

**Testimony of Narasimhan Ramarathnam,
President, Genox Corporation
Before
Senate Special Committee on Aging
Thursday, July 27, 2006**

Mr. Chairman and Committee Members:

My name is Narasimhan Ramarathnam. For convenience, I am generally known by my professional colleagues in Canada and the United States as Dr. Rama. I am the President of Genox Corporation, a position that I have held since November 1998. Genox is a small biotechnology company located in Baltimore, MD. The company was organized in October 1991 as a Minnesota Corporation by a small group of investors, along with Dr. Richard G. Cutler and his son, Roy Cutler.

Dr. Cutler is a well-known scientist in the field of molecular gerontology. Prior to founding Genox, Dr. Cutler spent 18 years as a research chemist at the National Institute on Aging (NIA) of the National Institutes of Health (NIH). He is internationally recognized for both his theoretical and his experimental work on the biology of aging and longevity. A list of his published research papers is attached. The Genox research laboratory was set up in Baltimore to be near the residences of Dr. Cutler and his son.

The late Dr. Hirotomo Ochi, the founder of Nikken Foods and the Nikken Group of Companies, was asked to invest in Genox shortly after the laboratory was established. Nikken Foods is a major supplier of natural flavorings and seasonings to food processing industries all over the world. Dr. Ochi had a life-long interest in the scientific study of aging processes. Prior to investing in Genox, Dr. Ochi had established a laboratory to pursue scientific work through the Japan Institute for the Control of Aging (JaICA), a division of Nikken Foods. His scientific temperament and interest in Dr. Cutler's scientific work on molecular gerontology while Dr. Cutler worked at NIH, led Dr. Ochi to invest in the establishment of Genox at Baltimore and continue to fund its operations. Dr. Ochi passed away in November 2005, but left a legacy in Japan and the United States for the continuing pursuit of scientific research on the processes of aging.

Dr. Cutler served as President and CEO of Genox Corporation from January 1995 until he resigned in November 1998 to pursue aging research at Kronos Science Laboratory in Phoenix, Arizona. His son, Mr. Roy Cutler, following his father's footsteps, now works for NIA at NIH.

During the past decade Genox has served the scientific community by providing to researchers products and services for the measurement of biomarkers that indicate oxidative stress levels. Oxidative Stress (OS) is a general term used to describe the steady state level of oxidative damage in a cell, tissue, or organ, caused by the reactive oxygen species (ROS). This damage can affect a specific molecule or the entire organism. Reactive oxygen species, such as free radicals and peroxides, represent a class

of molecules that are derived from the metabolism of oxygen and exist inherently in all anaerobic organisms. ROS can be generated internally or externally. Most ROS are by-products of normal metabolic reactions, such as energy generation from mitochondria. External ROS includes exposure to cigarette smoke, environmental pollutants and consumption of alcohol, to name three examples.

In layman's terms, oxidative stress is like a see-saw, a well-maintained balance between the oxidative damage that constantly occurs inside our body as a result of normal oxygen metabolism and the counterbalancing forces of the inherent anti-oxidative defenses in our body. When a tilt towards the damage side of the see-saw occurs, the aging process sets in, leading to the gradual loss of physiological functions, normally later in life.

Genox research tools include an Enzyme Linked Immuno-Sorbent Assay (ELISA) Kit, to be used by scientists in their laboratories, for their own research purposes. This kit was developed at JaICA, our parent company in Japan. JaICA holds the Japanese Patent (No. 3091974) for this kit. The kit helps scientists measure the DNA damage biomarker, 8-hydroxy-2'-deoxyguanosine (8-OHdG). The kit is not for "home test" applications. It does not analyze DNA directly. Very specialized skills are required to measure the precise volume of samples and the appropriate reagents needed for the analysis. Specialized equipment is also required, including a multi channel pipette, an incubator to maintain constant temperature during the analysis, a special microplate reader and analytical software to measure the samples after the experiment is completed.

The ELISA test kit is widely used by scientists all over the world. Among the many research institutions using the ELISA kit and are OXIS Health Products, located until last year in Portland, Oregon; the Medical College of Wisconsin; New York University; State University of New York; University of North Carolina at Chapel Hill; University of Pennsylvania; Penn State University; Yale University; Harvard University; Johns Hopkins University, and Emory University. Scientists working in federal research institutions such as Veterans Administration Medical Center, and United States Environmental Protection Agency have also purchased and used the kit for their work. Attached is a list of 28 publications by scientists who have used this product that demonstrate the importance and utility of this kit and Genox's services for the advancement of scientific research on the processes of aging.

