THE CANCER LETTER

Vol. 8 No. 15
April 9, 1982

Subscription $125 year North America/$150 yr elsewhere

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

WHITE HOUSE SEEKS ELIMINATION OF NCI'S BYPASS BUDGET AUTHORITY IN LEGISLATION RENEWING CANCER ACT

The Reagan Administration stunned supporters of the National Cancer Program last week with a last minute decision to attempt to

(Continued to page 2)

In Brief

STEVE CARTER ACCEPTS JOB WITH BRISTOL, PHILLIPS ELECTED NCOG CHAIRMAN; MURRAY COPELAND DIES

STEPHEN CARTER will leave his positions as director of the Northern California Cancer Program and chairman of the Northern California Oncology Group Aug. 1 to become vice president for anticancer research in the Pharmaceutical Research & Development Div. of Bristol Myers. He will be based in New York City. NCOG members have elected Theodore Phillips, chairman of the Dept. of Radiation Oncology at the Univ. of California (San Francisco) as new chairman. The NCCP Board of Directors has established a search committee for a new director. Carter will not continue as chairman of the Board of Scientific Counselors of NCI's Div. of Resources, Centers & Community Activities; "I just won't have the time," he said. . . . **MURRAY COPELAND**, director emeritus of the National Large Bowel Cancer Project, professor of surgery at M.D. Anderson Hospital, and former president of the American Cancer Society, died April 2 at a hospital in Easton, Texas. He was 79. Copeland had been ill for seven months, and retired last August as director of NLBCP, and was succeeded by his nephew, Edward Copeland. Murray Copeland was chairman of Georgetown Univ.'s oncology department from 1947-60, served on various NCI advisory groups, and in World War II commanded the largest Army general hospital in the South Pacific theater. . . . **VERNON RILEY**, chairman of the Dept. of Microbiology at Pacific Northwest Research Foundation in Seattle and a member of the Fred Hutchinson Cancer Research Center, died March 29 in Daytona Beach. He had made a presentation on his studies of the role of anxiety stress in experimental cancer at the ACS Science Writers Seminar. He collapsed in the hotel lobby after returning from a walk on the beach. Michael Glode, another seminar speaker and assistant professor of medicine at the Univ. of Colorado, worked for nearly an hour, assisted by paramedics, trying to revive Riley, who was pronounced dead at a local hospital. Authorities later said death was caused by an acute myocardial infarction. . . . **UNIV. OF NEBRASKA** has extended its search for a new director of Eppley Institute until April 30. Qualifications include, the university said, "an earned doctorate, outstanding research accomplishments, and administrative skills." Applications and nominations, with CVs and three references, should be sent to Dr. James V. Griesen, Vice Chancellor, Univ. of Nebraska Medical Center, 42nd and Dewey Ave., Omaha 68105.

HATCH RELUCTANTLY GOES ALONG ON OMB REQUEST TO KILL NCI BYPASS BUDGET

(Continued from page 1)

eliminate NCI's unique budget bypass authority in legislation renewing the National Cancer Act.

As late as March 30, the day before a hearing on the legislation by Sen. Orrin Hatch's Labor & Human Resources Committee, HHS Assistant Secretary for Health Edward Brandt had been prepared to recommend renewal of the Act with only one change –extending the period of cancer center core grants from three to five years, a change sought by the National Cancer Advisory Board and the Assn. of American Cancer Institutes.

Late that afternoon, Brandt was told by the White House that the Administration's position would be to drop the bypass. Thus Brandt's statement at the hearing included:

"In the interest of increased management efficiency, we are proposing to repeal the requirement that the NCI director submit an annual budget estimate, without change by the NIH director or the secretary, directly to the President for review and transmittal to the Congress."

Hatch agreed, without too much enthusiasm, to incorporate that recommendation into his bill, which included reauthorizations for other segments of NIH.

Congressman Henry Waxman (D.-Calif.), chairman of the House Health Subcommittee, also held a hearing on his NIH reauthorization bill last week. The section in Waxman's bill renewing the Cancer Act leaves the budget bypass intact and also adds a line item for cancer center core grant funding.

