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P.O. BOX 2370 RESTON, VIRGINIA TELEPHONE 703-620-4646

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FDA PROPOSES "CLARIFICATION" OF CLINICAL STUDIES REGULATIONS, INCLUDING SANCTIONS, INSPECTIONS

The Food & Drug Administration announced a "clarification" of its regulations pertaining to the conduct of clinical investigations of new

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In Brief

KENNEDY DROPS HEALTH CARE INSTITUTE PLAN; SENATE APPROVES DOLE AMENDMENT ON PATENTS

HEALTH SERVICES research bill (S.2466), which the Senate had previously rejected, was approved last week by a solid 74-19 vote after sponsor Ted Kennedy agreed to drop the provision creating a new National Institute of Health Care Research. The bill extends for three years authorization for the National Center for Health Statistics, expands somewhat its mandate for epidemiological research, and provides a legislative base for the Office of Health Technology which had already been established in the HEW assistant secretary for health office. Another amendment submitted by Sen. Robert Dole (R.-Kan.) was approved, transferring authority administrative responsibilities of the HEW patent counsel from the Office of General Counsel to the Office of Health Technology. Dole said this would end the "stonewalling" which he claimed general counsel is doing regarding patent requests (*The Cancer Letter,* Aug. 11). . . . **WILLIAM ROY**, an MD who as a congressman was a member of the House Health Subcommittee, won Democratic nomination for the U.S. Senate in the Kansas primary. Roy gave up his seat to run for the Senate four years ago, narrowly losing to Dole. This time he'll oppose the daughter of former Kansas Gov. and GOP Presidential nominee Alf Landon for the seat now held by retiring James Pearson. . . . **ARTHUR UPTON** told the Environmental Protection Agency that he supports proposed regulation to set a maximum contaminant level of 100 parts per billion for total trihalomethanes in drinking water. "Animal experimental data has demonstrated that many of the organic contaminants in water are carcinogens," Upton said. "Additive or more than additive effects from multiple exposures to an array of organic carcinogens in water are of such significance as to warrant an appraisal of the opportunity for magnification of the total carcinogenic burden which may be tractable or controllable by water processing to reduce the levels of total exposure. The lack of a recognizable threshold for carcinogens implies that even a low level of exposure may contribute to the total cancer risk. Any reduction in the exposure to a carcinogen may therefore contribute to reducing the cancer risk in the population". . . . **SECOND INTERNATIONAL** Conference on Adjuvant Therapy of Cancer will be held in Tucson March 28-31 under sponsorship of the Cancer Center Div. of the Univ. of Arizona. Sydney Salmon and Stephen Jones are co-chairmen. Deadline for submission of abstracts is Dec. 1. For abstract forms, other information, contact Dorothy Baker at Cancer Center Div., Univ. of Arizona, Tucson 85724, (602) 626-6044.

FDA FINDS VIOLATIONS; NO HAZARDS TO PATIENTS, STUDIES NOT COMPROMISED

(Continued from page 1)

drugs and medical devices. "Defining the obligations of investigators in conducting clinical investigations constitutes a major restatement and clarification of FDA policy," the agency said in its explanation of the proposals.

The 26 page statement of proposals and explanations was published in the Aug. 8 issue of the *Federal Register.* They could have broad implications for clinical investigators developing anticancer drugs and for physicians using anticancer agents still considered experimental by FDA.

The agency asked for comments on the proposals, to be submitted in writing by Nov. 6. They should be sent to Hearing Clerk (HFA-305), FDA Room 4-65, 5600 Fishers Ln., Rockville, Md. 20857.

"This proposal would clarify existing regulations concerning persons who conduct clinical investigations on new drug products and would extend these regulations to include persons who conduct clinical investigations on other products regulated by FDA," the summary of the announcement said. "This proposal is based upon findings in inspections of clinical investigators that existing requirements are not being fully followed and may be subject to varying interpretations, upon recommendations of the General Accounting Office regarding FDA regulation of new drug testing, and upon an evaluation of the need for such regulations to implement both the Medical Device Amendments of 1976 and the agency's bioresearch monitoring program for assuring the validity of scientific data from human and animal studies.

