THE CANCER LETTER

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"SLOPPY WORK" MAY INVALIDATE METHYLENE CHLORIDE STUDY; CONTRACTOR HINTS NTP PRESSURED BY INDUSTRY

NCI's problems with the Carcinogensis Testing Program in the 1970s led directly to establishment of the National Toxicology Program which absorbed carcinogenesis testing, along with other selected toxicity testing

(Continued to page 2)

In Brief

HHS DRAGS FEET, NCI CONSIDERING CONTRACT TO REVIEW CANCER RESEARCH FACILITY NEEDS

HHS IS DRAGGING its feet on the survey of cancer research facility needs requested by the President's Cancer Panel. The department previously had agreed to do the survey when Panel Chairman Armand Hammer, disturbed by the hatchet job done by the White House every year on NCI's requests for construction grant funds, said he would take up the issue with President Reagan if someone would supply him with an updated and unbiased estimate of construction needs. It's been five years since the National Cancer Advisory Board directed NCI to allocate at least $25 million a year for construction grants; the bypass budget request each year has been slashed by the Office of Management & Budget, this year to $1 million. With HHS apparently backing down on its offer to do the survey, Research Facilities Branch Chief Donald Fox has decided to ask the Board of Scientific Counselors of the Div. of Resources, Centers & Community Activities for concept approval of a contract to do the job. It will go to the DRCCA Board next week. Meanwhile, Fox has been swamped with construction grant applications. . . .

ROBERT GALLO, chief of NCI's Laboratory of Tumor Cell Biology, is winner of the 1983 Griffuel Prize. The prestigious award, by the French Assn. for Development of Research on Cancer, was made in recognition of Gallo's discovery of the human T-cell leukemia virus. It includes a hefty cash prize; when Vincent DeVita won it in 1983, it was worth $41,000. . . LUTHER BRADY, chairman of the Dept. of Radiation Therapy and Nuclear Medicine at Hahnemann Univ. and chairman of the Radiation Therapy Oncology Group, has received the American College of Radiology's Gold Medal for his "outstanding achievements in radiology and radiation oncology." It was only the third time since ACR started awarding the Gold Medal in 1927 that it went to a radiation oncologist.

NTP AUDIT FINDS SERIOUS PROBLEMS WITH BIOASSAYS, STUDIES IN DOUBT

(Continued from page 1)

efforts within the Dept. of Health & Human Services and housed within the National Institute of Environmental Health Sciences. NIEHS and NTP Director David Rall and his staff were expected to use the lessons learned in NCI's stewardship of carcinogenesis bioassays, and the new science that had evolved during the past decade, to shape up and modernize the program.

NTP in about four years has gone a long way toward improving the science in carcinogenesis testing and in smoothing out the wrinkles in the operation. But recently, Rall and his staff found that some of the mistakes of the past are still around, and the consequences are still rolling in.

Rall and NTP Acting Deputy Director Gene McConnell reported to the program's Board of Scientific Counselors that deficiencies uncovered in recent audits of one NTP contractor threaten to invalidate the very important bioassay of methylene chloride and perhaps others. In fact, McConnell said, every one of the studies of 12 to 15 compounds carried out by that contractor "has to be called into question."

The contractor is Gulf South Research Institute, a not for profit organization with three locations in Louisiana. The contracts now being questioned were awarded to GSRI from 1977 to 1982.

Before carcinogenesis testing was switched to NTP, the firm Tracor-Jitco had the prime contract from NCI to run the program and was supposed to monitor the efforts of subcontractors like GSRI. However, McConnell said, as the Tracor-Jitco contract was being phased out and NTP began taking over the monitoring in 1981, NTP discovered that very little monitoring had been done.

"Starting in November, 1981, NTP really got into monitoring those studies in some detail," McConnell said. "We discovered we had a significant problem at Gulf South." The problems included poor quality slides, inadequate histopathology, misdosing of animals, and "extremely poor observation of animals in my opinion," he said.

