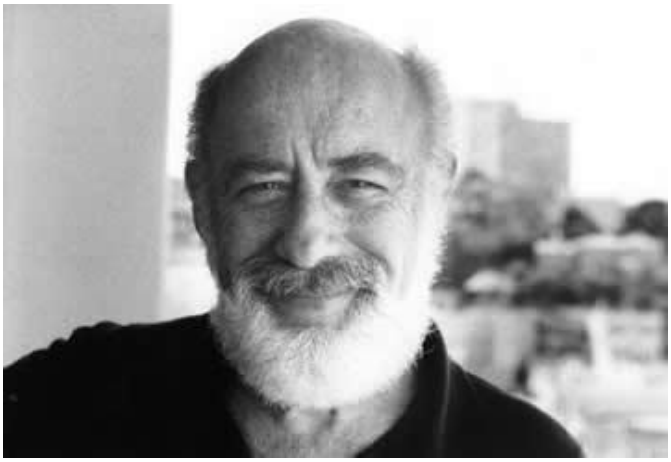

IN MEMORIAM

John W. Gofman
Professor of Molecular and Cell Biology, Emeritus
UC Berkeley
1918 – 2007

John William Gofman, internationally recognized as a scientist of great foresight and strong dedication to research benefiting human health and well- being, passed away at his home in San Francisco, California, on August 15, 2007.

His pioneering research on identification, quantification and clinical implications of cholesterol- bearing lipoproteins in human blood now stands as a foundation stone in the current paradigm for diagnosis and treatment of cardiovascular disease. Of equal significance to human health was his subsequent research on health risks associated with environmental and medical radiation, research that opened debates on the legally permissible public exposure from radioactive pollutants and on the need for reducing X- ray doses from medical procedures (especially from CT scanners and fluoroscopes).

Gofman was born in Cleveland, Ohio, on September 21, 1918, the son of David and Sarah (Kaplan) Gofman, each immigrating from czarist Russia in 1905. He attended Oberlin College, where in 1939 he graduated, academically first in his class, with an A.B. in chemistry. After a postgraduate year at Western Reserve School of Medicine, he felt he needed a deeper background in chemistry and was advised by his past Oberlin professor in chemistry, "there is only one place in the world for the kind of chemistry, physical chemistry, you'd like to study, and that's Berkeley." He applied for graduate study at the University of California, Berkeley, where then- Dean Gilbert Newton Lewis counseled him to take a course or two and get his research started in the next few weeks. He was attracted to the research in Glenn Seaborg's laboratory and, as described by Seaborg, "Fortunately Gofman and I chose each other, and within two weeks he was indeed getting his feet wet in the laboratory." He was awarded the Ph.D. degree in nuclear and physical chemistry in 1943.

His dissertation research, under Glenn Seaborg, resulted in the discovery of Pa-232, U-232, Pa-233 and U-233 and proved the fissionability of U-233, indicating it a potential source of nuclear energy. His experimental expertise was enlisted in the Manhattan Project and, at J. Robert Oppenheimer's request, he isolated 1.2 milligrams of plutonium, the world's largest existing quantity at that time. After working on the Manhattan Project, he enrolled at the University of California, San Francisco, to complete requirements for the M.D. degree, and graduated with the award of the Gold- Headed Cane for personifying the qualities of a true physician. Following his internship in 1947, Gofman joined the faculty at the University of California, Berkeley, as assistant professor in the Division of Medical Physics, Department of Physics. He also held an appointment as lecturer/ instructor in medicine at the University of California, San Francisco.

Gofman's academic background was an ideal match with the evolving programs on the Berkeley campus that promoted interdisciplinary interaction among the biological and physical sciences in both teaching and research. He was an early member of the faculty who organized the Graduate Group in Biophysics and

Medical Physics. He was uniformly recognized as a dynamic lecturer, superb teacher– thorough, systematic, inspiring — and a generous research mentor. He was promoted to professor in 1954.

In his research he wanted to address a big problem, such as heart disease or cancer. He chose heart disease because he was intrigued by early Russian studies indicating an association between atherosclerosis and blood cholesterol. His research, conducted at the Donner Laboratory, began with an innovative investigation of the molecular nature of cholesterol transport in blood. Gofman acquired one of the first analytic ultracentrifuges designed for detailed characterization of proteins and other large biomolecules. He elegantly demonstrated, with graduate student Frank Lindgren, that the key to ultracentrifugal isolation and analysis of cholesterol-bearing proteins, called lipoproteins, was to adjust the density of serum by salt addition, and thereby float them away from the other more dense sedimenting proteins.

He identified three major classes of lipoproteins: very low density (VLDL), low density (LDL) and high density lipoproteins (HDL) in human serum. He then proceeded with an extensive evaluation of the association between the different lipoprotein classes and the risk of heart disease. The cholesterol- rich LDL class, when elevated, was found to be highly predictive of risk and, subsequently, deemed the most atherogenic. The triglyceride- rich VLDL class was also associated with risk and assigned a causal role in atherosclerosis. Gofman's studies on HDL consistently indicated inverse relationships between HDL and the atherogenic LDL and VLDL classes. Subsequent studies by others definitively established HDL to be a strong inverse predictor of cardiovascular risk. Together, these findings are reflected in the current clinical terminology identifying LDL as "bad" cholesterol and HDL as "good" cholesterol.