"The proposed regulations are intended to assure adequate protection of the rights and safety of subjects involved in clinical investigations and the quality and integrity of the resulting data submitted to FDA in support of applications for permission to conduct further research or to market regulated products, while providing sufficient flexibility and latitude for innovative clinical research in the interest of the public health.

FDA Commissioner Donald Kennedy "believes that a complete revision of the regulations governing the conduct of clinical investigators is needed because (1) current regulations have not been comprehensively reviewed in 15 years, (2) FDA inspections have disclosed numerous deviations from current standards by investigators, (3) these discrepancies may be related, at least in part, to misunderstandings over the precise meaning of FDA requirements as currently written, (4) the GAO has recommended changes in current FDA regulations, (5) the Medical Device Amendments of 1976 mandate FDA to develop standards for clinical investigators of devices for human use, and (6) the new FDA bioresearch monitoring program, designed to assure the validity and reliability of clinical and nonclinical data submitted to the agency, can be more efficiently and effectively conducted with uniform, agencywide regulatory standards."

The announcement notes that FDA's Bureau of Drugs and Bureau of Biologics have conducted surveys of clinical trials recently and "numerous deficiencies were discovered. . . . Both bureaus concluded that most of the shortcomings constituted violations that did not present any significant hazard to the subjects or compromise the integrity of the specific studies. On the other hand, there was serious concern about certain deficiencies such as the failure to keep an institutional review committee informed of progress in the study, refusal to permit FDA inspectors to examine records containing a subject's name or prior medical history, inadequate documentation of subject consent, and use of exculpatory statements in consent forms. Although these actions and omissions are not acceptable behavior for clinical investigators, the commissioner emphasizes that the surveys do not support a conclusion that human subjects are routinely being exposed to unnecessary or avoidable risks in the course of research on new drugs and biologics, or that decisions to approve marketing of new drugs are being made upon that that are inaccurate or unreliable or accepted without analysis or means of verification.

"Nevertheless, these surveys do indicate that a serious problem of communication exists between FDA and at least some clinical investigators."

Those who will be affected by the new or "clarified" rules might be expected to ask, if patient safety has not been jeopardized and research results have not been compromised under the existing system, why tinker with it?

Because GAO (Congress' investigative agency) and the Medical Services Act require it, the announcement said, and because "FDA has recently reassessed its responsibilities, needs, and priorities in the entire area of biomedical research. . . . The agency, Congress and others have recently become concerned about the validity and reliability of scientific data on the safety and effectiveness of products regulated by FDA."

NCI and cancer clinical investigators have attempted to make the point with FDA that the catastrophic nature and high mortality of the disease should be a consideration in the enforcement of regulations. Administering a new drug to a cancer patient, for whom no other effective treatment may be available, is not the same as trying out a new variation of aspirin, they contend.

Kennedy admitted as much in providing for exemptions from the regulations.

"The commissioner is proposing to permit exemptions from all or part of the requirements . . . in appropriate cases," the proposal says. "These regulations have been drafted to make them applicable to

all clinical investigations regulated by or submitted to FDA, and the commissioner maintains that the principles are reasonably applicable to all such investigations. However, FDA has not been able to review every type of clinical investigation to guarantee that these standards are totally appropriate to each particular study. Therefore, the commissioner invites comments to identify any unique category of clinical investigation that should be exempted from any specific requirements of this proposal and to provide an adequate rationale to demonstrate why such requirements are not necessary to protect the rights and safety of subjects or to help assure the quality and integrity of the data produced.

"In addition, the commissioner proposes (that) individual investigators or their sponsors may request FDA for a waiver of any particular requirements for purposes of a specific study or group of studies. In emergency situations, such a request may be granted by telephone; otherwise, such requests should be in writing as part of the application for a research permit."

The proposal says that while FDA agrees that research on living animals and humans "requires flexibility," and that modifications of an investigational plan may be necessary at times, it has sometimes found "significant changes" which "undermine the validity of a study or expose subjects to different risks or innappropriately affect their rights" without notice to or approval of a sponsor.