Attempts to correct the problems met with some success, McConnell reported, "but when we corrected one thing, another problem would come up." NTP finally decided last March to remove all pathology from GSRI. "That's sitting with us now. We plan to bring up each study, look at it, try to clean it up, and bring it to the Board to determine if the problems are bad enough to affect the results."

Verne Schwetz of NTP staff said that the Board could decide either to not report the data from studies deemed so deficient that they are compromised, or it could report the data but with caveats, with the results of the audit included. The audit reports will be included in any case.

"How about not paying them?" Board member Jerry Hook asked. "We're stuffing money down a rathole and not getting anything for it."

"Our contracts people are talking to them," Rall said. "We had assumed Tracor-Jitco was doing it. Gulf South is in full compliance with GLP (Good Laboratory Practices). GLP was designed to detect fraud, and that is not the case here. I think this can be easily corrected. It's just sloppy work."

"When was the last Gulf South study started?" Hook asked.

"Fourteen months ago," McConnell said.

"After you recognized you had a problem?" Hook was incredulous.

"It was not recognized then as a severe problem," Rall said.

"Are we still giving them money?" Hook asked.

"Yes," McConnell replied. "It is a best effort contract, and there is nothing we can do. We're between a rock and a hard place. They are 14 months into the study, and we have to let it go to completion. But we're not giving them money for pathology."

"NTP is the premiere outfit in government for testing," Hook insisted. "We should set standards. We should come down hard on them."

"Sometimes you can get money back, but our lawyers say it's not worth the expense to try it," Rall said.

Board member James Swenberg pointed out that errors in the methylene chloride study had already been pointed out by some critics, that the report include some "erroneous assumptions."

"You're absolutely right," McConnell said.

Jim Clinton, GSRI president, admitted in a telephone interview with *The Cancer Letter* that his organization had not performed as well as he would have liked. But he inferred that pressure by industry may have influenced NTP's actions.

"I don't think Dr. Rall in any way is doing something wrong in deciding to withdraw the study," Clinton said. "But methylene chloride

carries considerable economic weight. Why did it take three years to reach this decision? It's been out there, it's been through peer review, and accepted by peer review. It was not until after industry had challenged the study that our problems became an issue. I don't think there is any question that the economic impact had a role in it."

Clinton insisted that a "good case can be made that adequate data are there to support the findings (of methylene chloride's carcinogenicity). I hope that an independent audit will confirm that."

GSRI is disillusioned with the business of toxicity testing as well as with its own performance, Clinton indicated.

"We've been looking at our performance in the bioassay program. We have some questions. We're not convinced that the quality of our work was what we would have had it be. . . . But while we've been singled out for the dubious honor of all this attention, I see they are going to audit all labs doing bioassays. GAO (U.S. General Accounting Office) did an audit of us in 1979 and found that conditions at GSRI were good, and that was not the case with other labs GAO audited then. If we were better than others then, it's obvious there may be some questions about others now."

Clinton said that a large part of the problem with methylene chloride has been "state of the art changes. GLP was just coming in then, and there were a large number of changes in the program. There were hundreds of contract changes during the course of the studies. The studies are enormously complex. If you want to question the findings of any study, at any lab, you can find problems without looking too hard."

Clinton said his board of directors has been looking at the situation and is "leaning more to the direction that we can't afford to be involved in this kind of study. You can't win. If the compound is politically hot, your work will be challenged and will be called sloppy."

NTP's audit procedures cover eight major aspects of a study:

1. Administrative information—the protocol and correspondence.

2. Pretest animal data—animal receipt (shipping tags), health at arrival, randomization to cages, randomization to groups, racks placed in rooms, quarantine observations, health when placed on study and release to study, animal identification (individual and group), and replacement of lost eartags.

3. Chemistry information—Chemical receipt (lots and when used), total amount used in dose prep vs. bulk received, total amount, chemical analysis and reanalysis, method of analysis (standard procedures and validation, analysis of test aliquots (animal room), referee samples, stability and homogeneity data, and corn oil analyses—peroxides.