David Sundwall, an M.D. member of Hatch's committee staff who deals with health legislation, told ***The Cancer Letter*** that Hatch had included the bypass elimination in his bill only because the White House Office of Management & Budget had requested it. Hatch previously had said he would seek a "quick and clean" renewal of the Act without major modification (***The Cancer Letter,*** March 5).

Sundwall said dropping the bypass could be justified because NCI's budget had reached the point, at nearly $1 billion a year, where it should be subject to the same scrutiny and controls that apply to all other NIH budgets.

Sundwall said Hatch was "astounded" by the negative reaction he had received from Cancer Program advocates who had learned of the action. He indicated that, since Hatch does not feel that strongly about eliminating the bypass, he might be persuaded to remove it from the bill before it goes to the Senate floor. Last week's hearing did not include public witnesses, other than former Congressman Paul Rogers and a representative of the Assn. of American Medical Colleges. No further hearings are planned, Sundwall said.

The fact that Hatch was surprised by the reaction of cancer scientists and that he and his staff accept the argument that NCI's budget process should be no different than that of other NIH institutes demonstrated an unawareness of the history of and rationale for the bypass.

The Senate Panel of Consultants whose deliberations and recommendations led to the National Cancer Act of 1971 recognized that the NIH and departmental structure, in which NCI was buried as only one of an array of health agencies competing for shares of the department's budget, was the greatest single impediment to substantially increasing the effort against cancer. The Panel suggested that NCI be entirely removed from the department and set up as a separate agency. The Senate bill, approved overwhelmingly, toned that down somewhat, leaving NCI within the department but with a great degree of independence, responsible for the most part only to the President and Congress.

Paul Rogers, who was chairman of the House Health Subcommittee, would not go along. Many scientists, including a majority of those at NCI, felt it would be a mistake for the institute to leave NIH. Rogers engineered a compromise with Sen. Edward Kennedy, who was then chairman of the Senate Health Subcommittee, in which NCI would remain within NIH but would be permitted to develop its annual budget request without interference from NIH or the department. The congressional intent was clear: National Cancer Program funding would be developed in a dialog between NCI and the President (represented by OMB). NIH and the department could comment on but not change the NCI budget proposal.

(There were other elements in the compromise: Presidential appointment of the NCI director and members of the NCAB; establishing the President's Cancer Panel to create direct access to the White House; unique authorities of the NCI director to award small grants, support construction, encourage development of cancer centers, and establish cancer control programs. These are all left intact in both the Hatch and Waxman bills,)

The Nixon White House went along with the intent of Congress, for the most part. Presidential appointments were just that, with White House staff rather than the department making the recommendations, and OMB working from the bypass budget. The NCI request was always cut, but the budget increases were substantial.

OMB began to ignore the bypass budget during the Ford Administration, and the gaps between the bypass request and the White House budget as submitted to Congress became ever larger. OMB under Carter and Reagan has totally disregarded the bypass budget, and now considers only the completely separate budget developed by NIH and HHS, which

includes NCI as "just another institute."

Why worry about keeping the bypass budget if no one pays any attention to it?

In the first place, Congress in the past did use the bypass figures as justification for increasing NCI appropriations above Administration requests. Appropriations committee members could ask the NCI director what his bypass request was in particular programs or categories and would get forthright answers. Now, when they ask what his original request was, the director, as a member of the Administration and under orders about "budget busting," must refer to the watered down NIH-HHS budget. If a committee member specifically asks for the bypass figure, he will get it, but that has not been happening much in recent years.

There has been some discussion among Cancer Program advocates that, rather than eliminate the bypass authority, Congress should be considering ways to strengthen it. One way: require NCI to send copies of the bypass budget to all members of Congress, or at least to members of the two appropriations committees.

Perhaps the most important aspect of the bypass authority is that it requires NCI staff to develop an optimal budget for each intramural and extramural research and control effort being supported or considered for support by the institute. These budget recommendations are peer reviewed, by nongovernment scientific advisors (the NCAB). They answer the question, "How much money can we wisely and usefully spend in each of these efforts?"

