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NCI RECEIVES 165 SBIR GRANT APPLICATIONS; COMBINED WITH SOLID CONTRACTS, NO MORE FIASCOS ARE EXPECTED

NCI's policy of encouraging academic scientists to develop relationships with commercial organizations and go after Small Business Innovative Research grants and contracts has paid off. The

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In Brief

CHABNER SAYS JOHN ANTOINE OF NEW MEXICO MAY HEAD RADIATION PROGRAM: GM WINNERS ANNOUNCED

JOHN ANTOINE, Univ. of New Mexico, has been offered the job of heading NCI's Radiation Research Program in the Div. of Cancer Treatment. DCT Director Bruce Chabner said Monday that Antoine has said he is very interested but wants to wait until later in the year to make the move. The position has been vacant for two years.... **GENERAL MOTORS** Cancer Research Foundation 1985 Awards went to Paul Lauterbur, professor of chemistry at SUNY (Stony Brook), who won the Kettering Prize for his work in developing magnetic resonance imaging; Christopher Wagner, Llandough Hospital, Wales, who won the Mott Prize for identifying asbestos as a cause of mesothelioma; and Robert Schimke, professor of biology at Stanford Univ., who won the Sloan Prize for his discoveries about drug resistance to anticancer chemotherapy. Each received $130,000, with $30,000 set aside to support a workshop or conference headed by the prizewinner.... **VICTOR DEMBROW,** Miami, assumed the presidency of the Society of Surgical Oncology at the organization's annual meeting in Houston. He replaces Hiram Polk. Robert Hutter, St. Barnabas Medical Center, Livingston, N.J., is the new president elect. Bradley Aust, San Antonio, was elected vice president. Blake Cady, New England Deaconess Hospital, and Richard Wilson, Brigham & Women's Hospital, continue as secretary and treasurer, respectively. Polk became chairman of the Executive Council, which includes John Daly, William Donegan, George Hill, Carmack Holmes, Peter Mozden and Claude Organ.... **OUTSTANDING NURSE** Oncologist Awards presented by the Brown Foundation to nurses at M.D. Anderson went to Eleanor Cole and Dorothy Smith this year. Each received $10,000.... **FLORIDA SOCIETY** of Clinical Oncology, not the Florida Cancer Council, publishes the newsletter which printed the rumor that NCI's Steven Rosenberg was being sought by Tampa's Moffitt Hospital to head its surgery department (**The Cancer Letter,** June 7). Rosenberg said he had not talked with anyone from Tampa about the job.... **ONS/SCHERING** Excellence in Cancer Nursing Research Award was presented to Patricia Cotanch and Marilyn Hockenberry of Duke Univ. at the recent Oncology Nursing Society annual congress. The award was for their work, "Self Hypnosis as Therapy in Children Receiving Chemotherapy."

SBIR GRANT FUNDING DEPENDS ON HOW MANY TOTAL GRANTS NIH MAY AWARD

(Continued from page 1)

Institute received, from the round of grant applications submitted by the April 15 deadline, 143 for R43 (phase 1) and 22 R44 (phase 2) grants. Phase 1 awards are up to $50,000 for six months; phase 2, up to $250,000 a year for two years.

Those numbers assure that even in the unlikely event the huge number of SBIR contract proposals (238) now being reviewed does not produce enough awards to use up the rest of the $9.2 million set aside by NCI for the program, the grants would. However, most if not all of this latest round of grants probably will be funded with FY 1986 money. The solid numbers provide a good start toward use of the money NCI must set aside for 1986 funding.

The April 15 grants presently are all in review, and there has been no indication yet on how they will stack up. NCI executives are becoming more confident, however, that there will not be any more fiascos like last year, when they were forced by the provisions of the law which created the program to fund SBIR grants all the way down to the worst possible priority scores. That was especially hard to take at a time when RO1 and PO1 grants exceeding 175 were not funded other than a few special exceptions.

The surge of contract proposals which poured in by the April 1 deadline could have assured that that would not happen again. There are probably enough good, solid approved contracts to use all the money left after funding the phase 1 and 2 grants which cleared the National Cancer Advisory Board last month.