"The agency is committed to . . . providing wide latitude to clinical investigators. The commissioner believes, however, that the sponsor and where required the institutional review board must be consulted in the event that certain types of changes are considered."

Five case studies were listed which illustrate the types of changes that warrant prior approval by the sponsor or institutional review board:

"1. A significant increase in the dosage or frequency of administration of the test article, or a change in the method of administration. In one recent drug investigation, the investigator sought to accelerate the pace of the study by moving to high-dose phase I exposure before low-dose exposure had been completed; some of the subjects developed liver toxicity and required extended medical care after exposure was discontinued.

"2. A significant increase in the number of subjects participating in the study. A recently discontinued drug investigation had reached the stage where a few phase III investigators had begun routine use of the drug in their practice and, in effect, the drug was being promoted before approval. The primary purpose of an investigation is to study a drug's benefits and risks in order to reach a conclusion on whether it should be introduced into medical practice. The conversion of a study phase into a promotional phase does not in the long run help the public, the investigators, or the sponsor. Each protocol should have a built-in maximum number of subjects which, at least initially, seems likely to provide a data base adequate to make a judgment on whether the scientific hypothesis under examination should be accepted or rejected. Any significant increases above this maximum properly require justification.

"3. The utilization of subjects with medical conditions unrelated to, but possibly affecting, the scope or validity of the study.

"4. The utilization of human subjects who require special consideration or protection and who are not specifically listed in the protocol. The recent concern for special protections for particular subject populations led to the enactment of the National Research Act (Pub. L. 93-348), which in turn mandated the creation of the National Commission for the Protection of Human Subjects in Biomedical and Behavioral Research. One of the functions of this commission is to review and recommend policies regarding research involving special populations such as children, prisoners, and the mentally disabled. The commissioner forsees specific proposals for FDA regulations to implement appropriate recommendations of the commission. In the interim, the commissioner believes that at a minimum the investigators should consult in advance with sponsors, and, when required, institutional review boards about utilization of such populations in clinical investigations.

"5. The administration of concomitant or concurrent therapy under conditions which confound interpretation of results. A recurring problem in investigational drug studies is the use of more than one pharmaceutical agent in the subject, often to treat the condition under study. The commissioner recognizes the medical necessity to provide quality medical care to subjects who participate in research. This means that drugs or therapies other than the one undergoing evaluation must be given to research subjects on occasion. Such concomitant medication can sometimes be anticipated and its use described in the protocol, and sometimes it cannot. The principle to be maintained is that concomitant medication is to be avoided whenever possible, introduced in such a way as not to confound the study whenever such medication is necessary, and in any event reported accurately so that the data can be interpeted correctly. If confounding concomitant medication is introduced with any frequency in a study, the validity of the study is seriously undermined, and such investigation raises a separate ethical issue of whether the subject should have received the test article in the first place."

The proposal emphasized that "none of these alterations of the protocol is being forbidden or even subjected to prior FDA approval, except in the case of (certain) investigational devices . . . the commissioner proposes that each protocol be in writing; that

any change in a protocol be documented and dated; and that significant modifications of an investigation, if not contemplated in the original protocol not be undertaken without prior consultation and agreement with the sponsor and institutional review board."

FDA presently requires annual progress reports be submitted by investigators to the agency but not specifically also to sponsors. The proposal would include sponsors in the requirement. It also would require notification of the sponsor within three months after a study has been completed or discontinued.

The new rules would tighten up adverse reaction reporting requirements.

"To specify more precisely when reports are required and how quickly they must be submitted, the commissioner proposes that a special report be required for any serious adverse effect, death, or life-threatening problem that may reasonably be regarded as caused by or associated with the test article and that was not previously anticipated (in nature, severity, or degree of incidence) in the written information given to the investigator by the sponsor. This requirement should eliminate any repeated reports of routine and minor side effects (nausea, dizziness, drowsiness) once these are inserted in the sponsor's brochure for investigators, but would require reports of unusual, serious, or unanticipated reaction.

