THE CANCER LETTER

P.O. Box 2370 Reston, Virginia 22090 Telephone 703-620-4646

Vol. 7 No. 29

July 17, 1981


Subscription $125.00 per year

## M.D. ANDERSON INVESTIGATOR GAVE DRUG TO PATIENTS WITHOUT IND; NCI PROBES INCIDENT, TO MAKE REPORT

This is the story of an incident that at first had the look of another scandal, in which drugs not approved for clinical use were administered to cancer patients—another Martin Kline case perhaps with the potential of developing into another congressional controversy. There is no assurance at this point that it will not.

An NCI staff member perusing the proceedings of the American Assn. for Cancer Research April meeting happened onto the abstract

(Continued to page 2)

*In Brief*

### HATCH BILL WOULD RELAX DELANEY CLAUSE; MALONE NAMED ACTING NIH HEAD; SEARCH COMMITTEE FORMED

**SEN. ORRIN HATCH** has drawn up legislation, the Food Safety Amendments of 1981, which would allow FDA greater flexibility in regulating food additives, including a relaxation of the Delaney Clause. Delaney, which forbids use of additives shown to be carcinogenic in animals, would be retained but would not apply to substances "that do not present a significant risk to humans," Hatch said. . . . **NCI IS** concerned about another bill, S. 881, introduced by Sen. Warren Rudman (R.-N.H.), which would require federal agencies to set aside a certain percentage of their research and development funds for small business. Hatch and other senators are cosponsoring the measure. Under the bill, NCI would have to set aside $2 million in the first year following enactment to $10 million the third year, based on a $1 billion budget. A number of exceptions is permitted which could exclude most biomedical research. . . . **NIH DEPUTY** Director Thomas Malone was named acting director by HHS Secretary Richard Schweiker. The secretary also established a search committee consisting of Edward Brandt Jr., asst. secretary for health; Robert Rubin, asst. secretary for planning and evaluation; and FDA Commissioner Arthur Hayes Jr. Schweiker asked them to submit nominations for the new NIH director to him by July 17. The job is a Presidential appointment which does not require Senate confirmation. . . . **JOSEPH RALL**, director of intramural research for the National Institute of Arthritis, Metabolism & Digestive Diseases, has been named acting deputy director for science of NIH. Robert Goldberger vacated that position last month for a job with Columbia Univ. . . . **DAVID YOHN**, director of the Ohio State Univ. Comprehensive Cancer Center, has been appointed Assn. of American Cancer Institutes liaison to the Assn. of Community Cancer Centers. . . . **ROBERT BYRNE**, acting director of the National Institute of Allergy & Infectious Diseases, died last week after a heart attack. Byrne, a virologist, played a leading role in NIAID's development of viral vaccines and hepatitis. He was 58.

NIH Negotiating On Straus Grant; Committee Asks For One Probe . . . Page 3

DCCP Board OKs Four New Concepts . . . Page 3

Steckel Urges AACI To Seek Increase In Core Funding . . . Page 5

RFA On Promoters, Hormones, Other Cofactors Available . . . Page 6

Sources Sought . . . Page 7

## INVESTIGATOR ASSUMED IND APPROVED; NO INTENT TO DECEIVE, FREIREICH SAYS

(Continued from page 1)

(No. 715) of a poster session presentation entitled, "Clinical Pharmacologic Studies of 5-methyltetrahydrohomofolate (MTHHF)." The NCI staff member was aware of the fact that studies published in the AACR and ASCO proceedings had to have been initiated no later than mid-1980, since abstracts had to be submitted in the fall.

The staff member also was aware that an IND for phase 1 studies of MTHHF had only recently been approved, within the previous three months. The inescapable conclusion: The drug had been given to patients without an IND.

Astounding. Not only had a cardinal FDA regulation been violated, but the study was submitted for publication, and accepted (not once but twice, it later developed. The same study was presented last September at the 1980 symposium on progress in cancer research, sponsored by Memorial Sloan-Kettering Cancer Center).

Even more astounding, the study was performed at one of the world's leading cancer research institutions, M.D. Anderson Hospital & Tumor Institute, by one of the world's leading pharmacologists in cancer research, Ti Li Loo.

NCI, the recent Senate hearings still scorchingly fresh in mind, notified officials at M.D. Anderson and FDA and launched an investigation to determine how this could have happened, whether internal review procedures were compromised, what can be done to prevent recurrence of similar incidents, how the matter might affect the NCI contract which supports Loo's studies.