In fact, NIH policy at the moment is that no grants in the May round scoring past 200 will be funded. Still not down to the RO1 level of 158, but a lot closer than 500.

NIH, with the enthusiastic concurrence of NCI, is leaning toward funding as many of the approved contracts as is consistent with good science, while taking only the cream of the SBIR grants. The reason: The ceiling placed on the total number of competing grants NIH may award this year, thanks to the brilliant minds at the Office of Management & Budget. Even if the Weicker compromise prevails and the limit is lifted from 5,000 to 6,000, the payline would still be in the range of 165 to 170. And, thanks to another flouting of congressional intent by OMB, the SBIR grants will count against the total number NIH can award.

The improvement in SBIR grant proposals was evident in the January round, when the payline was held at 300. NCI funded 10 phase 1 and three phase 2 grants then at scores under 300. In May, the NCAB approved 10 phase 1 grants up to 300 in scores and one phase 2, but only those with scores of 200 or less are assured of funding. If the Weicker compromise holds up, NCI may pick up the rest of those 300 and under.

Of the SBIR grants under review now, those that come in with scores under 200 may well be funded with FY 1985 money, with NCAB concurrence being obtained by mail ballot. The others considered fundable (probably those with scores under 300) would go to the NCAB at its October meeting and be funded from the 1986 set aside.

"We now have a lot of options," Vincent Oliverio, NCI's SBIR coordinator, said.

Oliverio, who is associate director for program coordination in the Div. of Extramural Activities, said the number of contracts which will be in the funding range may be known next week. He thinks the number that will be considered acceptable "will be way over 50 per cent, maybe as high as 70 per cent."

The contract proposals are reviewed for technical merit by an initial review group, and then go to staff groups for further evaluation. The IRG assigns scores, from 1 to 1,000, with 1,000 being the best.

Anything below 400 probably will not be considered competitive for this round. Decisions on which contracts will be funded probably will be made in July, when NIH hopes to have a definite answer on how many grants it can award.

ONE MORE VICTORY FOR SOL GARB: FDA APPROVES THC COMPOUND FOR MARKETING

The Food & Drug Administration's action last week in approving a THC-based compound for marketing as an antinausea drug could be considered a posthumous victory for Solomon Garb.

FDA approved the new drug application of Unimed Inc., but the compound, with the trade name Marinol, still must get Schedule 2 clearance from the Drug Enforcement Administration before it can go on the market.

When it does become available for prescriptions, NCI will cease providing it free to approved physicians, as it has done for about four years. An estimated 20,000 cancer patients have received the drug through the NCI program.

Garb was one of the activists whose lobbying of Congress and the public led to the National Cancer Act of 1971. He was scientific director of AMC Cancer Research Center in Denver, served on the Yarborough Commission which drew up the 1971 Act, lobbied constantly for it and subsequent renewals, camped in Congress during appropriations discussions, and fought ceaselessly against enemies of the Cancer Program.

Above all, Garb was a physician and clinical investigator who treated cancer patients. Finding an effective antinausea agent eventually became his top priority, and he filed an IND for a tetrahydrocannabinol based compound when FDA—after much pushing and shoving by Garb-led forces—reluctantly went along with testing the marijuana derivative.

Ironically, Garb eventually had to use the drug himself. He discovered in November, 1980, that he had stomach cancer. For a year, he was on a chemotherapy regimen that produces severe nausea and vomiting. He managed to keep it under control with THC, using the protocol he had developed. He noted his reactions and developed a method for overcoming the sometimes hallucinogenic effects. He died in February, 1982.

A number of other antinausea agents have been developed since Garb filed his IND, but it appears that THC still will have a place in cancer treatment.

NCAB COMMITTEE URGED TO PRESS BOARD CERTIFICATION FOR SURGICAL ONCOLOGY

The National Cancer Advisory Board's Committee on Innovations in Surgical Oncology has been urged to support development of board certification of surgical oncologists.

