tions in Latin America, bringing together for the first time the food laws and regulations of the Latin American countries. There is extreme variability in approach by the various countries.

Robert Angelotti gave a succinct and unequivocal summary of U.S. requirements, which have a major impact on the massive U.S. imports of fresh and processed foods from other American countries.

E. R. Méndez reviewed the existing and prospective international agreements on food standards under this important multinational program sponsored by the World Health Organization and the U.N. Food and Agriculture Organization. The world urgently needs to accelerate the development and acceptance of standards under the *Codex Alimentarius*. It also needs more bilaterally accepted standards to expedite food trade among nations. Standards, however, only reflect quality. Adequate technology applied in food production, processing, storage, and distribution is essential to assure foods that meet adequate standards of quality, safety, and wholesomeness. Continuing communications among food technologists of the Americas can be highly productive.

William Darby noted the essential and growing role of food technology in the adequate nutrition of the peoples of the world. He addressed the problem of chemical residues and concluded that chemicals are necessary to the production and protection of an adequate and safe food supply. Residues must be kept at nonhazardous levels through careful use of chemicals and surveillance of residues in food products.

As Darby emphasized in his summary, technology cannot make food absolutely safe, but its application can, and should, assure that all food in commerce meets standards reflecting "acceptable minimal risk." He noted the recent formation in the United States of the Citizens Commission on Science, Law, and Food Supply, which will examine questions of risk-benefit and develop guidelines for decision-making on important issues related to foods.

RAFAEL ROJAS GUTIERREZ
Laboratorios Nacionales de Fomento Industrial, Mexico D.F.

T. C. BYERLY
U.S. Department of Agriculture, Office of the Secretary (Retired), 6-J Ridge Road, Greenbelt, Maryland 20770

Environmental Mutagens

Increasing concern over release of genetically active materials into the environment was reflected in the organization of the First International Conference on Environmental Mutagens, held at Asilomar, California, 29 August to 1 September 1973. The conference was sponsored by the American Environmental Mutagen Society (EMS) and was organized by B. Ames (University of California, Berkeley), S. Wolff (University of California, San Francisco), and A. Sparrow (Brookhaven National Laboratory).

Representatives of the European, Japanese, and Indian Environmental Mutagen Societies were present; an International Association of Environmental Mutagen Societies had been formed before the end of the conference.

L. Fishbein (National Center for Toxicology Research, Jefferson, Arkansas) pointed out that about 500 new chemicals are introduced industrially each year; thousands are already in use. Most have not been adequately tested for mutagenicity, carcinogenicity, or teratogenicity. In his welcoming address, A. Hollaender (Oak Ridge National Laboratory) indicated that the EMS would like to see all chemicals that reach the public tested for mutagenicity.

T. Tazima (National Institute of Genetics, Mishima, Japan) emphasized that in our concern over man-made chemicals, we should not forget natural toxic compounds. The bracken fern *Pteridium aquilinum* is eaten in Japan and is now appearing in U.S. food markets. This fern contains an uncharacterized chemical which is carcinogenic and mutagenic in the fruit fly *Drosophila*. There is no evidence so far for species-specific carcinogens, according to U. Saffiotti (National Cancer Institute).

Cycads, used as both food and medicine in tropical and subtropical areas, contain toxic substances. Investigation revealed that nontoxic cycasin, methylazoxymethanol-β-D-glucoside, is metabolized to form methylazoxymethanol which is toxic and carcinogenic, and behaves as a mutagen in the bacterium *Salmonella* and in *Drosophila*.

The most important natural mutagens are the mycotoxins produced by various fungi which grow in stored grain and contaminate fermented food. Aflatoxins, the best known mycotoxins, induce mutations in mice, in *Vicia fava*, in *Salmonella*, and in human cells grown in tissue culture. Aflatoxins are also suspected to be a major cause of human liver cancer. Mycotoxins have a wide variety of chemical structures. The common element appears to be the presence of a lactone ring; destruction of this ring destroys their mutagenic effect. Besides mutations, mycotoxins cause mitotic injury, breaks in double-stranded DNA, and chromosome aberrations.

