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Senate Bill Would Require Clinical Trials To Test Gender, Racial Differences In Therapies

Women and minorities must be included equally in NIH-supported clinical research, and trials of new therapies will have to be designed to test gender and racial differences in response, under legislation reported out of the Senate Labor & Human Resources Committee last week.

(Continued to page 2)

In Brief

Alfred Ketcham Is New SSO President; Meyskens Receives NCI Year 2000 Award; Coltman Honored

ALFRED KETCHAM is the new president of the Society of Surgical Oncology. Other officers elected at the May annual meeting were Charles Balch, president-elect; Donald Morton, vice president; Bernard Gardner, secretary; Samuel Wells, treasurer; and Benjamin Rush, chairman of the executive council. . . . **FRANK MEYSKENS**, director of the Univ. of California (Irvine) Clinical Cancer Center, has received NCI's Year 2000 Award for "exemplary support of the nation's year 2000 goal of reducing the cancer death rate by one half". . . . **CHARLES COLTMAN**, chairman of the Southwest Oncology Group, was the recipient of the 1990 Philip S. Hench Distinguished Alumnus Award from the Univ. of Pittsburgh Medical Alumni Assn. . . . **INTERNATIONAL LIFE** Sciences Institute, based in Washington, announced a new awards program to support basic research on nutrition. Michael Gloth of Johns Hopkins Hospital, will study nutritional needs of the elderly, and Paula Morgan, of Univ. of California (Berkeley) will study zinc absorption in women. Each receives $20,000 a year for two years. . . . **COMMITTEE ON SCIENCE**, Engineering & Public Policy, a unit of the National Academy of Sciences, has formed a study panel to examine "the contemporary research environment as it affects the responsible conduct of research and to assess mechanisms for encouraging integrity in research." Panel chairman is Edward David, former White House science advisor under Richard Nixon and now president of EED Inc. of Bedminster, NJ. . . . **MORE NIH BIOMEDICAL** contract dollars end up in the Washington-Baltimore region than any other area of the U.S., according to a recent study by the Washington-Baltimore Regional Assoc. In 1989, 521 contracts, worth $275 million, were awarded to area companies. Boston-Lawrence-Salem, MA, ranks a distant second with $33.7 million, and San Francisco-Oakland-San Jose comes in third with $30.3 million. Top Washington-Baltimore area contract recipients are Program Resources Inc. ($95.7 million in 1989), Westat Inc. ($17.4 million) and Biometics Research Inc. ($16.3 million).

Tests Of Differences In Response Would Be Mandated In Senate Bill

(Continued from page 1)

The requirements were included in legislation reauthorizing NIH, including renewal of the National Cancer Act, for four years.

The bill, introduced by Sen. Edward Kennedy (D-MA), leaves intact NCI's special authorities, which the institute has had to defend vigorously in the past. It authorizes funding for NCI of $2.093 billion for FY 1991 and "such sums as may be necessary" for FY 1992 through 1994.

While NIH has had a policy on inclusion of women and minorities in research for three years, the institutes have been criticized recently for slow implementation. At a hearing in June, Rep. Henry Waxman (D-CA), chairman of the House Subcommittee on Health and the Environment of the Committee on Energy & Commerce, which authorizes NIH, released a General Accounting Office study finding that NIH has not consistently applied its policy in grant review (**The Cancer Letter,** June 22).

A spokesman for Waxman's committee said its version of the NIH reauthorization legislation would be introduced in September.

The Senate bill requires the HHS Secretary to ensure that women and members of minority groups are included as subjects in clinical research. The Secretary may designate circumstances under which this requirement does not apply, such as if the inclusion of women and minorities is inappropriate to the research or the health of the subjects.

The bill also requires that in any clinical research that is not exempted from this inclusion policy, "the Secretary shall ensure that the project is designed and carried out in a manner sufficient to provide for a valid analysis of whether the variables being tested in the research affect women or members of minority groups, as the case may be, differently than other subjects in the research."

This second provision raised concern at NCI last week about the implications for the time and costs of clinical trials.

"Women and minority groups should have full access to NCI sponsored clinical trials--and that's the case now," said Michael Friedman, director of the Cancer Therapy Evaluation Program. "To mandate any kind of restriction past that makes it very difficult to conduct clinical trials in the future because sample sizes would be mandated by gender and ethnicity rather than other variables."