NCI also notified the staff of the Senate Committee on Labor & Human Resources.

A site visit team was organized, headed by Div. of Cancer Treatment Deputy Director Saul Schepartz and including John Driscoll, acting director of the Developmental Therapeutics Program; Daniel Hoth, chief of the Investigational Drug Branch; David Johns, project officer for the contract; David Keefer, deputy chief of the Research Contracts Branch; Alan Sartorelli, chairman of the Yale Dept. of Pharmacology and a member of the DCT Board of Scientific Counselors; Lawrence Baker, Wayne State Univ.; and two other NIH representatives.

The site visit team conducted its investigation in Houston Monday and is in the process of writing its report. Schepartz told ***The Cancer Letter*** that "we had an excellent degree of cooperation from everyone there." He said no further comment would be made until the report has been completed, probably within a few days.

Charles LeMaistre, president of the Univ. of Texas System Cancer Center/M.D. Anderson, said he would withhold comment until the center's internal investigation has been completed and the NCI report issued.

Just how did an apparently flagrant violation of FDA (and NCI) regulations occur, involving a drug which had been supplied by NCI at that time strictly for animal experiments? Obviously, neither Loo nor his colleagues felt they had done anything wrong since they had published their findings.

Here is what happened, as pieced together by ***The Cancer Letter:***

Three years prior to the incident, Loo had completed the preclinical pharmacology on MTHHF. A protocol for a phase 1 study was written by Developmental Therapeutics at M.D. Anderson and submitted to NCI. For a number of reasons which are not yet clear, NCI did not file the IND with FDA.

The protocol had been reviewed and approved at three levels within M.D. Anderson—the department, the drug development research committee, and the human surveillance committee. It did not seem to be a controversial protocol, and three years later, Loo was under the impression that it had been approved.

Loo has developed contacts with colleagues in the People's Republic of China and has on occasion worked with visiting scientists from there. A delegation from Lanchow Medical College was at M.D. Anderson last year, and someone raised a question on the pharmacology of MTHHF. Assuming that an approved protocol was in existence, Loo agreed to administering small (15 mg/m$^2$) radiolabelled doses to four patients after obtaining informed consent.

The study found that the drug apparently is retained in the body and recommended that to prevent cumulated toxicity, frequent administration of the agent should be avoided.

Loo and the reviewers of the study for two international meetings obviously felt that finding was important enough to be published.

Emil Freireich, head of Developmental Therapeutics at M.D. Anderson, insisted "there was no intent to deceive anyone. No one was harmed. A minute amount of the drug was given, about 100 times less than that approved in the IND. It was a procedural violation only. Someone failed to file the IND. You can be sure that Dr. Loo would never knowingly violate an FDA regulation."

M.D. Anderson moved quickly, after officials there realized a violation had been committed, to establish new procedures which would protect against a repeat. Physicians working in preclinical research now are not permitted to collaborate with clinicians unless there is a written protocol and a note from Gerald Bodey, chief of the Chemotherapy Branch in Developmental Therapeutics, authorizing the study. Pharmacists are not permitted to issue any drug without a memo from Bodey approving it.

Freireich feels the reaction by NCI and others to the incident may have been exacerbated by his well

known and outspoken opposition to many of FDA's policies relating to anticancer drugs. He believes the IND process should be dispensed with for anticancer agents. He has submitted an editorial to the *New England Journal of Medicine* in which he contends that the requirement is immoral when 400,000 cancer patients are dying each year.

"I am not advocating that the law be violated, only that it be changed," Freireich said. "I advocate the elimination of INDs for cancer agents. But it is an institution policy and a Freireich policy that we will follow the law. We have never and certainly will not in the future deliberately avert policies NCI feels are necessary."

Loo temporarily at least has been removed as principal investigator for the NCI contract. The NCI report probably will recommend what further steps, if any, should be taken. Under the new NIH regulation, debarment procedures could be initiated if the incident is deemed that serious.

## NIH NEGOTIATING STRAUS GRANT; NEW COMMITTEE ASKS FOR SINGLE PROBE

NIH has begun negotiations with New York Medical College on what should be done with the program project grant awarded to Marc Straus. Funding of the Straus grant by NCI after he was accused of falsifying data as a cooperative group investigator at Boston Univ. was the focus of severe criticism by the Senate Committee on Labor & Human Resources.