John Potter, director of the Vincent Lombardi Cancer Research Center at Georgetown Univ., said at the meeting last month of the committee, "The surgical community is 10-15 years behind our colleagues in radiotherapy and medical oncology. We haven't been attracting the brightest and best minds into surgery."

NCI's training programs in surgical oncology "are a step in the right direction," Potter continued. "But the crux of the problem is the fact that surgeons don't have credentials certifying them as surgical oncologists. All the others have boards."

"This committee might encourage the NCAB and NCI to encourage organizations to establish board certification," committee member Victor Braren said.

Committee Chairman Ed Calhoon said that more surgeons might be interested in competing for NCI research grants if they could get some help in writing applications. "Surgeons need some direction in how to write grants," he said. "NCI could develop a video presentation, which would only take a modest amount of money."

Barney Lepovetsky, chief of the Cancer Training Branch in the Div. of Cancer Prevention & Control, described the several programs available for surgical oncologists, including a proposed new mechanism which would provide salary and research for a period long enough to permit the surgeon to become an established investigator. That proposal was still awaiting clearance by the NCI Executive Committee.

"The wonderful thing about this program is the flexibility," William Longmire, member of the President's Cancer Panel, said. "From one year support to support all the way through training and after to help him get established. The surgical community couldn't ask for anything more."

Frederick Avis, chief of the Surgery Section in the Div. of Cancer Treatment's Clinical Investigations Branch, said, "One of the problems is the lack of representation in extramural programs of surgeons."

"That was mentioned in the closed session of the Board today," NCAB member William Powers said. "There is an attempt to get surgeons into the extramural program and to recruit surgeons for advisory groups, boards of scientific counselors, review groups."

Avis said NCI is working hard to recruit surgeons for review committees. Along with the programs to support surgeons in basic and clinical research and the training programs, "There is a tremendous amount being done by NCI. That does not mean that is all that needs to be done."

Committee member Geza Jako read a statement in which he urged NCI to devote more attention to development of laser surgery in cancer treatment. "What is needed now is a better technique to reduce the cancer load, a technique which can detect and remove or destroy cancer cells with much greater precision," he said.

"Laser surgery provides an unprecedented precision in intraoperative detection and removal of cancer cells," Jako continued. "It provides a dry surgical field and allows detection under magnification. On dry cut surfaces, where good contrast exists between normal and cancerous cells, one can detect as few as 100 or 1,000 cancer cells, and follow them in the process of removal as a coal miner follows a vein in the coal mine. This precision compares with the present surgical techniques where the minimum detection is around 10 to the 7th or 8th cells at its best. The laser is giving unique opportunities in surgical research for improved intraoperative cancer detection and removal. . . In the past, as is still true of general surgery, incompatible surgical techniques are used in an attempt to handle such a microscopic disease as cancer. This can be likened to repairing a fine Swiss watch with a large screwdriver or plumber's wrench.

"In the past 12 years, microscopic laser surgery has made major progress in the diagnosis, treatment and management of cancer. . . It is time that NCI, members of the boards of scientific counselors and others educate themselves about laser surgery."

DCT BOARD APPROVES CONCEPTS FOR NEW TRIALS IN IMAGING, INTRAOPERATIVE RT

Multi-institutional imaging trials and a cooperative group of six institutions to carry out phase 2 and 3 clinical trials in intraoperative radiotherapy were given concept approval Tuesday by the Board of Scientific Counselors of NCI's Div. of Cancer Treatment.

Those concepts were among five presented by DCT's Radiation Research Program with an estimated first year total cost of $1.35 million, all approved by the Board.

The Board also approved at its meeting this week concepts presented by the Developmental Therapeutics Program (nearly $10 million in estimated first year awards, all contract recompetitions); the Cancer Therapy Evaluation Program, one contract recompetition at an estimated first year cost of $390,000 plus a no cost extension of another; and the Biological Response Modifiers Program, one contract recompetiton at an estimated first year cost of $160,000.

The concept proposals and Board discussion follow:

Radiation Research Program
Cooperative Agreement RFAs

Multi-institutional imaging trials in cancer. "Multiple" three year awards, estimated first year total, $600,000.

