American governments look on ecology as merely a professional extension of birdwatching or as "simply the anti-pollution science," whose chief impact might be to increase the cost of building factories and digging mines.

Strong tended to agree. But he said that, while the term "environment" had yet to acquire a charismatic appeal among developing nations, the issues it embraces—especially those of exploding urban populations—are of "real and growing concern to them."

Similarly, B. R. Seshachar, a zoologist at Delhi University and president of the Indian National Science Academy, said that it was "extremely important that the developing countries do not obtain the impression that advanced countries are attempting to thwart development," by using pollution-control as an excuse to slow industrialization.

But if the U.N. conference next year must contend with the reluctance of the poor, it seems that the petulance of the wealthy may be a problem too.

An East-West Flap

Christian A. Herter, Jr., the U.S. State Department's chief representative to the U.N. conference, told the colloquium that a diplomatic dispute over the status to be accorded East Germany during a pan-European environmental conference in Prague earlier this month had "nearly wrecked" the conference. The Prague meeting had been organized by the U.N. Economic Commission for Europe, and its purpose was to generate interest in the main event next year. Soviet delegates, Herter said, blocked proceedings for 5 days in an attempt to win membership privileges for the German Democratic Republic. "They nearly took it to the breaking point," he said, but the confrontation ended in "harmony" when participants agreed to demote the meeting to a "symposium," connoting a lesser meeting of experts, not of governments.

Senator Magnuson asked whether the German dispute might surface at Stockholm, and whether mainland China, with one-third of the earth's population, might be invited to attend.

In a burst of extreme optimism, Herter replied that, "We don't know what effect [this issue] will have at Stockholm, but I hope that it may be resolved by the two Germanys before the 1972 conference." China's attendance, he said, may be settled by a U.N. membership vote this fall.

Through it all, Maurice Strong remains buoyant: "Stockholm will be neither the beginning nor the end. . . . It will be, I trust, the launching pad for a major new international quest for global knowledge about the relationship between the human race and its earthly habitat."—ROBERT GILLETTE

Drug Efficacy Study: FDA Yields on Fixed Combinations

Our problems persist; in fact, they hardly ever change character or form. There are times I feel condemned like the mythical Sisyphus, who, you may recall, had to push a heavy stone up a steep hill in Hades, only to have it always roll down again when he approached the top.—W. H. CONZEN, outgoing chairman of the Pharmaceutical Manufacturers Association and president of Schering and Plough, Inc., discussing the problems of the drug industry.

In the above statement, Conzen is referring to the rocks of regulation that the federal government occasionally hurls into the drug manufacturers' valley of profit. And, in spite of the way they view their grim fate, Conzen and his colleagues have been quite successful over the years in pushing the government's rocks up that steep hill and out of their valley.

Just in the past few weeks, the drug companies have brought sufficient pressure on the Food and Drug Administration to lessen the impact of the agency's new drug effectiveness policies. Based on the 1962 Kefauver-Harris amendments to the Food, Drug, and Cosmetics Act, the effectiveness policies mark a major turning point in the regulation of prescription drug sales. The outcome of the current confrontation over these policies between the FDA and the pharmaceutical industry will have far-reaching implications for American medicine. Included among the issues in contention are the questions of whether controlled studies should replace empiricism in the determination of which drugs are put on the market, and the "rights" of doctors to treat their patients with anything they choose.

Passed in the wake of the thalidomide tragedy, the 1962 amendments require that drugs be shown to be effective, with respect to the manufacturers' claims, before they are put on the market. Prior to 1962, the drug companies had only to demonstrate product safety. The 1962 amendments applied not only to new drugs but also retroactively to all drugs introduced between 1938 and 1962. Thus, FDA was faced with the monumental task of evaluating the validity of over 10,000 claims made for some 3000 drugs, including most of the commonly prescribed drugs in the country.