Genox also offers analytic assay services to scientists who are involved in basic and applied research. The data provided by Genox enables these scientists to understand the mechanism of aging and investigate the causes for oxidative stress-mediated diseases. These research scientists lack either the necessary equipment or expertise to measure the levels of 8-OHdG in their research samples. Through the provision of its analytic services Genox enables more extensive research efforts on aging than would otherwise be possible.

The major institutions whose researchers use Genox's analytic services are the University of Pittsburgh, Johns Hopkins University, Colorado State University, Harvard School of

Public Health, Penn State University, Veterans Administration Hospital and the Gerontology Research Center or the National Institute on Aging of NIH .

In April of this year, I attended a conference on Experimental Biology held at San Francisco. I learned from scientists there that they want additional products from Genox. Many researchers are now asking for a method for analyzing protein oxidation. Work is already underway at JALCA to develop a new monoclonal antibody against 3,5-DiBrY, a protein oxidation biomarker.

I have attached to my written testimony seven publications by scientists who have used Genox services. These studies represent the type of work that our services facilitate. Take for example, the acknowledgement made by Professor Eldon Askew, Director of Division of Foods and Nutrition, of the University of Utah. He studied control of oxidative stress in individuals trained at high altitudes, research of great significance to the armed forces. Dr. Lloyd Greek of the University of Colorado Health Sciences Center, in his testimonial, has also emphasized the significance of the measurement of 8-OHdG produced in individuals who were subjected to diagnostic radiology (medical imaging) studies. Every time scientists like Dr. Askew and Dr. Greek call us and request our services, it only makes Genox and me personally grow younger and not older. The primary mission of Genox is to serve the scientific community so that the mechanism of aging and age-related disease processes will become easier to understand and interpret.

In closing, I again want to thank the committee for inviting me to testify, and commend you, Mr. Chairman, for holding this hearing. Our late founder, Dr. Ochi used to believe in three basic principles, "I am OK You are OK," "Affirmative Philosophy," and "Good Science Makes Good Business." Let's all take a broader perspective in life, and work together towards the betterment of mankind.

I will be happy to answer any questions you may have for me.

A short biography to be used by Chairman Smith for introductory purposes at the hearing:

Name: Narasimhan Ramarathnam, commonly known to his scientific colleagues in Japan, Canada, and the US as Dr. Rama.

President of Genox Corporation, a small biotech company, located in Baltimore MD, that is involved in the area of development of novel biomarkers to measure oxidative stress for the advancement of basic and applied research related to aging and free radical chemistry in medicine and biology.

Dr. Rama has a Ph. D in Food Science from Nagoya University in Japan and a Ph. D in Applied Biochemistry from the University of Bombay in India. He is a Professional Member of the American Chemical Society and the Institute of Food Technologists (USA). Dr. Rama is also a reviewer of scientific manuscripts related to the Chemistry of Natural Antioxidants, that are communicated to the Journal of Agricultural and Food Chemistry, published by the American Chemical Society.

Narasimhan Ramarathnam, Ph. D.

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PROFILE

President of Genox Corporation, a small biotech company involved in the development and marketing of oxidative stress biomarkers related products and testing services to research institutions.

EDUCATION

Master of Business Administration Fall 2007 (Anticipated)
(International Business Major)
Johns Hopkins University, Baltimore, MD

Doctor of Philosophy October 1987
(Food Science & Technology)
Nagoya University, JAPAN

Doctor of Philosophy June 1982
(Applied Biochemistry)
University of Bombay, INDIA

Master of Science – FIRST CLASS with Honors May 1975
(Organic Chemistry)
University of Bombay, INDIA

Bachelor of Science – FIRST CLASS with Honors May 1973
(Chemistry & Biology)
University of Bombay, INDIA

PROFESIONAL EXPERIENCE

LABORATORY DIRECTOR 1996 – present
Genox Corporation, Baltimore, MD

Develop and market in-house testing services of oxidative stress biomarkers, ELISA test Kits and monoclonal antibodies to research institutions
Troubleshoot problems related to the testing protocols, instruments, and report generation
Undertake the overall administration of the company including purchasing, accounts, and payroll.
Author, present, and publish scientific publications in peer-reviewed scientific journals and international conferences

