STATE OF VERMONT)
Washington County) ss.

Petition of Vermont
Yankee Nuclear
Power Corporation

Public Service Board
Docket No. 3445

A F F I D A V I T

I, Joshua Lederberg, of Palo Alto, County of Santa Clara, State of California, being duly sworn, do hereby depose and say as follows:

I am Professor of Genetics at Stanford University, a position I have held since 1959.

Attached hereto and by this reference incorporated herein is a list of the articles and books I have authored.

I have been awarded the following degrees, honors and awards:

Nobel Prize, 1958, for work in Genetics.

PhD, 1947, Yale University, in Microbiology.

Honorary Doctor of Science, Yale University, University of Wisconsin and Columbia University.

Honorary Doctor of Medicine, University of Turin.

Member, National Academy of Science.

Socially responsible scientists should be concerned about the potential hazards of chemical and radiation-induced mutation for at least three reasons. The most important is also the most remote in the scale of time: the human nature that defines our posterity is energized by our cultural tradition but is bounded by the integrity of the genetic information of which each generation is the vessel.

Second, genetic impairments already account for a very large part of our existing burden of disease and premature death. If we give proper

weight to the genetic component of many common diseases which have a more complex etiology than the textbook examples of mendelian defects, we can calculate that at least 25 per cent of our health burden is of genetic origin. This figure is a very conservative estimate in view of the genetic component of such griefs as schizophrenia, diabetes and atherosclerosis, mental retardation, early senility and many congenital malformations. In fact, the genetic factor in disease is bound to increase to an even larger proportion, for as we deal with infectious disease and other environmental insults, the genetic legacy of the species will compete only with traumatic accidents as the major factor in health.

Our existing genetic load is a summation of three kinds of process: the historical accumulation of recessive gene mutations reappearing from time to time as their heterozygous carriers chance to mate; the immediate manifestation of dominant mutations and chromosome anomalies, which are only rarely propagated; and the paradoxical segregational load, where deleterious recessives had been stabilized within the population through some present, or more often, historical, advantage of the heterozygotes.

Any assessment of the social and personal <u>costs</u> of mutation must take account both of absolute and of relative measures. (And of course we must use the same perspective in weighing the social and personal <u>benefits</u> claimed for a given environmental additive.) A ten percent increase in the existing "spontaneous" mutation rate is, in effect, the standard that has been adopted as the "maximum acceptable" level of public exposure to radiation by responsible regulatory bodies.

(2) This can be defended on the argument that we neglect to take a number of measures that could probably improve the mutation index to a comparable degree. It can be attacked by reciting the absolute level of eventual

biological injury that might come from public exposure at such a level, were this in fact to occur from the proliferation of nuclear power plants and unregulated weapons tests.

I believe that the present standards for population exposure to radiation should and will (at least de facto) be made more stringent, to about 1 percent of the spontaneous rate, and that this is also a reasonable standard for the maximum tolerable mutagenic effect of any environmental chemical (better for them in aggregate).

Accepting, for present argument, the formal arguments of the UN advisory group (5), I translate this standard into a rate of about one recessive mutation per 1000 gametes (10-7 per nominal locus) per generation of typical exposure. Dominant mutations and chromosome aberrations may deserve even more stringent scrutiny, in view of the immediacy of their personal and social cost. The corresponding standard of 50 per million induced, viable, chromosome anomalies and 2 per million dominant mutations entails a raw social cost of over $100 million.

The costs of recessive mutations are much more difficult to estimate, being quite sensitive to the proportion of the mutational to the segregational load. At equilibrium, a one percent increase in the mutation rate will generate an estimated economic loss of about $1 billion per year (measured in the 1970 economy of the U.S.), but taking at least ten generations to approach full impact. This calculation assumes

(1) that mutations account for half the health load,

(2) that this is $200 billion per year:

$ 85 billion direct medical

$ 15 billion gross lost time

$100 billion reduction of efficiency in life and work attributable to less than perfect health (judged by the standard of the healthiest genetypes).

This calculation also works out to an eventual health bill of $500 per person per rad. Most of this is paid many generations after the exposure, and we would need a complicated analysis of the relevant discount rate to compute its present value. Let me suggest $100 per rad. per person.

