THE CANCER LETTER

Vol. 9 No. 25
June 24, 1983

Subscription $125 year North America
$150 year elsewhere

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

BRANDT TELLS NIH THERE MAY BE NO EXCEPTIONS TO DRG REGULATIONS, MAYBE A FEW AT COMPREHENSIVE CENTERS

Assistant Secretary for Health Edward Brandt informed NIH officials last week that, upon orders from the White House, there may be no exceptions or adjustments made for any category of disease or institution in Diagnosis Related Group reimbursement regulations now being drafted by the Health Care Finance Administration. If any waivers are granted, they will be made only to a selected few comprehensive cancer centers.

In danger of being left out of any adjustments or exceptions are all

(Continued to page 2)

In Brief

DCT BOARD REJECTS MOVE TO COUNT INDIVIDUAL P01 PROJECTS TOWARD THE NIH TOTAL OF 5,000 GRANTS

MOTION RECOMMENDING that NIH count each individual project within a program project grant toward the goal of supporting 5,000 competing grants a year was voted down by the Board of Scientific Counselors of NCI's Div. of Cancer Treatment. Board member Paul Marks offered the motion, arguing that counting all projects in a P01 would relieve pressure on the 1984 budget. The Administration's agreement to fund 5,000 new and competing renewals, without putting enough money into the budget to pay for that many, forced NIH to make drastic cuts in support for centers, research resources, and other areas. "People should understand the P01 concept. A P01 grant is a number of related research projects, which are conceptually the same as R01s but more efficient," Marks said. DCT Director Bruce Chabner said that counting all P01 projects would merely result in adjusting the target level upward, and thus would not free up any money. Board member Brigid Leventhal added that counting individual projects "runs the risk of making it easier to reduce the budget." . . . NEW DCT STAFF appointments: Charles Grieshaber is chief of the Toxicology Branch in the Developmental Therapeutics Program; Matt Suffness, who has been acting chief of the Natural Products Branch in DTP, now has the permanent appointment; and Bruce Wachholz is chief of the Low Level Radiation Branch in the Radiation Research Program. Theodore Phillips, chairman of the Dept. of Radiation Oncology at the Univ. of California (San Francisco) and a member of the DCT Board, will spend a year at NCI on an Intergovernmental Personnel Agreement. He will work with Eli Glatstein in the Radiation Oncology Branch, concentrating on brain tumor therapy and intraoperative radiation. Phillips will continue as chairman of the Northern California Oncology Group during that period. Other radiation oncologists presently working in DCT on IPAs are Glenn Sheline of UCSF and Gabriel Wilson of UCLA.

KATTERHAGEN CALLS EMERGENCY MEETING OF NCAB COMMITTEE; ACCC GEARING UP

(Continued from page 1)

other institutions and clinics treating cancer patients and entering cancer patients on clinical trials, including community cancer centers, the new Community Clinical Oncology Program institutions, and possibly even some university based cancer centers.

"NCI's clinical research program is in serious jeopardy if some legitimate mechanism can't be found to fund that activity," William Dugan, president of the Assn. of Community Cancer Centers, said when informed of Brandt's statement. "Oncology units in community hospitals are in terrible shape financially anyway, without talking about research. The new CCOPs will be in great trouble. The money they are getting to fund clinical trials is woefully inadequate, and if they can't recover patient care costs above the DRG averages, I don't see how they can participate."

Gale Katterhagen, principal investigator for one of the CCOPs, in Tacoma, and a member of the National Cancer Advisory Board, called an emergency meeting of the NCAB committee he chairs, on Cancer Control & the Community. The committee will meet June 27 in NIH Bldg. 31, Rm. 6, starting at 9 a.m.

"Unless we act now, this will significantly damage the National Cancer Program, by severely hampering clinical trials," Katterhagen said. "There's no question that some centers would go out of business, and it could put an end to clinical trials in community hospitals."

"It will devastate community cancer programs, and have a special impact on the more sophisticated ones —they will lose heavily," ACCC Executive Director Lee Mortenson said. "CCOPs will have less than a year in existence when this is implemented. Hospital administrators will perceive that CCOP patients will be more expensive than typical patient care and will prohibit physicians from participating in the program."