4. Dose preparation and administration—Directions for preparation of each batch of solution /feed, notation of animal dosage, amount of chemical-vehicle mixture prepared vs. amount required to dose animals.

5. Environmental conditions (temperature, relative humidity)—Equipment used, frequency of observation, mean conditions, fluctuations—range and duration.

6. In-life observations—Body weights—N and means, unexpected trends; clinical signs, continuity through necropsy; mortality records—AM/PM room checks, body weight records IADRs, moribund sacrifices vs. animals found dead.

7. Pathology—Wet tissue bag count, slide/block match, IADR necropsy observations vs. histopathology findings, wet tissue bags—ear tag or ear punch vs. label, group identification vs. label, uncut lesions visible grossly; causes of death—accident vs. chemical induced vs. natural.

8. Report—Protocol vs. methods and materials, raw data vs. report—clinical signs, chemistry, mortality, tumor pathology.

McConnell reported briefly on seven audits being carried out now or recently completed at six labs:

* A gavage satudy on tris (2-ethylhexyl) phosphate by Litton Bionetics. "Very well done," McConnell said.

* An inhalation study on 1,3 butadiene by Battelle Northwest. "There were some problems—three chemicals in one room, chamber doors left open, problems with cages and animals in one chamber on the floor."

* A gavage study of benzene by Battelle Columbus. "Minimal problems. This was done very well considering the size of the study."

* A feed study of HC blue 1 by Southern Research Institute. "There were no major problems."

* Currently being audited are a gavage study of chlorodibromomethane by Mason, a gavage study of benzyl acetate by Southern,

and a gavage study of methyl chloroform by GSRI.

McConnell said NTP plans to audit all studies at critical stages in-life, and will audit studies prior to reporting. The audit team includes NTP scientists and contract consultants.

To date, the bioassay contracts awarded to GSRI either by NCI or NTP total approximately $5.5 million.

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The NTP Board of Scientific Counselors Peer Review Panel will meet Oct. 27-28 at Research Triangle Park to review bioassay reports. Among them will be reports on two important chemicals—the first American study of benzene, and 1,3 liutadiene, a compound to which rubber workers are widely exposed.

NCAB ASKS EARLIER REVIEW OF NEW ORGAN SYSTEMS COORDINATING CENTER

Only three applications for the new Organ Systems Program Coordinating Center were submitted despite NCI's efforts to drum up more by extending the deadline and personal calls from Director Vincent DeVita.

DeVita told the National Cancer Advisory Board last week that he had struck out in attempts to stimulate more applications. "I called several people who told me they wouldn't touch it with a 10 foot pole. But we did receive three excellent applications."

The coordinating center grant will replace the four headquarters grants which have supported the prostate, bladder, bowel, and pancreas programs for the past 10 years, and will add breast as a fifth organ system, assuming much of the work performed in the past by the Breast Cancer Task Force. The first four involved not only overview and updates on research in their respective areas but also the review of grants submitted specifically for the programs with earmarked NCI funds. The review has all been returned to NCI and NIH, the amount of money committed is less specific, and the coordinating center's role will be one of monitoring research and recommending new studies for concept consideration by the appropriate NCI board of scientific counselors.

The NCAB, which initiated the original organ site programs and defended them through the years against a host of critics, continues to maintain a keen interest in the new Organ Systems Programs. The Board's Organ Systems Programs Committee met last week and recommended that the NCAB once again endorse the concept of a strong OSP; that "interested scientists be reassured of continued NCI commitment for the program; and that we urge and recommend that consistent with NCI managerial practices there be expeditious review and recommendation of the Organ System Coordinating Center."

The full Board approved the recommendations without dissent.

The schedule for review of the coordinating center applications calls for submission to the NCAB at its meeting in May, 1984. William Powers, chairman of the Board's committee, asked that the review be moved up so that it could go to the Board at its meeting Jan. 31.