MANAGER 1993 - 1996
Nikken Foods Co., Ltd., Fukuroi-city, JAPAN

Optimized the extraction and concentration processes for the development of natural flavorings with antioxidant properties

Presented and published scientific papers related to the chemistry of natural antioxidants, in international conferences and peer reviewed scientific journals

Helped in organizing the First International Conference on Food Factors: *Chemistry and Cancer Prevention* (IcoFF), held in Hamamatsu, Japan, in December 1995, as a member of the organizing committee

RESEARCH ASSOCIATE

1988 - 1993

University of Toronto, Toronto, CANADA

Developed new methods to isolate and characterize key flavor components in nitrite-cured meat

Characterized the volatile components responsible for species differences among pork, beef, and chicken.

Published and presented research and development results in national and international conferences and peer-reviewed professional journals

VISITING SCIENTIST

1987- 1988

St-Hyacinthe Food Research and Development Center

Agriculture Canada, St-Hyacinthe, CANADA

Developed new technique for the extraction of food flavors with the use of microwave heat

Undertook projects to optimize conditions for the extraction of essential oils and oleoresins from spices using supercritical fluid extraction

LECTURER

1975 - 1982

Colleges Affiliated to the University of Bombay, INDIA.

Taught organic chemistry to undergraduate students

Lead groups of students in designing scientific projects for competitions

Taught and supervised undergraduate chemistry laboratory assignments

PROFESIONAL DEVELOPMENT

Instrumentation: Experienced in handling GC, HPLC, GC-MS, and ESR.

Computer Skills: Proficient in PeachTree Accounting Software, Microsoft Office, and Microsoft PowerPoint.

Language Skills: Fluent in English, Japanese (spoken), Tamil and Hindi.

Fellowships, Awards: NSERC (Canada) Visiting Research Fellowship, 1987-88.
Japanese Government Ministry of Education (Monbusho) Research Scholarship, 1983-87.
Council of Scientific & Industrial Research (C.S.I.R., New Delhi) Junior Research Fellowship, 1978-82.
University of Bombay Post-graduate Merit Scholarship, 1973-75.

Affiliations: Professional Member - **American Chemical Society**
(*Reviewer for the Journal of Agricultural and Food Chemistry*)

Professional Member - **Institute of Food Technologists**

LIST OF PUBLICATIONS

Ochi, H. R-Z. Cheng, S, Sri Kantha, M. Takeuchi, and N. Ramarathnam,. The JaiCA-Genox Oxidative Stress Profile – An Overview on the Profiling Technique in the Oxidative Stress Assessment and Management. *Bio Factors*: 13, 195-203, 2000.

Cutler, R. G., K. Crawford, R-Z. Cheng, N. Ramarathnam, M. Takeuchi, and H. Ochi. The Genox Oxidative Stress Profile – An Overview on its Assessment and Application. *Functional Foods for Disease Prevention II: Medicinal Plants and Other Foods*, (Shibamoto, T. J. Terao, and T. Osawa eds.), American Chemical Society, Washington, D. C., 188-197, 1998.

Ramarathnam, N. Flavour of Cured Meat in *Flavor of Meat, Meat Products and Sea Foods*, (Shahidi, F., ed.), Blackie Academic and Professional, London, 290-319, 1998.

Ramarathnam, N., H. Ochi, and M. Takeuchi. Antioxidant Defense System and Free Radical Scavenging Potentials of Cereals in *Food Factors for Cancer Prevention*, Springer Verlag, Tokyo, pp 293-298, 1997.

Sato, M., N. Ramarathnam, Y. Suzuki, T. Ohkubo, M. Takeuchi, and H. Ochi. Superoxide Radical Scavenging Activities of Wines, and Antioxidative Properties of Fractions Recovered from Merlot Wine Pomace in *Food Factors for Cancer Prevention*, Springer Verlag, Tokyo, pp 359-364, 1997.

Ramarathnam, N., H. Ochi, and M. Takeuchi. Antioxidant Defense System in Vegetable Extracts in *Natural Antioxidants*, (Shahidi, F., ed.) AOCS Press, pp 76-87, 1997.