Among the more prevalent man-made mutagens are some herbicides and pesticides. Dioxins, potent teratogens found as impurities in the herbicide 2,4,5-T (Agent Orange of the Vietnam war), were discussed by Fishbein and S. Epstein (Case Western Reserve University School of Medicine). After it was discovered that dioxins were powerful toxic agents, efforts were made to decrease the dioxin content of 2,4,5-T and related herbicides, such as the widely used Silvex [2-(2,4,5-trichlorophenoxy)propionic acid]. The herbicide 2,4,5-T was banned for use on food crops but is still commonly used by state and federal forest service personnel. Dioxins are formed when these herbicides are pyrolyzed; herbicide killed brush is often burned off.

In an extensive study of the cytological effects of pesticides on the cells of vascular plants, W. Grant (McGill University) found the following abnormalities: chromosome breakage, endopolyploidy, C-mitoses, multipolar anaphases, multinucleate cells, chromosome stickiness, despiralization of chromosomes, chromatin clumping, chromosome rearrangements, anaphase and telophase bridges, lagging chromosomes, and nuclear swelling.

Pesticides may also react with substances in the environment to form mutagens. For example, R. Elespuru (Oak Ridge National Laboratory) found that carbaryl reacts with nitrite to form nitrosocarbaryl which is highly mutagenic in the bacteria *Hemophilus* and *Escherichia coli*.

Increasing concern is now being expressed for the mutagenic effects of various drugs. Licit as well as illicit drugs may be harmful. G. Röhrborn (University of Heidelberg) found isoniazide mutagenic in one system and inactive in another. The widespread use of isoniazide therapy and prophylaxis of tuberculosis makes it important to evaluate the hazard of this drug.

L. Zetterberg (Department of Genetics and Plant Breeding, Uppsala,

Sweden) indicated that the tranquilizer chlorpromazine can induce genetic effects in *E. coli* and in yeast. This drug causes mutations in these organisms only if they are exposed to light. Possibly chlorpromazine could be carcinogenic in skin that has been exposed to the sun.

Phencyclidine is a veterinary anesthetic currently sold on the illicit market as a hallucinogen. F. Walker (Childrens Psychiatric Reseach Institute, London, Ontario) found this drug to be teratogenic. Users of phencyclidine had increased rates of fetal loss, decreased fertility, extensive chromosome breakage, and increased presence of a small chromosome that resembled the Philadelphia chromosome. Their offspring had an abnormally large incidence of spinal defects, limb reduction anomalies, triploidy, and trisomy.

Industrial chemicals are another source of potential mutagens. B. Kilbey (University of Edinburgh) studied effects of various amounts of the carcinogen diepoxybutane (DEB) on the rates of reversion of adenine-requiring mutants of *Neurospora.* This chemical is used to cure polymers and cross-link textile fibers. Effects on *Neurospora* that were related to the dose of DEB appeared only at low DEB concentrations. It is believed that DEB may interfere with both DNA and its repair systems. This theory is supported by increased sensitivity to mutagenic effects of ultraviolet light and of DEB after pretreatment with DEB. The effect is transient, indicating that the damage to the DNA repair system is itself repairable. Actidione prevents this repair, suggesting that the restoration of repair function requires protein synthesis.

Mutants of *Salmonella* and *E. coli* were used by F. Mukai and I. Hawryluk (New York University Medical Center) to demonstrate the mutagenicity of a series of haloethers and haloketones, including dimethyl carbamyl chloride, epichlorohydrin, chloropentafluoroacetone, and chlorotetrafluoroacetone.

