THE CANCER LETTER

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Judge Clears Way For Trial Pitting FDA Against Physicians Over First Amendment

A federal judge has cleared the way for a trial in which a Washington public interest group will argue that FDA has violated the First Amendment rights of physicians by denying them access to information concerning "off-label" use of drugs.

The suit, filed by the Washington Legal Foundation, a group generally associated with conservative causes, stems partly from FDA actions that

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In Brief

House Budget Committee Proposes 5% Cut To NIH In FY96; Steady Reductions Expected

A COST-CUTTING PLAN proposed by the House Budget Committee calls for a 5 percent reduction for NIH in fiscal 1996. If the plan is enacted, NIH could lose about $1 billion next year. The President's budget proposal seeks $11.8 billion for NIH. The Budget Committe's goal is to cut spending sufficiently to balance the budget and finance a tax cut. Several observers said the proposal would be unlikely to pass unaltered through the Senate and noted that it would be the appropriations rather than budget committtees that will make the final decisions. . . . **NIH IS NOT SPARED** in the President's budget, either. A program of steady reductions could decrease the NIH budget by as much as 9 percent by the year 2000. Though NIH is not on the list of programs protected from the cuts, Administration officials said other HHS programs may be cut instead. . . . **A RESCISSION BILL** approved by the House last week proposed a cut $70 million from NIH construction funds during the current year. . . . **DOMESTIC SPENDING**, including medical research, will be hit especially hard since the Administration's five-year projections as well as the Republican plans call for long-term increases for the Department of Defense, observers said. However, the DOD's $150 million breast cancer research program has survived rescission in the House. . . . **FOR THE RECORD:** In a recent radio interview, House Majority Leader **Richard Armey** (R-TX) made this statement about government sponsorship of research: "We know that the best research is not necessarily and not often government sponsored. There is always a political element in the decision where the government will spend your research dollars on your behalf. When you start taking a look at the research that comes out of the private sector of the economy and even to some extent, at least in the hard sciences,

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Trial To Test FDA's Criteria For Improper Drug Promotion

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prevented Bristol-Myers Squibb Co. from distributing to physicians complimentary copies of *The Chemotherapy Sourcebook,* edited by Michael Perry and chapters from *Cancer: Principles & Practice of Oncology*, a textbook by Vincent DeVita, Samuel Hellman and Steven Rosenberg.

In a ruling last week, Judge Royce Lamberth of the US District Court for the District of Columbia denied FDA's motion to dismiss the action, clearing the way for a trial. The case is likely to be the first Constitutional test of the criteria FDA employs to distinguish improper promotion of drugs from distribution of legitimate medical educational materials.

WLF claims that FDA has established a *de facto* ban on distribution of educational materials that contain information on off-label indications and that the agency has been enforcing that ban for several years. Claiming that no such policy exists, FDA moved that the case be dismissed. Lamberth denied the agency's motion in a ruling dated March 9.

"The stage is now set for a showdown in the courts as to the constitutionality of this policy," Richard Samp, executive legal director of WFL, said to **The Cancer Letter**. The case is expected to be tried later this year, he said.

Samp said that while the controversy over the oncology text was a particularly good illustration of FDA's stance on educational materials, the implications of the case reach beyond one book, one drug company and one medical specialty.

"This is an issue that affects a wide variety of regulated entities and health care providers across the board," he said.

Early in the controversy, the First Amendment issues were raised in correspondence between FDA and J.B. Lippincott, the publisher of the oncology textbook (**The Cancer Letter**, June 19, 1992).

"It is very useful that a court would look at the limits of FDA authority," said Alan Bennett, a Washington attorney who was involved in the initial stages of the controversy.

"FDA should not be in the role of protecting doctors from scientifically valid information contained in text books," Bennett said to **The Cancer Letter**. "In fact, it should encourage the distribution of exactly that kind of information."