After a 2-year grace period followed by a 2-year delay, FDA turned to the National Academy of Sciences and its National Research Council to implement the study. The NAS–NRC established 30 panels, each consisting of six academic and medical experts, to evaluate the claims of a certain group of remedies. On the basis of the scientific literature, information from the manufacturers and from the FDA, and "the experience and informed judgment of the members of the panel," the drugs were classified into a series of categories: effective, probably effective, possibly effective, ineffective, ineffective as a fixed combination, and a catchall category of effective but doubtful about certain claims.

At the conclusion of the NAS–NRC study, which spanned the 3 years from 1966 to 1969, the panelists said in their final report that they found a "deplorable situation" in the quality of the labeling of the drugs and in the quality of the evidence submitted by the drug manufacturers to back up their claims of effectiveness. They rated only 20 percent of all the drug claims as effective and 39 percent of the individual

Suit against Fast Breeder Reactor

The national Scientists' Institute for Public Information (SIPI) has filed suit against the Atomic Energy Commission (AEC) for failing to submit an environmental impact statement on the effects of the development of the liquid metal cooled, fast breeder reactor and its eventual commercial use in power plants.

The suit charges AEC with violation of the National Environmental Protection Act (NEPA) and asks that the AEC meet legal requirements by issuing a statement describing alternatives to the reactor and the potential impact of the program on the environment.

The AEC has announced it will circulate environmental impact statements on individual fast breeder nuclear reactors as they are built. SIPI's demand for submission of an impact statement early in the development stage is viewed as a departure from current practice. Such legal action in the past has been taken only against specific reactor projects. A precedent for the action, cited by SIPI, was the filing last year of a similar suit against the supersonic transport.

SIPI was particularly critical of the use of plutonium as a fuel for the fast breeder reactors and, in a statement issued when the suit was filed, the organization said that "By the year 2000, the AEC predicts that hundreds of these fast breeder reactors would be located throughout the United States. Such a situation would pose the risks of explosion, accidents, sabotage, and a plutonium black market, all of which might lead to radiation contamination of the environment."

SIPI is an organization of 15 distinguished American scientists established to provide the public with understandable scientific information on important public issues. Some 15 local scientific information committees are affiliated with the national organization.

The suit was filed in U.S. District Court in the District of Columbia by the Natural Resources Defense Council, a public interest law firm, on behalf of SIPI. It is the first such legal action undertaken by the national SIPI group.

drugs as effective; they found the majority of drugs lacking evidence of effectiveness as defined by the 1962 amendments.

As soon as FDA issued its first orders against ineffective drugs back in 1968, it was deluged with hearing requests, lawsuits, and other legal obstacles presented by the pharmaceutical manufacturers. These obstacles were finally removed by a 20 October 1970 court decision declaring that FDA could force the antibiotic product Panalba off the market (*Science*, 29 August 1969). The FDA was thus given a green light by the courts to proceed against those drugs ruled less than effective by the NAS–NRC panels.

Now, however, the FDA is facing a new wave of opposition. In the past several weeks, both Congress and the FDA have received hundreds of letters from irate physicians protesting the impending regulatory actions. During recent congressional hearings, FDA representatives charged that many of these letters resulted from drug company detailmen (salesmen) misinforming the doctors as to FDA's intentions and urging the doctors to write in protest.

Most of this protest focused on the FDA's policy regarding fixed combination drugs—that is, mixtures of prescription products. And it is in regard to fixed combination drugs that FDA has given in to the pressure.

The NAS–NRC panels established the designation of "ineffective as a fixed combination" because these drugs present a special problem in determining whether the product is effective as claimed. Usually, each component of the mixture is effective for some purpose when taken as a separate entity. Thus, each combination drug is bound to cure something. This was the case with Panalba, which was a mixture of two antibiotics, tetracycline and novobiocin. But the NAS–NRC panelists decided that a combination drug had to be more effective than either of its components taken alone. The NAS–NRC panel evaluating Panalba conceded that it cured everything that tetracycline alone would cure, but the panel declared the drug to be ineffective as a fixed combination because the presence of the second drug appeared not to enhance this process.