"We'll do the best we can," DeVita said.

"Would it be possible to speed things up by having reverse site visits?" Powers asked.

"I don't see why not," DeVita said.

Board member Rose Kushner expressed concern over maintaining NCI's commitment, noting that some organ systems RO1 grant applications "went into the general RO1 pool because they were not specifically marked organ systems." She suggested that organ systems applicants be asked to submit duplicate copies of their applications to NCI staff so they could be tracked by staff.

Andrew Chiarodo, chief of the Organ Systems Branch, insisted that "we do know when the grants come in and are tracking them."

Powers initiated a discussion on surgical oncology after noting, he said, that in the Board's review of grants during this meeting, surgical oncology grants did not seem to fare very well.

Div. of Cancer Treatment Director Bruce Chabner described efforts in his division, with the leadership of his Board of Scientific Counselors, to develop initiatives in surgical oncology. He noted that his Board has a committee for surgical oncology chaired now by Samuel Wells, chairman of the Dept. of Surgery at Washington Univ., "one of the major figures in cancer surgery."

At Powers' suggestion that the NCAB should have an ad hoc committee on surgical oncology, Chabner said, "We all recognize the problem and we are working to build up a cadre of surgical oncology scientists. Our efforts are directed at the major problem of getting more young people into surgical oncology, to help them get their basic science training so they can compete for grants." He said his Board's committee would endeavor to keep the NCAB advised on the program, but that "I don't think it would be productive to have a

parallel NCAB committee at this time."

After hearing Chabner's description of various DCT initiatives in surgical oncology and the makeup of the NIH Experimental Therapy study section which now has three surgeons among its 12 members, Board members appeared inclined to go along with him. Only Geza Jako continued to argue for an NCAB committee, "to make recommendations to the Board of Scientific Counselors, and to hold workshops for new approaches in surgical oncology."

Board Chairman Tim Lee Carter ended the discussion. "I hereby establish a committee on surgical oncology, to hold hearings and to make recommendations," Carter said. I appoint Dr. (Ed) Calhoon chairman, and any member of the Board can serve on it."

Janet Rowley suggested an alternative would be to encourage NCAB members to work with the DCT Board committee. "We should work together as a unit rather than as two separate groups," Rowley said.

"I've gone over this at great length," Carter said, "and this is the decision I have made."

The gavel came down and there was no further dissent.

For the first time since the early days of the National Cancer Program, the NCAB's Planning & Budget Committee had some happy news to report—the House and Senate figures for NCI's FY 1984 appropriations. The House added $81 million to the President's request, the Senate $99 million. But the committee, reflecting DeVita's concerns, still had something to complain about.

Both houses agreed that much of the increase would be earmarked to pay all grants at or near their recommended levels, ruling out the practice NCI has employed the last couple of years to "stretch" grant dollars over more grants by funding all of them at somewhat less than levels approved by study sections. DeVita decried the limit this places on the Institute's flexibility in keeping more laboratories operating, and he has pointed out that most scientists expressing opinions on the issue favor stretching at the expense of full funding.

The final figure which will be agreed upon in conference is likely to be close to the amount requested in the bypass budget of $1.074 billion, which raises the question of whether the bypass request was too low. If that amount of money, supposedly the optimal amount NCI could wisely spend, is not enough to pay grants at recommended levels and still fund an appropriate number, then obviously it was too low. It was the first of the "reasonable" bypass budgets which really did not ask for the optimal amount but rather for a figure closer to what NCI realistically might get. In view of the recent level budgets coming out of the White House and Congress for NCI, $1.074 billion (written in the bypass budget for FY 1984 in the spring of 1982) seemed like more than it actually turned out to be.