Those answers are available for scrutiny by OMB and Congress. No other NIH institute has the statutory obligation to provide that kind of information. NCI has that authority because Congress, with the solid support of the American people as repeatedly found in public opinion surveys, decided in 1971 that scientifically sound efforts to reduce the terrible toll exacted by cancer should not be impeded by lack of money.

The American Cancer Society and others feel that elimination of the bypass budget may kill the National Cancer Program. It won't put NCI out of business, of course, but it could lead to restoring the pre-1971 status quo and threaten the momentum which has generated so much progress in the past 10 years.

Hatch considers himself solidly on the side of the National Cancer Program. Along with Waxman and Sen. Robert Packwood, he has taken on the tobacco industry in legislation to strengthen the health warnings on cigarette packages. That is a courageous position for a politician involved in a tough reelection battle, inviting as it does tobacco interests to spend some of their millions on his opponent.

The Hatch bill contains other amendments to the Cancer Act and to other segments of the Public Health Service Act in reauthorization of biomedical research. Most will be welcomed by Cancer Program advocates:

- Requires cancer research and cancer control programs to include support for projects related to "continuing care of the cancer patient and the patient's family. This addresses concern that an increasing number of cancer victims suffer tremendous psychological, economic and social problems related to their illness. Many of them seek unconventional treatments, at great cost. More understanding is needed related to how optimal care might be provided for the cancer patient during prolonged phases of illness, and terminal stages. Research is also needed regarding psychosocial support of families, medical staffs, and patients," Hatch said.
- Cancer Control programs are authorized to conduct "developmental research, in addition to current programs. This will facilitate identification, field testing, and evaluation of cancer control methods and techniques."
- Increases the ceiling of direct costs from $35,000 to $50,000 of grants which may be approved by the NCI (and the National Heart, Lung & Blood Institute) without recommendation for approval by the national advisory boards.
- Repeal of payback requirement for National Research Service Awards.

That last amendment will be greeted with enthusiasm by prospective NRSA recipients and others who are concerned abou the decreasing number of students who are going into biomedical research.

In his statement at the hearing and in his presentation of the bill to Congress, Hatch asked the Administration to reconsider cutting indirect cost support by 10 percent. Extramural program support, "both direct to researcher and indirect to universities, has become essential to most institutions of higher learning, and benefits all students of health sciences as well as the nation as a whole," he said. "For this reason, I am hopeful that at least for the immediate framework of fiscal year 1983, the Administration will reconsider its proposal to cut indirect cost support by 10 percent. I would prefer to see instead an administration reexamination of how we can assure adequate institutional capability to support research while meeting necessary cost containment objectives."

Both Hatch and Waxman included in their bills dollar authorizations for the next three fiscal years. Hatch felt that his figures demonstrate his commitment to the Cancer Program:

—1983 fiscal year, $916.8 million for research, $58.6 million for cancer control, and $22.8 million for National Research Service Awards (the last item not included in this bill but NCI's share in the NRSA reauthorization legislation). The total for NCI, $998,242,740. The White House request for NCI in

FY 1983 is $956 million.

–1984 fiscal year, 5.5 percent above the 1983 figure.

–1985 fiscal year, 5 percent above the 1984 figure.

The Waxman authorization figures are somewhat higher:

–1983, $913 million for research, $63 million for control, and $83 million for centers, a total of $1 billion, 59 million.

–1984, $1 billion, 19 million for research, $70 million for control, and $93 million for centers, totaling $1.182 billion.

–1985, $1.131 billion for research, $78 million for control, $103 million for centers, totaling $1.312 billion.

The Waxman bill does not eliminate the NRSA payback, and does include the five year center grants.

Sen. Claiborne Pell (D.-R.I.) queried NCI Director Vincent DeVita about Pell's favorite cancer topic, the International Cancer Research Data Bank. That facility was established at Pell's insistence, when he wrote into the National Cancer Act of 1971 language which requires NCI to exchange research information with scientists around the world.