The NAS–NRC panelists generally came down very hard on fixed combinations. They rated as effective only 45 combinations out of some 1200 studied. The panel's overall attitude toward the fixed combinations threatens a good deal of the potential sales of the pharmaceutical industry. Combination drugs now account for over half of the products sold nationwide and some 40 percent of the best-selling drugs. In addition, they represent a large percentage of future markets, since selling combinations greatly expands a drug company's potential range of products.

Convenience and economy generally form the basis of the arguments offered in favor of retaining the combination drugs. The Pharmaceutical Manufacturers Association commissioned a study which concluded that prescription drug costs would somehow rise 59 percent if combination drugs were eliminated. And some practicing physicians believe that a patient is more likely to take multiple drugs if they are contained in one pill.

On the other hand, the panelists feared that the risk of a patient's receiving a drug he doesn't really need or taking an improper dose of a drug far outweighs considerations of convenience and economy. Nevertheless, the FDA seems to be moving much closer to the industry viewpoint regarding the combination drugs. In recent hearings before the House Health and Environment Subcommittee, Commissioner Edwards made it clear that the agency doesn't feel bound by the Academy's decisions on combination drugs and is preparing to further modify a proposed FDA statement governing the effectiveness of such products. This prompted the Pharmaceutical Manufacturers Association to declare that "Industry and FDA now appear to be in agreement that if a combination benefits a few patients but not most it should be kept."

This distinction between a "few" and "most" is critical to the entire efficacy review. The Kefauver-Harris amendments defined efficacy as "substantial evidence" based on "adequate and well-controlled investigations, including clinical investigations." In arguing against enactment of the Kefauver-Harris amendments in 1962, a rep-

resentative of the American Medical Association said that the efficacy requirement would "substitute the judgment of governmental officials for the time-proven system of the consensus of the medical profession as to the ultimate usefulness and efficaciousness of a particular drug." Stated in a different way, "Old Doc knows best." In its various forms, this argument is the primary weapon now being used against enforcement of the NAS–NRC efficacy finds. Many doctors, having successfully prescribed for years some of the drugs that are now threatened with extinction, feel it to be a professional insult.

This has resulted in something of a town versus gown battle regarding implementation of the panel's determinations, with some doctors decrying the lack of private practitioners on the NAS–NRC panels. One doctor's letter to his congressman criticized "the ivory tower thinking of bureaucrats or academicians who are out of touch with the realities of patient care." Responding to this criticism, Edwards said, "In my judgment, a physician is a physician and treating patients is treating patients, whether it is in a large medical center or in the family doctor's office."

One champion of the industry's position has, however, risen from the ranks of academia. Louis Lasagna, professor of Pharmacology and Toxology at the University of Rochester and a chairman of one of the NAS–NRC panels, wrote a long article in the 8 April *Wall Street Journal* arguing, among other things, that "a respectable minority opinion" should justify the approval of a new drug.

Lasagna said in the article that he never believed that the FDA would go to the lengths that they have in implementing the NAS–NRC recommendations. "I can only express dismay," he said, "at the impact our recommendations seem to be having. I'm not sure which metaphor is more apt, Pandora's box or Frankenstein's monster, but the results are frightening to view."

Several other panel chairmen contacted by *Science* did not share Lasagna's viewpoint. And some seemed outright perturbed that he had taken the stand that he did. All of those contacted said that they were aware of FDA's implementation plans before they began their deliberations. "Why else would we have gone to all that trouble?" asked one of the panel chairmen.—ROBERT J. BAZELL