Several imaging technologies of recent development (magnetic resonance, computed tomography, ultrasound, digital radiography, positron emission tomography, single photon emission tomography) have reached a stage of progress which justifies investigation into the capacity of each of these modalities to detect cancer and to determine its extent, that is, to stage the disease employing a single modality or a combination of modalities, and to monitor therapy. Early assessment of these technologies is important for evaluating their impact on the management of cancer.

Many studies have been carried out using these various technologies, and have been reported in literature. However, such studies usually consist of small numbers of cases so that statistical data have remained questionable. Further, the objectives of the studies have been diverse. Since one modality seldom provides all of the information needed, various combinations of the different technologies have been employed, but without successful solution of the proper sequence of the modalities. The algorithms employed at a given institution have represented opinions based on logic but not necessarily on fact.

A current contract supported study is assessing the value of magnetic resonance imaging compared to other modalities for cancer of lung, musculoskeletal sarcomas, brain gliomas, and liver disease. However, the objective of the contract study is quite different from the present proposal which is to diagnose, stage and monitor cancer in the most efficacious way rather than to assess a particular technology. A recent workshop sponsored by DCT on the subject "Imaging Requirements in the Staging of Patients with Lung Cancer" concluded that there is an insufficient data base presently available using modern technology to determine the imaging requirements in lung cancer. They further concluded that such information is necessary if the costs of imaging evaluation in the staging of lung cancer are to be reduced without adversely affecting the care of patients.

Objectives will be to diagnose, stage and monitor carcinoma employing single or multiple technologies of new and advanced type; and to develop algorithms for the appropriate sequential selection of these diagnostic procedures. Related aims will be improved quality and cost reduction of the imaging process.

These funds will support multiple institutions in diagnosing, staging and monitoring tumor responses of the more common malignancies. They would support an operations headquarters and statistical center and would cover expenses incurred by members of the cooperative group in performing studies required by specific protocol.

The assistance support mechanism with a cooperative agreement permit the accumulation of adequate numbers of patients needed for statistically significant results and at the same time would permit suitable programmatic control of the protocols for carrying out the studies, thus better ensuring attainment of the objectives. Further, the cooperative agreement mechanism would permit the development of a variety of protocols not obtainable by contract and allow researchers to respond effectively to the requirements of new scientific opportunities. In addition, the flexibility of the cooperative agreement, permitting participation by multiple groups would facilitate more rapid assessment of developing technologies while at the same time assuring coordination by NCI staff.

Board Chairman Samuel Wells said, "A lot of these data will be collected anyway. There are a lot of other areas that could use this money. It's not clear to me why we need this."

"That is a key comment," responded Board member

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.

David Bragg, who is chairman of the Dept. of Radiology at the Univ. of Utah Medical Center. "An example is prostate cancer. There are 75,000 cases, and a smorgasbord of procedures are being used. IVP and barium enemas are still being done by rote, although you and I know they're useless. We don't have a protocol for workup for any site. We need to develop a data base to determine which procedures can be thrown out and which are useful. We're talking about basic current technology. This is loose change compared to what we have approved for Developmental Therapeutics. It needs to be done and I don't see it being done anywhere else."

Board member Karen Fu said she was concerned about costs. "A single MRI costs $800."

Bragg pointed out that NCI funds would pay only for data management and collection and not for the procedure. DCT Director Bruce Chabner said it would be the same as for chemotherapy trials. "We pay for data collection, and most of the rest is paid by third parties."

There were no objections to the motion for approval.

Clinical trials in intraoperative radiotherapy. Six three year awards, total estimated cost $300,000 first year.

The contract effort in intraoperative radiotherapy was instituted in 1981. The awards were given to three institutions with the Radiation Oncology Branch participating in the working group as an ad hoc member. The purpose of the contract effort is to investigate the role of intraoperative radiotherapy in intra-abdominal malignancy and to develop a consensus on appropriate dose and technique for a given abdominal structure. These essentially constitute phase 1 studies, though followup information is being kept to obtain some estimate of efficacy. The most commonly investigated sites are pancreas, colorectal tumors and stomach tumors. Other sites include advanced cervix and bladder tumors as well as a few sarcomas. At present, no firm conclusions can be drawn about efficacy. Tolerance is becoming more well established in the primary abdominal sites, at between 2,500 and 3,000 rads in a single dose. Patient accrual continues on the contracts which expire in late 1985.