"Another change in special reporting obligations is the replacement of current nonspecific deadlines ("promptly" and "immediately") with a simple standard: As soon as possible but in no event later than 10 working days after discovery."

In another concession to cancer investigators, the proposal notes there have been objections to reporting a serious incident when it could be and in fact was foreseen, for example when an extremely serious or terminal medical condition for which no accepted therapy exists is being treated with the test article. "The commissioner agrees that special reports under such circumstances would be unnecessarily burdensome, and has revised this proposal accordingly. The comments on the 5-day reporting period argued that it was too brief to permit an adequate review of the case by the investigator to determine whether the incident could reasonably be regarded as caused by or associated with the test article. The commissioner is now proposing a period of 10 working days, which he believes is clearly adequate for the type of determination being requested. Absolute proof of causality is not necessary; a reasonable belief that an association may exist between the test article and the adverse phenomenon is sufficient to justify notification to the sponsor and the institutional review board."

The new proposals "raise the question of what to do if an investigator fails to carry out these requirements," the announcement said.

"Several options are available:

1. Notifying the investigator of deficiencies observed during an inspection.
2. Issuing more formal warnings concerning discrepancies, through formal regulatory correspondence.
3. Determining that data from one or more specific clinical investigations will not be considered by FDA in support of an application for a research or marketing permit.
4. Disqualifying an investigator as an acceptable researcher to conduct clinical investigations regulated by or submitted to FDA. "This sanction would be utilized when the deficiencies found in an investigator's work are of such a widespread or fundamental nature that the safety of subjects in, or the rights of human subjects in, or the quality and integrity of a number of studies conducted by the investigator have probably been compromised, or when the investigator has failed to comply with FDA regulations after previous warnings from the agency."
5. Court injunction against further violations. "This form of judicial action has not previously been utilized by FDA to enforce the obligations of clinical investigators, but will be considered in appropriate circumstances."
6. Criminal prosecution of an investigator and/or sponsor for violations of federal criminal laws.

The announcement noted that in 15 years, FDA has disqualified only 24 investigators—two by the Bureau of Biologics, the others by the Bureau of Drugs.

FDA's insistence that it has the right to inspect the scene of clinical investigations and pertinent records has led to some confrontations. Kennedy did not back down in drawing up the proposed rules.

"It follows from the authority to promulgate these regulations that FDA also has authority to prescribe the terms on which it will accept data generated in a clinical investigation." That means, it went on, that FDA will not consider data from a clinical investigation unless the investigator consents to inspection.

"The commissioner believes this requirement does not infringe on any rights or obligations of an investigator who at any time may refuse to consent to inspection or withdraw his or her consent. In this event, however, FDA will not consider the results of the study and may consider disqualifying the investigator. . . . The commissioner advises all persons who sponsor or perform under grant or contract clinical investigations that may be submitted to FDA to consider including in the grant or contract provisions regarding FDA inspections."

Despite the notation above that investigators "may at any time refuse to consent to inspection," the proposed rules go on to state that "inspections of many, perhaps most, clinical investigators will not be conditioned upon consent. FDA may inspect es-

tablishments, including consulting laboratories, in which certain drugs and devices are processed or held, an may examine research data that would be subject to reporting and inspection pursuant to (certain provisions of the law). . . . Thus, most sponsors and many investigators under INDs, INADs, IDEs and those institutions in which such studies are conducted would be subject to FDA inspection whether or not they consented."

The proposals acknowledged that confidentiality of records with names of patients is a problem, and attempt to deal with it.

"The commissioner finds it necessary to state clearly and publicly when FDA will request access to such records, and if such access is requested, how the agency will safeguard the privacy of subjects. . . . Agency personnel must invite the investigator to be present with them throughout FDA's records review, and they must inform the investigator that he or she may see the records which they may wish to copy and may review any records that are copied. Agency personnel may not copy medical records containing the names of research subjects, and the investigator is to be given the right to delete any information that could identify an individual subject, except when: (1) A more detailed study of the records regarding particular subjects is indicated; or (2) there is reason to believe that the records do not represent actual studies, or do not represent actual results obtained. The exceptions to the prohibition against the copying of individually identifiable medical records by FDA personnel rest primarily on the need to determine whether a given research subject in fact exists and whether the research subject in fact participated in the investigation. Where an individually identifiable medical record is copied and reviewed by the agency, the record is properly safeguarded within FDA and is used or disseminated under conditions that protect the privacy of the individual to the fullest possible extent consistent with laws relating to public disclosure of information (Freedom of Information and Privacy Act regulations) and the law enforcement responsibilities of the agency. . . .