NCI's record on inclusion of women in trials is good, Friedman and other NCI officials said. Excluding trials of gender-specific diseases such as breast or prostate cancer, between 40 and 45 percent of all patients in trials are women. Including gender-specific diseases, almost 60 percent of all patients on trials are women.

"In the Div. of Cancer Treatment, we pride ourselves on how much attention is given to women's issues," Friedman told **The Cancer Letter.** "But if you mandate such things, the cost of clinical trials would skyrocket, the duration of trials would be much longer. The whole hypothesis for clinical trials becomes much more cumbersome."

Others did not share that view, however. "It's not a difficult requirement," said Karen Antman, chairman of the American Society of Clinical Oncology's government relations committee. "I believe some data--age, gender, etc.--are usually available before you begin a trial. In fact, cancer studies are less likely to have gender bias. The work is already basically done."

The Senate bill also establishes a new infrastructure on women's health within NIH. Following are the bill's major new provisions:

Advisory council subcommittees. The bill requires the advisory council of each of the institutes to establish a subcommittee to be called the Clinical Research Equity Subcommittee.

Each of these subcommittees is to review all clinical research conduced by the agency to determine the extent to which the research is being conducted in accordance with the women and minorities requirement. This review is to take place annually and a report must be submitted to the NIH director.

The bill provides that if the HHS Secretary determines that any clinical research that should include minorities and women does not, the Secretary may suspend or revoke the authority for the project.

Peer review. In the technical and scientific peer

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review of each clinical research proposal, consideration must be made of the merit of the proposal regarding the inclusion of women and minorities as subjects in the research.

The bill establishes the same requirements for the Alcohol, Drug Abuse & Mental Health Administration.

Office of Women's Health. The bill requires NIH to establish an Office of Women's Health Research by January 1991, whose director will be appointed by the NIH director. This office shall "ensure that research pertaining to women's health is identified and addressed throughout the research activities conducted and supported" by NIH."

Through the Office of Women's Health, NIH must establish:

--an intramural research program in gynecology at the National Institute of Child Health & Human Development,

--a clinical service in gynecology,

--a Center for Women's Health Research to support research pertaining to women's health conditions, by Jan. 1, 1993.

The duties of the director of the Office of Women's Health are to:

--identify women's health research needs, including prevention research,

--identify needs for coordinated research activities, especially multidisciplinary research relating to women's health, to be conducted intra and extramurally,

--encourage researchers whose research is funded or supported by NIH to pursue research pertaining to women's health,

--support the development and expansion of clinical trials of treatments, therapies and modes of prevention that include women of all ages, races and ethnicities,

--establish a coordinating council that shall be composed of directors of the institutes, centers, offices and divisions of NIH and ADAMHA,

--establish within the office an advisory committee to be known as the Women's Health Clinical Research Advisory Committee. The committee is to be composed of 12 representatives, including physicians, practitioners, scientists and other women's health professionals.

Data bank. The bill directs NIH to establish a data bank to compile information on research, treatment and prevention relating to women's health, including a registry of ongoing clinical trials. The bill requires that drug sponsors provide information on trials to the data bank.

Biomedical Research Foundation

The Senate bill also establishes the National Foundation for Biomedical Research would be established under the bill.

The foundation would be a nonprofit corporation to provide funding to recruit and support endowed scientists within the intramural research programs of NIH and ADAMHA. The foundation also is to support the staffing, equipment and space requirements for the research undertaken by those scientists and support the stipends and research expenses of individuals appointed under the NIH Scholars program.

The foundation will have a board of directors consisting of nine voting members including the NIH director, the administrator of the Alcohol, Drug Abuse & Mental Health Administration, and the Surgeon General. Two members are to represent the general biomedical field, one is to represent the general behavioral field, and two will represent the public. The board is to appoint a chairman and an executive director.

The bill also includes a new general NIH authority that would allow institute directors to license information products, such as PDQ, rather than simply making them publically available.

NCI's special authorities, which remain in the reauthorization, include the requirement to submit directly to the President a "professional judgement" budget request outlining cancer research needs and opportunities. This budget, called the bypass budget, is formulated with the NCAB and not modified by the Executive Branch.