Intraoperative radiotherapy is moving into phase 2 and 3 studies. These studies are most easily done through cooperative agreements which by permitting participation by multiple qualified institutions allows reasonably rapid accrual of data under controlled circumstances (operational and statistical). The studies will be carried out with programmatic NCI staff input including protocol approval and general monitoring. The amount requested will permit participation by approximately six institutions providing support for data management personnel and administration overhead. Colocation is the preferred physical disposition of facilities.

Wells and Board member Carol Portlock expressed concern about morbidity from the procedure. Timothy Kinsella and William Sindelar, of DCT's intramural Clinical Oncology Program who are participating in the intraoperative radiotherapy studies at the NIH Clinical Center, said that investigators are learning how to limit morbidity and that a few institutions now have the background to carry out the trials needed to determine if the procedure has significant therapeutic effect.

Institutions with the existing contracts are Howard Univ., Mayo Clinic and Massachusetts General Hospital.

Chabner commented, "We're not sure about the money. It probably can be done for less."

The motion to approve was passed without objection.

RRP Contract Recompetition

Screening drugs for radiosensitizer activity. One five year award, estimated first year cost, $300,000. Present contractor is the Northern California Cancer Program.

The concept of compounds which sensitize cells to ionizing radiation has been demonstrated in many preclinical investigations. Some of these compounds, especially the nitroimidazoles, have been tested clinically but have not shown efficacy. This lack of clinical efficacy has been attributed to the dose limiting peripheral neuropathy which develops before effective dose level of the drug is achieved in patients. This toxicity is related to the nitro moiety of the nitroimidazoles. A search has been under way to develop new leads (target compounds which represent chemical classes which are devoid of nitro groups). These target compounds can then be optimized and the best analogues tested chemically.

The objective of this contract is to screen a large number of compounds representing numerous chemical classes from the NCI drug inventory for cellular cytotoxicity and radiation sensitization both in vitro and in vivo.

The proposed contract represents half of the Radiation Research Program's efforts in this area of radiation modifiers. The remainder of this effort consists of a contract for the synthesis, biological testing and optimization of those target compounds which result from the screening contract. The RRP effort is the only one world wide which has the development of new radiosensitizers as its goal. In addition, the screening of a large number of chemical classes is expected to provide the data base necessary for a future structure-activity approach to the development of radiosensitizers.

The proposed contract is the second recompetition of the Radiation Research Program effort for screening various classes of chemical compounds as potential radiosensitizers. There is a continuous need to discover new leads (compounds), especially non-nitro compounds, if a clinically useful radiosensitizer is to become a reality. During the last four and one half years apprxomately 440 compounds were sent for in vitro evaluation. The compounds come from various sources which include universities, pharmaceutical companies, and the NCI inventory. Approximately 106 compounds have been tested for cytotoxicity and radiation sensitization in

vitro. The other compounds were insoluble or too cytotoxic to be tested for sensitization. Twenty five of these compounds appeared to be better than or as good as misonidazole, the radiosensitizer standard against which they are being compared and were sent for in vivo testing. As a result of the leads discovered to date, three target compounds have been patented and are being optimized before being submitted to the NCI Decision Network as radiosensitizers for clinical development.

Francis Ruzicka, acting director of the Radiation Research Program, said the research effort has produced the first nonnitro radiosensitizer and has shown that electron affinity is not a necessary characteristic.

Board member Alan Rosenthal suggested that the process could be streamlined by eliminating those that are insoluble and those for which sufficient quantity is not available (another limiting factor) for testing before they reach the point where those deficiencies prohibit further tests. Ruzicka said the insolubility is not known until the in vitro evaluation is attempted.

