At a more basic scientific level, research in molecular epidemiology on understanding the molecular basis of predisposition toward and resistance to damage by radiation and toxic chemicals now is extremely promising. The identification of populations that are particularly susceptible or resistant to certain types of insults is not only of the greatest significance to medical sciences, but it will have a major positive impact on Federal regulatory activities by providing data for setting health standards that take into account both variations in the population and the doses to which human populations are ordinarily exposed.

The study of atomic bomb survivors in Japan has provided the best available estimates of the risk of various types of cancer resulting from exposure to external low-energy radiation. Some of the characteristics that make this study particularly useful are as follows:

1. The survivors are the only large population with a wide range of whole-body exposures, or exposure over the entire body.
2. The population was comparatively random with respect to health and work history.
3. An elaborate dosimetry program has yielded individual dose estimates for major organs.
4. The family registration system of Japan ensures 100 percent followup on mortality.

Although intensive study has been under way for over 30 years, the past decade has seen the identification of new potential cancer sites and revisions of previous estimates of risk. Most recently, a reassessment of calculated gamma and neutron dose received by individuals has led to a major change in the carcinogenic, or cancer-producing, role assigned to neutrons and to a modest revision in estimates of gamma doses.

A series of epidemiological studies designed to detect genetic effects among the offspring of atomic bomb survivors has shown no statistically significant difference between them and the offspring of groups not exposed to the radiation. The genetic studies have provided valuable assurance that the use of animal data (see section on "Animal Studies") does not seriously underestimate the effect on human populations. The epidemiological results are consistent with the mouse data and also allow us to confidently place an upper bound on the level of somatic effects in irradiated humans.

Although the study of bomb survivors was the predominant factor in developing a quantitative estimate of the effects of various levels of exposure, i.e., a dose-response relationship for radiation-induced cancer, it has inherent limitations, notably that the data were compiled from a single exposure at a high dose rate and the population samples are not large enough to define with any confidence the risk of very low dose rates. These factors made questionable the extrapolation of the dose-response curve to lower, prolonged exposures without additional information. Moreover, animal studies had shown that the results of high doses of low energy-transfer radiation (low energy particles or gamma radiation) received over a short period of time are of far more consequence than the same dose received over a long period of time. As a result, studies of industrial workers were begun by the AEC as early as 1964. The initia studies of Hanford and other DOE-contractor employees have subsequently been expanded to include naval shipyard workers and soldiers present at nuclear weapons tests in Nevada. The results to date have reinforced the low risk that would be predicted for workplace external exposures.

The AEC initiated a study of radium-dial painters subjected to radiation from internal radium deposits accumulated in the era before the health effects of radiation exposure were generally known. Radium emits high energy alpha-particles and a gamma ray. These epidemiological studies have provided the primary basis for setting all such standards for radium and for transuranic elements such as plutonium, which also emit alpha-particles and gamma rays. Epidemiological research on chronic internal exposure has more recently been expanded to include plutonium workers at several DOE facilities. Results of this ongoing work have corroborated the adequacy of current standards for these alpha emitters.

Animal Studies Important information about the risks from exposure to radiation has been derived from large-scale animal experiments. These studies determined the potential cancer or genetic effects from internally deposited radionuclides or from external radiation and revealed the importance of the rate with which the radiation is received, as well as the relative biological effectiveness of different types of radiation.

Because there was minimal human data on the effects of long-term exposure to low levels of radiation, animal data had to play a significant role in estimating guidelines for allowable human exposure to different types of radiation. Between 1956 and 1966, three large studies on mammals were conducted to determine (1) the latent effects of plutonium exposure in dogs and rodents, (2) the relative toxicity of strontium-90 and radium-226 deposited in the skeletons of humans and other mammals, and (3) the genetic effects of external radiation in mice. By 1974 ten major animal experiments were in place to determine the uptake, metabolism, dosimetry, and early and late effects of exposure to most major fission products of concern. There were also concerns about the importance of chemical forms of plutonium administered by different exposure routes and the importance of dose (quantity and rate) of external gamma ray or fission energy neutrons in the induction of late somatic or genetic effects.