An example which offers a gloomy picture of things to come is the result of participation by St. Barnabas Hospital in the DRG experiment conducted in New Jersey. Rodger Winn, director of St. Barnabas' oncology program and PI for the CCOP there, said that in six months, the hospital lost $80,000 on its cancer patients. The hospital sees about 1,100 new cancer patients a year, and is putting about 75 on research protocols.

"We're not talking about just a hospital or a center or a group of hospitals or centers," Mortenson said. "We're talking about NCI's clinical research program. That includes the cooperative groups and all others involved in clinical research."

Francis McKay, associate director for finance and administration at Fox Chase Cancer Center, has represented the Assn. of American Cancer Institutes in discussions with HCFA. McKay told ***The Cancer Letter*** that if the decision is to not provide any exceptions or adjustments, "it will be a disaster. We simply can't survive on a system based on average cost. I can't believe the federal government will allow cancer centers to go out of business."

The problem is not just with the extra costs involved in putting cancer patients onto research protocols. "The kind of cost we're talking out is state of the art medicine," McKay said.

That type of sophisticated treatment, available at most cancer centers and at the up to date community hospitals, will not be reflected much, if any, in the initial DRG averages. As it moves into standard practice, it eventually will be picked up, permitting reimbursement levels to cover those costs. But, "this lag time presents a serious financial problem to the cancer centers since the new treatments and new technologies are usually more expensive than in the current ones," McKay wrote in a letter to Michael Maher, director of HCFA's Office of Reimbursement Policy.

"A further concern we have is based on the type of patient we see. These are often the more difficult cases that cannot be handled by the community hospital and as a result their length of stay in the community hospital is considerably shorter than you would ordinarily expect. This will distort an average cost payment system based on diagnosis. Many of these patients come to us with recurrent disease having been unsuccessfully treated. They often have serious secondary problems such as infection, pneumonia, cardiac problems and compromised immune systems. It is in the nature of cancer centers to attract such patients. Therefore, the work done at our institutions incurs a number of extraordinary costs," McKay continued.

Those problems "are common to all institutions in the Cancer Centers Program, whether university based or free standing," McKay said. "Free standing cancer hospitals have an additional problem in that they are dealing only with cancer patients and have an extraordinary concentration of severity of illness. Not only are the patients sicker and the treatment modalities more expensive, these institutions do not have low cost DRGs to average against."

McKay presented AACI's suggestions for adjustment or exceptions:

- Adjust DRGs based on some standard factor such as an atypical service exception. This should be relatively easy to establish and to calculate once the component pieces of the DRGs, especially the average length of stay, are known.
- Develop institution specific DRGs.
- Develop group specific DRGs for the cancer research institutions. If this is followed, it may be necessary to develop several groups since even within

the Cancer Centers Program, there is considerable diversity.

Of the organizations which have taken the lead in seeking exceptions for cancer treatment, ACCC feels the most threatened. ACCC's leadership this week was in the process of organizing an all out effort to get help from Congress in securing exceptions for community cancer programs.

AACI was taking a more relaxed view of the situation. At the organization's annual meeting this week in Denver, most members reflected McKay's concerns, but no action had been taken by press time on the issue. McKay's discussions with Maher have led him and other AACI members to believe that an acceptable solution will be worked out.

The final decision will not be made by Maher, however, nor by his boss, HCFA Administrator Carolyn Davis. It will be made at the White House, and if enough furor is raised to push the issue past the Office of Management & Budget, by President Reagan.

LARGEST ONCOLOGIC SOCIETY EXERTS CLOUT, STARTING TO GET RESULTS

The largest and potentially the strongest and most politically influential of the oncologic societies, meeting last month in San Diego, considered a variety of actions which could have significant impact on clinical oncology and cancer research--professional certification, nationwide educational programs, development of guidelines for administration of chemotherapy and for safe handling of chemotherapeutic agents, lobbying Congress in support of the National Cancer Act and for increased NCI appropriations, pressuring the White House and Congress for appointment of at least one of its members to the National Cancer Advisory Board.