NCI also has special authorities to support construction of laboratories and other cancer facilities, appoint advisory and peer review committees, support a broad array of training initiatives and promote international information exchanges.

Other NCI authorities granted by the National Cancer Act include the President's Cancer Panel, which is a format for taking research and budget concerns directly to the President, as well as the Presidential appointments of the NCI director and NCAB members.

The bill also authorizes the National Heart, Lung & Blood Institute at $1.5 billion, the National Library of Medicine Medical Assistance program at $35 million, the National Research Service Award at $415 million, the Alzheimer's Disease Registry at $8 million, the National Center for Biotechnology Information at $10 million, and the Biomedical Ethics Board at $2.5 million.

All programs and institutes of NIH are authorized for "such sums as necessary" for fiscal years 1992 through 1994.

Investigator, Banned For Three Years, Intends To Resume Clinical Trial Role

A clinical investigator who was banned for three years from using experimental anticancer drugs for a series of FDA regulation violations is nearing the end of that period and intends to resume full participation in trials at that time.

Alexander Spiers, who is now professor of medicine at the Univ. of South Florida School of Medicine and director of the leukemia and lymphoma center at the Moffitt Cancer Center in Tampa, was barred by FDA from access to experimental drugs after an investigation turned up a series of irregularities by Spiers when he was at Albany Medical College.

Spiers signed a consent agreement with FDA on Dec. 16, 1987 which admitted the following charges:

* Failure to follow the plan of investigation in that dosing regimens were not adhered to; ineligible subjects were entered into studies; and prohibited concomitant chemotherapy was administered.

* Failure to maintain adequate and accurate case histories in that prohibited concomitant chemotherapy was not reported in case report forms, and administration of the test substance was not always reported and at other times was reported inaccurately.

* Failure to maintain adequate records of drug accountability.

* Distribution of investigational drug to unauthorized persons.

* Failure to obtain IRB approval for studies involving dose ranges outside the approved "in house" protocol.

Spiers agreed to conduct no further studies with investigational drugs and is ineligible to receive investigational drugs for a period of three years.

Frances Kelsey, director of FDA's Div. of Scientific Investigations, signed the agreement for the agency.

The studies were phase 2 and 3 trials of pentastatin (deoxycoformycin) for lymphomas and leukemias carried out from 1984 to 1986. Spiers was a member of the Eastern Cooperative Oncology Group and was the study chairman for those trials, as well as for an in house Albany trial with the same agent.

Prior to joining the Albany Medical College faculty as professor of medicine in 1980, Spiers was at Boston Univ. It is somewhat ironic that he was a clinical investigator there with Marc Straus, who in 1978 was charged with falsification and manipulation of clinical research data, charges Straus vehemently denies.

An affidavit signed by Spiers, implicating Straus in the data manipulation, was one of the crucial items of evidence which led to the disqualification of Straus from NCI sponsored trials and use of investigational drugs. That affidavit, incidentally, was obtained by the same FDA investigator who probed Spiers' alleged violations eight years later.

Straus contended that data alteration found by FDA had been done by others and that his signature on those documents had been forged. He has also said that in testimony under oath, taken in connection with a lawsuit he filed, one of his chief accusers admitted altering data without his knowledge or consent. Another accuser, also under oath, admitted that she had signed his name to documents requiring his signature, without his knowledge or consent, knowing those documents contained false information.

Straus is now in private practice in White Plains, NY.

FDA Report On Investigation

The FDA report on the Spiers investigation lists the following complaints on a phase 2 study to evaluate deoxycoformycin for treatment of refractory lymphoid neoplasms:

--Nine of the 21 patients treated were ineligible for the study according to protocol eligibility criteria. Three of those ineligible patients subsequently suffered drug related toxicities or "probable" drug related toxicities and died.

--Twelve of the 21 patients were not treated according to the dosing regimen required by the protocol.

--Two patients received concomitant chemotherapy prohibited by the protocol.

--Failure to maintain accurate records of the receipt and disposition of the test article [deoxycophormycin].

--Routine distribution of the test article to patients and physicians not under the director supervision of the investigator, and not identified on the appropriate FD-1573 "Statement of Investigator" form under which the test article was obtained.

