental agencies, who has factual knowledge of the following incidents:

a. Love Canal
b. Times Beach, Missouri
c. Seveso, Italy
d. Agent Orange, Vietnam
e. Production, delivery and/or application between 1925 at any of the plants of any of the Defendants manufacturing, 2CP, 2,4-D, 2,4,5-T, phenols, chlorine, or the acid, benzene, sodium hydroxide, petroleum hydrocarbons, and/or Agent Orange, including mishaps in the packaging, and transportation of the Defendants' products to the U.S. Armed Forces bases for eventual shipment to Vietnam.
f. Spraying of Vietnam between 1965-1970.

13. Any current or previous employee, contractor, subcontractor, in-house or private consultant of each of the Defendants or any other person who has factual knowledge of any surveys, tests, medical or clinical studies of any kind relating to the effects of exposure to Agent Orange, 2,4-D, 2,4,5-T or any constituent thereof including the contaminant by-product known as dioxins.

14. Any person with factual knowledge of how decisions are made within the United States government, particularly the decision to use and to continue to use phenoxy herbicides in Vietnam, particularly Agent Orange; any person with factual knowledge of government procurement orders and the invitation to bidders, particularly those parts which specified the government contracts for all phenoxy herbicides (green, white, blue, purple, pink, green, orange I and II) and that the individual defendants represented between 1965-1970.

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15. Any person with factual knowledge through any surveys, tests, epidemiological studies or research undertaken by any state government, any part of the public or foreign corporation, the U. S. Congress or the government of any nation concerning the chemical compounds, 2,5-D, 2,4,5-T, dioxins, or related chlorophenols relating to the creation of dioxins; the detection of dioxins, the dangers of dioxins' exposure, and/or the toxicity, carcinogenicity, fetotoxicity, teratogenicity, acute and/or chronic effects on plants, animals and the human population.

16. Any and all persons listed in The Chemical Scythe by Alastair Hay, as having factual knowledge regarding 2,4,5-T, 2,4-D, and its contaminant dioxins.

17. All workers compensation claims for the Defendants and documentation of all occupational exposures filed since 1928 which evidence industrial injuries or diseases at the TCP, 2,4,5-T, 2,4-D, Thirty-gallon, and/or transportation plants of the Defendants.

18. Any and all workers or public workers compensation claimants of the Defendants who have had alleged occupational exposures and/or relevant [illegible] and/or diseases and/or symptoms [illegible] (sub 17) above.

19. Any and all other of [illegible] Representatives Committee on Oversight [illegible] of the [illegible] Actions (1983) and/or any person cognizant with this [illegible] and demonstrative evidence given to them at said hearing, which will show the misbehavior of Hardin testimony herein [illegible] on the failure of the EPA to take prompt and effective action to ban the production of 2,4-D, 2,4,5-T, and its contaminant dioxins.

20. Any and all persons having knowledge of relevant facts regarding the financial status of the Defendants and their ability to respond in punitive damages, including, but not limited to, their past, present, and future position and earnings in the United States and abroad since 1928 through and including the present from the sale of the products made the basis of this lawsuit, i.e., 2,4-D, 2,4,5-T, phenoxy herbicides and the relevant herbicide market.

21. Any and all persons having knowledge of relevant facts regarding the ownership interests of the Defendants and their ability to respond in punitive damages, including, but not limited to, defendants' domestic and foreign subsidiaries, joint ventures, licensing agreements, and/or other public or private corporations in the U. S. and abroad, in which these defendants own a substantial financial [illegible] since 1928 through and including the present.

22. Any and all persons listed by Plaintiffs' in both original and amended [illegible] expert witness [illegible], scientific or causation), government's witness, government causation witness, defendants' employees and/or related personnel and/or any witnesses listed by all Defendants, may be called at time of trial to present factual information as to any issue involved in this case.

23. Any and all members of the scientific and/or medical community who have knowledge of relevant facts, including information on any of the previously listed subjects in this Answer, including, but not limited to:

a. David [illegible], M.D.
b. Dr. Alan [illegible]
c. Dr. Paul [illegible], Ph.D.
d. Dr. [illegible]
e. Dr. [illegible], Ph.D.
f. Dr. N. S. McDonald
g. Dr. H. S. Peters
h. Alvin Ali
i. Marilyn [illegible]

24. Any and all persons who have factual knowledge concerning the individual injuries that Plaintiffs' damages, including, but not limited to, the following:

a. Any and all medical persons who have examined, observed, treated and/or treated the Plaintiffs' for injuries, diseases and/or related physical and emotional conditions which resulted from Plaintiffs' exposure to Agent Orange, and/or phenoxy herbicides, their constituents, secondary by products, wastes, residuals, dioxin and TCDD.

b. Any and all hospital personnel who's Plaintiffs have been confined for treatment relating to their exposure to Defendants' products in Vietnam.

c. Any and all persons with knowledge of the economic losses, psychological and/or intangible damages sustained by your Plaintiffs as a result of their injuries and diseases resulting from their exposure to Defendants' products in Vietnam.

d. Any and all persons with knowledge of the past, present and/or future [illegible] who's claims your Plaintiffs have or will sustain in the future as a result of their loss of wage earnings and/or wages earning capacity resulting from the injuries and diseases made the basis of this lawsuit which were caused by Plaintiffs exposure to Defendants' products in Vietnam.

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e. Any and all persons with knowledge of past, present and/or future reasonable and necessary costs of doctors, hospitals, nursery care, medical equipment, drugs, and any other related medical services rendered or to be rendered in the future to Plaintiffs as a result of their injuries and disease resulting from their exposure to Defendants' products in Vietnam.

f. Any and all persons with knowledge of the physical disfigurement (past and present), physical and mental impairment (past and present), physical pain (past and present) and mental anguish (past and present) which Plaintiffs have endured as a result of their exposure to Defendants' products in Vietnam and which in reasonable probability Plaintiffs will continue to sustain for an indefinite time into the future from beyond the date of this trial.

Respectfully submitted,

James W. Henderson, Esquire
Allison Pettiette, Esquire

CERTIFICATE OF SERVICE

I hereby certify that a true and correct copy of the foregoing Supplement to Plaintiff's Interrogatories were mailed Federal Express to Mr. William Krohley, Kelley, Drye & Warren, Mr. Gene Locks, Plaintiffs' Management Committee Agent Orange Office, with copies to personally serve the remaining Defendants on the Schedule of Positions and Ms. Nancy Potrilla, U.S. District Court, E.D. of New York, 225 Cadman Plaza, Brooklyn, New York 11201 this 10th day of February, 1984.

Allison Pettiette

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United States
Environmental Protection
Agency

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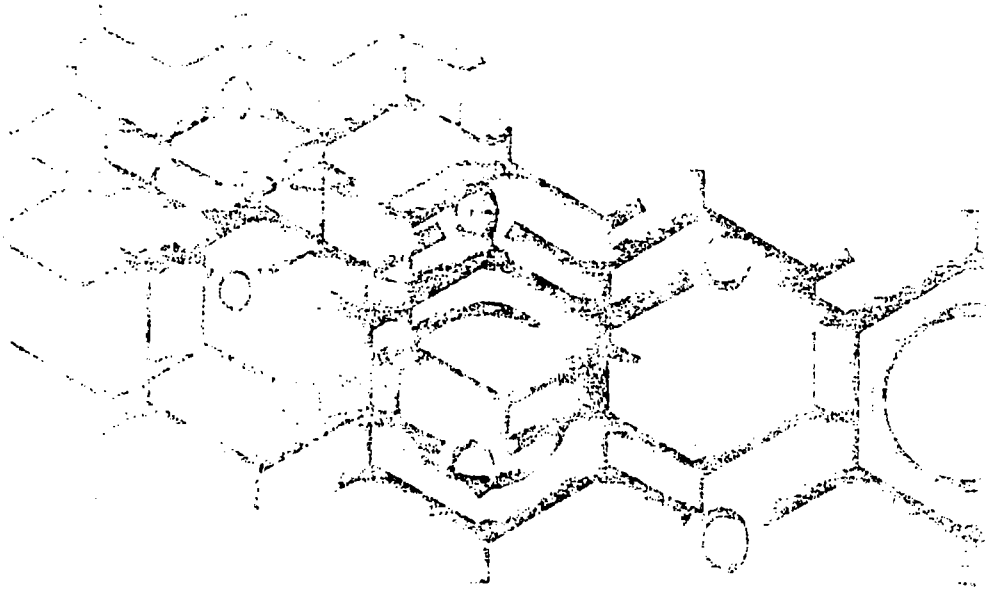
Cincinnati OH 45268

Research & Development

EPA Dioxins



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UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF NEW YORK

---X

In Re

"AGENT ORANGE"

MDL NO. 381

PRODUCT LIABILITY LITIGATION

---X

FILED
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TIME A.M. 1984
P.M.

DEFENDANTS LIST OF FACT WITNESSES SUBMITTED PURSUANT TO THE SCHEDULING ORDER FOR THE COMPLETION OF DISCOVERY

13127

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1944

UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF NEW YORK

---X

In Re

"AGENT ORANGE"

MDL NO. 381

PRODUCT LIABILITY LITIGATION

---X

DEFENDANTS LIST OF FACT WITNESSES
SUBMITTED PURSUANT TO THE SCHEDULING ORDER
FOR THE COMPLETION OF DISCOVERY

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DEFENDANTS LIST OF FACT WITNESSES
SUBMITTED PURSUANT TO THE SCHEDULING ORDER
FOR THE COMPLETION OF DISCOVERY

On behalf of all defendants, and pursuant to the Scheduling Order For The Completion Of Discovery dated January 10, 1984, counsel for Thompson Chemical Company hereby submits the following list of potential witnesses to be called at trial, attached hereto as Schedule A. These witnesses shall be called to testify as to the issue of the government contract defense.

Furthermore, attached hereto as Schedule B, defendants hereby submit a list of witnesses presently scheduled to be deposed at a future date. Therefore, defendants reserve the right, after these witnesses are deposed to determine whether or not these individuals shall be called upon at trial.

Each individual defendant also reserves the right to submit an additional list of witnesses on their own behalf which they may choose to call upon to testify.

Dated February 29, 1984

Respectfully submitted,

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By David R. Gross
David R. Gross, Esq.

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cc: Service List

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Cambridge, Mass. 02138

William Childs Westmoreland
Box 1059
Charleston, S.C. 29402

Jerome B. Wiesner
61 Shattuck Rd.
Watertown, Mass.

Jerome Wilkenfeld
5757 Owensmouth Ave.
Woodland Hills, California

Donald Whittam
10308 Brookmoor Drive
Silver Spring, Maryland 20901

James H. Wills
9706 Bellevue Dr.
Bethesda, Maryland

Herbert F. York
6110 Camino De LaCosta
LaJolla, California

Dr. Mitchell Zavon
Occidental Chemical Corp.
P.O. Box 728
Niagara Falls, New York 14302

Walter Leo Zielinski, Jr.
12705 Darnestown Rd.
Gaithersburgh, Maryland 20878

SCHEDULE B

DEPOSITIONS SCHEDULED AFTER FEBRUARY 29, 1984:

1. Donald Barnes
2. General Stanzwick Hay
3. Julius Johnson
4. Harold Kinney
5. Debdas Mukerjee
6. Elmer Wheeler

UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF NEW YORK

In Re

"AGENT ORANGE"

PRODUCT LIABILITY LITIGATION

MDL NO. 381

DEFENDANTS LIST OF FACT WITNESSES SUBMITTED PURSUANT TO THE SCHEDULING ORDER FOR THE COMPLETION OF DISCOERY

BUDD, LARNER, KENT, GROSS,
PICILLO & ROSENBAUM, P.C.

33 Washington Streert
Newark, New Jersey 07102
(201) 622-7400

Attorneys for Defendant
Thompson Chemical Company

FILED
IN CLERK'S OFFICE
U. S. DISTRICT COURT E.D. N.Y.
★ MAR 1 1984 ★
TIME A.M.
P.M.

UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF NEW YORK

In re	:	
"AGENT ORANGE"	:	MDL No. 381
Product Liability Litigation	:	

DEFENDANT DIAMOND SHAMROCK CHEMICALS COMPANY'S PRELIMINARY LISTING OF FACT WITNESSES

Pursuant to the Special Master's Final Amended Recommended Scheduling Order, approved by the Court on January 10, 1984, defendant Diamond Shamrock Chemicals Company ("Diamond Shamrock") sets forth below its preliminary listing of fact witnesses who may give live testimony at trial in support of Diamond Shamrock's claims and defenses. This listing does not address deposition testimony that may be used at trial, which will be identified as part of preparation of the pretrial order. In accordance with the Scheduling Order and the Magistrate's Pretrial Order No. 9, Diamond Shamrock reserves the right to supplement and amend this preliminary listing.

12:42

1949

Name and Present Address	Description of General Nature of Testimony
Dr. Donald J. Birmingham 19811 Wedgewood Drive Gross Point Woods, Michigan	Testimony concerning research and investigation of chloracne by U.S. Public Health Service in the 1950's and 1960's, including visits to Diamond Shamrock's former Newark plant.
Robert L. Chonoles Diamond Shamrock Chemicals Company Berry Avenue at Route 17 North Carlstadt, New Jersey 07072	Testimony concerning manufacturing operations at Diamond Shamrock's former Newark plant, including: the removal of dioxin from trichlorophenol; and the U.S. Public Health Service study of the Newark workers in 1968-69.
Sigmund R. Eckhaus 4208 Colonial Road Pikesville, Maryland	Testimony concerning United States' program for the construction of an Agent Orange manufacturing facility, and communications with producers of Agent Orange in connection with that program.
Dr. Marcus M. Key University of Texas Health Science Center P.O. Box 20186 Houston, Texas 77025	Testimony concerning research and investigation of chloracne by U.S. Public Health Service in the 1960's, including visit to Diamond Shamrock's former Newark plant.
Jane Lewis 5125 Temple Hills Road Temple Hills, Maryland 20748	Testimony concerning the procurement and production of Agent Orange pursuant to the Defense Production Act, including directives and priority ratings issued by the United States.
Dr. Alan P. Poland 2918 Nottingham Way Madison, Wisconsin	Testimony concerning medical study of the workers at Diamond Shamock's former Newark plant in 1968-69, and research and investigation of trichlorophenol, 2,4,5-T and dioxin at National Communicable Disease Center in the 1960's.
Dr. Paul A. Possick 46 Winding Way Woodcliff Lake, New Jersey	Testimony concerning medical study of the workers at Diamond Shamrock's former Newark plant in 1968-69.

Name and Present Address	Description of General Nature of Testimony
Warren C. Shaw 1907 Edgewater Parkway Silver Spring, Maryland	Testimony concerning USDA regulation of 2,4,5-T under FIFRA in 1950's and 1960's, and USDA research and investigation concerning health effects and efficacy of 2,4,5-T.
F. Gordon Steward Diamond Shamrock Agricultural Chemicals Inc. P.O. Box H Tuscaloosa, Alabama 35404	Testimony concerning manufacturing operations at Diamond Shamrock's former Newark plant, including: the development, installation and operation of a method for removing dioxin from trichlorophenol; the U.S. Public Health Service study of the Newark workers in 1968-69; and the production and shipment of Agent Orange pursuant to contracts with the United States.

Dated: New York, New York
February 29, 1984

Respectfully submitted,

CADWALADER, WICKERSHAM & TAFT

By Wenman B. Arnold Jr.
A Member of the Firm

Attorneys for Defendant
Diamond Shamrock Chemicals Company
One Wall Street
New York, New York 10005
(212) 908-7000

13144

AFFIDAVIT OF SERVICE

STATE OF NEW YORK)
: ss.:
COUNTY OF NEW YORK)

MICHAEL M. GORDON, being duly sworn, deposes and says:

1. I am not a party to this action, am over 18 years of age and reside in New York County, New York.

3. On February 29, 1984, I served the annexed Defendant Diamond Shamrock Chemicals Company's Preliminary Listing of Fact Witnesses on each of the persons named on the annexed list by depositing a true copy of same enclosed in a postpaid properly addressed wrapper, in an official depository under the exclusive care and custody of the United States Postal Service within the State of New York. The copy to David J. Dean, Esq. was sent by Federal Express. A copy was also sent by Federal Express to the Agent Orange Plaintiffs' Management Committee, 26 Court Street, Suite 905, Brooklyn, New York.

Michael M. Gordon

Sworn to before me this
29th day of February, 1984

Notary Public

CHARLES E. ERWAY III
Notary Public, State of New York
No. 4739184
Qualified in Kings County
Commission Expires March 30, 1985

SERVICE LIST

FOR DEFENDANTS

Leonard L. Rivkin
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(for DOW CHEMICAL)
100 Garden City Plaza
Garden City, New York 11530

Morton G. Silberman
Clark, Gagliardi & Miller
(for T H AGRICULTURE & NUTRITION COMPANY, INC.)
The Inns of Court
99 Court Street
White Plains, New York 10601

John C. Sabetta
Townley & Updike
(for MONSANTO)
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William Krohley
Kelley Drye & Warren
(for HERCULES, INC.)
101 Park Avenue
New York, New York 10178

John M. Fitzpatrick
Dilworth, Paxson, Kalish & Levy
(for HOOKER PLASTICS & CHEMICALS CORP.)
2600 The Fidelity Building
Philadelphia, Pennsylvania 19109

Richard Goldstein
Shea & Gould
330 Madison Avenue
New York, New York 10017

Thomas Beck
Arthur, Dry & Kalish, P.C.
(for UNIROYAL)
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New York, New York 10020

David R. Gross
Budd, Larner, Kent, Gross, Picillo & Rosenbaum
(for THOMPSON CHEMICALS)
33 Washington Street
Newark, New Jersey 07102

Arvin Maskin
Department of Justice
(for THIRD PARTY DEFENDANT USA)
Safeway Building
521 12th Street, N.W.
Washington, D.C. 20530

L. Kevin Sheridan
Executive Assistant
U.S. Attorney
Eastern District of New York
United States Courthouse
225 Cadman Plaza East
Brooklyn, New York 11201

COPIES OF ALL DOCUMENTS MUST BE SENT TO:

Clerk of the Panel
Judicial Panel on Multidistrict Litigation
1120 Vermont Avenue, N.W.
Suite 1002
Washington, D.C. 20005

FOR PLAINTIFFS

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Yannacone & Yannacone
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Benton Musselwhite
Law Offices of Benton Musselwhite, Inc.
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Houston, Texas 77002

Thomas Henderson
Baskin & Sears
Frick Building - 10th Floor
Pittsburgh, Pennsylvania 15219

David J. Dean, Esq.
Dean, Falanga & Rose
1 Old Country Road
Carle Place, New York 11514

FILED
IN CLERK'S OFFICE
U.S. DISTRICT COURT E.D. N.Y.
FEB 10 1984
TIME A.M.
P.M.

UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF NEW YORK

In re	:	MDL No. 381
"AGENT ORANGE"	:	
Product Liability Litigation	:	

DEFENDANT DIAMOND SHAMROCK'S OBJECTIONS TO PLAINTIFFS' PRELIMINARY LIST OF POTENTIAL DEPONENTS PRESENTLY OR FORMERLY EMPLOYED BY DIAMOND SHAMROCK

1869

CADWALADER, WICKERSHAM & TAFT
A PARTNERSHIP INCLUDING PROFESSIONAL CORPORATIONS
One Wall Street New York, N.Y. 10005
(212) 908-7000

13 17

UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF NEW YORK

----------x

In re : MDL No. 381

"AGENT ORANGE" :

Product Liability Litigation :

----------x

DEFENDANT DIAMOND SHAMROCK'S OBJECTIONS TO PLAINTIFFS' PRELIMINARY LIST OF POTENTIAL DEPONENTS PRESENTLY OR FORMERLY EMPLOYED BY DIAMOND SHAMROCK

Preliminary Statement

Pursuant to the direction of Magistrate Scheindlin at the February 9, 1984 pre-trial conference, defendant Diamond Shamrock Chemicals Company ("Diamond Shamrock") sets forth below its objections to plaintiffs' preliminary list of present or former Diamond Shamrock employees who may be deposed by plaintiffs, served on February 9, 1984 ("Plaintiffs' List"). Diamond Shamrock requests, however, that consideration of its objections by the Magistrate be deferred pending receipt and review of plaintiffs' "priority" deposition list.

DISCUSSION

Since the commencement of deposition discovery in the "Agent Orange" litigation in 1982, plaintiffs have deposed nine present or former Diamond Shamrock employees on substantive

issues. An additional three employees have been examined pursuant to Pretrial Order No. 57.

On December 12, 1983, counsel for plaintiffs confirmed in writing that their deposition discovery of Diamond Shamrock would be completed by the examination of five additional former employees: Richard Marrese, Donald Purdy, Cy Perkins, James King and Stanley Honour. See letter from Edward J. Gorman to Michael M. Gordon dated December 12, 1983 (Exhibit A hereto). Dr. Marrese and Mr. Purdy were examined on December 13, 1983 and January 5, 1984, respectively. The depositions of Mr. Perkins and Mr. King were both tentatively scheduled, and then postponed at plaintiffs' request for various reasons, including ill health of plaintiffs' counsel. The deposition of Mr. Honour remains unscheduled.

Now, only 12 weeks before trial, plaintiffs have identified ten former Diamond Shamrock employees that they may wish to depose, in addition to the three witnesses previously requested and remaining to be scheduled. Thus, if their List is accepted at face value, plaintiffs seek at the last minute to double the number of Diamond Shamrock depositions taken in this litigation. Their List similarly more than triples the number of outstanding depositions to be scheduled, in total repudiation of plaintiffs' most recent assurances to Diamond Shamrock.

Plaintiffs' unannounced new "wave" of Diamond Shamrock depositions, in the face of recent representations to the contrary, would seriously and unfairly prejudice Diamond Shamrock's own pre-trial preparations. Instead of the three remaining

depositions agreed to in December, Diamond Shamrock would now be compelled to locate and prepare for depositions of 13 former employees, most of whom reside far from New York and are unlikely to agree to travel here for their examinations. The strain on the resources of Diamond Shamrock's counsel that would result at this critical stage of the proceedings is obvious. Absent a compelling explanation for plaintiffs' failure to apprise Diamond Shamrock of their intentions and to pursue scheduling of Diamond Shamrock depositions during the past several months, plaintiffs should not be permitted to sidetrack Diamond Shamrock's trial preparations in the few precious weeks remaining before jury selection.

In fairness to plaintiffs, Diamond Shamrock recognizes that plaintiffs themselves estimate that only a fraction of the deponents they have listed will actually be examined. Plaintiffs have also stated their intention to submit by February 15, 1984 a "priority list" that is expected to contain only one-half to one-quarter of the names set forth in their original list. See tr. at 9214-15. Accordingly, Diamond Shamrock requests that consideration of its objections to the number of former Diamond Shamrock employees identified as deponents in Plaintiffs' List be deferred to permit receipt and review of plaintiffs' priority

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list, and discussion of that list between counsel for Diamond Shamrock and plaintiffs.

Dated: New York, New York
February 14, 1984

Respectfully submitted,

CADWALADER, WICKERSHAM & TAFT

By _____
A Member of the Firm
Attorneys for Defendant
Diamond Shamrock Chemicals
Company
One Wall Street
New York, New York 10005
(212) 908-7000

12151

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OF COUNSEL
HENRY J. O'HAGAN - DEC'D 1978
EDWARD G. DOUGHERTY - DEC'D 1977
GEORGE W. KELLY
ALLAN M. KAPLAN
RICHARD F. POHL
(ADM. PENN. BAR)
EDWARD F. HAYES, III

December 12, 1983

Cadwalder, Wickersham & Taft, Esqs.
One Wall Street
New York, New York 10005

Attention of Michael M. Gordon, Esq.

RE: In re "Agent Orange"
Product Liability Litigation
MDL No. 381

Dear Mr. Gordon:

This will confirm our telephone conversation of December 8, 1983 wherein you advised that Mr. S. S. Savage is deceased and Mr. S. B. Honour, still shares this earth with us although his exact whereabouts are unknown.

Presently scheduled for depositions are Mr. Marrese, Perdy, Perkins and King.

As you know Mr. Fiorella has written to Mr. Lex Creamer regarding his deposition but to date we have not heard from this gentleman. What we are looking for is a witness with knowledge of the various South American episodes involving chloracne and the use of 2, 4, 5,T. I doubt if we will hear from Mr. Creamer.

If you will be kind enough therefore to arrange to have Mr. Honour presented for deposition, he, in addition to those gentlemen mentioned above,will complete our discovery.

Thank you for your cooperation, I remain

Very truly yours,

O'HAGAN, REILLY & GORMAN, P.C.

Edward J. Gorman

EDWARD J. GORMAN

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CC: Albert Fiorella, Esq.
D. Russo, Esq.

AFFIDAVIT OF SERVICE

STATE OF NEW YORK)
: ss.:
COUNTY OF NEW YORK)

JEFFREY SAPER, being duly sworn, deposes and says:

1. I am not a party to this action, am over 18 years of age and reside in Queens County, New York.

2. On February 14, 1984, I served the annexed Defendant Diamond Shamrock's Objections to Plaintiffs' Preliminary List of Potential Deponents Presently or Formerly Employed by Diamond Shamrock on each of the persons named on the annexed list by depositing a true copy of same enclosed in a postpaid properly addressed wrapper, in an official depository under the exclusive care and custody of the United State Postal Service within the State of New York. The copy to David J. Dean, Esq. was sent by Express Mail. A copy was also sent by hand to the Agent Orange Plaintiffs' Management Committee, 26 Court Street, Suite 905, Brooklyn, New York.

Jeffrey Saper

Sworn to before me this
14th day of February, 1984.

Notary Public

MICHAEL MACKIN GORDON
Notary Public, State of New York
No. 31-4643965
Qualified in New York County
Commission Expires March 30, 1985

13153

SERVICE LIST

FOR DEFENDANTS

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Executive Assistant
U.S. Attorney
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TELEX: 129146/667465
RAPIFAX: (212) 269-2321
XEROX: (212) 785-1630

February 14, 1984

Honorable Shira A. Scheindlin
United States Magistrate
United States District Court
Eastern District of New York
United States Courthouse
225 Cadman Plaza East
Brooklyn, New York 11201

Re: In re "Agent Orange" Product
Liability Litigation, MDL No. 381

Dear Magistrate Scheindlin:

Pursuant to your direction at the February 9, 1984 pre-trial conference, I enclose Defendant Diamond Shamrock's Objections to Plaintiffs' Preliminary List of Potential Deponents Presently or Formerly Employed by Diamond Shamrock.

Very truly yours,

Michael M. Gordon

MMG/mam
Enclosure
BY HAND

cc(w/encl.): Clerk of the Court
Service List

UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF NEW YORK
----------X

In re

"AGENT ORANGE" MDL No. 381

Product Liability Litigation

----------X

PRESENT LIST OF PLAINTIFFS'
CAUSATION WITNESSES
WITH ATTACHED SUMMARIES
IN ACCORDANCE WITH FRCP 26(b)(4)(A)(i)

1.	Charles Baron, M.D.	Exhibit "A"
2.	Deborah Anne Barsotti, Ph.D.	Exhibit "B"
3.	Ronald Codario, M.D.	Exhibit "C"
4.	Arthur W. Galston, Ph.D.	Exhibit "D"
5.	John Garofalo, M.D.	Exhibit "E"
6.	Lennart Hardell, M.D.	Exhibit "F"
7.	Maureen C. Hatch, Ph.D.	Exhibit "G"
8.	Alastair W.M. Hay, Ph.D.	Exhibit "H"
9.	Herbert Kay, Ph.D.	Exhibit "I"
10.	Ronald H. Kerman, Ph.D.	Exhibit "J"
11.	Marvin S. Legator, Ph.D.	Exhibit "K"
12.	Alan Scott Levin, M.D.	Exhibit "L"
13.	Peter Orris, M.D., M.P.H.	Exhibit "M"
14.	Marvin A. Schneiderman, Ph.D.	Exhibit "N"
15.	Ellen K. Silbergeld, Ph.D.	Exhibit "O"
16.	Raymond Singer, Ph.D.	Exhibit "P"
17.	Theodor D. Sterling, Ph.D.	Exhibit "Q"
18.	Biostatistician/Mathematician (Additional)	Exhibit "R"

PLAINTIFFS' MANAGEMENT COMMITTEE

By Thomas W. Henderson
Thomas W. Henderson, Esquire

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Dr. Charles M. Baron, M.D., is a physiatrist practicing in Philadelphia, Pennsylvania. His curriculum vitae will be supplied.

Dr. Baron will testify as to the performance and interpretation of various tests in the veterans. These will include an eltroencephalogram on both sleep and waking states with nasopharyngeal leads. He will also perfrom electromyograms, nerve conduction velocity tests, and somato sensory evoked potentials of the upper and lower extemities.

Dr. Baron will then testify as to the mechanisms by which toxins produce the changes noted in the tests and what the various tests are capable of determining as to the medical status of the patient.

Then he will relate the results obtained in the testing of each plaintiff examined, give opinions as to the causation of those results where possible from the evidence revealed by the tests, and state the prognosis for the individual plaintiff for further deterioration in test results and/or for the individual's condition as a whole.

Dr. Deborah Anne Barsotti is an Assistant Professor of Toxicology in the Department of Pharmacology and Toxicology of the Philadelphia College of Pharmacy and Science in Philadelphia, Pennsylvania. Her curriculum vitae is attached.

Dr. Barsotti is a toxicologist who has done substantial personal investigative work with halogenated aromatic hydrocarbons. This category of chemicals includes various biphenyls and dioxins, and specifically includes tetrachlorodibenzo-p-dioxin (TCDD). She will testify as to the relative chemical stability and lipophilicity of these chemicals as well as their resistance to degradation, and will testify that these qualities are what account for the perceived and documented bioaccumulation of the chemicals in the human system. Dr. Barsotti will emphasize the difference in results between chronic and acute exposures to these chemicals, testifying as to the varying types of responses to acute and chronic exposures.

Dr. Barsotti will discuss her own work as well as review the literature in these areas, noting differences in routes of administration, and in the species and genetic strain of the animals involved. She will explain these variations and where they permit extrapolation of results from animals to humans. In particular, Dr. Barsotti will also testify as to the similarities in response to these chemicals by rhesus monkeys and by humans, and will explain how the similarities permit extrapolation in this instance.

Dr. Barsotti will also discuss reproductive toxicity,

teratology and post-natal toxicity, including instances where no gross or clinical signes of maternal toxicity could be detected.

CURRICULUM VITAE

DEBORAH ANNE BARSOTTI

ADDRESS: Home - 4818 Trinity Place
Phila., PA 19143
215-724-5387

Business - Phila. College of Pharmacy & Science
Dept. of Pharmacology & Toxicology
43rd & Kingsessing Mall
Phila., PA 19104
215-596-8978

CITIZENSHIP: USA

BIRTHDATE: September 14, 1949

MARITAL STATUS: Married; no children

EDUCATION:

Humboldt State University
Arcata, California - 1967-1972
Bachelor of Arts
Biology-Medical Technology

Humboldt State University
Arcata, California - 1972-1973
Graduate School
Coursework: Electron microscopy
Endocrinology
Instrumentation

University of Wisconsin
Madison, Wisconsin - 1973-1980
Doctor of Philosophy
Pathology
Thesis Title: Gross, Clinical & Reproductive Effects of Polychlorinated Biphenyls (PCBs) in the Rhesus Monkey

EXPERIENCE:

Phila. College of Pharmacy & Science
Phila., PA - January, 1983 to Present
Asst. Professor, Dept. of Pharmacology/Toxicology
Instruct Biological Methods in Toxicology, Toxicology III & Techniques in Electron Microscopy
Advise undergraduate students
Faculty advisor for Tox Club
Member, Advisory Committe for four graduate students
Conduct independent research

Assistant Scientist - July, 1982 to January, 1983
Project Associate - June, 1980 to June, 1982
University of Wisconsin
Dept. of Pathology
Madison, Wisconsin

Coordinated multifaceted research projects involving over 120 rhesus monkeys exposed to low levels of toxins (halogenated aromatic hydrocarbons) and integrated the clinical data and observations with the residue analyses of tissues and fluids obtained by gas chromatography (GC) and confirmed by mass spectrometry (MS).

Supervised the clinical and reproductive evaluations as well as the care of laboratory animals.

Developed data management and word processing systems utilizing on-site computers and tie-ins to a Sperry Univac 1100 to sort, collate and statistically evaluate data.

Conducted gross necropsies and microscopic evaluations and prepared necropsy reports.

Research Assistant - 1976-1980
University of Wisconsin
Dept. of Pathology
Madison, Wisconsin

Conducted radioimmunoassays for serum progesterone and estradiol for use in evaluating the reproductive parameters in rhesus monkeys.

Performed clinical assessments on lab. animals including hematology and clinical chemistries.

Supervised and evaluated data and prepared reports for contractural work.

Separated cellular fractions of tissue homogenates by ultracentrifugation and assayed homogenates and resultant fractions for content of various components.

Provided animal husbandry for rhesus monkey and rat colonies.

Supervised unit members on protocols for experimentation and proper methods of conducting basic laboratory analyses.

Pre-Doctoral Fellow - 1974-1976
University of Wisconsin
Dept. of Pathology
Madison, Wisconsin

Stocked and organized a laboratory for the clinical and reproductive analyses of laboratory animals.

13161

Prepared protocols for long-term feeding studies in the laboratory animals including those for gross, clinical and reproductive assessments.

Developed radioimmunoassay procedures for serum progesterone and estradiol.

Conducted metabolism and distribution studies in rats and rhesus monkeys using radiolabeled isomers of halogenated aromatic hydrocarbons and other chemicals.

Laboratory Assistant - 1970-1972
Humboldt State University
Student Health Center
Arcata, California

Duties included assisting in routine clinical laboratory practices involved in urinalysis, gonococcal screening, VDRLs, heterophiles for mononucleosis, throat cultures and pregnancy tests.

AWARDS/HONORS: National Sea Grant Graduate Student of the Year - 1976.

PROFESSIONAL SOCIETIES:

American Society for Primatologists
Mid-Atlantic Chapter, Society of Toxicology

SEMINARS/MEETINGS:

Participant - Federation of American Societies for Experimental Biology (FASEB), Atlantic City, NJ, April, 1976. Topic: "Effects of polychlorinated biphenyls on reproduction in the primate".

Participant - American Association of Pathologists and Bacteriologists, Boston, MA, March, 1976. Topic: "The Association of Transplacental and Mammary Movement of PCBs with Infant Morbidity and Mortality".

Invited Speaker - 9th Annual Sea Grant Association Meeting, Los Angeles, CA, November, 1976. Topic: "Toxicology of PCBs in the Adult and Infant Rhesus Monkey".

Participant - FASEB, Chicago, IL, April, 1977. Topic: "Effects of polychlorinated biphenyls in nonhuman primates".

Participant - American Chemical Society, 11th Great Lakes Regional Meeting, Stevens Point, WI, June, 1977. Topic: "Responses of infant primates to interuterine and neonatal exposure to polychlorinated biphenyls".

Invited Speaker - Community Meeting on PCBs, University of Wisconsin, Parkside, March, 1977.

13162

Participant - International Symposium on Pathobiology of Environmental Pollutants, Storrs, CT, June, 1977. Topics: "Pathology or rhesus macaques (Macaca mulatta) exposed to tetrachlorodibenzo-p-dioxin (TCDD)" and "Exposure of polychlorinated biphenyl (PCB) to infant rhesus macaques (Macaca mulatta)".

Invited Speaker - Community Meeting on PCBs, Door County, WI, September, 1977.

Invited Speaker - 45th Annual Convention of Association of Midwest Fish and Wildlife Agencies, Milwaukee, WI, July, 1978. Topic: "Consequences of dietary PCB consumption in rhesus monkeys".

Invited Consultant - Symposium on PBB Litigation, Traverse City, MI, July, 1978. Topic: "PBB toxicity in the rhesus monkey".

Invited Speaker - Smerkee's Conservation Club, Sheboygan, WI, February, 1979. Topic: "PCBs and their effects on rhesus monkeys".

Participant - FASEB, Dallas, TX, April, 1979. Topic: "Residual effects of polychlorinated biphenyls on adult nonhuman primates and their offspring".

Expert Witness - State of North Carolina, Halifax County; testimony on toxicity of PCBs, June, 1979.

Participant - Sea Grant Symposium on Toxic Materials and their Effects on Marine Resources, Madison, WI, July, 1979.

PUBLICATIONS:

Barsotti, D. A. and Van Miller, J. P.: Reproductive assessments of rhesus monkeys housed in climate controlled conditions. Amer. J. Primatol., submitted 1983.

Barsotti, D. A.: Long term reproductive assessment of rhesus monkeys exposed to chlorinated biphenyls (Aroclor 1248). Fd. Cosmet. Toxicol., submitted 1983.

Barsotti, D. A. and Van Miller, J. P.: Accumulation of a commercial polychlorinated biphenyl mixture (Aroclor 1010) in adult rhesus monkeys and their nursing offspring. Toxicology. In press.

Bowman, R. E., Heironimus, M. P. and Barsotti, D. A.: Locomotor hyperactivity in PCB-exposed rhesus monkeys. Neurotoxicol. 2:251-268, 1981.

Barsotti, D. A., Abrahamson, L. J., Marlar, R. J. and Allen, J. R.: The effect of climate controlled housing on the reproductive potential of the rhesus monkey. J. Reprod. Fertil. 59:15-20, 1980.

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Allen, J. R., Barsotti, D. A. and Carstens, L. A.: Residual effects of polychlorinated biphenyls on adult nonhuman primates and their offspring. J. Toxicol. Environ. Hlth. 6:55-66, 1980.

Allen, J. R., Barsotti, D. A. and Van Miller, J. P.: Toxicological effects of Aroclor 1016 on nonhuman primates. EPA Report #68-02:2464, 1980.

Barsotti, D. A., Abrahamson, L. J. and Allen, J. R.: Hormonal alterations in female rhesus monkeys fed diets containing 2,3,7,8-tetrachlorodibenzo-p-dioxin. Bull. Environ. Contam. Toxicol. 21:463-469, 1979.

Barsotti, D. A., Carstens, L. A. and Allen, J. R.: Residual effects of polychlorinated biphenyls on adult nonhuman primates and their offspring. Fed. Proc. 38:1119, 1979 (Abstract).

Allen, J. R., Barsotti, D. A. and Lambrecht, L. K.: Reproductive effects of halogenated aromatic hydrocarbons on nonhuman primates. New York Academy of Sciences, 320:419-427, 1979.

Allen, J. R., Barsotti, D. A. and Van Miller, J. P.: Pathology of rhesus macaçques (Macaca mulatta) exposed to tetrachlorodibenzo-p-dioxin (TCDD). International Symposium on Pathology of Environmental Pollutants, National Research Council, 346-355, 1979.

Allen, J. R., Van Miller, J. P. and Barsotti, D. A.: Toxicological responses of nonhuman primates to 1,2,4,6,7,8-hexachlorodibenzo-p-dioxin (HCDD). Toxicol. Appl. Pharmacol. 47:179, 1979 (Abstract).

Carstens, L. A., Barsotti, D. A. and Allen, J. R.: Exposure of polychlorinated biphenyl (PCB) to infant rhesus macaques (Macaca mulatta). International Symposium on Pathobiology of Environmental Pollutants, National Research Council, 339-345, 1979.

Schantz, S. L., Barsotti, D. A. and Allen, J. R.: Toxicological effects produced in nonhuman primates chronically exposed to fifty parts per trillion 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). Toxicol. Appl. Pharmacol. 46:180, 1979 (Abstract).

Allen, J. R., Lambrecht, L. K. and Barsotti, D. A.: Some general effects of polybrominated biphenyls in nonhuman primates. J. Am. Vet. Med. Assoc. 173 11:1485-1489, 1978.

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Allen, J. R., Barsotti, D. A., Van Miller, J. P., Abrahamson, L. J. and Lalich, J. J.: Morphological changes in monkeys consuming a diet containing low levels of 2,3,7,8-tetrachlorodibenzo-p-dioxin. Fd. Cosmet., Toxicol. 15:401-410, 1977.

Allen, J. R. and Barsotti, D. A.: Responses of infant primates to interuterine and neonatal exposure of polychlorinated biphenyls. American Chemical Society, Proceedings of 11th Great Lakes Regional Meeting, June, 1977 (Abstract).

Allen, J. R., Barsotti, D. A. and Van Miller, J. P.: Reproductive dysfunction in nonhuman primates exposed to dioxins. Toxicol. Appl. Pharmacol. 41:179, 1977 (Abstract).

Norback, D. H. and Barsotti, D. A.: Effects of polychlorinated biphenyls in nonhuman primates. Fed. Proc. 365:396, 1977 (Abstract).

Barsotti, D. A., Marlar, R. J. and Allen, J. R.: Reproductive dysfunctions in rhesus monkeys exposed to low levels of polychlorinated biphenyls (Aroclor 1248). Fd. Cosmet. Toxicol. 14:99-103, 1976.

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Allen, J. R. and Barsotti, D. A.: The effects of transplacental and mammary movement of PCBs on infant rhesus monkeys. Toxicology 6:331-340, 1976.

Allen, J. R., Barsotti, D. A. and Carstens, L. A.: Residual effects of short term, low level exposure of nonhuman primates to polychlorinated biphenyls. Toxicol. Appl. Pharmacol. 30:440-451, 1974.

Dr. Ronald Corderio, M.D., is an internist practicing in Philadelphia, Pennsylvania. His curriculum vitae will be supplied.

Dr. Corderio will testify that he is currently engaged in the private practice of medicine as an internist. He will testify that he personally has examined and/or treated over five hundred Vietnam veterans for complaints related to Agent Orange. He will testify as to the type of interview he has conducted with each veteran, the type of tests that each veteran should have performed, and the clinical significance of positive or negative findings on each of those tests. He will also discuss how toxins, and specifically Agent Orange, can cause changes in each of the tests and what such changes portend for the individual.

Dr. Corderio will next discuss some of the available medical literature in both animals and humans to further validate his own work.

Dr. Corderio will then outline in detail the results obtained from his own extensive investigation into Agent Orange toxicity based upon his examination of more than five hundred veterans, and will present those conclusions which he feels are reasonably appropriate based upon an analysis of his investigative work.

With this material as background, Dr. Corderio will then proceed to present the test results which have been obtained for each court-approved representative veteran plaintiff. He will

interpret each of the test results in terms of those individual plaintiffs.

Finally, he will testify on generic causation and specific proximate causation in relation to each representative veteran plaintiff. He will also testify as to prognosis for each representative veteran plaintiff.

ARTHUR W. GALSTON, Ph.D.

Dr. Galston is Eaton Professor of Botany, Department of Biology, at Yale University. His Curriculum Vitae will be supplied.

Dr. Galston is a plant physiologist and has personally observed the effect of the spraying of Agent Orange on the Vietnam ecosystem, i.e. the devastation of the Vietnamese countryside. Dr. Galston has been in Vietnam on four occasions between 1971 and 1982, and will describe those observations while in Vietnam, with such pictorial evidence as is available.

Dr. Galston will testify to the potential and actual effects of phenoxy herbicides and their contaminants, both in Vietnam and elsewhere, including the United States and Sweden, and other places. The testimony will include the chemistry and the mechanisms of action of such chemicals on plant life.

In addition, Dr. Galston will testify to the fate of Agent Orange and other phenoxy herbicides and their contaminants, especially TCDD, in the environment generally and in Vietnam in particular. Dr. Galston will testify to the persistence of such chemicals on plants, in water, and in soil, such that exposure to the phenoxy herbicides and their contaminants, especially TCDD, by the veterans in sprayed areas in Vietnam is presumed.

The bases or grounds for Dr. Galston's testimony as to any facts and opinions expressed are a review of the scientific literature and his personal research and experience.

Dr. John Garofalo is a immunologist practicing in Philadelphia, Pennsylvania. His curriculum vitae will be supplied.

Dr. Garofalo will testify to the performance of certain tests on the veteran plaintiffs and their wives and children and to the interpretation of those test results. Specifically, he will be conducting phenotyping assay tests for, among others, B-lymphocytes, K cells, T-lymphocytes, T-helper cells, T-cytotoxic cells, and T-suppressor cells. The purpose of these tests is to determine antigen levels, antibody levels, and the presence of a viral defenses and immune surveillance systems, and to identify various types of cells that may be indicators of and/or precursors of malignancy. Not only will the tests determine the presence of such factors, but they will also include functional assays of each.

LENNART HARDELL, M.D.

Dr. Hardell is employed by the University Hospital in its Department of Oncology in Umeå, Sweden, where he specializes in internal medicine and oncology. His work includes diagnosis, treatment, and evaluation of possible causes of cancer, and education of medical students.

Dr. Hardell will testify to several epidemiological studies which he and colleagues have conducted in Sweden. This research includes investigations concerning the relationship between the risk for different types of cancer and exposure to phenoxy herbicides and chlorophenols. The research has been published in the medical and scientific literature.

These studies utilized the case-control study as the vehicle for investigation. Certain methodological aspects, such as selection of cases, selection of controls, assessment of exposure, and statistical methods, were considered; and then utilization was based upon thoroughly considered aspects of bias, all of which were well controlled.

Specifically, these studies, four in number, involved soft tissue sarcomas, malignant lymphomas, and colon cancer. Highly statistically significant risks of soft tissue sarcomas and malignant lymphoma were found, whereas no association was found for colon cancer. In point of fact, the negative finding for colon cancer strongly supports the statistical significance of the increased risk demonstrated for soft tissue sarcomas and malignant lymphomas, i.e. a presumed causal relationship between exposure to phenoxy herbicides and human cancer particularly of soft tissue sarcoma and malignant lymphoma.

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Dr. Hardell has also seen in his clinical practice basal cell carcinoma of persons previously exposed to phenoxy herbicides, with no other known confounding variables.

With respect to those cases with soft tissue sarcoma, malignant lymphoma, and basal cell carcinomas, Dr. Hardell will testify that the presumed exposure to Agent Orange caused, in significant part, such neoplastic processes.

The bases for Dr. Hardell's testimony as to various facts and opinion include: educational background; professional training and experience; review of the applicable medical and scientific literature; personal research; and a review of the pertinent medical data of the relevant representative plaintiffs.

MAUREEN C. HATCH, Ph.D.

Dr. Hatch is Assistant Professor of Epidemiology at Columbia University, School of Public Health, in New York City. Her Curriculum Vitae will be supplied.

The subject matter about which Dr. Hatch will testify is reproductive toxicology and its specific applicability to miscarriages and congenital malformations (birth defects) in the wives and children of Vietnam veterans.

Dr. Hatch will testify at length to the data collected in Vietnam regarding untoward pregnancy outcomes. Dr. Hatch is one of two investigators who are to publish that portion of the International Symposium held in Ho Chi Minh City in January, 1983 having to do with reproductive toxicology as a result of exposure to Agent Orange and other phenoxy herbicide spraying in Vietnam.

The results of these data demonstrate a statistically significant increase in certain congenital malformations, e.g. cleft palate, limb deformaties, and anencephaly, as a result of paternal mediated reproductive effects. The exposure of the fathers was to the spraying of Agent Orange in Vietnam. The mothers were not exposed.

These human data are coupled with positive, consistent animal data. For example, such studies where males were exposed indicate the following; the male gonads are a target site of 2,3,7,8-TCDD action; at the endocrinological level, there has been demonstrated a major effect, i.e., AHH receptor in male gonads; which very nicely provides a mechanistic linkage; and finally, abnormal biochemical and morphologic characteristics of the sperm have been likewise demonstrated.

ALASTAIR W.M. HAY, Ph.D.

Dr. Hay is a lecturer on Chemical Pathology, Department of Chemical Pathology, Old Medical School, University of Leeds, Leeds, England. His partial Curriculum Vitae is attached.

Dr. Hay will testify to a broad spectrum of matters related to Agent Orange, phenoxy herbicides, and their contaminants, including dioxins, especially 2,3,7,8-TCDD.

Dr. Hay will discuss in detail his knowledge of the various phenoxy herbicides and their contaminants, including but not limited to the various aspects of: chemistry; biochemistry; manufacture and/or production; fate in the environment, animals, and humans; modes of exposure, i.e. absorption, ingestion and inhalation, specifically by the veterans who served in Vietnam; toxicity; and the state of the medical and scientific literature at various times since at least 1957 forward.

The medical and scientific literature, attendance and participation in various symposia, review of various documents of certain defendants, personal research, and experience form the bases of whatever facts and opinions to which Dr. Hay will testify.

Dr. Hay's testimony regarding the medical and scientific literature will include an exposition of the definitions and explanations, and their applicability to the troops exposed in Vietnam, of the phenoxy herbicides and their contaminants, in the following areas: plant physiology; toxicology; neuro-toxicology. both neurological and psychological; epidemiology; immunology; mutagenicity; teratology; reproductive toxicology; and carcinogenicity.

More specifically, the phenoxy herbicides, including Agent Orange, 2,4-D and 2,4,5-T, and their contaminants, including dioxins, especially TCDD are highly toxic, neuro-toxic, immuno-suppressive, teratogenic, potentially mutagenic, and certainly carcinogenic. As a carcinogen, e.g. TCDD, it has no safe level and indeed any single exposure may prove to result in human cancer many years later; said in another way, there is no "no effect" level that can be established.

Dr. Hay will testify to examples of the grounds which support the above, including: knowledge of spraying Agent Orange, especially its effect on the Vietnamese countryside; the purpose and historical tracing of the animal studies; historical tracing of the human data, including the various industrial incidents since 1949; references to specific documents, such as the EPA Dioxin document (presently in Draft form); various cancer epidemiology; pertinent teratology epidemiology; various studies of the Vietnamese, especially in area of reproductive toxicology; and those reports of the symptoms and diagnoses of the U.S. Vietnam veterans.

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Name:	Alastair Watt Macintyre HAY
D.O.B.:	21 April 1947
Marital Status:	Married
Children:	1 son (Tom)
Place of Birth:	Glasgow, Scotland
Nationality:	British
Degrees:	B.Sc.(Hons), Chemistry IIA - London 1969 Ph.D., Biochemistry, London 1973
Home Address:	School House, Arthington Lane, Arthington, Leeds LS21 1PE England.
Work Address:	Department of Chemical Pathology, Old Medical School, University of Leeds, Leeds LS2 9NL England.
Place of Secondary Education:	Gifford Technical High School, Bulowayo, Zimbabwe (formerly Rhodesia)
Present Appointment:	University lecturer in Chemical Pathology since April 1979 (University of Leeds) Leeds, England.
Former Appointments:	Research Fellow - Zoological Soc. of London September 1972 - November 1977 Research Fellow - University of Leeds, Department of Animal Physiology and Nutrition December 1977 - March 1979

PUBLICATIONS

Books

(i) Alastair Hay. The Chemical Scythe: Lessons of 2,4,5-T and Dioxin. Plenum Press. 265pp. August 1982

(ii) Sean Murphy, Alastair Hay and Steven Rose. No Fire: No Thunder. The threat of chemical and biological warfare. Pluto Press. (To be published in January 1984). 135pp.

Scientific Papers

Some 50 scientific papers including:

(i) Hay, A.W.M., Mawer, E.B., Hassan, A.G., Crawford, M.A., & Stevens, P.A. The role of essential fatty acids in vitamin D dependent calcium absorption in the intestine. Proc. of 5th Vitamin D Workshop. Williamsburg USA now in Vitamin D, Chemical, Biochemical and Clinical Endocrinology of Calcium

Metabolism. Walter de Gruyter. Berlin. 1982 pp309-311.

(ii) Hay, Alastair. Vitamin D: Sunlight and precursors. Nature. 297, 364 (1982)

(iii) Hay, A. Herbicides, Trichlorophenols and soft tissue sarcomas. Lancet I, 1240, (1982).

(iv) Hay, A. It kills weeds, but what about people? New Scientist. 94, No.1314. pp158-161 (1982).

(v) Hay,A ., Murphy, S., Robinson, J.P., and S. Rose. The poison cloud hanging over Europe. New Scientist. 93, No.1296 pp630-635 (1982).

(vi) Hay, Alastair. New Pathways for clorinated dioxins. Nature, 294, 514-515 (1981).

(vii) Hay, A. Experimental Toxicology and cytogenetics: an overview. In "Herbicides and War" to be published by Stockholm International Peace Research Institute. (1984) A. Westing, Ed.

(viii) Hay,A. The Mutagenic properties of 2,3,7,8-Tetrachloro-dibenzo-p-dioxin in "Chlorinated Dioxins and Dibenzofurans in the Total Environment. Vol II" Edit. by Keith, L.H. et al to be published in 1984.

Other Publications

I have written some 90 odd articles for the News, News and Views and books review section of the scientific journal Nature since 1976.

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Dr. Herbert Kaye, Ph.D., is a psychologist in the Department of Psychology at the State University of New York at Stoneybrook, Long Island and a visiting Associate Professor in the Department of Psychiatry at New York University Medical Center. His curriculum vitae will be supplied.

Dr. Kaye will testify concerning the significance of a battery of quantitative neurophysiological tests called neurometrics will which be performed on the veteran, wife and children plaintiffs. The procedures were developed in part by Dr. Kaye in conjunction with medical and psychological researchers from this and other countries. He will testify that neurometrics, on which he has written extensively, is a sophisticated battery of electrical tests in use for about fifty years, which are highly efficient in determing cortical EEG and evoked responses.

Dr. Kay will explain the model used in the computerization against which the test results are compared and will explain how deviations from normal produce certain effects.

Dr. Kaye will also discuss the mechanism by which toxins produce these altered responses, and what effect those altered responses have upon the individual veterans at present, and the prognosis for any additional changes or deterioration in the future based upon an assumed bioaccumulation of the toxic materials in the system. In doing so, he will rely on his experience in diagnosing many Vietnam veterans exposed to Agent Orange.

RONALD H. KERMAN, Ph.D.

Dr. Kerman is Associate Professor, and Chief, Cellular Immunology, Clinical Immunology Laboratories, the University of Texas Medical School at Houston. His Curriculum Vitae is attached.

Dr. Kerman will testify that 2,3,7,8-TCDD in particular causes, among others, immuno-suppressive effects, as reported in the literature regarding the various animal species studies. Specifically, TCDD has been demonstrated to suppress T-cell mediated immunity in such species. This effect likewise has been demonstrated in humans by Bekesi, specifically an alteration of mature T-cells.

Dr. Kerman will testify that the special scientific discipline involved is immuno-toxicology which has been defined as "the undesirable effects of an inappropriate response of the immune system". The bases for the facts and opinions to which Dr. Kerman will testify include a review of the applicable medical and scientific literature, his educational and professional background, and his work in connection with the Texas Agent Orange Study.

Dr. Kerman will discuss the following in his testimony: the immune system, with its organic, cellular, and humoral components - most especially with regard to the latter, T-helper cells, B-cells, plasma cells and immunoglobulin production; immune response, both beneficial and harmful; the various experimental studies, particularly those demonstrating atrophy of the thymus, weight loss, depletion of lymphoid organs, lymphopenia, cutaneous type delayed hypersensitivity (skin thickness) and altered bacterial immunity.

Dr. Kerman will testify that on the basis of the above a person exposed to TCDD might have increased predisposition to increased infection and neoplasm (cancer).

CURRICULUM VITAE

Ronald H. Kerman, Ph.D.