"I'm not sure I agree (with Rosenthal)," Chabner said. "If we throw them out because we don't have enough, we may overlook some good ones. Synthesizing the compounds is not that difficult."

New RRP Contract Procurement

Computer software development for magnetic resonance imaging. One three year award as a small business set aside for an 8a firm, estimated annual cost, $100,000.

The Radiation Research Program has awarded five contracts in the area of clinical magnetic resonance imaging research. The contractors constitute a working group which will carry out comparative imaging studies to evaluate the accuracy of MRI vs. other modalities in detecting and diagnosing disease in many parts of the body. None of the contractors under the current workscope can provide a centralized data storage and rapid retrieval system for all other contractors. Centralized data storage and analysis are necessary to assure adequate statistical control of high quality data as a basis for authoritative evaluation of the comparative imaging results.

This contract will be aimed at providing local ongoing computer programming and data analysis functions in close support and coordination with RRP. Computer programs will be needed to achieve data retrieval, analysis, display, and overall data management objectives.

RRP Interagency Agreement

Development of reference standards for hyperthermia thermometry. Two year interagency agreement with the National Bureau of Standards, estimated cost $50,000 a year.

Phase 2 clinical studies using hyperthermia in conjunction with radiation therapy are under way and phase 3 clinical trials are being planned. Currently used thermometer probes require frequent calibration against a standard and are nonlinear in their temperature response. The standards used now do not fall within the temperature range used for therapy. Accurate thermometry requires temperature measurement to 0.1 degree C or better. Reference standards will be purified from existing compounds known to have triple points at 40.9 degrees C and 44.4 degrees C. These temperatures occur at both ends of the range of clinical interest. Reference standards will be made available to the community at a low cost ($300-$400). Laboratory facilities will be provided by NBS.

Developmental Therapeutics Program Contract Recompetitions

Off site quick reaction synthesis. Multiple task order contracts, three years, estimated annual total cost, $450,000. Present contractors are Univ. of Alabama, Franklin Research Institute, Michigan Tech. Univ., Midwest Research Institute, Raylo Chemicals Ltd., Research Triangle Institute, SISA Inc., Univ. of South Florida, Southern Research Institute, SRI International and Starks Associates.

Objective of the task order synthesis contracts is the resynthesis of a variety of compounds, unobtainable from the original sources, for evaluation as potential anticancer agents in the primary screens. These contracts will synthesize compounds, selected on the basis of biological and/or chemical rationale, in quantities of 0.1 to 2 grams using the original synthetic methods.

Task order synthesis contracts have provided about 200 compounds for screening in a flexible, timely and cost effective manner during each contract year.

Through this mechanism, we propose to synthesize approximately 200 selected compounds a year for our primary screens that would not be obtainable by other means.

"Then, assuming we've found an interesting lead," DTP Director Michael Boyd said after the Board approved the concept, "we need resynthesis as an intermediate source."

Resynthesis contracts. Possible multiple awards for three and a half years, estimated annual amount, $500,000. Present contractors are those listed below which hold contracts for preparation of bulk chemicals and drugs.

Objective of the resynthesis contracts is the synthesis of promising compounds for secondary in vivo evaluation against the panel of tumors. This task entails the scale up of compounds in quantities of 2 to 50 grams. This may require modification of existing synthetic procedures or the development of more efficient alternate routes of synthesis.

Previously this task was accomplished through the numerous laboratories awarded under the large scale chemical and drug synthesis contracts.

We expect to synthesize approximately 80 to 100 compounds each year, depending on the complexity of their synthesis. We can expect cost reductions compared to the prior configuration of the contracts because the proposed solicitation will not require large scale equipment and the compounds need not be

synthesized under the requirements of Good Manufacturing Practices.

Preparation of bulk chemicals and drugs. Multiple awards anticipated, four and a half years, estimated annual cost, $2.35 million. Present contractors are Aerojet Strategic Propulsion Co., Aldrich Chemical Co., Ash Stevens Inc., Pharm-Eco Laboratories Inc., Starks Associates Inc., Warner-Lambert Co., Monsanto Research Corp.