The FDA report on the in house protocol, testing deoxycoformycin in the treatment of leukemias, lymphomas, multiple myeloma, and renal cancer, said that:

--For 12 of the 25 patients covered, failure to report all doses of the test article administered and/or inaccurately reporting dosing information to NCI.

--Failure to maintain accurate accountability records for the receipt and distribution of the test article.

--For one patient, unreported concomitant radiation therapy.

--Routine distribution of the test article to physicians not under the direct supervision of the investigator, and not identified on the appropriate FD-1573 under which the test article was supplied.

The report on the other ECOG studies revealed, FDA said:

--Treatment of three patients under special exception protocols that had not been approved by the hospital IRB, and for which the dosing was not in accordance with the in house protocol.

--The one patient entered into another study was ineligible.

--Failure to submit ECOG flow sheets to the sponsor for two of the patients treated in another study.

--One of two patients in a study was ineligible.

--Two of three patients in one study received concomitant medication prohibited by the protocol.

--The one patient treated under one of the protocols received concomitant radiation therapy prohibited by the protocol.

--Reporting of inaccurate x-ray data for the one patient in another study.

--Numerous instances of reporting nonverifiable data, including dosing information.

After the investigation had been completed, Kelsey wrote to Spiers:

"Based upon the information obtained during the inspection and our review of your responses, we believe that you have repeatedly or deliberately violated regulations pertaining to the proper conduct of clinical studies involving investigational drugs. . .

"The information provided by you in your reports never reflected the fact that these subjects were treated by physicians who had not signed a form FDA-1573 or were not listed on your FDA-1573 as being responsible to you. Further, there was no indication that the treatments were not administered at the Albany Medical College. The reports never reflected the fact that you were providing investigational drugs to physicians outside of the U.S. and reporting these treatments as if they were done at the Albany Medical College."

FDA acknowledged that "there was no knowing or willing submission of false data" and said that it "has no interest in pursuing criminal prosecution of Dr. Spiers." However, Alan Lisook, chief of the Clinical Investigations Branch, said in a letter to Kelsey, "We nevertheless feel that Dr. Spiers should be disqualified without condition, since his protocol violations contributed to increased mortality. This, indeed, was the reason that ECOG initiated an audit of his work."

FDA initially sought to bar Spiers from investigational drugs for life. He responded in a letter to Kelsey, "If you were to prohibit such activity for the remainder of my career, it would be a very severe penalty, crippling to my work. A prohibition of unlimited length assumes that I am not capable of learning better ways and of becoming dedicated to the strictest possible observance of FDA guidelines and regulations. I assure you that I am capable of so doing, and that I am unlikely ever to transgress again."

Spiers asked for a one year suspension, FDA came back with an offer of four and eventually settled on three.

Spiers also asked for permission to participate in trials "which are written, chaired, and supervised by individuals other than myself and are subject to scrutiny by data managers, toxicity monitors, study chairmen, and statisticians." Kelsey's response:

"Any investigator ineligible to receive investigational drugs is prohibited from participating in investigational drug studies sponsored by ECOG or any other cooperative group. Despite the fact that the [study in which patients reportedly died with drug toxicity] was reviewed by data managers and toxicity monitors, the excessive mortality in subjects with ECOG performance status ratings above protocol permitted levels was found only after the fact. Thus, depending on third parties to prevent violations of FDA regulations is insufficient."

Kelsey later modified that to the extent that Spiers was permitted to participate in the care of patients receiving investigational drugs from other physicians. She also stated, "It is important that you realize that your personal demeanor or abilities as a physician are not at issue. Our sole concern is your documented and admitted problems as a clinical investigator of investigational drugs."

'Never Felt Guilty About Treatment'

Spiers this week told **The Cancer Letter** that "I basically pleaded guilty to infringement of FDA regulations, but I never felt guilty about the treatment of my patients."

Spiers insisted that he had been under the impression at that time that ECOG study chairmen had the prerogative of altering doses if in his professional judgment it was to the patients' benefit. He also did not see anything wrong with letting the patients' own physicians have the investigational drugs so that patients could be treated nearer home, "as long as they were board certified hematologists."

As for the excess mortality, Spiers blamed that on what he said was a reality of clinical trials, that "you get more deaths early in a study. Those who go into remission show up later. An excessive number of deaths look a lot less excessive when all the reports are in."