APPOINTMENTS

Stephen H. Spurr, dean, Graduate School, University of Michigan, to president, University of Texas, Austin. . . . **John E. Corbally**, president and chancellor, Syracuse University, to president, University of Illinois. . . . **Stanford Cazier**, vice provost, Utah State University, to president, Chico State College. . . . **Harry P. Graham**, vice president for development, Voorhees College, to president of the college. . . . **J. Roger Miller**, executive vice president, Milliken University, to president of the university. . . . **Manson V. B. Jennings**, dean, Graduate School of Arts and Sciences, Adelphi University, to president, Southern Connecticut State College. . . . **Edward A. Gall**, acting vice president, University of Cincinnati Medical Center, named vice president. . . . **Aksel A. Bothner-by**, chairman, chemistry department, Carnegie-Mellon University, to dean, Mellon Institute of Science. . . . **Hilliard Roderick**, head, international cooperation in science division, Directorate for Scientific Affairs, Organisation for Economic Cooperation and Development, to director, Environment Directorate, OECD. . . . **David M. Gates**, professor of biology, Washington University, to director, University of Michigan Biological Station. . . . **Howard L. Hartman**, dean of engineering, Sacramento State College, to dean, School of Engineering, Vanderbilt University. . . . **Richard H. Wanner**, professor of psychology, Dickinson College, to dean of the college. . . . **Daniel Z. Gibson**, former president, Washington College, to academic dean, Salisbury State College. . . . **Charles E. Cornelius**, dean of veterinary medicine, Kansas State University, to dean, College of Veterinary Medicine, University of Florida. . . . **David J. Moore**, associate professor of biology, Radford College, to dean of natural sciences at the college. . . . **Walter T. Grandy, Jr.**, professor of physics, University of Wyoming, to chairman, physics department at the university. . . . **Loren J. Humphrey**, associate professor of surgery and microbiology, School of Medicine, Emory University, to chairman, surgery department, University of Kansas Medical Center. . . . **Benjamin F. Trump**, professor of pathology, Duke University, to chairman, pathology department, School of Medicine, University of Maryland. . . . **Albert Bush-Brown**, vice president for facilities planning, State University of New York, Buffalo, to chancellor, Long Island University. . . . **Robert H. Maier**, vice chancellor, University of Wisconsin, Green Bay, to chancellor, University of Michigan, Dearborn. . . . **Mark C. Ebersole**, program adviser, Ford Foundation, to dean, Graduate School, Temple University. . . . **Norman C. Nelson**, professor of surgery, School of Medicine, Louisiana State University, to dean of the medical school. . . . **Thomas Wartik**, chairman, dentistry department, Pennsylvania State University, to dean, College of Science at the university. . . . **Thomas B. Brewer**, chairman, history department, University of Toledo, to dean, College of Arts and Sciences, Texas Christian University. . . . **Hatten S. Yoder, Jr.**, petrologist, Geophysical Laboratory, Carnegie Institution of Washington, to director of the laboratory. . . . **Gerald L. Wilson**, associate professor of electrical engineering, Massachusetts Institute of Technology, to director, Systems Engineering Laboratory at M.I.T. . . . **Samuel P. Ellison, Jr.**, acting dean, College of Arts and Sciences, University of Texas, Austin, to dean, new College of Natural Sciences at the university. . . . **Daniel J. Zaffarano**, chairman, physics department, Iowa State University, to vice president for research and dean, Graduate College, at the university. . . . **J. Stewart Lott**, head, radiotherapy division, Johns Hopkins University, to director, Ontario Cancer Foundation Kingston Clinic, and head, therapeutic radiology department, Queen's University. . . . **F. James Rutherford**, associate professor of science education, Harvard University, to chairman, science education department, New York University. . . . **J. David Bristow**, professor of medicine, Medical School, University of Oregon, to chairman, medicine department at the university. . . . **Warren G. Bennis**, former vice president for academic development, State University of New York, Buffalo, to president, University of Cincinnati. . . . **Thomas N. Bonner**, provost for academic affairs, University of Cincinnati, to president, University of New Hampshire. . . . **E. Bruce Heilman**, president, Meredith College, to president, University of Richmond. . . . **Alfred C. Emery**, professor of law, University of Utah, to president of the university. . . . **Archie L. Buffkins**, executive assistant to the chancellor, University of Maine, to chancellor, University of Maryland, Eastern Shore.