Julio E. Celis
Chairman, EMBL Council,
Danish Centre for Human
Genome Research,
170 DK-8000 Aarhus C, Denmark

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Gene Technology and Democracy

I disagree with Rolf M. Zinkernagel about the issues involved in the current debate before next year's Swiss referendum on a constitutional prohibition of gene manipulation (Editorial, 14 Nov., p. 1207). Discussions of this topic are not confined to Switzerland; in fact, the rest of the German-speaking regions of Europe are intensely interested in the issue. Apprehension about gene manipulation is related not only to the particular mentality of the culture ("nature is good," and so forth), but also—arising from the pervasive awareness of the Nazi abuses of science and medicine—to a general perception of "pure biologic thinking" as tantamount to extreme right-wing ideology (*1*). The problem is not one of "not understanding molecular biology," as Zinkernagel seems to imply, but is a profound cultural issue that needs to be dealt with in that context.

Zinkernagel also does not acknowledge that in the debate in the Swiss Parliament, I, along with other members of the Labour Party, introduced a counterproposal that could have averted the referendum now threatening our biological research. This proposal would have eliminated major problems while retaining the prohibition on the patenting of genetically generated organisms. It was, however, defeated by the pharmaceutical industry and their political representatives.

There is distrust throughout Europe—not only in Switzerland—of giant companies whose solicitude for their shareholders appears to outweigh their concern for their thousands of workers. This is exemplified by the merger of Ciba and Sandoz into the mega-Novartis, notwithstanding the eminently sound financial states of both companies before the merger.

If it is felt that researchers are too heavily influenced by the economic interests of pharmaceutical giants, they tend to lose authority as opinion shapers in political and societal debates such as the one at issue. I am afraid that Zinkernagel (and many other researchers) incur that risk by their erroneous assessment of this situation.

Franco Cavalli
Division of Oncology,
Ospedale San Giovanni,
6500 Bellinzona, Switzerland, and
Member of the Swiss Parliament

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1. E. Schuster, *N. Engl. J. Med.* **337**, 1436 (1997).

The Swiss vote on the "gene protection initiative" is a blatant example of the failure of scientists to communicate the urgency of research in biotechnology and genetics to the public. The development of vaccines and fundamental knowledge is vital in medical research and must not be sacrificed to veto by technophobic and opportunistic politics. Bioethicists, biologists, and science educators in general must publicly challenge the conventional wisdom of "statists" who are jeopardizing the future and even human survival with pseudoscientific and reactionary misinformation about biotechnology. Society can ill afford to suppress the development of new treatments and approaches to research in molecular genetics. Suppression of new technology cannot guarantee prevention of abuse in biotechnology, because such work will proceed in secret even if it is banned.

Openness is the only choice for scientific advancement in biotechnology and for human survival.

Howard Olson
Medical Department,
Silicon Valley College,
Walnut Creek, CA 94598, USA

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FDA "Reform"?

The Food and Drug Administration (FDA) reform bill (ScienceScope, 14 Nov., p. 1215) passed by the U.S. Congress includes requirements to speed the review of new vaccines and drugs and to reauthorize the Prescription Drug User Fee Act (PDUFA). But to say that the bill "leaves FDA's research structure untouched " is incorrect.

To enhance the review process and expand FDA's capacity to responsibly manage new types of biologics, some of the "user fees" (charges to companies that submit products for FDA review and approval) supported relevant research by scientists who perform much of the regulatory review. During the negotiations for the new PDUFA, an ancillary agreement (which was not included in the text of the act, but was made between FDA negotiators and the Pharmaceutical Manufacturers Association) was written that specifically prohibits the use of PDUFA funds to support such research.

Also, research at FDA must now compete with new initiatives in tobacco and food safety, as these will require funding from an FDA budget that has remained flat since fiscal year 1996. These and other factors will result in an estimated reduction of

60 to 70% in funds available for research 1998 in the Division of Viral Products, Center for Biologics Evaluation and Research (DVP-CBER), the branch of FDA that reviews viral vaccines. These reductions will terminate most tenure-track scientists who review vaccines. Loss or transfer of this expertise will interfere with regulatory efficiency and compromise the intent of the new legislation, as well as DVP-CBER's responsibility to effectively represent the public in ensuring vaccine safety and efficacy.

These reductions come after FDA's own Science Board Subcommittee on Research strongly recommended supporting *and expanding* science and research programs [D. Korn, "FDA under siege: The public at risk" (Editorial, 13 June, p. 1627)].

The DVP reviews more than 800 product submissions a year (such as new vaccines against the human immunodeficiency virus) and is responsible for regulating existing viral vaccines, including those required for every child in the United States. The drastic change in the 100-year tradition in the way biologics will be regulated by FDA (that is, without review by active scientists on the staff) represents an uncontrolled experiment in regulatory management. In this era of emerging infectious diseases, genetic engineering, and xenotransplantation, this "experiment" carries with it unknown implications for the public health. The question is whether such an experiment should be imposed on the public without the benefit of public knowledge or debate.