"The commissioner recognizes the highly sensitive nature of this provision. He welcomes reasoned discussions of the issues involved and specific proposals under which patient confidentiality could be further protected without compromising the ability of FDA to verify clinical data submitted in support of applications for research or marketing permits."

A limited number of reprints of the proposed rules is available from FDA and will be sent on request on a first come first served basis. Write to Bureau of Drugs, Advisory Opinions Branch, HFD-35, FDA, 5600 Fishers Ln., Rockville, Md. 20857. Ask for the reprint from the Aug. 8, 1978 *Federal Register* of "Obligations of Clinical Investigators of Regulated Articles."

GORI GETS INTO ANOTHER CONTROVERSY — AT A TIME WHEN HE DID NOT NEED ONE

Gio Gori, deputy director of NCI's Div. of Cancer Cause & Prevention, has said he is not one to go looking for controversy and does not regard himself as a controversial figure. Nevertheless, controversy has a way of finding him.

Gori's latest flap has not only brought down on his head the wrath of NCI Director Arthur Upton but also that of HEW Secretary Joseph Califano.

The storm was touched off last week when the Associated Press sent out a story based on a report that Gori and Cornelius Lynch of Environ Control Inc. prepared for publication in the *Journal of the American Medical Assn.* Gori has headed NCI's Smoking & Health Program since its inception in 1970, and Enviro Control is the program's prime contractor, with Lynch as manager.

The report for *JAMA* essentially summarizes what has been known about the Smoking & Health Program's efforts to develop less hazardous cigarettes since the tobacco industry started marketing the various new brands of low tar and nicotine cigarettes more than two years ago (***The Cancer Letter,*** January 1976). The new brands, some with tar and nicotine levels as low as 1 mg and .1 mg, respectively, obviously are not as dangerous to health as those with 20 or 30 times those levels.

Gori and Lynch presented it in a somewhat different and more explicit way: They compared the present low t & n brands to the average pre-1960 cigarettes. Gori told AP that studies showed persons who smoked no more than two of the pre-1960 cigarettes per day had no higher death rate than nonsmokers. There are among present day cigarettes brands with levels of toxins a fraction of the pre-1960 brands. One brand—Carlton Menthols—is so low in tar and nicotine that most persons could smoke 23 a day with no more risk than incurred by those who smoked two a day before 1960.

Gori and Lynch compiled a list of these "tolerable" cigarettes, showing how many of each could be smoked to equal two pre-1960 cigarettes.

"I am not calling any cigarette safe," Gori emphasized. "The only cigarette that is safe is the cigarette that is not lit. I am not talking about what might happen to any individual. I am talking about averages. There may be a risk that still may be there even though we might not see it in overall, large population studies. But we can now begin to talk about tolerable levels of smoking from an overall, public health standpoint. I think we will begin to see some beneficial effects in this country in five or six years."

Since 1970, NCI has spent about $18 million on the effort to develop less hazardous cigarettes—that is, remove or reduce tars, nicotine, carbon monoxide, nitrogen oxides, and acrolein. The tobacco industry

participated in the program, as contractors and as advisors, and some companies carried on their own independent research. In 1975, using some of the methods that came from NCI's program, the industry began introducing one new brand after another of low tar and nicotine content.

One of the problems with such brands in the past had been that smokers considered them tasteless. Most of the new ones contain flavor additives developed by the firms. Most are closely guarded secrets.