Sato, M., N. Ramarathnam, Y. Suzuki, T. Ohkubo, M. Takeuchi, and H. Ochi. Varietal Differences in the Phenolic Content and Superoxide Radical Scavenging Potential of Wines From Different Sources. *J. Agric. Food Chem.*, 44, 37-41, 1996

Ramarathnam, N., T. Osawa, H. Ochi, and S. Kawakishi. The Contribution of Plant Food Antioxidants to Human Health. *Trends in Food Sci. and Technol.*, 6, 75-82, 1995.

H. Ochi, N. Ramarathnam, M. Takeuchi, and H. Sugiyama. Antioxidant Activities Wasabi (*Euterna Wasabi* MAXIM.) Leaf, Stem, and Root Extracts. *J. Jpn. Nutr. Food Sci.* 3, 236-238, 1995.

Ramarathnam, N. and L.J. Rubin. The Flavour of Cured Meat in *Flavor of Meat and Meat Products*, (Shahidi, F., ed.) Blackie Academic & Professional: Glasgow, pp 174-198, 1994.

Ramarathnam, N., L. J. Rubin, and L. L. Diosady. Studies on Meat Flavor. 4. Fractionation, Characterization, and Quantitation of Volatiles from Uncured and Cured Beef and Chicken. *J. Agric. Food Chem.*, 41, 939-945, 1993.

Ramarathnam, N., L. J. Rubin, and L. L. Diosady. Studies on Meat Flavor. 3. A Novel Method for Trapping Volatile Components from Uncured and Cured Pork. *J. Agric. Food Chem.*, 41, 933-938, 1993.

Ramarathnam, N., L. J. Rubin, and L. L. Diosady. Composition of the Volatiles of Cooked Pork, Beef, and Chicken, and of Cured-Meat. *Proceedings of the 38th International Congress of Meat Science and Technology*, Clermont-Ferrand, France, 1992, Vol. 3, pp. 575-578.

Osawa, T., N. Ramarathnam, S. Kawakishi, and M. Namiki. Antioxidative Defense Systems Generated by Phenolic Plant Constituents. in *Phenolic Compounds in Food and Their Effects on Health. II Antioxidants & Cancer Prevention* (M-T. Huang, Ho, C-T, and C. Y. Lee, eds.) American Chemical Society: Washington, DC, pp 122-134, 1992.

Ramarathnam, N., L.J. Rubin, and L.L. Diosady. Studies on Meat Flavor. 2. A Quantitative Investigation of the Volatile Carbonyls and Hydrocarbons in Uncured and Cured Beef and Chicken. *J. Agric. Food Chem.*, **39**, 1839-1847, 1991.

Ramarathnam, N., L.J. Rubin and L.L. Diosady. Studies on Meat Flavor. 1. Qualitative and Quantitative Differences Among Cured and Uncured Pork. *J. Agric. Food Chem.*, **39**, 344-350, 1991.

Ramarathnam, N., T. Osawa, M. Namiki and S. Kawakishi. Chemical Studies on Novel Rice Hull Antioxidants : 2. Identification of Isovitexin, a C-Glycosylflavonoid. *J. Agric. Food Chem.*, **37**, 316-319, 1989.

Ramarathnam, N., T. Osawa, M. Namiki and S. Kawakishi. Studies on Changes in Fatty Acid Composition and Contents of Endogenous Antioxidants During γ -Irradiation of Rice Seeds. *J. Am. Oil Chem. Soc.*, **66**, 105-108, 1989.

Kaneda, H., Y. Kano, T. Osawa, N. Ramarathnam, S. Kawakishi and K. Kamada. Detection of Free Radicals in Beer Oxidation. *J. Food Sci.*, **53**, 885-888, 1988.

Ramarathnam, N., T. Osawa, M. Namiki and S. Kawakishi. Chemical Studies on Novel Rice Hull Antioxidants : 1. Isolation, Fractionation and Partial Characterization. *J. Agric. Food Chem.*, **36**, 732-737, 1988.

Ramarathnam, N., T. Osawa, M. Namiki and S. Kawakishi. High Temperature Storage Effect on Longevity of Rice Seeds. *J. Food Sci.*, **52**, 835-836, 1987.

Ramarathnam, N., T. Osawa, S. Kawakishi and M. Namiki. Effect of Oxidative Damage Induced by γ -Irradiation on Germination Potentials of Rice Seeds. *J. Agric. Food Chem.*, **35**, 8-11, 1987.