If DeVita succeeds in getting Congress to give him some flexibility in stretching grant dollars, the next question will be just what is an appropriate number of grants to fund? NCI has been paying about 30-33 percent of approved competing grants, at priority score paylines of 175-185. The percentage is down about 10 points under what it was when money was easier, in the early 1970s, but the number of grants approved has increased significantly. Likewise, the payline is well under the 225-250 in the happier days, but that is due to the switch from using "normalized" scores to raw scores and to the compression of scores by study sections looking out for the interests of their respective specialties.

The House-Senate conference was not held prior to Congress' October recess, but may be held as early as next week. A quick agreement and early submission of the bill to the President is forecast, and he probably will sign it. Until then, NCI and the rest of HHS are operating on a continuing resolution which is in effect until Nov. 15 or the appropriation bill is signed, whichever comes first.

NCI CONTRACT AWARDS

TITLE: Epidemiologic study of black/white differences in cancer patient survival experience—data coordinating center
CONTRACTOR: Westat Inc., Rockville, Md., $993,585.

TITLE: Assessment of the factors affecting critical cancer research findings
CONTRACTOR: Computer Horizons Inc., Cherry Hill, N.J., $345,052.

TITLE: Holding facility for small laboratory animals
CONTRACTOR: Litton Bionetics, $347,332.

TITLE: Technical writing, publication distribution and telephone answering services in response to cancer related inquiries
CONTRACTOR: Biospherics Inc., $404,039.

DCT BOARD OKs CONCEPT OF FIVE RECOMPETITIONS WORTH $6.5 MILLION

The Board of Scientific Counselors of NCI's Div. of Cancer Treatment gave concept approval at its fall meeting to the recompetition of five contract supported projects totaling $6.5 million in first year awards, including the multi-institution phase I and phase II/III clinical testing of new anticancer drugs.

New drug development: Phase I and phase II/III studies of new anticancer agents. This will be recompeted for multiple awards. Estimated awards total $3 million a year for five years. Present contractors are Johns Hopkins Univ., Univ. of Maryland, Mayo Foundation, Memorial Hospital, Ohio State Univ., Univ. of Texas Health Science Center, Univ. of Texas/M.D. Anderson Hospital, Univ. of Vermont, Wayne State Univ., and Univ. of Wisconsin. Phase II/III contractors are Memorial Hospital, Univ. of Michigan, UT/M.D. Anderson, and Wayne State Univ. Staff narrative describing the program (with some editing to conserve space):

We plan to continue NCI's program in clinical new drug development by combining the phase I and phase II/III projects into a single project plan; to this we will also add a pharmacokinetics project. The specific goals of the contract will be: (1) to define the acute toxicities of new anticancer agents in patients with advanced cancer; (2) to define the dose of each agent which can be safely given in subsequent phase II studies of drug activity; (3) to provide information on the pharmacologic characteristics (absorption, distribution, metabolism, and elimination) of selected antitumor agents; (4) to explore the potential uses of pharmacokinetic analysis for optimizing dose escalation procedures in a phase I trial; (5) to determine the spectrum of activity of new agents across a variety of human cancers; and (6) to establish the role of a new compound, alone or in combination, in selected human cancers compared to standard therapy.

The project plan will be divided into two parts. For part 1, the program staff anticipates the award of six to eight contracts at a total estimated cost of $2,250,000 for phase I clinical trials and pharmacokinetics. Each contractor will be expected to perform at least three phase I trials per year with an average of 25 to 30 patients per trial. Contractors will be selected on the basis of their expertise and sophistication in dealing with the following essential issues in the design and conduct of phase I trials: (1) eligibility criteria; (2) selection of the starting dose, dose escalation procedure, and schedule of treatment; (3) numbers of patients to be entered at each dose level; (4) criteria for the definition of a maximum tolerated dose; (5) criteria of dose limiting toxicity for the major organ systems; and (6) definition of an evaluable drug course.

Each contractor will perform at least two pharmacokinetics studies per year on the compounds evaluated in the phase I trials. Contractors will be selected on the basis of their expertise in: (1) analytical methodology; (2) collecting and analyzing parent compound and metabolites in appropriate biological fluids; (3) determining characteristics of drug distribution, metabolism and elimination from pharmacokinetic data; and (4) analyzing pharmacokinetic behavior as a function of drug schedule and disturbances in organ function.