Society members, after two days of scientific and educational sessions, heard reports on the organization's solid financial status (cash reserves exceeding those of the other two societies meeting in San Diego combined); heard from their newly hired full time executive director; heard a report on their successful new journal.

AACR? ASCO? If you guess that the above report was referring to the 75 year old American Assn. for Cancer Research or to the 19 year old American Society of Clinical Oncology, you are probably a male chauvinist, as one ASCO member described himself after learning that his claim of belonging to the largest oncology society was incorrect. That honor belongs to the Oncology Nursing Society, barely eight years old and growing so fast that its membership is approaching 5,500, an 11.5 percent increase in the last year.

Connie Henke Yarbro, retiring after four smashing years as president, reported these accomplishments:

–Growth from 1,900 members in 1979 to nearly 5,500.

–Growth in the ONS annual budget from $100,000 to over a half million dollars.

–From one part time employee in 1979 to four employees, including executive director Pearl Moore.

–From no chapters to 37 now established around the country.

–Establishment of Oncology Nurse Foundation to raise money for research. ONS will award its first research grant at next year's congress, with a contribution from Mead Johnson helping to fund it. It will not be limited to members.

–Representation on the American College of Surgeons Commission on Cancer.

Yarbro noted that 81 percent of ONS members are involved in clinical care, 39 percent in education, 26.5 percent in administration, and 22.5 percent in research. Sixty-three percent of the members have a bachelor's degree or higher.

In her final presidential address, Yarbro said, "We must develop our political clout. We are the largest organization of professionals in the cancer field. One of 44 women voters are RNs. We have an obligation to make sure our message is heard."

The Society approved resolutions at last year's meeting calling on the President to appoint an oncology nurse to the NCAB and calling on Congress to mandate such an appointment in the renewal of the National Cancer Act. Neither effort was successful in last year's round of appointments, but ONS intends to keep applying the pressure.

ONS approved a resolution last year calling on NCI to establish a new program to support nursing research. NCI listened and is in the process of doing just that. Details of the new program will be available later this year, with award of the first grants to come in the 1985 fiscal year.

Yarbro told ***The Cancer Letter*** that ONS also will seek to have oncology nurses appointed to NCI boards of scientific counselors.

Ten years ago, one of the major deficits delaying improvement in cancer care was the lack of oncology nurses. It was estimated then that there were only a few hundred, most of those working at the major cancer centers. Now, with the ONS membership at 5,500, oncology nurses are present in nearly all cancer centers and are growing in number at community hospitals. Yarbro feels that the ONS membership may not start leveling off before it hits 9-10,000.

One of the major issues facing oncology nurses is that of certification. A survey of members, reported at San Diego, found that an overwhelming number support certification and would be willing to pay for it. Almost 80 percent said they would pay up to $200 for certification; 13 percent said they would pay $300; and two percent would pay $400. Seventy-

two percent said they would be willing to make a donation to get the process started.

One issue involved in certification is that the nursing diploma schools and associate degrees in nursing are being phased out in favor of bachelor degrees.

"Will bachelor degrees be required for certification, thus freezing out the diploma nurse?" members were asked. The general opinion was that certification should be opened to all RNs until all RNs have bachelor degrees.

Another controversial issue is whether certification should be limited to nurses who work in direct patient care.

The survey results will be published in *ONS Forum,* the society's journal.

An ONS task force was established last year to develop and publish guidelines and recommendations relating to the administration of cancer chemotherapeutic agents. The group polled nurses randomly to define practice on the national level; solicited materials relevant to policies and procedures, chemotherapy administration techniques, and course content outlines; and drafted "Chemotherapy: Guidelines and Recommendations for Nursing Education and Practice." The task force recommended publishing and distribution of the document and continued accruing of course content outlines and policies and procedures.

Members approved a resolution dealing with potential occupational hazards associated with cancer chemotherapeutic agents. It stated that ONS would "support local and national research to investigate potential health hazards to professionals who have handled in the past or who are currently handling and administering cancer chemotherapeutic agents, and that research be encouraged to scientifically define safe handling techniques in an attempt to minimize unnecessary exposure to potentially hazardous materials."