Despite Gori's careful disclaimer, critics reacted to the report as if he had endorsed smoking. Sidney Wolfe, who heads the Ralph Nader Health Research Group, reacted in typical Nader fashion, saying that Gori should be fired for making "the most damaging statement about smoking in the last 10 years."

Gori couldn't care less what Wolfe says, but the criticism from Upton and Califano carried considerably more weight. Upton responded as he had to, to make it clear that NCI was not endorsing any of the new cigarettes or taking the position that any smoking could be considered safe.

"It is the firm position of the National Cancer Institute, the National Heart, Lung & Blood Institute and the Public Health Service that no cigarette now on the market can be considered wholly without risk to health," Upton said. Gori's use of the word "tolerable" was "unfortunate" and his statements have "set back our cause, and even if we can correct the misinterpretation, we will have lost valuable momentum," Upton said.

Califano, who earlier this year announced his own program to halt cigarette smoking, said, "There is no such thing as a safe cigarette or anything like it." He said government scientists "are very disturbed that millions of people might think so."

Gori received some support from the American Cancer Society. "There is no such thing as a proven safe cigarette," said Arthur Holleb, senior vice president for medical affairs. But Holleb acknowledged that the low tar/nicotine cigarettes do impose less serious risk of lung cancer and other disease than the more hazardous brands.

Holleb called upon the tobacco industry to perform a service to consumers and public by stopping manufacture of the more hazardous brands. "Given the industry's own research findings as reported over the weekend by the American Medical Assn. together with research reports of the National Cancer Institute and the National Heart & Lung Institute and epidemiology studies of the American Cancer Society, there can no longer be any question about the toxicity of high tar/nicotine cigarettes," Holleb said. "The tobacco industry now must decide how much responsibility it feels toward the American public and its health. The industry must ask itself what good is being done for consumers by its continuous promotion of hazardous high tar/nicotine products when it has the demonstrated ability to concentrate on products of lesser risk."

The Naderites, some members of Congress and even some within NCI have been critical of the Smoking & Health Program.

Including the $18 million spent on developing less hazardous cigarettes, the program has received about $25 million since 1970—an insignificant amount considering the contribution even the critics say that smoking makes to the incidence of cancer. But the critics argue that NCI is in the position of funding research for the tobacco industry and that the money should be going into antismoking campaigns.

The pragmatists, for whom Gori seems to be the leading spokesman, contend that antismoking efforts have been dismally unsuccessful and that the only way to make an impact on incidence of smoking related disease is to produce less hazardous cigarettes.

The Smoking & Health Program is in the midst of the reorganization being carried on in the Div. of Cancer Cause & Prevention since Gregory O'Conor became director of the division earlier this year. The program has been moved into the extramural Carcinogenesis Branch, headed by Thadeus Domanski. Gori no longer is head of the program, although O'Conor said he expects Gori to provide "advice, consultation and assistance."

The controversy over the smoking program came at a time when Gori least needed it. Since O'Conor became director, it was obvious that Gori's days as deputy were numbered.

"We get along fine, our relationship is excellent," O'Conor told ***The Cancer Letter.*** "But when I took this job, in view of the visibility, the fact that the division was being reorganized with a new director, it would be good for all of us to have a new deputy."

Upton was quoted by the *Washington Post* as saying that he had been talking to Gori for several months about changing jobs because he and O'Conor "simply haven't found a comfortable working relationship."

Gori insisted that "Greg and I are good friends. In fact, he has been my strongest supporter in this fracas (on cigarettes). It is true that he would prefer someone else as his deputy. We do have different philosophical approaches on some things, but I have tremendous respect for him."

O'Conor said he was trying to find a position for Gori within DCCP "commensurate with his experience and grade."

The Cancer Letter learned that another possibility —at least until last week's furor—was O'Conor's old job as head of NCI's Office of International Affairs.

O'Conor said existing contracts in the Smoking & Health Program would be continued, including studies on the long range effects of nicotine. The program recently underwent an internal review, and O'Conor has recommended that it be expanded to

include more work on basic carcinogenesis related to smoking, and new research on education and behavioral factors. Both grants and contracts will be used to fund extramural projects.

O'Conor said the program would be coordinated with Califano's office.