Spiers said that all toxicity reports were forwarded immediately to the ECOG operations office.

ECOG Chairman Paul Carbone confirmed that study chairmen had had some leeway in adjusting doses, but said that Spiers' deviations of 30 to 40 percent "were way beyond what was acceptable." After the Spiers investigation, study chairmen were required to strictly adhere to protocols, with no discretion whatever.

Spiers said that most of the alleged ineligibility was due to "a matter of performance status."

All but two of the dose modifications were downward, Spiers said. Those downward adjustments later became accepted as the standard dose for deoxycoformycin. Two received larger doses than called for in the protocol only after permission in writing had been obtained from NCI, Spiers insisted.

Spiers pointed out that the ECOG study of deoxycoformycin for treatment of hairy cell leukemia was published in the "New England Journal of Medicine" in 1987, and that the trial proved it is a very active drug.

"I certainly know more than I knew four years ago," he said. "I know that FDA regulations have to be observed."

Gene Therapy Experiments In Cancer, Immune Disorder, Get RDAC Okay

The Recombinant DNA Advisory Committee last week gave NCI and National Heart, Lung & Blood Institute researchers approval to conduct two experiments that will be the first to treat human disease by inserting genes into cells.

The committee, which counsels the NIH director on all genetic engineering projects, voted 16-1 to approve a gene therapy to treat children suffering from adenosine deaminase (ADA) deficiency, the rare immune disorder similar to the disease that confined the "bubble boy" of Texas to a sterile environment for his life. NCI researchers Michael Blaese and Kenneth Culver, and NHLBI researcher French Anderson proposed the experiment.

The panel then unanimously approved NCI Surgery Branch Chief Steven Rosenberg's proposal to treat advanced melanoma patients with gene-modified tumor infiltrating lymphocytes, which would identify and attack cancer cells. The lymphocytes would be given extra potency by insertion of a gene for tumor necrosis factor.

The votes cleared the main hurdles in the long approval process to which both projects have been subjected. Still needed are approvals from NIH Acting Director William Raub and the FDA.

Raub said he had been "intrigued and excited" by the proposals and would consider the panel's recommendation "more than any other single thing." FDA is expected to approve the projects within a month or two.

The researchers said they would be ready to begin trials of the therapies immediately after FDA approval.

"This is a truly historic moment," said RDAC Chairman Gerard McGarrity, Coriell Institute for Medical Research. "Medicine has been waiting for this kind of therapy for thousands of years."

Both experiments will use similar techniques for introducing genes into cells. In the ADA proposal, the researchers will splice a copy of the gene that produces the missing ADA enzyme into blood cells isolated from the patient. The cells will be reintroduced into the child through blood transfusion. They hypothesize that the gene will "turn on" and begin producing ADA to salvage the patient's immune system.

The researchers believe the therapy will have a longer lasting effect than current treatments, such as enzyme replacement. They have identified five possible candidates for the trial, including an 18-month-old boy.

Tobacco Control Bill Requires Stronger Warnings, Ad Restrictions

Rep. Henry Waxman (D-CA) has introduced an anti-tobacco bill that proposes stronger, more prominent warning labels, tough new restrictions on tobacco advertising and promotion, regulation of ingredients in tobacco products, prohibition of sales to minors and the sale of candy cigarettes, and more public education about the health effects of smoking.

The bill, titled the "Tobacco Control and Health Protection Act," HR 5041, is designed to strengthen the 1984 cigarette labeling law, but it goes much further, prohibiting tobacco companies from sponsoring athletic, music or artistic events in the name of tobacco products, and outlawing all but "tombstone" advertising of tobacco. It also requires states to enforce laws restricting the sale of tobacco to minors, or risk the loss of block grants for treatment of drug abuse.

The Bush Administration supports more explicit warnings, but opposes sanctions against states that do not enact laws, according to HHS Assistant Secretary James Mason. Mason testified at a hearing last month on the Waxman bill.

Mason said the Administration would prefer to find incentives to enact such legislation, rather than depriving states of "vitally needed services." But he expressed the Administration's support for a licensing

system for stores selling tobacco products, signs in stores stating that it is illegal to sell tobacco to minors, and enforcement of state laws through license suspension and fines.