The chemical preparation laboratories are service laboratories designed and selected to prepare known chemicals and bulk drugs which are needed by the program. The compounds prepared are not readily available in the quality or quantities needed from the original supplier or on the open market.

The laboratories are used to obtain data for the preparation of the necessary quantities of clinically important chemicals and to develop the most economical means for their preparation. Many methods of synthesis which are practical for small quantities are not technically feasible or economically practical when used for large scale synthesis operation. The conversion of small scale to large scale production often requires developmental studies which are carried out by these contractors.

The preparation laboratories provide the means of obtaining nearly any type of chemical compound in large quantities. The materials are of very high purity and are well characterized. The quantity of a given material synthesized may range from 50 grams to 200 kilograms. Factors governing the amounts needed include the rate of usage, ease of preparation, chemical stability, and cost. Compounds received from these contractors are prepared under current Good Manufacturing Practices and are intended for formulation development, toxicology, pharmacology, and clinical use.

The chemical preparation laboratory contracts will be recompeted as a single package which will now include the Monsanto Research Corp. contract. The FY 1984 level of effort for the seven chemical preparation laboratory contracts was approximately 34 staff years per year. The recompetition of the contract package will reflect several changes. The synthesis of small quantities of compounds required for testing in the DCT preclinical in vivo tumor panel will no longer take place in this contract package. Funds ($500,000 for the first year) will be transferred from this contract package to the Drug Synthesis & Chemistry Branch to initiate new contracts to carry out this small scale synthesis (10-50 g). In addition, total funds available to this contract package have been previously reduced. It is anticipated that 4-5 smaller contracts will be awarded from this contract package.

Chabner noted that the entire Drug Development Program had been reduced from over $40 million at its peak to less than $30 million. "The fat has been trimmed away. We couldn't do drug development without these contracts."

Boyd commented that more money could be shifted away from bulk preparation of chemicals and drugs "as more and more biologicals come in."

Board member Susan Horwitz pointed out that the total package for drug synthesis and bulk preparation was over $7 million. "We're totally dependent on you. We have no way of making a judgment on the costs."

"This is a vote of confidence in you," Board member Efraim Racker added.

"You can be assured we will watch these very closely," Boyd said.

Quality control and protocol development. One three and a half year award, estimated annual cost, $400,000. The present contractor is Southern Research Institute.

As a part of current contract performance, Southern Research Institute has developed protocols for use of L1210 and P388 as subcutaneous tumor systems, resistant lines of P388 and for the LOX amelanotic melanoma in athymic mice, all of which are tentatively scheduled for use in conjunction with the use of human and murine cell lines in the recently approved new screening experiment. In addition, quality control studies involving experimental tumors and various animal supplier sources have been conducted. These studies have provided assurances that specific tumors perform within acceptable parameters and are sufficiently stable for use as reliable screening tools. This type of study is critical for a fair assessment of the scientific integrity of the in vivo screening program. Kinetic data has also been provided which is utilized on drug treatment scheduling and for the interpretation of experimental results.

It is imperative that an in vivo tumor system counterpart be available for testing active leads developed in the screening of compounds in human cell lines. While it is obvious that few of these systems will be used routinely for screening, it is intended that cells be utilized for testing in vivo upon demand. This will require that each cell line be checked for feasibility of use with a tentative protocol. Although work under this contract has already been accelerated to accommodate current cell lines in development, the use of human cell lines is to be phased in over a three year period and it is therefore essential that this effort be maintained to complement the changing program needs.

Services in support of the primary drug screening program. One three year award, estimated annual cost, $200,000. Present contractor is Biotech Research Laboratories. This will be a small business set aside.

One of the objectives of the Drug Evaluation Branch is the evaluation of antitumor activity of materials against in vivo and in vitro test systems. Materials are tested in multiple laboratories under contract to NCI. Because of the complex and interrelated nature of this work, it is necessary that the test data be monitored and analyzed on a timely basis so that this contract network can be effectively utilized. The primary objective of this particular contract support activity is to provide assistance to the Screening Operations Section of the Branch in maintaining an orderly flow of

of materials to screening laboratories, evaluating data, maintaining records of the status of compounds being studied, and requesting further testing as prescribed by protocols designed by the staff of the Branch.