Committee members insisted the grant be suspended. It is an NIH rather than an NCI matter at this point, and NIH Associate Director for Extramural Research & Training William Raub is handling it.

Both NIH and the Food & Drug Administration are conducting investigations of the charges. The NIH probe probably will not be completed before October, an NIH spokesman told ***The Cancer Letter.***

Meanwhile, an organization, "Scientists Supporting the Rights of Marc J. Straus, M.D.," has written to HHS Secretary Richard Schweiker, NCI Director Vincent DeVita and FDA Commissioner Arthur Hayes asking for a single review in place of the two investigations. The letter, signed by Mendel Krim, Brooklyn, and Ruth Moran, Valhalla, N.Y., as co-chairmen, follows:

"This committee of scientists and physicians has been formed to support the due process rights of Dr. Marc J. Straus. Dr. Straus' rights are at stake, as are the rights of all scientists, for this case may be a precedent for future inquiries of scientific conduct.

"Dr. Straus has repeatedly asked for a scientific peer review since allegations were made in 1978. We fully support his rights to: 1) a review which includes experts in oncology, 2) his presence at the review, 3) full disclosure of relevant documents, and 4) an evidentiary procedure which asks for testimony of his accusers as well.

"The FDA and the NIH, under the Dept. of Health & Human Services, are conducting simultaneous and competitive investigations. Neither agency has offered an appropriate judicial review. Moreover, the FDA has potentially jeopardized a fair review by disclosure of sensitive materials to the press and by public negative commentaries. This committee deplores the public exposure of material prior to a conclusion of the case.

"No individual should be expected to defend himself against simultaneous reviews which are overlapping, extraordinarily time consuming, and expensive. We urge that a unitary blue ribbon review be created in place of the current FDA and NIH investigations. We urge that this review be conducted in such a manner that its final resolution can be accepted and recognized by all as just.

"We support the principle that an individual is innocent until proved guilty. We further support that grant monies should not be withdrawn on the basis of unproved allegations. The principles which this committee support are the principles which should apply to any scientist seeking justice from his peers.

"We urge you to support these propositions."

In a note to ***The Cancer Letter,*** Krim and Moran said the committee is "joined by many others who believe that Dr. Straus has never had a fair hearing which he has requested from the beginning, and that an abrogation of Dr. Straus' rights is a threat to the rights of us all."

According to the committee's letterhead, its members are in addition to Krim and Moran:

Oliver Alabaster, Washington, D.C.; Edward Alexson, Santa Ana, Calif.; Jeffrey Ambinder, New York; Philip Burke, Baltimore; Howard Chester, New York; Harry Crissman, Los Alamos, N.M.; Louis Del Guercio, Valhalla, N.Y.; Robert Diasio, Richmond, Va.; Benjamin Drewinko, Houston; Rita Giralomo, Valhalla; Morris Glassman, Chappaqua, N.Y.; Edward Henderson, Buffalo; John Hodgson, Mamaroneck, N.Y.; Awtar Krishan, Miami, Fla.; Robert Madden, Valhalla; William Mahoney, New Rochelle, N.Y.; Mary Matthews, Washington D.C.; John McGiff, Valhalla; Mortimor Mendelsohn, Livermore, Calif.; Sara Rockwell, New Haven, Conn.; Lewis Schiffer, Pittsburgh; Oleg Selawry, Miami, Fla.; Victor Selmanowitz, Brooklyn; Stanley Shackney, Bethesda; Kenneth Siegel, Bridgeport, Conn.; Stephen Straus, Bethesda; Frederick Valeriote, St. Louis; Richard Vernick, Brockton, Mass.; John Weisburger, White Plains, N.Y.; Thomas Zipoli, New Bedford, Mass.

## DCCP BOARD APPROVES CONCEPTS OF FOUR NEW CONTRACTS, $680,000 FIRST YEAR

The concept of four new contract supported projects, two of them to be funded by NCI but awarded

and managed by the National Institute of Occupational Safety & Health, was approved by the Board of Scientific Counselors of NCI's Div. of Cancer Cause & Prevention.

**Data bank on environmental agents.** Estimated first year award, $300,000 on a two year contract.

The main objective of this procurement is to search the published literature for data and information which are relevant to areas of carcinogenesis, toxicology and mutagenesis of environmental agents. Involvement of the contractor may range from scanning data and information and supplying reports on information prepared by established guidelines to the actual involvement in preparation of manuscripts for possible printing and distribution.