"A major motivation for the legislation is the continuing use of tobacco by children," Waxman said in a statement released at the hearing. "It has become increasingly clear that the U.S. tobacco industry has pursued a marketing policy dependent upon recruiting youthful smokers. Three million Americans under the age of 18 smoke 947 million packs of cigarettes a year. Each day, 3,000 young people, many still in elementary school, strike the first match of what may become a lifelong and life-threatening addiction.

"Despite the existence of restrictions on the sale of tobacco to young people in 45 states, we now know what the industry has known for years--states do not enforce laws prohibiting the sale of tobacco to minors. Lax enforcement and the continued availability of cigarettes through vending machines make a mockery of tobacco control efforts. Current restrictions in most states are archaic--many reflect laws enacted in the 19th and early 20th Century.

"In fact, the Surgeon General's 1989 report concluded that 'the number of legal restrictions on children's access to tobacco products has decreased over the past quarter century.'

"The tobacco and advertising industries say they don't want kids to smoke. Baloney! The industry does nothing to stop youthful smoking because younger smokers are essential to replace the millions of smokers lost annually to death and quitting. Youthful smoking is essential to the long term stability of the tobacco industry. It is the driving force of their marketing strategy."

The bill is concerned with the following major areas of tobacco control:

Warning label reform. The bill requires the following new warning on cigarette and smokeless tobacco packages and advertising: WARNING: Tobacco is an Addicting Drug. The warning label format is made larger, so that the warning takes up 25 percent of the space on each of the two most prominent sides of the package and 20 percent of advertising, including billboards. The warning is to be placed at the top of all packaging and advertising, and is to appear in black lettering on a white background or white letters on a black background, with a contrasting border.

The wording of the warnings is shortened and the variety of statements increased to promote visibility, and would rotate on packaging in the same manner as the existing law. The following eight warnings would apply to cigarette packaging and advertising: Cigarettes Kill, Cigarettes Cause Lung Cancer, Cigarettes Cause Emphysema, Cigarettes Cause Heart Disease, Tobacco is an Addicting Drug, Quitting Cigarettes Will Improve Health, Cigarettes May Cause Fetal Injury or Miscarriage, Cigarette Smoke is Harmful to Nonsmokers, and Cigarettes Cause Stroke.

The following warnings would be placed on smokeless tobacco packaging and advertising: Smokeless Tobacco Can Cause Mouth Cancer, Smokeless Tobacco Can Cause Gum Disease and Tooth Loss, Smokeless Tobacco Is Not a Safe Alternative to Cigarettes, and Tobacco is an Addicting Drug.

Under the bill, compliance with federal warning label requirements would not relieve tobacco companies from liability for the product.

Advertising and promotion restrictions. The ban on advertising tobacco products on TV or radio is extended, but the bill also bans advertising through film, video tape, audiotape, audio disc and video arcade game. This includes cigars and pipe tobacco.

Three years after the bill is enacted, all tobacco print advertising would have to conform to a "tombstone" format, which excludes the use of human or cartoon figures and brand name logos or symbols. No picture, other than the picture of a single package of the tobacco product displayed against a white background, may be used.

All tobacco product advertising in sports stadiums would be prohibited and sponsorship of events in the name of a registered tobacco brand name would be prohibited. Corporate sponsorship would continue to be permitted.

No free samples, coupons, toys or nontobacco products which bear a tobacco product brand name would be permitted. No paid placement of tobacco products in movie or TV shows, or on equipment or vehicles used in sporting events would be permitted.

Regulation of tobacco ingredients. Under the bill, no tobacco advertisement or package label may make representations concerning the level of or removal, reduction, or addition of ingredients, additives, filters or other devices unless the HHS Secretary determines that such representation is significant in affecting health or safety. This provision is intended to prohibit misleading health claims about low tar or low smoke.

The bill authorizes the HHS Secretary to require that the levels of any tobacco additive be reduced or eliminated if it is determined to be unsafe or presents an increased risk to the health of the consumer or the public.

The Secretary would have the authority to require tobacco manufacturers to put additional labels on

packages about the adverse effects of the products. Under the bill, tobacco products must include a label disclosing the ingredients of the product in descending order of importance. In addition, results from tests establishing the tar, nicotine and carbon monoxide levels of the product would have to be submitted annually to HHS, which would make the test results public.