DATE OF BIRTH: June 10, 1943

PLACE OF BIRTH: Chicago, Illinois

NATIONALITY: U.S. Citizen

SEX: Male

EDUCATION:

1965	University of Illinois, B.S. (with Honors)
1967	University of Illinois, M.S.
1969	University of Illinois, Ph.D. in Immunology

HONORS:

1965	Bachelor of Science with General Honors in the College
1967-1969	Recipient of Public Health Service Predoctoral Traineeship
1967	Phi Sigma National Biological Honorary
1969-1971	Recipient of Public Health Service Postdoctoral Traineeship
1970	Society of Sigma Xi

RESEARCH AND PROFESSIONAL EXPERIENCE:

1983-	Associate Professor Department of Pathology, and Chief, Cellular Immunology, Clinical Immunology Laboratories, The University of Texas Medical School at Houston
1981-	Associate Professor Department of Surgery, and Head, Histocompatibility and Immune Evaluation Laboratories, Division of Organ Transplantation, The University of Texas Medical School at Houston
1977-	Member, Program in Immunology, Graduate School of Biomedical Sciences, The University of Texas Health Science Center at Houston
1977-1980	Assistant Professor Department of Surgery, and Head, Histocompatibility and Immune Evaluation Laboratories, Division of Organ Transplantation, The University of Texas Medical School at Houston
1974-1977	Assistant Professor Department of Surgery, Loyola University Stritch School of Medicine, Maywood, Illinois
1973-1977	Research Immunologist Chief, Immunobiology Research Laboratory, Research Service, V. A. Hospital, Hines, Illinois
1972-1973	Assistant Professor Department of Microbiology, Jefferson Medical College
1969-1971	Postdoctoral Fellow, (Immunology) Children's Hospital of Philadelphia and The University of Pennsylvania School of Medicine

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PROFESSIONAL SOCIETIES:

The Transplantation Society (Editorial Board, Transplantation and Member, Symposium Committee)
American Association of Immunologists
American Association for Cancer Research
New York Academy of Sciences
American Society of Transplant Physicians (Member, and Vice Chairman, Scientific Studies Committee)
Society for Experimental Biology and Medicine
International Society for Heart Transplantation
American Association for the Advancement of Science
American Society for Histocompatibility and Immunogenetics (Chairman, Finance and Audit Committee, and Member, Laboratory Accreditation Committee)

RESEARCH INTERESTS:

Immunologic response to allotransplantation and malignancy
Evaluation of immunocompetency

RESEARCH SUPPORT:

1974-1978	Co-principal Investigator: Bronchogenic Carcinoma: Immunologic Profile, Radio and Immunotherapy - V.A. Medical Research Grant No. MRIS-8121-08. $213,000
1976-1979	Co-principal Investigator: Immunotherapy Adjuvant to Radiotherapy of Head and Neck Cancer - V.A. Medical Research Grant No. MRIS-8121-06. $73,814
1976-1980	Co-principal Investigator: Factors Influencing Immunocompetence in Human Transplantation - V.A. Medical Research Grant No. MRIS-3068. $68,770
1977-1978	Principal Investigator: Functional and Surface Receptor Differences of Human T-lymphocyte Subpopulations - General Research Support Funds, The University of Texas Medical School at Houston. $5,000
1977-	Principal Investigator: The Role of HLA Typing in Renal Transplantation, ESRD Program, No. 450068. $377,400 (last year)
1977-	Principal Investigator: Immune Monitoring for the Diagnosis of Renal Allograft Rejection, ESRD Program, No. 450068. $544,800 (last year)
1983-1984	Principal Investigator: Immune Evaluation of Veterans Exposed to Agent Orange. Texas Veterans Agent Orange Assistance Program, IAC(83-84)1266. $93,352

OTHER ACTIVITIES:

Special Consultant in Immunology to the Epidemiology and Disease Control Study Section, NIH
Consultant in Immunology and Histocompatibility Testing to the Department of Laboratory Medicine, M.D. Anderson Hospital and Tumor Institute
Editorial Board, Transplantation
Review of manuscripts for the journal Human Immunology
Review of manuscripts for the journal Transplantation
Review of manuscripts for the journal Heart Transplantation
Book reviewer for Journal of American Medical Association
Literature Reviewer for The American Association of Clinical Histocompatibility Testing -- AACHTion News

Grant Reviewer for the Kidney Foundation of Canada
Grant Reviewer in Transplantation Immunology for The March of Dimes - Birth Defects Foundation
Outside Reviewer of Research Proposals in Immunology for the Research and Development Committee, The Veterans Administration Research Service
Invited Participant (as a testing laboratory) in The Third American HLA Workshop
Invited Participant (as a testing laboratory) in The Eighth International Histocompatibility Workshop "Relevance of DR typing to renal allograft survival"
Invited Participant (as a testing laboratory) in The International Transfusion and Transplantation Workshop
Invited Participant (as a testing laboratory) for the Ninth International Histocompatibility Workshop
Invited Presenter at an NIH Workshop, "The Biological Relevance of Immune Suppression as Induced by Genetic, Therapeutic and Environmental Factors"
Invited Participant (as a testing laboratory) in the International Collaborative Transplant Study
Laboratory Inspector for Clinical Laboratory Accreditation in Histocompatibility for The American Society for Histocompatibility and Immunogenetics and The College of American Pathologists
Chairman, Finance and Audit Committee for The American Society for Histocompatibility and Immunogenetics
Member, Symposium and Affiliations Committee, The Transplantation Society
Member and Vice-Chairman, Scientific Studies Committee, American Society of Transplant Physicians
Member, Acquired Immune Deficiency Syndrome (AIDS) Working Group for the Houston Area
Chairman, Organizing Committee and Host for The Fourth International Immune Monitoring Symposium: Immunological Evaluation and Monitoring of the Transplant Recipient (1983)
Member, Organizing Committee for the International Symposium on Relevant Immunological Factors in Clinical Kidney Transplantation, Heidelberg, West Germany, 1985

Member, UTMSH Admissions Interview Committee
Member, UTMSH Admissions Committee
Member, Medical Review Board, Organ Transplantation Center, UTMSH
Member, Committee on Subject Selection for The University of Texas System Agent Orange Study
Member, Steering Committee, Program in Immunology, UT-GSBS
Chairman, By-Laws Committee, Program in Immunology, UT-GSBS
Course Director, "Methods in Cellular Immunology," a Program in Immunology Course, UT-GSBS

BIBLIOGRAPHY

Ronald H. Kerman, Ph.D.

Publications

1. Kerman, R., Segre, D. and Myers, W.L.: Altered response to pneumococcal polysaccharide in offspring of immunologically paralyzed mice. Science 156:1514, 1967.

2. Kerman, R., Segre, D. and Myers, W.L.: The role of immune and natural specific antibodies in immunologic paralysis and immunity of mice to pneumococcal polysaccharide Type III. J. Immunol. 104:655, 1970.

3. Kerman, R. and Segre, D.: Anti-pneumococcal polysaccharide Type III hemolytic plaques in mice: Cellular response in immunity and immunologic paralysis. J. Immunol. 104:1262, 1970.

4. Kerman, R. and Harris, T.N.: Resistance to denaturation by periodate of a dialyzable histocompatibility antigen. Proc. Soc. Exp. Biol. Med. 141:179-183, 1972.

5. Kerman, R.H., Harris, T.N. and Harris, S.: Preparation of a dialyzable histocompatibility antigen from balb/c mice. Proc. Natl. Acad. Sci. 69:223-227, 1972.

6. Smith, R.A., Kerman, R., Ezdinli, E. and Stefani, S.: A modified assay for the detection of human adult active rosette forming cells. J. Immunol. Meth. 8:175-184, 1975.

7. Kerman, R. and Stefani, S.: Immunological evaluation of patients with solid tumors before and after radiotherapy. In Crispen, R.G. (ed.): Neoplasm Immunity: Mechanisms, pp. 109-120. University of Illinois Press, 1976.

8. Stefani, S., Kerman, R. and Abbate, J.: Immune evaluation of lung cancer patients undergoing radiation therapy. Cancer 37:2792-2796, 1976.

9. Stefani, S., Kerman, R. and Abbate, J.: Serial studies of immunocompetence of patients undergoing radiotherapy for malignancies of the head and neck. Am. J. Roentgenol. 126:880-886, 1976.

10. Kerman, R.H. and Geis, W.P.: Total and active T-cell kinetics in renal allograft recipients. Surgery 79:398-407, 1976.

11. Kerman, R., Smith, R., Stefani, S. and Ezdinli, E.: Active T-rosette forming cells in the peripheral blood of cancer patients. Cancer Res. 36:3274-3278, 1976.

12. Kerman, R., Smith, R., Ezdinli, E. and Stefani, S.: Unification and technical aspects of total T, active T and B lymphocyte rosette assays. Immunol. Comm. 5(7-8):685-694, 1976.

13. Dodson, M.G., Kerman, R.H., Lange, C.F., Stefani, S. and O'Leary, J.A.: T and B cells in pregnancy. Obstet. Gynecol. 49:299-302, 1977.

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14. Kerman, R.H. and Stefani, S.: PHA stimulation of lymphocytes from patients with lung cancer. Oncology 34:10-12, 1977.

15. Kerman, R.H. and Stefani, S.: Radio and immunotherapy of lung cancer: A preliminary report. In Crispen, R.G. (ed.): Neoplasm Immunity-Solid Tumor Therapy, pp. 29-35. Franklin Institute Press, 1977.

16. Stefani, S. and Kerman, R.H.: Lymphocyte response to PHA before and after radiation therapy in patients with carcinomas of the head and neck. J. Laryngol. Otol. 91:605-609, 1977.

17. Kerman, R.H., Ing, T.S., Hano, J.E. and Geis, W.P.: Prognostic significance of the active T-RFC in renal allograft survival. Surgery 82:607-612, 1977.

18. Marshack, M., Toto, P. and Kerman, R.H.: Delayed hypersensitivity in the hamster cheek pouch. J. Immunol. Meth. 15:325-330, 1977.

19. Marshack, M., Toto, P. and Kerman, R.H.: Immunotherapy of chemically-induced tumors in the hamster cheek pouch with dinitrochlorobenezene. J. Dental Res. 57:625-630, 1978.

20. Stefani, S. and Kerman, R.: Prognostic significance of pre-therapy delayed hypersensitivity and T-cell levels in patients with lung cancer. In Nieburgs, H.E. (ed.): Proceedings of the Third International Symposium on the Detection and Prevention of Cancer, Vol. 1, Part II, pp. 785-797. Marcel Dekker, Inc., 1978.

21. Geis, W.P., Iwatsuki, S., Molnar, Z., Giacchino, J.L., Kerman, R.H., Ing, T.S. and Hano, J.E.: Immunoblastic pseudo-lymphoma in renal allograft recipients. Arch. Surg. 113:461-466, 1978.

22. Dodson, M., Klegerman, M., Kerman, R.H., Lange, C., Tessler, J. and O'Leary, J.: Bechet syndrome: With immunologic evaluation. Obstet. Gynecol. 51:621-625, 1978.

23. Dodson, M.G., Klegerman, M.E., Menon, M., Kerman, R.H., Lange, C.F. and O'Leary, J.A.: Establishment and characterization of a squamous cell carcinoma of the vulva in tissue culture and immunological evaluation of the host. Am. J. Obstet. Gynecol. 131:606-619, 1978.

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Abstracts and Presentations

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4. Kerman, R., Stefani, S. and Geis, W.P.: Total and active T-cell dynamics in renal allograft recipients. Abstracts of the American Society Transplant Surgeons, Chicago, Illinois, May 1976.

5. Kerman, R., Stefani, S., Smith, R., Ezdinli, E. and Geis, W.P.: Immunological evaluation of patients with solid tumors and hematological malignancies. Presented at the 1975 Cancer Symposium, Neoplasm Immunity: Mechanism, Chicago, Illinois, September 1975.

6. Stefani, S., Kerman, R. and Abbate, J.: Immunological evaluation of patients with bronchogenic carcinoma. Presented at the American Society of Therapeutic Radiology, San Francisco, California, October 1975.

7. Stefani, S. and Kerman, R.: Determination and prognostic value of immunocompetence in patients with lung cancer treated by radiotherapy. Abstracts of the Third International Symposium on Detection and Prevention of Cancer, New York, April 1976.

8. Geis, W.P., Vaz, A.L. and Kerman, R.H.: Steroid sparing effect of ATG in high risk renal allograft survival. Presented at the American Society of Transplant Surgeons Meeting, Chicago, Illinois, May 1976.

9. Kerman, R.H., and Geis, W.P.: Prognostic significance of the active T-cell in renal allograft survival. Presented at the American Society Transplant Surgeons Meeting, Chicago, Illinois, May 1976.

10. Stefani, S. and Kerman, R.: BCG and radiotherapy in bronchogenic carcinoma: Preliminary report. Presented at the American Society of Therapeutic Radiology, Atlanta, Georgia, October 1976.

11. Kerman, R. and Geis, W.P.: T-RFC monitoring of CMI events in renal allograft recipients. Presented at the Sixth International Congress of the Transplantation Society Special Session Immunological Monitoring of Transplant Recipient, New York, August 1976.

12. Kerman, R. and Stefani, S.: Radio and immunotherapy of lung cancer: A preliminary report. Presented at the 1977 Chicago Symposium: Immunotherapy of Solid Tumors, Chicago Illinois, February 24-25, 1977.

13. Stefani, S. and Kerman, R.H.: Relevance of immunologic analysis for patients with inoperable lung cancer treated by radiotherapy. Presented at an NCI sponsored Symposium "The Second Conference on Lung Cancer Treatment," at Airlie House, Virginia, May 22-24, 1977.

14. Kerman, R.H., Ing, T.S., Hano, J.E. and Geis, W.P.: Prognostic significance of active T-RFC in renal allograft survival. Abstracts of First International Symposium on Immunological Monitoring of the Transplant Recipient. London, Ontario, June 8-10, 1977.

15. Kerman, R.H. and Geis, W.P.: T-RFC monitoring of CMI events in renal allograft recipients. Abstracts of First International Symposium on Immunological Monitoring of the Transplant Recipient. London, Ontario, June 8-10, 1977.

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17. Geis, W.P., Iwatsuki, S., Molnar, Z., Giacchino, J.L., Kerman, R.H., Ing, T.S. and Hano, J.E.: Immunoblastic pseudo-lymphoma in renal allograft recipients. Presented at the Western Surgical Association, Las Vegas, Nevada, November 15, 1977.

18. Kerman, R.H., Roesler, H. and Kahan, B.D.: Specific stimulation of active T-Rosette forming cells by 3M KCl solubilized antigen. Fed. Proc., 1978. Presented at the FASEB-AAI Meeting, Atlanta, Georgia, June 1978.

19. Kerman, R.H., Floyd, M., Conner, W., McConnell, B.J., McConnell, R. and Kahan, B.D.: Correlation of active T-RFC and spontaneous blastogenesis with decreased renal allograft function. Abstracts of the American Association for Clinical Histocompatibility Testing, Boston, Massachusetts, June 1978.

20. Kerman, R.H., Roesler, H. and Kahan, B.D.: Increased active T-RFC with in vitro stimulation by soluble donor antigen. Abstracts of the Amer. Assoc. of Clin. Histocomp. Testing, Boston, Massachusetts, June 1978.

21. Kerman, R.H., Floyd, M., Conner, W., McConnell, R., McConnell, B.J., Van Buren, C.T. and Kahan, B.D.: Combined immunological and radionuclide techniques to monitor renal allograft rejection. Presented at the VII International Congress of The Transplantation Society, Rome, Italy, September 1978.

22. Kerman, R.H.: Invited speaker to a special workshop "Immunological Monitoring of the Transplant Patients", VII International Congress of The Transplantation Society, Rome, Italy, September 1978.

23. Kahan, B.D., Kerman, R. and McConnell, R.: Combination of immunological and radionuclide techniques diagnoses allograft rejection. Presented at the American College of Surgeons, San Francisco, California, October 1978.

24. Michelson, J., McConell, Kerman, R. and Kahan, B.: Association of acute rejection episodes in renal transplant patients with scored results of computer analyzed data. Presented at the Southwest Society of Nuclear Medicine Meeting, March 16, 1979, San Antonio, Texas.

25. Kerman, R.H., Macek, C. and Kahan, B.D.: Increase in 3 different E-rosette markers on human T cells following PHA activation. Fed. Proc. 38 (No. 3, Part II):1282. Presented at the Annual Meeting of The American Association of Immunologists, Dallas, Texas, April 1979.

26. Kerman, R.H.: Immunological considerations in renal transplantation. Clinical Oncology Grand Rounds, M.D. Anderson Hospital and Tumor Institute, September 1979.

27. Kerman, R.H. and Kahan, B.D.: Assessment of immune parameters of transplant recipients on immunosuppressive therapy. Presented at an NIH Workshop on "The Biological Relevance of Immune Suppression as Induced by Genetic Therapy and Environmental Factors," Williamsburg, Virginia, November 1979.

28. Invited participant in a working cadre for the NIH to develop a "Consensus On Immunotoxicology" for the National Toxicology Program, November 1979, Research Triangle Park, N.C., NIEHS, NIH.

29. Kerman, R.H.: Histocompatibility testing in transplantation. Pathology Grand Rounds, St. Luke's Hospital, January 1980.

30. Van Buren, C.T., Kerman, R.H. Van Buren, D. and Kahan, B.D.: Correlation of immune responsiveness with nutritional indices in chronic renal failure patients. Presented at the American Society for Parenteral and Enteral Nutrition, Annual Meeting, Chicago, Illinois, January - February 1980.

31. Kerman, R.H.: Immune monitoring of renal allograft recipients. Surgical Grand Rounds, University of Miami School of Medicine, March 1980.

32. Kerman, R.H.: Pre- and postoperative immune monitoring of allograft recipients. Medical Grand Rounds, Division of Dialysis and Transplantation, Children's Hospital of Los Angeles, April 1980.

33. Kerman, R.H. and Semchuk, R.: Delineation of a radioresistant T cell subpopulation. Fed. Proc. 39(3):945. Presented at the Annual Meeting of The American Association of Immunologists, Anaheim, California, April 1980.

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35. Kerman, R., Peddada, L. and Kahan, B.D.: Correlation of hyperacute rejection with LDA and CDA vs. ^{51}Cr-labeled donor T and B cell targets. Presented at The American Association for Clinical Histocompatibility Testing, St. Louis, Missouri, April 1980.

36. Kerman, R., Floyd, M., Van Buren, C.T. and Kahan, B.D.: Improved allograft survival of strong responder-high risk cadaver recipients with adjuvant immunosuppressive therapy. Presented at the Annual Meeting of The American Association for Clinical Histocompatibility Testing, April 1980.

37. Kerman, R., Conklin, R., Cahall, D. and Kahan, B.D.: Association of cytomegalovirus and renal allograft survival. Presented at the meeting of the American Association for Clinical Histocompatibility Testing, St. Louis, Missouri, April 1980.

38. Kerman, R., Floyd, M., Van Buren, C.T. and Kahan, B.D.: Delineation of donor specific and nonspecific pretransplant immunocompetence as a predictor for LRD allograft survival. Presented at the Meeting of The American Association of Clinical Histocompatibility Testing, St. Louis, Missouri, April 1980.

39. Kerman, R.H., Floyd, M., Van Buren, C.T. and Kahan, B.D.: Improved allograft survival of strong immune responder-high risk recipients with adjuvant immunosuppressive therapy. Presented at the annual meeting of The American Society of Transplant Surgeons, Chicago, Illinois, May 1980.

40. Kerman, R.H., Floyd, M., Van Buren, C.T. and Kahan, B.D.: Correlation of nonspecific immune monitoring of renal allograft recipients with rejection and impaired renal function. Presented at the Annual Meeting of The American Society of Transplant Surgeons, Chicago, Illinois, May 1980.

41. Kerman, R., Floyd, M., Van Buren, C.T. and Kahan, B.D.: Prolonged allograft survival of strong pretransplant immune responders treated with ATG. Presented at the VIIIth International Congress of The Transplantation Society, Boston, Massachusetts, June 1980.

42. Kerman, R., Floyd, M., Van Buren, C.T. and Kahan, B.D.: Prediction of renal allograft survival based on pretransplant non-specific immunocompetence. Presented at The Second International Symposium on Immunological Monitoring of the Transplant Recipient, Leiden, The Netherlands, September 1980.

43. Kerman, R.H., Floyd, M., Van Buren, C.T., McConnell, B.J., McConnell, R. and Kahan, B.D.: Delineation of renal allograft rejection and impaired renal function by serial measurement of non-specific immune parameters. Presented at The Second International Symposium on Immunological Monitoring of the Transplant Recipient, Leiden, The Netherlands, September 1980.

44. Kerman, R.H. and Kahan, B.D.: Increased expression of the active T-RFC receptor as a measure of allosensitization following in vitro stimulation of recipient lymphocytes by soluble donor HLA antigens. Presented at The Second International Symposium on Immunological Monitoring of the Transplant Recipient, Leiden, The Netherlands, September 1980.

45. Kerman, R.H., Floyd, M., Van Buren, C.T. and Kahan, B.D.: Correlation of HLA A,B and DR typing to cadaveric and living related renal allograft survival. Presented at The Second International Symposium on Immunological Monitoring of the Transplant Recipient, Leiden, The Netherlands, September 1980.

46. Floyd, M., Kerman, R., Woo, J., Van Buren, C.T. and Kahan, B.D.: Relationships of beta-2-microglobulin metabolism, immune reactivity and renal allograft rejection. Presented at The Second International Symposium on Immunological Monitoring of the Transplant Recipient, Leiden, The Netherlands, September 1980.

47. Kerman, R.H.: Immune monitoring of renal allograft recipients. Surgical Grand Rounds, University of Chicago, June 1981.

48. Kerman, R.H., Van Buren, C.T., LeGrue, S.J. and Kahan, B.D.: Immunopharmacological monitoring of cadaveric renal allograft recipients receiving Cyclosporin A. Presented at the Annual Meeting of the American Society of Transplant Surgeons, Chicago, Illinois, June 1981.

49. Kerman, R.H., Conklin, R., Cahall, D., Van Buren, C.T. and Kahan, B.D.: CMV and renal allograft rejection. Presented at a Symposium on Host Defenses to Intracellular Pathogens, Franklin Plaza Hotel, Philadelphia, Pennsylvania, June 1981.

50. Schoenberg, L.P., Kahan, B.D. and Kerman, R.H.: The use of Cyclosporin A as immunosuppressive medication in renal transplantation. Presented at The National Kidney Foundation, Inc., Washington, D.C., November 1981. Amer. J. Kidney Diseases, Program for Clinical Dialysis and Transplantation Forum, p. 29.

51. Ettenger, R., Kerman, R., Arnett, J., Jordan, S., Warshaw, B., Harris, R., Wassner, S. and Fine, R.: Sensitization following donor-specific transfusions for live-related renal transplantation. American Society of Nephrology, Washington, D.C., November 1981.

52. Flechner, S., Boileau, M., Payne, W., Van Buren, C., Kerman, R. and Kahan, B.: The use of Cyclosporin A in strong immune responder, high risk renal transplant recipients. American Urological Association, Kansas City, Kansas, 1982.

53. Kerman, R., Van Buren, C., Payne, W., Flechner, S., Agostino, G., Conley, S., Brewer, E. and Kahan, B.: Influence of blood transfusions on immune responsiveness. Presented at The Transfusion and Transplantation Conference, Los Angeles, California, January - February 1982.

54. Agostino, G., Kahan, B.D. and Kerman, R.H.: Suppression of mixed leucocyte culture using mononuclear leukocytes from normals, uremics and allograft recipients. Presented at the Annual Meeting of The American Association of Immunologists, FASEB, New Orleans, Louisiana, April 1982.

55. Agostino, G.J., Kahan, B.D. and Kerman, R.H.: Measurement of suppressor cell status in potential allograft recipients. Presented at the Annual Meeting of The American Association of Clinical Histocompatibility Testing, San Francisco, California, April 1982.

56. Kerman, R.H.: Invited presenter at two workshops on 1) Immune monitoring of allograft recipients and 2) The effect of transfused blood and blood products on uremic hosts. Presented at the Annual Meeting of The North American Transplant Coordinators Organization, San Antonio, Texas, May 1982.

57. Kerman, R.H., Van Buren, C., Flechner, S., Agostino, G., Conley, S., Brewer, E. and Kahan, B.D.: The influence of pretransplant blood transfusions from random donors on immune parameters affecting cadaveric allograft survival. Presented at The Annual Meeting of The American Society of Transplant Surgeons, Chicago, Illinois, June 1982.

58. Agostino, G., Kahan, B.D. and Kerman, R.H.: Suppression of mixed leucocyte culture using leucocytes from normal individuals, uremic individuals, and allograft recipients. Presented at The Annual Meeting of The American Society of Transplant Surgeons, Chicago, Illinois, June 1982.

59. Kerman, R.H.: Invited presenter at a workshop on "Human T lymphocyte subpopulations: Their role in rejection and immunosuppression." Presented at the International Congress of The Transplantation Society, Brighton, England, August 1982.

60. Kerman, R.H.: Invited presenter at a workshop on "Mechanisms responsible for blood transfusion effects." Presented at The International Congress of The Transplantation Society, Brighton, England, August 1982.

61. Ettenger, R.B., Kerman, R., Jordan, S.C., Warshaw, B.L., Harris, R. and Fine, R.: Sensitization after donor-specific transfusions for live-related renal transplantation. Presented at The International Congress of The Transplantation Society, Brighton, England, August 1982.

62. Van Buren, C.T., Kerman, R.H., Agostino, G., Flechner, S. Payne, W. and Kahan, B.D.: Effect of cyclosporine on immunoregulatory cells of renal allograft recipients. Presented at The International Congress of The Transplantation Society, Brighton, England, August 1982.

63. Kerman, R.H., Van Buren, C.T., Payne, W., Flechner, S. and Kahan, B.D.: Monitoring T cell subsets and immune events in renal allograft recipients. Presented at The International Congress of The Transplantation Society, Brighton, England, August 1982.

64. Flechner, S., Kerman, R., Van Buren, C.T., Payne, W. and Kahan, B.D.: The use of cyclosporine and prednisone for high MLC haploidentical living related renal transplants. Presented at The International Congress of The Transplantation Society, Brighton, England, August 1982.

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66. Kerman, R.H., Agostino, G., Van Buren, C.T., Payne, W., Flechner, S., Conley, S., Brewer, E. and Kahan, B.D.: Effect of blood transfusions on graft survival and immune responsiveness. Presented at The International Congress of The Transplantation Society, Brighton, England, August 1982.

67. Kahan, B.D., Kerman, R., Payne, W.D., Flechner, S. and Van Buren, C.T.: Immunopharmacologic studies of cyclosporine-treated renal allograft recipients. Fifth Tripartite Meeting, Society of University Surgeons, Salzburg, Austria, September 1982.

68. Kerman, R.H., Flechner, S., Van Buren, C.T., Payne, W., and Kahan, B.D.: Cyclosporine improves allograft survival in immunologically high-risk renal allograft recipients. Presented at the Third International Immunological Monitoring Symposium, Key Biscayne, Florida, November 1982.

69. Kerman, R.H., Van Buren, C.T., Payne, W., Flechner, S., and Kahan, B.D.: Detection of host presensitization to donor alloantigens utilizing a comprehensive immune crossmatch. Presented at the Third International Immunological Monitoring Symposium, Key Biscayne, Florida, November 1982.

70. Kerman, R.H., Payne, W., Van Buren, C.T., Flechner, S., and Kahan, B.D.: Immune monitoring of renal allograft recipients treated with cyclosporine or azathioprine using donor-specific and nonspecific assays as well as monoclonal T cell reagents. Presented at the Third International Immunological Monitoring Symposium, Key Biscayne, Florida, November 1982.

71. Kerman, R.H.: Invited plenary speaker at the First Annual Meeting of The American Society of Transplant Physicians, "Optimizing immunosuppression: Mode of action of cyclosporine." Chicago, December 1982.

72. Kerman, R.H., Van Buren, C.T., Payne, W., Flechner, S., and Kahan, B.D.: Cyclosporine improves allograft survival in immunologically high-risk renal allograft recipients. Presented at The Annual Meeting, National Kidney Foundation, Clinical Dialysis and Transplant Forum, Chicago, December 1982.

73. Kerman, R.H.: Role of immune evaluation in clinical medicine. Clinical Immunology Grand Rounds, The Children's Memorial Hospital, Chicago, Illinois, December 1982.

74. Kerman, R.H.: Immunologic effects of toxic materials. Presented at Toxicology - Clinical Update, University of Texas Medical Branch, Galveston, Texas, January 1983.

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76. Kerman, R.H.: Immune evaluation of renal failure patients and allograft recipients. Presented at Surgical Grand Rounds, St. Louis University Medical Center, St. Louis, Missouri, March 1983.

77. Kerman, R.H.: Immunological evaluation of hemophiliacs. Presented at a Symposium on Current Problems in the Management of Hemophiliac Complications, Houston, Texas, April 1983.

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80. Van Buren, C., Kerman, R., Agostino, G., Flechner, S., Payne, W.D., and Kahan, B.: Effect of cyclosporine on immunoregulatory cells of renal allograft recipients. Presented at The First International Congress on Cyclosporine, Houston, Texas, May 1983.

81. Kahan, B.D., Van Buren, C., Flechner, S., Payne, W.D., and Kerman, R.: Improved outcome of 150 renal allografts in immunologically high risk recipients treated with cyclosporine. Presented at The First International Congress on Cyclosporine, Houston, Texas, May 1983.

82. Flechner, S.M., Van Buren, C., Kerman, R.H., and Kahan, B.D.: The nephrotoxicity of cyclosporine in renal transplantation. Presented at The First International Congress on Cyclosporine, Houston, Texas, May 1983.

83. Flechner, S.M., Van Buren, C.T., Kerman, R., and Kahan, B.D.: The effect of conversion from cyclosporine to azathioprine immunosuppression for intractable nephrotoxicity. Presented at The First International Congress on Cyclosporine, Houston, Texas, May 1983.

84. Kerman, R.H., Flechner, S., Van Buren, C.T., Payne, W., and Kahan, B.D.: Cyclosporine immunosuppression overcomes immunologic risk factors for recipients of cadaveric renal allografts. Presented at the Annual Meeting of The American Society of Transplant Physicians, Chicago, Illinois, June 1983.

85. Flechner, S.M., Kerman, R.H., Van Buren, C.T., and Kahan, B.D.: The high risk haploidentical living related recipient: Transplantation without blood transfusions and steroid withdrawal using cyclosporine. Presented at the Annual Meeting of The American Society of Transplant Physicians, Chicago, Illinois, June 1983.

86. Kerman, R.H.: Relationship of immunocompetence of hemophiliac patients and acquired immune deficiency syndrome (AIDS). Presented at the Gulf Coast Hemophilia Chapter Meeting, Houston, Texas, October 1983.

87. Kerman, R., Van Buren, C.T., Flechner, S., and Kahan, B.D.: Correlation of visual, ^{51}Cr-release and flow cytometry crossmatch results to graft survival. Presented at The Fourth International Symposium: Immune Monitoring of The Transplant Recipient, Houston, Texas, November 1983.

88. Rogers, A.J., Kerman, R.H., and Kahan, B.D.: The pharmacokinetic and immunobiological activity of cyclosporine in man. Presented at The Fourth International Symposium: Immune Monitoring of The Transplant Recipient, Houston, Texas, November 1983.

89. Kerman, R.H., Manner, C., Ford, K., and Hoots, K.: Comprehensive immune evaluation of 78 hemophiliacs. Presented at the New York Academy of Sciences Symposium on Acquired Immune Deficiency Syndrome, New York, New York, November 1983.

90. Kerman, R., Van Buren, C.T., Flechner, S.M., and Kahan, B.D.: DRW6 and DR3 phenotypes correlating with immune response. Presented at the Annual Meeting of The American Association for Clinical Histocompatibility Testing, Chicago, Illinois, November 1983.

91. Van Buren, C.T., Flechner, S.M., Kerman, R.H., Vaughn, W., and Kahan, B.D.: Cyclosporine improves outcome in high risk cadaveric renal allograft recipients. Presented at the First Meeting of The European Society for Organ Transplantation, Zurich, Switzerland, November 1983.

92. Kerman, R.H.: Cyclosporine immunosuppression for renal transplantation. Presented to Sandoz Pharmaceuticals, Inc., East Hanover, New Jersey, December 1983.

93. Kerman, R.H.: New horizons in transplantation: Influence of cyclosporine on renal transplantation. Invited presenter at the Western Dialysis and Transplantation Society, Park City, Utah, January 1984.

94. Sterling, R.P., Bradley, B.B., Khalil, K.G., Kerman, R.H., and Conklin, R.H.: Comparison of biopsy proven pneumocystis pneumonia in acquired immune deficiency syndrome (AIDS) patients versus renal allograft patients. Presented at The Society for Thoracic Surgeons, San Antonio, Texas, January 1984.

95. Rogers, A.J., Kerman, R.H., and Kahan, B.D.: Correlation of immunopharmacokinetic profiles of cyclosporine-treated allograft recipients and rejection. Presented at The Society for University Surgeons - Residents' Meeting, Chicago, Illinois, February 1984.

MARVIN S. LEGATOR, Ph.D.

Dr. Legator is Professor of Environmental Toxicology, University of Texas Medical School at Galveston. His Curriculum Vitae will be supplied.

The subject matter of Dr. Legator's testimony will include: the teratogenic and carcinogenic effects of TCDD, as well as its mutagenic potential; the multi-system effects of TCDD at extremely low concentrations; the demonstrable effects, both gross and more subtle, of TCDD on animals; the extrapolition of the animal studies to humans, that is, the inherent, intended predictive aspects of the animal data to man; and finally to his work as a geneticist with respect to reproductive toxicology, i.e. male (Vietnam Veterans) - mediated birth defects and certain untoward pregnancy outcomes.

Dr. Legator will testify to the extreme toxicity of dioxins, particularly 2,3,7,8-TCDD. Specifically, his testimony will indicate that TCDD is a complete carcinogen based upon certain animal studies, and that as a carcinogen, there is no safe level and does not have therefore a so-called no effect level. With respect to that, Dr. Legator will describe the extra-ordinary precautions which are taken, and the fears of the researchers, in connection with the laboratory use of TCDD.

In addition, Dr. Legator will testify to the reproductive toxicological effects, i.e. birth defects, and miscarriages of the children and wives of the exposed Vietnam veterans. The animal data in this regard are positive and consistent and provide a mechanistic linkage which confirms the Vietnamese epidemiological study of Hatch and others.

Specifically, therefore Dr. Legator will testify that the miscarriage

of Mrs. Dan G. Jordan and the congenital malformations of the children of Dan G. Jordan, as well as those of Kerry Ryan, daughter of Michael F. Ryan, were caused by the presumed exposure of representative plaintiffs Jordan and Ryan to phenoxy herbicides and dioxins - specifically 2,3,7,8-TCDD -- while serving in Vietnam.

The bases or grounds for such facts and opinions include Dr. Legator's: educational and professional experience; personal researches; review of the applicable medical and scientific literature; and a review of the medical records and/or data of the Jordan and Ryan families.

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ALAN SCOTT LEVIN, M.D.

Dr. Levin is engaged in the practice of medicine in San Francisco, His Curriculum Vitae is attached.

Dr. Levin will testify that phenoxy herbicides and their contaminants, including dioxins, most especially 2,3,7,8-TCDD, cause an assortment of immunological responses, i.e. immuno-toxicity, which predispose persons exposed - by absorption and/or ingestion and/or inhalation - to such chemicals to a whole host of adverse health effects, such as: chloracne or other skin rashes; various neuro-toxic effects; reproductive effects; and neoplasm. In connection with the carcinogenic effect, Dr. Levin will state there is no safe level for this or any other carcinogen, and that a single exposure several years earlier can result in human cancer many years later.

The bases for such facts and opinions expressed herein by Dr. Levin include: review of the medical and scientific literature, including both animal and human data; his personal researches; his clinical experiences; and his personal knowledge of the defoliation of Vietnam by such phenoxy herbicides and dioxins, with such chemicals in the presence of the veterans and their presumed exposure thereby; and review of all pertinent medical data of the representative plaintiffs.

Dr. Levin will discuss the following in his testimony: the immune system, with its organic, cellular, and humoral components - most especially with regard to the latter, T-helper cells, B-cells, plasma cells and immuno-globulin production; immune response, both beneficial and harmful; the various experimental studies, particularly those demonstrating atrophy of the thymus, weight loss, depletion of lymphoid organs, lymphopenia, cutaneous type delayed hypersensitivity (skin thickness) and altered bacterial immunity.

In addition, Dr. Levin will discuss the following and their significance: immunology as molecular biology; chemical-induced immune disregulation; T-cells (lymphocytes from thymus) acting as immune modulators, (for which again there is no "no effect" level); immune surveillance; the similarity of the immune, neurologic, and endocrine systems and their significance in the area of immuno-toxicity; the relationship of immune disregulation caused by chemicals and carcinogenicity.

Dr. Levin will then testify to the causal relationship of the various Agent Orange/dioxin related adverse health effects of the representative plaintiffs, including: chloracne; neuro-toxic effects, both neurological and psychological; reproductive toxic effects, both miscarriages and birth defects; and such neoplastic processes as soft tissue sarcoma, as here a rhabdomyosarcoma, lymphocytic lymphoma and basal cell carcinoma.

CURRICULUM VITAE

Alan Scott Levin, M.D.

Born:	January 12, 1938. Chicago, Illinois.
High School:	Austin, Chicago, Illinois
College:	University of Illinois, Champaign-Urbana, Illinois 1956-1960 B.S. Chemistry in L.A. with Honors.
Graduate School:	University of Illinois (Chicago Medical Center) M.S. in Biochemistry, 1963.
Masters Thesis:	Metabolism of Serum Albumin in Rats with Cirrhosis of the Liver, 1963.
Medical School:	University of Illinois (Chicago Medical Center) M.D. 1964 Alpha Omega Alpha Honor Medical Society, 1963
Internship:	Children's Hospital Medical Center, Boston, Mass.
Fellowships:	Traineeship Grant, Harvard Medical School 1964 Research Assistant, Children's Hospital Boston, 1965. USPHS Hematology Training Grant, University of California San Francisco, Medical Center 1969-1971 (Pediatric and General Immunology). American Cancer Society Faculty Research Award, 1971-1974
Specialty Board Certifications:	1. Certified Diplomate American Board of Allergy and Immunology, 1975. 2. Certified Diplomate American Board of Pathology-Clinical Pathology, 1977. 3. Fellow in the American College of Emergency Physicians. 4. Fellow College of American Pathologists. 5. Fellow American Society of Clinical Pathologists. 6. Member American Academy of Allergy. 7. Member American Association of Clinical Chemists.
Military:	USN attached to USMC as Flight Surgeon 1966-1968 Viet Nam Campaign ribbons and unit citation, Navy and Marine Corps Commendation, First through Fourth Air Medals Bronze Star Medal with Combat "V", Silver Star Medal, Honorable Discharge November 1969.
Marital Status:	Married to Vera S. Byers, Ph.D., M.D. No children.

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Academic
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Adjunct Instructor in Pediatrics
University of California
San Francisco Medical Center
1971 - 1972

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1972 - 1978

Adjunct Associate Professor of Immunology
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San Francisco Medical Center
1978 -

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1979 - 1981

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1981 -

Member, Medical Quality
Review Committee, #4
Board of Medical Quality Assurance
State of California
1982 -

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ALAN SCOTT LEVIN, M.D.

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20. Carter, J.B., Ponce, B.E., Stites, D.P., Levin, A.S., German, D.E., and Fudenberg, H.H.: Circadian Cycle of Spontaneous Thymidine-2^{14} C Incorporation by Unstimulated Normal Human Peripheral Lymphocytes In Vitro.

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22. Levin, A.S., Spitler, L.E., Wybran, J., Byers, V.S., and Fudenberg, H.H.: Treatment of Osteogenic Sarcoma (OS) with Tumor Specific Dialysable Transfer Factor (TF). Clinical Research, 1973

23. Levin, A.S., Byers, V.S., Fudenberg, H.H., and Wybran, J.E.: Immunologic Parameters for Monitoring Immunotherapy with Tumor Specific Transfer Factor. Clin. Res. 1974.

24. Gardner, R.D., Byers, V.S., Levin, A.S., and Fudenberg, H.H.: Frozen Human Lymphocytes: Dissociation between Tumor Specific Cytotoxicity and Mixed Leukocyte Reactivity (MLC Reactivity). Clin. Res. 1974.

25. Byers, V.S., Levin, A.S., and Fudenberg, H.H.: Detection of Tumor Specific Immunity in Normal Household Contacts of Tumor Bearing Patients. Clin. Res. 1974.

26. Levin, A.S., Byers, V.S., Johnston, J.O., Hackett, A.J., and Fudenberg, H.H.: Host-Tumor Relationships in Giant Cell Sarcoma of Bone (GCS): Measurement by Quantitative Immunofluorescence. Clin. Res. 1974

27. Fudenberg, H.H., Byers, V.S., Levin, A.S., and Hackett, A.J.: Evidence for Viral Etiology of Human Hypernophroma and Osteosarcoma. Perspectives in Virology. In Press, 1974

28. Levin, A.S., Byers, V.S., LeCam, L., and Johnston, J.O.: Evidence for Regression in Osteogenic Sarcoma Induced by Tumor Specific Transfer Factor. 2nd International Workshop on Transfer Factor. Frederick, MD., 1975.

29. Hackett, A., Springer, L., Levin, A.S., and Fink, M.: Transmission and Scanning Electron Microscopic Studies on Osteo Sarcoma Before and After Transfer Factor Therapy. Cancer Research 16:193, 1975

30. Levin, A.S., LeCam, L.M., Hackett, A.J. and Johnston, J.O.: Osteosarcoma (O.S.): 5 Year Followup of Epidemiology and Tumor Specific Transfer Factor Therapy (TSTF). Clin. Res. 1976

31. Levin, A.S., LeCam, L.M., and Agraz, J.M.: Dip-Stick Method of Quantitative Immunofluorescence. Clin. Res. 1976.

32. Newman, B.R., Byers, V.S., Levin, A.S., and Jerman, D.: Circadian Influences on T. Lymphocyte Function Mediated by Serum Factors. Clin. Res. 1976

33. Levin, A.S., Kassel, S.D., and Flam, M., A New Diagnostic Index: Collagen Disease vs. Malignancy vs. Infectious Disease. J.A.M.A. 237, 1916, 1977.

34. Levin, A.S., and Baldwin, R.W.: Solid Phase Fluoroimmunoassay to Detect Serum Immune Complexes. 6th International Congress on Immunofluorescence, Vienna, Austria. 1978

35. Levin, A.S., McGovern, J.J.,Jr., Miller, J.B., LeCam, L.L., and Lazaroni, J.: Non-Anaphylactic Food Allergies Mediated by Immune Complexes: Ann. Allergy, Abstract in Press. 1981

Dr. Peter Orris is an internist practicing in Chicago, Illinois. His curriculum vitae will be supplied.

Dr. Orris will testify as to the clinical aspects of the diseases in the representative plaintiff veterans. His testimony will be based upon a medical records review and an analysis of various test results that will have been performed upon the representative plaintiffs.

Dr. Orris will also testify on generic causation and specific proximate causation in relation to each representative veteran plaintiff. He will also testify as to prognosis for each representative veteran plaintiff

Marvin A. Schneiderman, Ph.D., of Bethesda, Maryland, is a statistician and epidemiologist who is the former Chief of Statistics and Epidemiology and the former Director for Science Policy of the National Cancer Institute and is currently a consultant. His curriculum vitae is attached.

Dr. Schneiderman will testify concerning mathematical models, statistics, and epidemiology in the area of cancer. He will first discuss the epidemiology of dioxins and their contaminants to human cancer insofar as it relates to soft tissue sarcomas, and particularly the EPA peer review group conclusions in regard thereto, stomach cancers and lymphomas. In that regard, he will discuss the relationship of exposure to the time the disease appears, the so-called latency period. He will also discuss the multiplication of base rates in the production of such cancer.

Next, Dr. Schneiderman will present a multi-stage model of cancer induction. He will discuss age relationships and the stage of cancer development as they are affected by dioxins and their contaiminants or other materials. He will also present certain pertinent animal data and discuss it as a predictor for human experience. He will also testify that TCDD is more toxic than many other carcinogens, including being more carcinogenic by a factor of 4 or 5 than benzene, for example. He will also explain the concept of risk assessment and how judgments as to such are capable of being made with regard to humans. This will include discussion of a mathematical model for association of the multi-faceted presentation of symptoms and signs in the same veteran to exposure to Agent Orange as a causative factor.

He will also discuss the population incidences of these rare cancers, presenting a comparison of the onset ages for them in the general population with the ages of onset for the cancers observed in the Vietnam veterans.

He will also discuss the relationship of cancer induction to immune deficiencies or deficits. He will place special emphasis upon lymphomas and soft tissue sarcomas and explain how the experience with transplant patients validates his opinions in this regard.

Finally, he will discuss the question of a threshold in the induction of cancer. This will include testimony to the effect that there is no "safe" dose for a carcinogen and that a single exposure may cause cancer. He will also discuss the disease-producing behavior of generalized carcinogens, i.e., the chance of a single carcinogen leading to cancer at multiple sites.

MARVIN A. SCHNEIDERMAN

Dr. Schneiderman is a Clement Associates Senior Science Advisor with principal responsibilities in biostatistics, epidemiology, risk assessment, and health surveillance. He has more than 30 years of experience in cancer research and related subjects, and he is the author of more than 130 scientific papers in areas of biostatistics, epidemiology, risk assessment, and science and regulatory policy. During his career with the National Cancer Institute (NCI), he was, successively, Associate Chief of the Biometry Branch, Associate Director for Field Studies (Epidemiology) and Statistics, and Associate Director for Science Policy. In this last position, he was one of the principal advisors to the Director of the Institute. Dr. Schneiderman is a member of the adjunct faculty of the Georgetown University Graduate School, and Professor of Biostatistics at the Uniformed Services University of the Health Sciences. He has held teaching positions at the University of Pittsburgh Graduate School of Public Health and the University of Miami (Florida), as well as at the Georgetown University Medical School. He was also a Rockefeller Public Service Fellow at the London School of Hygiene and Tropical Medicine. He has served on a number of expert advisory committees and is or has been an associate editor of Cancer Research, Blood, Journal of the National Cancer Institute, Biometrics, Statistics in Medicine, American Journal of Industrial Medicine, and a number of other scientific journals.

DEGREES

Ph.D., Statistics, American University, Washington, D.C., 1961

M.S., Statistics, American University, Washington, D.C., 1953

B.S., Mathematics and Statistics, City College of New York, 1939

NON-DEGREE EDUCATION

Harvard University Graduate School of Business, 1945
Management sciences, economics, statistics

Ohio State University Graduate School, 1946-1947
Economics

London School of Hygiene and Tropical Medicine, 1959-1960
Epidemiology, medical research involving humans, controlled trials, biostatistics

EMPLOYMENT HISTORY

1983-present	Senior Fellow, Environmental Law Institute, Washington, D.C.
1981-present	Professor (Division of Biometrics), Department of Preventive Medicine, USUHS, Bethesda, Md.
1980-present	Senior Science Advisor, Clement Associates
1975-present	Associate Professor, Graduate Faculty, Georgetown University
1980	Expert Consultant, Office of the Director, National Cancer Institute (NCI), National Institutes of Health (NIH)
1978-1980	Associate Director for Science Policy, Office of the Director, NCI
1970-1978	Associate Director NCI, Field Studies and Statistics Program, Division of Cancer Cause and Prevention, NCI
1967-1978	Adjunct Professor, Biostatistics, Graduate School of Public Health, University of Pittsburgh
1966-1975	Clinical Associate Professor, Medical Statistics, Georgetown University Medical School
1960-1970	Associate Chief, Biometry Branch, NCI
1960-1965	Professorial Lecturer, Georgetown University Medical School
1959-1960	Rockfeller Public Service Fellow, Statistical Research Unit of the British Medical Research Council, London School of Hygiene and Tropical Medicine
1955-1959	Mathematical Statistician and Acting Chief, Therapeutic Trials Section, NCI
1948-1955	Mathematical Statistician, Biometrics Section, NCI
1939-1948	Private Industry, Military Service (USAF), Other Federal government agencies

HONORS

Distinguished Lecturer, Lawrence Livermore Laboratories, University of California, 1982

American Conference of Government Industrial Hygienists, Symposium Speaker Award, June, 1982

Samuel Wilkes Public Lectureship, Princeton University, 1980

Keynote Lecturer, Society of Occupational and Environmental Health, 1979, North Carolina Public Health Association, 1980

Environmental Defense Fund, Public Interest Science Award, 1977

Distinguished Service Award, Department of Health, Education and Welfare (DHEW), 1974

Superior Service Award, DHEW, 1968

Rockefeller Public Service Fellow, London School of Hygiene and Tropical Medicine, 1959-1960

Phi Beta Kappa, 1939

SELECTED ADVISORY COMMITTEES

Committee on Toxicity Data Elements, National Academy of Sciences, 1981-present

Subcommittee on the Geochemical Environment in Relation to Health and Disease, NAS/NRC, 1980-present

Science Evaluation Board, National Health and Medical Research Council of Australia, 1980-present

American Cancer Society, Analysis and Projections Committee, 1976-1978, Institutional Grants Committee, 1980-present

Science Advisory Board, Howard University Cancer Center, 1979-present (External Review Committee)

Center for Science in the Public Interest, Board of Directors, 1983-present

Food Safety Council, Board of Directors, 1978-1982

Advisory Committee, Biomedical and Environmental Assessment Division, Brookhaven National Laboratory, 1978-present

Advisory Committee, International Cancer Research Data Bank (CIDAC), Franklin Institute, Philadelphia, 1981-present

Task Force on Heart Disease Epidemiology, National Heart, Lung, and Blood Institute, 1979-1980

Science Advisory Board, National Center for Toxicological Research, 1974-1979

Ad Hoc Subcommittee on Asbestos-Related Health Problems, Armed Forces Epidemiology Board, 1978-1979

International (American) Chairman, U.S./U.S.S.R. Working Group on the Epidemiology of Cancer, 1973-1979

Committee on Maritime Hazardous Materials, National Academy of Sciences, 1978

Committee to Coordinate Toxicology and Related Programs, DHEW, 1978

President's Biomedical Panel, 1975-1976

Consultative Panel on Hazards of Chemical Pesticides, National Academy of Sciences, 1974-1976

Chairman and Executive Secretary, Committee of Presidents of Statistical Societies, 1973-1976

Board of Directors, American Statistical Association, 1972-1974

International Council, International Biometric Society, 1971-1973

Immunology-Epidemiology Segment, Special Virus Cancer Program, NCI, 1969-1971

Advisory Panel on Carcinogenicity of Pesticides, Secretary's Commission on Pesticides and Their Relationship to Environmental Health, 1969-1970

Chairman, Subcommittee on Medical Biostatistics, American Therapeutic Society, 1967-1968

Subcommittee on Biologic Effects of Atomic Radiation, NAS/NRC, 1964-1965

SELECTED SOCIETIES

American Association for Cancer Research
American Society for Preventive Oncology (Founding Member)
American Statistical Association (Fellow)
Biometric Society (International)
International Epidemiological Association
Royal Statistical Society (Fellow)
Washington Statistical Society
American Association for the Advancement of Science (Fellow)
International Statistical Institute (Fellow)
Society for Occupational and Environmental Health

SELECTED PUBLICATIONS

Schneiderman, M.A. Standard setting: Implications of sensitivity, and a search for an ethical base. In: Protection of the Sensitive Individual, Annals of the American Conference of Government Industrial Hygienists, 3:133-138 (1982)

Schneiderman, M.A. A personal reminiscence (Austin Bradford Hill). Statistics in Medicine 1:307-308 (1982)

Schneiderman, M.A. Discussion of "Some Aspects of Cancer Epidemiology" by Abraham Lilienfeld. Biometrics (Supplement) 38:161-165 (1982)

Davis, D.L., Bridbord, K., and Schneiderman, M.A. Cancer prevention: Assessing cause, exposure, and recent trends in mortality for U.S. males, 1968-1978. Teratogenesis, Carcinogenesis and Mutagenesis. Pp. 105-135 (June 1982)

Schneiderman, M.A. Trends in cancer mortality and incidence in the United States: Is the future clear or clouded? In Miké, V., ed. Statistics in Medical Research. John Wiley and Sons, New York. Pp. 71-107 (1982)

Schneiderman, M.A. Description and reliability of trends in cancer incidence. In Magnus, K. Trends in Cancer Incidence. Hemisphere Publishing Corp., Washington, D.C. Pp. 1-2 (1982)

Schneiderman, M.A. Cost-benefit, social values and the setting of occupational health standards. In Lee, J.S., and Rom, W.N., eds. Legal and Ethical Dilemmas in Occupational Health. Ann Arbor Science, Ann Arbor, Michigan. pp. 191-205 (1982)

Peto, R., and Schneiderman, M., eds. Quantification of Occupational Cancer: Banbury Report No. 9. Cold Spring Harbor Laboratory, Cold Spring Harbor, New York (1981)

Davis, D.L., Bridbord, K., and Schneiderman, M.A. Estimating cancer risks: Problems in methodology production trends. In Peto, R., and Schneiderman, M., eds. Quantification of Occupational Cancer: Banbury Report No. 9. Cold Spring Harbor Laboratory, Cold Spring Harbor, New York. Pp. 285-315 (1981)

Schneiderman, M.A. Summary comments. In Crandall, R.W., and Lave, R., eds. The Scientific Basis of Health and Safety Regulation. The Brookings Institution, Washington, D.C. Pp. 297-299 (1981)

Schneiderman, M.A. Regulation of carcinogens in an imprecise world. Ann. N.Y. Acad. Sci. 363:217-232 (1981)

Schneiderman, M.A. Extrapolation from incomplete data to total or lifetime risks at low doses. Environ. Health Perspect. V. 42, Pp. 33-38 (December 1981)

Schneiderman, M.A. Toxic Substances in Our Environment-Can we manage them so that they don't manage to harm us? Health Forum 81, The Coalition for Health and the Environment, Washington, D.C. (1981)

Schneiderman, M.A. Epidemiology: What Can it Tell Us? Proceedings of the Conference on Environmental Risk, New Orleans, Louisiana, December 10, 1980. The Electric Power Research Institute, Palo Alto, California, EPRI EA-2064, Project 1316-6. Pp. 369 - 3-89 (October 1981)

Schneiderman, M.A., Nisbet, I., and Brett, S.M. Assessment of Risks Posed by Low Levels of Asbestos in the General Environment. Berichte: Bundesgesundheitsamt. No. 4, 1981. Dietrich Reimer Verlag, Berlin. Pp. 3/1-3/28 (1981)

Schneiderman, M.A., and Levin, D.L. Needs, problems and prospects in cancer epidemiology. In Levin. D.L., ed. Cancer Epidemiology in the U.S.A. and U.S.S.R. U.S. Department of Health and Human Services, PHS, Bethesda, Maryland. NIH Publication No. 80-2044 (1980)

Schneiderman, M.A. The Relationship Between Diet, Occupation, the Environment and Cancer. Proceedings: US/Egypt Symposium on the Biomedical Effects of Technology Transfer, Cairo, Egypt (February 9-13, 1980) (In Press: Environmental Health Perspectives)

Schneiderman, M.A. Scientific Issues in a National Cancer Policy. Proceedings of the 4th Toxic Control Conference. Government Institutes, Inc., Washington, D.C. Pp. 95-107 (1980)

Schneiderman, M.A. The uncertain risks we run: Hazardous materials. In Schwin, R.C., and Albers, W.A., Jr., eds. Societal Risk Assessment. Plenum Press, New York. Pp. 19-41 (1980)

Schneiderman, M.A. What's Happening to Cancer in our Advanced Industrial Society? Have the Risks been Overstated? Keynote Address: Society for Occupational and Environmental Health, Washington, D.C. (In Press: Proceedings) (December 3-5, 1979)

Blokhin, N.N., and Schneiderman, M.A., eds. Epidemiology of Cancer in the USSR and USA. Meditsina, Moscow (Russian) (1979)

Schneiderman, M.A., DeCouflé, P., and Brown, C.C. Thresholds for environmental cancer: Biologic and statistical considerations. Ann. N.Y. Acad. Sci. 329:92-130 (1979)

Schneiderman, M.A. Alpha, beta manitonne--a new industrial material with unknown benefits and risks. In Carcinogenic Risks/Strategies for Intervention. International Agency for Research on Cancer (IARC), Lyon, France. IARC Sci. Publ. 25:237-239 (1979)

Schneiderman, M.A. The Links Between the Environment and Health. Proceedings: National Conference on the Environment and Health Care Costs, U.S. House of Representatives (August 15, 1978)

Biersteker, K., and Schneiderman, M.A. Epidemiologic Aspects of Drinking Water-Health Relationship. Proceedings of the Health Effects Committee of the NATO committee on challenges of Modern Society. Bonn, W. Germany (April 23-27, 1978)

Schneiderman, M.A., Mason, T.J., and Hoover, R. Cancer, geography, and geology--a problem for interdisciplinary cross-fertilization. In Geochemistry and the Environment. Vol. 3. National Academy of Sciences, Washington, D.C. (1978)

Schneiderman, M.A. Legislative possibilities to reduce the impact of cancer. Prev. Med. 7:424-438 (1978)

Schneiderman, M.A. Water and epidemiology. In Russell, C.S., ed. Safe Drinking Water: Current and Future Problems. Proceedings of the National Conference on Resources for the Future. Pp. 111-148 (1978)

Schneiderman, M.A. Extrapolating animal and microbiological tests to humans. In Coling, G., ed. Environmental Cancer (Causes, Victims, Solutions). Proceedings of a conference of the Urban Environment Coalition, Inc. Pp. 9-11 (1978)

Schneiderman, M.A. Environmental Factors and Cancer Prevention. Marcel Dekker, New York (1978). (Third National Symposium on Detection and Prevention of Cancer, New York (April 26-30, 1976)

Schneiderman, M.A. Risk assessment of the health effects of water chlorination. In Jolley, R.L., Gorchev, H., and Hamilton, D.H., eds. Water Chlorination--Environmental Impact and Health Effects. Ann Arbor Science Publications, Ann Arbor, Mich. Vol. 2, pp. 509-515 (1978)

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DeVesa, S.S., and Schneiderman, M.A. Increase in the number of cancer deaths in the United States. Am. J. Epidemiol. 106:1-5 (1977)

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Schneiderman, M.A. Health effects--a scientific and statistical analysis. In Miller, M.L., ed. Proceedings of the First Toxic Substances Law Seminar. Washington, D.C. (1977)

Levin, D.L., and Schneiderman, M.A. Cancer. In Miller, S.S., ed. Symptoms. Thomas Y. Crowell, New York (1976)

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Schneiderman, M.A. Carcinogenesis as an end point in health impact assessment. In Anderson, E.C., and Sullivan, E.M., eds. Impact of Energy Production on Human Health: An Evaluation of Means of Assessment. National Technical Information Service, Springfield, Va. Pp. 65-74 (1976)

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Hoel, D.C., Gaylor, D.W., Kirschstein, R.L., Saffiotti, U., and Schneiderman, M.A. Estimation of risks of irreversible, delayed toxicity. J. Toxicol. Environ. Health 1:133-151 (1975)

Mantel, N., and Schneiderman, M.A. Non-parametric interval estimation of relative potency for dilution assays, including the case of non-monotone dosage response curves. Biometrics 31:619-632 (1975)

Mantel, N., and Schneiderman, M.A. Estimating "safe" levels--a hazardous undertaking. Cancer Res. 35:1379-1386 (1975)

Schneiderman, M.A., Mantel, N., and Brown, C.C. From mouse to man--or how to get from the laboratory to Park Avenue and 59th Street. Ann. N.Y. Acad. Sci. 246:237-248 (1975)

Schneiderman, M.A. How do you know you've done any better? Cancer 35:64-68 (1975)

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Fears, T.R., and Schneiderman, M.A. Pathologic evaluation and the blind technique. Science 183:1144-1145 (1974)

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Van Belle, G., and Schneiderman, M.A. Some statistical aspects of pollution and protection. Int. Stat. Rev. 41:315 (1973)

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Schneiderman, M.A., and Mantel, N. The Delaney clause and a scheme for rewarding good experimentation. Prev. Med. 2:165-170 (1973)

Schneiderman, M.A., and Levin, D.L. Parallels, convergences, and departures in case-control studies and clinical trials. Cancer Res. 33:1498-1503 (1973)

Graham, S., and Schneiderman, M.A. Social epidemiology and the prevention of cancer. Prev. Med. 1:371-379 (1972)

Scotto, J., and Schneiderman, M.A. Predicting survival in terminal cancer. Br. Med. J. 4:50 (1972)

Schneiderman, M.A., and Levin, D.L. Trends in lung cancer: Mortality, incidence, diagnosis, treatment, smoking and urbanization. Cancer 30:1320-1325 (1972)

Johnson, R.E., Thomas, L.B., Schneiderman, M.A., Glenn, D.W.., Faw, F., and Habermann, M.D. Preliminary experience with total nodal irradiation in Hodgkin's disease. Radiology 96:603-608 (1970)

Schneiderman, M.A., and Scotto, J. Computer-Investigator Interactions in Small-Scale Clinical Trials. Proceedings of the Fifth Scientific Meeting of the International Epidemiology Association, Primosten, Yugoslavia. Pp. 449-467 (1970)

Gold, G.L., Shnider, B.I., Salvin, L.G., Schneiderman, M.A., Colsky, J., Owens, A.H., Krant, M.J., Miller, S.P., Frei, E., III, Hall, T.C., Spurr, C.L., McIntyre, O.R., Hoogstraten, B., and Holland, J.F. The use of mechlorethamine, cyclophosphamide, and uracil mustard in neoplastic disease: A cooperative study. J. Clin. Pharmacol. 10:110-120 (1970)

Schneiderman, M.A. How to read the drug literature--or any other organized collection of numbers from experiments. Mod. Med. 37:92-96 (1969)

Malmgren, R.A., Bennett, J.M., DelVecchio, P.R., DeWhitt, S.H., Feld, M., Kazam, E., and Schneiderman, M.A. Evaluation studies of peripheral blood leucocyte changes in malignancy. Acta Cytol. 13:149-153 (1969)

Schneiderman, M.A. Quantitative thinking in medicine--biostatistics. (Using numbers to mark the route from cause to effect and back.) In Cantor, P., ed. Traumatic Medicine and Surgery for the Attorney. Matthew Bender, New York. Pp. 419-477 (1969)

Givelber, H., DiPaolo, J.A., and Schneiderman, M.A. The influence of actinomycin D on survival of x-radiated RF mice. Cancer Res. 28:2484-2488 (1968)

Pipberger, H.V., Schneiderman, M.A., and Klingeman, J.D. The love-at-first-sight effect in research. Circulation 38:822-825 (1968)

Carbone, P.P., Spurr, C., Schneiderman, M.A., Scotto, J., Holland, J.F., and Shnider, B. Management of patients with malignant lymphoma: A comparative study with cyclophosphamide and vinca alkaloids. Cancer Res. 28:811-822 (1968)

Hall, T.C., Nevinny, H.B., Holland, J.F., Maldia, G., Schneiderman, M.A., Salvin, L., Shnider, B.I., Gold, G.L., Frei, E., III, Carbone, P.P., Colsky, J., Franzino, A., Grob, D., Matiasevic, D., Olson, K.B., Horton, J., Owens, A., Santos, G.W., Chalmers, T.C., and Krant, M.J. Comparison of antimetabolites in the treatment of breast and colon cancer. JAMA 200:770-778 (1967)

Schneiderman, M.A. The Shin Tokaido to developing new treatments in medicine: Unbiasedness. In Harris, R.J.C., ed. Proceedings of the 9th International Cancer Congress. Springer-Verlag, Heidelberg. Pp. 194-198 (1967)

Bull, B.S., Schneiderman, M.A., and Brecher, G. Semi-automatic dilution system for the hematology laboratory. Am. J. Clin. Pathol. 47:549-553 (1967)

Schneiderman, M.A. Mouse to man: Statistical problems in bringing a drug to clinical trial. In LeCam, L., and Neyman, J., eds. Biology and Problems of Health. University of California Press, Berkeley. Vol. 4, pp. 855-866 (1967)

Schneiderman, M.A. Non-objective art and objective evaluation of cancer chemotherapy. In Brodsky, I., and Kahn, S.B., eds. Cancer Chemotherapy. New York, Grune and Stratton. Pp. 67-76 (1967)

Spurr, C.L., Carbone, P.P., and Schneiderman, M.A. Comparative evaluation of cyclophosphamide and vinca alkaloids in lymphomas. Proceedings of the 57th Annual Meeting of the American Association of Cancer Research 7:67 (1966)

Myers, M.H., Schneiderman, M.A., and Armitage, P. Boundaries for closed (wedge) sequential t-test plans. Biometrika 53:431-437 (1966)

Schneiderman, M.A. Experimental design considerations in multiclinic trials. In Radouco-Thomas, C., exec. ed. International Encyclopedia of Pharmacology and Therapeutics. Pergamon Press, Oxford. Vol. 2, pp. 617-636 (1966)

Schneiderman, M.A. The value of controlled trials. In Hayward, J.L., and Bulbrook, R.D., eds. Clinical Evaluation in Breast Cancer. London, Academic Press. Pp. 249-259 (1966)

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Williamson, C.R., and Schneiderman, M.A. The use of mass x-ray survey films for heart disease case finding. Mass. Health J. 30:7-14 (1950)

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Dr. Ellen Silbergeld, Ph.D., is an environmental scientist and toxicologist who is the Chief Toxicologist for the Environmental Defense Fund and a Research Scientist in the Reproductive Toxicology Laboratory of the National Institutes of Health in Bethesda, Maryland. Her curriculum vitae is attached.