**Mesothelioma and employment.** Estimated first year award, $205,000, on a three year contract.

To date, asbestos exposure has been identified as a causal agent in the development of mesothelioma, but information is incomplete on the full range of industries and occupations where known or suspected exposure to lower levels of asbestos may confer an increased risk. In addition, the role of non-asbestiform materials, such as fibrous glass products, as a possible cause of mesothelioma, is unclear. Incidence rates for mesothelioma, according to recent SEER data, may be increasing for white males, and to a lesser extent, for white females. Public speculation on the putative increase in incidence has focused on unidentified asbestos exposures as well as exposures to other agents. Although studies have been carried out in western Europe and Canada, there is a need for an objective evaluation of U.S. information on the etiology and environmental determinants of mesothelioma.

Objectives of this contract are:

1. To develop more complete information on the industrial and occupational sources of exposure to asbestos and to determine which, if any, other materials may also induce mesothelioma.

2. Evaluate epidemiologic potential of Social Security Administration files by comparing information on employment obtained through SSA Quarterly Earnings File with that available through conventional inquiries of medical providers and next-of-kin.

3. Evaluate occupational exposure patterns for a large group of mesothelioma cases compared with a suitable control group in an effort to determine the source(s) of the apparent increase in incidence.

4. Identify occupations and industries where asbestos exposure and the risk of mesothelioma is unknown.

The majority of the cases will come from population based tumor registries. In addition, cases will be selected from VA hospital pathology files. Controls for each tumor registry case will be drawn from mortality files of the appropriate state and further matched on age and sex. Controls for VA cases will be concurrent hospital deaths (excluding lung cancer patients) matched for age, sex, and race. Desired information includes histology, clinical diagnosis, and exposure history (including occupation, industry, and smoking). Interviews of next-of-kin will be done by telephone. A pathology review will be conducted in two stages: first, by a local pathologist or pathologist panel; and second, by a national panel of experts. The data collected in this study will be analyzed as a retrospective study using both pair- and group-matched control procedures. It is anticipated that the proposed study will generate a large enough series of cases (500-1,000) to allow separate analyses for histologic site.

**Industrial hygiene study of new agents.** Estimated first year award, $75,000 on a three year contract.

The purpose of this NIOSH project is to document past and present worker exposures to three substances and/or in three industries. The environmental data, industrial hygiene information and work practice and control technology procedures will be utilized to determine the extent and nature of worker exposure to the selected agents and/or in the given industries so that health effects can be assessed and appropriate epidemiologic studies planned. The substances and/or industries will be selected through the priority mechanisms established within NIOSH, which include recommendations from NIOSH surveillance activities, NIOSH health hazard evaluations, NIOSH and NTP toxicological results; OSHA and MSHA MSHA; severeity of the problem; number of workers exposed; and probability of success. NCI staff are consulted during the selection process. (This project is a followup to two previous funding efforts by NCI.)

**Dichloroethane: drug interactions.** Estimated first year award, $100,000 on a four year contract.

This NIOSH project is designed to assess the potential toxic effects of inhalation exposure to 1,2-dichloroethane (EDC) with the concomitant administration of either ethanol or disulfiram. A recent NIOSH-sponsored study demonstrated a toxic interaction between 1,2-dibromoethane, a compound similar to EDC, and disulfiram, an inhibitor of the enzyme aldehyde dehydrogenase used therapeutically in the management of alcoholism. Rats exposed to 20 ppm 1.2-dibromoethane and receiving dietary disulfiram had a significantly greater incidence of tumors of the liver, kidney, spleen and omentum as well as atrophy of the genital tract in males than animals exposed to 1,2-dibromoethane alone. A similar toxic interaction between inhaled vinul chloride and ingested ethanol has been reported by Radike et al. (1977). Sprague-Dawley rats of both sexes will be used to determine the chronic effects of exposure to inhaled EDC at the current OSHA permissible exposure limit of 50 ppm, with and without disulfiram in the diet or ethanol in the drinking water. Disulfiram levels employed will be within the range of doses utilized in the management of alcoholism in humans.

