US looking for short cuts to speed drug approval

- AIDS epidemic forces new approach
- Critics say changes just cosmetic

Washington

THE US Food and Drug Administration (FDA) is drafting regulations to streamline the review process for drugs to treat life-threatening illnesses. The FDA began the process of paring down the regulatory procedures for drugs to treat diseases such as AIDS, heart disease and some cancers last week, prodded by the Presidential Task Force on Regulatory Relief chaired by Vice President George Bush.

FDA Commissioner Frank Young was called in to make a presentation on proposals to speed up the drug approval process at a meeting of the Presidential Task Force late last month. At the meeting, Young laid out a plan which would eliminate extensive Phase III efficacy studies involving hundreds of people for drugs to treat life-threatening diseases.

Phase III studies are designed not only to prove a drug's effectiveness in a large patient sample, but also to monitor the drug for long-term side effects. Many have argued that it is more important to get life-saving drugs to patients quickly and take the chance that the drug may cause side effects than to wait and collect all the data while patients are dying.

Young's proposals would establish a mandatory conference between the FDA and company sponsoring the drug at the end of Phase I of the clinical trials, in which the drug's safety to humans and dose are evaluated in less than 50 patients.

At the post-Phase I conference, FDA would sit down with representatives from the company to go over proposed protocols for the Phase II studies — where the drug's effectiveness is tested for the first time in about 150 people — to make sure that the company understands what type of data the FDA is looking for. Phase II tests would be expanded to include enough patients to demonstrate efficacy without the need to move on to the more time-consuming Phase III tests. Once the drug is on the market, companies would be required to file 'Phase IV' data on the drug's side-effects, to enable the FDA to monitor the drug and to revoke its approval if side-effects proved to be severe.

The regulations differ from the 'treatment IND' exception created by FDA last year (see *Nature* **326**, 536; 1987). Under the 'treatment IND', a company may sell drugs for serious or life-threatening diseases only if it demonstrates that it needs the money to continue the clinical trials necessary to file an Investigational New Drug application for approval. The treatment IND exception was formulated to aid small drug companies — primarily biotechnology companies — who may be sponsoring a drug for the first time and have limited cash reserves. But so far, only five companies have taken advantage of the clause because of fears that it would prolong the review process by taking away the pressure on FDA to approve a new drug for use on patients.

The approval last year of AZT as a treatment for AIDS provided the impetus for the new clinical testing regulations. The Phase III testing requirement was dropped for AZT when the Phase II studies showed that it was indeed therapeutic. Because no alternative treatment was available and patients were not expected to live long enough to suffer long-term side-effects, the FDA allowed Burroughs Wellcome to sell the drug without the larger Phase III trials.

In response to pressures to act on drugs being developed for AIDS in a more timely manner, the FDA also established last year a fast-track '1AA' review process for AIDS therapies. But the new '1AA' designation simply ensures that the paperwork is handled faster once the clinical trial data are collected; it does not allow the sponsors of a drug to side-step any of the studies required to demonstrate a drug's safety or efficacy.

As Commissioner of the FDA, Young has been praised for increasing the communication between the agency and companies with drugs in the approval pipeline, but has been criticized for taking a hard line in requiring that a drug be tested adequately, especially in the cases of ribavirin for AIDS and tissue plasminogen activator (TPA) for heart attacks. Sidney Wolfe, of the Health Research Group of Ralph Nader's Public Citizen organization, calls the latest changes a "thinly disguised public relations ploy" to boost Young's image and to make Bush seem more sensitive to health issues as part of his Presidential campaign. Wolfe says the FDA is already empowered to carry out expedited drug reviews, as illustrated by the approval of AZT, without additional rulemaking.

Once the new regulations are drafted, a process expected to take several months, they will be published in the *Federal Register* and opened to public comment.

Carol Ezzell

Seal epidemic still spreading

London

THE epidemic that has killed 7,000 seals in the North Sea and the Baltic in the past six months remains a mystery to researchers from six European countries who took part in a two-day emergency conference organized by Greenpeace International in London last week.

No causal link has been established between the disease that has wiped out half the population of common seals in mainland Europe and two viruses that have been identified in the dead animals. And though it is thought likely that pollutants play a role in the epidemic, the researchers cannot yet say which chemicals are implicated or exactly what their role is. The working party of European researchers is recommending an international, multidisciplinary research project. Meanwhile, leakage into the sea of polychlorinated biphenyls (PCBs) and other persistent pollutants should be stopped until they are proved to be harmless. But questions arise as to the role of pollutants because the area in Denmark where the disease seems to have originated is relatively free from pollution.

A baby seal, surrounded by victims, Isle of Sylt.

The party's recommendations will be presented this week to a government-level meeting in Stockholm.

Symptoms of the disease vary, but those most prominent are lethargy, respiratory problems, skin lesions, abortion, diarrhoea and and nervous complaints. Most of the affected seals die within two days and are found to have inflammation of the lungs, brain, liver, intestines and skin. Two viruses have been identified in the dead seals. One is a herpes virus, already linked to pneumonia outbreaks in seals. The second virus is of the picorna family. How the virus spreads and why the seals react so badly is still unknown, says Dr Minnie Courtney of Queen Mary College, London. There are clear indications that the seals' immune system is being suppressed, and although the link between pollutants and this epidemic is not yet prove, persistent organic compounds such as PCBs and dioxin are known to affect immune response.

Christine McGourty