Potential carcinogens are under-regulated says OTA report

Washington

A KIND of paralysis seems to strike federal agencies when it comes to regulating carcinogens. According to a new report* by the congressional Office of Technology Assessment (OTA), regulatory agencies have set standards for fewer than half the chemicals listed in the government's *Annual Report on Carcinogens*.

Although Washington's bureaucratic jungle has always made setting regulatory standards difficult, the report identifies new hurdles added by the Reagan administration that have further slowed the process.

Since 1978, the National Toxicology Program has been collecting data on potential carcinogens. So far, it has tested more than 300 compounds, and on the basis of interagency discussions concludes that there is sufficient evidence that some 148 of these should be listed as carcinogens in its annual report.

A staggering alphabet soup of federal agencies is responsible for regulating these compounds. The Environmental Protection Agency (EPA), the Food and Drug Administration (FDA), the Occupational Safety and Health Administration (OSHA), the Mine Safety and Health Administration (MSHA), the Consumer Product Safety Commission (CPSC) and the Office of Management and Budget (OMB) all have a role in establishing safety guidelines for exposure to carcinogenic substances. Overlapping jurisdictions are not uncommon. EPA may set environmental standards for a particular substance for emission into the atmosphere, but OSHA may have different standards for acute exposure in the workplace.

Given the potential for bureaucratic tangles, it is of little surprise that OTA found "apparent gaps in regulatory coverage". As an example, OSHA has determined that it has regulatory responsibility for 110 carcinogens listed in the report, but has set standards for only 17.

Less than one month after he took office, President Reagan signed an executive order requiring OMB to review all new regulations, and stating that "regulatory action shall not be taken unless the potential benefits to society for the regulation outweigh the potential costs". The idea was to relieve industry from needless interference from Washington, but critics have argued that not only does this slow the regulatory process, but it is inappropriate for OMB to usurp the authority of other federal agencies.

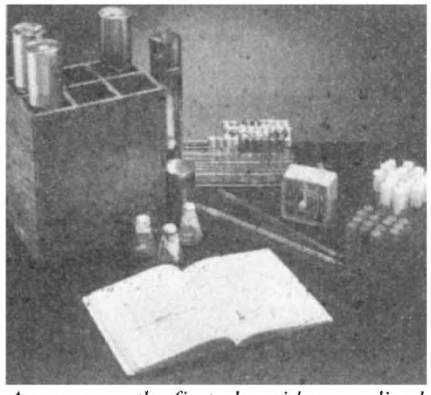
Karl Kronebusch, primary author of the OTA report, says agencies do not feel they have neglected their regulatory responsibilities. He says they argue that the law requires them to evaluate benefits and risks of using chemicals that may be carcinogens. The cost of regulating must also enter into the agency's decision on whether to act. But Kronebusch says it is often hard to tell just what an agency has in mind when it declines to publish regulations on a particular compound, with many compounds languishing in regulatory limbo for years.

The OTA report admits that most cases of cancer are not caused by exposure to environmental carcinogens created by humans. But the report states, "those carcinogenic chemicals that *can* be identified specifically and can be controlled are important for those very reasons: they are avoidable."

Joseph Palca

**Identifying and regulating carcinogens*. US Congress, Office of Technology Assessment, OTA-BP-H-42. US Government Printing Office, Washington, DC, 1987.

Historic exhibits



ALTHOUGH the first plasmid was spliced artificially only 15 years ago, the Smithsonian Institution has decided that an historical exhibit on genetic engineering techniques is in order. The Smithsonian has created an exhibit, "The Search for Life: Genetic Technology in the 20th Century" that opens this week at the National Museum of American History in Washington, DC. The exhibit includes artefacts from the laboratories of researchers who contributed to breakthroughs in the understanding of DNA: Hershey and Chase's Waring blender, Bruce Merrifield's prototype peptide synthesizer, two base plates from the original Watson and Crick DNA model, and the laboratory notebook in which Stanley Cohen first outlined gene-splicing (pictured above). The narrated exhibit is intended to explain the significance of the new biotechnology to the layperson, and also includes a 'cell theatre' with screens that close around the viewer like the petals of a flower to simulate being in the interior of a cell. C.E.

TPA freed for US use at last

Washington

THE long-awaited approval of Genentech's blood-clot-dissolving drug tissue plasminogen activator (TPA) was announced last week by the US Food and Drug Administration (FDA). As the first product of biotechnology with a large market — up to $1 million million per year — TPA is expected to become the first 'blockbuster' of the biotechnology industry. But with the recent approval of streptokinase for intravenous use and future competition, Genentech may have to share the wealth.

Genentech plans to charge between $2,000 and $2,500 for one dose of TPA, under the trade name Activase, according to a company spokesperson. This makes it more than ten times as expensive as streptokinase. But Genentech believes that data suggesting that TPA may be twice as effective in breaking down clots will persuade physicians and patients to spend the extra money.

Genentech's strongest competition will come from 'second generation' versions of TPA made by protein engineering. Genetics Institute — the current leader in the race for the next generation product — has a version of the TPA molecule with an extended half-life in the bloodstream that the company hopes will make the drug more effective. Others working on the natural TPA molecule are Smith-Kline, Integrated Genetics, Eli Lilly and G.D. Searle. Genentech also has a second-generation TPA under development.

The FDA has been under heavy pressure to approve TPA since its decision in May to send Genentech back to the clinic to collect more data on the drug's long-term effect on reducing mortality (see *Nature* **327**, 450; 1987). At that time, the FDA recommended against approval, citing the drug's infrequent side effect of inducing cranial bleeding and the lack of proof that clot dissolution decrease mortality from heart attacks. The decision drew strong criticism from cardiologists, patients and the media, who accused the FDA of allowing an internal battle to keep heart attack victims from receiving a drug that could save their lives. The FDA said the delay was due to Genentech's shoddy design of clinical studies.

After Genentech filed its additional data on 29 September, FDA took just seven weeks to give TPA final marketing approval. The company plans to begin shipping the drug to hospitals within 2–3 weeks. Genentech's foreign licensee, Boehringer Ingelheim, already markets TPA in Austria, West Germany, France, New Zealand, South Korea and the Philippines.

Carol Ezzell