Dr. Silbergeld will testify as to the scientific models for TCDD toxicity. She will emphasize the receptor model, its role in physiology, how to detect receptors and how to link receptors to function. She will discuss how receptors recognize TCDD by virtue of structural "fine-tuning". She will testify as to the existence of receptors in humans and in their various organs, together with the implications of their presence for TCDD potency. She will also discuss the extrapolations which are possible between animals and humans. She will further testify as to the mechanisms of toxicity including the sensitivity of the reproductive system, both endocrine and gonadal, to the receptor-mediated effects of TCDD. Finally, she will discuss the consequences of receptor interaction with TCDD insofar as that interaction produces results involving RNA-DNA, AHH induction, and heme synthesis regulation, among others.

In the field of neurotoxicity, she will discuss the experimental and clinical studies with particular emphasis upon dose-response mechanisms, acute versus chronic exposures and early versus long latency effects. She will also discuss the

biochemical and morphological effects of TCDD, the electrophysiology involved and the effects of TCDD on such things as cognition, mood, and affect.

She will also emphasize the basic mechanisms of toxicity on both the central and peripheral nervous systems, specifically dealing with the role of altered porphyrin synthesis on the nervous system. Three aspects of this problem will be discussed: First, the effects of decreased cellular energy supply on neuronal activity and viability; second, the effects of decreased heme systhesis on the integrity of myelin; and third, the neuroactive properties of certain porphyrin precursors.

CURRICULUM VITAE

Name: Ellen Kovner Silbergeld

Date and Place of Birth: July 29, 1945, Washington, DC

Education:

1967 - A.B.	Vassar College
1972 - Ph.D.	Johns Hopkins University

Chronology of Employment:

1967	Instructor, California International Summer Program, Uppsala Sweden
1968-70	Secretary and Program Officer, National Academy of Sciences, National Research Council, Washington, DC
1969-71	"Nader's Raiders", Center for the Study of Responsive Law, Washington, DC
1972-75	Postdoctoral Fellow in Environmental Medicine and Neurosciences, Johns Hopkins University, Baltimore, Maryland
1975	Assistant Professor, Department of Environmental Medicine, School of Hygiene and Public Health, Johns Hopkins University
1975-79	Staff Fellow and Head, Unit on Behavioral Neuropharmacology, Experimental Therapeutics Branch, NINCDS,NIH
1979-81	Chief, Section on Neurotoxicology, NINCDS,NIH
1982	Chief Toxics Scientist, Environmental Defense Fund, Washington, DC
	Guest Scientist, Reproductive Toxicology Section, Pregnancy Research Branch, NICHD,NIH

Other Professional Appointments:

Consultant, NSF Energy Program, 1974-1975

Member,	Nutrition Foundation National Committee on Food Additives and Hyperkinesis, 1975-1980
Member,	USDHEW-FDA Committee to Coordinate Toxicology and Related Programs, 1977-1981
Member,	US Delegation of the Joint US-USSR Health Agreement on Environmental Health, 1977-78
Member,	Society for Neuroscience Committee on Social Issues, 1978 -
Member,	OECD Chemicals Program Ad Hoc Expert Review Committees on Reproductive Toxicity and Neurotoxicity, 1982 -

Member, US Delegation to OECD Expert Meetings on Existing Chemicals, 1983 -
Member, Hazardous Waste Task Force and Hazardous Waste Facilities Siting Board, State of Maryland, 1983
Member, Govenor's Blue Ribbon Panel on Binghamton, NY, State Office Building, 1982 -
Member, Executive Committee, Science Advisory Board, US EPA, 1983 -
Member, Board on Toxicology and Environmental Health Hazards, National Academy of Sciences, 1983 -
Member, Public Policy Committee, American Society for Neurochemistry, 1983 -

Professional Society Memberships:

American Public Health Association
Society for Occupational and Environmental Health
Society for Neuroscience
Association of Women in Science
American Association for the Advancement of Science
International Brain Research Organization
American Society for Neurochemistry
American Society for Pharmacology and Experimental Therapeutics
Engineering Society of Baltimore

Other Activities

Secretary-Treasurer, Society for Occupational & Environmental Health, 1983-
Editorial Board: Neurobehavioral Toxicology, 1979-
American Journal of Industrial Medicine, 1980-
Neurotoxicology, 1981-
Environmental Research, 1983-
Hazardous Waste, 1983 -
Participant, NIH Consensus conferences, 1979 and 1982
Expert consultant on lead poisoning, U.S. Secret Service, 1979-81
Chairperson, Society for Occupational and Environmental Health Special Committee on El Paso Lead Poisoning, 1977-1979
Preceptor, NIGMS Pharmacology-Toxicology Research Associateship Program, 1977-1981
Graduate board examiner, University of Pittsburgh and University of Toronto
Lecturer, continuing medical education courses in environmental medicine (Johns Hopkins) and occupational medicine (NIOSH)

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Elected councillor, NIMH-NINCDS Assembly of Scientists, 1979-1981
Elected representative, NINCDS EEO Committee, 1977-1980
Co-organizer, Women in Neuroscience
Member, Solowey Lectureship selection committee, NIH, 1980-1981
Environmental Health Consultant, Oil, Chemical and Atomic Workers Union, AFL-CIO, Washington, D.C., 1970
Reviewer, EPA documents on lead, manganese, mercury, dioxin, risk assessment, and exposure, 1981-
Ad Hoc Member, Occupational Safety and Health Study Section, NIOSH, 1983-
Member, NIMH Committee on Frontiers of Neuroscience, 1983-
Grants reviewer, National Foundation - March of Dimes; National Science Foundation; Nutrition Foundation; Thrasher Foundation; Hereditary Diseases Foundation, NIH
Manuscript reviewer, Life Sciences, Biochemical Pharmacology, Environmental Journal Pharmacology, Science, Neurotoxicology, Neurobehavioral Toxicology Teratology, Pharmacology Biochemical Behavior, Procs. Society Experimental Biological Medicine, Experimental Neurology, etc.

Honors and Awards:

Graduated summa cum laude, 1967
elected to Phi Beta Kappa, 1967
undergraduate academic scholarship, 1963-1965
Woodrow Wilson National Foundation Fellow, 1967-1968
Leverhulme and Fulbright Fellowships to University of London, 1967
National Science Foundation Graduate Traineeship, 1968-1972
Public Health Service Research Fellowship to Woods Hole, 1970
Rockefeller Foundation predoctoral research fellowship, 1971-1972
NIH postdoctoral fellowship in environmental health sciences, 1972-1972
Joseph P. Kennedy, Jr. Fellowship in neurosciences, 1974-1975
Pharmaceutical Manufacturers Association Foundation Research Starter Award, 1974-1975
National Academy of Sciences Exchange Fellow to Yugoslavia, 1976
George Miller lectureship in environmental studies, University of Illinois, 1984

Professional Interests:

Neuropharmacology & Toxicology
Environmental Risk Assessment

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ELLEN KOVNER SILBERGELD

A. SCIENTIFIC PUBLICATIONS

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2. Silbergeld, E. K.: and Goldberg, A.M.: A lead-induced behavior disorder. Life Sci. 13(9):1275-1283, 1973.

3. Silbergeld, E. K.: Blood glucose: A sensitive indicator of environmental stress in fish. Bull. Environ. Contam. Toxicol 11(1):20-25, 1974.

4. Silbergeld, E. K., Fales, J. T. and Goldberg, A.M.: Lead: Evidence for a prejunctional effect on neuromuscular function. Nature 247:49-50, 1974.

5. Silbergeld, E. K., Fales, J. T. and Goldberg, A.M.: Lead: The effects of inorganic lead on the neuromuscular junction. Neuropharmacology 13:146-157, 1974.

6. Silbergeld, E. K. and Goldberg, A.M.: Lead induced behavioral dysfunction: An animal model of hyperactivity. Exp. Neurol. 42:146-157, 1974.

7. Silbergeld, E. K. and Goldberg, A.M.: Hyperactivity: A lead induced behavior disorder. Environ. Health Persp. 7:227-232, 1974.

8. Silbergeld, E. K. and Goldberg, A.M.: Pharmacological and neurochemical investigations of lead induced hyperactivity. Neuropharmacology 14:431-444, 1975.

9. Morrison, J. H., Olton, D. S., Goldberg, A.M. and Silbergeld, E. K.: Alteractions in consummatory behavior of mice produced by dietary exposure to inorganic lead. Dev. Psychobiol. 8(5):389-396, 1975.

10. Silbergeld, E.K.: Neurochemical and pharmacological studies of central nervous system lead toxicology. In Carnow, B.W. (ed.): Health Effects of Occupational Lead and Arsenic Exposure, USDHEW, PHS, CDC, NIOSH, Washington, D.C., pp. 74-85, 1976.

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64. Silbergeld, E. K., Hruska, R. E., Bradley, D., Lamon, J. M., and Frykholm, B. C.: Neurotoxic aspects of porphyrinopathies: lead and succinylacetone. Environ. Res., 29:459-471, 1982.

65. Silbergeld, E. K.: Experimental and environmental neurotoxins: correlation of behavioral and biochemical effects. In Levy, M. and Spiegelstein, A. (eds.) Behavioral Models and the Analysis of Drug Action Elsevier-North Holland, Amsterdam, pp 297-315, 1982.

66. DeRyck, M., Hruska, R.E., and Silbergeld, E.K.: Estrogen and haloperidol-induced versus handling-related catalepsy in male rats. Pharmacol. Biochem. Behav. 17:1027-1035, 1982.

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Hall, K.L., and Silbergeld, E.K.: "Reappraising Epidemiology" Harvard Environmental Law Review, 7:441-448, 1983

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Dr. Raymond Singer, Ph.D., is a neurotoxicologist and neuropsychologist practicing at Occupational Health Consulting, Inc., of New York, New York. Dr. Singer's curriculum vitae is attached.

Dr. Singer will prepare reports concerning each of the veteran plaintiffs. These reports will be based upon personal interviews and review of appropriate test findings performed by himself and/or by others. The personal interview will consist of a thorough account of the veteran's background and current and historic symptoms. It will also detail the educational and occupational background of each veteran. Various neuropsychologic tests will be given and discussed with particular reference to whether any deficits or changes noted are due to the results of any toxic chemical exposures. Neurophysiologic tests will also be given or reviewed and interpreted, with particular emphasis placed upon nerve conduction velocity findings, and the results will be set out and discussed, with particular reference to whether the findings are related to toxic chemical exposures. To the extent warranted, Dr. Singer will relate any findings to Agent Orange exposure.

Dr. Singer will also testify to the effects of toxic chemical exposures as they have been studied in a number of research efforts in both animals and humans. He will discuss the findings reported in various populations exposed to toxic chemicals

and particularly to TCDD through the mechanism of industrial accidents. He will also discuss the findings concerning demyelination of the fatty sheaths surrounding the nerves and the "dying-back" neuropathy which has been associated with toxic chemical exposures.

Dr. Singer will also discuss the results of his own work in relation to occupational exposures to TCDD, and will explain how his results are consistent with those obtained from tests performed on the veterans here, and how those results are consistent with causation by phenoxy herbicides and their contaminants.

RESUME

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EDUCATION AND DEGREES

Ph.D.	Washington State University	1978	Psychology
M.S.	Washington State University	1975	Psychology
B.A.	University of Rochester	1972	Psychology

PROFESSIONAL ORGANIZATIONS

Certified Psychologist, New York State Board of Psychology
Member, American Psychological Association
Member, National Academy of Neuropsychologists
Member, Society for Occupational and Enviromental Health
Member, American Public Health Association
Associate Member, College of Toxicology

PROFESSIONAL EXPERIENCE

1983 -	Adjunct Instructor, Mount Sinai School of Medicine Department of Community Medicine, New York City
1983 -	Consultant, New York State Department of Social Services, Office of Disability Determinations
1982 -	President, Occupational Health Consulting, Inc.
1982 -	Clinical Psychologist, Private Practice, New York City
1982 -	Reviewer, The American Journal of Industrial Medicine
1981 - 1982	Fellow, Mount Sinai School of Medicine, Department Community Medicine, Enviromental Sciences Laboratories, New York City
1979 - 1981	NIH Post-Doctoral Fellow in Environmental Epidemiology, Mount Sinai Medical School of Medicine, New York City
1978 - 1979	NIH Post-Doctoral Fellow in Biological Psychiatry, Millhauser Laboratories, New York University Medical Center, New York City
1978 - 1979	Clinical Psychology Intern, Park East Psychological Associates, New York City

Dr. Raymond Singer December 5, 1983

1972 - 1978 Teaching and Research Assistant, Department of Psychology, Washington State University, Pullman, Washington

PUBLICATION AND PAPERS

Singer, Raymond. Peripheral nervous system assessment in the evaluation of toxic chemical exposure. Paper to be presented at the 12th Annual Meeting of the International Neuropsychological Society, Houston, February, 1984.

Singer, Raymond. Neural indicators of phenoxy herbicide exposure. Paper presented at the 1983 Annual Meeting of The Society for Occupational and Environmental Health, Washington (D.C.), December, 1983.

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Singer, R. The role of the psychologist in the prevention of myopia. Paper presented at the annual meeting of the American Psychological Association, New York, New York, September, 1979.

Singer, R. The Camphill approach to the education of the retarded person. Symposium presented at the annual meeting of the American Psychological Association, New York, New York, September, 1979.

Singer, R. The behavioral etiology of myopia. Paper presented at the annual meeting of the Eastern Psychological Association, Philadelphia, Pennsylvania, May, 1979.

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Singer, R., Young, F., and Rokeach, M. Values as predictors of visual refractive error (in Barrow Eskimos). Paper presented at the Western Psychological Association Convention, Seattle, Washington, April, 1977.

Singer, R. Can myopia be prevented? Invited address - Presented to the Washington State University Chapter of Sigma XI, February, 1976.

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Young, F., Singer, R., and Foster, D. The psychological differentiation of male myopes and non-myopes. American Journal of Optometry, October, 52, 10, 679-686, 1975.

1984

THEODOR D. STERLING, Ph.D.

Dr. Sterling is Professor in the Facility of Interdisciplinary Studies and Department of Computing Science, Simon Fraser University, Vancouver, British Columbia, Canada. His Curriculum Vitae is attached.

Dr. Sterling is a mathematician, statistician, and epidemiologist; as well, Dr. Sterling is intimately familiar with existing data and analyses concerning the effects of phenoxy herbicides and impurities, e.g. 2,3,7,8-TCDD, contained therein. Dr. Sterling has devoted much of his teaching and research to the collection and analysis of data and their use for scientific inference.

Dr. Sterling will testify that there exists a considerable body of medical and scientific evidence which demonstrates that the preparations of 2,4,5-T and 2,4-D are toxic, teratogenic, and carcinogenic. Further, there is no credible scientific evidence of a no effect level; said another way, as a carcinogen, there is no safe level and therefore a single exposure years ago may be responsible for human cancer which develops today.

In addition, Dr. Sterling will testify that there is ample evidence that exposure to 2,4,5-T is teratogenic in humans when the mother is exposed, and convincing evidence is now extant that the outcome of pregnancy is influenced by exposure to the father alone.

Most especially, Dr. Sterling will testify of the incidence of subjective symptoms and/or medical records documenting such symptoms. These symptoms are those which have been compiled by the National Center for Health Statistics, and will be compared, to the extent available, to those symptoms of the Vietnam veterans, particularly those of the representative plaintiffs.

The purpose will be to ascertain the incidence of such symptoms in the general population so as to analyze statistically the symptoms of the plaintiffs. The product of such overall incidence will be calculated to examine the possibility or likelihood of such a constellation of Agent Orange/dioxin related symptom complex to occur in a random fashion.

The bases or grounds for the facts and opinions of Dr. Sterling's testimony are: educational and professional background; publications regarding the subject phenoxy herbicides; review of the applicable medical and scientific literature; attendance and participation in various symposia dealing with the scientific issues in question; training as a mathematician, statistician, and epidemiologist; and training and experience in the computer sciences.

CURRICULUM VITAE

Theodor D.Sterling

EDUCATION

B.A. (CUM LAUDE), 1949, M.A., 1952, University of Chicago; Ph.D., 1955, Tulane University.

PROFESSIONAL AFFILIATIONS

Present: Professor, The Faculty of Interdisciplinary Studies and Department of Computing Science, Simon Fraser University.

Previous: Visiting Professor, Department of Statistics, Princeton University, (78). Chairman, Department of Computing Science, Simon Fraser University, (72-77). Professor in the Department of Applied Mathematics and Computer Science, Washington University, St. Louis, Missouri (66-72). Also Joint appointment as Professor in the Department of Sociology (66-68), and Visiting Professor in Computers and Humanities, Hebrew Union College, Cincinnati, Ohio (68-70). Professor of Biostatistics and Director of the Computing Center, College of Medicine, University of Cincinnati, Ohio (58-66). Previously instructed in the Department of Statistics, Michigan State University and Department of Mathematics, University of Alabama.

PROFESSIONAL ACTIVITIES

ACM Committee on Scientific Freedom and Human Rights; President of the Computer Science Association of Canada (75-80); Chairman, Ombudsman Committee, Canadian Information Processing Society (73-80); Chairman, President of Biological Information Processing Organization (64-65); Chairman, CIPS Special Interest Groups, Humanization of Information Systems (73-80); Chairman, SIGCAS Committee of Information and Public Policy (72-); President of Missouri Chapter, American Association of Workers for the Blind (70-72); Member of the Panel for Biology, Management, and Social Sciences of the Mathematics Association of America (62-67); Chairman, Committee on Professional Activities of the Blind of the Association for Computing Machinery (63-71); Chairman, Ad Hoc Committee on Accreditation, Association for Computing Machinery (66-67); Committee on Radiation Dosimetry, American Association of Physicists in Medicine (66-69); National Lecturer for Association for Computing Machinery (72-3, 75-6).

EDITORIAL ACTIVITIES:

Associate Editor - Canadian Journal of Statistics (73-78); Editorial Board - International Journal of Biomedical Computing (69-); Computers and Applied Mathematics (73-), Humanist in Canada (73-).

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GOVERNMENT AND OTHER SERVICES:

(Consultant/adviser, now and previous): (In Canada) - Canadian Standards Board; Environment Canada, The Royal Commission (B.C.); Consumers Association of Canada; Society for Professional and Environmental Control. (In U.S.) - NIH; PHS; EPA; FTC; SRA; U.S. National Academy of Science, National Research Council; American Lung Association; Natural Resource Board (Wisconsin); Environmental Defense Fund, MECCA (Minnesota); Citizens Against Toxic Sprays (Oregon). (In Kuwait) - Ministry of Health.

PROFESSIONAL SOCIETIES:

Can. Inf. Proc. Soc.; Can. Comp. Sci. Assoc.; Assoc. Comp. Machinery; Amer. Math. Assoc.; Math. Soc.; Inst. Math. Stat.; Amer. Stat. Assoc.; Biometric Soc.; N.Y. Acad. Sci.; Amer. Assoc. Phys. Med.; Assoc. Res. Opthamology.

HONORS AND AWARDS:

Fellow, Amer. Assoc. for Advancement of Science; Fellow, Amer. College of Epidemiology; Fellow, Amer. Stat. Assoc.; Fellow, Can. Com. of Scientists and Scholars; Sigma Xi; Pi Nu Epsilon, Morrison Cressy Award in National Science; University Research Professor (1980-1981).

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1957

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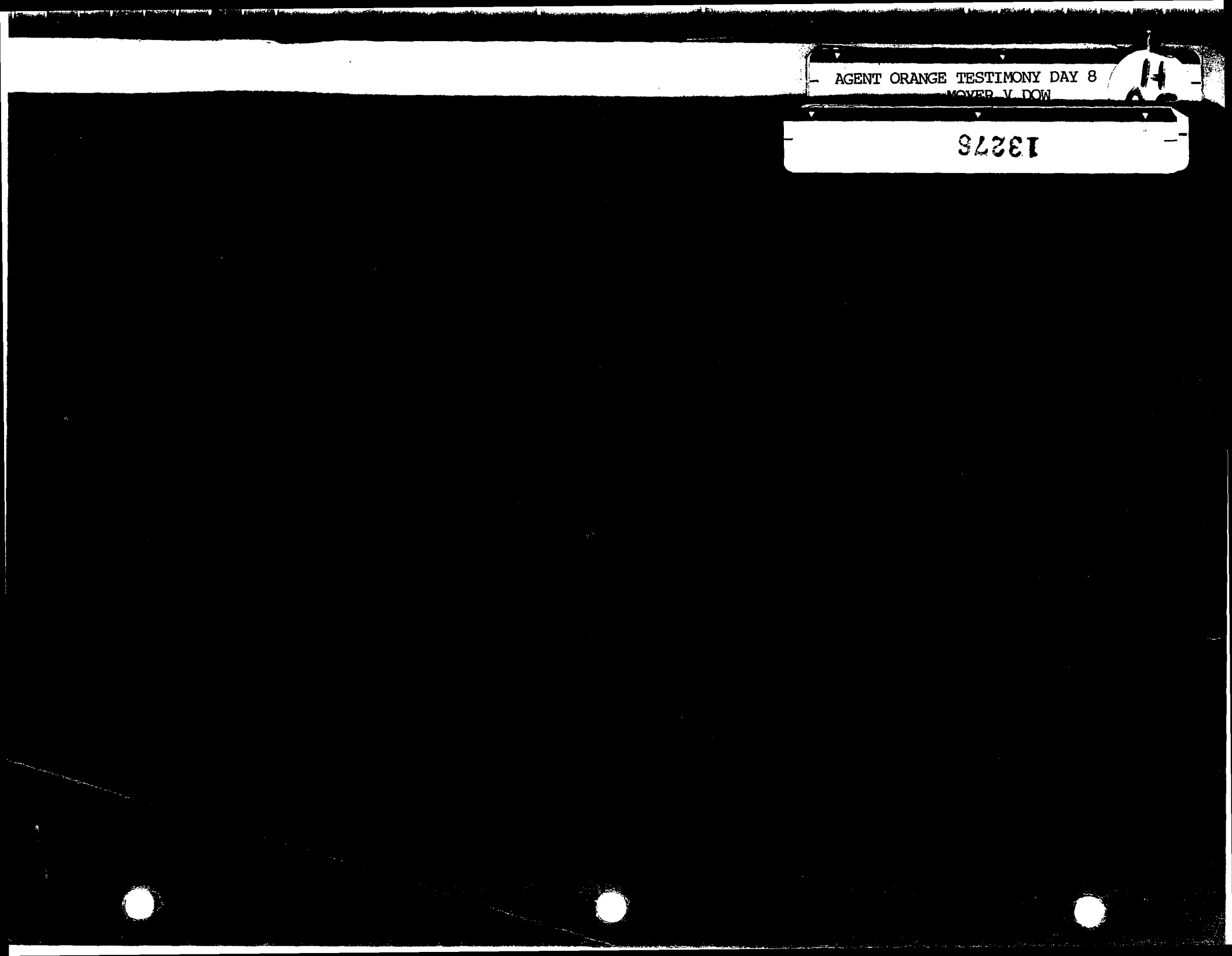
Bio-Statistician/Mathematician-

This witness will be identified in the near future. At that time a curriculum vitae will be supplied.

This witness will describe the mathematical/statistical model which will be used in the presentation of the figures to which the witness will testify. The theory subserving the testimony is that the multi-faceted presentation of symptoms and signs and test results in the same veteran makes a random composition of such an array extremely unlikely in view of the relative in-frequency of each facet of the array. As such, this testimony will be used in the generic and specific proximate causation areas.


AGENT ORANGE TESTIMONY DAY 8
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February 13, 1984

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U.S. DISTRICT COURT E.D. N.Y.
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TIME A.M.
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Honorable Shira Schneindlin
Magistrate & Special Master
United States District Court
Eastern District of New York
225 Cadman Plaza East
Brooklyn, New York 11201

Re: In re "Agent Orange" Product Liability Litigation - MDL No. 381

Dear Magistrate Scheindlin:

In conformity with the representation made by the Plaintiffs to you at the hearing he d on February 9, 1984, we are tendering the following as our preliminary list of our priority witnesses.

Plaintiffs wish to depose:

Debdas Mukerjee, EPA - D.C.

Philip J. Landrigan, CDC, NIOSH

Janet Springer, EPA - D.C.

Vernon N. Houk, CDC - Atl.

James Mason, CDC - Atl.

Dr. Diane Courtney, EPA - D.C.

Peter Infante, NIOSH, D.C.

Umberto Saffiotti, NCI - D.C.

Donald Barnes, EPA - D.C.

1848

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DIAMOND-SHAMROCK WITNESSES

I. Diamond-Shamrock employees:

David J. Porter

S. B. Honour

J. O. King

Melvin Hochberg

Howard E. Edison

Lex Creamer (Would like to depose, but unable to locate)

II. Government witnesses:

M. Isele, DCAS - Contracting officer

J. K. Murphy, Chief - Contracts branch

E. R. Sabala, DCAS - Contracing officer

I. Wolin, DCAS - Cleveland, Ohio

DCASR - Commander
Contracting officer
1367 E. 6th
Cleveland, Ohio

DOW CHEMICAL COMPANY

I. Employees:

George E. Lynn

Julius Johnson

H. R. Hoyle

Ross Mulholland

Larry G. Silverstein

Ray Holmes

R. D. Wilcox

V. K. Rowe

G. Goergen

Paul Orrefice

Sam Birkman

John Barber

Joseph G. Temple, Jr.

Etcyl H. Blair

David L. Rooke

HERCULES' WITNESSES

I. First priority list:

C. L. Dunn

T. Eagon

A. E. Sidwell

A. L. Triesback

H. E. Wilder

II. Second priority list:

J. G. Copeland

Rafael H. Huston

Charles E. Minarick, U.S. Army - Biochemical

Custodian of Records of NACA - National Agriculture Chemicals Association, Washington, D.C.

Custodian of Records of Bionetics Research Laboratories, Bethesda, Maryland

III. Third priority list:

Otis Fancher, Industrial Biotests Laboratories

Custodian of Records of Industrial Biotests Laboratories, Illinois

R. T. Yates

Custodian of Records of Hazleton Laboratories, Falls Church, Virginia

HERCULES' WITNESSES - cont.

IV. Defense Personnel Supple Center - Contracting officers: Government witnesses

Donald Elmore

Thomas P. Dalby

Jacob L. Bolton

Ellis Cash

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MONSANTO WITNESSES

I. Charles Luecke

John Mullendore

Carl Bohl

Phillip Balderson

Homer Payton

Frederick L. Rupel

Ronald R. Smith

R. L. Payne

Tom K. Smith

Richard Wallace, M.D.

Nel Putzel

Louis Schwartz

Robert R. Rumer (Recall)

U. L. Sims

R. L. Null

Toby White

Howard Minkler

E. Weger

Nick Machacrola

Paul Ekberg

Jim Starrett

Bruce Ely

MONSANTO WITNESSES - cont.

II. Contracting officers - Richmond, Virginia:

John Blish

George Collins

Jesse Gershberg

III. Monsanto inspectors - St. Louis region:

Ten Eyck

R. D. Fisher

M. McCalley

Roy Meyers

N. Wirz

R. Wright

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THOMPSON CHEMICAL COMPANY
WITNESSES

I. Employees:

John Mayer

Leo Crivello

D. Halleck

Cecil McGill

James Reagan

F. Vargas

II. Government witnesses:

DCSR, Director Commander - St. Louis, Missouri

III. Miscellaneous witnesses:

Dr. Earnest Velasco
Kosciusko Medical Clinic
St. Louis, Missouri

American Mutual Liability Insurance Company
St. Louis, Missouri

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UNIROYAL, INC. WITNESSES

I. Defense Contract Administration Service Office:

F. H. Placet (Process inspector)

A. Matasauage - Industrial Specialist

M. Dojny - Quality Assurance Rep. (Chemical inspector)

A. W. Glenn - Preservation Packing Specialist

Harold A. Lloy - Administration Contracting officer

Wayne Vandervendor - Specialist for Technical Orange Herbicides

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T-H AGRICULTURE & NUTRITION CO.
WITNESSES

I. T-H Agriculture & Nutrition Co. employees:

L. S. DeAtley

Bill Sulzen

Art Wilson

Dr. Charles Lewis

Bob Mayer

Jack Hallen

II. Government witnesses:

Edward E. Adams - St. Louis, Missouri

A. A. Block - Kansis City, Missouri

James E. Bowers - St. Louis, Missouri

Charles Dilley - Kansas City, Missouri

Frank W. Kleman - St. Louis, Missouri

Joseph W. Fowler - Kansis City, Missouri

Respectfully submitted,

Stephen J. Schlegel

On behalf of the Plaintiffs' Management Committee

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AGENT ORANGE SERVICE LIST

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Magistrate - Special Master
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UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF NEW YORK
----------X

In re:

"AGENT ORANGE" MDL #381

Product Liability Litigation
----------X

PRESENT LIST OF PLAINTIFFS'
CAUSATION WITNESSES
WITH ATTACHED EXPANDED SUMMARIES
IN ACCORDANCE WITH FRCP 26(b)(4)(A)(i)

AND

GENERAL STATEMENT OF SCIENTIFIC
PRINCIPLES AND ASSUMED FACTS

PLAINTIFFS' MANAGEMENT
COMMITTEE

By Thomas W. Henderson
Thomas W. Henderson, Esquire

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1904

GENERAL STATEMENT OF
SCIENTIFIC PRINCIPLES AND ASSUMED FACTS

A. BACKGROUND

The Plaintiffs' experts represent a cross-section of the scientific and medical community who have individualized areas of specialization, but, who, because of their training and expertise, have a common nucleus of scientific principles and assumed facts, which would be virtually unknown to the lay person and the jury without some explanation. This will serve to inform the Court and the Defendants of those areas which any one or more of the Plaintiffs' individual experts may testify to and which represent a "common consensus" of scientific principles and assumed scientific facts which the credible medical and scientific community, including all plaintiffs' experts, share.

The complexity of the instant litigation from the perspective of a layman necessitates a rather comprehensive overview of the basis scientific and medical disciplines. See Plaintiffs' Supplemental Answer to Interrogatory No. 2(d) which lists the basic scientific medical disciplines involved.

Plaintiffs have attempted to select causation experts who have unique areas of specialization which will in large part form the bases of their testimony, but, more importantly, these particular experts, because of their broad based experiences and qualifications, will hopefully be able to synthesize for the jury the broad scope of issues which are at the crux of

this lawsuit including:

(1) The chemistry, biochemistry of the defendants' products, including Agent Orange and its dioxins;

(2) The manufacturing and industrial processes used by the defendants to formulate Agent Orange and as a by-product the formation of dioxins;

(3) The extreme toxicity of one particular dioxin, 2,3,7,8-TCDD, which is the most toxic chemical ever synthesized by man. Specifically, the toxic effects of Agent Orange and 2,3,7,8-TCDD and its other dioxins, on our entire ecosystem and the balance of life that nature tries to maintain, including TCDD's threat to plant life, animal life, and human life, and more specifically, to the Veteran class of plaintiffs who were exposed to this most toxic of all poisons while serving their country in Vietnam.

Plaintiffs have exerted their best efforts to avoid repetition and unnecessary overlap of testimony. While the plaintiffs' experts testimony may in some instances overlap, each individual expert will be able to enlighten the Court and jury within their own specialty areas.

B. DEFINITIONS AND SHORT EXPLANATIONS OF EACH DISCIPLINE
(Tabers' Cyclopedic Medical Dictionary, 11th Ed., F.A. Davis Co., (1915 Arch St., Phil) 1970)

I. Chemistry/Botany

1. Botany/Plant Physiology -

Science of cells, tissue and organs of plants

2. Biochemistry -

The chemistry of living things; the science of the chemical changes accompanying the vital function of plants and animals

3. Bio-Assay -

Greek bios - life
French essayer - to try

Estimation of strength of a drug by noting its effect in test animals and comparing such with effect of a standard preparation

4. Chemistry

The science that treats the molecular and atomic structure of matter and composition of substances, their formation, decomposition, and various transformations which they may undergo.

5. Biological Chemistry

The chemistry of living things involving all chemical processes which take place within an organism, such as, digestion of food, anabolism and catabolism.

6. Inorganic Chemistry

The chemistry of compounds not containing carbon.

7. Organic Chemistry

The chemistry of carbon compounds.

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8. Pathological Chemistry

The study of chemical change by disease processes; changes in

chemistry or organs and tissues, blood, secretions, excretions, etc.

9. Physiological Chemistry

Study of chemical nature of living matter and the changes occurring in the metabolic activities of plants and animals

II. Animal Toxicology

10. Animal Toxicology

The study or science of poisons, their nature, effects and antidotes in animals

11. Toxic

Greek: poison/poisonous
To, resembling or caused by poison

12. Toxicity

The extent, quantity and degree of being poisonous

13. Toxicide

A chemical antidote for poisons

14. Toxicology

The study or science of poisons, their nature, effects and antidotes.

15. Toxigenic/Toxigenicity

Producing toxins or poisons; the virulence of a toxin - producing pathogenic organism.

16. Toxins

A poisonous substance of animal or plant origin

17. Bacterial Toxin

A. Exotoxins (extracellular)

Toxin produced by bacteria, which diffuse from bacterial cells into surrounding medium

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B. Endotoxins (intracellular)

Toxin produced by bacteria, which are liberated only when bacterial cell is destroyed

III. Neuro-Behavorial

18. Neurotoxicity

Study of the behavior of poisons on the neurological system (nervous tissues) of animals and humans, particularly TCDD

19. Neurology

The branch of medicine that deals with the nervous system and its diseases

20. Neurolysin

A substance which destroys nerve cells

21. Neuron

A nerve cell, the structural and functional unit of nervous system consisting of a cell body (perikaryon) and its processes (on axon and one or more dendrites) initiators and/or conductors of messages from the terminal branches of cell to the cell body or receptor

22. Peripheral Nervous System

Whose processes (messages) constitute the nerves conducting messages from the brain and the spinal cord throughout the body of animals and humans into the body's extremities

23. Central Nervous System

The brain and spinal column nervous of an animal and human which send messages to all other parts of body via peripheral nerves.

24. Porphyrin Levels

One group of cells forming basis of animal and plant respiratory pigments, obtained from hemoglobin (blood - human/animals) and chlorophyll (plants)

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25. Porphyria (PCT)

Porphyrin in the blood; a rare metabolic disease characterized by excessive excretion of porphyrins, acute abdominal pain and neurologic disturbances, sensitivity to light is characteristic

26. Myelin Sheath

A fat-like substance or protective covering for nerve fibers; Greek word: myelos = marrow)

A complex lipoid (fatty) substance present in the brain in small quantities, but predominantly a protective shield for the nerves conducting messages throughout the bodies of animals and humans

IV. Immunology

27. Immunology

Study of how body responds to foreign (antigenic) stimulation and tries to protect itself

28. T - Lymphocytes; B - Lymphocytes

Immunoregulatory cells of immune system - regulates a number of responses which destroy host cells bearing foreign substances; and regulates cell - mediated resistance to infectious agents

29. Immune Bodies

Substances in those afflicted with an infectious disease or toxic foreign substance formed by the tissue and possessing power to destroy or injure the disease producing or poison producing agent or to neutralize the toxins.

These substances are formed in serium of coagulated blood, in blood plasma and in lymph glands - called antibodies; each is result of specific antigen (foreign substance) or disease producing factor which acts only upon the same antigen. They are determined by the effect they cause. If the antigen is poisonous it is called toxin and its antibody, is called an Antitoxin.

29a. Immuno-Toxicology

The undesirable effects of an inappropriate response of the immune system.

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V. Oncology

30. Oncology

The diagnosis, treatment and care of cancer victims with emphasis upon the cause of the cancer so that preventive medicine may prevent the occurrence of cancer in others.

31. Carcinogen

Any substance that has been shown to cause tumors in animals or man. As a matter of principle all chemical carcinogens which are shown to be active in men are also active in animals. Scientifically, there is no way to determine a "safe" level for substances (chemical) known to produce cancer in animals or man.

A malignant tumor or neoplasm; a sarcoma or carcinoma.

VI. Reproductive Toxicology

32. Reproductive Toxicology

Study of poisons which affect the process by which plants, animals and humans give rise to offspring or create a similar structures or living beings (the act of duplicating oneself).

VII. Other Definitions

33. Internal Medicine

The study of the human body as a whole with emphasis on the internal body structure and organs, their functions and interrelationships of the various body systems.

34. Psychology

The study of medicine dealing with mental processes, both normal and abnormal and their effects upon behavior, including four primary methods: (1) experimental; (2) comparative; (3) genetic; and (4) pathological.

35. Physiologic; Psychology

The study of the structure and function of nervous system and other bodily organs and their relationship to behavior.

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36. Fetotoxicity/Teratotenicity

Fetotoxicity is a general term used to describe all abnormalities (both transient and permanent) originating in an embryo or fetus regardless of the timing of any such action. A special fetotoxic effect is called teratotenicity which is an abnormality from impairment of an event which occurs at a specific time in an embryo's or fetus' development in the mother.

37. Mutagenicity/Cytotoxicity

Sudden, permanent variation with offspring differing from the parents in a marked characteristic as differntiated from gradual variation through many generations; a dramatic change in genes and/or chromosomes potentially capable of being transmitted to offspring.

38. Epidemiological and Biostatistics

The methods by which cause and effect relationships are determined in the medical and scientific community.

The study of medicine concerned with explaining the interrelationships of the host, agent and environment in causing or contributing to cause a disease or physical condition.

39. Gonadotoxicity

The study of substances which poison the gonads; "Gonad" refers to both the female sex glands or ovaries, and the male sex gland or testes. The embryonic sex gland before differentiation into testes or ovary.

40. Genetics

The science that accounts for natural differences and resemblances among organisms related by descent; the study of heredity and its variation

41. Dermatology

The study of the skin and the diseases of the skin.

C. CHEMISTRY/BIOCHEMISTRY

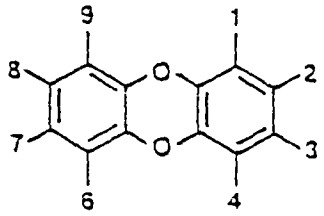
I. Chemical Formulation of 2,4-D, 2,4,5-T and 2,3,7,8-TCDD

Plaintiffs as a class represent the veterans who served in Vietnam between 1961 and 1972 and were exposed to the spraying of a herbicide known as Agent Orange which was composed of 2,4-D (Dichlorophenoxyacetic acid) and 2,4,5-T (trichlorophenoxyacetic acid), which chemical compounds are known to be neurotoxins by the credible scientific and medical community. It has further been established that a family of chemical compounds, commonly known as dioxins (dibenzo-p-dioxins), are produced in the manufacturing processes utilized by the Defendants in the instant lawsuit since the date production of these herbicides began in approximately 1925 through the last days of spraying operations in Vietnam in approximately 1972. The Defendants comprise almost 99% of the relevant herbicide production market between 1961-1972 which was sold to the U. S. Government for spraying operations in Vietnam. The World Health Organization in 1971 found "no acceptable daily intake for man" for 2,4,5-T. Because of the extreme toxicity of all dioxins, and particularly of 2,3,7,8-TCDD, a known contaminant of 2,4,5-T and hence of Agent Orange, it is important to understand the chemical formation of dioxin 2,3,7,8-TCDD, the "most toxic chemical synthesized by man."

II. Chemistry of Dioxin Formation

The basic chemical composition of the family of compounds known as "dioxin" consists of two double-bonded benzene rings interconnected with a pair of oxygen atoms which close a third center ring. The nucleus of a "dioxin" is clearly shown in the diagram below, and represents a triple ring structure. Each of the numbered positions as shown in the diagram can hold a chlorine or

other halogenated or organic radical. Or, if there are no other substituents in the formula in the manufacturing or process formula, a hydrogen will be attached at one or more of the numbered positions.



The only difference in the "dioxin" family is the nature and positions of the substituents which are attached to the benzene rings at the numbered positions above. Most of the environmental interest in the dioxin group is centered in chlorinated dioxins where chlorine atoms are attached to one or more of the eight positions on the two benzene rings. There are theoretically seventy-five (75) positions available for chlorine atoms to attach in various formations. These represent differences in the number of chlorine atoms which attach to the eight positions available and to the relative positioning of chlorine atoms in the "dioxin" nuclues itself. See list of all seventy-five theoretical Chlorinated Dioxins on the Table which follows.

For example, there are two possible isomers of monochlorodibenzo-p-dioxin (MCDD). Therefore, there are two places on the two benzene rings which allow only one chlorine atom to attach and those are at positions no. 1 or no. 4. Also important is that the particular type of dioxin, tetrachlorodibenzo-p-dioxin (TCDD's) which has been classified as most toxic, has twenty-two (22) isomeric possibilities. On page 4 of the EPA Chart which follows is the diagram of the 2,3,7,8-TCDD nuclues, the most toxic contaminant of Agent Orange and of all dioxins.

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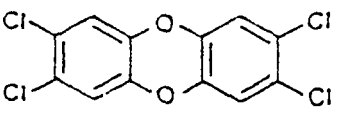
Table 1 lists the 75 possible chlorinated dioxins, and also notes the 40 that have been prepared and identified and whose analytical characteristics have been published (Buser, Bosshardt, and Rappe 1978; Buser 1975; Pohland and Yang 1972; Bolton 1978). Five others, as noted in the table, have been identified as distinct compounds but have not been clearly differentiated from each other (Buser, Bosshardt, and Rappe 1978; Buser 1975; Rappe 1978).

TABLE 1. CHLORINATED DIOXINS

1-chloro	a	1,2,3,4-tetrachloro	a,d	1,2,3,4,6-pentachloro	a
2-chloro	a	1,2,3,6-tetrachloro		1,2,3,4,7-pentachloro	a
1,2-dichloro	a	1,2,3,7-tetrachloro		1,2,3,6,7-pentachloro	
1,3-dichloro	a	1,2,3,8-tetrachloro	a	1,2,3,6,8-pentachloro	c
1,4-dichloro	a	1,2,3,9-tetrachloro		1,2,3,6,9-pentachloro	
1,6-dichloro	a	1,2,4,6-tetrachloro		1,2,3,7,8-pentachloro	a
1,7-dichloro		1,2,4,7-tetrachloro		1,2,3,7,9-pentachloro	c
1,8-dichloro		1,2,4,8-tetrachloro		1,2,3,8,9-pentachloro	
1,9-dichloro		1,2,4,9-tetrachloro		1,2,4,6,7-pentachloro	
2,3-dichloro	a	1,2,6,7-tetrachloro	a	1,2,4,6,8-pentachloro	
2,7-dichloro	a	1,2,6,8-tetrachloro		1,2,4,6,9-pentachloro	
2,8-dichloro	a	1,2,6,9-tetrachloro	a	1,2,4,7,8-pentachloro	a
1,2,3-trichloro	a	1,2,7,8-tetrachloro	a	1,2,4,7,9-pentachloro	c
1,2,4-trichloro	a	1,2,7,9-tetrachloro		1,2,4,8,9-pentachloro	
1,2,6-trichloro		1,2,8,9-tetrachloro	a	1,2,3,4,6,7-hexachloro	a
1,2,7-trichloro		1,3,6,8-tetrachloro	a	1,2,3,4,6,8-hexachloro	a
1,2,8-trichloro		1,3,6,9-tetrachloro	a	1,2,3,4,6,9-hexachloro	a
1,2,9-trichloro		1,3,7,8-tetrachloro	a	1,2,3,4,7,8-hexachloro	a
1,3,6-trichloro		1,3,7,9-tetrachloro	a	1,2,3,6,7,8-hexachloro	a
1,3,7-trichloro	a	1,4,6,9-tetrachloro	a	1,2,3,6,7,9-hexachloro	a
1,3,8-trichloro		1,4,7,8-tetrachloro		1,2,3,6,8,9-hexachloro	b
1,3,9-trichloro		2,3,7,8-tetrachloro	a	1,2,3,7,8,9-hexachloro	a
1,4,6-trichloro				1,2,4,6,7,9-hexachloro	a
1,4,7-trichloro				1,2,4,6,8,9-hexachloro	b
2,3,6-trichloro				1,2,3,4,6,7,8-heptachloro	a
2,3,7-trichloro	a			1,2,3,4,6,7,9-heptachloro	a
				Octachloro	a

a—Identified compounds.
b—One or the other of these compounds has been prepared.
c—A mixture of these three compounds has been prepared.
d—The Dow Chemical Company has recently reported the synthesis of all 22 TCDD isomers.

The interest of health and environmental researchers in dioxins arose principally because of the toxicity and distribution of one of these compounds, 2,3,7,8-TCDD, whose structural formula is as follows:



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The nucleus of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) is unusual in its symmetry on the horizontal and vertical axes and represents a chemically stable and non-reactive molecule. It is not soluble. in water and most organic liquids. It is extremely lipophilic molecule and colorless crystaline solid at room temperature. The only other formation of dioxin which is similar to the TCDD's is the OCDD's which has the same two-fold symmetry.

III. Precursors/Predioxins

Dioxins apparently are not constituents of a normal growing environment. They are not formed biosynthetically by living organisms. In order to cosntitute a dioxin precursor, a chemical compound used in industry has to meet two conditions:

(1) the precursor compound must be an ortho-substituted benzene ring in which one of the substituents includes an oxygen atom directly attached to the right.

It should be noted that a singe oxygen atom is very unstable and does not occur by itself; therefore, usually a phenol group (OH) is used in order to detach the oxygen atom from the hydrogen in a process known as hydrolosis.

(2) it must be possible for the two substituents excluding the oxygen atom to react with each other to form an independent compound.

The most common manufacturing for this two step reaction is the hydroxal group of phenols, which supplies the ring attached oxygen and the hydrogen of the hydroxal atom is capable of reacting with chlorine. The most common predioxins are trichlorophenol potasium salt and trichlorophenol sodium salt. The condensation of 2,4,5-trichlorophenol (TCP), the first step in the process, results in the formation of a dibenzo-p-furran (two benzene rings with

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four symmetrical chlorine atoms (2,3,7,8) and one oxygen atom connected at the top of the two benzene rings, and also produces industrial salt NACL or KCL, sodium chloride or potassium chloride.

The second step then substitutes the second oxygen which closes the benzene ring or which has the potential for closing the benzene ring with the second oxygen connecting it and allows the sodium or potassium to react with chlorine to make industrial salt used primarily in fertilizers.

All of these reactions occur under heat and pressure and over and in the presence of metal catalysts. The importance of the manufacturing process itself is emphasized because process engineers choose various chemical compounds to create an end product, not based on its safety, but simply based on the ability of the manufacturer to produce the maximum amount of the product at the lowest possible cost; hence, various manufacturing processes themselves yield differing amounts of the 2,3,7,8-TCDD contaminant based on factors such as (1) heat, (2) pressure, (3) photostimulation, (4) precursor chemical compounds used and (5) the catalysts, reagents and solvents which are used to encourage the reaction from the clorinated precursors to the predioxins and into dioxins themselves.

The importance of chemical structure of the compounds of 2,4-D, 2,4,5-T emphasize their close similarity with polychlorinated biphenols and other chlorinated napthalenes which have similar chemical structures although somewhat less complex than the triple bonded ring structure of dioxin and have a long history of toxic effects and hazards to humans.

The following quotations from the EPA Dioxin Report, 1978 are relevant:

"On a molecular basis, 2,3,7,8-TCDD is perhaps the most poisonous, synthetic chemical . . . only bacterial exotoxins are more potent poisons."

"It is reasonable to presume, therefore, that the slightest trace of 2,3,7,8-TCDD in the environment may have adverse effects on the health of both human and animal populations."

Toxicity of 2,3,7,8-TCDD

"Because of the remarkable stability of this substance (2,3,7,8-TCDD) in biological systems and its extreme toxicity, cumulative effects of extremely small doses are a major concern."

EPA Dioxin Report, 1978, p.1

D. EXPOSURE TO DIOXINS

I. Modes

Because of the extreme toxicity of all dioxins, but particularly of 2,3,7,8-TCDD, it is important to carefully scrutinize the probable avenues of contamination of the environment. It is known that 2,3,7,8-TCDD can be produced in the manufacture of 2,4,5-Trichlorophenol and other chlorophenols. The amounts of dioxin may vary in each commercial product with temperature and pressure.

Since dioxin contaminants are present in the manufacturing process, the amounts of dioxins varying with different process controls by each individual manufacturer, they are present in chemical waste and sludges remaining from these processes. If these waste products are indiscriminately discharged into the environment or not properly disposed of, contamination of water, air, or food stuff results in widespread exposure of the population to TCDD's and other dioxins. Humans can absorb these chemicals by absorption through the skin; by inhalation while breathing; by ingestion through food and water; and exposure from the use, of proximity to and/or spraying of herbicides. Occupational exposure has occurred in the following situations: (1) in manufacturing plants when TCDD was formed in excessive amounts because the reaction temperature and pressure were high enough to favor dioxin formation, but not high enough to produce an explosion; (2) in explosions at manufacturing plants where the reaction temperature and pressure levels reached exothermic proportions; and (3) from contaminated waste products of these same manufacturers which were released into the environment and/or handled by scientists testing these products. See attached charts on documented human exposures (VA Review of Literature, Exhibit A1-A3). Military exposure to TCDD resulted from the spraying of enormous quantities of 2,4,5-T in South Vietnam which was contaminated with TCDD.