The harmful effects of radiation exposure emphasize the need for tests that can measure radiation exposure and chromosome damage in man. In an effort to validate the extrapolation of animal data to man, J. Brewen and J. Preston (Oak Ridge National Laboratory) studied x-ray–induced aberrations in the chromosomes of peripheral leukocytes of six mammalian species. They concluded that in vitro radiation experiments correlated well with in vivo ones. They found human leukocytes twice as sensitive to radiation-induced translocations as those of the mouse. Marmoset leukocytes, cultured for the first time, may be particularly useful because the marmoset has the same number of chromosomes as man.

W. Brandon (University of Denver) found a marked increase in the occurrence of chromosomal aberrations in cultured peripheral lymphocytes from workers exposed to plutonium. He also found that uranium miners exposed to radon-222 showed an increase in chromosomal aberrations. This may prove of value as a biological indicator of mining radiation exposure.

It was the consensus among conference participants that environmental mutagens constitute a significant social problem, the magnitude of which must be carefully evaluated, and that adequate methods of societal control of genetically active substances should be established.

SELINA BENDIX
Bendix Research, 1103 The Alameda, Berkeley, California 94707

Enzyme Engineering

Considerable worldwide interest has arisen in recent years in the controlled use of enzymes as catalysts in industrial processing, analytical chemistry, and medical therapy. Significant new approaches with high economical and technological potential for solution of a number of problems in each of these areas currently are under investigation. Much of this potential has evolved from the development of techniques for enzyme immobilization on a wide variety of support materials, improved enzyme purification, and induction of microorganisms to produce large amounts of selected enzymes. This interest has generated the new interdisciplinary field of enzyme engineering, which includes both the scientific and technological aspects of the production, isolation and purification, immobilization, and application of enzymes in a variety of situations and reactor configurations.

Although several applications of immobilized enzymes are in commercial use or appear very promising, a number of technical problems limit other practical applications in industry, chemical analysis, and medicine. In order to generate ideas and direction for overcoming these problems, the Engineering Foundation with financial support from the Corning Glass Works sponsored the Second International Conference on Enzyme Engineering held on 5 to 10 August 1973 at Henniker, New Hampshire. More than 190 selected speakers and scientists from 18 countries participated, including biochemists, chemical engineers, microbiologists, and a variety of other specialists from industry, government, and universities. L. B. Wingard, Jr. (University of Pittsburgh) served as executive chairman and E. K. Pye (University of Pennsylvania) was program chairman with the assistance of an international advisory board.

Two major emphases of the conference were the application of immobilized enzymes and the problems of utilizing cofactor-requiring enzyme systems. L. B. Wingard, Jr. (University of Pittsburgh) opened the conference by citing the developments since the 1971 conference and by challenging the participants with the need for definitive economic and technical evaluations of specific applications of immobilized enzymes, for greatly improved feedback on economic and operational problems from industry to universities and granting agencies, and for more academic input toward resolving the more difficult problems of enzyme stability, cofactor systems, multienzyme systems, and enzyme moderated energy transfer.

Many of the potential applications of immobilized enzymes necessitate systems that require cofactors, which like the enzymes may be too expensive to use once and discard. By the immobilization of cofactors to either soluble or insoluble supports together with the provision for regeneration of these cofactors, several reaction schemes and reactor configurations can be visualized that may lead to the development of practical immobilized enzyme-cofactor catalytic systems. M. K. Weibel (University of Pennsylvania) and K. Mosbach (University of Lund) described the immobilization of nicotinamide adenine dinucleotide (NAD) and I. Chibata (Tanabe Seiyaku Co., Japan) reported the immobilization of coenzyme A. Several cofactor regeneration schemes were described: nicotinamide adenine dinucleotide phosphate by N. L. Smith (University of California at Irvine), NAD by R. P. Chambers (Tulane University), and adenosine triphosphate by D. Marshall (Battelle at Columbus) and C. K. Colton (Massachusetts Institute of Technology).

Reports on industrial applications of immobilized enzymes included the treatment of milk with proteases (N. Olson,