Pell commented that physicians in the U.S. and scientists in other countries seem unaware of the availability of the data bank. DeVita said NCI was attempting to make its availability known, and he described the new "PDQ" system which will provide protocol information through home and office computers to physicians and pertinent information to cancer patients and their families.

Armand Hammer, chairman of the President's Cancer Panel, had been scheduled to appear at the hearing, but withdrew because of illness. In his statement prepared for the record, Hammer said that since his appointment to the Panel, "I have become increasingly aware of the high regard in which NCI is held throughout the country. I believe deeply in the mandate of the National Cancer Program as described in the National Cancer Act of 1971. The impetus given to NCI by this Act has worked, and we have just witnessed a remarkable decade of discovery .... The program is working and working well."

Waxman criticized the Administration's budget proposals for NIH in a statement opening the hearing on his bill. "Dramatic, unprecedented cutbacks are being proposed in the areas of competing grants, research training and institutional support," he said. "Under this budget we will be training fewer researchers, pursuing fewer scientific leads and placing an unwarranted restriction on institutional support. I am confident about the future of biomedical research and the promise it holds. But the serious reductions proposed by this Administration jeopardize our nation's continued progress toward developing more effective and less costly health care services for its citizens. . . . Our task is not to devise shortsighted strategies to enable NIH to make do with less but rather to chart a course for future research priorities that will enhance the mission of NIH, not only in the current fiscal year but in the decade ahead."

Congressman Claude Pepper, chairman of the House Select Committee on Aging, said at the Waxman hearing, "NIH has not fared quite as badly as other programs that have come under the budget scalpel. But the institutes must do more than survive; they must flourish if they are to fulfill their mission of finding the answers the nation and the world await."

NCAB SUBCOMMITTEE OKAYS COMPROMISE ON CHANGES IN ORGAN SITE PROGRAM

The National Cancer Advisory Board Subcommittee on Organ Site Programs agreed unanimously last week to recommend sweeping changes in the program but retaining certain elements, including a consolidated headquartaers that would oversee coordination and communication activities.

The new arrangement envisioned by the subcommittee would comply with most of the recommendations of the ad hoc committee which reviewed the four projects in the program (***The Cancer Letter***, Feb. 5). In addition, it would broaden the scope of the program by opening it to additional organ sites.

The four projects (bladder, prostate, bowel, and pancreas) have their own "off site" (that is, nongovernment) headquarters and working cadre which serve as program advisory and grant review groups.

The subcommittee's proposal, a compromise initiated by Harold Amos and NCAB Chairman Henry Pitot, would:

- Change the program's name to "Organ Site Systems."
- Abolish the four headquarters and establish a new one through a competitively awarded grant. There would be two divisions initially, one for genitourinary systems and the other for gastro-intestinal systems. Each of the divisions would have an advisory group which would provide "concept review" and program advisory functions. The headquarters, with the divisions, would provide the coordinating and communication functions now done by the individual groups.
- Basic research and epidemiology grant applications would be referred either to the NIH Div. of Research Grants for study section review as R01s or to NCI's Div. of Extramural Activities as program projects.
- Clinical research initiated within the program would be reviewed through NCI/DEA, probably by the Cancer Clinical Investigation Review Committee with cooperative agreements as the funding mechanism. The cooperative groups could assume some of

the existing and new organ specific clinical trials.

"This is a sensible and reasonable approach," Subcommittee Chairman William Powers commented when agreement was reached on the Amos-Pitot proposal. The recommendation will go to the full NCAB May 17, after another meeting of Powers' subcommittee May 16 to work out details.

Three of the four headquarters are presently undergoing review for renewal of their grants. Andrew Chiarodo, chief of NCI's Organ Sites Branch, obtained subcommittee concurrence that those grants be extended administratively until the new headquarters is established (provided the NCAB concurs with the recommendation).

Also, clinical trials presently under way in the program would be continued until they can be recompeted or renewed through the new system.

Funds now supporting the basic and clinical research grants in the program would be placed in the appropriate R01/P01 and clinical trials pools. Pitot noted that the program's grantees now, instead of competing for the $10-15 million budgeted for the four projects, would have access to the entire R01/-P01 clinical trials budget.

