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LETTERS

Geological Models

As the lead author and the Department of Energy monitor for one of the reports (1) cited by N. Oreskes *et al.* in response to letters (15 Apr., p. 329) about the issue of validation and verification of codes and models (2), we take exception to their representation of our work. The Yucca Mountain Site Characterization Project has long recognized that “validation” in the common sense is not possible for models of long-term geological processes. Thus, we have restricted the use of the term to the verification that codes which embody models accurately implement the mathematical equations that describe the model, without regard to the verity of that model. This can be done.

We use the term “validation” in the sense of provisional acceptance, as E. J. Rykiel Jr. points out in his letter (p. 330). It is certain that there will be debate over who should decide the acceptance criteria, as pointed out by Oreskes *et al.* (Articles, 4 Feb., p. 641), and there certainly has been in the arena which they appear to criticize, that is, the radioactive waste management community. To the extent the public cares to listen, the caveats have been far better presented than Oreskes *et al.* indicate with their selective citation. Warnings about the impossibility of absolute proof are even embodied in the regulations.

As scientists involved in the difficult task of supporting credible policy decisions, we are regularly made aware of the limitations of our models by the scientific community. The statements of Oreskes *et al.* are, we feel, exaggerated.

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SIDS Research

Ginger Pinholster (News & Comment, 8 Apr., p. 197) suggests that pioneering sudden infant death syndrome (SIDS) research by Alfred Steinschneider may be called into

question because the mother of two SIDS victims is now charged with having murdered her babies. In 1972, Steinschneider described five infants with severe apneic episodes who subsequently died from SIDS (1). He suggested that SIDS may be due to apnea.

These murder charges do not refute Steinschneider’s ideas. SIDS is the most common cause of death in infants between the ages of 1 month and 1 year, yet its cause remains unknown. Leading hypotheses about the cause of SIDS are related to brain-stem dysfunction, especially neurologic control of breathing and sleep-wakefulness. The relation between control of breathing, apnea, and SIDS is currently being investigated, and many studies support an association between SIDS and respiratory dysfunction. Thus, one should not conclude that the “apnea hypothesis of SIDS” is unpopular, has been disproved, or that it is of little scientific interest.

Child abuse exists, and it is a serious pediatric problem. Similarly, SIDS exists, and it is a serious pediatric problem. Occasionally, infants whose deaths were originally attributed to SIDS are found to have died from child abuse. These deaths, and those described in the article, are tragic, but they represent child abuse. That child abuse exists does not decrease the credibility of legitimate scientific inquiry into the cause of true SIDS deaths. Steinschneider’s ideas have inspired 20 years of sustained SIDS research in which the relation between SIDS and apnea has been investigated, and that research continues today.

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Embargo on Biomaterials

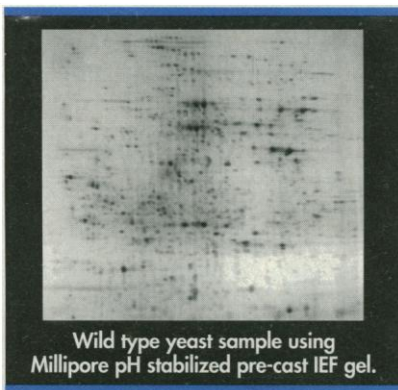
The article “New challenges in biomaterials” (25 Mar., p. 1715) by N. A. Peppas and R. Langer points out significant opportunities for the creation and characterization of biomaterials that are essential com-

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ponents of therapeutic implants. Materials that are reasonably biocompatible with use in the human body (for example, polyester for vascular grafts, polyurethanes for pacemaker leads, and silicone elastomers for hydrocephalus shunts) are becoming increasingly difficult to obtain from primary producers. The reason is that chemical companies have determined that unpredictable and excessive liability costs of doing business with manufacturers of implantable medical devices no longer allow unrestricted sale of standard polymers to these customers. Under current U.S. product liability laws, any remote supplier of commodity materials can be joined in lawsuits involving medical products that are alleged to have failed unexpectedly, not lived up to expectations, or caused complications. As the sales of such materials represent a tiny fraction of the business of chemical companies, but account for a major part of their liability or legal costs, it is expedient for the companies to opt out of the medical device market.

