FDA ACTION

Out with combination drugs

A year ago, the Food and Drug Administration took what was, on the surface, a clear and decisive action. It ordered 78 combination antibiotics off the market, as recommended by the National Academy of Sciences-National Research Council. The NAS-NRC had found those drugs to be either ineffective, dangerous, or both (SN: 4/19/69, p. 378).

Six months earlier the agency had similarly declared a ban on nine other combination antibiotic products (SN: 1/11/69, p. 33).

Some manufacturers, whose drugs were not important to their profit profiles, quietly withdrew their antibiotic combinations from the market. Others took their cases to court, and while FDA and company lawyers fought drawn-out battles, the drugs in question continued to be sold. While the court cases were active the FDA took little definitive action on other types of drugs criticized by the NAS-NRC. Instead, it took considerable criticism for failing to move quickly and protect the public health.

Some of those legal snarls have finally been untangled and the FDA is beginning to move. It has reissued its ban on the combination antibiotics and this time expects it to stick; by the end of July, 48 fixed combinations of penicillin and sulfa drugs, and penicillin and streptomycin will be off the market. From that point on, the three widely used types of antibiotics will be sold singly but not in combination.

The legal blockades to prior FDA action involved procedural matters: the issue of whether FDA could act without granting the manufacturer a prior hearing, and the question of the kind of data that qualified as substantial evidence of drug efficacy.

The Upjohn Co., Wyeth Laboratories and Philadelphia Laboratories challenged FDA on the former issue.

The Pharmaceutical Manufacturers Association had won a court injunction against FDA on the latter. The agency had drawn the PMA fire for ruling that acceptable data must include animal studies and controlled clinical trials; the PMA, on behalf of the drug companies, raised technical arguments about FDA authority to discount testimonial letters from physicians.

As the matter stands now, after receiving word from FDA that a product is to be either banned or subject to relabeling, manufacturers have an alloted period during which to submit evidence in their behalf. If the data fail to conform to FDA standards, the agency can act without a hearing.

Its most recent court suit was filed not by a drug company but jointly by the American Public Health Association and the National Council of Senior Citizens (SN: 6/20, p. 599). This was from the other direction. It charged that the FDA, in failing to act on the NAS-NRC drug evaluations, was negligent in its duty under the law.

The NAS-NRC reviewed for efficacy some 3,600 drugs marketed between 1938 and 1962. Of the 1,200 the FDA has itself subsequently re-reviewed, some, like the combination antibiotics, have been taken off the market; others are in the process of being relabeled, in most cases to modify previous claims; still others, found to meet standards, are being left alone. FDA Commissioner Charles Edwards says that by July 1 the agency should have given at least preliminary review to the remaining 2,354 drugs on the NAS-NRC list so that initial announcements of evaluative findings can be published. □

GEODYNAMICS

From the how to the why

In 1960 an international research program was proposed to direct the attention of geophysicists to the outermost 1,000 kilometers of the earth's sphere, the part that has the most direct influence on the earth's crustal features. After three years in limbo the Upper Mantle Project Committee selected three major international program areas for emphasis: continental margins and island arcs, the world rift system and studies of the viscosity and mechanical behavior of the upper mantle. The committee also accepted a recommendation of Dr. J. Tuzo Wilson of Canada that a prime objective of the program should be to prove whether continental drift occurs.

This year the Upper Mantle Project comes to an end. The period in which it operated has been a revolutionary one for the earth sciences. The mantle has been found to be not a radially symmetrical shell but a layer with significant lateral inhomogeneities. Continental drift, as refined by the hypotheses of seafloor spreading and of plate tectonics, has been demonstrated. The extreme top layer of the mantle couples with the crust to form vast slabs of lithosphere that creep slowly about the earth.

"Although one might reasonably question whether the Upper Mantle Project should get credit for all of the geophysical activities which took place during its period of activity, one cannot question that major advances have been made in the fields selected by the Upper Mantle Committee of 1964," says Dr. Charles L. Drake of Dartmouth College.

With the end of the UMP the natural question concerns the future. An international committee published a report earlier this year outlining a program built on the accomplishments of the UMP, but focusing on the thermodynamics and structure of the lithosphere. Now the International Council of Scientific Unions, which organized the UMP, has created an Interunion Commission on Geodynamics to implement the report's recommendation. Dr. Drake is its president; it has two members from the Soviet Union and one each from Australia, France, the Netherlands and the United Kingdom.

Last week in Arizona, where geologists and geophysicists were gathering for an international symposium held this week in Flagstaff on the mechanical properties and processes of the mantle—the last large symposium of the UMP—the Commission on Geodynamics held its first two meetings. It began outlining the new program.

The focus of the program will be on geodynamics: the dynamic processes, present and past, that have shaped the earth's surface. The focus can be approached in two ways. The first is a study of all relevant physical properties of the earth's interior. Except for some important evidence coming from geochemistry and petrology, most new knowledge of the physics of the earth's interior will have to come from laboratory experiments and theoretical studies. The second concerns all observations relevant to past and present deformations of the earth's surface.

Basically the new program will attempt to gain an understanding of the underlying forces at work producing the horizontal movements of the earth's surface. Despite all the work picturing what happened at the surface, little is known about the driving forces within the earth. Knowledge of the physical properties and behavior of rocks under mantle conditions is also limited. Earth scientists want also to explain not only the horizontal but also the sometimes extensive vertical movements of the plates, such as the uplifting of the Colorado Plateau of Southern Utah and Northern Arizona. The thinking of the commission is that the program would start in a year or so and last about five years.

The geodynamics program will attempt to capitalize on the new-found unity of the earth scientists. "This concept of plate motion has been almost the biggest thing to come along in the history of the earth sciences in bringing together geologists and geophysicists," Dr. Drake says. "It used to be that everybody just did his own thing. The geologists worked on a small scale, studying local regions, and the geophysicists worked on a large scale, studying planet-wide phenomena. Now the two scales are coming together." □