NTP BOARD APPROVES BIOASSAY CHANGES; INDUSTRY GROUP QUESTIONS ASSUMPTIONS

A variety of changes and modification in the National Toxicology Program's two year animal bioassays were approved at the recent meeting of the NTP Board of Scientific Counselors in Research Triangle Park, N.C.

The American Industrial Health Council, in a statement presented by Carrol Weil, of Bushy Run Laboratory, Export, Pa., had a dissent:

"Before we fiddle with peripheral questions about frequency of sacrifice, numbers of tissues to be examined, or doses to be used, it is important to examine what the results of these 500-600 experiments have shown about our underlying assumptions."

Weil, a former president of the Society of Toxicology, referred not only to NTP's some 200 bioassays, but also to the lifetime feeding studies conducted by industry, private foundations and other government agencies over the last 10 to 15 years.

The changes proposed by NTP staff included adding an interim sacrifice, at 15 or 18 months; routinely conducting histopathologic examination on fewer than the 31 organs or tissues now studied; and changing the dose schedule to four from three while increasing the number of animals per sex/species to 200 from 150.

The staff also proposed adding the inhalation route to the basic chemical disposition study now conducted on compounds selected for NTP testing, as well as funding research on two short term in vivo rodent liver carcinogenesis models, the Peraino and the Pitot. Both of these were presented as new "concepts," and as such had to be, and were, approved by the NTP Board.

There also was an interim report of NTP's experience in testing the Shimkin and Stoner strain A mouse pulmonary tumor bioassay model at two laboratories. The result was a striking lack of congruence and consistency.

In the first laboratory, 54 chemicals that had been tested "adequately" in a two year rodent bioassay were submitted for blind testing in the pulmonary tumor model.

The report, presented by NTP's R.R. Maronpot, said:

"The strain A mouse test system correctly predicted the carcinogenicity or lack thereof for 20 (37 percent) of the 54 chemicals. There were 7/16 (44 percent) fals positives and 27/38 (71 percent) false negatives.

He said, of the 27 false negative strain A test results, 14 were carcinogenic in rat and mouse in two year bioassays, eight were carcinogenic in rats only, and five were carcinogenic in mice only.

Thus far, 16 of the 54 chemicals have completed blind testing in the second laboratory, Maronpot said.

"Eleven of these 16 chemicals were found carcinogenic in rats and/or mice in conventional two year rodent bioassays. Of these 11 positive chemicals, Laboratory 2 produced 10 (91 percent) false negatives with the strain A pulmonary tumor model," he said.

Maronpot concluded:

"Failure of the strain A pulmonary tumor bioassay to give similar results to those obtained in the two year rat and mouse carcinogenesis bioassay may be a reflection of different pharmacokinetic and metabolic considerations. Species differences in metabolism could account for results from eight chemicals which were negative in strain A mice and positive only in rats in the two year bioassay.

"Strain differences in pharmacokinetics and metabolism may account for other situations in which there was a lack of congruity. The B6C3F1 mouse was used in the two year bioassay and the strain A mouse was used in the pulmonary tumor bioassay. Routes of chemical administration differed between the two bioassays. In the strain A pulmonary tumor bioassay, chemicals were given by intraperitoneal injection. In the two year bioassay, chemicals were given by gavage or in the feed. Although not determined at present, it is quite probable that the total dose of chemical given differed between the two bioassays. In addition, the duration of exposure to chemicals differed between the two bioassays.

"All of these variables could impact on chemical disposition, detoxification, and activation and account for the lack of congruity between the two bioassays.

"Another factor which might explain the apparent failure of the pulmonary tumor bioassay relates to the relative sensitivity of the two bioassays. It is entirely conceivable that the so-called false positives in the pulmonary tumor bioassay represent situations wherein the pulmonary tumor bioassay is correct in predicting carcinogenicity, while the two year bioassay is relatively insensitive. . . . In situations where an organ or tissue-specific response is obtained in the two year bioassay, the pulmonary tumor bioassay may be relatively insensitive because the target organ in the latter bioassay is the lung."

