

## Gene-splice product designated 'orphan'

A protein that may benefit emphysema patients is the first recombinant DNA product to be granted "orphan drug" status by the Food and Drug Administration (FDA). CooperBiomedical, Inc., of Palo Alto, Calif., plans to begin this year clinical tests of the protein, which is called alpha-1 antitrypsin (AAT), on patients who lack it due to a genetic deficiency. An estimated 54,000 people in the United States suffer from emphysema because they are genetically deficient in AAT. The FDA expects that about half of these would benefit from the drug.

In normal people AAT is produced in the liver and circulates through the blood. In lung tissue, AAT inhibits excessive activity of elastase, an enzyme that helps destroy bacteria. With insufficient AAT, elastase attacks lung's elastic connective tissue and thus prevents effective breathing. Cigarette smoke can inactivate AAT, suggesting that it and other irritants may lead to some forms of emphysema (SN: 3/26/83, p. 199).

Alpha-1 antitrypsin is the third pharmaceutical to receive orphan drug status under a 1983 act (SN: 1/8/83, p. 22). The act provides tax credits and speeds testing and approval for drugs developed to counter rare diseases. The two other drugs that have been granted orphan status are cancer treatments, one for ad-

vanced ovarian carcinoma and the other for primary brain malignancies.

Scientists at CooperBiomedical, which announced the FDA approval this week, have placed copies of the human gene for AAT into yeast cells. These genetically engineered yeast are expected to be a far more abundant source of the protein than is human blood, from which AAT has also been isolated. Preliminary work by Ronald G. Crystal of the National Institutes of Health in Bethesda, Md., has demonstrated that infusions of AAT derived from human blood can raise the levels of AAT in people with genetic deficiencies, but it is not yet known whether this change can protect a person against emphysema or whether it can change the clinical course.

CooperBiomedical plans to start clinical trials of the yeast-produced AAT this October, and the drug could be available to treat patients routinely as early as the end of 1985.

The drug eventually may also benefit other emphysema patients, who number about 11 million in the United States. "Theoretically it could be used for all emphysema victims," says Joseph A. Dornig of CooperBiomedical. But, he adds, such an extension would require going through the longer FDA approval process. — J.A. Miller

## Risks calculated for dioxin in water

To prevent water contaminated with 2,3,7,8-TCDD — the most toxic form of dioxin — from posing a cancer risk to humans, the chemical's concentration in water "should be zero," according to the Environmental Protection Agency (EPA) in a hazard assessment it issued on the pollutant last week. Acknowledging that "zero may not be an attainable level at this time," it gives human-cancer risk estimates both for drinking water contaminated with dioxin and for eating fish raised in polluted water.

"These criteria are published as the best scientific assessments on the effect of a particular chemical that we can do," explains EPA's Frank Gostomski, who helped develop the guidelines. They have no regulatory impact themselves, he says, until they are picked up as part of a state's water-quality standard. However, EPA expects states to borrow and adapt the data to account for regional differences in rates of fish consumption, types of fish eaten and values about what constitute "acceptable" levels of risk.

One can expect a dioxin-related cancer to develop for every 100,000 persons who consume drinking water contaminated at concentrations of  $2.2 \times 10^{-6}$  mi-

crograms per liter, the report says. This level is too low to measure directly, Gostomski notes. However, ambient levels of dioxin in water can be extrapolated from levels found in fish. EPA's laboratory data have shown a concentration within the fat of fish and shellfish of between 390 and 13,000 times the level in their water.

In estimating the risk posed by dioxin-contaminated fish, EPA assumed a bioaccumulation factor of 5,000 — the average associated with rainbow trout. Data on diet among Great Lakes area residents — where dioxin-contaminated fish have been found — show an average consumption of 6.5 grams (about 0.2 ounces) of locally caught fish daily. From this EPA estimates that eating this much fish from water contaminated with dioxin at levels of just  $1.4 \times 10^{-7}$  micrograms per liter could cause one excess cancer per 100,000 persons. This risk is roughly 10-fold higher than that given by the Food and Drug Administration for similarly contaminated fish. The variance is explained by differences both in the risk-assessment methodologies used and in assumptions about what proportion of the diet is made up of contaminated fish. — J. Raloff

## Holographic eagles wing across country



National Geographic Society

Nearly 11 million three-dimensional eagles — clones to those being checked for defects in the photo above — will fly across the nation this month, affixed to the covers of March NATIONAL GEOGRAPHIC magazines. The eagles are white-light transmission holograms (SN: 3/4/78, p. 141), laser-light recordings of a small 3-D model. Viewable using ordinary (non-laser) light, these holograms draw attention to the magazine's 44-page feature on lasers; they are also the first holograms to be printed in a national magazine.

NATIONAL GEOGRAPHIC acknowledges that it was American Bank Note Co.'s development of low-cost holographic reproduction that made its cover possible. American Bank Note is a subsidiary of International Banknote Co., Inc., a firm that prints stock certificates and foreign currency. Not only did American Bank Note produce NATIONAL GEOGRAPHIC's cover art, but also it used as its subject a sculpture of the company's unofficial trademark — a flying bald eagle.

American Bank Note is currently producing holograms for MasterCard and Visa credit cards, and for an undisclosed foreign nation's passport, as protection against the forging or altering of those items. The newest Visa cards, for example, carry a hologram over the last four digits of the identification number, making those digits unalterable without damaging the hologram.

Though NATIONAL GEOGRAPHIC will not divulge the cost of the holograms it used, it did acknowledge they more than doubled the cost of the regular cover. According to NATIONAL GEOGRAPHIC, similar holograms are being tested for use on travelers checks, U.S. currency and identification cards. — J. Raloff