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INDUSTRIAL EXPLOSIONS

References on Industrial Explosions That Involved TCDD

LOCATION	REFERENCES
Monsanto Nitro, WV	Suskind (1973); VA (1980) Zack and Suskind (1980)
BASF Ludwigshafen, W. Germany	Goldmann (1972); Goldmann (1973) Thiess and Frentzel-Beyme (1977)
Rhone Poulenc Grenoble, France	Dugois et al. (1958)
Italy	Joint NIESH/IARC Working Group (1978) Young et al. (1978)
Philips-Duphar Amsterdam, Netherlands	Dalderup (1974); Berlin et al. (1976) Rawls and Sullivan (1976); Hay (1977)
Rhone Poulenc Grenoble, France	Dugois et al. (1968) Rawls and Sullivan (1976)
Coalite & Chemicals Products Bolsover, Derbyshire, U.K.	Jensen and Walker (1972) Jensen et al. (1972; May (1973)
ICMESA Seveso, Italy	Commoner and Scott (1976; Hay (1976) Rawls and Sullivan (1976); Fara (1977) Gianotti (1977); Walsh (1977) Bonaccorsi, et al. (1978); Greim (1978) Laporte (1978); Reggiani (1978) Homberger, et al. (1979) Malizia, et al. (1979) Pocchiari, et al. (1979) Reggiani (1979); Strik (1979) Reggiani (1980); VA (1980); VA (1981)

References Which Review Industrial Exposures to TCDD

Forth (1977)
IARC (1977)
IARC (Joint NIESH/IARC-1978)
Hay (1979)
Moses and Moore (1979)
Esposito et al. (1980)
Hay (1977)
Firestone (1978)
Young et al. (1978)
Malizia et al. (1979)
Crow (1980)
Suskind (1980)

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INDUSTRIAL EXPOSURES

References on Industrial Exposures to TCDD

YEAR	LOCATION	REFERENCES
1949	Nordheim, Westfallen, West Germany	Baader & Bauer (1951)
1951-52	2 factories in Middle Rhein, W. Germany	Bauer et al. (1961)
1954	Boehringer, Ingelheim Hamburg, West Germany	Kimmig & Schulz (1957) Kimmig & Schulz (1957) Schulz (1957); Bauer et al. (1961)
1956	Diamond Alkali Newark, N.J.	Bleiberg et al. (1964) Poland et al. (1971)
1964	U.S.S.R.	IARC (1977)
1964	Dow Chemical (2,4,5-trichlorophenol production) Midland, Michigan	Firestone (1978) Cook et al. (1980) Rowe (1980)
1965-9	Spolana Czechoslovakia	Jirasek et al. (1973) Jirasek et al. (1974) Pazderova et al. (1974) Jirasek et al. (1976) Pazderova-Vejlupkova et al. (1980)
1970	Japan	Miura et al. (1974)
1972	U.S.S.R.	Zelikov and Danilov (1974)
1950-1975	Dow Chemical (2,4,5-T production) Midland, Michigan	Kramer (1974)* Ott et al. (1980) Townsend et al. (1980)*
1955 - 1977	Monsanto Nitro, West Virginia	VA (1980)

*unpublished reports

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. REFERENCES ON OTHER HUMAN EXPOSURES TO TCDD

YEAR	LOCATION	POPULATION DESCRIBED	REFERENCES
1971	Missouri	Farm residents	Carter et al. (1975) Case (1976) Beale et al. (1977) Kimbrough et al. (1977) Crow (1980)
1970	England	3 laboratory workers	Oliver (1975)
1967-1970	Vietnam	Vietnamese residents	NRC (1974)
		Vietnamese refugees	Tung et al. (1971) Rose and Rose (1972) Tung et al. (1980)
		Vietnam veterans	Bogen (1979) Halprin (1980) Stellman & Stellman (1980) VA (1980)
		Vietnam military	Harmon (1971) Allen (1980)

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II. The Fate of 2,4,5-T and Its Dioxin Impurities

Conclusions about the environmental fate of 2,4,5-T vary somewhat with the exosystem being considered. There is general agreement, however, that it is (a) rapidly degrated microbiologically in soil (Norris 1966); (b) not readily leached from soil into the water table (Wiese and Davis 1964); (c) immobilized by soil organic matter (Helling, et al. 1973); and (3) photodecomposed on the soil surface by ultraviolet light (Crosby and Wong 1973). In animals, 2,4,5-T is known to be hydroxylated, degraded to the halogenated phenol, detoxified by coupling to glycine and taurine, and rapidly excreted in the urine (Grunow and Bohme 1974; Shafik, et al. 1971). Where massive doses are given, some residues are detectable in the milk (Leng 1972) and bodily organs (Clark, et al. 1975). In microbes and plants, 2,4,5-T is degraded to the phenol (Fitzgerald, et al. 1967; Sharpee 1973) and subsequently to carbon dioxide in water.

TCDD, by contrast is relatively immobile in soil and not photo-decomposed[1] when attached to soil (Helling, et al. 1973; Kearney, et al. 1972). TCDD is not readily removed from soil to plant, and in the plant does not accumulate in the edible seeds or fruits of soybean or oats (Isensee and Jones 1971). However, in aquatic systems, soil containing 0.1 parts per billion (ppb) TCDD (a concentration that could occur under normal field use of 2,4,5-T) caused appreciable TCDD accumulation in algea, crustaceans, snails, and fish (Isensee and Jones 1975).

In order to decompose this molecule, Crummet of Dow Chemical Co. has done studies that indicate that dioxin survives burning up to 1150° C.

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[1] Recently, evidence has been presented that TCDD breaks down in ultraviolet light (Wong and Crosby 1978).

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Further, although certain higher chlorinated dioxins may lose chlorine atoms on exposure to sunlight or to some types of gammaradiation, the basic dioxin structure is largely unaffected and TCDD is highly stable (Crosby, et al. 1971; Buser, Bosshardt, and Rappe 1978).

> "In comparison to any other organic compound, the biological degradation rate of chlorinated dioxins is slow, although measured rates differ widely."

It has been further established that . . . 2,3,7,8-TCDD can enter the human body from a 2,4,5-T - treated food chain and can accumulate in the fatty tissues and secretions including milk (Galston 1979).

> "Because of the remarkable stability of this substance (2,3,7,8-TCDD) in biological systems and its extreme toxicity, cumulative effects of extremely small doses are a major concern." (EPA at p. 1)

1. Metabolism

A large portion of guinea pigs administered 2,3,7,8-TCDD show that this chemical persists in unmetabolized form in the liver and is responsible for its toxic effects in animals and men. There is some indication that persons with high dietary iron intake are more susceptible to 2,3,7,8-TCDD liver toxicity than persons with marginal iron intake.

(a) Pharmacokinetics & Tissue Distribution

Pharmacokinetics is the study of the rate of elimination and retention of any chemical in animals or humans. Tests performed on tissue distribution of ingested 2,3,7,8-TCDD on rats, guinea pigs, monkeys and chick embryos, as well as the tests performed on humans show accumulation of this toxin in animals as well as humans.

(b) Enzyme Effects

Several investigations show that 2,3,7,8-TCDD has a dramatic influence upon various enzyme systems in many species including man. Several

studies show that 2,3,7,8-TCDD induces many enzyme systems and suppresses others. The mechanism of AHH induction of 2,3,7,8-TCDD and possible the mechanism by which the substance produces other toxic effects had been advanced; 2,3,7,8-TCDD moves into a cell and binds to a specific receptor. The receptor-dioxin complex then moves into a cell's nucleus where it "turns on" the synthesis of a specific messenger RNAs which direct the synthesis of cytochrome P1/450 and related enzymes. This enzyme induction increases the metabolism of TCDD itself as well as other compounds; as a consequence, reactive and cytotoxic and carcinogenic compounds are formed.

(c) Effect on Lipids

2,3,7,8-TCDD has dramatically altered the lipid profiles in laboratory animals and man.

Studies of workers occupationally exposed to 2,3,7,8-TCDD have shown lipid abnormalities, elevated serum cholesterol levels, abnormalities in lipid metabolism and liver function. Further, these lipid abnormalities resulting from 2,3,7,8-TCDD exposure may be a significant risk factor to ischemic vascular disease.

(d) Gross and Histopathologies

The macroscopic-gross pathology and histopathology-microscopic of tissues of dioxin-exposed chickens, rats and monkeys have been examined extensively. At post-mortem examination, the most striking findings in dioxin-exposed animals are usually:
(1) substantial loss of body fat; (2) involution lesions of thymus;
(3) testicular alterations, including atrophy, necrosis, and abnormal spermatocyte development; and (4) liver cell pathology.

(e) Acute Toxicity

2,3,7,8-TCDD is a highly toxic material, several orders of magnitude more potent than many pesticides or herbicides. Some consider it to be the most toxic small molecule made by man (Poland & Kende, 1976).

E. ADVERSE HEALTH EFFECTS

Plaintiffs will testify to their individual exposures to Agent Orange in Vietnam and all experts will base their testimony upon the presumed fact of exposure. Experts will testify that there is no "safe" level of any carcinogen to humans. Agent Orange is a chemical caricnogen and/or carcinogen. There is no "safe" level for any human exposure to 2,3,7,8-TCDD and other dioxins.

Human exposure to 2,3,7,8-TCDD has induced chloracne, and often disfiguring and persistent dermatologic disorders, polyneuropathy (multiple lesions of peripheral nerves), mystagmus (involuntary rapid movement of the eye ball), and liver dysfunction as manifested by hepatomegaly (increase in liver size), and enzyme elevations. In animals and man, this compound has been shown to be teratogenic, mutagenetic, immunotoxic, embryotoxic, carcinogenic, and co-carcinogenic, and caused untoward pregnancy outcomes and birth defects in the wives and children of the veteran plaintiffs. For further explanation of all adverse effects of Agent Orange in the Plaintiffs and the human population, see Plaintiffs' Answers and Supplemental Answers to Defendants' Interrogatories Nos. 1, 2(d), 3(a), 4(a), and 4(c).

ERNEST M. BARAN, M.D.

I. Qualifications (See Curriculum Vitae)

II. Subject Matter

Dr. Baran will testify as to the performance and interpretation of various tests in the veterans. These will include an electroencephalogram on both sleep and waking states with nasopharyngeal leads. He will also perform electromyograms, nerve conduction velocity tests, and somato sensory evoked potentials of the upper and lower extremities.

Dr. Baran will then testify as to the mechanisms by which toxins produce the changes noted in the tests and what the various tests are capable of determining as to the medical status of the patient.

Then he will relate the results obtained in the testing of each plaintiff examined, give opinions as to the causation of those results where possible from the evidence revealed by the tests, and state the prognosis for the individual plaintiff for further deterioration in test results and/or for the individual's condition as a whole.

III. General Scientific Principles

Various substances cause sensory conduction deficits. Among them are neurotoxins. Agent Orange is a neurotoxin capable of causing a sensory conduction deficit.

The mechanisms by which such deficits are caused are either by a demyelinating process in which the sheath of the nerve itself is gradually erroded or by an axonal degeneration in which the nerve itself is broken.

The result of the demyelinating process is that nerve impulses are slowed and, on a functional basis, cause lack of sensation in coordination.

The result of axonal degeneration is that the impulse stops where the break has occurred. If enough of the nerve fibers themselves are caught, there is no response whatsoever. If a lesser number of fibers are caught, there is a smaller response. Functionally, a severence of the nerve chain results in impairments dealing with feeling, touch, and discriminative sensation (i.e. telling rough from smooth surfaces, etc.).

Additional tests may help to specify the particular causative agent for the sensory conduction deficit. Tests would include those which show which fibers had degenerated, tissue assays and a study of antibody deposits on the nerves.

IV. Substance of Opinion

1. Agent Orange could cause sensory conduction deficit.

V. Grounds for Opinion

Dr. Baran has been out of town and has not been able to prepare the grounds for his opinion as yet. He must do some library work in preparation for it, and he indicates that he will forward the grounds for his opinion as soon as he has done his library work.

Dr. Baran will also rely, in addition to medical and scientific articles, on testing on which he has done on 10 to 15 Vietnam Veterans.

Additionally, Dr. Baran served as an Army medical officer in Vietnam from August, 1969 to July, 1970. During that time, he was an orthopedic and general surgeon. For approximately six months, he operated in the fields in various Vietnamese villages. He has personally observed defoliation in Vietnam, especially on the perimeters of the compounds in which he was stationed as a surgeon.

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DEBORAH A. BARSOTTI, Ph.D.

I. QUALIFICATIONS

Dr. Barsotti is an Assistant Professor of Tocicology in the Department of Pharmacology and Toxicology of the Philadelphia College of Pharmacy and Science in Philadelphia, Pennsylvania. Her curriculum vitae is attached.

II. SUBJECT MATTER

Dr. Barsotti is a toxicologist who has done substantial personal investigative work with halogenated aromatic hydrocarbons. This category of chemicals includes various biphenyls and dioxins, and specifically includes tetrachlorodibenzo-p-dioxin (TCDD). She will testify as to the relative chemical stability and lipophilicity of these chemicals as well as their resistance to degradation, and will testify that these qualities are what account for the perceived and documented bioaccumulation of the chemicals in the human system. Dr. Barsotti will emphasize the difference in results between chronic and acute exposures to these chemicals, testifying as to the varying types of responses to acute and chronic exposures.

Dr. Barsotti will discuss her own work as well as review the literature in these areas, noting differences in routes of

D. That TCDD accumulates and persists in the lipid stores.

E. That TCDD, in chronic doses, is toxic, is particularly toxic to reproductive system, is teratogenic, and is fetotoxic.

F. There are ample scientific bases, for extrapolating animal experimental data to man, in the case of TCDD, for example, as demonstrated by Dr. Barsotti's work on rhesus monkeys.

V. GROUNDS FOR EACH OPINION

A. General

Review of applicable medical and scientific literature; education and training; personal research. The work on the chronic toxicity of HAHs in rhesus monkeys has culminated in numerous publications as presented in Dr. Barsotti's curriculum vitae. In addition, she has been invited to speak or present her work in various atmospheres including community meetings and scientific symposia.

B. Specific

1. With respect to opinion IV A, see generally references attached.

2. With respect to Opinion IV B, note the following:

Dr. Barsotti will contrast the acute toxicity that one observes in accidental or intentional ingestion of toxic or lethal doses of chemicals with the effects of chronic or lower levels of exposure to chemicals such as HAHs.

4. With respect to Opinion IV D, note the following:

Dr. Barsotti will comment on the state of the literature on the fate of TCDD once in the body, i.e. TCDD metabolism (Vinopal and Cassida, 1973; Ramsey et al., 1979; Schlatter, 1979). Efforts to identify metabolites in tissues and excreta from various studies have been unsuccessful. Recent advances in detection methodology indicate elevated levels of TCDD in Vietnam veterans and other exposed persons. Generally, however, the data indicate that if metabolism does occur the rate is slow (Guenthner et al., 1979) The ramification of this finding is that the body would be incapable of or slow in ridding itself of TCDD and TCDD would accumulate and persist in the lipid stores. In Dr. Barsotti's work, as well as others', this appears to be the case with rhesus monkeys and man (Montagna et al., 1979; Van Miller, 1981; McNulty et al., 1983).

5. With respect to opinion IV E, note the following:

Not only did the rhesus monkey appear a good model for HAH toxicity but established, as had been in other animal species, that the reproductive system was extremely sensitive to PCBs at intake levels below that required for the manifestation of toxic signs in the adult (Barsotti et al., 1976). In addition to PCB induced reproductive toxicity, PCBs were found to be fetotoxic

three months in animals receiving TCDD in the diets at levels of 500 parts per trillion (ppt) and in animals consuming diets containing 50 ppt TCDD these same symptoms occurred after consuming the diets for 30 months (Allen et al., 1977; Schantz et al., 1979). This indicates cumulative toxicity associated with ingestion of TCDD. Thus, there is evidence for bioaccumulation and associated chronic toxicity at lower doses than that required for acute toxicity in rhesus monkeys and presumably man (Pazderova et al, 1981; Ideo et al., 1982.)

6. With respect to Opinion IV F, see generally references attached and V A above.

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S.L. Schantz, D.A. Barsotti and J.R. Allen, Toxicol. Appl. Pharmacol., 46, 180. 1979.

S.L. Schantz and R.E. Bowman, The Toxicologist, Vol. 4, Abstract number 333, March, 1984.

J.P. Van Miller, Doctoral Thesis, University of Wisconsin, 1981.

J.H. Vinopal and J.E. Cassida, Arch. Environ. Contam. Toxicol. 1, 122, 1973.

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DR. RONALD CODARIO

I. QUALIFICATIONS

See the attached curriculum vitae.

II. SUBJECT MATTER

Dr. Codario will testify concerning acute and chronic toxicity of herbicides and TCDD in animals and humans. He will also testify concerning the metabolism of TCDD in body fat, and its mechanism of action, and its persistance in the environment, including both the surrounding environment and the body itself. He will also testify concerning exposures and the amounts of herbicides sprayed, the particular types, and the component elements of TCDD therein.

III. GENERAL SCIENTIFIC PRINCIPLES

Dr. Codario will testify that an organism can have varying types of exposures to toxins, including acute and chronic exposures. An acute exposure, according to the literature, is that which is used to define all the effects of a single exposure on an organism. A chronic exposure is a continuous exposure for up to thirty days or more. A chronic exposure can be an exposure to an exterior toxin, or an exposure to a toxin contained in some manner within the body itself after an exterior exposure. Toxins can have effects upon the following systems:

a. Teratogenicity

b. Mutagenicity

c. Carcinogenicity

d. Neurotoxic affects

e. Gastro-intestinal disturbances, including porphyrins.

f. Immunologic and hematologic

g. Renal

h. Cardiovascular

i. Endocrine and metabolic

j. Pulmonary

The metabolism of herbicides, including Agent Orange, and TCDD is known for animals, but not directly known for humans. It is located in all body tissues in animals, but the herbicides are eliminated through the renal system because they are water soluble. The elimination period in humans appears to be between twelve and twenty-four hours. However, TCDD is not water soluble but is fat soluble. Therefore, it is not eliminated by the kidneys unless it is converted to a water soluble substance, which does not appear to occur in humans. In animals, TCDD is metabolized in the following manners:

a. It is broken down to a water soluble substance and eliminated in the urine.

b. It is eliminated in bile fluid.

c. It is sequestered in fat.

d. It is converted to a different toxic substance.

The mechanism of action of herbicides and TCDD in particular is determined at the micromolecular level. At that level, TCDD changes the body chemistry and initiates enzyme induction. TCDD is persistent, especially in the human environment, both externally and internally. In the external environment, it was thought that

the half-life of TCDD in the soil after being sprayed in Agent Orange was approximately three years (900 days). However, the measurements were done in the top soil and it appears that the under-soil has both five to seven times higher concentrations than the top-soil does and that its half-life is longer at the sub-soil level. At least one of the herbicides sprayed in Viet Nam has been determined to exist in soil ten years after spraying, and recent reports indicate concentrations both longer and deeper than previously thought.

The amount of exposure any individual had in Viet Nam may be determinable in part through use of HERBSTAPES,which record the spraying missions flown by aircraft in Viet Nam. However, the HERBSTAPES do not cover nearly all of the spray missions flown there by various aircraft. The doctor will testify as to the totals of each type of herbicide sprayed per year and in total, how much TCDD was was in each type of herbicide, and the acreage sprayed each year for each herbicide.

IV. SUBSTANCE OF OPINIONS

Dr. Codario will testify to the following opinions:

1. Agent Orange, and in particular, TCDD is a chemical toxin.

2. Animal research experience is relevant to humans.

3. Agent Orange and its constituents and its contaminant TCDD effect all of the systems listed above in both man and animals.

4. The doctor will furnish conclusions as to individual plaintiffs in his reports on those individual plaintiffs.

5. TCDD, the particularly harmful toxin, is stored in body fat and furnishes a constant source of exposure to all body systems.

6. The literature and his research documents that chronic exposure to TCDD exhibits many more deleterious effects than single or acute exposures.

7. TCDD binds to a cytosol receptor, which is a gene product of the Ah locus on the chromosomes.

8. TCDD drifts.

9. The Ah locus of the chromosome determines whether the organism will demonstrate toxic effects and whether the liver will go about breaking the substance down. This is what accounts for individual susceptability and the fact that different people exposed to the same toxin do not necessarily get any effects or the same effects.

10. TCDD persisted in the soil of Viet Nam for the duration of the war.

11. The individuals serving in Viet Nam were exposed to TCDD by spraying operations, by drinking contaminated water, by eating wild animals, and by clearing underbrush and digging in the soil.

12. Substantial amounts of TCDD were sprayed throughout Viet Nam to the point that the presence of any veteran in Viet Nam,

in any location, means that he was exposed to TCDD through one mechanism or another, which exposure was sufficient to give him some form of disease depending upon the genetic predetermination of the Ah locus of his chromosomes.

V. GROUNDS FOR OPINIONS

The grounds for Dr. Codario's opinions include:

1. See the attached bibliography.

2. Young, Toxicity And Persistance Of Agent Orange And TCDD In The Environment.

3. Herbicides And Related Dioxins - A Review Of The Literature, J.R.B. Associates.

4. The doctor's own clinical and research work on approximately 500 veterans whom he has personally examined. This work is currently being translated into computer language, and will be computerized for analysis and comparison purposes. The computer data will be furnished as soon as it is completed.

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CURRICULUM VITAE

ADDRESS: Home - 205 Porter Street
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DATE OF BIRTH: 12-9-47 (Pennsylvania Hospital)

PERSONAL: Married Celeste DiSabatino
Children: Ronald Anthony (6-16-81) (Pennsylvania Hospital)
Maria Celeste (6-14-83) (Pennsylvania Hospital)

EDUCATION: LaSalle High School (1961-1965)
LaSalle College (1965-1969 B.A. Biology)
Hahnemann Medical College (1969-1973 M.D.)
St. Agnes Hospital (1973-1974 Medical Internship)
University of Pennsylvania Division of Philadelphia Genera
Hospital (Medical Residency 1974-1976)

PROFESSIONAL SOCIETIES: American Medical Society
Philadelphia County Medical Society
Pennsylvania Medical Society

AWARDS: WHO'S WHO OF MEDICAL SPECIALISTS 1977-1978
MARCONI RECOGNITION AWARD - June 1980 (Outstanding contributio
in the efforts to build Marconi Plaza)
DISTINGUISHED ACHIEVEMENT AWARD - St. Agnes Hospital, Dept. of
Medicine - February, 1980
FREEDOM'S FOUNDATION AT VALLEY FORGE GOLD MEDAL - April, 1981 -
(Outstanding achievement and humanitarian efforts
in treating Vietnam veterans and their families
free of charge)
GUBERNATORIAL CITATION: April 1981 - (Special achievement in
working with Vietnam veterans exposed to herbicides)
PENNSYLVANIA HOUSE OF REPRESENTATIVES CITATION - December 7, 1
(Special citation-sponsored by Rep. Paul Clymer and
Rep. George Sauerman in recognition of work done to
aid Vietnam veterans)
AGENT ORANGE NATIONAL HOTLINE CERTIFICATE OF APPRECIATION -
December 10, 1981 (Volunteer work with Vietnam veter
CHAPEL OF FOUR CHAPLAINS LEGION OF HONOR AWARD - February 28,
UNITED STATES CONGRESSIONAL CERTIFICATE OF MERIT - June 24, 19
SPECIAL CITATION -DISABLED AMERICAN VETS - July, 1982
(Outstanding service to Vietnam veterans)
CHAPEL OF FOUR CHAPLAINS LEGION OF HONOR - September 12, 1982
UNITED STATES CONGRESS CERTIFICATE OF MERIT - September 19, 19
(Outstanding service to Vietnam Vets)
VIETNAM VETERANS OF AMERICA AWARD OF MERIT - November, 1982
(Outstanding volunteer service to Vietnam vets)
HONARARY MEMBER OF THE ADVISARY BOARD OF THE UNITED VIETNAM
VETERANS ORGANIZATION - May, 1982- (honorary position due to
"your position as a leader of the community")
SIGNUM FIDEI MEDAL - November 18, 1983 - (Awarded annually to
the individual who has manifested the highest tradi
tions of Christianity and humanitarianism) LaSalle

 Colleg

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LECTURES/TEACHING:
Administrative Head - Division of Internal Medicine 1978 (St. Agnes Hospital)
Director of Clinical Pathological Conferences 1977-1978 (St. Agnes Hospital)
Lecture - Clinical Pathological Conference (January 1977 - Pseudomonas septicemia in a burn patient)
Lecture - Medical Grand Rounds - St. Agnes Hospital December 1981 - "Human Manifestations of Herbicide Poisoning"
Lecture - Medical Grand Rounds - Methodist Hospital, February, 1982 - "Medical Effects of Agent Orange Exposure"
Lecture - Medical Grand Rounds - Albert Einstein Hospital, August 1982 - "Medical Effects of Herbicide Poisoning
Lecture - Clinical Pathological Conference - "Sudden Death in a Patient with Lung Carcinoma" January, 1984
Lectures - 1983 - Lecture tour of senior citizen homes and meetings to promote health care and Albert Einstein Medical Center
Lectures - 1981 to present - series of 36 lectures on the East coast (Connecticutt to Alabama) on Agent Orange toxicity along with special lectures to the Pennsylvania, New York, West Virginia, Illinois Agent Orange Commissions
Lectures - October 19, 1983 and November 16, 1983 "Agent Orange Toxicity" - sponsored by the Pennsylvania Medical Society
Lecture - April 28, 1983 - "Agent Orange Effects on Vietnam veterans" - sponsored by the Pennsylvania Health Department

HOSPITAL APPOINTMENTS:
Internship - St. Agnes Hospital 1973-1974
Medical Residency - University of Pennsylvania Division - Philadelphia General Hospital 1974-197
Assistant Chief Admitting Physician - Emergency Room of Philadelphia General Hospital, 1976-1977
St. Agnes Medical Center - Attending Physician 1976-present
Methodist Hospital - Attending Physician - 1980-present
Albert Einstein Daroff Medical Center - 1982-pres Attending Physician
Police Surgeon, City of Philadelphia, 1978-presen
MEDICAL EXECUTIVE COMMITTEE - St. Agnes Hospital 1983
UTILIZATION REVIEW COMMITTEE - St. Agnes Hospital 1984 and Albert Einstein Hospital (1983-presen

PUBLICATIONS:
September 1976 - "Stroke" - Goldberg,H., Codario, R. et al. REGIONAL CEREBRAL BLOOD FLOW IN PATIENTS WITH SEVERE HYPERTENSION FOLLOWING THE ADMINISTRATION OF DIAZOXIDE

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January, 1984 - Agent Orange-Myths and Realities, THE VETERAN EXPERIENCE , Jan./Feb. page 12

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RELATED ARTICLES/BOOKS/TELEVISION/RADIO

PHILADELPHIA INQUIRER: October 25, 1981 -Investigat Agent Orange: a doctor's personal project. Darryl Sifford

PHILADELPHIA JOURNAL: November 20, 1981 - Agent Orange Makes South Philly Doc See Red. Bruce Bea

CAMDEN COURIER-POST: May 17, 1982 - Doctor treats Vets but has no answers, Julie Busby

ALUMNI - feature article of the Hahnemann Medical College - Spring, 1982

OMNI - August, 1982 - THE AGENT ORANGE MYSTERY - Pamela Weintraub

PHILADELPHIA DAILY NEWS, November 10, 1982 - Battleground - Viet Vets Still Fighting the War. Maria Gallagher

Television

October, 1981 - KYW-TV Special Report on Agent Oran

October 9, 1982 - PRIME TIME - feature on my work with Vietnam veterans (WPVI-TV)

September 20, 1982 - PEOPLE ARE TALKING - discussio group on Agent Orange (KYW-TV)

November 11, 1982 -(Channel 29) - DEL VAL - discussion group on Agent Orange

January 4, 1983 - EVENING MAGAZINE - (KYW-TV) feature presentation on Agent Orange

June 16, 1983 - WCAU-TV - discussion on herbicide toxicity with Herb Dennenberg

June 18, 1983 - Niagara School of Applied Arts - Documentary on Agent Orange

Radio

July 28, 1983 - WIP People Talk with Michele Iaia - featured discussant on Agent Orange

September, 1983 KSTP News Talk (Minnesota) - The Dick Pomerantz Program - discussion on Agent Orange

BOOKS

WAITING FOR AN ARMY TO DIE, the tragedy of Agent Orange by Fred Wilcox. pp. 114-125

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ARTICLES PENDING:

Review of the Signs and Symptoms of 500 Vietnam Veterans with Special Attention to Porphyrin Analysis
Case Report: Dying Back Neuropathy Due to Dioxin Exposure
Case Reports: Review of 10 Liver Biopsies in Vietnam Veterans (exposed to herbicides)with porphyrin disturbances
Instructive Manual : Toxic Herbicide Poisoning-Diagnosis and Management (Sponsored by the Pennsylvania Health Dept. and the Pennsylvania Medical Society)

LITIGATION EXPERIENCE

As a Police Surgeon for the City of Philadelphia for the past seven years I have been called to testify as an expert witness 50-60 times in matters related to drivers under the influence of drugs, illness, alcohol; as well as the health and physical state of police officers injured in the line of duty.

I have testified in the disability hearings of 18 patients as the expert witness (treating physician)

I have recently finished testifying in the 3-M vs. Hedges case. This case dealt with the neurological effects caused to the plaintiff by his exposure to the 3-M developer. (This case was recently won by the plaintiff).

I have testified at the Veterans Administration hearings of several patients (Vietnam vets and WW II vets) in attempts to obtain service connected disability

PERSONAL EXPERIENCE

In the last three years I have examined close to 500 Vietnam veterans free of charge and have conducted the largest independent survey of their health problems ever recorded. This survey is presently being computerized and statistically analyzed.

ARTHUR W. GALSTON, Ph.D.

I. QUALIFICATIONS

Dr. Arthur W. Galston is Eaton Professor of Botany in the Department of Biology, Yale University, New Haven, Connecticut. See attached curriculum vitae.

II. SUMMARY OF TESTIMONY

Dr. Galston is a plant physiologist and has personally observed the effect of the spraying of Agent Orange on the Vietnam ecosystem, i.e. the devastation of the Vietnamese countryside. Dr. Galston has been in Vietnam on four occasions between 1971 and 1982, and will describe those observations while in Vietnam, with such pictorial evidence as is available

Dr. Galston will testify to the potential and actual effects of phenoxy herbicides and their contaminants, both in Vietnam and elsewhere, including the United States and Sweden, and other places. The testimony will include the chemistry and the mechanisms of action of such chemicals on plant life.

In addition, Dr. Galston will testify to the fate of Agent Orange and other phenoxy herbicides and their contaminants, especially TCDD, in the environment generally and in Vietnam in particular. Dr. Galston will testify to the persistence of such chemicals on plants, in water, and in soil, such that exposure to the phenoxy herbicides and their contaminants, especially TCDD, by the veterans in sprayed areas in Vietnam is presumed.

III. SCIENTIFIC PRINCIPLES AND ASSUMED FACTS

See General Summary of Scientific Principles and Assumed Facts.

IV. SUBSTANCE OF OPINION

Dr. Galston will testify to the following opinions:

1. Agent Orange, phenoxy herbicides and their contaminants have had a long-term catastropic effect upon the environment in Vietnam.
2. 2,3,7,8-TCDD, one contaminant of Agent Orange, persists in the ecosystem for long periods of time.
3. The level of use of Agent Orange in Vietnam exposed servicemen there to significant levels of TCDD.
4. 2,3,7,8-TCDD can enter the human body from a 2,4,5-T treated food chain and can accumulate in the fatty tissues and secretions including milk.
5. The level of use of phenoxy herbicides and the persistence of the herbicides and their contaminants in the environment means that all veterans in sprayed areas in Vietnam can be presumed to have been exposed to the phenoxy herbicides and their contaminants, including TCDD.

V. FACTUAL BASIS OF OPINION

Dr. Galston's opinion is based upon his personal observations regarding the long-term effects of the use in Vietnam, his knowledge of the persistence of TCDD in the environment, his knowledge as to how TCDD can be transmitted to humans through the food chain and all or part of the following references:

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BIOGRAPHICAL SKETCHES

ARTHUR W. GALSTON, Ph.D., Eaton Professor of Botany, Department of Biology,

Yale University

Born April 21, 1920, New York City. Married, 2 children. B.S. Cornell University 1940; M.S. University of Illinois 1942; Ph.D. University of Illinois 1943. U.S. Navy, 1944-46; Agriculture Officer, U.S.N. Military Government, Okinawa, 1945-46.

Elected to Phi Beta Kappa, Phi Kappa Phi, Sigma Xi, American Academy of Arts and Sciences; National Sigma Xi Lecturer, 1966; National Phi Beta Kappa Visiting Scholar, 1972-3. Award of the New York Academy of Sciences, 1979. Honorary LL.D., 1980, Iona.

Plant Physiologist, Emergency Rubber Project, California Institute of Technology 1943-44; Instructor in Botany, Yale University, 1946-47; Senior Research Fellow, California Institute of Technology, 1947-50; Associate Professor of Biology, California Institute of Technology, 1951-1955. Professor of Plant Physiology, Department of Botany, Yale University 1955-61; Chairman, Department of Botany, 1961-62; Director, Division of Biological Sciences, Yale University, 1965-66; Professor of Biology, 1962-73; Eaton Professor of Botany, 1973-

Fellow of the John Simon Gugenheim Memorial Foundation, Stockholm and Sheffield, 1950-51; Fulbright Fellow, Canberra, Australia, 1960-61; National Science Foundation Faculty Fellow, London, 1967-68; Albert Einstein Fellow and Visiting Professor, Hebrew University of Jerusalem, 1980. Visiting Fellow, Wolfson College, Cambridge, England, 1983.

Secretary, American Society of Plant Physiologists, 1955-57; Vice President, 1957-58:,President, 1962-63. Secretary-Treasurer, International Association for Plant Physiology, 1962-67. Vice-President, Botanical Society of America, 1967-68; President, 1968-69; Merit Award, 1970. Formerly Council, Federation of American Scientists; President, Society for Social Responsibility in Science; Board Member, Scientists' Institute for Public Information. Member, Committee on Space Biology and Medicine, National Research Council.

Editorial Board Member: Journal of Plant Growth Regulation, Pesticide Physiology and Biochemistry, Environment.
Formerly Chemical and Engineering News, Science Year, Plant Physiology, Phytochemistry, American Journal of Botany, Lloydia. Formerly regular columnist, Natural History magazine.

Former member: Metabolic and Regulatory Biology Panels, Nation Science Foundation; Executive Committee, Growth Society; and Governing Boards, Biological Sciences Curriculum Study, Commission on Undergraduate Eduation in the Biological Sciences and American Institute of Biological Sciences. First American scientist to visit the People's Republic of China, 1971. Return visits to Far East, 1972, 1975, 1977, 1980.

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Lisansky and A. W. Galston. Phytochrome stability in vitro: I. Effect of metal ions. PLANT PHYSIOL 53(3): 352-359. Illus. 1974.

Applewhite, Satter and A. W. Galston. Protein synthesis during endogenous rhythmic leaflet movement in Albizia. J GEN PHYSIOL 62(6): 707-713. Illus. 1973.

Satter, Applewhite, Kreis and A. W. Galston. Rhythmic leaflet movement in Albizia julibrissin: Effect of electrolytes and temperature alteration. PLANT PHYSIOL 52(3): 202-207. Illus. 1973.

Satter, A. W. Galston. Leaf movements: Rosetta stone of plant behavior? BIOSCIENCE 23(7): 407-417. Illus. 1973.

1973

Satter, Applewhite and A. W. Galston. Phytochrome-controlled nyctinasty in Albizzi julibrissin: V. Evidence against acetycholine participation. PLANT PHYSIOL 50(4): 523-525. 1972.

JOHN A. GAROFALO, M.D.

I. QUALIFICATIONS

See attached curriculum vitae.

II. SUBJECT MATTER

The subject matter of Dr. Garofalo's testimony will pertain to the field of immunology. He will elaborate on the effect that Agent Orange (dioxin) can have on the immune system.

III. GENERAL SCIENTIFIC PRINCIPLES

The field of immunology involves the study of how the body responds to antigenic (foreign) stimulation. Peripheral blood lymphocytes are made up of B-cells; T-cells; and T cell subsets (also referred to as the immunoregulatory cells of the immune system). During the past two decades, the field of immunology has recorded a number of dramatic advances. The most significant of which have been the recognition of the various classes of T and B lymphocytes, hybridoma technology (provides a reliable and consistent method for providing large quantities of monoclonal antibodies directed against specific cell surface antigens) and the technological advances in flow cytometry. T lymphocytes (65-85% of lymphocytes) are responsible for a spectrum of immune responses referred to as cell-mediated immunity which include delayed hypersensitivity; allograph rejection; tumor cytotoxicity, whereby they destroy host cells bearing foreign antigens; and cell-mediated resistance to infectious agents (fungi, viruses, and intracellular faculative bacteria). Two functionally

distinct subsets of T cells have been defined with monoclonal antibodies. T4+ cells represent the helper/inducer population 38-53%) whereas T8+ cells represent the suppressor/cytotoxic population (18-30%) (cytotoxic refers to the major effector functions of T cells, the capacity to kill specific cells to which they are sensitized). T4+ (helper/inducer) cells regulate the immune response by means of cell-cell interactions as well as by producing biologically potent regulatory molecules. T4+ cells provide inducer function in T-T cell (required for optimal development of cytotoxicity by the T8+ cells); T-B cell (induces B cells to proliferate and differentiateinto immunoglobulin containing plasma); and T-macrophage interactions. T4+ cells produce humoral factors such as lymphocyte mitogenic factor, which induces proliferation of all major lymphocyte subclasses. Antigen stimulated T4+ cells produce helper factors that modulate erythroid stem-cell production and are important in hematopietic differentiation. T8+ cells contain cells with suppressor/cytotoxic functions. This subset suppresses B cell immunoglobulin synthesis and has the capacity to kill cells to which they are sensitized. B lymphocytes are cells coded to product immunoglobulins, which are proteins found in blood and various secretions. B cells product Ig which belong to four major gorups: IgG - responsible for defense against bacterial infections i.e. pneumonia and strep throat; IgM - responsible for the defense against anerobic bacterial infections i.e. bowel pathogens; IgA - defends us against viral infections and is found in large quantities in our secretions; IgE - responsible for our defense against allergens.

HYBRIDOMA TECHNOLOGY -- The advent of hybridome technology has provided a new approach to immunology research. With its application monoclonal antibodies capable of recognizing with precision the functional components of the immune system provide the medical community with highly specific reagents for the study of T lymphocyte maturation and for the identification of T lymphocyte syb-populations.

ORTHO SPECTRUM III utilizes the observation that human lymphocytes, monocytes and granulocytes posses different light scattering characteristics. Cells undergoing analysis travel in single file through a quartz cuvette where they intersect a narrowly focused 488nm wavelength beam of light from an argon-ion laser. The illuminated cells scatter the light in all directions. A solid-state sensor collects low angle forward scatter to discriminate size of cells, and a photomultiplier tube (PMT) set at 90°. These signals produce a histogram of cells counted based on intensity of green fluorescence. Analysis of peripheral blood samples is performed using whole blood. The cells are labeled by direct immunofluorescence, in which the monoclonal antibody directed against the desired cell surface antigen is conjugated with a flourescent dye, or by indirect immunofluorescence, in which the monoclonal antibody, having been found to the cell surface, is visualized with a second fluoresceinated antibody directed against the monoclonal immunoglobulin.

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In the evaluation of lymphocyte populations both percentages and absolute values are taken into consideration. The mechanism of how abnormal lymphocyte populations affects the im-

mune response will be set out. The basic theorem is that changes in lymphocyte populations are suggestive of disease processer and often but not universally relate to dysfunction. For the purposes of this litigation, it is important to distinguish between immune deficiencies and immuno-suppression. Suppression referring to an acquired immune deficiency that can be the result of exposure to chemical toxins.

Dr. Garofalo has had particular clinical experience relevant to this litigation. He has, since December, 1983, examined about thirty-five (35) Vietnam veterans for Agent Orange-related immune abberations. To the best of his knowledge, the published literature does not contain any reports of data comparable to that which he has acquired. A general review of his date indicates that the Vietnam veterans exposed to Agent Orange have slightly elevated levels of lymphocytes, with particular reference to T helper cells. There is even some elevation of suppressor T cells.

IV. SUBSTANCE OF OPINIONS

1. Agent Orange can affect the immune system by producing changes in the numbers and distribution of T cells, T helper cells, and T suppressors cells, though it is much more likely that it has its effect through changes in the latter two types of cells.

2. The effect on helper T cells may result in a heightened immune response, leading to the formation of auto-immune diseases. These in turn may lead to excess cancer formation, arthritis, and nerve damage, the latter including both central

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nerve damage and peripheral neuropathy, of which the "dying back" variant is typical.

3. Agent Orange can cause an excess of T8+ cells (suppressor/cytotoxic). This may represent an increase in either the suppressor population which in turn can interfere with helper T cell and B cell function or the cytotoxic cell population which have the capacity to kill specific cells to which they are sensitized.

4. Agent Orange may act as an antigen bound to body tissues resulting in the formation of autoantibodies and cytotoxic cells directed against the sensitized tissue.

Auto Antibody: "Auto" refers to self; "Antibody" refers to a protein formed by the immune system in a response to antigen exposure. An autoantibody is thus an antibody that is formed within a person against their own tissues, i.e., red blood cells, platelers, nerve tissue, skin).

5. Individual opinions concerning the representative plaintiffs are contained in their individual reports.

V. GROUNDS FOR OPINIONS

Dr. Garofalo will rely upon his own experience in the evaluation of other veterans he has evaluated in the past or whom he will evaluate in the future, and upon the attached list of articles.

ARTICLES UPON WHICH DR. GAROFALO MAY RELY IN WHOLE, OR IN PART, ARE:

J. Hopkins
Dioxin: Carcinogenicity
FD. COSMET. TOXICOL.
1980
Vol. 18, pp. 739-741

J. Hopkins, P. Cooper
Dioxin Dangers to Man
FD. COSMET. TOXICOL.
1980
Vol. 18, pp. 541-546

J. E. Huff, J. A. Moore, R. Caracci and L. Tomatis
Long-Term Hazards of Polychlorinated Dibenzodioxins and Polychlorinated Dibenzofurans
ENVIRONMENTAL HEALTH PERSPECTIVES
1980
Vol. 36, pp. 221-240

David Palen & Edward Glover
Our Promotion by O in Skin of HRS/J Hairless Mice
MACMILLAN JOURNAL
November 18, 1982
Vol. 300, pp. 271-273

G. Reggiani, F. Hoffmann
Acute Human Exposure to TCDD in Seveso Italy
JOURNALOF TOXICOLOGY AND ENVIRONMENTAL HEALTH
1980
Vol. 6, pp. 27-43

Michael I. Luster, Gary A. Boorman, Jack H. Dean, Martha W. Harris, Robert W. Luebke, Martin L. Padarathsingh and John A. Moore
Examination of Bone Marrow, Immunologic Parameters and Host Susceptibility Following Pre- and Postnatal Exposure to 2,3,7,8-Tetrachlorodibenzo-p-Dioxin (TCDD)
INT. J. IMMUNOPHARMACY
1980
Vol. 2, pp. 301-310

William G. Dunagin, M.D.
Dioxin Effects on Human Health
MISSOURI MEDICINE
March, 1983
Vol. 80, No. 3, pp. 127-131

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R. P. Sharma, P. J. Gehring
Effects of 2,3,7,8-Tetrachlorodibenzo-p-Dioxin (TCDD) On Splenic Lymphocyte Transformation in Mice After Single and Repeated Exposures
ANNALS NEW YORK ACADEMY OF SCIENCES
1979
pp. 487-497

S. J. Stohs, M.Q. Hassan and W. J. Murray
Lipid Peroxidation as a Possible Cause of TCDD Toxicity
BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS
March 29, 1983
Volume 111, No. 3, 1984, pp. 854-859

David A. Clark, Jack Gauldie, Myron R. Szewczuk and George Sweeney
Enhanced Supressor Cell Activity as a Mechanism of Immunosuppression by 2,3,7,8-Tetrachlorodibenzo-p-Dioxin (41275)
PROCEEDINGS OF THE SOCIETY FOR EXPERIMENTAL BIOLOGY AND MEDICINE
1981
pp. 290-299

Graziella Filippini, M.D., Bianca Bordo, M.D., Paolo Crenna, M.D., Nicoletta Massetto, M.D., Massimo Musicco, M.D., Renato Boeri, M.D.
Relationship Between Clinical and Electrophysiological Findings and Indicators of Heavy Exposure to 2,3,7,8-Tetrachlorodibenxo-dioxin
SCAND J WORK ENVIRON HEALTH
1981
Vol. 7, pp. 257-262

C. M. Bishop, A. H. Jones
Non-Hodgkin's Lymphoma of the Scalp in Workers Exposed to Dioxins
THE LANCET
August 15, 1981
p. 369

Jana Pazderova-Vejlupkova, M.D., Marcela Nemcova, Ph.D., Jane Pickova, Ph.D., Lubor Jirasek, Ph.D., Edgar Lukas, Ph.D.
The Development and Prognosis of Chronic Intoxication by Tetrachlordibenzo-p-dioxin in Men
ARCHIVES OF ENVIRONMENTAL HEALTH
January/February, 1981
Vol. 36, No. 1, pp. 5-11

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Henry C. Pitot, Thomas Goldsworthy, H. A. Campbell, and Alan Poland
Quantitative Evaluation of the Promotion by 2,3,7,8,-Tetrachloro-dibenzo-p-dioxin of Hepatocarcinogenesis from Diethylnitrosamine
CANCER RESEARCH
October, 1980
Vol. 40, pp.3316-3620

J. G. Vos, J. G. Kreeftenberg, H. W. B. Engle, A. Minderhoud and L. M. Van Noorle Jansen
Studies on 2,3,7,8-Tetrachlorodibenzo-p-Dioxin-Induced Immune Suppression and Decreased Resistance to Infection: Endotoxin Hypersensitivity, Serum Zinc Concentrations and Effect of Thymosin Treatment
TOXICOLOGY
1978
Vol. 9, pp. 75-86

Michael I. Luster, Robert E. Faith and George Clark
Laboratory Studies on the Immune Effects of Halogenated Aromatics
ANNALS NEW YORK ACADEMY OF SCIENCES
1979
pp. 473-483

Ralph R. Cook
Dioxin, Chloracne, and Soft Tissue Sarcoma
THE LANCET
March 14, 1981

A. Mantovani, A. Vecchi, W. Luini, M. sironi, G. P. Candiani, F. Spreafico and S. Farattini
Effect of 2,3,7,8-Tetrachlorodibenzo-p-Dioxin on Macrophage and Natural Killer Cell-Mediated Cytotoxicity in Mice
BIOMEDICINE
1980
Vol. 32, pp. 200-204

Michael I. Luster and Robert E. Faith
Assessment of Immunologic Alterations Caused by Halogenated Aromatic Hydrocarbons
ANNALS NEW YORK ACADEMY OF SCIENCES
1979
pp. 572-577

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John A. Garofalo, M.D.
847 Old Lancaster Road
Bryn Mawr, PA 19010
Date of Birth: August 15, 1946

SPECIALTY: Hematology - Oncology - Immunology

AFFILIATIONS: Assistant Professor of Medicine
Thomas Jefferson University Hospital
Philadelphia, Pennsylvania

Assistant Attending
Department of Medicine
Bryn Mawr Hospital
Bryn Mawr, Pennsylvania

EDUCATION:

1977-1980	Clinical Fellow - Immunology - Oncology Memorial Sloan Kettering Cancer Center New York, New York.
1977-1980	Research Fellow - Immunobiology Memorial Sloan Kettering Cancer Center New York, New York.
1976-1977	Medical Resident - Pennsylvania Hospital, Philadelphia, Pennsylvania.
1975-1976	Medical Intern, Philadelphia General Hospital, Philadelphia, Pennsylvania.
1974-1975	Research Fellow - Immunobiology, Memorial Sloan Kettering Cancer Center New York, New York.
1969-1974	University of Rome, Faculty of Medicine.
1964-1969	Oklahoma State University, Stillwater, Oklahoma - Bachelor of Science in Physiology.
1983	Medical Director - Home Cancer Care, INC. Home Health Care Agency
1983	Medical Director - Immunodiagnostics Clinical Laboratories, INC., Reference Immunology Laboratory.

BIBLIOGRAPHY

John A. Garofalo

I. Letters to the Editor

1. AIUTI, F., GAROFALO, J.A.: Rectal immunoglobulin synthesis in ulcerative colitis. To The Editor: New England Journal of Medicine vol 287, No. 22, 1151, 1972.

2. GAROFALO, J.A., STRONG, E., GOOD, R.A.: Zinc and intestinal bypass procedures. To the Editor: Annals of Internal Medicine, June 1979.

II. Abstracts

1. GAROFALO, J.A., CUNNINGHAM-RUNDLES, S.: In vitro effects of zinc chloride on lymphocyte transformation. Fed. Proc. 37(6), 3154, 1978.

2. GAROFALO, J.A., STRONG, E., CUNNINGHAM-RUNDLES, S., ERLANDSON, E., MENENDEZ-BOTET, C., SCHWARTZ, M., GOOD, R.A.: Serum zinc in patients with epidermoid cancer of the head and neck. Fed. Proc. 38(3), 2561.

3. CUNNINGHAM-RUNDLES, C., CUNNINGHAM-RUNDLES, S., GAROFALO, J., IWATA, T., INCEFY, G., TWOMEY, J., GOOD, R.A.: Increased T lymphocyte function and thymopoietin following zinc replacement in man. Fed. Proc. 38(3), 5259, 1979.

4. CUNNINGHAM-RUNDLES, S., CUNNINGHAM-RUNDLES, C., GAROFALO, J., DUPONT, B., GOOD, R.A.: Effect of zinc on human B cell activation. Fed. Proc. 38(3), 3735, 1979.

5. GAROFALO, J.A. et al.: Serum zinc and copper and the Cu/Zu ratio in patients with cancer. AACR/ASCO, 733, 1980.

III. Publications

1. AIUTI, F., LACAVA, V., GAROFALO, J.A., D'AMELIO, R., D'ASERO, C.: Surface markers on human lymphocytes: Studies of normal subjects and of patients with primary immunodeficiencies. Clin. Exp. Immunol. 15: 43-52, 1973.

2. AIUTI, F., CIARLA, M.V., D'ASERO, C., D'AMELIO, R., GAROFALO, J.A.: Surface markers on lymphocytes of patients with infectious diseases. Infection and Immunity 8(1), 110-117, 1973.

3. AIUTI, F., PAPA, G., LACAVA, V., CIARLA, M.V., D'AMELIO, R., GAROFALO, J.: Lymphocyte membrane markers in acute lymphoblastic leukemia. Brit. J. Haem. 27, 635, 1974.

4. CUNNINGHAM-RUNDLES, S., DE SOUSA, M., GAROFALO, J.A., BOGNACKI, J.J., LEE, B.J., DUPONT, B., GOOD, R.A.: Differential analysis of spontaneous uptake of thymidine and transferrin by mononuclear cells in vitro in Hodgkin's disease. 13th International Leukocyte Conference, 1979.

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5. SCHLOEN, L.H., FERNANDES, G., GAROFALO, J.A., GOOD, R.A.: Nutrition, Immunity and Cancer - A Review, Part II. Clinical Bulletin, 9, #2, 1979.

6. GAROFALO, J.A., CUNNINGHAM-RUNDLES, S., BRAUN, D.W., GOOD, R.A.: In Vitro Effect of Zn^{++} on Peripheral Blood Lymphocytes in Patients with Cancer. Inter. J. of Immunopharmacology, 2, 37-44, 1980.

7. GAROFALO, J.A., ASHIKARI, H., LESSER, M., MENENDEZ-BOTET, C., CUNNINGHAM-RUNDLES, S., SCHWARTZ, M.K., GOOD, R.A.: Serum Zinc, Copper and the Cu/Zn Ratio in Patients with Benign and Malignant Breast Lesions. Cancer, 46, 2, 2682-2685, 1980.

8. GAROFALO, J.A., ERLANDSON, E., STRONG, E., LESSER, M., GEROLD, F., SPIRO, R., SCHWARTZ, M., GOOD, R.A.: SErum Zinc, Serum Copper and the Cu/Zn Ratio in Patients with Epidermoid Cancer of the Head and Neck. J. of Surgical Oncology, Vol. 15, issue 4, 381-386, 1980.

9. SCHULOF, R.S., GAROFALO, J.A., GOOD, R.A., GUPTA, S.: Concanavalin A Induced Suppressor Cell Activity for T Cell Proliferative Responses: Autologous and Allogenic Suppression in Aging Humans. Cellular Immunology, 56, 80-88, 1980.

10. GOOD, R.A., FERNANDES, G., CUNNINGHAM-RUNDLES, C., CUNNINGHAM-RUNDLES, S., GAROFALO, J.A., RAO, K., INCEFY, G.S., IWATA, T.: The Relation of Zinc Deficiency to Immunologic Function in Animals and Man. In Primary Immunodeficiencies, Inserm Symposium No. 16, 223-234, Editors: M. Seligmann and W.H. Hitzig, Biomedical Press, 1980.

11. GOOD, R.A., FERNANDES, G., GAROFALO, J.A., CUNNINGHAM-RUNDLES, C., IWATA, T., WEST, A.: Zinc and Immunity. In: International Conference on Clinical and Public Health Significance of Trace Minerals in the World Population, Detroit, 1980; Proceedings (A.S. Prasad, ed.), New York, Alan R. Liss.

LENNART HARDELL, M.D., Ph.D.

I. QUALIFICATIONS

Dr. Hardell is employed by the University Hospital in its Department of Oncology in Umea, Sweden, where he specializes in interna medicine and oncology. His work includes diagnosis, treatment, and evaluation of possible causes of cancer, and education of medical students. His Curriculum Vitae is attached. A list of seminars is also attached.

II. Subject Matter

Dr. Hardell will testify to several epidemiological studies which he and his colleagues have conducted in Sweden. This research includes investigations concerning the relationship between the risk for different types of cancer and exposure to phenoxy herbicides and chlorophenols. The research has been published in the medical and scientific literature.

These studies utilized the case-control study as the vehicle for investigation. Certain methodological aspects, such as selection of cases, selection of controls, assessment of exposure, and statistical methods, were considered; and then utilization was based upon thoroughly considered aspects of bias, all of which were well controlled.

Dr. Hardell has also seen in his clinical practice basal cell carcinoma of persons previously exposed to phenoxy herbicides, with no other known confounding variables.

III. Scientific Principles

See General Statement of Scientific Principles and Assumed Facts attached.

Dr. Hardell will use as a factual base for his testimony his hands-on diagnoses and treatment of various cancer victims as well as his review of the medical records and examinations of cases involved in his epidemiological studies. His additional clinical experiences also form a factual basis for his testimony, especially those patients with basal cell carcinoma.

Dr. Hardell will also review the medical records of George Ewalt, Danny Ford, and David Lambiotte for the opinions which he will express regarding the causation (in the legal sense) and their exposure to Agent Orange and basal cell carcinoma, rhabdomyosarcoma (form of soft tissue sarcoma) and malignant lymphocytic lymphoma.

IV. Substance of Opinions

A. Specifically, Dr. Hardell's studies, four in number, involved soft tissue sarcomas, malignant lymphomas, and colon cancer. Highly statistically significant risks of soft tissue sarcomas and malignant lymphoma were found, whereas no association was found for colon cancer. In point of fact, the negative finding for colon cancer strongly supports the statistical significance of the increased risk demonstrated for soft tissue sarcomas and malignant lymphomas, and that there exists a presumed causal relationship between exposure to phenoxy herbicides and human cancer, particularly of soft tissue sarcoma and malignant lymphoma.

B. With respect to those cases with soft tissue sarcoma, malignant lymphoma, and basal cell carcinomas, Dr. Hardell will testify that the presumed exposure to Agent Orange caused, in significant part, such neoplastic processes.

V. Grounds for Each Opinion

A. General

The bases for Dr. Hardell's testimony as to various facts and opinions include: educational background, professional training, and experience; diagnosis and treatment of patients, review of the applicable medical and scientific literature; personal research; and a review of the pertinent medical data of the relevant representative plaintiffs.

B. Specific

1. Soft tissue sarcomas and malignant lymphoma

References:

Cook RR (1981): Dioxin, chloracne, and soft-tissue sarcoma. Lancet i. 618-619.

Eriksson M, Hardell L, Berg NO, Moller T, Axelson O (1981): Soft-tissue sarcomas and exposure to chemical substances; a case-reference study. Br J Ind Med 38: 27-33.

Hardell L (1979): Malignant lymphoma of histiocytic type and exposure to phenoxyacetic acids or chlorophenols. Lancet i: 55-56.

Hardell L (1981): Relation of soft-tissue sarcoma, malignant lymphoma and colon cancer to phenoxy acids, chlorophenols and other agents. Scand J Work Environ Health 7: 119-130.

Hardell, L, Sandstrom A (1979): Case-control study; soft-tissue sarcomas and exposure to phenoxyacetic acids or chlorophenols. Br J Cancer 39: 711-717.

Hardell L, Eriksson J, Lenner P, Lundgren E (1981): Malignant lymphoma and exposure to chemicals, especially organic solvents, chlorophenols and phenoxy acids; a case-control study. Br J Cancer 43: 169-176

Honchar PA, Halperin WE (1981): 2,4,5-T trichlorophenol, and soft tissue sarcoma. Lancet i: 268-269.

Johnson FE, Kugler MA, Brown SM (1981): soft-tissue sarcomas and chlorinated phenols. Lancet I: 1370.

Moses M, Selikoff IJ (1981): soft-tissue sarcomas, phenoxy herbicides and chlorinated phenols. Lancet i: 1370

Pitot HC, Goldsworthy T, Poland H (1980): Promotion by 2,3, 7,8-tetrachlorodibenzo-p-dioxin of hepatocarcinogenesis from diethylnitrosamine. Cancer Res 40: 3616-3620.

Poland A, Palen D, Glover E (1982): Tumour promotion by TCDD in skin of HRS/J hairless mice. Nature 300: 271-273.

Sarma PR, Jacobs J (1982) Thoracic soft-tissue sarcoma in Vietnam veterans exposed to agent orange. N. Engl J. Med 306: 1109

2. Basal Cell Carcinoma

Case history:

Woman born in 1946. In 1964 operated for a cyst on one of her ovaries. No other diseases. In the end of the 1960's she developed a blister on her left shoulder and in the 1970's several ones on her back. In June 1977, two basal cell carcinomas were surgically removed from her back. In September 1977 nine more and in December 1977, two more basal cell carcinomas were excised from her back. In January 1983 one basal cell carcinoma on her shoulder and another on her back were cured by radiotherapy. In October 1983 five tumors were removed from her back; two basal cell carcinomas and three basal cell carcinomas in situ.

During summertime in 1959, 1960, and 1961 the patient afforested for one month each summer. The seedlings were treated with DDT. Moreover, she carried water for the dilution of phenoxy acids used by back pack sprayers. She walker in newly sprayed areas. In 1960 she used to basal bark spray for six weeks and in 1961 for two weeks. The chemical used was a combination of 2,4,5-T and 2,4,-D. She was thereby stripped to her waist but for a brassiere. She used no gloves.

The patient reported no heredity for basal cell carcinoma. She had not used any special drugs or been exposed to arsenic.

Curriculum Vitae

Lennart Hardell M.D.,Ph.D. Department of Oncology, University Hospital, S-901 85 UMEÅ, Sweden

Born in October 18, 1944.

Medical degree from University of Upsala, Sweden October 27, 1971.

Authorization to practice the medical profession, National Board of Health and Welfare, Stockholm, November 5, 1971.

Specialized in internal medicine October 18, 1976.