Samp said WLF stepped into the controversy as a plaintiff of last resort. "FDA has been known to threaten retaliation against those who dare to challenge its regulatory programs and policies," Samp said. "That is why it is important for organizations like WLF to challenge FDA head-on."

The WLF suit names as defendants FDA Commissioner David Kessler and HHS Secretary Donna Shalala.

Ruling Rejects FDA's Arguments

Lamberth's ruling is signficant because it rejects several arguments that have been central to FDA's ability to maintain power over the industries it regulates, several observers said.

- Lamberth rejected the agency's argument that the physicians on whose behalf WLF filed its suit had no enforceable First Amendment rights before FDA.

"WLF is alleging that the FDA's actions with respect to manufacturer-supported distribution of off-label usage information have resulted in a significant curtailment of this source of information to doctors," Lamberth wrote.

"The law is clear that where a law or other official act has resulted in silencing of an otherwise willing speaker, those who wished to receive information from that speaker may challenge the constitutionality of the law or act," he wrote.

- The judge rejected the argument by FDA that the entities it regulates have the option to mount a direct challenge to the agency's actions.

"The reality of the situation, as alleged by plaintiff, is that few if any companies are willing to directly challenge the FDA in this manner... The

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company must expose itself to the FDA's power to seize an entire product line if FDA finds the products to be `misbranded.'

"Although the company can then litigate the validity of the seizure (and therefore the policy pursuant to which the seizure was made), the prospect of lost sales and protracted litigation is understandably discouraging to these companies...

"It is evident that manufacturers are most reluctant to arouse the ire of such a powerful agency," Lamberth wrote.

● The judge rejected the argument by FDA that the agency's policy on industry support of continuing medical education cannot be challenge because the policy is still being developed.

"If an agency's own characterization of the *finality of its policy* were to be determinative, that agency could effectively regulate industry without ever exposing itself to judicial review," Lamberth wrote in his opinion.

"A powerful agency such as FDA could achieve this result through the simple expedient of (1) never formally declaring the policy to be `final,' and (2) threatening (but never actually initiating) enforcement procedures against companies which failed to comply with the agency's *de facto* policies," he wrote.

Central Question: Is There A Policy?

Three years ago, FDA published a "Draft Policy Statement on Industry-Supported Scientific and Educational Activities" (**The Cancer Letter**, Feb. 5, 1993). However, the final policy is still being formulated, FDA said in court documents.

The WLF suit contends that statements by FDA officials point to a definitive agency position on off-label usage information. According to court documents, in 1991 Kessler made the following statement:

"I would urge all members of the pharmaceutical industry to take a long hard look at their promotional practices. I do not expect companies to wait until this guidance becomes final to put their advertising and promotional houses in order."

In another reference to FDA's draft policy on distribution of educational materials, David Adams, director of the policy development and coordination staff in Kessler's office said:

"Although this document was published as a draft policy statement with an invitation to submit comments, it reflects actual agency policy.

"It tells you how the agency makes decisions from day to day in determining whether activities are subject to regulation and are potentially illegal..."

FDA argued that these statements reflected views of individual officials rather than policy of the agency. Lamberth disagreed:

"The question here is not whether any single act on the part of the FDA signifies the existence of a final agency policy; rather, the aggregate effect of these acts must be analyzed to determine whether the agency by its conduct has objectively demonstrated the existence of such a policy," he wrote.

The ruling also discussed the controversy over Bristol's attempt to distribute the oncology text:

"In one... instance, WLF alleges that a pharmaceutical company which planned to distribute a standard oncology textbook (which included references to off-label uses of some of the company's products) to doctors was informed by a representative of the FDA that the company would have to include package inserts from each of the company's drugs that were mentioned in the textbook.

"In subsequent phone calls, however, FDA allegedly rescinded this limited approval and stated that pharmaceutical companies would no longer be permitted to have any involvement in the distribution of medical textbooks in which off-label uses of their drugs were discussed.

"Companies attempting to support scientific and educational activities by providing information or samples of their products encountered similar warnings from representatives of the FDA."