The major tasks of this contract are:

1. Evaluating test results, requesting further testing of materials as required, scheduling them for timely review by the Prescreen Subcommittee and participating in these meetings.

2. Initiating requests for testing to screening contractors for those compounds designated for testing in additional systems; assisting in the evaluation of these test results and entering these evaluations to an on line file which contains summary evaluation data and status information on all compounds being tested in the DCT panel of test systems. The contractor will also assist in the evaluation of test results and the establishment of protocols for developmental systems.

The Branch has established a number of other automated files, such as the files for the Prescreen Subcommittee, the Operating Committee, and the file for compounds of interest to staff. The contract will provide personnel for data entry to these files and the staff to record and enter minutes of meetings of the Prescreen and Operating Committees. The Operating Committee file was designed to provide a management tool for Branch staff and includes such data items as procurement requirements, screening test results, and toxicology and Decision Network status. The contractor will provide for the coordination of this data from various program areas as well as for the data entry. This contract will also provide clerical support staff for data entry, typing and maintenance of files of selected agents and progress reports.

It is anticipated that this project will continue to provide the support personnel to assist in the evaluation of the screening data for materials being tested in the DCT panel of test systems and the maintenance of the necessary related records and files.

Primary genetic centers. Multiple awards are anticipated, three years, estimated total annual cost, $4.68 million. Of that amount, users are reimbursing about $2 million. Present contractors are Charles River, Leo Goodwin, Harlan Sprague Dawley and Simonsen Labs.

These contracts produce most of the animals raised in the DCT animal production program. It is within these contracts that the isolator maintained foundation colonies are housed as well as the pedigreed expansion colonies. These contracts supplied breeders to the rodent production contracts and to hybrid contracts. These primary genetic center contracts raise animals in a maximum barrier environment. During the past year, there has been a decrease in program demand for animals. As a result, the six hybrid contracts were not renewed in FY 1985. There has been an increase in the demand for nude mice. Since the hybrids were not renewed, these primary genetic centers were restructured to produce a large percentage of the needed hybrids and to meet the demand for additional nude mice. This enables the Animal Genetics & Production Branch to supply a greater percentage of pathogen free animals.

It is DCT's intent to recompete these contracts with a renewal date effective July 1, 1986, for a three year period. The new contracts will continue to maintain our foundation colonies and operate under strict barrier conditions. Should a future decrease in demand occur for animals, the production decrease would take place at the rodent production centers and not at these primary genetic centers.

Task managed computer programming support. One five year award, estimated annual cost, $150,000. Present contractor is ORI Inc.

This contract provides rapid computer programming support for the Information Technology Branch. It is intended to provide programs for maintenance support, operations support, and development support. Programming may involve the conversion of a file from one format to another, the interfacing of a software package or new equipment with the DIS, the generation of a new output, adaptation to change in procedure, resolution of problems, and so on. Without the ability to quickly perform such tasks, the ITB would be unable to maintain the various computer systems used by DCT.

Following is a sampling of tasks that have been accomplished under this contract: Transfer of the Hodes model from the CAS computer to the DCRT machine; the development of programs allowing the IBM XT to be used for the input of chemical structures; the programming of a laser printer to obtain output combining both text and chemical structures on one page.

In the still rapidly advancing computer field, the capability to deal with problems or opportunities without delay is required for a computerized system to remain useful. The task order mechanism has provided the ITB with an effective means for addressing the needs that arise in the operation of the systems that it maintains. A continuation of this contract is essential for the operation and improvement of these systems.

Chabner, referring to the entire Drug Development Program, said, "What you're getting is about six drugs a year (going to clinical trials). Boyd noted that preclinical drug development is costing NCI $25-26 million. "About $5 million per drug per year," Chabner said. "With about one in 10 turning out to be useful, that"s $50 million per drug."

Rosenthal said industry spends $70-80 million per drug.

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