Specialized in oncology, June 20, 1979.

Medical dissertation University of Umeå, May 15, 1981.

Direct testimony before the United States Environmental Protection Agency in the matter of the hearing of 2,4,5-T and Silvex, Washington DC, September 29-30 1980 and February 9, 1981.

Receiver of the Fernström Award, University of Umeå, October 9, 1982. Delivered by the King Carl XVI Gustaf of Sweden.

Member of "Expert Panel on Dioxin Documents", United States Environmental Protection Agency, Cincinnati, Ohio, July 27-29, 1983.

Qualified for Associate Professor of oncology, University of Umeå, December 9, 1983.

Member of the Swedish Medical Association.
Member of Nordic Radiotherapy Club
Member of Swedish Association of Radiotherapy
Member of Swedish Association of Oncology
Member of Swedish Epidemiological Association

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Appointments by Dr Lennart Hardell

After authorization worked as:

General practitioner, Primary Health Centre, Haparanda, November 1 1971 - - August 31 1972.

Junior registrar, Department of Psychiatry, County Hospital, Kristinehamn, September 1-30, 1972.

Junior registrar, Department of Psychiatry, County Hospital, Boden, October 1 - December 31 1972.

From January 1 1973 to August 31 1976 various appointments as Junior registrar, Senior registrar and consultant at the Department of Internal Medicine, County Hospital, Boden.

From September 1 1976 various appointments as a Junior registrar, Senior registrar and consultant at the Department of Oncology, University Hospital, Umeå.

September 1 - December 31 1983 Head and consultant, Centre of Oncology, University Hospital, Umeå.

For the moment appointed as consultant at the Department of Oncology, University Hospital, Umeå, Sweden.

COURSES IN WHICH DR LENNART HARDELL HAS PARTICIPATED

Cardiology	University of Lund	April 2-6 1973
Hypertonia, hypotonia and blood vessel diseases	Regional Hospital of Malmö	November 5-9 19
Lung diseases, especially astma, autoimmune and work related lung diseases	University of Upsala	March 11-15 197
Gastroenterology and liver diseases	University of Gothenburg	May 13-17 1974
Acute medicine	Regional Hospital of Örebro	November 18-22 1
Hematology, nephrology	University of Linköping	April 7-11 1975
Course in endocrinology	Karolinska Institute, Stockholm	November 3-7 197
Intrathoracal tumours	Regional Hospital Huddinge	February 23-27 1
Infectious diseases and antibiotic therapy	University of Gothenburg	February 15-19 1
Cancer epidemiology, cancer statistics and early diagnoses of cancer	Karolinska Institute, Stockholm	October 11-15 19
Postgraduate course in clinical oncology, soft tissue sarcomas, plasma cell tumours, cancer of the esophagus and stomach	Royal Marsden Hospital, The Chester Beatty Research Institute, London	November 14-18 19
Biological and medical effects of irradiation, course for oncologists	Karolinska Institute, Stockholm	May 2-6 1977
Biostatics in epidemiology, methods and applicability	University of Umeå	March 11-18 1978
Therapy with cytostatic drugs and hormones of malignant tumours and orientation about progress in tumour immunology	Karolinska Institute, Stockholm	May 8-12 1978
Cancer epidemiology	IARC, Lyon, France	July 31-August 11 1
Radiation physics for oncologists	Karolinska Institute, Stockholm	October 2-6 1978

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Clinical oncology II and radiation therapy	University of Lund	October 16-20 1
Clinical oncology I	University of Umeå	March 19-23 197
Course on epidemiological approach to occupational cancer	IARC, Lyon, France	March 17-21 198
Methods of epidemiology	University of Umeå	Course for three weeks June 1980. January 1981

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Publications

1. Hardell L. Maligna mesenkymala mjukdelstumörer och exposition för fenoxisyror - en klinisk observation. Läkartidningen 71 (1977) 2753-2754. (In Swedish, English summary)

2. Hardell L. Kemiska substanser och maligna mesenkymala tumörer. Svensk förening för medicinsk radiologi. Förhandlingar nr 9 (1978) 18-21. (In Swedish).

3. Hardell L, Sandström A. Case-control studie: Maligna mesenkymala mjukdelstumörer och exposition för fenoxisyror eller klorfenoler. Läkartidningen 75 (1978) 3535-3536. (In Swedish).

4. Hardell L, Sandström A. Case-control study: Soft-tissue sarcomas and exposure to phenoxyacetic acids or chlorophenols. Paper presented at the conference on pesticides and human health. Society for Occupational and Environmental Health, Washington D.C., USA December 10-13, 1978.

5. Hardell L. Malignant lymphoma of histiocytic type and exposure to phenoxy acetic acids or chlorophenols. Lancet i (1979) 55-56.

6. Hardell L, Sandström A. Case-control study: Soft-tissue sarcomas and exposure to phenoxy acids or chlorophenols. Br. J. Cancer 39 (1979) 711-717.

7. Eriksson M, Hardell L, Berg NO, Möller T, Axelson O. Case-control studie över maligna mesenkymala mjukdelstumörer och exposition för kemiska substanser. Läkartidningen 76 (1979) 3872-3875. (In Swedish).

8. Hardell L. Cancer epidemiology in northern Sweden. Nordic Council Arct. Med. Res. Rep. No. 26 (1980) 94-97.

9. Hardell L. The clofibrate problem: A differenct viewpoint. Lancet ii (1980) 1081-1082.

10. Hardell L. Case-control studies: Soft-tissue sarcomas and malignant lymphomas and exposure to phenoxy acids or chlorophenols. In: Progress in Mutation Research, Vol. 2, Ed. Koppas. Elsevier/North-Holland. Biomedical Press, pp. 105-108, 1981.

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11. Hardell L. Direct testimony before the United States Environmental Protection Agency. Washington DC. Exihibit No. 762, September 29-30, 1980.

12. Hardell L, Eriksson M, Lenner P. En fall-kontroll studie: Maligna lymfom och exposition för kemiska substanser, särskilt organiska lösningsmedel, klorfenoler och fenoxisyror. Läkartidningen 77 (1980) 208-210. (In Swedish).

13. Hardell L, Eriksson M, Lenner P. (Hodgkins sjukdom - en komplettering). Replik Läkartidningen 77 (1980) 983. (In Swedish).

14. Hardell L. Relation of soft-tissue sarcoma, malignant lymphoma and colon cancer to phenoxy acids, chlorophenols and other agents. Scand. J. Work. Environ. Health 7 (1981) 119-130.

15. Hardell L, Eriksson M. Soft-tissue sarcomas, phenoxy herbicides and chlorinated phenols. Lancet ii (1981) 250.

16. Hardell L. Epidemiological studies on soft-tissue sarcoma and malignant lymphoma and their relation to phenoxy acid or chlorophenol exposure. Umeå University Medical Dissertations. New Series No 65 - ISSN 0346-6612. 1981.

17. Hardell L. Direct testimony before the United States Environmental Protection Agency. Washington D.C. Exihibit No 956, February 9, 1981.

18. Hardell L, Eriksson M, Lenner P, Lundgren E. Malignant lymphoma and exposure to chemicals, especially organic solvents, chlorophenols and phenoxy acids: A case-control study. Br. J. Cancer 43 (1981) 169-176.

19. Hardell L, Eriksson M. Fenoxisyror, klorfenoler och cancer. Läkartidningen 78 (1981) 2862-2863. (In Swedish).

20. Axelson O, Flodin U, Hardell L. A comment on the reference series with regard to multiple exposure evaluation in a case-referent study. Scand. J. Work. Environ. Health 8 (1982) suppl. 1, 15-19.

21. Eriksson M, Hardell L, Berg NO, Möller T, Axelson O. Soft-tissue sarcomas and exposure to chemical substances: a case-referent study. Br. J. Ind. Med. 38 (1981) 27-33.

22. Hardell L. Fall-kontroll studier: Maligna mesenkymala mjukdelstumörer, maligna lymfom och exponering för fenoxisyror eller klorfenoler. NJF-serminar 12-13 november 1980. Nordisk jordbruksforskning 1 (1981) 58-59. (In Swedish).

23. Osterman B, Hardell L, Holm J, Lenner P, Lindholm C, Wahlin A. Erfarenheter av intensiv cytostatikabehandling vid akut myeloisk leukemi. Läkartidningen 79 (1982) 2107-2109. (In Swedish).

24. Sandahl C, Hardell L. Koststudie vid onkologisk klinik. Delstudie. Maten på sjukhuset. I. Patient- och II. personalsynpunkter. Näringsforskning 27 (1983) 14-21. (In Swedish, English summary).

25. Hardell L. Cancer. Kapitel i lärobok i invärtesmedicin för sjuksköterskor. (1982), 263-268. (In Swedish).

26. Hardell L, Axelson O. Soft-tissue sarcoma, malignant lymphoma and exposure to phenoxy acids or chlorophenols. Lancet i (1982) 1408-1409.

27. Hardell L, Johansson B, Axelson O. Epidemiological study on nasal cancer and nasopharyngeal cancer and their relation to phenoxy acid or chlorophenol exposure. Am. J. Ind. Med. 3 (1982) 247-257.

28. Hardell L. Exposure to chlorophenols and phenoxy herbicides in the working environment. Abstract before the 13th International Cancer Congress. September 8-15, 1982. Seattle, Washington USA.

29. Hardell L. Exposure to polychlorinated dibenzo-p-dioxins and dibenzofurans in the environment. In: 13th International Cancer Congress, Part E. Cancer Management. Eds. Mirand, Hutchinson, Mihich. Alan R Liss, New York, pp. 357-369, 1983.

30. Hardell L, Eriksson M, Lenner P, Lundgren E. Malignant lymphoma and exposure to chemicals, especially organic solvents, chlorophenols, and phenoxy acids: A case-control study. Poster at the 13th International Cancer Congress, September 8-15, 1982. Seattle, Washington USA.

31. Hardell L. Epidemiological studies on soft-tissue sarcoma, malignant lymphoma, nasal, and nasopharyngeal cancer and their relation to phenoxy acid or chlorophenol exposure. In: Chlorinated Dioxins and Dibenzofurans in the Total Environment. Eds. Choudhary, Keith, Rappe. Butterworth Publishers, Boston, pp. 367-374, 1983.

32. Bengtsson NO, Hardell L, Eriksson M. Asbestos exposure and malignant lymphoma. Lancet ii (1982) 1463.

33. Hardell L, Bengtsson NO. Epidemiological study of socioeconomic factors and clinical findings in Hodgkin's disease, and reanalysis of previous data regarding chemical exposure. Br. J. Cancer 48 (1983) 217-225.

34. Sandahl, Rönnlund U, Hardell L. Koststudie vid onkologisk klinik. Nutritionsstatus hos radioterapibehandlade head- och neckpatienter. Umeå Universitet 1983. (In Swedish).

35. Hardell L. Epidemiological studies on soft-tissue sarcoma, malignant lymphoma, nasal, and nasopharyngeal cancer and their relation to phenoxy acid or chlorophenol exposure. Abstract before Dividsion of Environmental Chemistry, American Chemical Society, Kansas City, Missouri, September 15-16, 1982.

36. Direct testimony of Dr. Lennart Hardell, "The Herbicide Court Case", Nova Scotia, Canada, May 1983 (presented by Dr. M. Eriksson).

37. Hardell L. Axelson O, Rappe C. Nasal cancer and chlorophenols. Lancet i (1983) 1167.

38. Sandahl C, Rönnlund U, Hardell L. Bättre näringsstatus hos cancerpatienter med hjälp av nutritionsgrupp och kostombud? Läkartidningen 80 (1983) 2234-2235. (In Swedish).

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39. Domellöf L. Hansson M. Hardell L. Nygren M. Rappe C. Levels of polychlorinated dibenzodioxins (PCDDs) and dibenzofurans (PCDFs) in fat tissue from cancerpatients and controls. Abstract before the AACR annual meeting May 9-12, 1984, Toronto, Ontario, Canada.

HARDELL, Lennart

1. Conference organized by the Swedish Society of Medical Radiology (Invited speaker)

2. Conference by the Finnish Medical Association; Duodecim and Medical Faculty

3. Malignant Tumors and Chemical Risk Sectors in the Environment (Invited speaker)

4. Meeting on Phenoxy Acids; The Committee on Agriculture of Swedish Parliment (Invited speaker)

5. Soft-tissue Sarcoma and Exposure to Phenoxy Acids or Chlorophenols; Meeting by the Swedish Pharmaceptical Association in Umeå (Invited speaker)

6. Conference on Pesticides and Human Health - Society for Occupational and Environmental Health (Invited speaker)

7. Symposium by Nordic Counsel on Arctic Medical Research (Invited speaker)

8. Seminar by Umeå University Before The Swedish Work Environmental Fund; Chemical Substances in the Environment (Invited speaker)

Umeå, Sweden	September 23-24, 1977
Oulu, Finland	
Oulu, Finland	February 22-23, 1978
Stockholm, Sweden	October 17, 1978
Umeå, Sweden	November 9, 1978
Washington, D.C.	December 10-13, 1978
Leykgavik, Iceland	June 29-30, 1979
Umeå, Sweden	September 11-12, 1979

9. Seminar on the Work with Pesticides and Associated Risk; The National Swedish Environmental Protection Board (Invited to participate)

10. Seminar on the Use of Phenoxy Acids in the Agriculture; Swedish National Board of Occupational Safety and Health (Invited to participate)

11. Conference on the Use of Pesticides in Forestries - Swedish Association of Churches (Invited speaker)

12. Conference by the Swedish Association of Pesticide Manufacturers; Phenoxy Acids and Cancer (Invited speaker)

13. Committee on the Use of Pesticides in Forestry and Agriculture - The Swedish Parliment (Invited speaker)

14. Conference on Use and Regulation of Pesticides - Nordic Counsel of Workers in Agriculture and Horticulture; Health Effects of Phenoxy Acids (Invited speaker)

15. Tenth Annual Meeting of European Environmental Mutagen; Society on Environmental Mutagenisis (Invited speaker)

16. Seminar on Demands Made by the Society for Registration and Use of Pesticides- Association of Nordic Agricultural Research (Invited speaker)

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Stockholm, Sweden	September 20, 1979
Stockholm, Sweden	October 3, 1979
Sodrahoka, Sweden	November 6, 1979
Stockholm, Sweden	November 27, 1979
Stockholm, Sweden	February 20, 1980
Istab, Sweden	September 1-5, 1980
Athens, Greece	September 14-19, 1980
Helleiud, Norway	November 12-13, 1980

17. Seminar on Phenoxy Adics and Cancer; Institute of Occupational Health (Invited speaker)

18. International Symposium on Prevention of Occupational Cancer; Institute of Occupational Health, Helsinki, Finland; and International Labor Office and World Health Organization

19. Staff Meeting - University Hospital, Linkoping, Sweden; Phenoxy Acids or Soft-tissue sarcoma and Malignant Lymphoma (Invited speaker)

20. Thirteenth International Cancer Congress; The Environment and Cancer; Recent Epidemiologic Developments (Invited speaker)

21. Symposium on Chlorinated Dioxins and Dibenzo Phurons in the Total Environment; The 184th American Chemical Society Meeting (Invited speaker)

22. Seminar on Pesticides - of Benefit or Environmental Pollutant; County Hospital at Karlshamn (Invited speaker)

23. Expert Panel on Dioxon Documents; United States Environmental Protection Agency (Invited member)

24. Symposium on the Swedish Cancer Registry; Yesterday, Today and Tomorrow (Invited speaker)

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Helsinki, Finland	December 12, 1980
Helsinki, Finland	April 21-24, 1981
Linkoping, Sweden	October 22, 1981
Seattle, Washington	September 8-15, 1982
Kansas City, Missouri	September 12-17, 1982
Karlshamn, Sweden	March 11, 1983
Cincinnati, Ohio	July 27-29, 1983
Liding, Sweden	November 11, 1983

25. Seminar on Drugs and Pesticides; The Swedish Branch of Friends of Earth International ((nvited speaker)

Conference on Biological Mechanisms of Dioxin Action

Symposium on Toxicology; Swedish and Finnish Association of Toxicology
(Invited speaker - unable to attend)

Symposium on Leukemia and Related Diseases; International Association for Comparative Research
(Invited speaker - unable to attend)

Internation Symposium on Herbicides and Defoliants in War; The Long-Term Effects on Man and Nature
(Invited speaker - unable to attend)

Symposium on Public Health and Risks of Chlorinated Dioxins
(Invited speaker - unable to attend)

Congress on the Scientific and Social Response from Exposure to Dioxins and Related Material; Association of Occupational and Environmental Health
(Invited speaker - unable to attend)

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Biskopnarno, Sweden	November 26-27, 1983
Banbury Center, NY	April 1-4, 1984
Stockholm, Sweden	May 16, 1981
Los Angeles, CA	August 31-September 4, 1981
Ho Chi Minh City, Vietnam	January 13-20, 1983
Rockefeller University New York	October 19-20, 1983
Arlington, Virginia	December 6-7, 1983

MAUREEN C. HATCH, Ph.D.

I. Qualifications

Dr. Hatch is Assistant Professor Of Epidemiology at Columbia University, School of Public Health, in New York City. Her Curriculum Vitae and an Addendum listing non-scientific work experience and scientific meetings attended are attached.

II. Subject Matter

The subject matter about which Dr. Hatch will testify is reproductive epidemiology and toxicology, and their specific applicability to miscarriages and congenital malformations (birth defects) in the wives and children of Vietnam veterans.

Dr. Hatch will testify at length to the data collected in Vietnam regarding untoward pregnancy outcomes. Dr. Hatch is one of two investigators who are to publish that portion of the International Symposium held in Ho Chi Minh City in January, 1983 having to do with reproductive problems as a result of exposure to Agent Orange and other phenoxy herbicide spraying in Vietnam.

III. Scientific Principles

See General Statement of Scientific Principles and Assumed Facts attached.

IV. Substance of Opinions

A. That exposure to Agent Orange in Vietnam has resulted in certain epidemiological data showing a statistically significant increase in certain congenital malformations, e.g. cleft palate, limb deformaties, and anencephaly, as a result of paternal mediated reproductive effects where only the fathers were exposed to Agent Orange.

B. That animal experiments confirm the epidemiological data in that TCDD exposure of the male has shown reproductive toxicity.

V. Grounds for each Opinion

A. General

Review of applicable medical and scientific literature; personal research; attendance and/or participation at various seminars; education and training.

REFERENCES CITED

Allen JR, Carstons LA. Light and electron microscopic observations in Macaca mulatta monkeys fed toxic fat. Am J Vet Res 28:1513-1526, 1967.

Constable J, Hatch M. Herbicide exposure and reproductive outcome. In: Herbicides in War: The Long-term Effects of Man and Nature, AW Westing, ed. New York: Taylor & Francis, 1984 (in press).

Khera KS, Ruddick JA. Polychlorodibenzoistar-p-dioxins: Perinatal effects and the dominant lethal test in Wistar rata. In: Chlorodioxins - Origin and Fate, EH Blaire, ed. Washington DC: American Chemical Society, 1973, pp 70-84.

Kociba RJ, Keeler PA< Park CN, Gehring PJ. 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD): Results of a 13-week oral toxicity study in rats. Toxicol Appl Pharmacol 35:553-575, 1976.

McConnell EE< Moore JA< Haseman JK, Harris MW> The comparative toxicity of chlorinated dibenzo-p-dioxins in mice and guinea pigs. Toxicol Appl Pharmacol 44:335-356, 1978.

Mattison DR, Thorgeirsson SS. Gonadal aryl hydrocarbon hydroxylase in rats and mice. Cancer Res 38:1368-1373, 1978.

Norback DH, Allen JR. Biological responses of the nonhuman primate, chicken and rat to chlorinated dibenzo-p-dioxin ingestion. Environ Health Perspect 5:233-240, 1973.

Peterson, R. Hormonal changes and "wasting" observed in moderately-high-dose animal experiments. Presented at the Symposium on Public Health Risks of the Dioxins, The Rockefeller University, October 19-20, 1983. (Proceedings in press, Alan R. Liss Inc.)

Poland A, Knutson JC. 2,3,7,8-tetrachlorodibenzo-p-dioxin and related aromatic hydrocarbons: Examination of the mechnanism of toxicity. Ann Rev Pharmacol Toxicol 22:517-554, 1982.

Tofilon PJ, Piper WN. 2,3,7,8-tetrachlorodibenzo-p-dioxin-mediated depression of rat testicular heme synthesis and microsomal cytochrome P-450. Biochem Pharmacol 31:3663-3666, 1982.

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RELEVANT EMPLOYMENT:

Curriculum Vitae

MAUREEN C. HATCH
412 Mountain View Road
Englewood, New Jersey 07631
Home: (201) 569-4139
Business: (212) 694-3944

Born: 26 March, 1942
SS # 054-34-6077

EDUCATION:

B.A., 1963: Manhattanville College, Purchase, N.Y.
Graduate studies in urban planning, 1965-67: Hunter College, N.Y.C.
M.P.H., Epidemiology, 1979: Columbia Unversity School of Public Health, N.Y.C.
Ph.D., Epidemiology, 1983: Columbia University Graduate School of Arts and Sciences, N.Y.C.
Thesis Topic: Paternal Risk Factors for Spontaneous Abortion.

HONORS:

1977-79: N.I.C.H.D. Fellowship, Epidemiology of Mental Retardation and Other Developmental Disorders
1978: Selected for the Society for Epidemiologic Research Student Workshop

PROFESSIONAL SOCIETIES:

Society for Epidemiologic Research, Occupational Reproductive Hazards Committee

COMPUTER SKILLS:

Computer languages: Wylbur, UC360
Statistical software: SAS, SPSS, CROSSTABS

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Hatch, M., Kline, J. Epidemiology Studies: Spontaneous Abortion and Exposure to the Herbicide 2,4,5-T. U.S. Environmental Protection Agency, Washington, D.C., 1981 (EPA 560/6-81-006).

Stein, Z., Hatch, M., Kline, J., Shrout, P., Warburton, D. Epidemiologic Considerations in Assessing Health Effects at Toxic Waste Sites. In: Assessment of Health Effects at Chemical Disposal Sites, William W. Lowrance, Ed. The Rockefeller University, New York City, 1981.

Edmonds, L., Hatch, M., Holmes, L., Kline, J., Letz, G., Levin, B., Miller, R., Shrout, P., Stein, Z., Warburton, D., Weinstock, M., Whorton, D., Wyrobek, A. Report of Panel II: Guidelines for Reproductive Studies in Exposed Human Populations. In: Guidelines for Studies of Human Populations Exposed to Mutagenic and Reproductive Hazards, Arthur D. Bloom, Ed. March of Dimes Birth Defects Foundation, 1981.

Kline, J., Stein, Z., Hatch, M., Strobino, B. The Role of Spontaneous Abortion Studies in Environmental Research. EPA Technical Report, 1983 (in press).

Kline, J., Stein, Z., Hatch, M., Hutzler, M., Lai, A., Pantel-Silverman, J. Surveillance of Parental Occupational and Spontaneous Abortion. NIOSH Technical Report, 1983 (in press).

Hatch, M. Occupational and environmental hazards to human reproduction. In: Double Exposure: Women's Health Hazards on the Job and at Home, Wendy Chavkin, Ed., Monthly Review Press, 1984 (in press).

Stein, Z., Hatch, M. Outcomes of occupational exposures: Antenatal and postnatal impairment. In: Review of Occupational Hazards to Reproductive Health, World Health Organization, Geneva, Switzerland, 1983, pp 79-91.

Constable, J., Hatch, M. Herbicide exposure and reproductive outcome- an overview. In: Herbicides in War: The Long-term Effects on Man and Nature, A.W. Westing, Ed., New York: Taylor & Francis, Pubs., 1983 (in press).

Hatch, M. Parental occupation and cytogenetic findings in abortuses. In: Reproduction: The New Frontier in Occupational Health, James Lockey, Grace Lemasters, William Keye, Eds., New York: Alan R. Liss, Inc., 1984 (in press).

Hatch, M. Reproductive effects of the chlorinated dioxins. In: Public Health Risks of the Dioxins, William W. Lowrance, Ed., The Rockefeller University, New York City, 1984 (in press).

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PRESENTATIONS:

Hatch, M. Testing Clusters of Reproductive Anomalies to Screen for New Teratogens. Presented at the Society for Epidemiologic Research, Student Workshop on Epidemiologic Methods, Iowa City, Iowa, June 1978.

Hatch, M. Environmental Hazards to Human Reproduction. Presented at the March of Dimes Nursing Symposium, New York City, March 1981.

Hatch, M. Social Context, Concepts of Safety, and Occupational Epidemiology. Presented at the Conference on Work and Health, Case Western Reserve University, Cleveland, Ohio, April 1981.

Hatch, M. Spontaneous Abortion as an Endpoint in Environmental Research. Presented at the Latin American Course on Genetic Toxicology, Mexico City, August 1981.

Hatch, M. Reproductive Hazards in the Workplace: Research Findings, Research Issues. Presented at the New Jersey Family Planning League Symposium on Occupational Hazards and Reproductive Health, Clark, New Jersey, October 1981.

Hatch, M., Kline, J., Stein, Z., Hutzler, M., Silverman, J., Lai, A. Parental Employment and Spontaneous Abortion. Presented at the American Public Health Association Meetings, Montreal, November 1982.

Hatch, M., Kline, J., Stein, Z., Hutzler, M., Lai, A., Pantel-Silverman, J., Parental Employment and Spontaneous Abortion. Presented at the Conference on Reproductive Health Studies in Industry, East Millstone, New Jersey, December 1982.

Hatch, M. Reproductive Effects of Herbicide Exposure in Humans. Presented at the International Symposium on Herbicides and Defoliants in War: The Long-term Effects on Man and Nature, Ho Chi Minh City, Vietnam, January 1983.

Hatch, M. Agent Orange and the Herbicide 2,4,5-T. Presented at the American Chemical Society Conference on Dioxins, Old Westbury, May 1983.

Hatch, M. Environmental Influences on Reproduction. Medical Department Seminar, Brookhaven National Laboratory, Upton, Long Island, September 1983.

Hatch, M. Environmental Agents and Aneuploidy in Human Spontaneous Abortions. Presented at the Environmental Protection Agency Workshop on Approaches for Assessing the Risk of Aneuploidy Induction by Chemicals, Washington, D.C., October 1983.

Hatch, M. Reproductive Epidemiology. Presented as part of the University of Ottawa refresher course, Recent Advances in Occupational and Environmental Health, Ottawa, Ontario, October 1983.

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CONSULTING EXPERIENCE:

Council on Environmental Quality: Scientific advisory panel for report entitled "Chemical Hazards to Reproduction."

Environmental Protection Agency: Reviewer for study by Dow Chemical Co. on the reproductive effects of occupational exposure to chlorinated dioxins.

National Opinion Research Center: Reviewer for reproductive portion of survey instrument developed for the Air Force study of herbicide-exposed personnel.

TEACHING EXPERIENCE:

Coordinator for Columbia core course in epidemiology for public health students.

Teaching Assistant and section leader for courses in epidemiology and cancer epidemiology for public health and medical students.

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ADDENDUM

Nonscientific Work Experience:

1963-64 Harper & Row Publishers: designed promotional brochures , wrote jacket copy.

1964-68 Architects' Renewal Committee in Harlem, Inc.: administrative assistant, junior planner.

1968-69 Model Cities Program, Hoboken, NJ: Planner.

1970-73 C. Richard Hatch Associates, Inc.: conceived and wrote educational materials on urban planning and ecology.

1973-76 Parttime freelance editing for such firms as Harry Abrams, Inc. and World Publishing Co.

Scientific Meetings Attended in Addition to Those on CV:

. Society for Epidemiologic Research, Iowa City, 6/78

. Society for Epidemiologic Research, New Haven, 6/79 or 6/80

. Birth Defects Symposium X: Human Embryonic and Fetal Death, Albany, 9/79

. Birth Defects Symposium XI: Human Mutation, Albany, 9/80

. American Public Health Association Meetings, New York City 1980 (?)

. First Annual Symposium on Environmental Epidemiology, Pittsburgh, 4/80

. Changing Risk of Disease in Women, Johns Hopkins University, 10/81

Please note also that the last two papers mentioned on p.3 of the attached CV were originally presented at scientific meetings whose proceedings are currently in press; Reproduction: The New Frontier..., a symposium at the Rocky Mountain Center for Occupational and Environmental Health of the University of Utah, Park City, 4/83, and Public Health Risks of the Dioxins, a symposium at The Rockefeller University, 10/83.

I also attended an allegedly impartial scientific meeting on 2,4,5-T convened in June, 1980 (?) by Dr. Frederick Coulston, at which there were many Dow scientists whose names had not

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appeared on t original list of conferees.

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ALASTAIR W. M. HAY, Ph.D.

I. QUALIFICATIONS

Dr. Hay is a lecturer on Chemical Pathology, Department of Chemical Pathology, Old Medical School, University of Leeds, Leeds, England. His Curriculum Vitae is attached. A list of seminars, meetings and awards is also attached.

II. SUBJECT MATTER

Dr. Hay will provide background testimony on a broad range of matters relating to Agent Orange, phenoxy herbicides, and their contaminants, including 2, 3, 7, 8-TCDD.

Dr. Hay will discuss in detail his knowledge of the various phenoxy herbicides and their contaminants, including but not limited to the various aspects of: chemistry; biochemistry; manufacture and/or production; fate in the environment, animals, and humans; modes of exposure, i.e. absorption, ingestion and inhalation, specifically by the veterans who served in Vietnam; toxicity; and the state of the medical and scientific literature at various times since at least 1957 forward.

Dr. Hay's testimony regarding the medical and scientific literature will include an exposition of the definitions and explanations, and their applicability to the troops exposed in Vietnam, of the phenoxy herbicides and their contaminants, in

the following areas: plant physiology; toxicology; neuro-toxicology, both neurological and psychological; epidemiology; immunology; mutagenicity; teratology; embryotoxicity; reproductive toxicology; and carcinogenicity.

III. SCIENTIFIC PRINCIPLES

See General Statement of Scientific Principles and Assumed Facts attached.

IV. SUBSTANCE OF OPINION

Dr. Hay will testify to the following opinions:

A. That phenoxy herbicides, including Agent Orange, and 2, 4, 5-T, and their contaminants, especially TCDD, are:

1. Highly toxic
2. Neurotoxic
3. Immunosuppressive
4. Teratogenic and Embryotoxic
5. Potentially Mutagenic
6. Carcinogenic.

B. That there is no "minimum effect" level for 2, 3, 7, 8-TCDD and all other dioxins or, in other words, there is no known "safe level" for any human intake of 2, 3, 7, 8-TCDD and all other dioxins.

V. GROUNDS FOR EACH OPINION

A. General

The medical and scientific literature, attendance and participation in various symposia, review of various documents of certain defendants, personal research, and experience form the bases of whatever facts and opinions to which Dr. Hay will testify.

B. More specifically, the phenoxy herbicides, including Agent Orange, 2,4,-D and 2,4,5-T and their contaminants, including dioxin, especially TCDD, are:

1.	Highly toxic	McConnell, E.E., et al. Toxicology & Applied Pharmacology 44, 355-356 (1978); Schwetz, B.A., et al. Advances in Chemistry Series, ed. E. H. Blair, 120 55-69 (1973); Greig, J.B., et al. Food & Cosmetics Toxicology, 11,585-595 (1973);
2.	Neurotoxic	Kimmig, J. & Schultz, K. H. Dermatologica 115, 540-546 (1957); Bauer, et al. Archiv. Fuer Gewerbepathology un Gewerbehygin, 18,538-555 (1961)
3.	Immunosuppressive	Vos, J.G., & Moore, J.A. Internal Archives of Allergy and Applied Immunology 47,777-794 (1974); Faith, R.E., and Luster, M.I. Annals of The N.Y. Acad. of Sciences, 320, 564-571 (1979)

4.	Teratogenic and Embryotoxic	Neubert, D., and Dillmann, I. Naunym Schmiedebergs Archives and Pharmacology (Berlin) 272 (3), 243-264 (1972) Neubert, D. Environmental Health Perspectives 5, 67-79 (1973); Courtney, K.D., and Moore, J.A. Toxicology and Applied Pharmacology, 20, 396-403 (1971); Courtney, K.D. Bulletin of Environmental Contamination and Toxicology, 16, 674-681 (1976); Smith, F.A., et al. Toxicology and Applied Pharmacology 38, 517-523 (1976); Moore, J.A., et al. Environmental Health Perspectives 5, 81-85 (1973); Sparschu, G.L., et al. Food and Cosmetic Toxicology, 9, 405-412 (1971); Roll, R. Food and Cosmetic Toxicology, 9,671-676 (1971)
5.	Potentially Mutagenic	Rogers, A.M., et al., Mutation Research 105, 445-449 (1982); Bronzetti, G., et al. in Chlorinated Dioxins and Related Compounds: Impact on the Environment (pergamon Press, Oxford, NY (1982) pp 429-436; Hay, A. in The Chemical Scythe (Plenum Press, 1982) pp. 43
6.	Carcinogenic	Allen, et al., Chemosphere, 9,537-544 (1977); Kociba, R.J., et al. Toxicology and Applied Pharmacology. 46, 279-303 (1978); Anonymous. Bioassay of 2,3,7,8-tetrachlorodibenzo-p-dioxin for possible carcinogenicity (gavage study), National Cancer Institute DHHS Publication No. (NIH) 80-1757 (1980); Toth, K.S., et al. Nature (London) 278,548-549 (1979); Anonymous. National Cancer Institute Technical Report Series No. 123 (1979); Anonymous. Bioassay of a mixture of 1,2,3,6,7,8- and 1,2,3,7,8,9-hexachlorodibenzo-p-dioxin for possible carcinogenicity (gavage study), National Cancer Institute, Technical Report Series No. 198 (1980); Anonymous. Bioassay of a mixture of 1/2/3/6/7/8- and 1/2/3/7/8/9-hexachlorodibenzo-p-dioxin for possible carcinogenicity (dermal study), National Cancer Institute, Technical Report Series No. 202 (1980)

Dr. Hay will testify to examples of the grounds which support the above, including: knowledge of spraying Agent Orange, especially its effect on the Vietnamese countryside; the purpose and historical tracing of the animal studies; historical tracing of the human data, including the various industrial incidents since 1949 (Hay, A. The Chemical Scythe, Plenum, N.Y. (1982) pp 95-146); references to specific documents such as the EPA Dioxin document (presently in draft form); various cancer epidemiology; (Hardell, L. & Sandstrom, A. British Journal of Cancer, 39, 711-717 (1979); Hardell, et al. British Journal of Cancer, 43, 169-176 (1981); Honchor, P.A. and Halperin, W.E. Lancet, I. 268-269 (1981); and Cook, R.R., Lancet, I. 618-619 (1981); pertinent teratology epidemiology (Hanity, J.A., et al., Science, 212, 349-351 (1981); Field, B., and Kerr, C. Lancet I. 1341-1342 (1979)); various studies of the Vietnamese (Tung, T.T., LaRevue de Medicine, 14, 653-657 (1977)); especially reproduction toxicology (Constable, J. Report of the Workshop on Reproductive epidemiology. International Symposium on Herbicides and Defoliants in War: The long term effects on Man and Nature. Ho Chi Minh City 13-20 January 1983; to be published in Herbicides in War. Ed. A.H. Westing, SIPRI); and those reports of the symptoms and diagnoses of the U. S. Vietnam veterans.

C. The above will be relied upon to show that there is no "minimum effect" level for 2,3,7,8-TCDD or other dioxins.

Name:	Alastair Watt Macintyre HAY
D.O.B.:	21 April 1947
Marital Status:	Married
Children:	1 son (Tom)
Place of Birth:	Glasgow, Scotland.
Nationality:	British
Degrees:	B.Sc.(Hons), Chemistry IIA - London 1969 Ph.D., Biochemistry, London 1973
Home Address:	School House, Arthington Lane, Arthington, Leeds LS21 1PE England.
Work Address:	Department of Chemical Pathology, Old Medical School, University of Leeds, Leeds LS2 9NL England.
Place of Secondary Education:	Gifford Technical High School, Bulowayo, Zimbabwe (formerly Rhodesia)
Present Appointment:	University lecturer in Chemical Pathology since April 1979 (University of Leeds) Leeds, England.
Former Appointments:	Research Fellow - Zoological Soc. of London September 1972 - November 1977 Research Fellow - University of Leeds, Department of Animal Physiology and Nutrition December 1977 - March 1979
Societies:	Biochemical Society Nutrition Society
Expert Committees:	1983 EPA Review Panel on Dioxins for Environmental Criteria and Assessment Office.

PUBLICATIONS:

Books

1. Alastair Hay. The Chemical Scythe: Lessons of 2,4,5-T and Dioxin. Plenum Press. 265 pp. August 1982.

2. Sean Murphy, Alastair Hay and Steven Rose. No Fire: No Thunder. The threat of chemical and biological warfare. Pluto Press. (To be published in January 1984). 135pp.

Scientific Papers and Abstracts

1. Sinclair, A.J., Fiennes, R.N.T.W., Hay, A.W.M., Watson, G., Crawford, M.A., & Hart, M.G. Linolenic acid deprivation in Capuchin monkeys. Proc. Nutr. Soc., 33, 49A (1974).

2. Hay, A.W.M., Sinclair, A.J., & Ray, W.G. Some useful techniques in thin layer chromatography. J. Lab. Pract. 23, 483-484 (1974).

3. Hay, A.W.M. & Ray, W.G. A simple macrotome. J. Lab. Pract. 24, 35 (1975).

4. Hay, A.W.M. Comparative aspects of vitamin D transport. In: Calcium Regulating Hormones (Excerpta Medica, Amsterdam). The Proc. of the 5th Parathyroid Conference, Oxford. pp 405-407 (1975).

5. Hay, A.W.M. & Watson, G. Binding of 25-hydroxyvitamin D_2 to plasma protein in New World monkeys. Nature, 256, 150 (1975).

6. Hay, A.W.M. The transport of 25-hydroxycholecalciferol in a New World monkey. Biochem. J. 151, 193-196 (1975).

7. Hay, A.W.M. & Watson, G. The plasma transport proteins of 25-hydroxycholecalciferol in mammals. Comp. Biochem. Bhysiol. 53B, 163-166 (1976).

8. Hay, A.W.M. & Watson, G. The plasma transport protein of 25-hydroxychclecalciferol in fish, amphibia, reptiles and birds. Comp. Biochem. Physiol. 53B, 167-172 (1976).

9. Hay, A.W.M. The transport of vitamin D in the Giant Panda. Trans. Zool. Soc. Lond., 33, 139-140. (1976).

10. Hay, A.W.M. Vitamin D transport in vertebrates. Proc. Anat. Soc. J. Anat. 122, 195 (1976).

11. Hay, A.W.M. A possible role for vitamin D_3 in vertebrate evolution. Proc. of the 2nd Internation Workshop on Calcified Tissues. (Abstract). Isr. J. Med. Sci. 12, 31-32 (1976).

12. Hay, A.W.M. & Watson, G. The binding of 25-hydroxycholecalcifer and 25-hydroxyergocalciferol to tissue binding proteins in a New World and an Old World primate. Comp. Biochem. Physiol. 56B, 131-134 (1977).

13. Hay, A.W.M., & Watson, G. Vitamin D_3 in vertebrate evolution. Comp. Biochem. Physiol. 56B, 375-380 (1977).

14. Hay, A.W.M. & Watson, G. Binding properties of serum vitamin D transport proteins in vertebrates for 24R, 25-hydroxycholecalcif and 24S, 25-hydroxycholecalciferol *in vitro*. Comp. Biochem. Physiol. 58B, 42-48 (1977).

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15. Hay, A.W.M. & Watson, G. Evolution of vitamin D serum transport proteins in vitamin D: Biochemical, Chemical and Clinical Aspects related to Calcium Metabolism (Ed. by Norman, A.W. et al) Walter de Gruyter, Berlin & New York (1977) pp 483-489.

16. Hay, A.W.M. Vitamin D at Asilomar, Report of 3rd Workshop on Vitamin D. Nature 266, 17-18 (1977).

17. Hay, A.W.M. Combatting rickets. Nature 270, 289 (1977).

18. Hay, A.W.M. Vitamin D_2 metabolism in New World primates. Proc. of the 3rd International Workshop on Calcified Tissues, Israel 6-9th March 1978 (in press).

19. Hay, A.W.M., Darling, M. & Watson, G. Rickets and vitamin D metabolism in primates. Proc. Nutr. Soc. 37, 42A. (1978).

20. Hay, A.W.M. Tetrachlorodibenzo-p-dioxin release at Seveso. Disasters 1(4) 289-308 (1977).

21. Hay, A.W.M. Identifying carcinogens. Nature, 269, 468-470 (1977).

22. Hay, A.W.M. Seveso: No answers yet. Disasters 2, 163-168 (1978).

23. Hay, A.W.M. Vitamin D transport (Review). C.R.C. Handbook series in Nutrition and Food (in press).

24. Hay, A.W.M. Resurgence of Vitamin D. Nature, 273, 426-427 (1978).

25. Hay, A.W.M. Halogenated Hydrocarbon Effects. Nature, 274, 533-534. (1978).

26. Hay, A.W.M. & Jones, G. The elution profile of vitamin D_2 metabolites on Sephadex LH20. Clin. Chem. 25, 473-475 (1979).

27. Hay, A.W.M. Accidents in trichlorophenol plants: a need for realistic surveys to ascertain risk to health. Proc. of N.Y. Acad. of Sci. 320, 321-324 (1979).

28. Rivers, J.P.W., Frankel, T.L., Juttla, S., & Hay, A.W.M. Vitamin D in the Nutrition of the Cat. Proc. Nutr. Soc. 38, 36A (1979).

29. Hay, A.W.M., Hassam, A.G., Crawford, M.A., Stevens, P.A., Mawer, E.B. & Case, L. The ability of 1α,25-dihydroxycholecalciferol to alter the fatty acid composition of phosphoglyceric in rat intestinal mucosa and smooth muscle in Vitamin D Basic Research and its Clinical Application (Ed. by Norman, A.W., et al). Walter de Gruyter, Berlin, & N.Y. (1979).

30. Care, A.D., ickard, D.W., Ross, R., [illegible], A.W.M., Garel, J.M. & Recel, J. A comparison of the effects of 25,26-dihydroxycholecalciferol (25,26-DHCC) and 24,25-DHCC on calcitonin secretion rate in vitamin D depleted pigs. J. Endocrinology 85, (2), 54p-55p (1980).

31. Fleming , J. Cooper, E.H., Hay, A.W.M., Morgan, D.B., and Parapia, L. Tubuloproteinuria in Cancer Chemotherapy. La Ricerca Clin Lab. 10, 135-141 (1980).

32. Hay, A. Complecation of vitamin D metabolism still increasing Nature, 278, 509-510 (1979).

33. Hay, A.W.M. Essential fatty acid restriction inhibits vitamin D dependent Calcium absorption. Lipids. 15, 251-4 (1980).

34. Intestinal, 1α,25-dihydroxycholecalciferol-dependent calcium absorption inhibited by essential fatty acid restricton. Proceedings of Nutri. Soc. 39, 89A (1980).

35. Halogenated hydrocarbon. Hay, A.W.M. in 1981 EST Yearbook of Science & Technology. McGraw-Hill pp198-200.

36. Hay, A.W.M. Exposure to TCDD: the health risks. - Chlorinated dioxins and related compounds. Impact on the Environment. O. Hutzinger, et al. Pergamon Press, Oxford, N.Y. (1982).

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39. Hay, A.W.M., Mawer, E.B., Hassan, A.G., Crawford, M.A. & Stevens, P.A. The Role of essential fatty acids in vitamin D dependent calcium absorption in the intestine. Proc. of 5th vitamin D workshop. Williamsburg, U.S.A. New in Vitamin D, chemical biochemical and clinical endocrinology of calcium metabolism. Walter de Guyter. Berlin, N.Y.(1982) pp309-311.

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41. Sheltawy, M., Hay, A.W.M., Hullin, R.P., and Morgan, D.B. Vitamin D_2 and D_3 in the nutrition of elderly. Clin. Sci. 62, 15-16 (1982) (abstract).

42. Hay, A. Herbicides, trichlorophenols and soft tissue sarcomas. Lancet I, 1240 (1982).

43. Hay, A. It kills weeds, but what about people? New Scientist. 94, No.1314 pp158-161 (1982)

44. Hay, A., Murphy, S., Robinson, J.P. & Rose, S. The poison cloud hanging over Europe. New Scientist 93, No. 1296 pp630-635 (1982)

45. Hay, A. Experimental Toxicology and cytogenetics: an overview. In "Herbicides and War" to be published by Stockholm International Peace Research Institute 1984 A. Westing. Edit.

46. Hay, A. The Mutagenic Properties of 2,3,7,8-Tetrachlorodiben p-dioxin in "Chlorinated Dioxins and Dibenzofurans in the Total Environment. Vol II. Edit. by Keith, L.H. et al to be published in 1984.

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48. Sheltawy, M., Newton, H., Hay, A., and Morgan, D.B. and Hull, R.P. The contribution of diet and sunlight to the plasma 25-hydroxy vitamin D. (abstract) to be published in November 1983. Proceedings of UK Bone and Tooth Society.

49. Feely, M., Hay, A., Clarke, N., Price, D., and Cooke, J. "mini-Dose" Phenobarbitone: A useful marker of compliance - submitted to IUPHAR 9th International Congress of Pharmacolog

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2. Hay, Alastair. Recipe for less disaster. Nature 263, 270 (1976)

3. Hay, Alastair. Seveso: the aftermath. Nature 263, 538-540. (1976)

4. Hay, Alastair. Towards anticipating disaster. Nature 264 310 (1976).

5. Hay, Alastair. Seveso:putting it right. Nature 264, 504 (1976)

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6. Hay, Alastair. Seven months on. 265, Nature, 490 (1977).

7. Alastair Hay, Seveso: Dioxin damage. Nature 266,7-8(1977).

8. Hay, Alastair. Zoo story. Nature 267, 94-95 (1977).

9. Hay, Alastair. Italy: Distant drums. Nature 267, 301 (1977).

10. Hay, Alastair. Seveso solicitude. Nature. 267, 384-385 (1977)

11. Hay, Alastair. An aid to development? Nature, 267, 571-572 (1977)

12. Hay, Alastair. Roche's reply. Nature, 267, 749 (1977)

13. Hay, Alastair. Twelve months after Seveso. Nature, 268 90 (1977).

14. Hay, Alastair. Seveso Row. Nature, 268, 395 (1977)

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16. Hay, Alastair. Informing on 2,4,5-T. Nature, 269, 749-750 (1977).

17. Hay, Alastair. Health and safety 3 years on. Nature, 270, 91-93(1977).

18. Hay, Alastair. Combatting rickets. Nature, 270, 289 (1977).

19. Hay, Alastair. Science Key to Vietnams Recovery, Nature 271, 101-2 (1978).

20. Hay, Alastair. Science helps to rebuild Vietnam. Nature, 271, 101-102 (1978).

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26. Hay, Alastair. Commonwealth Science Council Coordinates approach to UNCSTD. Nature, 273, 697-698 (1978).

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29. Hay, Alastair. Dioxin source is 'safe'. Nature, 274, 526 (1978).

30. Hay, Alastair. Vietnam still looking for foreign aid. Nature, 275, 6-7 (1978)

31. Hay, Alastair. Vietnam's scientists wait for books and equipment. Nature, 276, 203 (1978).

32. Hay, Alastair. Dioxin workshop. Nature, 276, 304 (1978).

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39. Hay, Alastair. Critics challenge data that led to 2,4,5-T ban. Nature, 279, 3 (1979).

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44. Hay, Alastair. Rickets under control again in UK. Nature, 279, 749 (1979).

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50. Hay, Alastair. Seveso: the crucial question of reactor safety Nature. 281, 521 (1979).

51. Hay, Alastair. Dispute over Dow Chemicals theory of dioxin traces. Nature, 281, 619-620 (1979).

52. Hay, Alastair. UK to tighten asbestos controls. Nature, 282, 5 (1979).

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54. Hay, Alastair. Short term tests can predict potential carcinogens, says study. Nature, 282, 664 (1979).

55. Hay, Alastair. Dioxin as a health hazard. Book Review. Nature, 283, 229-230 (1980).

56. Hay, Alastair. Health monitoring endangered at Seveso. Nature, 283, 237 (1980).

57. Hay, Alastair. Dioxin detection. Nature, 283, 426 (1980).

58. Hay, Alastair. Study finds malnutrition in 7% of elderly. Nature, 283, 612 (1980).

59 Hay, Alastair. Chemical company study shows no dioxin hazard. Nature, 283, 613 (1980).

60. Hay, Alastair. Chemical company suppresses dioxin report. Nature, 284, 2 (1980).

61. Hay, Alastair. Dioxin and 2,4,5-T: what are the risks? Nature, 284, 111 (1980).

62. Hay, Alastair. The CIA's toxic agents. Nature, 284, 296 (1980).

63. Hay, Alastair. Coalite health survey talks. Nature, 284, (1980).

64. Hay, Alastair. Red faces (and hot tempers) on 2,4,5-T. Nature, 286, 97 (1980).

65. Hay, Alastair. A plea for 2,4,5-T. Nature, 287, 659-570 (1980).

66. Hay, Alastair. Herbicide safety: Bill of Health. Nature, 289, 4 - 5 (1981).

67. Hay, Alastair. Rickets at bay. Nature, 289, 113 (1981).

68. Hay, Alastair. Chlorinated dioxins and the environment. Nature, 289, 351-352, (1981).

69. Hay, Alastair. Seveso: the intrigue and the infighting. Book Review. Nature, 290, 71-72 (1981).

70. Hay, Alastair. Disposing of dioxins by oxidation. Nature, 290, 294, (1981).

71. Hay, Alastair. Secrecy at Coalite. Nature, 290, 729, (1981).

72. Hay, A., Murphy, S., Robinson, J.P. On Chemical War. Nature, 294, 204 (1981).

73. Hay, Alastair. Spot the potential carcinogen. Nature, 296, 100, (1982).

74. Hay, Alastair. Relating to halenated hydrocarbons. Nature, 296, 688 (1982).

75. Hay, Alastair. Chemistry at War. Nature, 298, 205-206 (1982).

76. Hay, Alastair. The official's book of risky business. Book Review. Nature, 301, 640 (1983).

77. Hay, Alastair. Defoliants in Vietnam: the long term effects. Nature, 302, 208-209 (1983).

78. Hay, Alastair. Empowered to set standards. Book review. Nature, 305. 77 (1983).

79. Hay, Alastair...and its control. Journal Review. Nature. 305, 486 (1983).

80. Hay, Alastair. Fresh support for apian origin. Nature. 306, 8 (1983).

HAY, Alastair W.M.

Additional Papers

1. Paper: "Relationship between Sex Hormones and Fructose Metabolisms in Rat Liver"; Presented at Nutrition Society, London, December 7, 1972.

2. Participant: International Agency for Research on Cancer, NIEHS/IARC Working Group on the Coordination of Epidemiological Studies on the Long-Term Hazards of Chlorinated Dibenzo Dioxins-Chlorinated Dibenzo Phurons; Lyon, Lyon, France, January 10-11, 1978.

3. Member: Panel on Human Observation of the Consequences of Dioxon Exposure; Meeting: International Symposium on Chlorinated Dioxins and Related Compounds, Arlington, Virginia, October, 1981.

4. Paper: "The Role of Membrane Lipids in the Expression of Vitamin D Function in the Intestinal Nucosal Cell"; Presented at the Biochemical Society, London, December, 1981.

5. Paper: "The Manufacture of 2,4,5-Trichlorophenol and its Social Consequences"; Presented at the Royal Society of Chemistry, Education Division Meeting, Leeds, England, September, 1981.

6. Presentation: "Renal Toxicity to the Yorkshire Regional Health Authority Meeting on Aspects of Pathology:; Harigat, January, 1980.

7. Paper: "TCDD Mutagenic Property"; Presented at the International Symposium on Herbicides and Defoliants in War; Long-Term Effects on Man and Nature; held in Ho Chi Minh City, Vietnam; Also, repertoire of working group on experimental toxicology and cytogentics at this Conference.

HERBERT KAYE, Ph.D.

I. QUALIFICATIONS

Dr. Herbert Kaye, Ph.D., is a psychologist in the Department of Psychology at the State University of New York at Stoneybrook, Long Island and a visiting Associate Professor in the Department of Psychiatry at New York University Medical Center. See attached curriculum vitae.

II. SUBJECT MATTER OF TESTIMONY

Dr. Kaye will testify concerning the significance of a battery of quantitative neurophysiological tests called neurometrics which will be performed on various plaintiffs. The procedures were developed in part by Dr. Kaye in conjunction with medical and psychological researchers from this and other countries. He will testify that neurometrics, on which he has written extensively, is a sophisticated battery of electrical tests in use for about fifty years, which are highly efficient in the determining cortical EEG and evoked responses.

Dr. Kaye will explain the model used in the computerization against which the test results are compared and will explain how deviations from normal produce certain effects.

Dr. Kaye will also discuss the mechanism by which toxins produce these altered responses, and what effect those altered responses have upon the individual veterans at present, and the prognosis for any additional changes or deterioration in the future based upon an assumed bioaccumulation of the toxic materials in the system. In doing so, he will rely on his experience in diagnosing many Vietnam veterans exposed to Agent Orange.

III. GENERAL SCIENTIFIC PRINCIPLES RELEVANT TO AREA:

The scientific principles arise from three general disciplines: neurophysiology, mathematics, and neuropsychology.

The area of neurophysiology includes the work on neuro-anatomy, neurochemistry, neuropharmacology, and applied or clinical electrophysiology. The work in mathematics represents multivariate statistics. The work in neuropsychology includes direct and indirect brain-behavior research and clinical diagnostics.

The neurophysiological basis of the development of neurometrics is presented in Volumes I and II of Functional Neurosciences, published in 1977 by Lawrence Erlbaum Associates, publishers, Hillside, New Jersey. However, this work represents an integration of research and applications in the neurosciences over a period four decades, initiated with the seminal EEG work of Gibbs (see, for example, Atlas of Electroencephalography, Cambridge, Massachusetts, Addison-Wesley) W. Gray Walter (see, for example, Electronic Engineering, 1943, 16, pp. 9-13) and going through the specific and extensive quantitative work of Matousek and Peterson (Automation of Clinical Electroencephalography, New York, Raven Press, 1973, pp. 75-102) and current work by quantitative electrophysiologists such as A. S. Gevins, C. Shagass, Theodore Gasser, Enoch Calloway, T. M. Itil, L. Goldstein, and others. (See, for example, Neuro-psychopharmacology, Proceedings of the Tenth Congress of the Collegium Internationale Neuro-psycho-psychopharmacologicum,

eighth relevant norm. (See John, et al., Science, Volume 210, 1980).

Neuropsychological literature represents the third strand. This represents the melding of brain electrophysiology and other neurophysiological techniques with those of psychology, or the study of mental and behavioral processes. There is a huge literature in the area, and recent work by such researchers as Gevins, Galin, Tucker, Thatcher, Needleman, and others, as well as those studies of Dr. Kaye and his students and colleagues indicate that quantitative electrophysiology is valuable in diagnosing underlying cortical processes serving certain behaviors.

IV. SUBSTANCE OF OPINION

1. Agent Orange represents a neurotoxic agent that works indirectly by affecting liver function and the liver's production of heme; and in doing so makes an individual, so affected, vulnerable to neurohypoxia.

2. Agent Orange may also work at a local level on enzymes relevant to the production and mobilizations of neurotransmitters.

3. Agent Orange, which is lipid, soluable, is likely to be stored in myelin and other fatty material and is collectively "time released" under "stress".

4. Storage is likely to be greater in the long fiber tracts, such as the major pathways from spinal cord to peripheral cutaneous receptors, pathways from frontal cortical regions to the thalimus and in spinal cortical motor pathways.

5. Changes in cortical functioning, represented by each EEG's slowing, represent breakdown of neural metabolic function occurring as a result of progressive neurotoxic assault.

6. Changes in cortical functioning represented by inter-hemispheric asymmetries and wave-shape incoherence represent the disruption of neural

timing either through the breakdown of cortical pacers, or through the failure of transcortical communication via the corpus collosum.

7. The occurrence of sharp-wave activity is caused by disruption of inhibitory neurotransmitters and represents a mechanism that can partially account for mood lability, which along with selective suppression of frontal lobe function would provide the basis for behavioral discontrol.

V. GROUNDS FOR MY OPINION

A recent study by Needleman (Acta Psychiatrica-Scandinavica, 1983, Supplement No. 303, pp. 26-37) indicates the ability to utilize simple quantitative EEG spectral measures along with the psychological measures to classify children from the "normal" population to have high and low lead levels (using dentyne lead levels). The disrciminating variables for the EEG were the variables associated in our and inconventional EEG work with abnormalities; that is, excessive slow wave energy.

Recent work in our evaluation unit has examined the abnormality profiles of thirty-two Vietnam veterans. In summary, approximately fifty percent showed spectral abnormalities, fifty percent showed power asymmetries, fifty percent showed wave-shape incoherence, and fifty percent showed sharp wave activity. In all, eighty-four percent showed some significant degree of abnormality. Correlation of these patients' neurometrics profiles with other behavioral and physiological data is progressing. Specific correlation of neurometrics profiles and behavioral reports of individual patients who were exposed to herbicides while engaged in non-military activities is also proceeding.