Court Orders NIH To Retract Flags On Fisher Publications

A Federal judge earlier this week issued a preliminary injunction precluding NIH from distributing databases containing any annotations on publications that list Bernard Fisher as an author.

Under the court order, drafted by attorneys representing Fisher and the US government, the following corrections will be placed as part of the "log-on sequence" on the NIH-operated databases:

"Medline, Cancerlit, and PDQ erroneously annotated certain articles authored or co-authored by Dr. Bernard Fisher with the phrase `scientific misconduct—data to be reanalyzed.' All such annotations have been removed or are being removed. We apologize for any problems or concerns this may

have caused. Users should disregard those prior annotations."

The court order also applies to the Journal of the National Cancer Institute and Monographs of the National Cancer Institute.

The injunction is the consequence of a legal action in which Fisher claims that federal agencies including NCI and the HHS Office of Research Integrity had violated his rights under the Privacy Act when "scientific misconduct" flags were placed on articles that list him among authors (**The Cancer Letter**, Feb. 24, March 10).

The injunction permits annotation of articles to reflect any reanalysis of data from the National Surgical Breast & Bowel Project. However, annotations would have to be placed with the input from Fisher and Judge Ricardo Urbina of the US District Court for the District of Columbia.

Should NIH attempt to place annotations on Fisher's work, it would have to give Fisher and the judge at least a 60-day notice. Should Fisher contest the annotations, NIH would have 15 days to respond in writing to his objections.

If the two sides fail to resolve their differences, the judge would step in to resolve the disagreements.

Reinventing NCI

DCE Plans Reorganization To Stablize, Stem Departures

The NCI Div. of Cancer Etiology has begun planning its first major reorganization since the early 1980s.

The immediate goal of the reorganization is to stabilize the division and protect from further loss of staff, Jerry Rice, acting division director, said to **The Cancer Letter**. Ten top positions are vacant in the division, which has an annual budget of $105 million.

"We are looking at what is the best way to plan for cancer etiology research in view of the projected future downsizing and the departure of key senior scientists," Rice said in an interview last week. "We are going to have to close and consolidate some labs in order to strengthen other programs and even establish some new programs."

Rice said the reorganization, which was discussed in a closed session of the DCE Board of Scientific Counselors earlier this month, will proceed incrementally. "We won't do anything radical without the involvement of a new NCI director," he said.

A subcommittee of the National Cancer Advisory Board is expected to issue recommendations for the Institute's intramural program in May. Michael Bishop, co-chairman of the NCAB Working Group on NCI Intramural Programs, has been kept informed about the DCE reorganization, Rice said.

Maintain Strong Causation Research

Current plans call for grouping the division's laboratories in a single intramural program, while reorganizing the extramural branches into a single extramural program, Rice said.

Staffing levels will remain the same in "strong laboratories, the Epidemiology and Biostatistics Program, and the extramural branches," Rice said to the DCE board at its meeting March 9.

"The plan will serve as a blueprint to be refined by further discussion within the division and to be presented when the incoming NCI director addresses the question of the organization of the Institute," Rice said.

Rice said that in his testimony to the NCAB working group last December, he stressed "the importance of a strong and highly visible focus for causation research" within NCI.

"The Congress, the federal regulatory agencies, and the public expect that the NCI respond vigorously and with authority to evaluate perceived carcinogenic risks," Rice said.

Rice said agreed with Div. of Cancer Treatment Director Bruce Chabner, who opposed the creation of a single NCI intramural program (**The Cancer Letter**, March 3).

What Is NCI's Future Role In AIDS?

The new NCI director will have to help DCE and its advisors grapple with the question of the division's involvement in AIDS research, Rice said.

AIDS funding—which now must go through the NIH Office of AIDS Research and is therefore vulnerable—comprises about 30 percent of the in-house and contract funds available to the division, a total of about $30 million.