Gori denied that he told a *Post* reporter that Califano was putting pressure on Upton to fire him (which Upton denied). Gori admitted that he did say Califano probably was unhappy in that he might consider the report on less hazardous cigarettes would undercut the secretary's antismoking initiatives.

Gori fell into considerable disfavor with some NCI and NIH brass about 18 months ago when he participated in an effort to go over their heads directly to Congress in an appeal for more money for nutrition research.

When the Diet, Nutrition & Cancer Program was established following a mandate by Congress in renewal of the National Cancer Act three years ago, Gori was given the job of heading it (along with his other duties). Working with an advisory committee of nongovernment experts in that field, Gori got the program started and contracts were awarded.

NCI's budget levelled off about that time, and when the nutrition program was given a no-growth budget, the advisory committee drafted a strong letter criticizing the decision, NCI policymakers and other NCI programs. Copies were sent to the White House, members of Congress and other key individuals.

The letter brought on a tirade by Cancer Panel Chairman Benno Schmidt at a meeting of the National Cancer Advisory Board, who objected to the criticism of other cancer programs. It also earned the disfavor, according to some observers, of NIH Director Donald Fredrickson, who they say blamed it all on Gori. Others felt that Gori and his committee had gone too far and had unfairly and unnecessarily embarraased NCI's leadership.

It was not long after that NCI Deputy Director Guy Newell, who was then acting director of the institute, was required by HEW to immediately reduce the number of advisory committees. Among those Newell elected to eliminate was the Diet, Nutrition & Cancer Program Advisory Committee. Newell denied he was exacting revenge, but committee members wondered.

A few months ago, Sen. George McGovern sicced his Nutrition Committee onto NCI. The Cancer Program was severely criticized for not making a greater effort on nutrition research, and Upton was required to explain, defend and promise to do better.

Gio Gori could not be blamed if he had commented, "It wouldn't have happened if they had listened to me."

As part of the response to Congress, Upton agreed to provide more coordination of nutrition research with other agencies, along with giving it more money and attention. He also relieved Gori from responsibilities with the program, and turned it over to, ironically, Guy Newell.

SENATE APPROPRIATIONS COMMITTEE SLASHES $25 MILLION FROM NCI TOTAL

The Senate Appropriations Committee this week cut $25 million from the 1979 fiscal year allocation for NCI that had been approved last June by the HEW Appropriations Subcommittee. It was the first time the full committee has cut any money from the amounts recommended for NCI by the subcommittee since the National Cancer Program's inception in 1971.

The subcommittee, with Sens. Edward Brooke, Birch Bayh and Richard Schweiker supporting increased cancer funding, had approved $950 million, not including training funds which will have to be included in a separate bill after authorization legislation has been passed. Training funds are expected to be about $20 million, which would have brought the total NCI appropriation to $970 million—$100 million more than NCI is getting this year and also $100 million more than requested by the Administration.

The House has voted $888 million, plus training.

A cut of $50 million by the full committee was asked by Sen. Henry Bellmon (R.-Okla.). In arguing for the cut, Bellmon quoted from a letter published in the Congressional Record which charged that NCI has mismanaged its funds and that there has been no progress in cancer research since the 1971 Cancer Act. Bellmon commented that the letter was written by Sidney Wolfe.

Appropriations Committee Chairman Warren Magnuson said, "Well, I'm as well versed on the Cancer Program as anyone, and I never heard of Sidney Wolfe. Who is he?" (Wolfe is head of Health Research Group, a Ralph Nader affiliate.)

Sen. Lawton Chiles (D.-Fla.) pointed out that Magnuson had first requested $925 million (plus training) from the subcommittee. "Why not compromise at that?" Chiles asked. The committee agreed without any formal vote being taken.

Neither Brooke nor Bayh was present when the decision on cancer funding was made. Brooke appeared later to make a futile effort to add $25 million to the amount approved by the subcommittee for the National Heart, Lung & Blood Disease Institute.