The lack of consistency between the two laboratories, Maronpot said, may be explained because two different substrains of strain A mice were used, with Lab 1 using strain A/ST and Lab 2 strain A/J. Also, Lab 2 used only male mice, while Lab 1 used both sexes, he said. He noted that Lab 1's data indicated a difference in pulmonary tumor responsiveness between males and females.

"In a certain sense it is wrong to attempt to validate any short term bioassay by simply comparing its results to those of the two year rodent carcinogenesis bioassay. The two year bioassay itself has not been definitively validated and, in some instances, the short term bioassay under investigation may be more predictive of carcinogenicity, Maronpot said.

"More appropriately, a validation exercise should take into account all that is known about how the chemicals under test are metabolized in each bioassay model, organ specificity of the carcinogenic response, the degree of positivity of the response, available genotoxicity data, whether the bioassay under validation has been optimized for maximum sensitivity, etc."

Maronpot concluded that these issues "must be rigorously addressed" before valid claims regarding the utility of the pulmonary tumor bioassay can be made.

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: *Experimental developmental, test and research work—Biochemical genetic monitoring in rodents*

Deadline for capability statements: *April 29*

The National Institutes of Environmental Health Sciences, National Toxicology Program is seeking small business sources to provide a genetic monitoring resource using biochemical methods in testing of loci involved in producing cellular enzyme or protein variants to verify the phenotypic profile of commonly utilized laboratory rodents. This is a call for capability statements for a possible small business set-aside.

The project officer will provide rats and mice of various strains or hybrids to the principal investigator for creating of a genetic profile and genetic monitoring of designated gene products in erythrocyte lysates, kidney homogenates or serum proteins. The contractor must be capable of detecting variants by either electrophoresis or immunochemical methods. In addition, frozen tissues will be received monthly for isozyme analyses.

Personnel must demonstrate experience in biochemical genetics and genetic monitoring, i.e., extent of experience and expertise of the PI specifically in genetics of rodents, analytical biochemistry, immunology and statistics.

Organizations submitting capability statements must have working laboratory facilities in operation by the date of contract award which is anticipated by Sept. 30, 1982, i.e. adequate equipment for electrophoresis and immunochemistry, frozen storage capability, animal holding capacity, quality of record keeping, and quality of report format.

Contracting Officer: Dorothy Britton
NIEHS/NTP
8300 Colesville Rd. Rm 2A01
Silver Spring, Md. 20010

SOURCES SOUGHT

Title: *Hybridoma assays and related laboratory tests*

Deadline for capability statements: *Approx. April 26*

NCI is seeking small business sources (500 employees or less) within a 35 mile radius of the NIH campus in Bethesda with the ability to carry out a project for performance of hybridoma assays and related laboratory tests. Interested organizations will perform the following tasks:

1. Routine immunoperoxidase assays

a. Cutting of tissue sections. Approximately 300 paraffin embedded tissue samples per year will be supplied by the NCI project officer. For each sample, 20 serial five micron sections will be cut via a microtome and placed on microscope slides for subsequent immunoperoxidase techniques. The number of sections cut per sample may vary as indicated by the PO.

b. Immunoperoxidase staining of tissue sections. The PO will supply monoclonal antibodies and protocols for which dilution of antibody is to be used per slide. The standard ABC and PAP immunoperoxidase methods to be used were previously described in Schlom, J. et al. (Proc. Natl. Acad. Sci. 77: 6841-6845, 1980), Wunderlich, D. et al. (Eur. J. Cancer 17: 719-730, 1981), and Hsu, S. et al. (J. Histochem. and Cytochem. 29: 577-580, 1981).