"The era of this division's extensive involvement in AIDS research is reaching a turning point," with the retirements of Robert Gallo, chief of the Laboratory of Tumor Cell Biology, and William Blattner, chief of the Viral Epidemiology Branch, Rice said. Both will accept academic appointments later this year, Rice said.

Gallo's lab received more than $7 million in FY93, according to budget documents.

"The choices we make for the future of AIDS research within this division and this Institute will have to proceed in the context of the dramatic paradigm shift that began in 1994 and will continue until the end of the century, from an era of progressive expansion in positions and funds allocated to this Institute, to one of progressive annual reductions," Rice said to the board. "This is a new era and one in which future planning is extremely important regarding allocation of increasingly scarce resources.

"Future cuts cannot be distributed pro rata among all existing units," Rice said. "Pro rata reduction has the effect of weakening what currently exists.... Choices must be made."

Rice said the relatively large number of vacancies in DCE is the result of normal attrition over the past three years. The NIH hiring freeze made it impossible for DCE to fill the positions as they became vacant.

"The freeze put a hold on organizational changes, so as people left, you couldn't do anything," Rice said to **The Cancer Letter**. "It left DCE looking like Pickett's brigade after the Battle of Gettysburg."

DCE has placed 10 laboratory scientists and 12 staff of the Epidemiology and Biostatistics Program on the new NIH tenure track through the "grandfathering" process in place for staff who joined NIH prior to the new tenure track rules, Rice said to the board.

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Michael Sporn, chief of the Laboratory of Chemoprevention in DCE, will retire at the end of April after 35 years in the Public Health Service, including 33 years at NCI. Sporn has accepted a position as professor of pharmacology at Dartmouth Medical School.

Anita Roberts, deputy chief of the laboratory, will become the acting chief.

ORI Bars Cleveland Clinic Scientist From Federal Funds

A former Cleveland Clinic Foundation researcher has been barred from federal grants and contracts for three years after allegedly falsifying data in a study of a rare form of eye cancer.

The HHS Office of Research Integrity said last week that over a period of several years Vivian Tanner fabricated the dates of examinations, the qualifications of examiners and the results of laboratory tests.

Tanner was the coordinator for the clinic's participation in a wider study of choroidal melanoma. The problems came to light in 1993 during a routine audit and she resigned the following year.

John Clough, chairman of the Cleveland Clinic's health affairs division, said the 24 patients in the study at the time of the audit were notified by letter and telephone, and all chose to remain in the study. ORI said that while inaccurate data was submitted for the clinical trial database, no scientific reports affected by the false data were published.

The study is still going on and has not yet produced any treatment recommendations, the agency said. The Cleveland Clinic has received $294,928 in federal research for the study since 1985.

Tanner has not appealed the agency's finding or the decision to bar her from grants and contracts for three years. Tanner had an unlisted phone number in Cleveland and could not be reached for comment.

Clough said the Cleveland Clinic "cooperated fully with all aspects" of the government's review. "Only the coordinator of the study was found guilty of scientific misconduct," he said.

"The routine methods that were put in place to detect this kind of problem did detect it. The feeling was the methods worked. Errors were found before any harm was done and the problem was corrected," he said.

Clough said Tanner had cooperated with investigators but provided "no satisfactory explanation."

In Brief

Government Funded Research Not The Best, Armey Says

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out of our American universities, I think we probably get better research value for our dollar than we do so often from the government expenditures." (*Charlie Rose*, Feb. 2, 1995). . . . **DANA-FARBER** Cancer Institute has received a gift of $8 million from Abraham Gosman, a member of the board of trustees. The contribution is one of the largest ever received by the institute, and will make possible the creation of new state-of-the-art outpatient clinics and facilities, the center said. The clinics will be collectively named the Abraham D.