Ramarathnam, N., T. Osawa, M. Namiki and T. Tashiro. Studies on Relationship Between Antioxidative Activity of Rice Hull and Germination Ability of Rice Seeds. *J. Sci. Food Agric.*, **37**, 718-726, 1986.

Osawa, T., N. Ramarathnam, S. Kawakishi, M. Namiki and T. Tashiro. Antioxidative Defense Systems in Rice Hull Against Damage Caused by Oxygen Radicals. *Agric. Biol. Chem.*, **49**, 3085-3087, 1985.

Ramarathnam, N. and P.R. Kulkarni. Effect of Storage on the Physicochemical Properties of Rice Starch and Cooking Quality of Rice Grain. *Z. Ernährungswiss.*, **23**, 143-150, 1984.

Ramarathnam, N. and P.R. Kulkarni. Volatiles of Scented Ambemohor Rice and Leaves of *Pandanus odoratissimus*. *Naturwissenschaften*, **71**, 215, 1984.

Ramarathnam, N. and P.R. Kulkarni. Effect of Ageing on the Fatty Acid Composition of Some Indian Varieties of Brown Rice. *J. Food Sci. Technol.*, **20**, 284-287, 1983.

Ramarathnam, N., C. Bandopadhyay and P.R. Kulkarni. Comparative Studies on Volatile Components of Scented and Non-Scented Rice. *J. Food Sci. Technol.*, **20**, 43-47, 1983.

CONFERENCE PRESENTATIONS

Ochi, H. R-Z. Cheng, S, Sri Kantha, M. Takeuchi, and N. Ramarathnam,. The JaiCA-Genox Oxidative Stress Profile – An Overview on the Profiling Technique in the Oxidative Stress Assessment and Management. 2nd International Conference on Food Factors, Kyoto, Japan, December 9-13, 1999.

Ramarathnam, N. R. G. Cutler, T. Yoshikawa, T. Osawa, M. Takeuchi, and H. Ochi. The Genox Oxidative Stress Profile. III. DNA Damage. Symposium on Functional Foods, 213th National Meeting of the American Chemical Society, San Francisco, April 13-15, 1997.

Cutler, R. G., K. Crawford, R. Chen, N. Ramarathnam, M. Takeuchi, and H. Ochi. The Genox Oxidative Stress Profile. I. Introduction. Symposium on Functional Foods, 213th National Meeting of the American Chemical Society, San Francisco, April 13-15, 1997.

Cheng, R. A. Patel, N. Ramarathnam, R. G. Cutler, M. Takeuchi, and H. Ochi. The Genox Oxidative Stress Profile. II. Lipid Peroxidation. Symposium on Functional Foods, 213th National Meeting of the American Chemical Society, San Francisco, April 13-15, 1997.

N. Ramarathnam, M. Takeuchi, and H. Ochi. Antioxidant Activities of Cereals and Beans. International Conference on Food Factors: Chemistry and Cancer Prevention, Hamamatsu, Japan, December 12-15, 1995.

Sato, M., N. Ramarathnam, Y. Suzuki, T. Ohkubo, M. Takeuchi, and H. Ochi. Free Radical Scavenging Potential and Health Benefits of Components in Wine. Annual Meeting of the Japanese Society of Agricultural and Biological Chemists, Sapporo, August 1-3, 1995.

Ochi, H., N. Ramarathnam, and M. Takeuchi. Antioxidant Defense Role of Vegetable Extracts. IFT Annual Meeting, Anaheim, CA, June 3-8, 1996.

Ochi, H., N. Ramarathnam, and M. Takeuchi. Oxygen Radical Scavenging Potential and Antioxidant Activity of Spices and Herbs. 86th AOCS Annual Meeting, San Antonio, TX, May 7-11, 1995.

Ramarathnam, N., L. J. Rubin, and L. L. Diosady. A Comparative Study of the Volatile Flavor Components of Cured Meat and those that are Generated During Cooking of Defatted Meat. IFT Annual Meeting, Chicago, IL, July 10-14, 1993.

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Ramarathnam, N. and L.J. Rubin. The Flavor of Cured Meats - a Review. 8th IUFOST World Food Congress, held in Toronto, Canada, September 1991.

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Ramarathnam, N., T. Osawa, M. Namiki and S. Kawakishi. Chemical Studies on Novel Rice Hull Antioxidants : Isolation, Fractionation and Partial Characterisation. Annual Meeting of the Agricultural Chemical Society of Japan, held in Tokyo, Japan, April 1987.

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