2. Cell fusions and cloning of hybridomas. Approximately three fresh samples per well (lymph nodes or spleens) from either rodent or primate species will be supplied by the PO. Standard hybridoma protocols are to be used in fusion of the lymphocytes from these samples with myeloma cell lines supplied by the PO. The protocols are as described in (a) Koprowski, H. et al., (Proc. Natl. Acad. Sci. 75: 3405-3409, 1978), and (b) Wunderlich, D. et al. (Eur. J. Cancer 17: 719-730, 1981) and may be slightly modified by the PO. Approximately 100 microtiter wells will be seeded post-fusion (total of approximately 300 per week), and passaged using standard hybridoma techniques (see above references). Following assay of supernate culture fluids for approximate antibody production (see next section), approximately 10 individual cultures will be specified by the PO for double cloning using standard endpoint dilution techniques as described in Wunderlich, D. et al. (Eur. J. Cancer 17: 719-730, 1981).

3. Routine assays for monoclonal antibodies

Supernatant fluids of cloned and uncloned cultures as designated by the PO will be assayed for appropriate antibodies using protocols and reagents (e.g., cell extracts, viral extracts, second antibodies) furnished by the PO. The methodology for the solid phase RIAs has been described in detail in Teramoto, Y. et al. (Cancer Res. 41: 1451-1459, 1981) and Wunderlich as above.

4. Delivery of samples and records to investigators

Provide transportation of samples to and from NCI investigators. One to two trips may be required per day.

Resumes of experience and capability must cover:

1. The name, professional qualifications and experience of the key personnel and adequate documentation that they have experience working on projects of a similar nature, including the generation of interspecies hybridomas and assay of subsequent immunoglobulins produced.

2. Availability and description of facilities. Minimum requirements are that proposers shall supply necessary facilities and equipment to perform the workscope, including laminar flow hoods and adequate tissue culture facilities, and access to an iodination facility.

3. Knowledge of the organizational and administrative procedures necessary for the operation of a multifacted hybridoma and immunology facility and providing of related technical services.

Interested organizations qualifying as small businesses are invited to submit a resume of experience and capability based on the information provided above. NCI will evaluate qualification statements and will issue an RFP to those firms judged to be qualified.

Responses should reference synopsis No. 62 and should be submitted in 20 copies to:

Contracting Officer: Elizabeth Osinski
RCB, Blair Bldg. Rm. 117
301-427-8888

Project No. NCI-CM-37535-W

Title: *Prime contractor for performance of protocol toxicology studies (small business set aside)*

Deadline for resume of experience & capabilities: *April 19*

The Toxicology Branch, Developmental Therapeutics Program, Div. of Cancer Treatment, is seeking an organization to serve as prime contractor and assume responsibility for the development of toxicologic data suitable for filing with the Food & Drug Administration as part of investigational new drug applications.

Such a prime contractor must have both technical management and laboratory capabilities. Technical management capabilities are essential to select subcontractors to conduct preclinical toxicology protocol studies of new oncologic agents, to supervise, monitor and analyze the results of such studies and to develop new protocols for the toxicologic evaluation of various types of agents intended for clinical use in cancer patients.

The current protocol for the toxicologic testing of cytotoxic agents utilizes mice and dogs on a single dose schedule and a daily times five schedule. Modifications to the existing protocols are necessary when the mouse cannot be used because of the unusual nature (limited solubility, instability, etc.) of various oncolytic agents. This is especially important since the mouse is the primary animal species used for the prediction of safe human starting doses of oncolytic agents being developed for phase 1 trials and since the data developed in the mouse studies serve as the basis for testing done in the dog. Therefore, laboratory facilities that are in full compliance with the Good Laboratory Practice Regulations are necessary for the rapid evaluation of proposed modifications to the existing protocols when these situations arise.

Laboratory capability is also essential so that the program director of the prime contractor and technical subcontractor monitors can periodically spend time in the laboratory in order to maintain currentness in the rapidly developing field of toxicology and to be fully cognizant of the impact of the FDA Good Laboratory Practice Regulations.