These estimates are surely subject to an uncertainty of a factor of ten or so. They predicate the value of a human life as between $50,000 and $1 million per capita, depending on the age at which disability or death occurs and the level of custodial care entailed by it, as well as loss of economic productivity. They assign no value to early prenatal losses, though some would regard these as beneficial for the aim of zero population growth. This kind of cost-accounting is morally insufferable, but we must find some de facto standard of value in making hard decisions. If lives are valued at much more than a "million per bod", there is little evidence of this from the pragmatic behavior of the community or of most individuals in the choices they make in their daily lives (6). However, these choices are made in a hindered market where the cost of safety is a side issue, more often obscured than intelligently ventilated.

A health cost (from the "acceptable" standard) of $200 million per year is a grievous burden in absolute terms, but is immediately lost in an overall budget of over $100 billion. ($60 billion of this is direct health care; the indirect economic costs of disease, injury and premature senscence are open-ended.) This is to say that a level of risk that approaches the intolerable, once we are well aware of it, may be impossible to verify by direct measurements of disease diffused throughout the population! In exceptional circumstances, an effect like the peculiar malformations induced by thalidomide comes to the surface, and then achieves a visibility and notoriety all out of proportion to other agents. If the malformation induced

by thalidomide were a mental retardation of ten percent of the I.Q., instead of a highly characteristic and unusual deformation of the limbs, in an equal number of subjects, we would be unaware of it to this day.

All this is to say that we must look to extrapolations from laboratory measures for the only reliable indication of mutagenicity in the human population!

Someday, it will be argued that the standard risk should be elevated in a particular case, for example were there to be a demonstrable net social benefit of, say, $1 billion per year from the use of an agent that elevated the mutation rate by 5 percent. The argument should not be rejected out of hand. For example, I believe that an acceleration of health research by $1 billion per year would improve the genetic and the overall health climate so as to more than outweigh the penalties of more mutations. If there were a harmonious redistribution of the resource benefit, we could foresee an advantageous tradeoff. The problem is to produce that harmony, to insure that the people, who bear the risk and eventually pay the price, will reap the benefits. Perhaps we will invent a tax on pesticides or on atomic energy earmarked for compensatory research. This makes sense only if we have exhausted alternative sources of income for such restorative purposes.

Geneticists must not now overlook the other side of the coin - the enormous value of reliable measures to decrease the spontaneous mutation rate. There has been very little followup of the pioneering work on anti-mutagenic chemicals by Novick and Szilard two decades ago (9).

Dated at Palo Alto, California, September 8, 1970

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Joshua Lederberg

State of California)
) ss.
County of Santa Clara)

At Palo Alto aforesaid, this 8th day of September 1970, personally appeared Joshua Lederberg, who, being duly sworn by me, acknowledged that he is the person mentioned in the foregoing Affidavit, that the substance thereof is true to the best of his knowledge and belief and he further executed the same in my presence.

(SEAL)

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Notary Public

BIBLIOGRAPHY

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2. Federal Radiation Council, "Radiation Protection Standards", Report No. 1, May 13, 1960. See also Federal Register, 4402, May 18, 1960.

3. Auerbach, Charlotte and J.M. Robson, Production of mutations by allyl isothiocyanate. Nature 154:81 (1944).

4. Rusch, H.P., Dorothy Bosch, and R. K. Boutwell, The influence of irritants on mitotic activity and tumor formation in mouse epidermis. Acta Un. Int. Canc., 11:699-703 (1955).

5. Scientific committee on the effects of atomic radiation, Report to U.N. General Assembly, Official Records, 21st session. Suppl. 14 (A/6314), (1966).

6. Starr, C., Social benefit versus technological risk. Science 165:1232-1238 (1969).

7. Goldstein, Avram, Lewis Aronow, and S. M. Kalman, Principles of Drug Action. Harper and Row Publishers, N.Y. 1968.

8. Cleaver, J. E., "Xeroderma Pigmentosum: A Human Disease in Which an Initial Stage of DNA Repair is Defective". Proc. N.A.S., Vol. 63:428-435 (1969).

9. Nature 1951.