Part 2, phase II/III clinical trials. Program staff anticipates the award of three contracts for these efforts at a total estimated cost of $750,000 the first year. Our current plans are that 10 percent of these funds will be devoted to phase III trials and the rest to phase II trials.

In all categories of disease, patients to be selected for trial will be those with excellent performance status and the minimum amount of prior treatment that is consistent with ethical medical practice. (a) For diseases which currently lack effective systemic therapy (carcinomas of the large bowel, kidney, liver, and pancreas, as well as malignant melanoma) entry of patients with no prior chemotherapy will be required. (b) For diseases in which partially effective but noncurative systemic therapy is available (carcinomas of the head and neck, cervix, esophagus, prostate, bladder, stomach and non-small cell lung) entry of patients with no prior therapy will also be required. In certain situations which present legitimate clinical dilemmas (extensive small cell lung cancer, disseminated indolent lymphomas, and breast cancer) patients who have received prior treatment with no more than one regimen may be entered on study, provided that the performance status is high. (c) For diseases which are potentially curable with systemic treatment (the acute leukemias, diffuse non-Hodgkins lymphomas, Hodgkins disease, testicular cancer, limited small cell lung cancer, ovarian cancer) patients having the minimum extent of prior treatment compatible with current ethical standards of care will be required.

For any proposed trial, offerors will be required to document their ability to accrue the required number of patients within a reasonable time period. For relatively rare tumors (e.g. thyroid cancer, apudomas, mesothelioma, salivary gland cancer) intercontract trials will be encouraged. Studies of regional drug administration will be permitted, where appropriate, in those centers having demonstrated expertise with the necessary techniques of drug delivery and pharmacology. Similarly, exploration of the upper end of the dose response curve, using appropriate approaches for protection of normal tissues, may be permitted in suitable circumstances.

Randomized phase III trials to identify the comparative efficacy of a new agent vs. standard treatment or the possible contribution of a new agent in combination with standard treatment are more suitably performed by the clinical cooperative groups. Under exceptional circumstances, however, such trials may be permitted within the scope of the present contract provided the offeror can demonstrate convincingly the ability to accrue appropriate numbers of patients to answer the question posed within reasonable statistical power. Unrandomized studies of the activities of combinations involving investigational agents will not be permitted in the absence of an overall plan by the offeror for the development of the drug in a given disease; such plans will be developed jointly by the offeror and NCI staff.

Rodent production center. Estimated annual

award, $1.7 million. Present contractors are Charles River Breeding Labs, Simonsen Labs, Southern Animal Farms, and Microbiological Associates. Awards will be for three years. The narrative:

Historically, these contracts have been part of a tightly integrated program of animal production directed by the Div. of Cancer Treatment. Primary genetic center contractors receive initial and replacement breeders from the NIH repository. These animals were then cesarian rederived into the germfree state after which they received a designated flora of six nonpathogenic organisms. (This flora is necessary in order to maintain an acceptable reproductive capability). Foundation colonies of these inbred strains were expanded and maintained in isolator cages at production levels large enough to support breeder replacements for barrier maintained pedigreed expansion colonies at these same primary genetic centers. Offspring from the pedigreed expansion colonies were used to support one random mating for each inbred strain at the rodent production centers which are proposed here for recompetition. Cost savings were realized because of decreased labor (no pedigree charts, etc.) and a somewhat cheaper price for maintaining production cages. However, as the demand for animals completely free of known pathogens has increased from both DCT investigative contracts and other users, it has become necessary to reassess DCT's animal production system. Currently, the number of producers who can meet our highest criteria from an animal health viewpoint is limited, and confined to primary genetic center producers. Consequently, the number of rodent production center contracts has been reduced from seven to four since the last competition. Production has been primarily increased at the remaining centers by recently adopted breeding system where two females are placed in each breeding cage (one male). This system has worked with a number of inbred strains and has reduced cost per cage at rodent production centers significantly. The quality of animal production has improved providing an animal with an excellent health profile, and production numbers have been increased to meet the demands of the program.