The prime contract is divided into four tasks for ease of monitoring by the government and because the nature of the work falls naturally into distinct categories. Task 1 is designed to cover protocol studies of oncolytic agents, radiosensitizers, biological modifiers, radioprotectors, etc. Protocols for cytotoxic agents have been developed to the stage where they are documented and workable for many of the

drugs. However, insoluble drugs and drugs which are relatively nontoxic in the mouse at the maximum achievable dose demand development of new methodologies to elucidate the toxicities inherent in these drugs. Protocols for the testing of radiosensitizer drugs are also developed and tested. Protocols for biological modifiers have have not been developed and will require a literature search, protocol development and laboratory validation before they will reach a stage where the laboratory work can be subcontracted.

Task 2 is any part of the protocol study used in Task 1 or any portion of the earlier published protocol (1973, Prieur et al.) and is used to evaluate agents that have had previous clinical use, preclinical study, etc., but where existing data are not considered adequate for investigational new drug applications.

Task 3 covers organ specific toxicity testing, in vitro and in vivo, from development of protocols to the actual inhouse testing of the protocols to disclose any potential problems that might occur prior to being sent out to subcontractors for implementation.

Task 4 covers cost management, subcontractor management, quality assurance monitoring, protocol development for each specific agent (as required by the GLP regulations), computerization of toxicology protocols and results, etc.

A well equipped laboratory component is mandatory for adequate assessment of the validity of the data obtained from all studies. Experience in the toxicologic evaluation of drugs intended for human use is an important aspect of any potential offeror which may propose for the toxicology prime contract. Evidence of such experience should be reflected in the curriculum vitae of the principal investigator, who should be trained in toxicology/pharmacology at the PhD or equivalent level at an accredited school, scientists and technical monitors employed by such a small business and should be supplied to the government as part of a response to this solicitation. Additionally the offeror must supply documentation demonstrating its corporate stability and the management experiences of the actual staff involved in the conduct of the contract.

Laboratory facilities and equipment must be described in sufficient detail to assess their capabilities and capacity. The prime contractor office facility must be within 35 miles of the NIH reservation to permit the proper level and frequency of interaction between the contractor, the Toxicology Branch and various other segments of the Div. of Cancer Treatment.

Since resumes will be used to assist in making a determination as to whether or not a small business set-aside should be made, only small business concerns should submit their resumes. Offerors are to provide a statement certifying their status as a small business. Twenty copies of the resume of experience and capabilities must be submitted.

Contracting Officer: Clyde Williams
RCB, Blair Bldg. Rm. 228
301-427-8737

RFP NCI-CP-31000-78

Title: *Animal holding facility and attendant services for various laboratory animals*
Deadline: *Approximately May 27*

NCI has a requirement for a small business organization (500 employees or less) to maintain an animal holding and breeding facility within a 50 mile radius of the NIH campus in Bethesda. This procurement is a 100 percent small business set-aside.

This facility must be capable of holding up to 5,700 standard inbred mice; 1,180 nude mice; 275 rats; 90 rabbits and 10 guinea pigs. Also, the contractor must be able to breed inbred strains of mice. In addition, the organization must provide related animal services, e.g., inoculations, fluid collection (milk, sera, urine), monitoring of experimental animals for disease, tumor removal, necropsy, pathology and autopsy.

Contracting Officer: Elizabeth Osinski
RCB, Blair Bldg. Rm. 117
301-427-8888

RFP 200-82-2520

Title: *In vitro tests for workplace cocarcinogens*
Deadline: *April 30*

The National Institute for Occupational Safety & Health proposes to procure services to conduct in vitro tests for workplace cocarcinogens. Three laboratories will be selected to study the effects of selected chemicals (cocarcinogens, both positive and negative) on inhibitions of metabolic cooperation in Chinese hamsters V-79 cells. The protocol, statistical analysis and chemicals to be employed will be supplied by NIOSH. It is anticipated that multiple awards will be made and that cost-reimbursement type contracts will result from this solicitation for a period of 14 months.

Contracting Officer: R.E. Heil
PGO, Centers for Disease Control, NIOSH
255 E. Paces Ferry Rd. N.E.
Atlanta, Ga. 30305

The Cancer Letter _Editor Jerry D. Boyd
Published forty-eight times a year by The Cancer Letter, Inc., P.O. Box 2370, Reston, Virginia 22090. Also publisher of The Clinical Cancer Letter.