Gosman Clinic. In addition, a building on the Dana-Farber campus will carry the Gosman name. . . . **HAROLD SLAVKIN** was named director of the National Institute of Dental Research. Slavkin, director of the Center for Craniofacial Molecular Biology of the Univ. of California School of Dentistry, will replace **Harold Loe**, who retired last June. . . . **APPLICATION DEADLINE** for the NCI Cancer Prevention Fellowship Program is Sept. 1. The program offers Masters of Public Health training at accredited universities, folowed by independent research at the Div. of Cancer Prevention & Control. The three-year program is designed for MDs, other clinicians and PhDs. Contact Douglas Weed, 301/496-8640, fax 301/402-4863. . . . **FIRST RUSSIAN-AMERICAN Breast Cancer Conference** will be held in Moscow June 7-9. Originally, the conference was to be held in the city of Saratov, but "to accommodate a growing interest among both US and former Soviet Union physicians," the conference organizers decided that Moscow would be a more convenient location. "The move to Moscow makes the conference infinitely more accessible, reduces travel time and makes the experience more culturally appealing to American and Canadian physicians," said **Barrie Cassileth**, organizer of the conference. Cassileth said a tour package for Moscow and St. Petersburg is also available. For additional information, call 919/967-2184.

NCI Cooperative Breast Cancer Tissue Registry Established

NCI has established a new resource for scientists seeking breast cancer tissue for research.

The NCI Cooperative Breast Cancer Tissue Registry is a collection of formalin-fixed, paraffin-embedded breast cancer tissues with associated clinical and follow-up data.

The registry is available for research studies, particularly those to translate basic research findings to clinical application.

Available clinical and outcome data includes demographic data, diagnosis, extent of disease, treatment, follow-up, recurrence, survival, and vital status.

The registry cannot identify patients or provide family history information.

Researchers pay for preparation of sections and the costs of shipping.

Registry tissues are from existing collections of material from four geographically diverse areas of the US.

Additional information and application forms may be obtained from Sherrill Long, Information Management Services, 12501 Prosperity Dr., Suite 200, Silver Spring, MD 20904, Tel: 301/680-9770.

RFAs Available

RFA HG-95-005

Title: **Pilot Projects For Sequencing Of The Human Genome**

Letter of Intent Receipt Date: June 1

Application Receipt Date: Aug. 4

The National Center for Human Genome Research invites applications to develop and implement pilot projects to test strategies that have the potential to lead to full-scale production sequencing of mammalian DNA, resulting in achieving the goal of the complete, accurate, finished sequence of human DNA by the year 2005. This RFA will use the NIH individual research grant (R01), pilot project/feasibility study (R21), research program project (P01), exploratory grant (P20) and center (P50) grant mechanisms. $20 million has been set aside to fund approximately 15 awards.

Inquiries: Jane Peterson or Jeffery Schloss, Mammalian Genomics Branch, NCHGR, Tel: 301/496-7531, fax: 301/480-2770, Email: jane_peterson @nih.gov, Email: jeff_schloss @nih.gov

RFA HG-95-004

Title: **Improved Electrophoretic Dna Sequencing Technology**

Letter of Intent Receipt Date: June 15

Application Receipt Date: Aug. 29

NCHGR invites applications for research projects to develop novel automated sequencing technology suitable for large-scale genomic sequencing through the reduction in scale and increased parallelization of existing approaches that utilize Sanger sequencing reactions coupled with electrophoretic separation of fragments.

The RFA encompasses front end sample preparation, separation, detection, and data acquisition and handling. Technologies solicited include, but are not limited to, a spectrum of approaches ranging from capillary and ultrathin gel electrophoresis to microfabricated and microelectro mechanical systems that could yield reductions in scale and increased throughput.

Support will be through the individual research project grant (R01), pilot project/feasibility study (R21), research program project (P01), and exploratory grant (P20) mechanisms. $20 million has been set-aside to fund approximately 15 awards made under this RFA and RFA HG-95-005.

Inquiries: Carol Dahl or Robert Strausberg, Sequencing Technology Branch, NCHGR, Tel: 301/496-7531, fax: 301/480-2770, Email: carol_dahl@nih.gov, Email: robert_strausberg@nih.gov