DCT intends to recompete at a level of caging necessary to support the program in FY 1985. However, as the demand for highest quality production increases, further modifications will be made to accommodate needs.

Hybrid contracts. Estimated annual awards total $740,000, for three years. Present contractors are Taconic Farm, Southern Animal Farms, King Animal Labs, Murphy Breeding Labs, Simonsen Labs, and Engle Laboratory Animals. The narrative:

These contracts have been traditionally awarded on a fixed price basis, i.e. from those offerors which are determined to be technically acceptable, awards are made to the lowest bidders. This system has certain advantages, including a somewhat lower purchase price and a small business set aside capability. However, there are several disadvantages associated with this system, including:

1. A higher cost of contract administration to DCT. Current plans are to move the administration of these contracts back to NCI's Research Contracts Branch, which will eliminate this problem.

2. A lack of flexibility. As program needs change, e.g. the recent shift from RDF1 to B6C3F1 mouse required to accommodate the M5076 ovarian tumor, it is difficult to make adjustments to these contracts.

3. Quality of production with these contractors is satisfactory but they have difficulty keeping pace with the highest quality demands of DCT, NCI, and other users. Production has shifted to rodent production centers (increased flexibility) and primary genetic centers (increased quality and flexibility). Over the last four years, the number of hybrid contracts has decreased from 11 to six and the number of mice per contractor from 6,000 to 2,000 on a weekly basis. Thus, total production has decreased from 66,000 to 12,000 per week with a compensating shift from hybrid to primary genetic and rodent production contractors.

DCT plans to recompete the contracts at a level required to meet the needs of the screening program in FY 1985. Further adjustments will be made to meet investigator needs from both a quality and quantity production viewpoint.

Operation and maintenance of the Developmental Therapeutics Program biological data processing system. Estimated annual award, $960,000, five years. Present contractor is VSE Corp. The narrative:

The Information Technology Branch manages the contract which provides the data processing services required for the screening data from candidate antitumor agents. Processed information includes in vivo, in vitro, and colony forming assay data. The data processing contractor provides summarized antitumor data to suppliers of compounds tested, the laboratories which performed the tests, the staff of DTP and DTP archives. This is done in the form of screening data summaries, screening experiment analysis reports, and management reports such as the production report (number of tests) and the quarterly control performance report (quality control). Special reports are created upon demand. Main task areas of the contract and the percent they represent are: (a) production, including data input and data distribution 46%; (b) program maintenance 17%; (c) development of data processing systems for new screens 9%; (d) materials 8%; (e) documentation 8%; (f) management 7%; and (g) statistics (5%).

The data processing contractor collects and processes raw data supplied by the screening contractors and submits this product to the NIH Div. of Computer Research & Technology which holds our biological file. Updates of the biology master files occur biweekly. The contractor documents all programs designed, written and operated by them; they also supply DCRT with documentation for the programs run there. Other support provided includes the production of data for statistical evaluation of test systems, the evaluation of test system parameters, and management reports which DTP branches use to measure their requirements and productivity. Assistance is provided to ITB's new Drug Information System development effort (integrated structural and biological files) in the form of extensive collaboration with the DIS contractor in restructuring the biology file for input into the DIS. Significant modification of current programs is required to accomplish this task, e.g., since the biology master file contains proprietary information, programs allowing access only to

the nonproprietary data must be written for certain user classes.

This is the sole contract which supplies biological data to compound suppliers and staff. As the results of compound activity or inactivity are reported, suppliers, contractors and NCI make decisions concerning the direction of new synthesis work or compound acquisition. The biological data are the single most important factor in the selection of agents for clinical trial and access to this information is a necessity.