This research is a logical extension of NIOSH studies on the interaction of halogenated hydrocarbons with disulfiram or ethanol, since we have not yet established whether or not the interaction noted between 1,2-dibromoethane and disulfiram is limited to that particular compound or is representative of other, more widely used halogenated hydrocarbons such as EDC. A study of the interaction of inhaled EDC with ingested ethanol has been included because of the widespread use of alcoholic beverages and because ethanol or its metabolites could interfere with the EDC biotransformation pathway in a manner similar to that of disulfiram.

Noncompetitive renewals of contracts receiving concept approval from the Board included:

—Application of Epstein-Barr virus markers to diagnostic and prognosis of NPC and occult tumors of the nasopharynx area in the U.S. Mayo Foundation is the contractor, with proposed first year award of $261,000. Staff had asked for a two year renewal, but the Board voted for a one year renewal.

—Surveillance of effects of tobacco products. Kaiser Foundation Research Institute is the contractor, with proposed first year award of $180,000, total project cost of $540,000 over two years.

—Development of a low tar/low nicotine reference cigarette. An interagency agreement with the U.S. Dept. of Agriculture, one year at $200,000. The reference cigarette is needed to perform routine and frequent surveillance of current and new cigarettes for specific chemical constituents

–Cancer risk in x-ray technologists. Univ. of Minnesota is the contractor, with an estimated first year award of $250,000 on a three year contract.

–Conference on laboratory methods and research advances for occupational carcinogenesis studies. Courtesy Associates is the contractor, with an estimated award of $50,000.

–Mortality analysis of United Auto Workers cohorts. An interagency agreement with NIOSH, with a first year award of $75,000 on a three year contract.

–Effect of polychlorinated biphenyls on reproductive outcome. Another NIOSH interagency agreement, with a proposed first year award of $160,000 on a three year contract.

–Studies related to passive serum therapy of AKR leukemia. Duke Univ. is the contractor, with a proposed award of $189,000 on a one year contract.

–Genotoxic potential of medical device material. American Health Foundation, estimated first year award, $70,000, two years.

–Interaction between normal human diploid cells and chemical carcinogens/mutagens in vitro. Northrop Services Inc., $100,000, three years.

–Transplacental carcinogenesis and tumor promotion in nonhuman primates. Meloy Laboratories, $100,000, three years.

–Comparative carcinogenesis data base and quantitative species comparisons. Interagency agreement with the Dept. of Energy–Lawrence Berkeley Laboratory, $187,500, 15 months.

–Animal morbidity/mortality survey of colleges of veterinary medicine in North America. Assn. of Veterinary Medicine Data Program Participants Inc., $140,000, five years.

–Studies on radiation induced chromosome damage in humans. Interagency agreement with the Dept. of Energy, $73,000, three years.

–Feasibility of using state unemployment insurance records for occupational epidemiology. Dept. of Labor, $32,000, one year.

–Feasibility of coding occupation on IRS Form 1040. Internal Revenue Service, $250,000, one year.

–Study of human health consequences of polybrominated biphenyls contamination of farms in Michigan. Center for Disease Control, $165,000, three years.

–Evaluation of the transformation assay using C3H 10T½ cells for use in screening chemicals for carcinogenic potential. Arthur D. Little Inc., $298,-000, two years.

–Evaluation of the tranformation assay using C3H 10T½ cells for use in screening chemicals for carcinogenic potential. Microbiological Associates, $290,000, two years.

## STECKEL URGES AACI TO GO ON OFFENSE, INSIST ON INCREASED CORE FUNDING

Cancer center executives, who have been on the defensive for the past five years since NCI proposed drastic changes in the way centers are funded, were urged to go on the offensive by Assn. of American Cancer Institutes President Richard Steckel.

Steckel, director of the UCLA Jonsson Comprehensive Cancer Center, called upon AACI at the organization's recent meeting at Duke Univ. to "insist on a fair and objective appraisal of what the existence of centers means to the National Cancer Program as well as to the quality of research conducted within these centers' walls."

Steckel said AACI should take a "vigorous stance" to "encourage" NCI "and if necessary, the Congress" to reestablish the core grant budget at 25 percent of the total budget for R01 and P01 grants. He pointed out that that proportion existed in 1977 but since then has dwindled to 21 percent.

The core grant, Steckel argued, provides major support for R01s and P01s in addition to other core services.