Stephen M. Feinstone,* *3021 Cathedral Avenue, NW, Washington, DC 20008, USA*; **Andrew M. Lewis Jr.,*** *15958 Limestone School Road, Leesburg, VA 20176, USA*; **Lewis J. Markoff,*** *6908 Nevis Road, Bethesda, MD 20817, USA*; **Kathryn Carbone,*** *5613 Doubs Road, Adamstown, MD 21710*; **Hana Golding,*** *14321 Woodcrest Drive, Rockville, MD 20853*

*The signatories are laboratory chiefs in the Division of Viral Products, Center for Biologics Evaluation and Research, U.S. Food and Drug Administration.

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Reauthorization of the "user fees" paid by regulated companies should have provided the Clinton Administration with a strong incentive to push for meaningful reforms in FDA. Instead, the legislation approaches reform in inconsequential ways.

First, it calls for "promptly and efficiently reviewing clinical research" and making decisions "in a timely manner." But these words will not have any impact on the agency's 30-year tradition of risk aversion and foot-dragging.

Second, it calls on FDA to develop a plan by the year 2000 for clearing the legendary backlog of products awaiting approval. Congress here makes itself a hostage to an endless series of demands for additional resources the agency will claim are essential for doing this.

Third, it codifies many policies that are already in place, giving the impression of a lengthy list of improvements.

The most important provision offers drug companies greater latitude in supplying scientifically sound information to doctors about drugs' "off label" uses (those not yet approved by FDA). Companies are currently prohibited from distributing such critical information. But even this improvement comes at a high price: substantial additional paperwork to convince FDA that formal applications for approval of the new uses are forthcoming.

A welcome provision permits manufacturers to submit "health care economic information," such as data on a drug's cost-effectiveness, to hospitals and HMOs.

The bill contains other minor improvements, such as loosened restrictions on health claims for food products and expanded use of third parties, including academic institutions, to review medical devices.

However, one provision actually *increases* the scope of FDA's regulation by ex-

panding its jurisdiction to activities that occur completely within a single state—small-scale research by an academic or a practicing physician testing an innovative therapy.

Many critical reforms recommended by blue-ribbon panels are conspicuously absent. These include reducing the redundancy of regulation of early-stage clinical trials and a binding reciprocity provision that, for example, would limit the duration of FDA review of a new drug to a maximum of, say, 60 days after its approval in the United Kingdom or by the European Medicines Evaluation Agency (thereafter, FDA would have to show cause why the drug should not be marketed in the United States, or it would automatically be approved).

Following Congress's failure to accomplish significant FDA reform, the costs of drug development (already averaging more than $500 million to bring a single product to market) will continue to rise, fewer drugs will be developed, and market competition will erode. Patients will suffer higher prices and benefit from fewer breakthrough drugs.

Henry I. Miller*
Hoover Institution, Stanford University, Stanford, CA 94305-6010, USA

*FDA official from 1979 to 1994.

Thumbs Down on Acupuncture

The U.S. National Institutes of Health (NIH) consensus statement on acupuncture (Random Samples, 14 Nov., p. 1231) should not prompt physicians to use acupuncture or to refer patients to acupuncturists.

The panel convened by the NIH, in fact, presented meager conclusions. It announced that there is "clear evidence that needle acupuncture is efficacious for adult postoperative and chemotherapy nausea and vomiting, and probably for the nausea of pregnancy," and that there was "evidence of efficacy for postoperative dental pain." It did not quantify the degree of "efficacy" of needle acupuncture in these conditions, or discuss its actual usefulness.

The nausea of some forms of chemotherapy is severe, but current medications used for its suppression are increasing highly effective and do not present major side effects. Why torment patients just emerging from surgery, or suffering from the effects of chemotherapy, with multiple and repeated needle insertion and manipulation?

The precise cause of nausea of pregnancy is enigmatic. The NIH statement qualified its comments on this point. It did not comment on hyperemesis gravidarum, the real problem, or the possible effects of painful daily needling of pregnant women over a period of months.

"Postoperative dental pain" is well handled by the brief administration of minor analgesics, which presents minimal risk and is much to be preferred over 20-minute, painful needling.

The panel also points out "there are also studies that do not find efficacy for acupuncture in pain..." and that there is "evidence that acupuncture does not demonstrate efficacy for cessation of smoking and may not be efficacious for other conditions."

In short, it appears that the panel concluded that acupuncture was virtually useless, declared a "victory" as ordered up, and called for more research expenditure to heap on that already wasted.

Arthur Taub
Department of Anesthesiology, Yale University School of Medicine, New Haven, CT 06520, USA

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Drug Abuse and Therapy

The special section "Frontiers in neuroscience: The science of substance abuse" (3 Oct., p. 45) highlights many of the exciting advances in this field. From molecular neu-