mutagenic, and toxic effects of energy related chemicals and complex mixtures of chemicals;

6. Define mechanisms involved in the induction of biological damage following exposure to low levels of energy-related pollutants by supporting research on biomolecular structure, gene function and control, genetic damage and repair, and cell transformation; and

7. Develop new approaches, instruments, and methodology for the improved diagnosis and therapy of human diseases, and in the study of human physiological processes, including the brain and heart.

The research is carried out in the following major program activities.

Health Effects Research This program is primarily concerned with evaluating the delayed types of health effects—tumors, heritable defects, developmental effects, and damage to body organs—that are caused by chronic low-level exposure to energy-related physical and chemical agents. The research utilizes molecular, cellular, and animal test systems to obtain quantitative data on dose response relationships and to develop an understanding of differences in species sensitivity. Because credible extrapolation of such data to man requires a knowledge of the mechanism underlying the induction of adverse effects in different species and because the production of delayed effects is not clearly understood, extensive use is made of generic and basic research to provide experimental systems, techniques, and insights having the broadest application to health-risk prediction. Included is the development of improved biological test systems and improved techniques for the extrapolation of experimental data to man.

Health effects research cuts across virtually all of the energy technologies. Areas of ongoing research include those that address health effects associated with the broad spectrum of ionizing radiation and a variety of energy-related chemicals, including indoor air pollutants, PAHs, and related compounds associated with synthetic fuels production. Extensive research is conducted to elucidate the mechanisms which cause cancers and mutations, metabolism of energy-related chemicals, and mechanisms of DNA repair. Categories of research include:

1. Carcinogenesis (the production of cancer)—Both established and developing energy technologies produce or involve physical and/or chemical agents that can cause human cancer. Carcinogenesis research emphasizes evaluation of the tumor-causing potential of such agents, detection and characterization of carcinogens, elucidation of pathways and ways to detect formation and growth indicators of tumor, investigations to correlate exposure conditions (carcinogen dose) with tumor incidence in animal populations, and elucidation of mechanisms of carcinogenesis.

   Because the production of cancer is a complex process that may include discrete initiation and promotion steps, research into cancer induction often involves the study of complex interactions among different causative agents. Emphasis is also being given to researching free radicals and other oxidizing species that play a role in both chemical and radiation carcinogenesis.

2. Mutagenesis (the production of mutations)—Alteration of genetic material by physical and chemical agents may produce heritable defects as a result of mutations in reproductive, or germ, cells. Mutations in nonreproductive, or somatic, cells may result in cell modifications, leading to cancer or other health effects. The mutagenesis research program emphasizes investigations of the mutagenic potential of energy-related physical and chemical agents; metabolism of chemical agents in target cells; correlation of mutation frequency with level of exposure to a mutagen; evaluation of health consequences that mutations may produce at the population level; measurement of chemical damage to DNA formation; and elucidation of mechanisms of mutagenesis, including the relationship of mutagenesis to tumor induction. Effects on germ cells (chromosomal modifications) are also studied in detail.

3. Systems damage—Many hazardous environmental agents manifest their toxic potential by impairing one of the body's functional systems. Such effects—particularly delayed impairment of the respiratory, immune, nervous, reproductive, and blood forming systems or the developing embryo/fetal system—may lead to chronic disease with attendant health costs. The major efforts in this research area include the identification of early indicators of biological damage, interspecies comparison of major functional systems and their sensitivity to environmental agents, the development of improved biological test systems, and the conduct of dose response studies that support risk estimates for man.

4. Basic research—This is a substantial research effort aimed at providing the mechanistic and conceptual foundation that is needed to understand how physical and chemical agents interfere with life processes. Emphasis is on molecular and cellular studies to elucidate the normal structure and function of key biological systems or processes. Included is research in biophysics (structure of macromolecules and organelles), genetics (including DNA damage and repair), and cell biology (cell growth, cell differentiation, and cell regulation).

Human Health and Assessment The Human Health and Assessment program supports research to provide information on the response of individuals and human populations to toxicants and the feasibility