Finally, there is a growing body of data relating research with people who were exposed to low levels of toxic material and who show the range of effects present in the Vietnam veterans exposed to Agent Orange. In particular,

research on the mechanisms underlying heavy metal toxicity (such as with lead and with methyl mercury) suggests possible mechanisms for both neurotoxic and genetic effects. (See, for example, Chang, L.W. "Pathogenetic Mechanisms of the Neurotoxicity of Methyl Mercury" in Mechanism of Actions of Neurotoxic Substances, edited by K.N. Prasad and A. Vernagakis, Raven Press, New York, 1982; and, Egan, et al., "Experimental Design for Animal Toxicity Studies" in Experimental and Clinical Neurotoxicology, edited by P.S. Spenser and H.H. Schaumberg, Williams and Wilkins, Baltimore, 1980.

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Cirriculum Vita - Herbert Kaye

Date of Birth and Birthplace: May 23, 1935, New York City

Marital Status: Married, one child

Business Address: Psychology Department
S.U.N.Y. at Stony Brook
Stony Brook, New York 11790
Phone: (516) 246-7638

Clinic Address: Neurometrics Evaluation Unit
Hauppauge Professional Building
111 Smithtown Bypass
Hauppauge, New York 11787

Education:

Rennslear Polytech. Institute, from 9/53 to 1/56, field: engineering

Hunter College, from 1/56 to 6/56

Columbia University, from 7/56 to 7/60 B.S.C. (1/60), psychology

Brown University, 9/60 to 6/62, M.S.C. (6/62), psychology

Brown University, 9/62 to 6/64, Ph.D. (6/64), psychology

Professional Experience:

Brown University, 7/64 to 8/66
Research Associate, Department of Psychology

Emory University, 9/66 to 6/67
Assistant Professor, (joint position) Graduate School of Psychology and in the Medical School, the Department of Obstetrics and Gynecology

Emory University, 7/67 to 3/71
Associate Professor, (joint appointment) Graduate School of Psychology and in the Medical School, the Departments of Obstetrics and Gynecology

State University of New York at Stony Brook, 4/71 to present
Associate Professor of Psychology

New York University Medical Center, Dept. of Psychiatry
Brain Research Laboratories, 1977 to present
Visiting Associate Professor

Professional Service

(1) University:

Director Institute for Research in Learning and Instruction: (1971-1974)
Director Developmental Psychology Program: (1971-1976; 1977;1978*;1982-present)
Department Executive Committee (8 of 12 years through 1983-4 Academic year)
Department Graduate Committee (2years)
Department Undergraduate Committee (2 years)
Director of Undergraduate Psychology Program (1975-6)
University Special Committees:
- (a) Behavioral Medicine
- (b) Chair Tenure Committee: Kenneth Gado
- (c) Chair Special Education Committee
- (d) Day Care
- (e) Undergraduate Studies
- (f) University Awards Program of S.U.N.Y. (1982-83)

Department Special Committees:
- (a) Applied Child and Family Concentration
- (b) Setting of S.C.D.C. on South Campus
- (c) Day Care

Dissertations and Theses:
- (a) Ph.D's: 5 Students
- (b) Master's: 12 Students
- (c) I have been on about 15 dissertation committees of students other than my own.

(2) Outside University:

Consulting Editor:
- (a) Journal of Experimental Child Psychology (1967-1974)
- (b) Development Psychology (1969-1974)
- (c) Journal of Infant Behavior and Development (1976-forward)
- (d) Journal of Learning Disabilities (1977-forward)
- (e) Child Development (1977-1980; 1983-forward)

Associate Editor: Journal of Learning Disabilities; Game's Application:
Guest Editor
- (a) Science
- (b) Journal of Animal Behavior
- (c) Psychological Review
- (d) S.R.C.D. Monograph
- (e) Human Development
- (f) Behavior Research Methods and Instrumentation
- (g) Journal exp. Child Psychology

N.I.H. Member of Clinical and Personality Fellowship Review-Committee (1970-73)
N.S.F. Guest Reviewer of Research Grants (1982)
A.C.L.D./N.I.N.C.D.S 5 year Support Priorities Subcommittee (1978)

(3) Outside Consultant Activities:
United Nations Development Program (1976-forward)
World Health Organization, Pan American Health Organization (1978-1980)
Jamaica Ministry of Education and Ministry of Social Security (1979-1980)

(4) Outside Committee Activities:

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Committee for Research in Infancy (one of the founding members, 1963)
The Brazelton Infant Behavior Scale (committee on use for premature infants, 1972)
Committee for Research in Infancy (Recording secretary 1967; coorganizer of meet.

B.O.C.E.S., III, Committee on Student Adjustment Center, (I have served as an occasional member for several school districts in Suffolk County in helping to develop Special Education facilities.)
(I have served as an outside evaluation for tenure and/or promotion decisions for professionals at 7 universities: Finstein University; C.U.N.Y.; Rutgers University; University of Connecticut; University of Alabama; University of Illinois; and University of Chicago.)

Membership in Professional Associations:

Sigma Xi
American Psychology Association
Mid Atlantic Association of Developmental Psychologists
Suffolk County Psychological Association
International Conference for Infant Studies
Committee for Research in Infancy
Society for Research in Child Development
New York Neuropsychological Group
Infancy Group of New York
New York Academy of Sciences
International Neuropsychological Society
Society for the Neurosciences (pending)
National Academy of Neuropsychology (pending)
International Society for the Study of Infant Behavior

Honors:

A.P.A. Fellow, Division 7, 1974
A.F.A. Division 7 Candidate for Credentials Committee
Merrill-Palmer Annual Meeting: Keynote Speaker, 1972
Association of Children with Learning Disabilities: Special Presentation: (1976-1
Association of Children with Learning Disabilities/National Institute of Neurolo and Communicable Diseases and Stroke Special Committee on Research Priorities for Government support (1978)
Pan American Health Organization International Workshop Participant: Effects of Maternal Nutrition on Infants Health, Pandjachel, Guatemala, (1979)

Grants on Which I Was Principle Investigator or Co-principle Investigator:

N.I.C.H.D. Infant Behavior (1966-1970)
McCandless Fund: Early Language Development (1967-1969)
N.I.E. Male/Female Differences in Free Word Associations (1969-70)
S.U.N.Y. Biomedical Fund: Infant Behavior (1972-1973)
N.S.F./R.A.N.N.: Brain-Behavior Relationships (1971-73; 73-76; 76-79)
N.I.C.M.D. Infant Behavior (1975-78)
Office of Education, B.E.H. (N.Y.U. Med. Center) Brain Function and Remediation o Learning Disabilities (1976-81)

Affilliation to Other Grants:

U.N.D.P. Caribbean Nutritional and Infant High Risk Longitudinal Study

Major Invited Lectures (last 8 years):

W. Virginia Life Span Development Conference: Dialectic Approaches to Developmen Methods (1976)
S.R.C.D. Conversation Hour on Physiology Measurements (1982)
A.P.A. Conversation Hour with H. Kaye (1976)
S.R.C.D. Introductory Speaker at Symposium: Infant Conditioning and Develop. (197
Minnesota Symposium on Development: Brain Function in Infancy (1976)
I.N.S. (European Division) Computer Applications in Neuropsychology (Italy, 1980)
Mid-A.H. Developmendtal Psychological Meetings (1981)
A.C.L.D./N.I.N.C.D.S. (1978)

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Joint U.S.S.R.-U.S.A. Conference: Theoretical Conceptualizations of Experimental Methodology; U.P.: H., L.R.P. Center, (1980)
Suffolk Bar Association, Criminal Division; 1981
Vietnam Veterans Survivors Symposium, 1983
Vietnam Veterans Agent Orange Victims Assoc. (Invited Participant, 1982)
(I have given about 30 lectures to local school groups, Special Education Parent-Teachers Associations, and local interest groups in the last 8 years.)

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Publications:

"Developmental changes in the olfactory threshold of the neonate". Child Develpm., 1963, 34, 371-376. (with Lipsitt, L.P. and Engen, T.)

"Two attempts to demonstrate tonal suppression of non-nutritive sucking in neonates." Percept. Mot. Skills, 1963, 17, 521-522. (with Levin, G.R.)

"Conditioned sucking in the human newborn." Psychon. Sci., 1963, 1, , 29-30, (with Lipsitt, L.P.)

"Olfactory responses and adaptation in the human neonate." J. comp. physiol. Psychol., 56, 1964, 73-77. (with Engen, T. and Lipsitt, L.P.)

"Skin Conductance in the Human Neonate." Child Develpm., 1964, 35, 1297-1305

"The relation of electronactual threshold to basal skin conductance in the human neonate, Child Develpm., 1964, 35, 1307-1312. (with Lipsitt, L.P.

"Non-nutritive sucking by human neonate." Child Develpm., 1964, 35, 479-758. (with Levin, G.R.)

"Primary and secondary punishment of toe sucking in the infant rhesus monkey." Psychol. Sci., 1965, 3, 73-74. (with Cox, J., Rosack, R., and Anderson, K.)

"Change in neonatal response to optimizing and non-optimizing sucking stimulation." Psychon. Sci., 1965, 2, 221-222. (with Lipsitt, L.P.)

"The conditioned Babkin response in human newborns." Psychon.Sci., 1965, 2, 287-288

"Operant Avoidance in an infant rhesus within the first month of life." Psychon. Sci., 1965, 3, 371-372

"Rearing of M. Mulatta from birth." Laboratory Animal Care Panel, 1966, 16, 176-486.

"Enhancement of neonatal sucking through reinforcement." J. Exp. Child Psychol. 1966, 163-168. (with Lipsitt, L.P. and Rosack, T.)

"Sucking behavior in the human infant: An evaluation of the process and its modification." Advances in Child Development and Behavior, 1967, III, 1-50.

"The effects of feeding and tonal stimulation on non-nutritive sucking in the human newborn." J. Exp. Child Psychol., 1966, 3, 146-154. (with Levin, G.R.)

"Work decrement and rest recovery during non-nutritive sucking in the human neonate." J. Exp. Child Psychol., 1966, 3, 146-154. (with Levin, G.R.)

"Sensory Processes in Infancy." In Reese, H. and Lipsitt, L.P. (eds.) Experimental Child Psychology, New York: Academic Press, 1969, Vol. 3

"Agreement among Subjects in choosing trigram labels for random shapes." Amer. Jour. of Psychol., Vol. 83, No. 1, March, 1970.

"Effects of variation of oral experience upon suckle." In Bosma, J. Oral

Publications: (Cont'd.)

Sensation and Perception, Vol. 3, C. C. Thomas, N. Y., 1973.

"Feedback from the sucking environment and subsequent modification of sucking behavior in the human neonate." J. Exp. Child Psychol., 1974; (with Brassell, W.R., Jr.)

"Some suggestions for reclassification of ontogenetically relevent early psychomotor behavior." In Schopler, E. and Reichler, R.J., First International Leo Kanner Symposium, (Pergamann Press, London, 1976).

"Early Experience as the Basis for Unity and Cooperation of "Differences", West Virginia Symposium in Life Span Development, Vol. 5, 1975.

"Neurometrics: Numerical taxonomy identifies different profiles of brain functions within groups of behaviorally similar people." Science, 1977, Volume 196, Number 4297 (with John, E. Roy and others)

Karmel, B.Z., Kaye, H. & John, E.R. Developmental neurometrics: the use of quantitative analysis of brain electrical activity to probe mental function throughout life-span. In Minnesota Symposia on Child Psychology. A. Collins, Ed., L E A, 62 Maria Drive, Hillsdale, N.J. 07642. 1978, pp 141-198.

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Publications: (Cont'd.)

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RONALD H. KERMAN, Ph.D.

I. Qualifications

Dr. Kerman is Associate Professor, and Chief, Cellular Immunology, Clinical Immunology Laboratories, the University of Texas Medical School at Houston. His Curriculum Vitae is attached.

II. Subject Matter

Dr. Kerman will testify that the special scientific discipline involved is immuno-toxicology which has been defined as "the undesirable effects of an inappropriate response of the immune system".

Dr. Kerman will discuss the following in his testimony: the immune system, with its organic, cellular, and humoral components - most especially with regard to the latter, T-helper cells, B-cells, plasma cells and immunoglobulin production; immune response, both beneficial and harmful; the various experimental studies, particularly those demonstrating atrophy of the thymus, weight loss, depletion of lymphoid organs, lymphopenia, cutaneous type delayed hypersensitivity (skin thickness) and altered bacterial immunity.

III. Scientific Principles

See General Statement of Scientific Principles and Assumed Facts attached.

IV. Substance of Opinions

A. That TCDD is immunosuppressive.

B. That a person exposed to TCDD might have increased predisposition to increased infection, neoplasm (cancer), and other diseases.

V. Grounds for each opinion

A. General

The bases for the facts and opinions to which Dr. Kerman will testify include a review of the applicable medical and scientific literature, his educational and professional background, and his work in connection with the Texas Agent Orange Study.

B. Specific

As indicated above, Dr. Kerman will testify that 2,3, 7,8-TCDD in particular causes, among others, immuno-suppressive effects, as reported in the literature regarding the various animal species studies. Specifically, TCDD has been demonstrated to suppress T-cell mediated immunity in such species. This effect likewise has been demonstrated in humans by Bekesi, specifically an alteration of mature T-cells. A more complete exposition of the substance and grounds for Dr. Kerman's opinions is set forth below.

Between 1961 and 1971, the United States Air Force dropped more than 100 million pounds of herbicides in Vietnam to defoliate certain forest regions. Chief among the herbicidal agents used was "Agent Orange" which is a mixture of equal parts of 2,4-dichlorophenol (2,4-D) and 2,4,5 trichlorophenol (2,4,5-T). Agent Orange contains a toxic contaminant, 2,3,7,8-tetrachlorodibenzo-p-dioxin (variously referred to as TCDD or dioxin), which has been called by some authorities "the most potent small-molecule toxin known" (1-2).

TCDD produces toxic effects in various mammalian species; the toxic manifestations often depend on the species. Guinea pigs are very sensitive to the toxic effects of TCDD, the single LD50 dose for this chemical being less than 1 ug/kg body weight. The LD50 value for mice and rabits is about 100 ug/kg. The toxic effects of the chemical include hepatic damages, thymic atrophy, hematological alterations and teratological effects in various species (3-7).

A consistent toxic effect of TCDD in various test animals is damage to the thymus gland. A dose-related depletion of hymocytes from this organ leading to cortical atrophy and hymic involution has been described in various species. Buu-Hoi et al (4) were first to suggest that sublethal doses of TCDD produced thymus atrophy and proposed that the thymus, liver and heart were the target organs of dioxin toxicity. Single or repeated toxic doses of TCDD caused a decrease in body

weight and several vital organs and often reduced organ: body weight ratios. TCDD has been reported to cause a reduction of body weight in guinea pigs, rats, mice, rabbits and monkeys (as reviewed in 8). In all species, a consistent reduction in thymus weight was seen. This is often associated with atrophy of the thymic cortex subsequent to the gradual depletion of lymphocytes in this area at low doses of TCDD.

Vos and co-workers (6) reported the effects of TCDD on the immune system of guinea pigs, rats and mice. Several tests were employed in these three species and the authors concluded that the Effect of TCDD was primarily on cell mediated immune mechanisms of these animals. Guinea pigs treated with 1 ug/kg of TCDD per week either died or were moribund after 4 doses. At this dose and also at smaller doses (0.008, 0.04 and 0.2 ug/kg), guinea pigs showed severe loss of body weight, depleting of lymphoid organs, particularly the thymus and lymphopenia. At sublethal doses the effects were primarily on the thymus. In selected experiments, the treated and control animals were challenged with a subcutaneous dose of tetanus toxoid or an oil suspension of killed mycobacterium tuberculosis. One and two weeks after a second challenge

dose, the TCDD animals had significantly lower tetanus antitoxin titers. Similarly, TCDD animals displayed deceased skin thickness reactions when tested for delayed type hypersensitivity to intradermal tuberculin injections. Female albino rats treated orally with TCDD once a week for 6 weeks displayed reduced body and thumus weights (The relative thymus weight of TCDD treated was about half of the controls). On the basis of these experiments Vos et al (6) concluded that TCDD suppressed the cell-mediated immunity in guinea pigs, mice and rats. The humoral immunity (antibody response) in guinea pigs was also slightly suppressed.

Thigpen et al (9) challenged groups of mice treated orally with TCDD to either Salmonella born or Herpesvirus suis. Treatment of mice with TCDD reduced the time of death after bacterial challenge and also increased the mortality to S.bern. The influence of challenge to similar animals with H. suis influenced neither the period of death nor mortality rate. The conclusion was that treatment with TCDD had a differential effect on bacterial vs. viral challenge. The possibility of alterations in phagocytic cell-junction or in the interaction of T-cells with phagocytic cells was suggested. In similar experiments Dean et al (10) reported

that mice treated pre and post natally with TCDD displayed decreased host resistance and increased susceptibility to bacterial challenge (listeria monocytogenes). Additionally, these mice were more susceptible to tumor formation following challenge with PYBG tumor cells from syngeneic transplantable tumors. Finally, these mice displayed depressed lymphoproliferative responses to PHA which correlated with the decreased host resistance.

Sharma et al (11) reported that rabbits orally exposed to TCDD for 8 weeks and then innoculated with tetanus toxoid displayed depressed thymus and popliteal lymph node weights. Serumantitetanus titers showed a decrease at treatment levels starting from 0.1 ug/kg. Similarly, a significant decrease in the number of plasma cells in popliteal nodes was observed. Skin reactivity to tuberculin was depressed at all TCDD levels. These results were somehwat comparable to those reported in mice by Sharma and Gehring (12) using a similar protocol. It may be concluded that treatment of animals with TCDD produced effects on cell-mediated immune reactions at very low doses, whereas the effect on humoral immunity was observed at high dose levels. The effect on humoral immune responses may be an indirect one, produced by an initial suppression of T cells involved in such mechanisms. Recently, Clark et al (13) reported

on the chronic immunotoxic effects of TCDD in mice. Total doses of 100 ug/kg or greater produced cellular depletion in thymus, spleen and lymph nodes and the animals appeared sick. The antibody response to sheep red blood cells was impaired following 40 ug/kg TCDD, the delayed hypersensitivity response to oxazolone was impaired by 4 ug/kg and the generation of allo-antigen specific cytotoxid T-cells (CTL) was sensitive to as little 0.004 ug/kg TCDD. In vitro analysis of the mechanism of suppression indicated generation of cells capable of suppressing CTL generation in vitro following TCDD.

Several studies have been reported where exposure of animals to TCDD has been shown to decrease the responsiveness of lymphocytes to various mitogens in culture. Exposure of rats to various doses of TCDD, pre and postnatally through maternal treatments decreased the synthesis of DNA by splenic and thymic lymphocytes when cultured in the presence of PHA (14). The decreased responsiveness of thymus cells to mitogens, together with the fact that there was depletion of cells in the thymus, suggest a strong immunosuppressive effect of TCDD.

A similar effect to that described above for rats was observed in mice and rabbits when these animals were challenged

with an appropriate antigen (tetanus toxoid). The effects of a single dose of TCDD in suppressing mitogen responsiveness was most marked in younger animals (10).

The influence of direct addition of TCDD to mouse splenic cultures was reported by Sharma and Gehring (12). TCDD decreased the unstimulated DNA synthesis in lymphocytes at concentrations as low as 10^{-9} M. The relative effect of mitogens such as PHA and PWM was also reduced. Luster and co-workers exposed spleen cells to TCDD and reported DNA, RNA and protein synthesis in spleens were inhibited.

In man several episodes of accidental or purposeful exposure to TCDD have occurred including 1) Sevese, Italy, 1976 where a transient decrease in lymphocytes was reported (15); 2) Monsanto incident, 1949 (Bekesi, personal communications) reporting alterations in mature T cells and 3) the United Kingdom incident at Coalite (reported out in a Transcript from EPA Cancellation Hearings on 2,4,5-T and Silvex (November 14, 1980) wherein the highly exposed group was observed to display depressed PHA response and IgM and IgD immunoglobulin levels.

This brief review (as cited above) indicates that TCDD is a potent immunosuppressive. What is most distressing

and of greatest concern is the data reflecting decreased immunocompetence following TCDD exposure leading to increased susceptibility to infection and/or possible tumor challenge in experimental animals. It indicates a fundamental inbalance in immunoregulation.

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Sharma, R.P., Kociba, R.J. and Gehring, P.J.: Immunotoxicological effects of TCDD in mice and rabbits. J. Environ Pathol. Toxicol. (In Press).

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Reggiani, G.: Medical problems raised by TCDD contamination in Seveso, Italy. Arch. Toxicol. 40: 161, 1978.

CURRICULUM VITAE

Ronald H. Kerman, Ph.D.

DATE OF BIRTH: June 10, 1943

PLACE OF BIRTH: Chicago, Illinois

NATIONALITY: U.S. Citizen

SEX: Male

EDUCATION:

1965	University of Illinois, B.S. (with Honors)
1967	University of Illinois, M.S.
1969	University of Illinois, Ph.D. in Immunology

HONORS:

1965	Bachelor of Science with General Honors in the College
1967-1969	Recipient of Public Health Service Predoctoral Traineeship
1967	Phi Sigma National Biological Honorary
1969-1971	Recipient of Public Health Service Postdoctoral Traineeship
1970	Society of Sigma Xi

RESEARCH AND PROFESSIONAL EXPERIENCE:

1983-	Associate Professor Department of Pathology, and Chief, Cellular Immunology, Clinical Immunology Laboratories, The University of Texas Medical School at Houston
1981-	Associate Professor Department of Surgery, and Head, Histocompatibility and Immune Evaluation Laboratories, Division of Organ Transplantation, The University of Texas Medical School at Houston
1977-	Member, Program in Immunology, Graduate School of Biomedical Sciences, The University of Texas Health Science Center at Houston
1977-1980	Assistant Professor Department of Surgery, and Head, Histocompatibility and Immune Evaluation Laboratories, Division of Organ Transplantation, The University of Texas Medical School at Houston
1974-1977	Assistant Professor Department of Surgery, Loyola University Stritch School of Medicine, Maywood, Illinois
1973-1977	Research Immunologist Chief, Immunobiology Research Laboratory, Research Service, V. A. Hospital, Hines, Illinois
1972-1973	Assistant Professor Department of Microbiology, Jefferson Medical College
1969-1971	Postdoctoral Fellow, (Immunology) Children's Hospital of Philadelphia and The University of Pennsylvania School of Medicine

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PROFESSIONAL SOCIETIES:

The Transplantation Society (Editorial Board, Transplantation and Member, Symposium Committee)
American Association of Immunologists
American Association for Cancer Research
New York Academy of Sciences
American Society of Transplant Physicians (Member, and Vice Chairman, Scientific Studies Committee)
Society for Experimental Biology and Medicine
International Society for Heart Transplantation
American Association for the Advancement of Science
American Society for Histocompatibility and Immunogenetics (Chairman, Finance and Audit Committee, and Member, Laboratory Accreditation Committee)

RESEARCH INTERESTS:

Immunologic response to allotransplantation and malignancy
Evaluation of immunocompetency

RESEARCH SUPPORT:

1974-1978	Co-principal Investigator: Bronchogenic Carcinoma: Immunologic Profile, Radio and Immunotherapy - V.A. Medical Research Grant No. MRIS-8121-08. $213,000
1976-1979	Co-principal Investigator: Immunotherapy Adjuvant to Radiotherapy of Head and Neck Cancer - V.A. Medical Research Grant No. MRIS-8121-06. $78,814
1976-1980	Co-principal Investigator: Factors Influencing Immunocompetence in Human Transplantation - V.A. Medical Research Grant No. MRIS-3068. $68,770
1977-1978	Principal Investigator: Functional and Surface Receptor Differences of Human T-lymphocyte Subpopulations - General Research Support Funds, The University of Texas Medical School at Houston. $5,000
1977-	Principal Investigator: The Role of HLA Typing in Renal Transplantation, ESRD Program, No. 450068. $377,400 (last year)
1977-	Principal Investigator: Immune Monitoring for the Diagnosis of Renal Allograft Rejection, ESRD Program, No. 450068. $544,800 (last year)
1983-1984	Principal Investigator: Immune Evaluation of Veterans Exposed to Agent Orange. Texas Veterans Agent Orange Assistance Program, IAC(83-84)1266. $93,352

OTHER ACTIVITIES:

Special Consultant in Immunology to the Epidemiology and Disease Control Study Section, NIH
Consultant in Immunology and Histocompatibility Testing to the Department of Laboratory Medicine, M.D. Anderson Hospital and Tumor Institute
Consulting Immunologist to the UpJohn and Sandoz Pharmaceutical Companies
Editorial Board, Transplantation
Review of manuscripts for the journal Human Immunology
Review of manuscripts for the journal Transplantation
Review of manuscripts for the journal Heart Transplantation
Book reviewer for Journal of American Medical Association
Literature Reviewer for The American Association of Clinical Histocompatibility Testing -- AACHTion News

Grant Reviewer for the Kidney Foundation of Canada
Grant Reviewer in Transplantation Immunology for The March of Dimes - Birth Defects Foundation
Outside Reviewer of Research Proposals in Immunology for the Research and Development Committee, The Veterans Administration Research Service
Invited Participant (as a testing laboratory) in The Third American HLA Workshop
Invited Participant (as a testing laboratory) in The Eighth International Histocompatibility Workshop "Relevance of DR typing to renal allograft survival"
Invited Participant (as a testing laboratory) in The International Transfusion and Transplantation Workshop
Invited Participant (as a testing laboratory) for the Ninth International Histocompatibility Workshop
Invited Presenter at an NIH Workshop, "The Biological Relevance of Immune Suppression as Induced by Genetic, Therapeutic and Environmental Factors"
Invited Participant (as a testing laboratory) in the International Collaborative Transplant Study
Laboratory Inspector for Clinical Laboratory Accreditation in Histocompatibility for The American Society for Histocompatibility and Immunogenetics and The College of American Pathologists
Chairman, Finance and Audit Committee for The American Society for Histocompatibility and Immunogenetics
Member, Symposium and Affiliations Committee, The Transplantation Society
Member and Vice-Chairman, Scientific Studies Committee, American Society of Transplant Physicians
Member, Acquired Immune Deficiency Syndrome (AIDS) Working Group for the Houston Area
Chairman, Organizing Committee and Host for The Fourth International Immune Monitoring Symposium: Immunological Evaluation and Monitoring of the Transplant Recipient (1983)
Member, Organizing Committee for the International Symposium on Relevant Immunological Factors in Clinical Kidney Transplantation, Heidelberg, West Germany, 1985

Member, UTMSH Admissions Interview Committee
Member, UTMSH Admissions Committee
Member, Medical Review Board, Organ Transplantation Center, UTMSH
Member, Committee on Subject Selection for The University of Texas System Agent Orange Study
Member, Steering Committee, Program in Immunology, UT-GSBS
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54. Flechner, S., Kerman, R., Van Buren, C.T., Payne, W., and Kahan, B.D.: The use of cyclosporine and prednisone for high MLC haploidentical living related renal transplants. Transpl. Proc. 15:442-445, 1983.

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73. Kerman, R.H., Manner, C., Ford, K., and Hoots, K.: Comprehensive immune evaluation of 78 hemophiliacs. Ann. N. Y. Acad. Sc. 1984 (In press).

Abstracts and Presentations

1. Kerman, R., Clark, J. and Wheelock, E.F.: Mononuclear infiltrate into an air pouch: A new in vitro cell mediated immune assay. Fed. Proc. 32:973, Atlantic City, New Jersey, April 1973.

2. Wheelock, E.F., Kerman, R.H., Clark, J. and Toy, S.: Cell mediated immunity in dormant friend virus infections. Proc. Am. Assoc. Cancer Res. 14:68, Atlantic City, New Jersey, April 1973.

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12. Kerman, R. and Stefani, S.: Radio and immunotherapy of lung cancer: A preliminary report. Presented at the 1977 Chicago Symposium: Immunotherapy of Solid Tumors, Chicago Illinois, February 24-25, 1977.

13. Stefani, S. and Kerman, R.H.: Relevance of immunologic analysis for patients with inoperable lung cancer treated by radiotherapy. Presented at an NCI sponsored Symposium "The Second Conference on Lung Cancer Treatment," at Airlie House, Virginia, May 22-24, 1977.

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19. Kerman, R.H., Floyd, M., Conner, W., McConnell, B.J., McConnell, R. and Kahan, B.D.: Correlation of active T-RFC and spontaneous blastogenesis with decreased renal allograft function. Abstracts of the American Association for Clinical Histocompatibility Testing, Boston, Massachusetts, June 1978.

20. Kerman, R.H., Roesler, H. and Kahan, B.D.: Increased active T-RFC with in vitro stimulation by soluble donor antigen. Abstracts of the Amer. Assoc. of Clin. Histocomp. Testing, Boston, Massachusetts, June 1978.

21. Kerman, R.H., Floyd, M., Conner, W., McConnell, R., McConnell, B.J., Van Buren, C.T. and Kahan, B.D.: Combined immunological and radionuclide techniques to monitor renal allograft rejection. Presented at the VII International Congress of The Transplantation Society, Rome, Italy, September 1978.

22. Kerman, R.H.: Invited speaker to a special workshop "Immunological Monitoring of the Transplant Patients", VII International Congress of The Transplantation Society, Rome, Italy, September 1978.

23. Kahan, B.D., Kerman, R. and McConnell, R.: Combination of immunological and radionuclide techniques diagnoses allograft rejection. Presented at the American College of Surgeons, San Francisco, California, October 1978.

24. Michelson, J., McConell, Kerman, R. and Kahan, B.: Association of acute rejection episodes in renal transplant patients with scored results of computer analyzed data. Presented at the Southwest Society of Nuclear Medicine Meeting, March 16, 1979, San Antonio, Texas.

25. Kerman, R.H., Macek, C. and Kahan, B.D.: Increase in 3 different E-rosette markers on human T cells following PHA activation. Fed. Proc. 38 (No. 3, Part II):1282. Presented at the Annual Meeting of The American Association of Immunologists, Dallas, Texas, April 1979.

26. Kerman, R.H.: Immunological considerations in renal transplantation. Clinical Oncology Grand Rounds, M.D. Anderson Hospital and Tumor Institute, September 1979.

27. Kerman, R.H. and Kahan, B.D.: Assessment of immune parameters of transplant recipients on immunosuppressive therapy. Presented at an NIH Workshop on "The Biological Relevance of Immune Suppression as Induced by Genetic Therapy and Environmental Factors," Williamsburg, Virginia, November 1979.

28. Invited participant in a working cadre for the NIH to develop a "Consensus On Immunotoxicology" for the National Toxicology Program, November 1979, Research Triangle Park, N.C., NIEHS, NIH.

29. Kerman, R.H.: Histocompatibility testing in transplantation. Pathology Grand Rounds, St. Luke's Hospital, January 1980.

30. Van Buren, C.T., Kerman, R.H. Van Buren, D. and Kahan, B.D.: Correlation of immune responsiveness with nutritional indices in chronic renal failure patients. Presented at the American Society for Parenteral and Enteral Nutrition, Annual Meeting, Chicago, Illinois, January - February 1980.

31. Kerman, R.H.: Immune monitoring of renal allograft recipients. Surgical Grand Rounds, University of Miami School of Medicine, March 1980.

32. Kerman, R.H.: Pre- and postoperative immune monitoring of allograft recipients. Medical Grand Rounds, Division of Dialysis and Transplantation, Children's Hospital of Los Angeles, April 1980.

33. Kerman, R.H. and Semchuk, R.: Delineation of a radioresistant T cell subpopulation. Fed. Proc. 39(3):945. Presented at the Annual Meeting of The American Association of Immunologists, Anaheim, California, April 1980.

34. Kerman, R.H.: Effect of heat on the ability of human T cells to express the active T and total T receptors. Fed. Proc. 39(3):1137. Presented at the Annual Meeting of The American Association of Immunologists, April 1980, Anaheim, California.

35. Kerman, R., Peddada, L. and Kahan, B.D.: Correlation of hyperacute rejection with LDA and CDA vs. ^{51}Cr-labeled donor T and B cell targets. Presented at The American Association for Clinical Histocompatibility Testing, St. Louis, Missouri, April 1980.

36. Kerman, R., Floyd, M., Van Buren, C.T. and Kahan, B.D.: Improved allograft survival of strong responder-high risk cadaver recipients with adjuvant immunosuppressive therapy. Presented at the Annual Meeting of The American Association for Clinical Histocompatibility Testing, April 1980.

37. Kerman, R., Conklin, R., Cahall, D. and Kahan, B.D.: Association of cytomegalovirus and renal allograft survival. Presented at the meeting of the American Association for Clinical Histocompatibility Testing, St. Louis, Missouri, April 1980.

38. Kerman, R., Floyd, M., Van Buren, C.T. and Kahan, B.D.: Delineation of donor specific and nonspecific pretransplant immunocompetence as a predictor for LRD allograft survival. Presented at the Meeting of The American Association of Clinical Histocompatibility Testing, St. Louis, Missouri, April 1980.

39. Kerman, R.H., Floyd, M., Van Buren, C.T. and Kahan, B.D.: Improved allograft survival of strong immune responder-high risk recipients with adjuvant immunosuppressive therapy. Presented at the annual meeting of The American Society of Transplant Surgeons, Chicago, Illinois, May 1980.

40. Kerman, R.H., Floyd, M., Van Buren, C.T. and Kahan, B.D.: Correlation of nonspecific immune monitoring of renal allograft recipients with rejection and impaired renal function. Presented at the Annual Meeting of The American Society of Transplant Surgeons, Chicago, Illinois, May 1980.

41. Kerman, R., Floyd, M., Van Buren, C.T. and Kahan, B.D.: Prolonged allograft survival of strong pretransplant immune responders treated with ATG. Presented at the VIIIth International Congress of The Transplantation Society, Boston, Massachusetts, June 1980.

42. Kerman, R., Floyd, M., Van Buren, C.T. and Kahan, B.D.: Prediction of renal allograft survival based on pretransplant non-specific immunocompetence. Presented at The Second International Symposium on Immunological Monitoring of the Transplant Recipient, Leiden, The Netherlands, September 1980.

43. Kerman, R.H., Floyd, M., Van Buren, C.T., McConnell, B.J., McConnell, R. and Kahan, B.D.: Delineation of renal allograft rejection and impaired renal function by serial measurement of non-specific immune parameters. Presented at The Second International Symposium on Immunological Monitoring of the Transplant Recipient, Leiden, The Netherlands, September 1980.

44. Kerman, R.H. and Kahan, B.D.: Increased expression of the active T-RFC receptor as a measure of allosensitization following in vitro stimulation of recipient lymphocytes by soluble donor HLA antigens. Presented at The Second International Symposium on Immunological Monitoring of the Transplant Recipient, Leiden, The Netherlands, September 1980.

45. Kerman, R.H., Floyd, M., Van Buren, C.T. and Kahan, B.D.: Correlation of HLA A,B and DR typing to cadaveric and living related renal allograft survival. Presented at The Second International Symposium on Immunological Monitoring of the Transplant Recipient, Leiden, The Netherlands, September 1980.

46. Floyd, M., Kerman, R., Woo, J., Van Buren, C.T. and Kahan, B.D.: Relationships of beta-2-microglobulin metabolism, immune reactivity and renal allograft rejection. Presented at The Second International Symposium on Immunological Monitoring of the Transplant Recipient, Leiden, The Netherlands, September 1980.

47. Kerman, R.H.: Immune monitoring of renal allograft recipients. Surgical Grand Rounds, University of Chicago, June 1981.

48. Kerman, R.H., Van Buren, C.T., LeGrue, S.J. and Kahan, B.D.: Immunopharmacological monitoring of cadaveric renal allograft recipients receiving Cyclosporin A. Presented at the Annual Meeting of the American Society of Transplant Surgeons, Chicago, Illinois, June 1981.

49. Kerman, R.H., Conklin, R., Cahall, D., Van Buren, C.T. and Kahan, B.D.: CMV and renal allograft rejection. Presented at a Symposium on Host Defenses to Intracellular Pathogens, Franklin Plaza Hotel, Philadelphia, Pennsylvania, June 1981.

50. Schoenberg, L.P., Kahan, B.D. and Kerman, R.H.: The use of Cyclosporin A as immunosuppressive medication in renal transplantation. Presented at The National Kidney Foundation, Inc., Washington, D.C., November 1981. Amer. J. Kidney Diseases, Program for Clinical Dialysis and Transplantation Forum, p. 29.

51. Ettenger, R., Kerman, R., Arnett, J., Jordan, S., Warshaw, B., Harris, R., Wassner, S. and Fine, R.: Sensitization following donor-specific transfusions for live-related renal transplantation. American Society of Nephrology, Washington, D.C., November 1981.

52. Flechner, S., Boileau, M., Payne, W., Van Buren, C., Kerman, R. and Kahan, B.: The use of Cyclosporin A in strong immune responder, high risk renal transplant recipients. American Urological Association, Kansas City, Kansas, 1982.

53. Kerman, R., Van Buren, C., Payne, W., Flechner, S., Agostino, G., Conley, S., Brewer, E. and Kahan, B.: Influence of blood transfusions on immune responsiveness. Presented at The Transfusion and Transplantation Conference, Los Angeles, California, January - February 1982.

54. Agostino, G., Kahan, B.D. and Kerman, R.H.: Suppression of mixed leucocyte culture using mononuclear leukocytes from normals, uremics and allograft recipients. Presented at the Annual Meeting of The American Association of Immunologists, FASEB, New Orleans, Louisiana, April 1982.

55. Agostino, G.J., Kahan, B.D. and Kerman, R.H.: Measurement of suppressor cell status in potential allograft recipients. Presented at the Annual Meeting of The American Association of Clinical Histocompatibility Testing, San Francisco, California, April 1982.

56. Kerman, R.H.: Invited presenter at two workshops on 1) Immune monitoring of allograft recipients and 2) The effect of transfused blood and blood products on uremic hosts. Presented at the Annual Meeting of The North American Transplant Coordinators Organization, San Antonio, Texas, May 1982.

57. Kerman, R.H., Van Buren, C., Flechner, S., Agostino, G., Conley, S., Brewer, E. and Kahan, B.D.: The influence of pretransplant blood transfusions from random donors on immune parameters affecting cadaveric allograft survival. Presented at The Annual Meeting of The American Society of Transplant Surgeons, Chicago, Illinois, June 1982.

58. Agostino, G., Kahan, B.D. and Kerman, R.H.: Suppression of mixed leucocyte culture using leucocytes from normal individuals, uremic individuals, and allograft recipients. Presented at The Annual Meeting of The American Society of Transplant Surgeons, Chicago, Illinois, June 1982.

59. Kerman, R.H.: Invited presenter at a workshop on "Human T lymphocyte subpopulations: Their role in rejection and immunosuppression." Presented at the International Congress of The Transplantation Society, Brighton, England, August 1982.

60. Kerman, R.H.: Invited presenter at a workshop on "Mechanisms responsible for blood transfusion effects." Presented at The International Congress of The Transplantation Society, Brighton, England, August 1982.

61. Ettenger, R.B., Kerman, R., Jordan, S.C., Warshaw, B.L., Harris, R. and Fine, R.: Sensitization after donor-specific transfusions for live-related renal transplantation. Presented at The International Congress of The Transplantation Society, Brighton, England, August 1982.

62. Van Buren, C.T., Kerman, R.H., Agostino, G., Flechner, S. Payne, W. and Kahan, B.D.: Effect of cyclosporine on immunoregulatory cells of renal allograft recipients. Presented at The International Congress of The Transplantation Society, Brighton, England, August 1982.

63. Kerman, R.H., Van Buren, C.T., Payne, W., Flechner, S. and Kahan, B.D.: Monitoring T cell subsets and immune events in renal allograft recipients. Presented at The International Congress of The Transplantation Society, Brighton, England, August 1982.

64. Flechner, S., Kerman, R., Van Buren, C.T., Payne, W. and Kahan, B.D.: The use of cyclosporine and prednisone for high MLC haploidentical living related renal transplants. Presented at The International Congress of The Transplantation Society, Brighton, England, August 1982.

65. Agostino, G., Kahan, B.D. and Kerman, R.: Detection of nonspecific suppressor cells from normal individuals, uremic patients and allograft recipients. Presented at The International Congress of The Transplantation Society, Brighton, England, August 1982.

66. Kerman, R.H., Agostino, G., Van Buren, C.T., Payne, W., Flechner, S., Conley, S., Brewer, E. and Kahan, B.D.: Effect of blood transfusions on graft survival and immune responsiveness. Presented at The International Congress of The Transplantation Society, Brighton, England, August 1982.

67. Kahan, B.D., Kerman, R., Payne, W.D., Flechner, S. and Van Buren, C.T.: Immunopharmacologic studies of cyclosporine-treated renal allograft recipients. Fifth Tripartite Meeting, Society of University Surgeons, Salzburg, Austria, September 1982.

68. Kerman, R.H., Flechner, S., Van Buren, C.T., Payne, W., and Kahan, B.D.: Cyclosporine improves allograft survival in immunologically high-risk renal allograft recipients. Presented at the Third International Immunological Monitoring Symposium, Key Biscayne, Florida, November 1982.

69. Kerman, R.H., Van Buren, C.T., Payne, W., Flechner, S., and Kahan, B.D.: Detection of host presensitization to donor alloantigens utilizing a comprehensive immune crossmatch. Presented at the Third International Immunological Monitoring Symposium, Key Biscayne, Florida, November 1982.

70. Kerman, R.H., Payne, W., Van Buren, C.T., Flechner, S., and Kahan, B.D.: Immune monitoring of renal allograft recipients treated with cyclosporine or azathioprine using donor-specific and nonspecific assays as well as monoclonal T cell reagents. Presented at the Third International Immunological Monitoring Symposium, Key Biscayne, Florida, November 1982.

71. Kerman, R.H.: Invited plenary speaker at the First Annual Meeting of The American Society of Transplant Physicians, "Optimizing immunosuppression: Mode of action of cyclosporine." Chicago, December 1982.

72. Kerman, R.H., Van Buren, C.T., Payne, W., Flechner, S., and Kahan, B.D.: Cyclosporine improves allograft survival in immunologically high-risk renal allograft recipients. Presented at The Annual Meeting, National Kidney Foundation, Clinical Dialysis and Transplant Forum, Chicago, December 1982.

73. Kerman, R.H.: Role of immune evaluation in clinical medicine. Clinical Immunology Grand Rounds, The Children's Memorial Hospital, Chicago, Illinois, December 1982.

74. Kerman, R.H.: Immunologic effects of toxic materials. Presented at Toxicology - Clinical Update, University of Texas Medical Branch, Galveston, Texas, January 1983.

75. Kerman, R.H.: Cyclosporine improves allograft survival in immunologically high risk renal allograft recipients. Presented at Pathology Grand Rounds, University of Pittsburgh School of Medicine, February 1983.

76. Kerman, R.H.: Immune evaluation of renal failure patients and allograft recipients. Presented at Surgical Grand Rounds, St. Louis University Medical Center, St. Louis, Missouri, March 1983.

77. Kerman, R.H.: Immunological evaluation of hemophiliacs. Presented at a Symposium on Current Problems in the Management of Hemophiliac Complications, Houston, Texas, April 1983.

78. Flechner, S., Kerman, R.H., Van Buren, C.T., Payne, W., and Kahan, B.D.: Successful transplantation of high mixed lymphocyte culture haplo-identical living related donors using cyclosporine and prednisone. Presented at the Annual American Urological Association, Las Vegas, Nevada, April 1983.

79. Kerman, R.H., Flechner, S., Van Buren, C.T., Payne, W., and Kahan, B.D.: Immunological monitoring of renal allograft recipients treated with cyclosporine. Presented at The First International Congress on Cyclosporine, Houston, Texas, May 1983.

80. Van Buren, C., Kerman, R., Agostino, G., Flechner, S., Payne, W.D., and Kahan, B.: Effect of cyclosporine on immunoregulatory cells of renal allograft recipients. Presented at The First International Congress on Cyclosporine, Houston, Texas, May 1983.

81. Kahan, B.D., Van Buren, C., Flechner, S., Payne, W.D., and Kerman, R.: Improved outcome of 150 renal allografts in immunologically high risk recipients treated with cyclosporine. Presented at The First International Congress on Cyclosporine, Houston, Texas, May 1983.

82. Flechner, S.M., Van Buren, C., Kerman, R.H., and Kahan, B.D.: The nephrotoxicity of cyclosporine in renal transplantation. Presented at The First International Congress on Cyclosporine, Houston, Texas, May 1983.

83. Flechner, S.M., Van Buren, C.T., Kerman, R., and Kahan, B.D.: The effect of conversion from cyclosporine to azathioprine immunosuppression for intractable nephrotoxicity. Presented at The First International Congress on Cyclosporine, Houston, Texas, May 1983.

84. Kerman, R.H., Flechner, S., Van Buren, C.T., Payne, W., and Kahan, B.D.: Cyclosporine immunosuppression overcomes immunologic risk factors for recipients of cadaveric renal allografts. Presented at the Annual Meeting of The American Society of Transplant Physicians, Chicago, Illinois, June 1983.

85. Flechner, S.M., Kerman, R.H., Van Buren, C.T., and Kahan, B.D.: The high risk haploidentical living related recipient: Transplantation without blood transfusions and steroid withdrawal using cyclosporine. Presented at the Annual Meeting of The American Society of Transplant Physicians, Chicago, Illinois, June 1983.

86. Kerman, R.H.: Relationship of immunocompetence of hemophiliac patients and acquired immune deficiency syndrome (AIDS). Presented at the Gulf Coast Hemophilia Chapter Meeting, Houston, Texas, October 1983.

87. Kerman, R., Van Buren, C.T., Flechner, S., and Kahan, B.D.: Correlation of visual, ^{51}Cr-release and flow cytometry crossmatch results to graft survival. Presented at The Fourth International Symposium: Immune Monitoring of The Transplant Recipient, Houston, Texas, November 1983.

88. Rogers, A.J., Kerman, R.H., and Kahan, B.D.: The pharmacokinetic and immunobiological activity of cyclosporine in man. Presented at The Fourth International Symposium: Immune Monitoring of The Transplant Recipient, Houston, Texas, November 1983.

89. Kerman, R.H., Manner, C., Ford, K., and Hoots, K.: Comprehensive immune evaluation of 78 hemophiliacs. Presented at the New York Academy of Sciences Symposium on Acquired Immune Deficiency Syndrome, New York, New York, November 1983.

90. Kerman, R., Van Buren, C.T., Flechner, S.M., and Kahan, B.D.: DRW6 and DR3 phenotypes correlating with immune response. Presented at the Annual Meeting of The American Association for Clinical Histocompatibility Testing, Chicago, Illinois, November 1983.

91. Van Buren, C.T., Flechner, S.M., Kerman, R.H., Vaughn, W., and Kahan, B.D.: Cyclosporine improves outcome in high risk cadaveric renal allograft recipients. Presented at the First Meeting of The European Society for Organ Transplantation, Zurich, Switzerland, November 1983.

92. Kerman, R.H.: Cyclosporine immunosuppression for renal transplantation. Presented to Sandoz Pharmaceuticals, Inc., East Hanover, New Jersey, December 1983.

93. Kerman, R.H.: New horizons in transplantation: Influence of cyclosporine on renal transplantation. Invited presenter at the Western Dialysis and Transplantation Society, Park City, Utah, January 1984.

94. Sterling, R.P., Bradley, B.B., Khalil, K.G., Kerman, R.H., and Conklin, R.H.: Comparison of biopsy proven pneumocystis pneumonia in acquired immune deficiency syndrome (AIDS) patients versus renal allograft patients. Presented at The Society for Thoracic Surgeons, San Antonio, Texas, January 1984.

95. Rogers, A.J., Kerman, R.H., and Kahan, B.D.: Correlation of immunopharmacokinetic profiles of cyclosporine-treated allograft recipients and rejection. Presented at The Society for University Surgeons - Residents' Meeting, Chicago, Illinois, February 1984.

MARVIN S. LEGATOR, Ph.D.

I. QUALIFICATIONS

Dr. Legator is Professor of Environmental Toxicology, University of Texas Medical School at Galveston. His Curriculum Vitae is attached. Dr. Legator has been associated with many committes investigating various toxins, including TCDD, and most especially the recent EPA committee involved with dioxin exposure.

II. SUBJECT MATTER

The subject matter of Dr. Legator's testimony will include: the teratogenic and carcinogenic effects of TCDD, as well as its mutagenic potential; the multi-system effects of TCDD at extremely low concentrations; the demonstrable effects, both gross and more subtle, of TCDD on animals; the extrapolation of the animal studies to humans, that is, the inherent, intended predictive aspects of the animal data to man. Dr. Legator will testify that the animal data are positive and consistent and provide a mechanistic linkage which confirms the Vietnamese epidemiological study of Hatch and others. Further he will testify to his work as a geneticist with respect to reproductive toxicology, i.e. male (Vietnam Veterans) - mediated birth defects and certain untoward pregnancy outcomes. Further,

insofar as the reproductive toxicological effects, i.e. birth defects and miscarriages, of Agent Orange and/or TCDD, et al. Dr. Legator will testify that such can occur through one or more of the following biological mechanisms: (1) decreased quality of sperm resulting from gonadal lesion during spermatogenesis, altered hormonal regulation, or transmittable defects in heritable characteristics of sperm; (2) potentiation of xenobiotic metabolism in gonadal tissue; (3) secretion of chemicals in Agent Orange or their metabolites into seminal fluid and subsequent transfer to the womb. These mechanisms can result from either the long-term effects of past exposure to Agent Orange or from the continuing presence of biologically active concentration of Agent Orange and metabolites of its constituent chemicals within the bodies of exposed persons.

III. SCIENTIFIC PRINCIPLES

See General Statement of Scientific Principles and Assumed Facts attached.

Dr. Legator will describe the extraordinary precautions which are taken, and the fears of the researchers, in connection with the laboratory use of TCDD.

IV. SUBSTANCE OF OPINIONS

A. That dioxins are extremely toxic, particularly 2,3,7,8-TCDD.
B. That TCDD is exceptionally toxic at extremely low levels;
C. That TCDD is a complete carcinogen;
D. That, as a carcinogen, there is no safe level of exposure.

E. That there is therefore no "no-effect" level of TCDD:
F. That TCDD is the most toxic substance ever synthesized by man;
G. That TCDD is acnegenic;
H. That TCDD is immunosuppressive;
I. That TCDD is teratogenic;
J. That TCDD is fetotoxic;
K. That TCDD is gonadotoxic;
L. That TCDD is capable of transmitting genetic damage;
M. That the miscarriage of Mrs. Dan G. Jordan and the congenital malformations of the children of Mr. and Mrs. Dan G. Jordan, as well as those congenital malformations and birth defects of Kerry Ryan, daughter of Mr. and Mrs. Michael F. Ryan, are consistent with the presumed exposure of representative plaintiffs Jordan and Ryan to phenoxy herbicides and dioxins - specifically 2,3,7,8-TCCD -- while serving in Vietnam.

V. GROUNDS FOR OPINIONS

A. General

The bases or grounds for such facts and opinions include Dr. Legator's: educational and professional experience; personal research; review of the applicable medical and scientific literature; and a review of the medical record and/or data of the Jordan and Ryan familes.

B. Specific

The additional grounds for Dr. Legator's opinions can be found in:

1. Dioxins are extremely toxic:
   the EPA Criteria Documents, Publications and associated references.
2. TCDD toxic at low levels:
   the EPA Criteria Documents, Publications and associated references.
3. TCDD complete carcinogen:
   National Cancer Institute 1980a. Bioassay of 2,3,7,8 - tetrachloro-dibenzo-p-dioxin for possible carcinogenicity (dermal study) U. S. Department of Health and Human Services Pub. No. 80-1757.

National Cancer Institute 1980B. Bioassay of 2,3,7,8-tetrachloro-dibenzo-p-dioxin for possible carcinogenicity (gavage study) U. S. Department of Health and Human Services Pub. No. 80-1765.

4. No safe level:
IARC: Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans.
5. No "no effect" level:
IARC: Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans.
6. TCDD most toxic substance:
EPA (cited above)
IARC (cited above)
7. TCDD - acnegenic:
Kearney, D.C., et al. 1973 Environmental Significance of chlorodioxins. Adv. Chem. Ser. 120:105
8. TCDD - immunosuppressive:
- Harris, M.W., J.A. Moore, J.G. Vos and B. N. Gupta. 1973. General biological effects of TCDD in laborator animals. Environ. Health Perspect. 5: 101.
- Kearney, D.C. et al. 1973. Environmental significance of chlorodioxins. Adv. Chem. Ser. 120: 105.
9. TCDD - teratogenic:
- Courney, K.D., D. W. Gaylor, M.D. Hogan and H. L. Falk. 1979. Teratogenic evaluation of 2,4,5-T. Science 1968: 864.
- Kociba, R. J., P. A. Kesler, C. N. Park and P. J. Gehring. 1976. 2,3,7,8-Tetrachlorodibenzo-p-dioxin results of a 13-week oral toxicity study in rats. Toxicol. Appl. Pharmacol. 35: 553.
- Kociba, R. J., D. G. Keyes, J. E. Beyer, R. M. Carreon, C. E. Wade, D. A. Dittenberg, R. P. Kalnins, L. E. Frauson, C. N. Park, S. D. Barnard, R. A. Hummel and C. G. Humiston. 1978. Results of a two-year chronic toxicity and oncogenicity study of 2,3,7,8-tetrachlorodibenzo-p-dioxin in rats. Toxicol. Appl. Pharmacol. 46: 279.
- Kociba, R. J., D. G. Keyes, J. E. Beyer, R. M. Carreon and P. J. Gehring. 1979. Long term toxicologic studies of 2,3,7,8-tetrachlorodibenzo-p-dioxin in laboratory animals. Ann. N.Y. Acad. Sci. 320: 397-404.
10. TCDD - fetotoxic:
- McConnell, E.E., J. A. Moore and D. W. Dalgard. 1978a. Toxicity of TCDD in Rhesus monkeys (Macaca mulatta) following a single oral dose. Toxic. Appl. Pharmacol. 43: 175.

11. TCDD - gonadotoxic:
- Neubert, D., P. Zens, A. Rothenwallner and H. J. Merker. 1973. A survey of the embryotoxic effects of TCDD in mammalian species. Environ. Health Perspect. 5: 67.

12. TCDD can cause genetic damages:
- Murray, F. J., F. A. Smith, K. D. Nitschke, C. G. Humiston, R. J. Kocibe and B. A. Schwetz. 1979. Three-generation reproduction study of rats given 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in the diet. Toxicol. Appl. Pharmacol. 50: 241.
- Seiler, J. P. 1977. Inhibition of testicular DNA synthesis by chemical mutagens and carcinogens. Preliminary results in the validation of a novel short-term test. Mutat. Res. 46: 335.
- Green, S. et al. 1977. Cytogenetic effect of 2,3,7,8-tetrachlorodibenzo-p-dioxin on rat bone marrow cells. U. S. Food and Drug Admin., Washington, D.C. FDA By-Lines 7: 292.

Allen JR, Carstons LA. Light and electron microscopic observations in Macaca mulatta monkeys fed toxic fat. Am J Vet Res 28:1513-1526, 1967.

- Constable J, Hatch M. Herbicide exposure and reproductive outcome. In: Herbicides in War: The Long-term Effects of Man and Nature, AW Westing, ed. New York: Taylor & Francis, 1984 (in press).

- Khera KS, Ruddick JA. Polychlorodibenzo-p-dioxins: Perinatal effects and the dominant lethal test in Wistar rats. In: Chlorodioxins - Origin and Fate, EH Blaire, ed. Washington DC: American Chemical Society, 1973, pp 70-84.

- Kociba RJ, Keeler PA, Park CN, Gehring PJ. 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD): Results of a 13-week oral toxicity study in rats. Toxicol Appl Pharmacol 35:553-575, 1976.

- McConnell EE, Moore JA, Haseman JK, Harris MW. The comparative toxicity of chlorinated dibenzo-p-dioxins in mice and guinea pigs. Toxicol Appl Pharmacol 44:335-356, 1978.

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- Norback DH, Allen JR. Biological responses of the nonhuman primate, chicken and rat to chlorinated dibenzo-p-dioxin ingestion. Environ Health Perspect 5:233-240, 1973.

- Peterson, R. Hormonal changes and "wasting" observed in moderately-high-dose animal experiments. Presented at the Symposium on Public Health Risks of the Dioxins, The Rockefeller University, October 19-20, 1983. (Proceedings in press, Alan R. Liss Inc.)

- Poland A, Knutson JC. 2,3,7,8-tetrachlorodibenzo-p-dioxin and related aromatic hydrocarbons: Examination of the mechnanism of toxicity. Ann Rev Pharmacol Toxicol 22:517-554, 1982.

- Tofilon PJ, Piper WN. 2,3,7,8-tetrachlorodibenzo-p-dioxin-mediated depression of rat testicular heme synthesis and microsomal cytochrome P-450. Biochem Pharmacol 31:3663-3666, 1982.

In addition, Dr. Legator may rely on some of the following references for his specific opinions:

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Allen, J.R., D.A. Barsotti, J.P. Van Miller, L.J. Abrahamson and J.J. Lauch. 1977. Morphological changes in monkeys consuming a diet containing low levels of TCDD. Food Cosmet. Toxicol. 15: 401.

Berry, D.L. et al. 1976. Transplacental induction of carcinogen hydroxiylating systems with 2,3,7,8-tetrachlorodibenzo-p-dioxin. Toxicol. Appl. Pharmacol. 36: 569.

Berry, D.L. et al. 1978. Studies with chlorinated dibenzo-p-dioxins, polybrominated biphenyls, and polychlorinated biphenyls in a two-stage system of mouse skin tumorigenesis: potent anticarcinogenic effects. Ann. N.Y. Acad. Sci. 320: 405.