RFPs AVAILABLE

Requests for proposal described here pertain to contracts planned for award by the National Cancer Institute, unless otherwise noted. Write to the Contracting Officer or Contract Specialist for copies of the RFP, citing the RFP number. Some listings will show the phone number of the Contract Specialist, who will respond to questions. Listings identify the respective sections of the Research Contracts Branch which

are issuing the RFPs. Their addresses, all followed by NIH, Bethesda, Md. 20014, are:
Biology & Diagnosis Section – Landow Building
Viral Oncology & Field Studies Section – Landow Building
Control & Rehabilitation Section – Blair Building
Carcinogenesis Section – Blair Building
Treatment Section – Blair Building
Office of the Director Section – Blair Building
Deadline date shown for each listing is the final day for receipt of the completed proposal unless otherwise indicated.

SOURCES SOUGHT

RFP NO1-CP-85646-58

Title: *Resource effort for microscopic and autoradiographic technology*
Deadline: *Sept. 7*

NCI is interested in entering into a basic ordering agreement for a two year period with an organization(s) to obtain assistance in preparation and examination of tissues by high resolution light microscopy, transmission and scanning electron microscopy and quantitative light and electron microscopic autoradiography.

Respondents should have experience and expertise in use of these methodologies and expertise in interpreting the results. Specific tasks will be identified. Pick up and delivery of specimen from the NIH reservation is required. Respondents should have proven abilities and equipment to perform the above described ultrastructural techniques to provide data on (1) the pathogenesis of tumors of various target organs and (2) the localization of labeled and unlabeled compounds, including chemical and physical carcinogens into cellular organelles by autoradiographic and x-ray defraction techniques.

For information purposes, the incumbent performers of tasks under this basic ordering agreement for the past two years have been Litton Bionetics Inc. and Experimental Pathology Laboratories Inc.

Contract Specialist: Mary Armstead
Carcinogenesis
301-427-7957

RFP NIH-ES-78-1

Title: *Development of somatic cell mutation systems in humans*
Deadline: *Approximately Oct. 5*

Proposals solicited from qualified sources having the capability to develop methods for study of somatic cell mutations in vivo. Offerors must have access to and be able to purify several (at least 10) different hemoglobin variants from the human population; must be able to produce and purify monospecific antibodies against these hemoglobin variants; must be able to deliver purified monospecific FTCT and rodamin-labelled antibodies to the government; must be able to develop methods to prove that the detected variants are mutant cells; and when the above techniques are sufficiently developed, must be able to screen a number of humans exposed to chemical mutagens and compare them to matched controls.

National Institute of Environmental Health Sciences
Procurement Office, OAM
PO Box 12233, Building 11, Room 1101
Research Triangle Park, NC 27709

NCI CONTRACT AWARDS

Title: Biologic, biochemical and immunologic characteristics of "premalignant" human mammary epithelial hyperplasias
Contractor: Duke Univ., $223,500.

Title: Relationship of thyroid function to growth of mammary tumors, continuation
Contractor: Albany Medical College, $37,000.

Title: Estrogen/progestin effects on breast in neonatal period, continuation
Contractor: Univ. of California (Santa Cruz), $92,400.

Title: Data management system and statistical support for NCI Serum Panel
Contractor: U.S. Small Business Administration, $57,362.

Title: Ten alteration/renovation/upgrading projects and provision for additional support at Frederick Cancer Research Center
Contractor: Litton Bionetics, $410,670.

Title: Development of an assay for genetic damage to mammary gland cells
Contractor: Ohio State Univ., $382,300.

Title: Resources modelling and analysis, renewal
Contractor: JRB Associates, $24,666.

Title: Isolation and tissue culture of human tumor cells
Contractor: Sloan-Kettering Institute, $91,035.

Title: Cervical Cancer Screening Program
Contractor: Maryland Dept. of Health & Mental Hygiene, $233,042.

Title: Diagnostic use of leukemia-associated antigens
Contractor: Health Research Inc. Roswell Park Div., $67,376.

Title: Development and validation of an in vitro mammalian cell mutagenesis system for carcinogenesis screening, continuation
Contractor: Litton Bionetics, $478,262.

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