AACI had already carried its message to Congress prior to Steckel's call to arms. Nathaniel Berlin, director of the Northwestern Univ. Cancer Center and chairman of AACI's Policy & Program Committee, asked the House Labor-HHS Appropriations Subcommittee to support NCI's budget request "and within those appropriations. . . recommend that the Institute provide increased financial support for its centers."

Finally, the AACI Board of Directors adopted a resolution calling on NCI "to restore funds for cancer center core grants to the levels recommended by peer review. Furthermore, in view of the complementary relationship of center core grants and research grants, for the present a target goal within the overall NCI budget should be to restore the proportionality of at least 25 percent between the dollars allotted for core grants and the combined dollar shpport allotted for R01 and P01 grants."

The core grant budget this year (FY 1981) is $70 million. That will not permit all approved renewals to be funded at recommended levels but rather on a sliding scale determined by priority scores (***The Cancer Letter,*** June 12). Those at the bottom of the scale might have to take reductions from the current level, while those at the top might get close to the recommended levels.

Steckel calculated that if the 25 percent ratio were in effect this ydar, the center core budget would be increased by about $15 million, probably enough to pay all grants at recommended levels.

"We must not lose sight of the fact that NCI recognition and funding of centers has contributed substantially to the quality of all of our activities, particularly–but not exclusively–in the research realm, and that core support has complemented the R01 and P01 research grant support that our member investigators and programs receive," Steckel said.

"The only justification for core support of research in our centers is in fact the quality and breadth of our research activities, most of which is supported in turn by R01 and P01 grants. Furthermore, increasingly over recent years the core grants have effected a transfer in salary support of staff investigators at certain centers from R01 and P01 grants to the core grant itself. In 1980, center core grants paid $9.3 million in staff investigator salaries alone, based on the peer reviewed efforts on R01 and program project grants.

"While this transfer of salary funding sources from research grants to core grants has placed an increasingly severe strain upon cancer centers' program funds, one cannot argue with the premise that the support of peer reviewed cancer investigators of the highest quality through the core grant mechanism has contributed to stability at many of our institutions and has made more NCI funds available overall for individual research grants through assumption of certain staff investigators' salaries by core grants.

"If the quality of cancer research efforts is the major issue, then core grants for centers should be counted as an enormous success. If on the other hand the overall costs of member investigator salaries charged to core grants were assumed to be the overriding issue, then the transfer of investigators' salaries from R01 and P01 grants to core grants might seem to gain great significance and one might even take the unwarranted position that cancer center core grants threatened to bankrupt the National Cancer Program.

"As always, a compromise solution seemed best, meaning a solution which would be completely satisfactory to no one. One must therefore conclude that the revised guidelines for core grants were an expectable result."

Steckel displayed a graph drawn up by Denman Hammond, director of the USC Comprehensive Cancer Center and shown to the National Cancer Advisory Board and others. It shows the trend over the past 10 years of sharply increasing funds for R01s and P01s with core support failing to keep pace.

"None of us believes that the National Cancer Institute, functioning as it has in the past two years with constant dollar budgets, has an unlimited capcity to fund centers or their member investigators. What we do insist upon is a fair and objective appraisal of what the existence of centers means to the National Cancer Program as well as to the quality of research conducted within these centers' walls. Furthermore, we expect that the NCI budget for centers core support will be formulated in an atmosphere which takes full cognizance of the complementary role that this support plays with respect to R01 and P01 research programs at our institutions, and at other institutions nationally."

Berlin told the House subcommittee, chaired by William Natcher (D.-Ky.) that the core grant is "the glue that binds the investigators in a cancer center together by providing for scientific leadership through the center director and the program leaders. It is the principal mechanism by which the center director guides his center." Berlin said, "Given the time required to construct new facilities and to organize programs, given the demonstrated ability of cancer centers to attract outstanding investigators, and given the track record of these cancer investigators in attracting their own research support, we must conclude that center core grants are critical elements for the effective functioning of cancer centers and that they have not yet reached their full development. For these reasons, we believe that continued and increasing support of the cancer centers through the core grant mechanism is highly desirable, if not essential."

## REQUEST FOR RESEARCH GRANT APPLICATIONS

### RFA NIH-NCI-DCCP-CPCB-81-2

**Title:** *Role of tumor promoters, hormones, and other cofactors in human cancer causation*

**Application receipt date:** *Dec. 1, 1981*

The Div. of Cancer Cause & Prevention of NCI invites grant applications from interested investigators for both basic and applied studies intended to provide insights and approaches to an understanding of the role of tumor promoters, hormones, and other cofactors in human cancer causation. As pertains to tumor promoters, the intended emphasis is on the use of non-phorbol agents.