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CURRICULUM VITAE

NAME: Marvin Seymour Legator, Ph.D. DATE: November, 1983

PRESENT POSITION AND ADDRESS:

Professor and Director
Division of Environmental Toxicology
Department of Preventive Medicine and Community Health
University of Texas Medical Branch
Galveston, Texas 77550
Office phone: 409/761-1803

BIOGRAPHICAL:

Date of Birth:	June 27, 1926
Place of birth:	Chicago, Illinois
Marital Status:	Married
Children:	Three
Home Address:	70 Colony Park Galveston, Texas 77551
Social Security Number:	348-16-3682

EDUCATION:

1948	Microbiology-Biochemistry	B.A.	University of Illinois Urbana, Illinois
1948	Biochemistry	M.S.	University of Illinois Urbana, Illinois
1951	Microbial Genetics-Biochemistry	Ph.D.	University of Illinois Urbana, Illinois

PROFESSIONAL AND TEACHING EXPERIENCE:

1976-present	Professor and Director	Division of Environmental Toxicology Department of Preventive Medicine and Community Health University of Texas Medical Branch

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		Galveston, Texas
1972-1976	Professor of Genetics	Brown University Providence, Rhode Island
1968-1972	Professor (part-time) General and Medical Genetics	George Washington University Washington, D.C.
1962 - 1972	Chief, Branch Genetic Toxicity Branch	Food and Drug Administration Washington, D.C.
1952-1962	Head, Animal Health Program	Shell Development Company Modesto, California
1951-1952	Senior Microbiologist	Julius Hyman Company Denver, Colorado
1948-1950	Instructor	University of Illinois Urbana, Illinois

COMMITTEE RESPONSIBILITIES:

UTMB Committees:

University Cancer Center Committee (through 1982)

University Appointment, Promotion and Tenure Committee (through 1980)

University Fellows Grants Committee

Department of Preventive Medicine and Community Health Executive Committee

Department of Preventive Medicine and Community Health Steering Committee

Department of Preventive Medicine and Community Health Application, Promotion and Tenure Committee

Outside Committees:

1983	Environmental Protection Agency Science Review Panel for Health Research
1983	Subject Selection Committee of the Texas Veterans Agent Orange Assistance Program
1980	March of Dimes Committee on Reproductive Hazards (Chairman)
1980	Environmental Protection Agency Research Grant Review Panel
1980	Environmental Protection Agency Criteria Document Panel

1980	Environmental Protection Agency Committee Chairman, Gene-Tox Program (HMA)
1980	Science Committee of Food Safety Council
1975	Oversight Committee for Proctor and Gamble to determine adequacies of toxicological procedures
1975	Committee 17, Analysis of Methodology of Mutagenicity Testing
1973	National Academy of Science Committee on Biological Hazards of Low Levels of Radiation
1972	Member of Swedish Government Sponsored Committee on Mutagenicity Testing
1971	Japanese and United States Government Committee on Toxicology
1971	Member of World Health Organization Committee on Use of Hycanthone
1971	Chairman of Government Hearing on Safety of Immunological Preparations
1970	Member Steering Committee on Industry-Academic, Committee on Toxicology
1970	National Institute of Mental Health - Committee on Genetics Effects of Drug Abuse

MEMBERSHIP IN SCIENTIFIC SOCIETIES:

American College of Toxicology
Environmental Mutagen Society
New York Academy of Sciences
Society of Occupational and Environmental Health

HONORS:

Honorary Health Advocate Award - "... awarded in recognition of outstanding contributions in health advocacy and promotion of the public's health to Marvin S. Legator." Health Policy Advisory Center, New York, New York, November 15, 1983.

Food Safety Council 1976-1982 - "With deep appreciation for the tireless effort that Marvin Legator devoted to help the Food Safety Council achieve its goals. This experiment in concensus building has shown that representatives from industry and non-industry with different viewpoints can work together toward a better way for making food safety decisions."

U.S. Environmental Protection Agency Certificate of Award - Presented to Marvin S. Legator in recognition of noteworthy contribution and special achievement for the U.S. Environmental Protection Agency, Cincinnati, Ohio

Visiting Scholar Award at Western Michigan University 1980

Nominated for 1980 Distinguished Faculty Research Award

F.D.A. Award of Merit - Presented to the Genetic Toxicology Branch (M. Legator, Chief), 1971

Key Lecture Award by the American Genetics Association for Outstanding Contributions on the Implementation of Genetics for Human Welfare and Improvement, 1970

U.S. Government Award - Technique Advance in Cell Culture, 1965

ADDITIONAL INFORMATION:

Areas of Teaching and Research Competency:

Mutagenicity
Cytogenetics
Reproductive Studies
Biochemistry
Molecular Biology
Tissue Culture (Post Doctorate Course, University of Wisconsin, Madison, Wisconsin)

Consulting Activities:

Panel Member, Toxicology Panel on Psychochemicals, Commission on Life Sciences, National Research Council, National Academy of Sciences, 1983
Expert Witness, Texas Senate Subcommittee on Consumer Affairs, 1982
Expert Witness, U.S. House Subcommittee on Oversight and Investigations of the Committee on Energy and Commerce, 1982
Consultant, Hooker Chemical Company, 1980
Consultant, JRB Associates, 1980
Consultant, Toxi-Genics (Fabrizio), 1980
Consultant for Environmental Protection Agency, 1976-1980
Consultant for Lady Clairol, 1976-1978
Expert Witness, Committee on Science and Technology, 1975
Dow Chemical Company, 1974-1979
National Institute of Drug Abuse, 1973-1980
Consultant, Senate Committee on Public Works, 1970

Other Activities:

Elected Member, Collegium Ramazzini, 1983
Member of the Board of Directors, Committee for Responsible Genetics, 1983.

Member, Critical Issues Committee on Accreditation, Certification and Standardization, Environmental Mutagen Society, 1983-84.
Co-chairperson, Workshops and Training Committee, Environmental Mutagen Society, 1983-84.
Member of the Board, Texas Center for Rural Studies, Inc. The corporation is organized to provide research and educational services regarding the quality of life in Texas, including, but not limited to, the health, economic and environmental effects of pesticides and other chemicals; public policies effecting the rural economy; and the enhancement of the role of family farmers, farm laborers and rural residents in Texas agriculture, 1983, Austin, Texas.

Co-Director of Workshop, Environmental Influences on Fertility, Pregnancy, and Development: Directions for Future Research, May 24-25, 1982, Cincinnati, Ohio
Director of CME Workshop for Practicing Physicians, Recognizing, Diagnosing, and Treating Chronic Toxic Chemical Effects, July 16-18, 1981, Galveston, Texas
Director of Annual Genetic Toxicology Course, Galveston
Director of Annual Genetic Toxicology Course, Hunt Valley
Co-Director of Annual Toxicology and Law Course, Houston
Director of Annual Workshop on Carcinogenicity, Mutagenicity and Teratogenesis sponsored by the March of Dimes Birth Defects Foundation
Faculty member of short course on Toxicology at Wayne State University, 1976-1979
Coordinator of Workshop on Occupational Monitoring for Genetic Hazards, March 27-29, 1975
Visiting lecturer to Heidleburg University, Germany, 1971

Editorial Responsibilities:

Editor, Journal of Teratogenesis, Carcinogenesis, and Mutagenesis
Editorial Board of Environmental Mutagenesis Journal (through 1981)

BIBLIOGRAPHY:

Journal Articles:

Legator, M.S., and Gottlied, D. 1954. The Biosynthesis of Chloramphenicol 1 Precursors Stimulating the Synthesis. J. Bacteriol. 2.

Legator, M.S., and Racussen, D. 1959. Mechanism of Ally Alcohol Toxicity. J. Bacteriol. 2.

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Wragg, J., Ross, V.C., and Legator, M.S. 1967. Effect of Aflatoxin B1 on Deoxyribonucleic Acid Polymerase of Escherichia Coli. Proceedings of the Society for Experimental Biology and Medicine 125:1052-1055.

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Green, S., Palmer, K.A., and Legator, M.S. 1970. In Vitro Cytogenetic Investigation of Calcium Cyclamate, Cyclohexylamine and Trifluoropromazine. Food and Cosmetics Toxicology 8:617-623.

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Green, S., Sauro, F.M., and Legator, M.S. 1973. Cytogenetic Effects of Hycanthone in the Rat. Mutation Research 17:239-244.

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Committee 17 of the Environmental Mutagen Society. 1975. Environmental Mutagenic Hazards. Science 187:503-514.

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pp. 95-103.

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Weber, E., Bidwell, K., and Legator, M.S. 1975. Evaluation of the Micronuclei Test using Triethyleneamine, Trimethylphoshate, Hycanthone and Niridazole. Mutation Research 28:101-106.

Zimmering, P.H., Legator, M.S., and Weber, E. 1975. Effect of Pyrogen Treatment on Cytogenetic Response with Chemical Mutagens in Mice. Mutation Research 31:339-340.

Green, S., Zeiger, E., Palmer, K.A., Springer, J.A., and Legator, M.S. 1976. Protocols for the Dominant Lethal Test, Host-Mediated Assay and In Vivo Cytogenetic Test Used in the Food and Drug Administration's Review of Substances in the GRAS (Generally Recognized As Safe) List. Journal of Toxicology and Environmental Health 1:921-928.

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Connor, T.H., Stoeckel, M., Evrard, J., and Legator, M.S. 1977. The Contribution of Metrinidazole and Two Metabolites to the Mutagenic Activity Detected in Urine of Treated Humans and Mice. Cancer Research 37:629-633.

Kilian, D.J., Moreland, F.M., Benge, M.C., Legator, M.S., and Whorton, E.B., Jr. 1977. Collaborative Cytogenetics Study to Measure and Minimize Interlaboratory Variation. Mutation Research 44:97-104.

Connor, T., and Legator, M.S. 1978. Method for Separation and Analysis of Body Fluids in Rodents and Humans for Mutagenic Components Using Salmonella typhimurium as the Indicator of Mutagenicity. Mutation Research 53:71-72.

Coutino, R., Meyne, J., and Legator, M.S. 1978. Cytogenetic Studies in Chinese Hamster Ovary Cells With the Narcotic Antagonistic Naltrexone. Mutation Research 53:80.

Kilian, D.J., Pullin, T.G., Connor, T., Legator, M.S., and Edwards, H.N. 1978. Mutagenicity of Epichlorohydrin in the Bacterial Assay System: Evaluation by Direct In Vitro Activity and In Vivo Activity of Urine from Exposed Humans and Mice. Mutation Research 53:72.

Kilian, D.J., Whorton, E.B., Jr., and Legator, M.S. 1978. Response to Critique of Paper 'A Collaborative Study to Measure and Minimize Interlaboratory Variation'. Mutation Research 50:293-294.

Meyne, J., Rinkus, S., and Legator, M.S. 1978. Distribution of Chromosomal Breaks Induced by Three Chemicals. Mutation Research 53:80.

Molina, L., Rinkus, S., and Legator, M.S. 1978. Evaluation of the Micronucleus

Procedure Over a 2-Year Period. Mutation Research 53:125.

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Troung, L., and Legator, M.S. 1978. In Vivo Determination of Alkylation of Amino Acids in Hemoglobin and Urine to Detect Potential Mutagenic-Carcinogenic Effects. Mutation Research 53:121.

Nienhold, I. and Legator, M.S. 1978. Assessment of Unscheduled DNA-Synthesis in Lupus-Erythematosus (SLE) Patients. Clinical Genetics 13(1):130.

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ALAN SCOTT LEVIN, M.D.

I. QUALIFICATIONS

Dr. Levin is engaged in the practice of medicine in San Franciso. His Curriculum Vitae and Addendum, listing Professional Societies and Awards, are attached.

II. SUBJECT MATTER

Dr. Levin will discuss the following in his testimony: the immune system, with its organic, cellular, and humoral components - most especially with regard to the latter, T-helper cells, B-cells, plasma cells and immunoglobulin production; immune response, both beneficial and harmful; the various experimental studies, particularly those demonstrating atrophy of the thymus, weight loss, depletion of lymphoid organs, lymphopenia, cutaneous type delayed hypersensitivity (skin thickness) and altered bacterial immunity.

In addition, Dr. Levin will discuss the following and their significance: immunology as molecular biology; chemical-induced immune disregulation; T-cells (lymphocytes from thymus) acting as immune modulators (for which there is "no effect" level); immune surveillance; the similarity of the immune, neurologic, and endocrine systems and their significance in the area of immuno-toxicity; the relationship of immune disregulation caused by chemicals and carcinogenicity, including cancer and the oncogene theory.

Also, Dr. Levin will discuss clinical uses of the epidemologic approach, i.e., clinical epidemiology.

And, Dr. Levin will discuss the problems of diagnosing "psychiatric disease" and the misdiagnosis which frequently occurs.

III. SCIENTIFIC PRINCIPLES

See General Statement of Scientific Principles and Assumed Facts attached.

IV. SUBSTANCE OF OPINIONS

A. That phenoxy herbicides and their contaminants, specifically dioxin, most especially 2,3,7,8-TCDD, cause an assortment of immunological responses, i.e. immuno-toxicity, which predispose persons exposed, by absorption and/or ingestion and/or inhalation, to such chemicals to a whole host of adverse health effects, such as: chloracne or other skin rashes; liver and other organ damage; various neuro-toxic effects; reproductive effects; and neoplasm.

B. That, in connection with the carcinogenic effect, there is no safe level for TCDD or any other carcinogen, and that a single exposure several years earlier can result in human cancer many years later.

C. Dr. Levin will then testify to the causal relationship of the various Agent Orange/dioxin related adverse health effects of the representative plaintiffs, including: chloracne; liver damage; neuro-toxic effects, both neurological and psychological; reproductive toxic effects, both miscarriages and birth defects; and such neoplastic processes as soft tissue sarcoma, as here a

ALAN SCOTT LEVIN, M.D.

ADDENDUM

Professional Societies

1. Alpha Omega Alpha Honor Medical Society
2. Certified Diplomate-American Board of Allergy and Immunology
3. Certified Diplomate-American Board of Pathology-Clinical Pathology
4. Member-Medical Quality Review Committee #4, Board of Medical Quality Assurance, State of California
5. Fellow-American College of Emergency Physicians
6. Fellow-College of American Pathologists
7. Fellow-American Society of Clinical Pathologists
8. Member-American Academy of Allergy
9. Member-American Association of Clinical Chemists
10. Member-Americal Medical Association
11. Member-California Medical Association
12. Member-San Francisco Medical Society
13. Member-Society for Clinical Ecology

Awards

1. American Cancer Society Faculty Research Award

Dr. Levin will also rely on the following articles:

Gallo, R.C. The Virus-Cancer Story: Hospital Practice pp. 79-89, June 1983.

Leder, P. Genetic Control of Immunoglobulin Production: Hospital Practice pp 73-82, February 1983.

Bishop, J.M. Oncogenes and Proto-Oncogenes: Hospital Practice pp. 67-74, August 1983.

Biological Relevance of Immune Suppression as Induced by Genetic, Therapeutic and Environmental Factors: J. H. Dean and M. L. Padarathsingh Editors, Litton Bionetics, Van Nostrand Reinhold Co. New York, Cincinanti, London, 1981.

Inadvertent Modification of the Immune Response: The Effects of Foods, Drugs and Environmental Contaminantsl Proceedings of the 4th FDA Science Symposium August 28-30, 1978.

Immunologic Considerations in Toxicology Vol 1 & 2, Raghubir P. Sharma, CRC Press, Inc. Boca Raton, Fla. 1981.

Pathology of Drug-Induced and Toxic Diseases: R.H. Riddell editor. Churchill Livingstone, New York and London, 1983.

Goldberg, R.J. Clinical Uses of the Epidemiologic Approach: Hospital Practice pp. 177-188, August 1983.

C. With respect to Opinion IV B, note the following

IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans.

EPA Criteria Documents, Publications and Assorted References Re: TCDD

A PLEA FOR THOUGHTFUL CONSIDERATION

Submitted to

THE BOARD OF MEDICAL QUALITY ASSURANCE

By

THE SOCIETY FOR CLINICAL ECOLOGY
(Northern California Chapter)

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II. Clinical and Scientific Demonstration of the Efficacy and Safety of Provocation Testing and Neutralization Therapy.

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I. INTRODUCTION

The members of the Society for Clinical Ecology, Northern California Chapter ("Petitioners") are most anxious that this presentation be given the closest, most thoughtful attention by the Board of Medical Quality Assurance. They are acutely aware of the attacks on their techniques that have emanated from certain quarters for some time. The Petitioners understand that medical break-throughs and innovations are often resisted by those who have become comfortable with accustomed techniques. The Petitioners have each made the extremely modest intellectual and clinical journey represented in testing and treating their allergy patients with the subject techniques, which are but precise refinements, albeit important refinements, of the more traditional techniques.

The Petitioners have been dismayed by the virulence of the attacks on their techniques and upon themselves. They have been dismayed at the refusal of their antagonists to engage in a good faith, collaborative scientific dialogue in which an exchange could take place. Indeed, Petitioners have been amazed as much at the refusal of their antagonists to observe patients or to examine carefully the statistical and

immunological research as they have been embarrassed for their antagonists over the seriously flawed analyses upon which they have been forced to rely in rejecting the provocation/neutralization modalities.

The Board of Medical Quality Assurance should at once acknowledge this internecine conflict and yet avoid getting drawn into it. It should acknowledge it for what it is -- the manifestation of pains of scientific growth and advancement.

New clinical and research findings, which are explained by corroborative evidence in basic immunology, have led a large number of allergy practitioners to modify the classical techniques of testing and treatment. The results have been dramatic. Many individual allergy sufferers who have each typically been treated by several classical practitioners without success have had their symptoms relieved. The newer techniques of testing are quicker, and the treatment far less burdensome to the patient. The newer techniques rely far less on drug therapy. The newer techniques in the entirety of their application are demonstrably less costly.

These various indices of effectiveness can be threatening to those who do not use the techniques and who are not knowledgeable about the literature or the immunological bases of the techniques. In the end, however, the controversy is a classic of innovation and change. In the past it has been viewed also as a clinical vs. academic conflict, but the immunological discourse presented below should erase that false dichotomy.

The Petitioners appreciated the opportunity to meet with officers of the Board of Medical Quality Assurance some months ago. Petitioners in this Presentation bring to BMQA's attention a number of rigorously scientific studies that document and explain the safety and efficacy of the sublingual, intracutaneous and subcutaneous provocative and neutralization testing and neutralization therapy techniques. They detail the immunological framework and mechanisms which explain not only why these techniques are sound, but also why they are more consonant with modern medical knowledge than parallel testing and therapeutic techniques of certain other allergists.

An extensive methodological and statistical critique is also

made of the reports critical of the provocative neutralization techniques. Finally, the scientific soundness of the alternative allergy testing and treatment are placed in perspective.

Petitioners request the Board to review these comments carefully, and stand ready to assist the Board and its staff in securing further clarification.

(These Comments were originally prepared for submission to the Health Care Financing Administration of the U. S. Department of Health and Human Services for its enlightenment and assistance in evaluating the Petitioners' techniques as eligible for Medicare coverage. Hence the odd section numbering and pagination.)

II. CLINICAL AND SCIENTIFIC DEMONSTRATION OF THE EFFICACY AND SAFETY OF PROVOCATION TESTING AND NEUTRALIZATION THERAPY

(Prepared by Alan S. Levin, M.D.
with the assistance of Joseph D. Miller, M.D.
and Sidney Weinstein, B.A.)

INTRODUCTION

Opponents brand the provocation and neutralization techniques of allergy testing and treatment as "experimental" and unreliable. Yet this technique has proven safe and effective in thousands of clinical trials. Furthermore, it has afforded relief to patients whose allergies have proven unresponsive to less precise methods of allergy testing and treatment, either because of the type of sensitivity (for example, poison oak-ivy)[1] or because the extent of sensitivities ("chemical hypersensitivity" or "immune dysregulation"[2]) have seriously compromised their immune system's ability to respond appropriately to antigens. It is a method whereby permanent relief from food, inhalant, and chemical allergies and other antigen-related illnesses can be obtained without the use of harmful alternatives such as psychotropic drugs, artificial prostaglandin inhibitors, or

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synthetic adrenal corticosteroids. Provocation and neutralization also obviate the need for antihistamine, bronchodilator, or steroid therapy, the long-term side effects of which have never been tested.

The efficacy of this approach is well-supported by well-known immunological mechanisms. Three recent rigidly controlled, double-blind placebo-controlled studies[3,4,5] have demonstrated the scientific validity of this approach and have substantiated the immunological mechanisms of action as well. A number of earlier studies also statistically validate the efficacy of provocation/neutralization.

In support of the safety, reliability, efficacy, and scientific soundness of provocation and neutralization techniques, this section will describe:

II. CLINICAL AND SCIENTIFIC DEMONSTRATION OF THE EFFICACY AND SAFETY OF PROVOCATION TESTING AND NEUTRALIZATION THERAPY

A. What is provocation testing and neutralization treatment?

B. The clinical observations which initiated the development of the provocation/neutralization techniques

C. How does provocation/neutralization differ from conventional allergy techniques?

D. Which kinds of medical illnesses are best treated with provocation/neutralization?

E. The controlled double-blind clinical trials which establish the efficacy of provocation/neutralization

F. Modern concepts of the immune response and how they relate to provocation/neutralization

1. The highly regulated and controlled immune system

2. The phasic phenomenon of immune response

3. How provocation/neutralization works

4. The immune response is often mediated by factors other than IgE

5. Two interacting immune mechanisms explain non-IgE mediated allergic reactions

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a. Role of macrophages

b. Basophils and mast cells: role of histamine

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d. Role of neutrophils

G. Why do intradermal and sublingual administration of antigen provoke and neutralize symptoms?

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A. WHAT IS PROVOCATION TESTING AND NEUTRALIZATION THERAPY?

The provocation and neutralization method of testing and treating allergies is a technique by which the clinician can quickly ascertain the doses of allergen that will induce ("provoke") symptoms of allergy, then relieve ("neutralize") the induced symptoms.[6]

To determine the precise beneficial concentration of each antigen to be tested, a concentration of an inhalant extract designed to induce ("provoke") mild symptoms is injected intradermally. The wheal size is measured initially 10 minutes later. Wheal growth of greater than 2x2 mm is considered "positive". Less than 2x2 mm growth or reduction in wheal size is considered "negative". Consecutively stronger or weaker concentrations, depending on whether the initial wheal is negative or positive, are then injected at 10-minute intervals until the strongest concentration is found which relieves ("neutralizes") the induced symptoms in 10 minutes and produces a negative wheal. This is the therapeutic or neutralizing dose.

To use this technique correctly, the practitioner must systematically evaluate the effects of a series of different dose levels in each individual. Provoked signs and symptoms are sometimes strikingly intensified rather than relieved by

subsequent administration of a much less concentrated dilution of extract than the provoking dose.

Therapy is begun with intradermal injections of a solution containing the full individually determined neutralizing dose of each antigen. In some cases, relief can be achieved during the first testing session. Most patients beginning immunotherapy with this technique note marked improvement or complete clearing of symptoms within two to three weeks. Thereafter, marked relief usually begins within 30 minutes after each injection and lasts a week. Scientific evidence has shown that sublingual drops are generally as effective as intradermal injections and provide relief in less than 10 minutes. When indicated, practitioners conduct oral and inhalation challenges with allergens or placebo in a single-blind manner to verify the validity of their patients' responses.

As will be seen later in this section, provocation and neutralization techniques initiate a biochemical process that alters the ratio of suppressor to helper|inducer T-cell subsets, thereby changing the phase of immune response and resulting in immune unresponsiveness to challenge with additional specific antigen.

B.THE CLINICAL OBSERVATIONS WHICH INITIATED THE DEVELOPMENT OF PROVOCATION/NEUTRALIZATION TECHNIQUES

Virtually every practicing allergist has noted a strange phenomenon in some patients receiving build-up immunotherapy. When these patients reach a particular dosage level, they report that each injection provides marked relief which begins in minutes or hours and lasts about a week. Some return once a week requesting another "relieving injection".

This immediate response is unanticipated. It does not fit the doctors' accepted concepts of immunotherapy, yet many allergists have wished they could duplicate this phenomenon in all of their patients.

This relieving phenomena is duplicatable in most cases. For most patients, a specific symptom-relieving therapeutic concentration for each antigen extract exists and can be determined individually by skin testing. This is the clinical principle behind provocation/neutralization. In the case of multiple allergies, the relieving concentration for each antigen may differ considerably. However, all of the relieving doses can be combined into a single vial to provide response to all the allergens at once.

C. HOW DOES PROVOCATION/NEUTRALIZATION DIFFER FROM TRADITIONAL ALLERGY TECHNIQUES?

Provocation/neutralization has been in use for close to 40 years, and represents a refinement of older techniques. Both use the same allergy extracts supplied by the same supply houses. Both skin test intradermally with stock solutions of extracts.

Practitioners of the newer techniques, however, use certain crucial refinements of the traditional methods. (1) They test one item at a time, in 1:5 concentrations, rather than 20-40 allergens at one time in 1:10 dilutions. (2) They carefully observe the patients during the 10 minutes between tests. The wheal size is always monitored, but they also observe every nuance of the patient's affect behavior. When indicated, they measure: nasal passageway patency; pulse; blood pressure; pulmonary function (using a peak flow meter); handwriting changes; and picture-drawing abilities. On the basis of the above monitored criteria, a decision is made concerning the correct treatment dose for therapy for the individual item which is being tested on that particular patient.

The most radical difference between traditional and newer techniques is the determination of the therapeutic dose. Traditional allergists start therapy with a dose that

produces a "safe" wheal, that is, where the increase in wheal size is not excessive within 10 minutes. In contrast, the refined approach determines the correct dilution that will neutralize symptoms for that particular patient for the items tested. The traditional therapy requires injections by the physician 1-3 times a week for up to 30 weeks, and then once a month for many years. With the refined approach, once the correct therapeutic dilution is determined, it is combined with the correct dilutions of the other tested items. The patient can then self-treat safely, using sublingual therapy 3 times a week to once every two weeks, or injection therapy once daily and in time once every week or two, as indicated.

D. WHAT KINDS OF MEDICAL ILLNESSES ARE BEST TREATED WITH PROVOCATION/NEUTRALIZATION ?

Provocation and neutralization techniques can be used to test and treat a wider variety of allergic disorders than can those employed by conventional allergists. The patient's response is often most gratifying. Most physicians using provocation/neutralization report that use of specific neutralizing doses of specific stock allergy extracts results in improved "tolerance" to offending antigens when compared to conventional hyposensitization techniques.

Traditional allergists are often perplexed by patients who have classical year-round or seasonal asthma or hayfever without having positive skin reactions. The newer techniques of provocation testing and neutralization therapy enable these patients to be effectively treated with stock allergy extracts once it is realized that their illnesses are not caused by an IgE mechanism.

Conventional allergists are somewhat successful in treating traditional allergic reactions to pollen, dust, and mold for traditional nasal symptoms, asthma, post-nasal drip, conjunctivitis, urticaria, and at times atopic dermatitis. Most of these reactions are mediated by IgE mechanisms. Practitioners using provocation/neutralization modalities have successfully treated these and other symptoms that have

Finally, these techniques have proven useful for treating various syndromes and infectious diseases[10,167-171] such as resistant vaginal candidiasis[12], dysmenorrhea[12], and active viral infections[10] as well as certain autoimmune disaeses such as lupus erythematosus.[12,13]

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been linked for the past 40 years to a wide variety of environmental factors, including foods, pets, toxic chemicals, and infectious diseases. These immune reactions are mediated by factors other than IgE (including IgG, IgA, etc.) and frequently involve diverse parts of the body.[7]

A surprising number of patient complaints include both the typical and less well-recognized signs and symptoms of allergy. Both types of illnesses respond equally well to neutralizing immunotherapy once the appropriate specific antigenic material has been determined and injected in appropriate symptom-relieving doses. Examples of such illnesses include: aphthous stomatitis; chronic diarrhea; chronic ulcerative colitis; atopic dermatitis; chronic urticaria; hyperkinesis; migraine; and some resistant respiratory inhalant syndromes including perennial allergic rhinitis, asthma, and recurrent laryngeal edema.[6,8,9]

Some patients sensitive to foods, inhalants, and/or chemicals have multi-system disease with symptoms referable to many organs. In these patients, immune complexes or other vascular perturbation factors affect almost the entire vasculature. Formerly, these patients were often considered neurotic because of the multiplicity of their complaints and intractable because no adequate therapy was available. Many of these patients have multiple sensitivities that are readily relieved by neutralization therapy.

E. THE CONTROLLED DOUBLE-BLIND CLINICAL TRIALS WHICH ESTABLISH THE EFFICACY OF PROVOCATION/NEUTRALIZATION

Three rigidly controlled, double-blind placebo studies on allergy testing and treatment clearly demonstrate the efficacy of provocation/neutralization techniques. In addition, several earlier studies also illustrate their efficacy.

Boris et al (1983)[3]. These researchers have recently reported a double-blind controlled study on the effect of neutralization therapy on asthma. They evaluated 19 subjects with a history of wheezing to animal dander. The subjects were challenged with inhaled animal antigen to determine the dose causing a 20% decrease of FEV_1. The neutralizing dose was determined by the five-fold serial dilution skin technique. On two subsequent days, one week apart, the specific antigen neutralizing dose of placebo was injected and bronchoprovocation was performed with the dose previously ascertained by the provocation test. FEV_1 decreased 31.8% from baseline in the controls, 27.4% post-placebo, and 10.7% post-neutralization injection (p less than 0.01). FVC and FEF 25-75, and PEF had similar responses. These results demonstrate that neutralization therapy, when properly performed, produces a statistically significant improvement in bronchospasm in asthma patients sensitive to animal dander.

Rea et al (1983)[4]. This group performed a similar study using food-sensitive patients. In this study, 22 subjects were selected who had a documented adverse reaction to certain foods. A neutralizing dose was obtained by intradermally titrating the subjects to the sensitizing foods. The patients were then given oral food challenge and injected with neutralizing dose or placebo in a double-blind controlled experiment. Signs and symptoms, Visual Analogue Discomfort Rating, heart rate, Aaron Smith Symbol Digit Modalities Test, Symbol Digit Modalities Subtest, and patient signature were evaluated. The neutralizing dose, compared to placebo, produced a protective effect on all parameters measured. Statistical analysis showed the difference between neutralizing dose and placebo to be highly significant (p less than 0.001-0.05) in all parameters with the exception of the Symbol Digit Modalities Subtest. These results demonstrate that neutralization therapy, when properly performed, produces a statistically significant improvement in the symptoms of food intolerance.

McGovern et al (1983)[5]. McGovern et al studied the reliability of the provocative challenge test in six patients and controls. This study used a double-blind, randomized, placebo-controlled protocol. In addition to clinical parameters, it measured cellular and humoral immune factors in the blood of these subjects. The investigators measured IgG, IgA, IgM, IgD, C3, C4, IgE, immune complexes (by the

polyethylene glycol technique which detects both complement-associated and non-complement-associated immune complexes), total white blood cell count, absolute lymphocytes, total T cells, T-helper cells, T-suppressor cells, and helper/suppressor ratios.

The injection of specific doses of allergenic extracts and haptens induced objective physical abnormalities with statistically significant frequency in patients, when compared with placebo injections. In ten additional patients and controls, the authors showed that the neutralization, but not the placebo injection, brought about a reversal of the patients' induced clinical reaction with statistically significant frequency. Blood samples taken before and after provocation and neutralization injections in allergic subjects showed markedly fluctuating levels of parameters of inflammation when compared with controls. These levels directly correlated with the onset of systemic reactions after provocative injection and with the disappearence of systemic reaction after neutralization.

This study is unique. Not only does it demonstrate that provocation/neutralization testing techniques, when performed correctly, produce statistically significant clinical responses when compared to placebo, but it also objectively demonstrates the marked instability of allergy patients' immune systems.

In addition to these 3 most recent double-blind placebo controlled studies, there are 9 other controlled studies which establish the efficacy of provocation/neutralization testing and treatment techniques. Of these nine studies, three[8,17,18] stand out as well-controlled scientific studies which when considered alone, clearly demonstrate the efficacy of the provocation/neutralization technique. Two[19,20] of the remaining reports are well-controlled, very convincing studies performed in double-blind crossover-controlled fashion on single patients. The remaining four[21,6,22,23] studies, when viewed with the others, further corroborate the efficacy of provocation/neutralization.

Miller, J. (1977)[8]. This is a well-designed, double-blind, crossover-controlled study which was the first in a series of confirmatory studies on the provocation/neutralization technique. The major attribute of this study was that it was carefully performed in a double-blind fashion by the recognized leader in the development and clinical use of the technique. Patients were selected who presented with symptoms found from extensive clinical experience to be caused frequently by food sensitivities. Prior to the double-blind phase, subjects underwent a trial treatment period with neutralization therapy. For the double-blind phase, eight subjects were treated during four separate 20-day periods either with the putative neutralizing antigens or phenolated saline colored with mushroom extract to

simulate the neutralizing vaccine. A careful symptom survey was made during the first office visit and symptom changes were recorded during and at the end of each of the four 20-day courses of therapy. Each subject received two courses of antigen and two of placebo in a crossover fashion. During neutralization dose therapy the average improvement score was 3.68 while that for the placebo was 2.25. The difference is stasitically significant (p less than .002).

This study clearly demonstrates that provocation/neutralization therapy produces statistically significant improvement when compared to controls.

King, D. (1982)[17]. This is one of the most definitive studies ever performed to test the efficacy of sublingual provocation/neutralization testing. The author evaluated allergy patients who had also had at least one psychological symptoms such as anxiety, depression, confusion, or difficulty concentrating. The major question was whether sublingual provocation with antigen or placebo would induce psychological symptoms more frequently. Selection of the antigens for challenge was based on the patient's individual history. Thirty patients were challenged with four selected foods and with triple distilled water as placebo. There were four kinds of trials: 1) allergen trials (four antigens, each given three times), 2) placebo trials (two tests, each give three times), 3) base-rate trials in which the subjects

received nothing sublingually but for which the dependent end points were measured (three trials), and 4) open placebo trials to assess the biological reactivity to the placebo (three trials). Two blinded judges independently assessed symptoms. Symptom severity was reported quantitatively. The integrity of the double-blind was evaluated, and data points in which the double blind might have been jeopardized were excluded. Average symptom scores for psychological symptoms were four times higher after antigen than after placebo provocation. This difference was statistically significant ($p=0.001$). Severe reactions were also more frequent after antigen challenge ($p=0.006$). Mixed psychological-somatic symptoms were more frequent after antigen provocation ($p=0.02$). Somatic symptoms were significantly more frequent after antigen provocation according to one method of analysis, but this difference was not statistically significant using a different analysis.

This comprehensive study demonstrates that psychological symptoms can be provoked with statistically significant frequency using active antigen administered sublingually when compared to placebo controls.

Lee, L.K. (1982)[18]. This controlled study measured the relative efficacy of skin endpoint therapy as compared to conventional treatment and finds the titration technique superior.

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Rapp, D. (1978)[19]. This is a double-blind, placebo-controlled study of milk sensitivity in one 9-year-old boy. The patient was treated with neutralization therapy after the study and improved dramatically. A study of one patient does not prove the case when considered alone, However, when considered in conjunction with other confirmatory studies, this well-designed double-blind, placebo-controlled study further corroborates the efficacy of provocation/neutralization therapy.

Rapp, D. (1982)[20]. This is another double-blind, placebo-controlled study performed on one patient with documented wheat allergy. This patient was diagnosed by two opthalmologists as having moderately severe chronic allergic blepharo-conjunctivitis. These symptoms improved markedly on a wheat-elimination diet. The patient was then tested intradermally with wheat antigen and opthalmologic symptoms returned. A neutralizing dose of wheat antigen was then determined. The patient was then asked to avoid wheat in all forms and to ingest 24 capsules (six teaspoons) each day for a period of 12 days. The capsules for each three-day period contained either wheat germ or similarly colored group peanut which had been coded in a double-blind manner. The patient remained asymptomatic throughout the entire 12-day period. She was then told to eat large quantities of wheat. Shortly after reintroducing wheat into her diet, her opthalmologic

symptoms recurred. During the next 12 weeks, she limited her wheat ingestion to 1 slice of bread per day while she was treated sublingually with the neutralizing dose of wheat antigen. Her eyes returned to the asymptomatic condition and remained in that condition throughout the 12-week test period. Three bottles, identical in color and taste were then prepared and double-blinded. Two contained phenolated saline while the third contained phenolated saline and her neutralizing dose of wheat antigen. While ingesting large quantities of wheat each day, the patient found that her eyes began to tear for the first time in three months after she had used a placebo solution for five days. Her eyes continued to tear for the next three days while she tried the second placebo solution. Her symptoms cleared within 1 1/2 days of using the bottle containing the active neutralizing dose.

This study constitutes a brilliant investigative effort for a busy practicing clinican and a cooperative patient. Although this study involved only one patient, every busy practitioner will appreciate that this patient was definitely responding favorably to the active treatment dose and was not benefitting from a placebo response.

Mandell, M and Conte, A. (1982)[21]. In the Mandell study, the investigators studied 30 volunteers with documented arthritic pain. Each received a sublingual challenge of 19 food

antigens, 9 inhalants, and 4 placebos of distilled water. The positive symptomatic response was 61% for the foods, 38% for the inhalants, and 6.6% for placebos. Each difference is highly significant statistically.

The data and structure of this study are somewhat difficult to assess and the method of assuring the double-blind are not clearly outlined. Despite these flaws, this report adds further corroborative evidence to the efficacy of sublingual provocation/neutralization techniques when it is considered in conjunction with the other positive double-blind controlled studies.

Miller, J.(1972)[6]. This book represents a comprehensive text on the "how to" of provocation/neutralization techniques.

O'Shea, J., and Porter, S. (1981)[22]. In this study, fifteen children were chosen who met the clinical criteria of hyperkinetic syndrome. The mean score by both parents and teachers was 20 on the Abbott's Hyperkinetic Index (an adaptation of Conner's hyperkinesis scale). A detailed history and physical examination confirmed the diagnosis of hyperkinetic syndrome. Food and inhalant extracts were serially diluted in multiples of five for intradermal testing. The food dyes were commercial food colors sold in most food stores. Placebo was preservative-free chlorophyll. The study lasted for seven weeks and consisted of two 3-week

periods separated by one weeks's vacation. During each 3-week period, every child was randomly given either the allergy extract or the placebo. The same Hyperkinetic Index was used as in the Connor study. However, in contrast to that study, the children were monitored daily. The allergy extract could be differentiated from the placebo solution by 11 of 14 (78%) of the parents and 7 of 13 (54%) of the teachers because of improved activity and behavior patterns in the children studied.

This study indicates that allergy extract therapy can produce significant symptomatic improvement in documented hyperkinetic children, often obviating the need for the dangerous practice of treating these children with amphetamine-like drugs.

Rapp, D. (1979)[23]. In this study, eleven children were treated with a food extract after titration food allergy testing. Extract was administered sublingually or subcutaneously. These patients remained improved, as measured by the Abbot Hyperkinesis Index Scale, for one to three months while ingesting the foods to which they were sensitive. Five of eight patients then completed a double-blind evaluation of the food extract and successfully differentiated the latter solution from two placebo ones. All solutions were dispensed in opaque bottles to avoid patient recognition of color. Two of the three children who

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failed to correctly identify the food extract relapsed when food therapy was discontinued. They responded favorably when the therapy was reinstituted.

This study, like the O'Shea one, further corroborates the efficacy of sublingual provocation/neutralization therapy for food allergy treatment.

F. MODERN CONCEPTS OF THE IMMUNE RESPONSE AND HOW IT RELATES TO PROVOCATIVE/NEUTRALIZATION

Although the efficacy of provocation/neutralization has been firmly established clinically and by placebo-controlled double-blind studies, controversy still surrounds the techniques. This is based, in part, on the critics' assumptions that the treatable allergic reactions are mediated by IgE, and that no immunologic mechanisms exist which can explain the provocation/neutralization phenomenon.

The past decade has brought major changes in the concepts underlying the mechanisms of allergy. We originally thought that the immune response was a specific reaction to challenge from a specific antigen, mediated by IgE antibody. The immune response was seen as a linear function of ever-increasing doses of specific antigen producing ever-increasing amounts of antibodies, until the immunologically reactive cells were exhausted and immunologic unresponsiveness ("tolerance") resulted.[24] Although immunologic tolerance is the goal of build-up immunotherapy modalities, these conventional allergy methods have been unsuccessful in treating non-IgE-mediated allergies (Type 1, immediate response) as well as some classical IgE-mediated illnesses.

We now know that many types of allergies, e.g., those due to

foods and environmental chemicals, cause other-than-IgE mediated reactions. The immune response is a complex series of well-programmed interactions and counteractions between various cellular and humoral components of the immune system. These interactions follow a biphasic or multiphasic curve if plotted out. Because the immune system is part of a larger interactive network involving the lymphoreticular, nervous,[25,26] and endocrine systems,[25,26] an immune response may involve multiple systems and organs and result in such diverse clinical signs and symptoms as migraine,[27] food addiction,[7] behavior or mood changes,[28,29,30] hyperkinesis,[22,23] heart problems,[31] or joint diseases.[21]

Provocation/neutralization is the clinical correlate of the phasic immune response, where one dose of antigen provokes an immune response, a lower dose cancels ("neutralizes") it, and a still lower dose again provokes it. This pattern occurs because the various components of the immune system involved in an immune reaction are dynamically interacting to return the organism to homeostasis or nonreactivity. Physicians using these modalities can safely and effectively treat antigen-related allergies in most cases because administration of a neutralizing dose of specific antigen alters the body's phase of immune response, thereby enabling it to return to homeostasis.

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1. THE HIGHLY REGULATED AND CONTROLLED IMMUNE SYSTEM

The immune system is a highly regulated system which monitors and responds to changes in the chemical composition of the body. These changes trigger signals from cellular and molecular elements of the immune system which distinguish between harmless and harmful agents. The signals switch various cellular and humoral effectors "on" or "off" to control and modulate growth and development within the organism. They interact not only with elements of the lymphoreticular system but with those of the neuroendocrine system as well. Immunologic regulation is effected by a tightly controlled interactive balance between inducer and suppressor T-cell subsets, idiotypic and anti-idiotypic antibodies, and a multitude of other immunomodulatory molecules and cells

Once the immune system has distinguished between harmful and harmless agents, it must induce the appropriate molecular and cellular reactors to ignore (suppress active inflammatory reactions) or challenge (induce active inflammation). Many of the factors secreted by immune-reactive cells are soluble peptides and lipids which circulate to remote sites of the body and cause effector functions.[135,41-44] Objective changes in brain chemistry,[25] joint metabolism, and endocrine glands result from remote immunologic reactions.

The immune system's tightly controlled interaction of

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antibodies and cells are directed against specific antigens and are called idiotypes. Production of these idiotypes is modulated by specific antibodies (anti-idiotypes) against the antigen-combining site of these antibodies and cells. The production of these anti-idiotypes are in turn controlled by anti-anti-idiotypes and these by anti-anti-anti-idiotypes. The presence of the family of anti-idiotypic antibodies lends smoothness to the immune response, much like extra cylinders provide smooth function to a gasoline engine.[32-50]

2. THE PHASIC PHENOMENON OF IMMUNE RESPONSE

Specific immunologic unresponsiveness ("tolerance") occurs when responsive cell clones have been eliminated by prior contact with antigen, with the result that no immune response against that antigen occurs on re-administration.

One of the original workers to note the phasic nature of immunological responsiveness and unresponsiveness was Mitchison.[51] In his study, newborn rats were injected daily for 2 weeks with a wide range of doses of bacterial flagellin antigen. Control rats received no antigen. All animals, including controls, were then given a stimulatory dose (10 mcg) of flagellin twice a week for 4 more weeks, and their antibody responses measured. The results are shown in figure 1 at the end of this subsection.

As can be seen in the figure, the response to varying doses of antigen in the tolerized animals produced a biphasic distribution. At very low tolerizing doses of antigen (less than 10^{-3} pg of flagellin antigen/gr body weight) the animals responded to the immunizing dose with near-normal (control) levels. As the tolerizing doses approached 10^{-3} pg, the animals developed specific immunologic unresponsiveness (low-dose tolerance). As the tolerizing dose increased to around 10^{-1} pg, the animals responded with a supernormal ("overshoot")[59] immune response. When the tolerizing dose

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approached 100 pg and above, the animals again exhibited specific unresponsiveness.

This phenomenon has been shown to be due to the modulatory effects of suppressor T cells which respond to various concentrations of antigen. These suppressor cells can be categorized as non-antigen-specific and specific. Most react through soluble factors which can circulate throughout the body. "Tolerance" occurs when the specific suppressor T-cell factors are dominant over specific helper/inducer T-cell factors.[60-74].

Biphasic and multiphasic responses to antigen and other mediators of the inflamatory process are not unusual. Although not specifically discussed, they have been found by a number of investigators in their studies. For example, in experiments using spin label probes to detect the release of myelin-basic protein from lipid vesicles in an artificial membrane, Boggs et al.[52] showed a reciprocal and essentially biphasic response between specific antibody-dependent and antibody-independent release as a function of increased antigen concentration.

Eichmann[53] found that 50% of the antibodies to a specific bacterial carbohydrate produced by a strain of mice had cross-reacting idiotypes. When these animals were pretreated with anti-idiotypic antibody, their idiotype response was

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suppressed. The amount of suppression followed a biphasic curve. Small amounts of anti-idiotype produced little idiotypic suppression, intermediate doses produced maximum suppression, and larger doses produced less suppression.

A similar phenomenon was demonstrated by Szewczk et al[54] when they measured the affinity distribution of the IgG anti-TNP plaque-forming cells in the spleen of animals treated with various doses of histamine which is a suppressor cell inducer.

Sullivan et al[55] found that modulation of cyclic AMP in purified rat mast cells by pharmacologic stimuli follows a biphasic mode. They demonstrated a biphasic response of purified rat mast cell cAMP to carbamycholine, exogenous adenine, and diazoxide.

A biphasic response develped in rats' capacity to respond to sensitization with a supraoptimal dose of oxazolone when they were pre-treated with various doses of oral cyclophosphamide.[56]

Serial assessment of antibody concentrations weeks after immunization with antigen often shows a multiphasic curve.[57] These biphasic and multiphasic responses to varying concentrations of antigen are due to the phasic nature of the immune network which is a complex interaction of idiotypes

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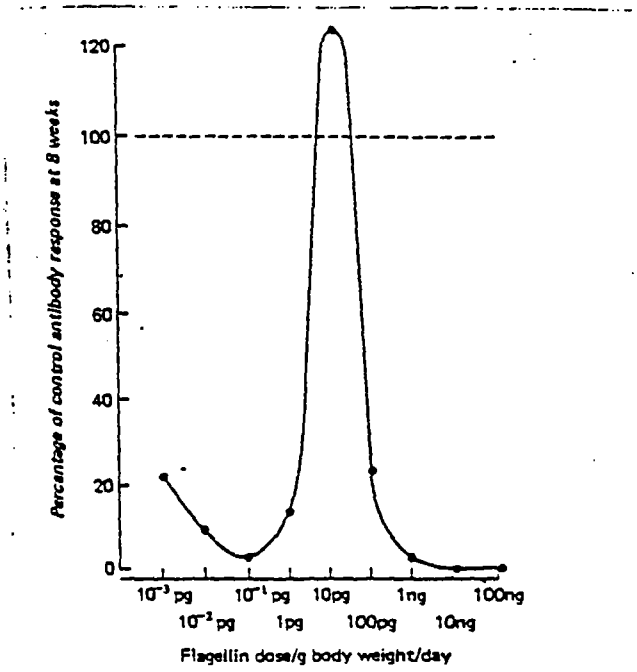
and anti-idiotypes.[58] When the helper/inducer cells are dominant in function, idiotypes are synthesized. This provokes a reciprocal synthesis of anti-idiotypes which enhance the activity of the suppressor cells. The suppressor cells then suppress the action of the idiotype-producing B cells. This cycle continues with ever-decreasing intensity until the base line is re-established.[75-77]

figure 1:
The Phasic Nature of the Immune Response[51]



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3. HOW PROVOCATION/NEUTRALIZATION WORKS

Many types of allergic reactions are mediated through the formation of immune complexes. Provocation/neutralization works because it alters the ratio of antibody to antigen by addition of a small amount of antigen.

The combination of antibody with antigen is one of the fundamental life-preserving processes of immunology. Yet these complexes,once formed, must be completely removed from the circulation quickly, for their persistence is itself a threat to survival of the organism. This is because such persistence can call complement and polymorphonuclear leucocytes into action to destroy the remaining complexes. Since these destructive effects are nonspecific, cells in the vicinity of the complexes may be damaged or destroyed, possibly resulting in lethal immune-complex-mediated disease.

The existence and potential pathogenicity of immune complexes were first suggested in 1905 by von Pirquet and Schick.[78] Immune complexes are formed daily in everyone from foods, inhalants, micro-organisms, and many other antigens,[79-81] but their size, level, and rate of removal from the circulation are such that clinical immune complex disease does not normally occur.

Very small complexes which are formed in antigen excess are less likely to be pathogenic than somewhat larger ones.[82]

This is because they may contain only one IgG antibody which is incapable of activating complement. They are small enough to pass completely out of the circulation through inter-endothelial cell pores in vascular basement membranes. These very small complexes do very little harm since they activate complement and do not deposit in vessels.

Very large complexes (over 19S) formed in antibody excess are efficiently cleared from the circulation by macrophages of the reticulo-endothelial system.[82] They are also relatively harmless.

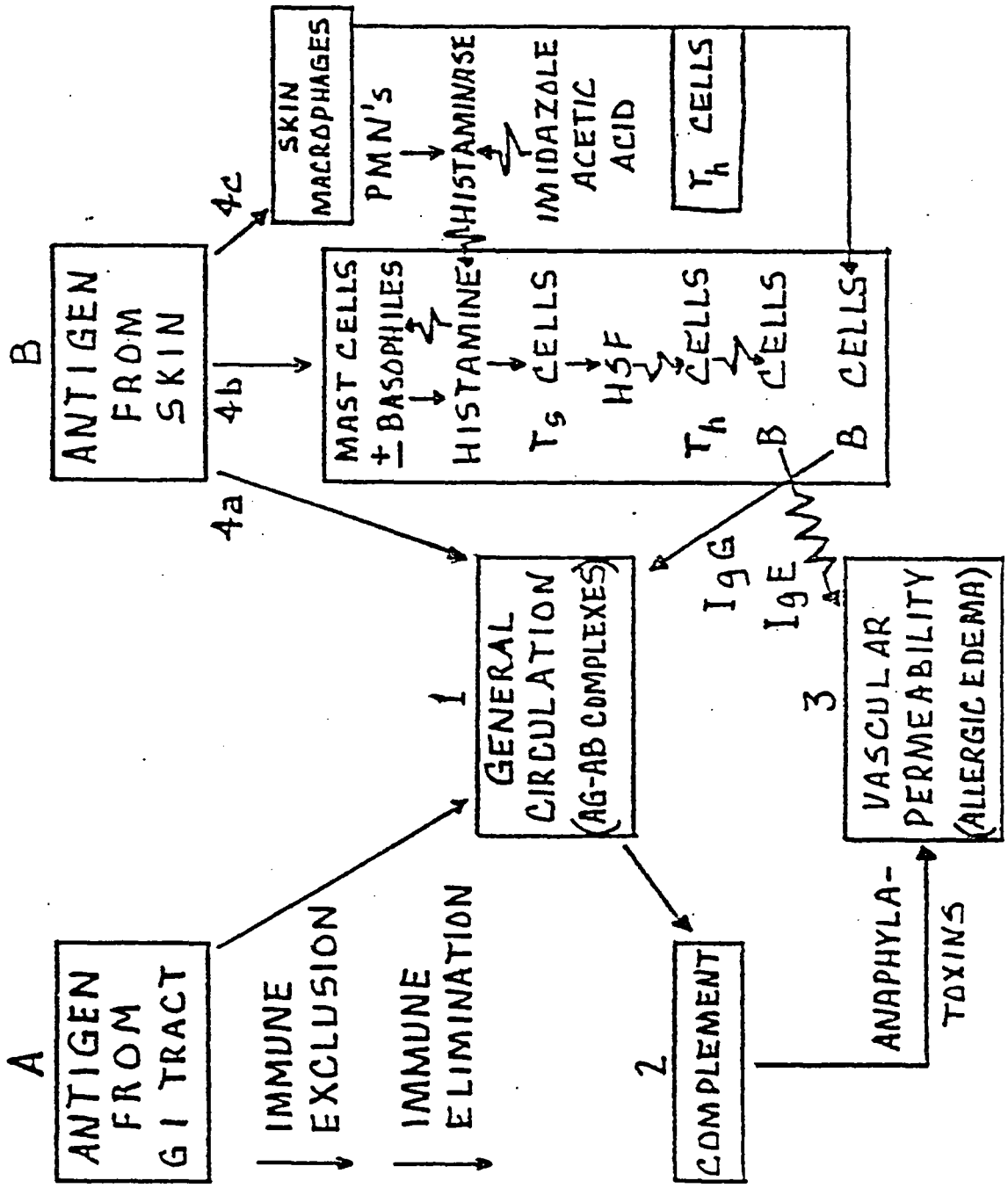
Intermediate-sized complexes formed at approximate equivalence (ag:ab ratio of approximately 3:2) with a molecular weight of about one million, are the potentially toxic ones. They are too small to be efficiently phagocytosed by macrophages, and are too large to completely traverse the pores of vascular basement membranes. They tend to persist in the circulation and become lodged in these pores. This automatically activates the complement cascade which in turn attracts polymorphonuclear leukocytes. The destruction of neighboring endothelial and tissue cells flows from two mechanisms, destruction by complement cascade proceeding to C8 and C9, and neutrophil enzymatic digestion.[82]

If complement activation proceeds only to the point of liberating anaphylatoxins, particularly if only to C3a, there is much less likelihood of inducing irreversible cell injury by either mechanism. Anaphylatoxins can cause release of histamine and other mediators from mast cells and basophils, inducing reversible enlargement of inter-endothelial cell pores resulting in increased capillary permeability and local edema. It is chiefly by way of such edema that allergic symptoms can be initiated without the involvement of IgE and without the cellular destruction associated with full complement activation and neutrophil participation.

Antigen-antibody interaction in immune complex formation is a highly dynamic process. Antigens and antibodies in complexes can quickly dissociate and recombine in other ratios. Complement activation and inactivation and anaphylatoxin-induced mediator release can occur in seconds or minutes.[83] Adding a small amount of antigen or antibody can shift the reaction rapidly and markedly. This shift results in smaller or larger complexes, thereby altering the potential for complement activation. If the right amount of antigen is added to shift the curve from pathogenic to a nonpathogenic mode, rapid symptom-relief occurs. This is what happens in neutralization. Repeatedly adding this dose of antigen keeps equilibrium reactions stable and symptoms controlled. If the amount of antigen added is too small or too large, symptoms are induced. The induction and relief of

symptoms in this manner are consistent with the "turn-on"/"turn-off" phenomena noted during provocation and neutralization testing and with the long-term relief provided by regularly administered neutralization injections. See figure 2 (next two pages) for a diagram of how provocation/neutralization works, and an explanation of the diagram.

figure 1: How Provocation/Neutralization Works



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Legend to figure 1
How Provocation/Neutralization Works

1. Antigen from G-I tract (A) enters circulation, is bound by antibody to from ag-ab complexes.

2. If complexes persist in circulation, complement is activated, anaphylatoxin released.

3. Anaphylatoxin triggers mast cells and basophils to release mediators, resulting in vascular permeability, edema, and allergic symptoms.

4. Antigen injected into skin (B) in appropriate doses takes three pathways

a. Enters circulation to alter circulating antigen-antibody ration and affect immune complex formation.

b. Combines with IgE antibody on surfaces of mast cells in skin, and also possibly with basophils in circulation, or arriving in tissue at site of antigen injection. This stimulates local release of mast cell mediators, including histamine.

Histamine stimulates mast cells and basophils to stop mediator release, and stimulates T-suppressor cells to secrete HSF.

HSF suppresses T-helper cells, which turns of B-cell release of IgE, reducing vascular permeability, edema, and allergic symptoms.

c. Stimulates skin macrophages to transmit signals to T_h cells to turn on increased B-cell formation of IgG, which enter circulation and favorably affect antigen-IgG ration, reducing formation of toxic complexes.

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4. THE IMMUNE RESPONSE IS OFTEN MEDIATED BY FACTORS OTHER THAN IgE

The past 10 years have changed many of our concepts of allergy and immune response. For example, the common consideration of IgG only as a blocking ("good") antibody in allergy, and IgE only as a symptoms-inducing ("bad") antibody is obsolete. Such a simplistic scenario is too incomplete to explain recently accumulated data concerning complicated interactions among humoral and cellular reactants and the two cell types (helpers and suppressors) that can effect opposite reactions.[46,84] For example, IgG can form immune complexes to produce harmful allergic syndromes as well as lethal diseases.[80] Conversely, IgE can induce local histamine release which itself can quickly turn off allergic symptoms and stimulate expansion of clones of protective suppressor lymphocytes.[85-99]

Allergy symptoms are mediated by the formation of specific antigen-induced immune complexes rather than by specific antibodies. As demonstration of this, symptoms of non-IgE mediated allergy may be produced in some patients by antigen-induced immune complexes, and relieved by antigen injection which induces rapid clearing of these complexes.