This embargo, which already affects the main sources of fluorinated polymers (for example, Teflon), polyacetals (for example, Delrin), silicone compounds, polyurethanes and polyesters (for example, Dac-

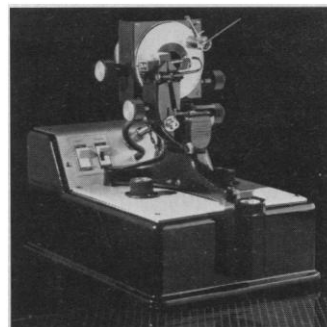
ron), is progressively extending to other elements of medical devices, such as the small, but essential, amount of PTFE powder used in the fabrication of batteries for cardiac pacemakers or the electric components of such devices, as well as to the specialty metals used for pacemaker casings and joint replacement prostheses. The resulting crisis could bring to a halt the fabrication of implantable devices in the United States, resulting in a shortage of widely used devices approved by the Food and Drug Administration (FDA) on the market, inadequate treatment for thousands of patients, and the loss of jobs in a major sector of U.S. industry. Other potential consequences include a shortage of materials for artificial organ and cell transplantation research, the loss of engineering and medical experience as material fabrication and clinical trials are shifted abroad, the closing of career opportunities for graduates of U.S. training programs, and a diminished incentive to develop new materials.

The leadership of the National Institutes of Health is needed in addressing this issue and in directing research to establish a scientific base for technological advances in the field of medical devices and implants. The Health Industry Manufacturers Associ-

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ation is coordinating efforts with the FDA to establish "equivalence" criteria for substitute materials in shortage areas and to keep critical devices on the market (1).

In the short run, the most effective remedy would be to change tort law to bar product liability claims against remote suppliers of "off the shelf" commodity materials and components of devices that have received FDA approval. The entire liability burden would then fall on the device manufacturer, who could decide whether or not to market a device.

Better solutions might be generated through discussion with all involved parties. However, a temporary resolution is urgently needed if we are to avoid a shortage of chronic implants for critically ill patients.

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Cholesterol Vaccines

John Travis's Research News article of 24 December (p. 1974) discusses vaccines to protect against atherosclerosis. Variations of this approach have been tested previously (1-6). Cholesterol-fed rabbits were protected against atherosclerosis by immunizing them with β -lipoproteins (1), and the response of rats to dietary cholesterol was reduced by stimulating the reticuloendothelial (RE) system using zymosan (2). In our work, cholesterol-fed rabbits were immunized with synthetic antigens in which cholesterol-esters were covalently linked, as haptens, to various protein carriers (3-7). Significant reductions in serum cholesterol and up to 90% protection against atherosclerotic plaques were obtained.

In a discussion of the work of the Army group (8), the question was raised whether the immune system will develop antibodies to a common constituent such as cholesterol. We found that significant titers were retained against cholesterol after absorption with carrier protein, and extensive cross-reaction was exhibited with cholesterol conjugates of unrelated carrier proteins. This confirmed that antibodies directed specifically against cholesterol could be induced by immunization.

The article also questions how immunization lowers blood cholesterol. We observed increases of greater than 70% in the clearance of ^{14}C -cholesterol-esters from serum of immunized animals (5). Significant amounts of cholesterol-antibody complexes were also detected in serum. These observations led to the proposal that the antibodies might label cholesterol-containing lipoproteins for clearance by scavenging macrophages (6).

Travis mentions possible long-term adverse effects of the vaccination procedure. In experiments lasting up to 9 months, the hypocholesterolemic effects of immunization persisted, but the protective effects against atherosclerosis gradually declined, despite monthly booster shots. No evidence of autoimmune phenomena or other side effects were noted (7).

The cholesterol-fed rabbit may be too severe a test for the cholesterol vaccination procedure. Serum cholesterol in this model frequently exceeds 2000 milligrams per deciliter (mg/dl), whereas the clearance capacity of the RE system is about 300 mg/dl (7). The bulk of the public health problem involves cholesterol in the range of 200 to 500 mg/dl. If the procedure can be validated in a more appropriate model, it could become a useful adjunct to diet or drug therapy. However, many technical obstacles would need to be overcome before the scenario of a routine "cholesterol vaccination" could become a reality.

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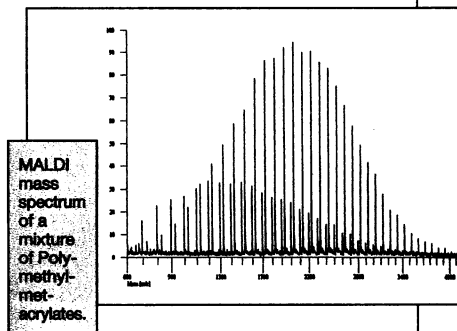
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Opinion

A New View of Synthetic Polymers

The current methodology for the analysis of synthetic polymers, although well established, leaves a lot to be desired. Reliable results depend heavily on the availability of known and well characterised standards. A variety of techniques – for example GPC, light scattering, viscosity measurements and NMR may have to be used to characterise a single polymer.

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