Experimental tumor promotion, originally demonstrated in mouse skin, has been analogously modeled in organs of laboratory animals, notably the liver, and in culture systems. It has been widely postulated that the phenomenon of tumor promotion may also apply to people and may constitute an important consideration relative to the occurrence of cancer in humans.

Applications submitted in response to the RFA should be responsive to one or more topics selected from any one or from a combination of the following categories:

1. Development of non-phorbol tumor promotion models in experimental animals, in one or more of the following: breast, colon, lung, prostate, stomach, urinary bladder, and/or uterus. Development of cocarcinogenesis models in experimental animals in one or more of the same organs.

2. Development of non-phorbol tumor promotion models and/or cocarcinogenesis models in human and/or nonhuman cell culture and/or organ culture systems.

3. Studies to test the possibility that hormones may serve a tumor promotion role or other cofactor role in carcinogenesis in experimental animals.

Studies to test the existence of a tumor promotion role or other cofactor role with respect to one or more of the following: bile acids, saturated/unsaturated dietary fat, alcohol abuse, salt abuse, and/or free oxygen radicals.

4. Identification of non-phorbol tumor promoters and/or cocarcinogens present in the human environment. Elucidation of mechanisms of action of non-phorbol tumor promoters and/or cocarcinogens present in the human environment. Dose-response studies on non-phorbol tumor promoters in experimental animals.

5. Interdisciplinary studies involving epidemiologists and experimentalists, to test hypotheses concerning tumor promoters generated by either.

In studies involving use of one or more chemical carcinogens, agents used should be chosen from among those those which are organic compounds, are present in the human environment, and are known to be carcinogenic for humans or for experimental animals, or for both. The choice of cocarcinogen(s) and/or non-phorbol tumor promoter(s) should be from among those present in the human environment. The choice of experimental animal(s) should be from among those commonly used in carcinogenicity testing.

This RFA will use the NIH grant in aid. Responsibility for the planning, direction and execution of the proposed research will be solely that of the applicant. The total project period for applications submitted in response to this RFA should not exceed four years. Intent is to fund multiple projects, with total costs amounting to approximately $2.5 million for the first year. This funding level is dependent on the receipt of a sufficient number of applications of high scientific merit. Also, although this program is provided for in the financial plans of NCI, the award of grants pursuant to this RFA is contingent upon availability of funds for this purpose.

Applications must be responsive to this RFA, in the sense of being directed towards the attainment of the stated programmatic goals and fall within one or more of the specified research categories. If the application is judged by NCI not to be responsive, the applicant will have the opportunity of having the application considered, along with other unsolicited applications, in the next regular review cycle.

Factors considered in evaluating each response to this RFA will be:

1. Scientific merit of research approach, design, and methodoloty.

2. Research experience and competence of the principal investigator and staff to conduct the proposed studies.

3. Adequacy of time (effort) which the principal investigator and staff would devote to the proposed studies.

4. Adequacy of existing/proposed facilities and resources. Applications which specify a proposed use of cultures and specimens derived from humans need to provide assurance and details concerning the nature, source, and availability of these specimens.

5. Adequacy of practices, procedures and facilities relative to the safe handling and use of chemical carcinogens, if applicable.

Applications must be submitted on form PHS 398, the application form for research project grants, available at most institutional business offices, or may be obtained from the Div. of Research Grants, NIH. The conventional presentation in format and detail applicable to regular research grant applications should be followed, and requirements specified must be fulfilled. The words "Proposal in Response to RFA NIH-NCI-DCCP-CPCB-81-2, Role of Tumor Promoters, Hormones, and other Cofactors in Human Cancer Causation" must be typed in bold letters across the face page of the application.

The completed original application and six copies should be sent or delivered to: Div. of Research Grants, NIH, Rm. 240 Westwood Bldg., Bethesda, Md., 20205.

A copy of the applications and any inquiries should be directed to: Dr. Thaddeus J. Domanski, Chemical & Physical Carcinogenesis Branch, NCI-DCCP, Rm. 8C-29, Landow Bldg., Bethesda, Md. 20205, phone 301-496-9448.