Gofman's proposition that measurement of the lipoprotein pattern provides more specific predictive information of heart attack risk than measurement of total cholesterol level in blood sparked considerable controversy and debate. While both measures were acknowledged to provide a valid assessment of risk, Gofman's work made clear that the total cholesterol level in blood is comprised of the sum of contributions made by lipoproteins that exhibit different predictive strengths as well as different roles in lipid metabolism and cholesterol transport.

In collaboration with E. Virginia Dobbin, senior dietician at Cowell Memorial Hospital, Gofman conducted the first study evaluating the effect of diet on blood levels of specific lipoprotein classes. Their findings indicated that a diet high in animal fat (saturated fat) increased LDL levels, while a diet high in carbohydrates increased VLDL levels. Gofman initiated a wide range of collaborative studies with physicians to examine patients exhibiting premature atherosclerosis or familial lipid disorders and to conduct anatomical studies on the distribution and intensity of atherosclerotic lesions in human heart and brain arteries. Gofman's graduate students and postdoctoral fellows provided a wealth of basic information on the physical, biochemical and metabolic properties of the newly discovered lipoproteins.

The impact of this work on the field was vast, enduring and universally recognized. Gofman received many honors, including the Modern Medicine Award (1954) for outstanding contributions to heart disease research, the Lyman Duff Lectureship Award (1965) of the American Heart Association for his research on atherosclerosis and coronary heart disease, the Stouffer Prize (1972, shared) for outstanding contributions to research in arteriosclerosis, and the American College of Cardiology (1974) selection as one of 25 leading researchers in cardiology of the past quarter century. In May 2007, the Journal of Clinical Lipidology republished his classic paper covering his laboratory's work between 1949 and 1955 and honored Gofman with the title "The Father of Clinical Lipidology".

Drawing on his background in physical chemistry, Gofman, in 1960, redirected his research to an investigation of trace elements in blood and their possible relationship to disease, especially heart disease. His plan was to use mostly X- ray fluorescence spectroscopy, with some neutron- activation analysis (for light elements), initially to measure a wide range of chemical elements in blood from a population sample whose lipoprotein profiles had previously been analyzed.

Halfway into the trace element study, in 1962, John Foster, director of Lawrence Livermore National Laboratory (LLNL), and Glenn Seaborg, then commissioner of the Atomic Energy Commission (AEC), urged him to assume a leadership position at Livermore and to establish a Biomedical Research Division. The mission was to conduct research evaluating health effects of ionizing radiation and radionuclide release from a range of activities including weapons testing, nuclear power and medical applications. Gofman accepted the post in 1963 as associate director of LLNL and director of biomedical research. Among the many projects he initiated was research into the role in carcinogenesis of double- strand chromosome breaks, readily caused by

ionizing radiation. In addition, he participated directly with Arthur Tamplin, a former student, in evaluating the epidemiologic data from humans exposed to the atom bombs in 1945 and to medical X- rays. The existing evidence showed, with positive dose- responses, excess cancers of several types, and they predicted that future evidence would establish positive dose- responses for virtually all types of cancer. Based on their analysis, they reported, in 1969, that ionizing radiation was a much greater contributor to mutagenesis and cancer than previously assumed and recommended at least a tenfold reduction in the legally permissible dose to the public from nuclear pollutants. They further expressed concern about and opposition to using underground nuclear explosives to liberate natural gas, and by 1971, urged a five- year moratorium on licensing additional nuclear power plants to allow time for realistic consideration of the requirement, based on health considerations, for nearly perfect containment of radioactive by- products at every stage of the nuclear fuel cycle.

Proponents of increased nuclear utilization countered with claims critical of the Gofman- Tamplin interpretation of the health data. While the ensuing debate severely strained his relationship with the AEC, the Livermore leadership, and the Congressional Joint Committee on Atomic Energy, it activated many ardent supporters both in and out of academia. In 1971, Gofman helped to establish the research and educational Committee for Nuclear Responsibility, joined by three Nobel laureates, to disseminate information on the radiation debate.

In 1973, with cessation of his research funding from the AEC, Gofman returned to full- time teaching at Berkeley and in the following year retired as professor emeritus. He was a most prolific emeritus, publishing six scholarly books, providing expert testimony, giving speeches and interviews, and publishing a stream of articles for the Committee for Nuclear Responsibility. In 1992, he was awarded the Right Livelihood Award (Sweden) for “vision and work forming an essential contribution to making life more whole, healing our planet, and uplifting humanity.”

While the Gofman- Tamplin findings about the magnitude of hazard of ionizing radiation and later findings by Gofman were widely debated, subsequent independent estimates of risk- per- radiation dose by the Committee on Biological Effects of the National Research Council were progressively increased. In 1990, Gofman presented an analysis that rules out any threshold dose below which genetic damage from ionizing radiation is always perfectly repaired; subsequently, national and international radiation committees have reached the same conclusion. In 1999, Gofman’s last monograph addressed epidemiologic evidence leading him to postulate that somatic mutations, caused in coronary arteries by medical X- rays, became in the twentieth century an important causal cofactor in coronary artery disease, an hypothesis awaiting further exploration.

John’s courageous spirit will be deeply missed by all who knew him.

Gofman is survived by his son, John David Gofman, M.D. His wife, Helen Fahl Gofman, M.D., passed away in 2004.

Alexander V. Nichols
Robert M. Glaeser
Howard C. Mel