

radars in hardened sites.

The radars, the computers and missiles must also be integrated and tested, a task that is to begin this summer. Individual components have already been tested. The MSR, operating at Kwajalein Atoll in the Pacific since 1968, has been combined with four data processors and has tracked ICBM launches from California. Out of 15 launches, the Spartan has had 11 complete successes. The Sprint, out of 38 launches, has had 19 complete successes and 9 partial ones. The PAR is nearing production, and the Defense Department is convinced that, short of an actual attack, the system will be adequately tested.

But whether it is because the system has been changed to meet such technical criticisms as the vulnerability of the radar to attack and the inadequacy of piecemeal testing, or the critics have conceded that other objections to Safeguard are more telling, the tenor of the argument seems to have shifted away from the technical.

According to Dr. Jerome B. Wiesner, provost of Massachusetts Institute of Technology and President Kennedy's science adviser, the debate has shifted this year because the Administration has conceded a key point—the over-all capabilities of the system against an all-out Soviet attack against the Minuteman installations. In his presentation of the Defense Program and Budget in February, Secretary of Defense Melvin R. Laird admitted that that threat “could actually turn out to be considerably larger than the Safeguard defense is designed to handle.” The Administration defends the deployment of the system, however, maintaining the cost to the United States would be less than the cost to the Soviet Union of enough ICBM's to overwhelm the ABM.

Opponents, therefore, have focused their attacks this year on belief that the deployment of Safeguard would hinder Strategic Arms Limitation Talks with the Soviet Union currently under way in Vienna. The Administration, on the other hand, believes that Safeguard will strengthen the United States' position. The Soviet negotiators will know, Laird says, that should the talks fail, the United States is in a position to enlarge and continue the program.

“To an observer from a distant planet,” says Dr. Donald F. Hornig of Eastman Kodak Co., and President Johnson's science adviser, “this futile pursuit of actions which only increase the risks we face every day, which progressively threaten the existence of the civilization we have painfully constructed over six thousand years, and which divert the precious resources from things we badly need, must make the earth look like a vast insane asylum.” □

METHOTREXATE

Prescribing without approval

Federal law prohibits the transport of drugs across the state line for uses not approved by the Food and Drug Administration. But legally there is no way a physician can be held liable for prescribing a drug, once it is in his hands, for a use that is not indicated on the FDA-approved label.

Theoretically, doctors are expected to file appropriate forms for such ostensibly experimental activities. Many doctors, nevertheless, claim they are unaware of the need to file the forms, while others find it time-consuming and inconvenient. If a doctor has at hand a drug he believes to be beneficial, it is hard to dissuade him from using it.

A case in point is a drug called Methotrexate, a highly toxic anticancer drug. Physicians have been prescribing it in the treatment of psoriasis, even though the Food and Drug Administration has not approved it for such use. Some 20 years ago physicians stumbled onto the fact that, though Methotrexate does not cure psoriasis, the drug suppresses the scaly, itchy symptoms of the skin disease. Thousands of psoriasis victims have been given the drug in the past 15 years, according to FDA.

Methotrexate is widely used in the United States, says Dr. Gordon A. Caron, a dermatologist at the University of Oregon Medical School in Portland. He says the drug has in fact become standard dermatologic practice for treating severe psoriasis. A recent poll has shown that 56 of 64 institutions that train dermatologists in the United States treat cases of severe psoriasis with the drug. Moreover, recent indications are that the drug is being used more frequently for less severe psoriasis cases.

The official approval for Methotrexate, marketed by Lederle Laboratories of Pearl River, N.Y., is limited to treatment of leukemia and other cancers. The drug acts by inhibiting cell division and has well-known toxicities, including effects on bone marrow and disorders of the gastrointestinal tract (SN: 12/27, p. 595). Leukemic patients get periodic dosages. After a drug-caused remission, a period of time elapses before the drug must be administered again.

The control of psoriasis, however, requires prolonged administration of the drug. Doctors currently use a host of different regimens, most of them consisting of something like one dose every 7 to 14 days, over long periods of time. And a review of such recurrent administration over the past 15 years has disclosed toxic effects not seen in leukemia and other cancers.

Some doctors now suspect that chronic use of Methotrexate may cause severe liver damage, including cirrhosis, which could appear without warning. Dr. Thomas Hayes of FDA's Office of Marketed Drugs says toxicity is difficult to recognize and is not picked up in early stages when symptomatic questions are asked and routine laboratory surveillance tests for bone marrow and peripheral changes are made.

Mouth ulcers, often painful, have appeared in many cases as a side effect, and because the drug suppresses the white cells that fight bacteria, infections are common. In addition, says Dr. Hayes, esophageal bleeding, indicating liver disease, has shown up in some patients on the drug for 12 to 60 months.

Physicians claim they are trained to make decisions daily as to whether the benefits to the patients outweigh the risks of the drug. According to Dr. William M. Sweeney, Lederle's director of medical research, “To warn physicians not to prescribe any medication available on the pharmacist's shelves for a purpose judged to be within the bounds of good medical practice would be irresponsible. To offer directions on how to use the drug in psoriasis is not possible under current Federal regulations. There is no meaningful in-between course of action to take.”

The FDA has remained silent on the subject because, as it sees its primary responsibility, it is to regulate industry and not the medical profession. But last week Dr. Hayes publicly stated that the FDA is aware Methotrexate is prescribed extensively for treating psoriasis and that prolonged use may cause systemic toxicity. “Such risks may be less acceptable in psoriatic patients than in those with leukemia or other neoplastic diseases for which the use of this drug has been approved,” the regulatory official declared.

The FDA's position at this time is based on lack of evidence of safety for prolonged clinical use, but according to Dr. Hayes, there is not a tremendous impact the FDA can have on the prescribing habits of the nation's physicians.

“We are studying what action is necessary, but we don't know what the action will be,” says Dr. Henry Simmons, director of the agency's Bureau of Drugs. “FDA expects to discuss the situation with Lederle shortly.”

Most officials feel that publicizing the problem is a good place to begin, and that at this stage warnings from the manufacturer would have more impact on the prescribing habits of physicians than would the FDA. “Physicians can only be advised,” asserts William Goodrich, chief counsel for the FDA. “It is up to the state medical societies to control them.” □