## 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. NCI listings will show the phone number of the Contracting Officer or Contract Specialist who will respond to questions. Address requests for NCI RFPs to the individual named, the Blair Building room number shown, National Cancer Institute, 8300 Colesville Rd., Silver Spring, Md. 20910. RFP announcements from other agencies reported here will include the complete mailing address at the end of each.*

## SOURCES SOUGHT

**Title:** *NCI Cancer Communication Program support*
**Deadline for statement of capability:** *Aug. 7*

NCI is seeking small business sources capable of responding to a potential request for proposals to provide support services proposals to the Office of Cancer Communication.

OCC has a requirement for a contractor to provide technical services to support some of its numerous efforts to carry out its mandate, and to improve communication approaches and techniques for motivating both health professionals and the public to take the necessary steps which would help:

—decrease the exposure of individuals and groups of people to cancer-causing agents,

—increase the use of early cancer detection techniques, and

—increase the use of improved diagnostic, treatment, and rehabilitation programs.

This contract will require the successful firm to undertake the following scope of work:

I. Assist OCC in the development and staffing of an exhibits program for health professional audiences.

II. Provide graphic and design services needed for communications programs and materials produced by OCC.

III. Assist OCC in conducting a program to monitor, collect, and analyze research studies which can provide direction and insight into cancer communications.

IV. Support the development and promotion of information projects concerning subjects determined by NCI to be of special priority and needing long-term efforts.

V. Support the development and promotion of communications activities by cancer-concerned institutions and organizations.

VI. OCC, in cooperation with the Office of Public Affairs, HHS; the National Heart, Lung & Blood Institute; and the Office of Health Information & Health Promotion; operates a message testing service for cancer and other health related broadcast and print messages known as the Health Message Testing Services. The contractor shall assist OCC in conducting and managing the HMTS, refining HMTS methodologies, and analyzing aggregate test data.

VII. Assist OCC in conducting special public awareness programs with a national scope (e.g., hazards of asbestos exposure, DES exposure), requiring short-term intensive planning, implementation, and evaluation efforts.

VIII. Planned and structured meetings and conferences will be necessary for the optimum development of OCC communications programming as outlined in the above tasks and for exchange of information among organizations and individuals participating with OCC in its programs. OCC anticipates holding one national meeting during the contract year, in addition to approximately six smaller meetings of specific working groups assembled to consult/advise on project areas assigned under this contract.

IX. Assist OCC in the development and maintenance of a mailing list system to be used for various specialized functions related to the OCC mission.

Sources responding to this sources sought announcement must demonstrate the following minimum qualifications.

1. Staff proposed for working on this project must be located within a 50 mile radius of Bethesda, Md., and be available for frequent on site consultation (approximately three times per week) with the project officer.

2. Substantial experience in designing and conducting national health communications programs is required. This may consist of experience with nonprofit, voluntary, and/or government agencies in programs to reach public, professional, and patient audiences about major health problems.

3. Experience in working with intermediary organizations to enlist in the health information dissemination process is required. This should be with a variety of entities representing business, labor, voluntary groups, health professional organizations, minorities, trade groups, mass media, consumer organizations and special interest groups.

4. Experience in designing and conducting evaluation research, including both formative and summative evaluation of health information programs to public and patient audiences.

5. Experience in planning health communications programs, including conducting needs assessments and literature reviews, program objective, target audience and strategy selection.

6. Capability to implement a system to test public service announcements, develop normative values and conduct analyses of message performance factors.

7. Capability to provide professional exhibit services.

8. Experience and capability in the development of communications materials, including the design and creation of print, broadcast and audiovisual materials.

9. Experience and capability to provide planning and logistical support for national conferences and special working group meetings.

Other pertinent information:

Current program activities and materials used in program activities are available in the reading room in Blair Bldg. Room 327, 8300 Colesville Rd., Silver Spring, Md.

Questions should be directed to Diane Smith on 301-427-8877 or the address above.

Responses should be highly specific and include such information as dates of experience, telephone numbers of references, and employees names and telephone numbers.

Please submit two copies of capability statements and supporting documentation.

**Contract Specialist:** Diane Smith
RCB Blair Bldg. Rm. 327
301-427-8877

**The Cancer Letter** _Editor Jerry D. Boyd

Published fifty times a year by The Cancer Letter, Inc., P.O. Box 2370, Reston, Virginia 22090. Also publisher of The Clinical Cancer Letter. 