Prohibition of tobacco sales to minors. States would be required as a condition of receiving federal drug and alcohol abuse block grants to adopt state laws that make it unlawful to sell tobacco products to persons under age 19 and to sell tobacco through vending machines unless the machines are located where minors do not have access. The bill requires state licensing for tobacco vendors and civil penalties and license revocation for violation of state law. The bill gives states two years to enact the necessary legislation.

Other areas. The bill also prohibits the sale of candy or gum designed to resemble tobacco products. In addition, the bill elevates the existing HHS Office on Smoking and Health to the stature of a Center on Tobacco and Health. The bill authorizes the center to conduct paid advertising campaigns to discourage tobacco use by youth.

Similar legislation introduced by Sen. Edward Kennedy (D-MA) was reported out of the Senate Labor and Human Resources Committee in May. Some provisions were deleted, such as the warning label saying that tobacco is addictive, disclosure requirements for tar and nicotine, federal penalties to encourage states to enforce laws on sale of tobacco to minors. Kennedy plans to offer these provisions when the bill reaches the Senate floor.

Staff To Disperse During Next Two Weeks, No More Issues Until Aug. 31

The Cancer Letter editorial staff will flee the Washington scene the next two weeks, some for a vacation, others to cover the International Cancer Congress in Hamburg.

The office will remain open, Monday-Friday, with Subscription Manager Esther Cureton on hand to take new orders, answer questions, field complaints, and take messages. Calls (202/543-7665) during nonbusiness hours will get the message recorder and will be responded to as soon as possible. The fax machine (202/543-6879) is always on duty.

The Cancer Letter will not be published during those two weeks. The next issue, Volume 16 Number 33, will be dated August 31. Librarians please note.

RFPs Available

Requests for proposals described here pertain to contracts planned for award by the National Cancer Institute unless otherwise noted. NCI listings will show the phone number of the Contracting Officer or Contract Specialist who will respond to questions. Address requests for NCI RFPs, citing the RFP number, to the individual named, the Executive Plaza South room number shown, National Cancer Institute, Bethesda MD 20892. Proposals may be hand delivered to the Executive Plaza South Building, 6130 Executive Blvd., Rockville MD. RFP announcements from other agencies will include the complete mailing address at the end of each.

RFP NCI-CP-05647-18

Title: Synthesis of derivatives of polynuclear aromatic hydrocarbons
Deadline: Approximately Nov. 5

The Chemical & Physical Carcinogenesis Branch of NCI's Div. of Cancer Etiology has a requirement for the synthesis of labeled and unlabeled derivatives of polynuclear aromatic hydrocarbons. This procurement involves two tasks: Task 1, for the synthesis, purification and characterization of selected derivatives of polynuclear aromatic hydrocarbons in gram quantities; and Task 2, for the operation of a radiolabeled polycyclic aromatic hydrocarbon derivative repository.

The successful operation of the second task also involves the resynthesis and purification of compounds in the repository as stocks are depleted. As a result, the Task 2 award will be made only to an applicant who successfully competes for Task 1.

This acquisition is a recompetition and two awards are anticipated, one for Task 1 and one for Task 1/2. Each award is expected to be for a five-year period.

Contract Specialist: Catherine Baker
RCB Executive Plaza South Rm 620
301/496-8611

NCI Contract Awards

Title: Storage and distribution of clinical drugs
Contractor: ERC BioServices Corp., Gaithersburg, MD; $3,615,885

Title: Editorial services to the International Cancer Information Center
Contractor: Grammarians Inc., Arlington, VA; $1,035,617

Title: Booklet printing
Contractor: Progress Printing Co., Lynchburg, VA; $95,446

Title: Pamphlet printing
Contractor: Whittet & Shepperson Inc., Richmond, VA; $26,250

Title: Analysis of physician training in smoking cessation techniques
Contractor: Schulman, Ronca & Bucuvalas Inc., New York, NY; $454,917

Title: Evaluation of cohort survey for community intervention trial for smoking cessation
Contractor: Westat Inc., Rockville, MD; $254,791

Title: Endpoint cohort tracking survey for community intervention trial for smoking cessation
Contractor: Westat Inc., Rockville, MD; $261,772