DTP plans to continue the project with no major changes to the scope of work.

CONCEPT REVIEW FIGURES ARE ESTIMATES ONLY: RFPs, RFAs NOT YET AVAILABLE

The dollar estimates with each concept review brought before the various boards of scientific counselors are not intended to represent maximum or exact amounts which will be spent on those projects. They are intended only as guides for board members to help in determining the value of the projects in relation to resources available to the entire program or division. Responses should be based on the workscope and description of goals and methods included in the RFPs (contracts) and RFAs (grants and cooperative agreements). Availability of RFPs and RFAs will be announced when the Institute is ready to release them.

Conference and logistical support services. Estimated annual award, $100,000, five years, within the 8(a) minority business set aside program. Present contractor is Social and Scientific Systems Inc. The narrative:

Twenty five tasks have been undertaken by this contractor, although one was canceled. Thirteen tasks have been completed. Support has been given for meetings of scientific importance to the extramural clinical programs. Examples of these meetings include the phase I and II working group meetings and meetings to discuss the role of computers in cooperative clinical research. Several meetings on AIDS have been supported. Minutes from various meetings have been produced and distributed. We expect the contractor to continue to support 15 to 25 meetings a year which enable clinical scientists to assess their current research and develop new directions for studies. The level of effort proposed is based on the actual effort expended bu this contractor over the past 12 months. The amount is a reduction from our proposal presented to the Board in the fall of 1980.

RFPs AVAILABLE

Requests for proposal described here pertain to contracts planned for award by the National Cancer Institute unless otherwise noted. NCI listings will show the phone number of the Contracting Officer or Contract Specialist who will respond to questions. Address requests for NCI RFPs, citing the RFP number, to the individual named, the Blair building room number shown, National Cancer Institute, NIH, Bethesda, MD. 20205. Proposals may be hand delivered to the Blair building, 8300 Colesville Rd., Silver Spring, Md., but the U.S. Postal Service will not deliver there. RFP announcements from other agencies will include the complete mailing address at the end of each.

RFP NCI-CN-45167-50

TITLE: Phase I studies of new chemopreventive agents
DEADLINE: Dec. 12

The Div. of Resources, Centers & Community Activities, NCI, is seeking proposals for provision of all necessary personnel, labor, facilities, and equipment, not otherwise provided by the government, to provide necessary technical support to the Prevention, Detection & Diagnosis Program to establish clinical trials resources to perform phase I clinical trials of new cancer chemoprevention agents and to perform human pharmacokinetic studies during phase I studies. These will provide the phase I clinical evaluations of investigational agents which are developed through the Chemoprevention Linear Array and are sponsored by the Food & Drug Administration under an IND held by DRCCA.

The RFP will be available Oct. 27.
CONTRACT SPECIALIST: David Monk
RCB, Blair Bldg Rm 2A07
301-427-427-8745

RFP NCI-CM-47650-64

TITLE: Collection, storage and quality assurance and distribution of biological response modifiers
DEADLINE: Approximately Nov. 25

(This RFP announcement appeared in last week's issue of The Cancer Letter. NCI subsequently made the following additions and corrections).

1. The contract will be awarded for three years, incrementally funded.
2. Task B was modified, inserting the following language:

(Offerors will be requested to) perform one or more of the following assays at least twice a week according to protocols provided by the project officer to confirm stated biologic properties of BRM preparations: (a) in vitro determination of the antitumor property of BRM; (b) in vivo determination of adjuvanticity; (c) assays for tumor cytotoxicity and/or cytostasis; (d) assays for the effect of BRM on susceptibility of tumor cells to lysis by cytotoxic cells; (e) assays for interferon and interferon like activity; (f) assays for tumor cell lysis; (g) assays for antibody binding to discrete subpopulations of mouse or human lymphoid cells; (h) activation of macrophage mediated tumor cell lysis and cytostasis; (i) assays for lymphokines/cytokines; and (j) assays for augmentation of antibody response with cell assays.

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