It is well-recognized that immune complex-mediated disease can be associated with symptoms in virtually any organ. A classic example is systemic lupus erythematosus. Lupus

patients with central nervous system involvement may experience headache, hyperactivity, visual changes, disorientation, aggressiveness, and frank psychosis. These symptoms have been shown to be related to the presence of immune complexes in the peripheral circulation and to changes in complement components in the cerebrospinal fluid.[30,100,101] They are caused by anaphylatoxin-induced histamine release from mast cells and basophils leading to increased capillary permeability in the brain or adjacent structures. Similar symptoms occur after the ingestion of allergenic foods.[102-104]

In lupus, the immune complexes are generally made up of double-stranded DNA antigen and a complement-fixing IgG anti-DNA antibody.[30,100,105-108] In allergic patients, antigens complexed with circulating and cell-fixed antibodies activate complement to produce anaphylatoxin-mediated histamine release resulting in the increased capillary permeability which causes the observed allergic symptoms. A recent series of papers by Brostoff et al[80,81] and Paganelli et al[79] confirm the existence in food allergic patients of circulating immune complexes composed of food antigen and a variety of immunoglobulins including IgG, IgA, and IgE.

Matthews and Soothill[109] and Atherton et al[110] have demonstrated complement activation secondary to immune complex mediation in food allergic patients undergoing food

challenges with their allergenic foods. Minor, Tolber, and Frick[111] also found that immune complexes participate in delayed food allergy. May[112] has similarly demonstrated chronic high background blood levels of histamine in food-allergic patients.

5. TWO INTERACTING IMMUNE MECHANISMS EXPLAIN NON-IgE MEDIATED ALLERGIC RESPONSES

Two interacting immune mechanisms explain non-IgE mediated allergic reactions. The first mechanism concerns allergic symptoms caused by increased capillary permeability due to antigen-induced, immune complex-mediated phenomena, and relief of such symptoms by injecting precisely determined doses of antigen to beneficially alter antigen-antibody ratios and allow for more efficient clearing of these complexes. This is accomplished through interactions of immune complex-clearing systemic macrophages, antigen-stimulated skin macrophages, T cells, B cells, and various humoral products. Injected antigen interacting with macrophages, T cells, and B cells also stimulates B cells to produce specific IgG, thus increasing specific IgG levels to favorably alter the ratio of antigen to antibody in immune complex formation.

Secondly, injected antigens interacting with mast cell-bound IgE in the skin cause the release of histamine which can produce two opposing effects. Histamine causes symptoms by stimulating effector cells to "turn on" allergic symptoms. However, at known concentrations, histamine also quickly "turns off" further histamine release by mast cells and basophils, "turns off" IgE-forming B cells by stimulating T-cell secretion of histamine-induced suppressor factor, and stimulates and expands T suppressor populations.[85,86]

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Injected antigen interacting with macrophages, T cells, and B cells also stimulates B cells to produce specific IgG, thus increasing specific IgG levels to favorably alter the ratio of antigen and antibody in immune complex formation.

These two mechanisms are interdependent facets of a single system. Their operation is reflected in experimental evidence and clinical experiences from many laboratories and clinics. Resulting predictions can be tested by available laboratory and clinical techniques, and correlations can be made that place hitherto puzzling observations of responses to allergy and immunotherapy in the mainstream of current immunological understanding.

6. CELLULAR AND HUMORAL EFFECTORS OF THE PHASIC IMMUNE RESPONSE

The cellular systems (macrophages, mast cell-basophils, neutrophils, platelets, and lymphocytes) are inextricably interwoven with the humoral system to produce allergic responses. The humoral elements, including antibodies, endocrine and non-endocrine hormones, eicosanoids, plasma kinins and coagulation cascades as well as many other humoral participants, including neurotransmitters, are also integral parts of the same system.

The sequence of biochemical events that produce symptoms of allergy, for example food allergy, is: 1) food antigens combine with food antibodies to form immune complexes, 2) which trigger complement activation to produce anaphylatoxins, 3) which induce release of histamine and other mediators from mast cells and basophils, 4) which result in increased capillary permeability, edema, and allergic symptoms. It is chiefly by way of such edema that allergic symptoms can be initiated without the involvement of IgE and without the cellular destruction associated with full complement activation and neutrophil participation.

a. Role of Macrophages

Macrophages serve two functions in this process: clearing of immune complexes, and secretion of suppressor and helper factors.

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It is well-known that the rapidity with which immune complexes can be cleared from the circulation depends upon the integrity of the phagocytic cells of the blood and tissues. The macrophages of intact animals clear complexes rapidly. Animals with reticulo-endothelial blockade caused by injection of bentonite or carbon particles are unable to clear their circulation of immune complexes. The same is true of animals whose reticulo-endothelial cells are engorged with viruses or bacteria from overwhelming infection.[113,114]

Chronic or repeated showers of immune complexes in the circulation of humans also produce varying degrees of reticulo-endothelial blockade. The slower or more limited clearing of symptoms seen in some patients with multiple sensitivities indicates a temporary or prolonged overload on the phagocytic system.

Macrophages also participate in the initiation and regulation of immune responses[45] by secreting humoral factors, including some with helper and some with suppressor functions.[46,47] These substances are antigen-specific and genetically restricted.[47-49] Thus, for example, macrophages can secrete specific suppressor and helper factors for ovalbumin just as can ovalbumin-sensitive suppressor and helper T cells.

The symptoms seen in some patients with non-IgE mediated allergy are caused by: 1) transient showers of

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antigen-antibody complexes initiating partial complement activation, 2) which induce anaphylatoxin formation, 3) which leads to release of histamine and other mediators from mast cells and basophils, and 4) which results in allergic edema. The presence, severity, and duration of symptoms is, in part, a function of the level, size, and persistence of such complexes.[82]

Provocation and neutralization of symptoms result from alterations in blood and tissue levels of pathogenic complexes.[2,5] Circulating monocytes and fixed macrophages are important participants in these reactions through removal of immune complexes.[113,114]

When antigen is introduced into the skin, antigen-stimulated skin macrophages are the cells most intimately involved in secretion of antigen-specific helper and suppressor factors which can affect antibody formation and in turn alter circulating antigen-antibody ratios.[115-119] When T suppressor lymphocyte function becomes inadequate to control IgE-forming B cells, allergy results.[120-130] Injecting precisely chosen doses of specific antigens into the skin can stimulate and "train" skin macrophages to assume a greater portion of the needed suppressor function.[120-130]

b. Basophils and Mast Cells: Role of Histamine

Histamine released from mast cells and basophils by IgE and

non-IgE mechanisms can turn on immediate allergic symptoms by binding to H1 receptors on target cells such as bronchial smooth muscle (a proflammatory effect). At higher concentrations, histamine can also quickly turn off symptoms through a feedback loop to the H2 receptors on mast cells and basophils, stopping further histamine release (an anti-inflammatory effect).[85,86]

In addition, histamine has a delayed and prolonged effect on other cellular interactions. By binding to H2 receptors on T lymphocytes, neutrophils, and eosinophils, histamine modulates the function of these cells involved in delayed as well as immediate reactions.[87-92] After antigen injection into the skin, mast cell-released histamine in the skin can stimulate local T supresssor cells to release their Histamine-induced Suppressor Factor (HSF).[93] HSF traverses the circulation and suppresses distant helper T cells, thus turning off antibody synthesis by B cells, and altering circulating and cell-fixed antigen-antibody ratios.[91,94,95] Histamine levels are themselves modulated by histamine released from complement-stimulated neutrophils,[96] and histamine levels are regulated by a product of histamine degredation, imidazole acetic acid.[134]

Specific local concentrations of histamine are critical in determining which mode is operative. Histamine release from mast cells and from basophils recruited to the skin in

cutaneous basophil hypersensitivity is inhibited in vivo by locally released histamine in the concentration range of 10^{-6} to 10^{-4} M.[92] High levels of histamine are found in the blood of persons with food allergies.[97] Significant elevations in blood histamine levels[94] occur with subcutaneous injection of an allergenic food extract. These patterns reflect the high local histamine concentrations occuring transiently in the micro-environment around degranulating mast cells and basophils.[92]

In neutralization therapy, a dual therapeutic response occurs consisting of rapid relief in minutes or hours after each subcutaneous treatment injection, and increasing ability to tolerate exposures ("hyposensitization") to the antigen over weeks, months, and years. Rocklin et al[99] and Evans et al[131] have demonstrated that antigen-specific suppressor cells are induced by repeated injections of antigen. Decreased suppressor activity leads to clinical allergic sensitivity. Stimulation of increased suppressor activity and increased suppressor T cell populations account for much of the long-term improvement in allergic patients on immunotherapy.

Thus, it is well established that symptoms of allergy can be caused by histamine released from mast cells and basophils by both IgE and non-IgE mediated mechanisms. These symptoms can be quickly relieved by injecting a quantity of antigen which induces the release of the precise amount of histamine

required to turn off further histamine release. Maintenance treatment with these extracts repeatedly stimulates suppressor T cells to release HSF, further suppressing specific IgE antibody production. This effect of antigen on suppressor T cells can be direct or mediated by histamine or by stimulated macrophages. As discussed earlier, suppressor T cell populations are increased by repeated antigen injections. Finally, repeated antigen injections acting through macrophages, T cells, and B cells also stimulate increased specific IgG antibody production, favorably altering antigen-antibody ratios in immune complex interactions and diminishing the potential for complement activation and symptom induction.

c. Role of Lymphocytes

Minor, Tolber, and Frick[109] have reported that leucocyte migration inhibition factor (LIF) was frequently elevated in patients with delayed type food allergy. The presence of this lymphocyte-secreted product supports the fact that lymphocytes take part in delayed allergic reactions. They postulate that LIF release is a result of antigen-antibody complexes on the surface of lytmphocytes or neutrophils (Type III response).

May[97] reported a high nonspecific background leucocyte histamine release in food-sensitive patients. He suggested that these chronically high histamine blood levels can be

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explained by immune complexes on the surface of basophils. Circulating food antigen complexed with antibodies and attached to basophils induce a constant discharge of histamine from the basophils. It is evident from such observations that food antigen-induced, immune complex-mediated phenomena cause commonly encountered food allergy symptoms by several pathways, and that further study of these interacting pathways might well illuminate puzzling clinical observations.

The phenomena of intradermal provocation and neutralization is thus tied into the interactions of: 1)intradermally injected antigen, 2)antigen-processing macrophages in the skin, 3)T and B lymphocytes which come in contact with the antigen-stimulated macrophages or soluble factors to participate in signal transmissions, and 4)the subsequent T cell action of suppressing or stimulating B cell responses.[132] Langerhans cells themselves can be damaged by immune complex-activated complement and destroyed by killer T lymphocytes.[61,33] Thus, the regulators are themselves regulated.

Mast cell histamine release can participate in this series of interactions by increasing local capillary permeability to facilitate the movement of antibodies and cells into the site of the reaction. As local histamine levels rise, histamine can then terminate increased capillary permeability by

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turning off further histamine release through H2 receptors on mast cells and basophils. Histamine can also act by stimulting local T cells to release HSF and turn off IgE-forming B cells. Injected antigen can also act by increasing specific IgG levels to favorably alter the ratio of antigen and antibody in immune complex formation, and by stimulating and expanding T cell populations. If additional histamine release is required by the mast cells to accomplish their ends, these cells can recruit basophils to enter the reacting site and provide the additional histamine. All the individual facets of these multiple interactions are well documented and conform to the clinical phenomena observed in intradermal provocation and neutralization.

c. Role of Neutrophils

A major factor in food allergy disease process is the generation of an immune complex complement-consuming process which precipitates intravascular inflammatory events. These inflammatory events produce endothelial damage in various target organs. Inflammatory events can be the result of the action of one or a few cells. Complement activation by immune complexes can cause the aggregation of leukocytes through the action of the chemotactic factors of C3a and C5a.[136] Granulocytes are capable of causing both endothelial and interstitial injury. Neutrophils liberate superoxide radicals and other highly reactive oxidant byproducts of phagocytosis. The superoxide radical has been shown in

tissue culture to injure endothelial cells.[137] In addition, neutrophils produce neutral and acid proteases[138] that destroy structural proteins such as collagen elastin and the adhesive glycoprotein fibronectin,[139] a necessity for ordering the interstitial topography of cells and connective tissue.[140] These proteases also cleave fibrinogen, the Hageman factor, complement, and other plasma proteins.

Thus, neutrophil proteases can both destroy intersitial architecture and permit local amplification of tissue injury by activating plasma precursors that ultimately result in further leukocyte aggregation and intravascular coagulation.[141]

Using the lung as a model target organ for immune tissue damage, it has been demonstrated that the tissues' natural defense against damage induced by superoxide radicals,[142] alpha 1 antitrypsin from plasma, can be inactivated by the superoxide radical or by oxygen leaking into damaged tissue.[143]

The sequence of events is as follows: 1)circulating immune complexes lodge in a target organ, 2) which results in local activation of complement, 3) which generates C5a and C3a, and 4) which cause leukocyte aggregation in the target organ. As in the case of the heart or brain, very small numbers of leukocytes could produce wide-ranging symptoms. Aggregated

neutrophils injure endothelial cells by the generation of toxic oxygen radicals. The neutrophil liberates proteases that destroy structural proteins such as collagen, elastin, and fibronectin as well as promote further local inflammatory changes by proteolysis of circulating plasma proteins such as the Hageman factor, fibrinogen, and complement. At the same time, protective antiproteases are inactivated by oxygen radicals released from immune effector cells.

Endothelial damage caused by small numbers of inflammation cells can cause wide-ranging symptoms with little or no histologically definable target organ damage. For example, microscopic inflammatory events in the heart can cause fatal arrythmias with little or no detectable histologic changes. Microscopic inflammatory events in the brain can cause wide-spread symptoms of behavioral changes and epilepsy with little or no detectable histologic changes.[144]

Thus, reversible microvascular inflamatory events caused by small numbers of neutrophils are most probably the basis of many antigen-associated allergies, for example to foods.

(no page 72)

G. WHY DO INTRADERMAL AND SUBLINGUAL ADMINISTRATION OF ANTIGEN PROVOKE AND NEUTRALIZE SYMPTOMS?

The epidermis (and sublingual tissue) is one of the most immunologically active organs in the body. It contains most if not all of the cells known to be functional in immune response. The epidermis is the first line of defense in bacterial, fungal, and parasitic infestation. Complement-consuming dermatopathologic processes induced by immune complex formation have been documented as being caused by the inhalation of aerosolized petrochemicals from copying machines,[145] various petrochemicals used in plastics,[147] and foods.[146] Mediators originating from immunologic reactions in the skin can quickly become systemic due to the skin's vascular structure, making the skin the ideal organ for testing overall immune reactivity.

The epidermis (and sublingual tissue) contains a meshwork of fixed macrophages, the Langerhans cells, with long contracting cytoplasmic extensions. These cells contain Ia antigens[48] and are very active antigen-processing cells. Just below the basement membrane of the epidermis is a rich capillary network. Materials injected intradermally reach this network and absorb very rapidly by comparison with materials injected into subcutaneous fat or muscle tissue[150] where macrophages and capillaries are less concentrated.

Fixed macrophages in the skin are therefore well-equipped and well-situated to quickly detect and process specific antigens injected intradermally and to secrete specific modulating humoral factors which can quickly find their way to the systemic circulation. Once in the circulation, they can traverse the entire body in approximately 15 seconds. These factors thus can quickly suppress or stimulate specific antibody secreting B cells in the gastrointestinal tract, central nervous system, and other distant regions.

Langerhans cells in the epidermis can migrate to the dermis and also through lymphatic channels to regional nodes.[148,116] In nodes they are capable of transmitting signals to many T and B cells. They are known to function in contact dermatitis[117] as well as in herpes simplex virus infections, responses to intradermally injected PPD,[116] DNFB,[118] various haptens, and other allergens.[119]

While macrophages in the subcutaneous tissues perform similar functions, those in the epidermis do so more rapidly and vigorously. This fits observed clinical phenomena, including more rapid and vigorous symptom provocation and neutralization with intradermal as compared to subcutaneous antigen administration. Intradermal injection of antigen characteristically induces marked symptom provocation or neutralization beginning within three to four minutes and reaching peak effect in ten minutes. Sublingual

administration works as fast as and by the same mechanisms as intradermal injections. Subcutaneous administration usually induces such changes more gradually over a period of thirty minutes.

III. FLAWS IN THE OPPONENTS' CASE AGAINST PROVOCATION/NEUTRALIZATION

The opponents' case against provocation/neutralization techniques is flawed and scientifically unsound. In addition, the studies supporting the efficacy of traditional techniques are also flawed and fail to demonstrate their efficacy as an alternative to provocation/neutralization. This section will contain:

A. Critique of the opponents' case against provocation/neutralization

B. Representative flaws in the science supporting the clinical techniques of conventional allergists

A. CRITIQUE OF THE OPPONENTS' CASE AGAINST PROVOCATION/NEUTRALIZATION

The careful reviewer of these comments may note an information gap between the NCHCT 1981 Evaluations, upon which the proposed HCFA action is based, and the empirical and scientific justification for the efficacy and safety of provocation/neutralization outlined in the preceeding sections of these Comments. The gap is real. The NCHCT Evaluations cite only one of the 12 laboratory studies supporting provocation/neutralization. They do not even attempt to examine the immunological mechanisms behind these techniques. The latest critical bibliographic entry for the intradermal/subcutaneous NCHCT report is dated 1976, and the latest citation in support of provocation/neutralization is dated 1978. For the sublingual report, the latest critical citation is 1980, and the latest supportive one is 1980. Finally, both NCHCT reports were issued in 1981, before 3 of the strongest double-blind studies[3,4,5] in support of provocation/neutralization had been published. Yet no attempt has been made to incorporate the new data into HCFA's rule-making.

NCHTC references criticizing provocation/neutralization techniques lack scientific credibility. In support of its

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criticisms of the intradermal/subcutaneous modalities, NCHTC offers: 2 abstracted reports (one 7 years old, the other 12 years old, and neither have been followed up by full-length scientific articles); one letter to the editor (12 years old and never followed up by a full-length scientific article); and one uncontrolled study which appeared as a 1-page article in the Archives of Otolaryngology. The other references cited are favorable. For the sublingual modalities, the report cites: the same 12-year-old abstract; a seriously flawed 9-year-old committee report; and a more recent study whose author has acknowledged " many inadequacies in the study".[157] The other references cited were favorable.

Kailen and Collier(1971)[151]. This study is a 12-year-old, 3-paragraph letter to the editor. The authors are still alive yet the letter has never been followed up by a full-length article in a refereed journal. The only possible reason for this is that the study was not good enough. Nothing more need be said about it.

Hirsch et al(1981)[152]. This study has been roundly criticized by pediatric, internal medicine, and otolaryngologic allergists as well as by immunologists familiar with provocation/neutralization techniques. Among the more obvious errors in this study is its poor structure. The individuals administering the test had less than 4 hours of didactic training in the technique (physicians practicing

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this method are usually trained through graduate or continuing education courses). In addition, the observers' objectivity has been questioned by a variety of investigators.

The only parameter identified by critics as significant is the so-called "Symptoms Medication Index". Symptoms are very subjective and difficult to assess. Most practitioners using provocation/neutralization techniques use far fewer prescription medications than practitioners of conventional build-up immunotherapy. Therefore, the information derived through this index must be considered unreliable.

The worst aspect of this study is that although the investigators measured certain biochemical parameters in an attempt to correlate them with the clinical findings, they never measured any of the immunological factors known to effect neutralization in immunotherapy. Any allergist who is current with the immunology literature of the last decade knows that effective immunotherapy is characterized by the generation of antigen-specific suppressor cells. The investigators in this study never bothered to examine suppressor cell activity.

In summary, this study was conducted by people who were unfamiliar with the technique being evaluated. The provocation/neutralization techniques were performed in a

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manner inconsistent with current clinical practice. The only statistically significant finding is based solely on unreliable subjective observations. Finally, the investigators never attempted to measure obvious objective immunological parameters which would have truly established the efficacy or inefficacy of the techniques.

The remaining studies attempt to assess provocation testing. The critiques of these critiques are expanded in Appendix A, excerpted from a paper prepared by Dr. David S. King, M.D. of the Department of Psychiatry, University of California, San Fransico Medical Center. Dr. King examines the concepts of reliability and validity as well as the proper statistical techniques by which to assess them. He then reviews the research purporting to evaluate provocation testing methods.

In reviewing this critical literature, Dr. King includes the 4 studies upon which the American Academy of Allergy based its position statement (issued May 1981) branding subcutaneous and sublingual testing as ineffective. These same studies also form the basis for the 1980 American Academy of Allergy communication to the NCHCT declaring provocation techniques to be unproven and therefore "experimental". Since NCHCT and HCFA, by adoption of NCHCT's positions, rely so heavily on the American Academy of Allergy's conclusions, reviewers should give their very deliberate and detailed attention to these critiques.

Dr. King's review finds that serious flaws in study design and analysis are common in the critical literature. These shortcomings include: 1) comparison of subjects' responses to antigen and placebo without verification of their having specific sensitivities to the antigens administered, 2) failure to incorporate double-blind procedures with placebo controls in the study design or execution, 3) failure to analyze study results statistically, 4) improper statistical analysis, and 5) in some cases, re-analysis of the original data, seriously affecting the conclusions of the study.

Bronsky et al(1971)153. This is a 12-year-old abstract, the authors of which are still alive. The data was never presented in a full-length report which could be analyzed by unbiased observers. Since no placebo was given, double blinding seems unlikely. The design of the study does not rule out the possibility that the children were not sensitive to some or all of the foods tested. It is also not known whether the children were medicated.

Caplin, I.(1973)[154]. This report describes a study in which subjects were challenged sublingually with five standard foods and also placebo. Each antigen was challenged on two separate occasions. Although the results are reported as statistically insignificant, the committee's statistical consultant stated, "because of the design of this study one

must be careful of drawing any conclusions". Despite this warning, the committee reached the conclusion that the "test doesn't discriminate between control and food extracts". The protocol called for substantially more patients than were actually tested and even fewer received feeding tests. Additionally, the data on 17 of the patients was rejected without explanation. It is not stated whether this attrition occurred before or after the double-blind code was broken. Fifty percent of the remaining data was rejected for analysis because of "faulty protocol". An additional confounding factor in data analysis is the fact that most of the investigators were unfamiliar with the techniques used. Of the 10 physicians participating, only 3 had had previous experience with sublingual provocation.

In summary, this study is seriously flawed by its poor design and irregular handling of the data. The investigators were inexperienced, and the data was manipulated in an unexplained fashion. Despite the warning by its statistician, the committee chose to form a conclusion based on this study. (Surprisingly, this data was used in the 1974 follow-up report discussed below.) The numerous methodological and analytical flaws in this study have been extensively noted and critiqued.

Crawford et al(1976)[155]. This is a 7-year-old abstract which was never followed up by a full-length article. Since this

study has only been published in abstract form, it is impossible to evaluate the materials, methods, or data analysis. It is curious that the scientists who were charged with assessing a technique which has been in continuous use for close to 40 years chose to cite studies whose data is unavailable for critical analysis by unbiased observers.

Draper, L.W.(1972)[156]. This is a 1-page article which reports the findings of a study for which lack of proper controls renders clear interpretation of the data impossible. No statistical tests were reported. The absence of blinding and the failure to incorporate placebos in the design both seriously detract from the study. Since the intradermal tests were given only once, nothing can be said regarding their reliability.

Breneman et al(1974)158. This report contains the 1973 data, mentioned above, as well as information on additional patients. The placebo response rate as calculated from the data was 50%. This is inordinately high and leaves the objectivity of this study in serious doubt. In addition, as in the 1973 report, there is unexplained attrition of patients in this study. The protocol called for 30 patients, but the data on only 20 patients are included in this analysis. No mention is made of precautions taken to insure blind conditions. The data are presented in summary form in tables, with no statistical analysis provided.

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In summary, this report relies on seriously questionable data to form the conclusion that the technique evaluated was not effective. It is curious that the investigators were apparently oblivious to the obvious flaws in their experimental design and data analysis.

Lehman, C.(1980)[157]. This study claims to assess the efficacy of sublingual food allergy provocation. The investigator attempts to quantitate changes in the edema and swelling of the nasal mucosa as induced by specific food antigens and placebo. The major design error in this study is cited by the author himself, "the nasalmucosal edema is constantly changing from one 10-minute interval to another, independently of placing food antigens under the tongue".

This choice of an inherently non-stable endpoint compromises any assessment based on that endpoint. Another design error is that patients were not required to be sensitive to specific antigens to be tested. Subjects were supposed to have a "history of food allergy or other demonstration of food allergy". However, according to the reported data, clinical sensitivity was suspected for only 11 of the 60 antigens which were challenged. There is no reason to expect to provoke symptoms with an antigen to which the subject is not sensitive. No statistical analysis was reported.

In summary, this study used an unreliable endpoint to test

the reaction of poorly selected patients against antigens to which they were not sensitive. In fairness to the author, it should be noted that he acknowledged "many inadequacies in the study".

B. REPRESENTATIVE FLAWS IN THE SCIENCE SUPPORTING THE CLINICAL TECHNIQUES OF CONVENTIONAL ALLERGISTS

Although some good science is being performed by immunologists associated with classical allergists, most of the double-blind, placebo-controlled clinical trials by which they attempt to establish the efficacy of their treatment modalities are seriously flawed. The data from these studies is questionable, and the conclusions drawn by the authors are consequently unsound. An analysis of some representative studies follows.

Conners et al (1976)[160]. This article is one of the major studies frequently cited by the conventional allergists in support of their methods. This Nutrition Foundation-supported study purports to be a controlled double-blind experiment although its conclusions have been severely criticized. The "control" conditions of the challenge diet and "placebo-controlled" challenge trials are invalid and misleading. In this study of allergic children, milk, corn, wheat, eggs, chocolate (all common allergy-producing foods) were used as inert placebo. In addition, the challenge dose of food coloring constituted as little as 1/12 of the real-world exposure of children to food coloring additives. The children were evaluated weekly for evidence of allergic responses, a schedule that completely ignored the wide diversity of reaction times among allergic

children. It is doubtful that the aberrant behavior of even a single child would become apparent on such an observation schedule.

This study clearly demonstrates the lack of scientific training and bias of the investigators. That it was published as the lead article in Pediatrics is a telling commentary on the peer reviewers.

Norman and Lichtenstein (1978)[163]. This study purported to show clinical and immunological specificity of therapy in a group of patients with rhinitis caused by ragweed and grass pollen. The investigators used ragweed antigen only. They showed an increase in IgG "blocking antibodies" and significantly reduced symptom response scores to ragweed without a corresponding reduction in the symptom response to grass pollen or production of IgG in these patients. This paper is widely cited as establishing the efficacy of conventional build-up immunotherapy for pollen sensitivity.

The major flaw is that the investigators were measuring parameters which had nothing to do with clinical efficacy. The concept that IgG "blocking antibodies" effect clinical responses in patients treated with specific antigen immunotherapy had been obsolete for at least 3 years at the time of publication. Worse yet, this concept is still cited in text books used by conventional allergist today as the

reason for symptomatic improvement, even though it has been proven unsound for more than a decade. In addition to this parameter, the authors used a "Symptom Medication Index", which is highly subjective and vulnerable to investigator and patient bias. Of interest, too, is the investigators' failure to consider whether foods were a major factor in their subjects' symptoms.

Conventional allergists, in the main, lack sufficient scientific understanding of basic immunological principles and practices to perform credible clinical trials. In addition, the safety of conventional allergy treatment has been questioned. In one report,[165] 5 of 19 patients who developed polyarteritis nodosa received conventional immunotherapy. No such finding has ever been reported in patients receiving provocation/neutralization therapy.

Thus, based on the design and performance of the "classical studies" cited by conventional allergists as proof, it is far from clear that conventional allergy testing and treatment is either safe or effective.

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37TH ACA (AMERICAN COLLEGE OF ALLERGISTS) SCIENTIFIC CONGRESS, WASHINGTON, D.C., USA, APRIL 4-8, 1981. ANN ALLERGY 47 (2). 1981. 129. CODEN: ANAEA

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23011227
CHEMICAL SENSITIVITY RELATED TO PESTICIDE OVER EXPOSURE.
REA W J; KAHN A A; JOHNSON A R; FENYVES E J; SMILEY R E; SPRAGUE D E; EDGAR R T
DALLAS, TEXAS.
37TH ACA (AMERICAN COLLEGE OF ALLERGISTS) SCIENTIFIC CONGRESS, WASHINGTON, D.C., USA, APRIL 4-8, 1981. ANN ALLERGY 47 (2). 1981. 124. CODEN: ANAEA

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23011226
THE EFFECTS OF ENVIRONMENTAL CONTROL AND FASTING ON HEAD ACHES.
GREENBERG M R; REA W J; STROUD R M
DALLAS, TEXAS.
37TH ACA (AMERICAN COLLEGE OF ALLERGISTS) SCIENTIFIC CONGRESS, WASHINGTON, D.C., USA, APRIL 4-8, 1981. ANN ALLERGY 47 (2). 1981. 124. CODEN: ANAEA

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ACUTE LARYNGEAL EDEMA.
REA W J
DALLAS, TEXAS.
37TH ACA (AMERICAN COLLEGE OF ALLERGISTS) SCIENTIFIC CONGRESS,

W SHINGTON, D.C., USA, APRIL 4-8, 1981. ANN ALLERGY 47 (2). 1981. 119.
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COMPREHENSIVE ENVIRONMENTAL CONTROL AND ITS EFFECT ON RHEUMATOID ARTHRITIS

STROUD R M; KROKER G ... REA W J; SMILEY R E; ... ERG H; CARROLL P H;
BULLOCK T M; MARSHALL R ...; RANDOLPH T G
UNIV. ALA.
MEETING OF THE AMERICAN RHEUMATISM ASSOCIATION, CENTRAL REGION, CHICAGO, ILL., USA, NOV. 7, 1980. CLIN RES 28 (4). 1980. 791A. CODEN: CLREA

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File55:BIOSIS Previews - 1977 thru 1980
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AIR POLLUTION ANALYSIS USED IN OPERATING AN ENVIRONMENTAL CONTROL UNIT
EDGAR R T; FENYVES E J; REA W J
SUITE E 305, 12110 WEBB CHAPEL RD., DALLAS, TEX. 75234, USA.
ANN ALLERGY 42 (3). 1979. 166-173. CODEN: ANAEA

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67031938

FOOD AND CHEMICAL SUSCEPTIBILITY AFTER ENVIRONMENTAL CHEMICAL OVER EXPOSURE CASE HISTORIES
REA W J; BELL I R; SUITS C W; SMILEY R E
SUITE E305, 12110 WEBB CHAPEL RD., DALLAS, TEX. 75234, USA.
ANN ALLERGY 41 (2). 1978 101-110. CODEN: ANAEA

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ENVIRONMENTALLY TRIG..RED CARDIAC DISEASE
REA W J
8345 WALNUT HILL LANE, SUITE 240, DALLAS, TEX. 75231, USA.
ANN ALLERGY 40 (4). 1978 243-251. CODEN: ANAEA

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64024295
ENVIRONMENTALLY TRIGGERED SMALL VESSEL VASCULITIS
REA W J
ANN ALLERGY 38 (4). 1977 245-251. CODEN: ANAEA

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63005822
ENVIRONMENTALLY TRIGGERED THROMBO PHLEBITIS
REA W J
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77075477
ECOLOGIC ORIENTATION IN THORACIC AND CARDIO VASCULAR SURGERY
REA W J
DICKEY, LAWRENCE D. (ED.). CLINICAL ECOLOGY. XVI+807P. ILLUS. CHARLES C THOMAS PUBLISHER: SPRINGFIELD, ILL., USA. ISBN 0-398-03409-5. 1976 650-661 CODEN: 05358

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77075423
RELATIONSHIP OF FOOD AND CHEMICAL SENSITIVITIES TO ACUTE RESPIRATORY FAILURE
REA W J
DICKEY, LAWRENCE D. (ED.). CLINICAL ECOLOGY. XVI+807P. ILLUS. CHARLES C THOMAS PUBLISHER: SPRINGFIELD, ILL., USA. ISBN 0-398-03409-5. 1976 180-183 CODEN: 05358

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CROSS LINKED HEPARIN BINDING OF A MEMBRANE OXYGENATOR SYSTEM
EBERLE J W; MANTON J R; MEALS C R; WHITLEY D E; REA W J
J BIOMED MATER RES 7 (2). 1973 145-153. CODEN: JBMRB

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56017058
HYPER ALIMENTATION IN PULMONARY SURGERY
REA W J; ECKER R R; EBERLE J W; SUGG W L
CHEST 62 ((5 PT 1)). 1972 577-580. CODEN: CHETB

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55029919
ZINC IN CARDIAC SURGERY
REA W J; ECKER R R; SUGG W L
J SURG RES 12 (3). 1972 164-167. CODEN: JSGRA

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55021777
DIAZEPAM AS AN ADJUNCT TO BRONCHOSCOPY
ECKER R R; SUGG W L; REA W J
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73015673
MANAGEMENT OF INJURIES OF THE INNOMINATE AND PROXIMAL LEFT COMMON CAROTID ARTERIES
ECKER R R; DICKINSON W E; SUGG W L; REA W J
J THORAC CARDIOVASC SURG 64 (4). 1972 618-624 CODEN: JTCSA

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73009410
LONG-TERM MEMBRANE OXYGENATION WITHOUT SYSTEMIC HEPARINIZATION
REA W J; WHITLEY D; EBERLE J W
AM SOC ARTIF INTERN ORGANS. TRANSACTIONS AMERICAN SOCIETY FOR ARTIFICIAL INTERNAL ORGANS, VOL. 18. SEATTLE, WASHINGTON, APRIL 17-18, 1972. XII+634P. ILLUS. AMERICAN SOCIETY FOR ARTIFICIAL INTERNAL ORGANS: WASHINGTON, D.C., U.S.A. 1972 316-320 CODEN: 02735

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53059137
CONTROL OF INTRACTABLE VENTRICULAR TACHY CARDIA BY CORONARY RE

VASCULARIZATION
ECKER R R; MULLINS C B; GRAMMER J C; REA W J; ATKINS J M
CIRCULATION 44 (4). 1971 666-670. CODEN: CIRCA

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72096498
IMPORTANCE OF VENTRICULAR FUNCTION IN PREDICTING OPERATIVE MORTALITY IN

...RONARY BYPASS GRAFTS
REA W J; ECKER R R; ...JLLINS C B; SHAPIRO W; POMBO J F; SUGG W L
CIRC SUPPL 44 (4). 1971 II-215 CODEN: CISUA

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72084252
HYPER ALIMENTATION IN CHEST SURGERY
REA W J
COWAN, GEORGE S. M. JR. AND WALTER L. SCHEETZ (ED.). INTRAVENOUS HYPERALIMENTATION. XXIII+225P. ILLUS. LEA & FEBIGER: PHILADELPHIA, PA., U.S.A. 1972 176-184 CODEN: 02504

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GAS TRANSFER IN A HEPARINIZED MEMBRANE OXYGENATOR
REA W J; EBERLE J W; WATSON J T; ECKER R R; SUGG W L
SURG FORUM 22. 1971 188-190 CODEN: SUFOA

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71073996
INTRA VENOUS HYPER OSMOLAR ALIMENTATION
REA W J; WYRICK W J JR; MCCLELLAND R N; WEBB W R
ARCH SURG 100 (4). 1970 393-398 CODEN: ARSUA

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NECROTIZING FASCIITIS
WYRICK W J JR; REA W J
REV SURG 28 (2). 1971 143 CODEN: RESUA

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PETER ORRIS, M.D.

I. QUALIFICATIONS

Dr. Orris is a practicing physician, specializing in internal medicine. His practice is based in Chicago, Illinois where he is a member of the Division of Occupational Medicine at Cook County Hospital, Southwest Physicians Limited in Chicago, and part of NIOSH Region V. His curriculum vitae is attached. He is currently involved in a research study of truck drivers in the St. Louis, Missouri area through the Teamsters Central States Fund for potential exposure to dioxin at Times Beach and a study through the Veterans Administration of Wisconsin in surveying approximately 61 veterans twin pairs wherein one of the twins served in Vietnam and the other did not. He is participating in these separate studies of potential dioxin-related health effects from the clinician's point of view in preparing an initial survey questionaire to be followed by examinations. His clinical practice has involved the hands-on diagnosis and treatment of veterans who had served in Vietnam.

II. SUBJECT MATTER

The subject matter of Dr. Orris' testimony will include his clinical evaluation of Vietnam veterans in his own practice, a methodology for the assessment of TCDD intoxication and the diagnosis of symptoms and/or syndromes of TCDD intoxication. He will testify that the diagnosis of TCDD intoxication rests upon three categories of evidence, i.e. a history of exposure, a clinical syndrome consistent with that exposure history and chronologically appropriate, and laboratory evidence consistent with the exposure history and clinical syndrome. His testimony will finally include a review of the representative plaintiffs' medical records and clinical evaluations.

III. SCIENTIFIC PRINCIPLES

See General Statement of Scientific Principles and Assumed Facts Attached.

IV. SUBSTANCE OF OPINIONS

A. Dioxins are extremely toxic particularly 2,3,7,8-TCDD.
B. That TCDD is extremely toxic at extremely low levels.
C. That TCDD is acneogenic.
D. That TCDD is teratogenic.
E. That TCDD is fetotoxic.
F. That TCDD is capable of transmitting genetic damage.
G. That TCDD is capable of causing liver dysfunction.
H. That TCDD can cause peripheral neuropathy.
I. That TCDD is carcinogenic, specifically causing soft tissue sarcomas and lymphomas.
J. That TCDD as a carcinegen does not affect one organ, but many.
K. That additional sites of cancer may be caused by exposure to TCDD.
L. That TCDD may cause neuropsychiatric disorders.

V. GROUNDS FOR OPINIONS

A. General

The bases or grounds for such facts and opinions include Dr. Orris' educational and professional experience; personal research; review of the applicable medical and scientific literature; and a review of the medical records and/or data of the representative plaintiffs.

B. Specific

For several of the opinions articulated above, Dr. Orris will rely in part on the following references:

1. Van Miller, J. T., Lalich and Allen, 1977, Increased incidence of Neoplasm in Rats Exposed to Low Levels of 2,3,7,8-tetrachlorodibenzo-p-dioxin, Chemosphere 6(9, 10), 537-544 and 625-632.
Kociban, R. M., Keyes, and Beyer, 1978, Results of a two-year Chronic Toxicity and Oncogenicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin in Rats, Toxicology and Applied Pharmacology, 46 (2): 279-303.

Esposito, M. P., Tiernan and Dryden. 1980. Dioxins. Prepared for industrial pollution control division, U.S. EPA, Cincinnati, Ohio Contract Nos. 68-03-2577, 68-03-2659, and 68-03-2579. EPA 600/2-80-197.
The EPA Advisory Committee and Criteria Documents.

The additional specific references for the specific opinions articulated are being compiled by Dr. Orris but as of this submission, because of the requirements of his clinical practice, has been unable to compile the entire list of references but he shall forward those references within two weeks.

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CURRICULUM VITAE

November 18, 1983

NAME	Peter Orris	
ADDRESS & PHONE	Residence: 5205 South Kenwood Chicago, Illinois 60615 (312) 752-7680	Business: Division of Occupational Medicine Cook County Hospital 720 S. Wolcott Chicago, Ill. 60612 (312) 633-5310 NIOSH Region V. 300 S. Wacker, Chicago, Ill. 60606 (312)886-3651 Southwest Physicians Ltd. 3214 W. 63 Street Chicago, Illinois 60629 (312) 434-0556
BIRTHDATE	October 7, 1945	
BIRTHPLACE	Los Angeles, California	

EDUCATION

Undergraduate	June, 1967	Bachelor of Arts (B.A.) Harvard College Cambridge, Massachusetts
Graduate	June, 1970	Master of Public Health (M.P.H.) Yale University New Haven, Connecticut
	June, 1975	Doctor of Medicine (M.D.) Chicago Medical School Chicago, Illinois
Post Graduate	1975-1978	Internal Medicine Residency Cook County Hospital Chicago, Illinois
	1977-1979	Occupational Medicine Residency Cook County Hospital Chicago, Illinois
Additional	July, 1965	Bio-medical Electronics Harvard University Cambridge, Massachusetts

1967-1968	Advanced Electrical Circuit Theory Department of Engineering and Applied Physics Harvard University Cambridge, Massachusetts
January, 1979	UICC/ILO System of Radiographic Evaluation of Pneumocconiosis NIOSH approved American College Chest Physicians Continuing Medical Education Course.

CERTIFICATION AND LICENSES

1979	Diplomat, American Board of Preventive Medicine in Occupational Medicine
1976	State of Illinois, Physician and Surgeon, #36-53014

CURRENT EMPLOYMENT

July, 1979-	Attending Physician, Divisions of General and Occupational Medicine Department of Medicine Cook County Hospital Chicago, Illinois

Responsibilities include:

1) Internal Medicine Housestaff supervision and direct patient care in the out-patient clinic and on a general medicine ward service.

2) Occupational Medicine housestaff supervision and direct patient care on the inpatient consultation service and in the outpatient clinic.

3) Didactic sessions with the housestaff on both Internal and Occupational Medicine topics.

4) Clinical research in Occupational Medicine.

5) Supervision of the Epidemiologic Research of the Occupational Medicine Housestaff.

July, 1980- Medical Officer,
Region V
National Institute For
Occupational Safety
and Health
U.S. Public Health Service
Chicago, Illinois

Responsibilities include:

1) Conducting epidemiologic studies to evaluate industrial health hazards in the States of Ohio, Indiana, Illinois, Michigan, Wisconsin, and Minnesota.

2) Providing Occupational Medical consultative services to the medical community.

3) Lecturing management, labor, and medical groups on Occupational Health topics as requested.

ACADEMIC APPOINTMENTS

Department of Preventive
Medicine
Abraham Lincoln School of
Medicine
University of Illinois
Chicago, Illinois

1975-1980 Instructor
1980- Lecturer

Department of Community
Health and Preventive
Medicine
School of Medicine
Northwestern University
Chicago, Illinois

1979-1981 Associate
1981- Assistant Professor, Clinical

School of Public Health
University of Illinois
Chicago, Illinois

1983- Lecturer

HOSPITAL STAFF APPOINTMENTS

1979- Dept. of Internal Medicine
Cook County Hospital
Chicago, Illinois

1982-	Dept. of Internal Medicine Mount Sinai Hospital Chicago, Illinois
1983-	Dept. of Internal Medicine Mercy Hospital and Medical Center Chicago, Illinois

OCCUPATIONAL MEDICAL CONSULTANT TO:

Occupational Health Program of
Mercy Hospital and Medical Center
Miles Laboratories, Inc.
H. Kramer and Company
Industrial Medical Program of Mt.
Sinai Hospital

TEACHING OF UNDERGRADUATE MEDICAL COURSES

1977	The Epidemiology of Cardiovascular Disease University of Illinois, Abraham Lincoln School of Medicine.
1978	International Health Care Systems University of Illinois, Abraham Lincoln School of Medicine.
1980-1983	International Comparison of Health Care Systems Northwestern University Medical School
1981,1982	Occupational Health Northwestern University Medical School.

PAST EMPLOYMENT

1966-1967	Research Assistant to Dr. David T. Denhardt Dept. of Biology Harvard University Cambridge, Massachusetts
1967-1968	Research Assistant to Dr. J. A. Hobson Dept. of Psychiatry Harvard Medical School Boston, Massachusetts

1970	Administrative Intern Hill Health Center New Haven, Connecticut
1970-1982	Editorial Consultant Academy Professional Services New York, N.Y.
1971-1972	Nurse Technician Trauma Unit Cook County Hospital
1972-1975	Research Assistant Division of Emergency Medical Services Illinois Dept. of Health Chicago, Illinois
1979-1980	Attending Physician Div. of Emergency Medicine Cook County Hospital Chicago, Illinois
1979-1980	Medical Director HMO Feasibility Study Southeast Health Plan Chicago, Illinois.

BIBLIOGRAPHY

Orris, P., Daniels, W., Health Hazard Report 80-201 Health Effects of 1,1,1, Trichloroethane on Spray Can Assembly Employees U.S. Department of Health and Human Services, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, Cincinnati, Feb. 1980

Orris, P.: Unjustified Conclusion?(Letter) Journal of Occupational Medicine, Vol. 23, No. 1, Jan. 1981, p.7.

Edmonds, L., McQuilkin, S., Orris, P., Daniels, W. Health Hazard Report 80-058-874, An Evaluation of Potential Abortifactants At A Plant Producing Machine Tools Department of Health and Human Services, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, Cincinnati, May, 1981.

Orris, P., Daniels, W., Health Hazard Report 81-048-969 An Evaluation of Possible Carcinogenic Effects of Aromatic Hydrocarbons U.S. Department of Health and Human Services, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, Cincinnati, October 1981

Orris, P., Daniels, W., Health Hazard Report 80-244-992 Health Hazards of Diatomacious Earth and Phosphoric Acid at a Manufacturing Plant in Chicago U.S. Department of Health and Human Services, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, Cincinnati, Ohio, November, 1981

Orris, P., Daniels, W., Health Hazard Report 80-025-989 Health Effects of Low Dose Sulfuric Acid U.S. Department of Health and Human Services, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, Cincinnati, Ohio, November, 1981

Orris, P., Almaguer, D., Health Hazard 81-185-1007 Health Effects of a Spray Paint and Shot Blast Process U.S. Department of Health and Human Services, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, Cincinnalti, Ohio, November, 1981

Orris, P. Daniels, W., Health Hazard Report 81-064-1035, Polychlorinated Biphenyl Exposure to Electrical Workers in a Steel Mill, U. S. Department of Health and Human Services, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, Cincinnati, Ohio, January 1982

Orris, P. Health Hazard Report 80-235-1056, Cancer Mortality of Electrical Workers in a Steel Rolling Mill, U. S. Department of Health and Human Services, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, Cincinnati, Ohio, March 1982

Orris, P. Almaguer, D. Kramkowski, R. Health Hazard Report 81-128-1107, Low Dose TDI Exposure in a Foam Seat Manufacturing Process, U. S. Department of Health and Human Services, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, Cincinnati, Ohio, May 1982

Kahn, H.S., Orris, P., The Emerging Role of Salaried Physicians: An Organizational Proposal Journal of Public Health Policy, Vol. 3, No. 3, 1982

Orris, P. Kennedy, M.J. Guerriero, J. Hessl, S.M. Hryhorczuk, D.O. and Hoffman, D. Activities Of An Employer Independent Occupational Medicine Clinic American Journal of Public Health, Vol. 72, No. 10, October, 1982

Forum Monograph, Academy Professional Information Services, Inc. New York, N.Y. 982

Orris, P. Almaguer, D. Krankowski, R. Health Hazard Report 82-054-1194, Low Dose Solvent Exposure In A Small Engine Manufacturing Plant, U. S. Department of Health and Human Services, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, Cincinnati, Ohio, Sept. 1982

Fagan, K. Orris, P. & Daniels, W. Health Hazard Report 81-299-1201, Low Dose Carbon Monoxide Exposure in a Steel Mill, U. S. Department of Health and Human Services, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, Cincinnati, Ohio, Oct. 1982

Orris, P. Daniels, W. Health Hazard Report 81-317-1202, Health Effects of Oil Mist Exposure In A Machine Shop, U. S. Department of Health and Human Services, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, Cincinnati, Ohio, Oct. 1982

Orris, P. Baron, S. Occupational Medicine: A Role for the Primary Care Physician, Hospital Practice, Vol. 18, No. 3, March, 1983.

Orris, P. Daniels, W. Health Hazard Report 80-112-1261, Health Effects of Iron Oxide Exposure in A Steel Tubing Mill, U. S. Department of Health and Human Services, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, Cincinnati, Ohio, Feb. 1983

Orris, P. Cone, J, Dozier, E., McQuilkin, S. Health Hazard Report 80-096-1359, Health Effects of Vanadium Pentoxide In Thermal Battery Manufacture, U. S. Department of Health and Human Services, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, Cincinnati, Ohio, Aug. 1983

Orris, P. Health Hazard Report 82-239-1355, Evaluation of a Suspected Cancer Excess in an Electrical Coil Manufacturing Department, U. S. Department of Health and Human Services, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, Cincinnati, Ohio, Aug. 1983

Layon, J. Idris, A. Narzynski, M. Sherer, R. Brauner, D. Patch, O. McCulley, D. and [illegible]ris, P. Impaired Immunologic Function In Hospitalized Intravenous Drug Abusers, Archives of Internal Medicine, Accepted for publication November, 1983.

PRESENTED PAPERS

OCTOBER, 1975	Orris, P., Sheaf, L., Boyd, D., Freeland, J., & Zydlow, S. Mobile Intensive Care Units, Costs, and Effectiveness: An Assessment of Two Pilot Projects in Illinois American Public Health Association Annual Convention
	Orris, P., Carlson, C., & Conibear, S. Occupational Health Education of Industrial Workers: A New Approach American Public Health Association Annual Convention
OCTOBER, 1976	Kientz, R., Orris, P. The Economic Feasibility of a National Health Service American Public Health Association Annual Convention.
OCTOBER, 1979	Orris, P. Occupational Medicine in a Public General Hospital American Public Health Association Annual Convention.
JULY 8, 1981	Orris, P. The Cook County Hospital Occupational Medicine Clinic NIOSH Conference on Occupational Health and Safety of Minority Workers
NOVEMBER 3, 1981	Orris, P., Kahn, H.S., Sayres, B.B., Physician's Forum Task Force Report: The Salaried Physician American Public Health Association Annual Convention
NOVEMBER 4, 1981	Orris, P., Kennedy, M.J. Guerriero, J. Hessl, S.M. Hryhorczuk, D.O. and Hoffman, D. Activities of An Employer Independent Occupational Medicine Clinic American Public Health Association Annual Convention

MAY 25, 1983	Saxena, K., Johnson, P., Hryhorczuk, D., and Orris, P. Initial Medical Management of a Mini-Disaster with a Transformer Fire Emitting Polychlorinated Biphenyls. Third World Congress on Emergency and Disaster Medicine, Rome, Italy.
June, 2, 1983	Orris, P. Hryhorczuk, D. Diagnosis of TCDD Intoxication, American Public Health Association, Occupational Health Section Midwest Regional Meeting
AUGUST 1, 1983	Orris, P. Socioeconomic Determinants of Adult Disease, National Medical Association, 88th Annual Convention, Chicago, Illinois

LECTURES

Graduate Medical Education:

Health Effects of 2,3,7,8 Tetrachlorodibenzo-p-dioxin.	Case Western Reserve University School of Medicine, University of Tennessee Medical School, Wayne State University School of Medicine, Mt. Sinai Hospital, Chicago.
Epidemiology as a Tool of the Occupational Health Professional	Wisconsin Association of Occupational Health Professionals, Milwaukee, Wisconsin.
Occupational Disease in Primary Care Practice	Amalgamated Clothing & Textile Workers Union, AFL-CIO, New York City., Grant Hospital, Chicago., Alexian Brothers Medical Center, Chicago., University of Tennessee School of Medicine .
Occupational Renal Disease	University of Illinois Great Lakes Educational Resource Center, United States Navy, Virginia Beach, VA.
Occupational Lead Nephropathy	Case Western Reserve University School of Medicine, Cleveland, Ohio
Respiratory Hazards of Workers in the Port of New Orleans	New Orleans General Hospital, New Orleans, La.

Undergraduate Medical Education:

Agent Orange: Current Knowledge	The American Medical Student Association 31st Annual Convention,
Can Humanism Survive Medical School?	State University of New York Medical School, Syracuse, New York
Is Competition Healthy For Medicine?	Dept. of Preventive Medicine, Wayne State University School of Medicine, Detroit, Michigan.
Occupational Medicine: An Overview	Dept. of Preventive Medicine, St. Louis University, St. Louis, Mo.

Continuing Education in Occupational Health:

Medical Surveillance For Foundry Workers	Allied Industrial Workers, AFL-CIO, National Foundry Conference, Milwaukee, Wisc.
Health Hazards of Women in the Electrical Industry	Health Services Seminar, Motorola, Inc., Chicago, Illinois.
Infectious Disease Risks of Hospital Workers	American Federation of Government Employees, AFL-CIO, Chicago, Illinois.
PCBs: Current Knowledge	International Brotherhood of Electrical Workers, North Chicago, Illinois.

TESTIMONY BEFORE GOVERNMENTAL AND CITIZEN'S COMMITTEES

OCTOBER, 1975	Sub Committee on Health, U. S. House of Representatives Re: National Health Insurance
APRIL, 1976	Democratic National Committee Re: Housestaff Trade Unions
NOVEMBER, 1976	U. S. Congressional Hearings Re: Black Lung Compensation
SEPT. 25, 1981	Illinois Commission on the Status of Women. Re: Reproductive Hazards in Industry
NOVEMBER 6, 1982	Illinois Legislative Study Commission on Agent Orange. Re: Health Effects of Dioxin (TCDD)
MARCH 21, 1983	Citizens Commission On Justice At Hanes, Chicago, Illinois. Re: Carpal Tunnel Syndrome

JUNE 9, 1983	Illinois Senate Public Health, Welfare, and Corrections Committee. Re: Reporting of Parental Occupations After Adverse Reproductive Outcomes
September 25, 1983	Illinois Legislative Study Commission on Agent Orange. Re: Diagnosis of TCDD Intoxication

AWARDS AND HONORS

1973	Ciba Community Affairs Award
1980-	Fellow, American College of Preventive Medicine

PROFESSIONAL SOCIETY MEMBERSHIPS

1969-	American Public Health Association
1974-1975	American Trauma Society.
1975-	Physicians Forum
1978-	American Occupational Medical Association.
1978-	Illinois Public Health Association
1978-	American Academy of Occupational Medicine
1979-	Chicago Medical Society
1979-	Illinois State Medical Society
1979-	American Medical Association
1981-	American College of Preventive Medicine

COMMITTEE MEMBERSHIPS

1972-1975	Executive Committee, Chicago Area Committee on Occupational Safety and Health.
1975-1979	Executive Medical Staff, Cook County Hospital

1977-1980	Committee on National Health Proposals, Medical Care Section, The American Public Health Association
1978-1980	Resolutions Committee, Illinois Public Health Association
1978-	Occupational Health Committee, Cook County Hospital.
1979-1982	Program Committee, Medical Care Section, American Public Health Association
1980-1982	Chairman, Sub Committee on Public Hospitals Illinois Public Health Association.
1982-	Action Board, American Public Health Association.
1982-	Joint Policy Committee, American Public Health Association.
1983-	Member, Scientific Review Panel of the American Occupational Medical Association's Self Assessment Examination.

13593

MARVIN A. SCHNEIDERMAN, Ph.D.

I. QUALIFICATIONS

Marvin A. Schneiderman of Bethesda, Maryland is a statistician and epidemiologist who is the former Chief of Statistics and Epidemiology and the former Director for Science Policy of the National Cancer Institute. He is currently a consultant. His curriculum vitae is attached.

II. SUBJECT MATTER

Dr. Schneiderman will testify in areas concerning mathematical models, statistics, and epidemiology particularly in the area of the determination of cancer causation. He will also discuss the epidemiology of dioxins and their contaminants specifically as that relates to cancer in humans specifically soft tissue sarcoma, stomach cancers and lymphomas. He will further testify to the relationship of exposure to the time of manifestation of disease, i.e. the "latency period" for the development of neoplasms.

Included within his testimony will be a discussion of the multiplication of base rates in the production of cancers; the presentation of a multi-stage model for cancer induction; the age relationships and the role age plays in the various stages of cancer development as they are effected by dioxins and/or their contaminates. He will also discuss and present the pertinent animal data and the fact that the animal data in the reputable and respected medical and scientific literature is consistent with the epidemiological

studies pertaining to dioxin effects in humans and that the animal data is an accurate and appropriate method for the extrapolation and prediction of disease in humans.

His presentation will include a discussion of a mathematical model for the association of the multi-faceted presentation of signs and symptoms in the veteran who was exposed to Agent Orange and the correlation between those signs and symptoms and said exposure and the causal relations between those two elements. Dr. Schneiderman will, of necessity, discuss the incidence of these rare cancers in the general population for a comparison of the onset ages in the general population as compared to the ages of onset for these cancers observed in the Vietnam veterans.

His testimony shall also include a discussion of the relationship of cancer induction to immune deficiencies or deficits as brought about by the immuno-suppressive effects of exposure to dioxin and will rely upon the experience with organ transplant patients and the development of lymphomas and soft tissue sarcomas which he will testify validates his opinions as to the cancer induction in the representative veterans.

Finally, his testimony shall include a discussion of the question of a threshold exposure to a known carcinogen for the induction of cancer. This will include testimony to the effect that there is no "safe" level for exposure to a carcinogen, that a single exposure may cause cancer, and that there is no "no effect" level to a known carcinogen. In his testimony he will present his opinion that TCDD is the most toxic and potent carcinogen ever synthesized by man. And, finally, his testimony shall cover the widely held belief in the respected medical and scientific community that an

sarcomas, lymphomas and skin cancers.

12. A carcinogen capable of causing cancer in one organ or system is more probably than not capable of causing cancer in a variety of organs or systems.

13. The cancers present in representative plaintiffs Lambiotte and Ford are consistent with TCDD exposure.

14. It is more probable than not that the cancers present in Plaintiffs Ford and Lambiotte were caused by their exposure to Agent Orange.

V. BASES FOR OPINIONS

A. General

Dr. Schneiderman's opinion will be based upon his education, training, experiences, participation in on-going scientific research and investigations, a review of the medical and scientific research, and a review of the medical records of the plaintiffs.

B. Specific

1. Epidemiology of Cancer

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