But the members rejected a resolution to endorse recommendations for safe handling of parenteral antineoplastic drugs written last year by NCI. Some members objected to the fact that an insufficient number of copies of the recommendations was available. "I appreciate the work of NCI but I'm not sure all of its recommendations will work at my institution," one member said. "I would want to look at each recommendation in detail."

The NCI recommendations could result "in taking on a lot of baggage you might not need in handling chemotherapeutic drugs," another member said. "It could be a large burden on individuals and institutions."

"I don't understand the concern over finances and not over our health," another member responded. "Ten thousand dollars for a laminar flow hood could prevent a $20 million lawsuit."

"To adopt this would be premature and irresponsible," another member said. Another said that to implement the recommendations would cost her hospital "well over $200,000."

DCT BOARD APPROVES RECOMPETITIONS, DELAYS DECISION ON CLONOGENIC ASSAY

The Div. of Cancer Treatment Board of Scientific Counselors gave concept approval at its recent meeting to the recompetition of contracts for the Developmental Therapeutics and Biological Response Modifiers Programs, along with a division support contract for planning and conferences.

Biochemical and biological characterization of antitumor drugs. Present contractor is Arthur D. Little Inc. Estimated first year award, $170,000, three years. Staff description of the project:

The primary objective of this contract is to provide basic information on the cytotoxic and biochemical effects of antitumor agents being considered by DCT for development to clinical trial. The studies are not intended to elucidate definitively the mechanism of action of a developmental drug but to provide a clear lead as to how the agent exerts its effects. Agents are evaluated for their in vitro growth inhibitory and cytocidal properties and for their effects on DNA, RNA and protein synthesis. Other experiments are designed to answer specific questions raised by the initial findings or the compound's structure. For example, experiments may be conducted to determine the agent's effects on DNA, the mitotic process or cell membranes or to determine whether the agent has alkylating activity or inhibits specific enzymes. This contract is the only resource available to DCT for obtaining preliminary biochemical information on new agents in a time frame that enables the information to be of use to DCT in drug selection and development.

The contract has been very productive and has provided useful information on diverse compound types. Most compounds evaluated have been in the preclinical stages of the Decision Network Linear Array: A few have been studied in earlier stages of drug development. Significant findings include (1) properties of acodazole HCL are those of a DNA intercalator; rapamycin is a relatively selective inhibitor of DNA synthesis and causes DNA strand breaks; (3) macromolecular precursor incorporation assays indicate that bactobolin and phyllanthoside act as inhibitors of protein synthesis; (4) the major effect of caracemide appears to be on DNA; DNA single strand breaks are produced and inhibition of DNA synthesis is more pronounced than are inhibitions of RNA and protein synthesis; (5) studies conducted for the antifol coordinating group showed that a diaminoquinazoline derivative acts as a classical antifol; and (6) as part of a larger study

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.

to examine the properties of several fluoroethylnitrosoureas (FNUs) for the alkylating agent coordinating group, the carbamoylating activities of the FNUs were compared.

Objectives of the new project will be similar to those of the current contract. Experiments will be conducted to (1) answer specific biological questions on new antitumor agents raised by the Decision Network Committee; (2) provide in vitro biological data to DCT committees to aid them in their choice of new agents, or analogs of lead compounds, for development; and (3) establish whether agents with novel structures have biochemical activities similar to those of clinically evaluated drugs.

In addition, greater emphasis will be placed on the cytotoxicity experiments in order to provide information to the newly formed Drug Blood Level Working Group which will coordinate in vitro and in vivo preclinical data to improve schedule selection and dose escalation for phase I clinical trials. Each year, approximately six potential antitumor agents will be assigned to the contract as they enter the DCT decision network process or become of interest to committees in earlier stages of drug development. Several other agents will be assigned at the pre-decision network stage in order to help facilitate a DN choice. The level of effort on the contract is projected to be maintained at three staff years per annum.

Board member Paul Calabresi commented, "It is not clear why this is a unique resource. Why can't this be done by Georgetown, or Southern Research?"

"We want fast turnaround," DTP Director John Driscoll said. "We don't have a contract with Georgetown. The workscope of the Southern Research contract is such that they don't investigate biochemical mechanisms. That was taken out of their contract completely, when our budget (DTP's) was cut from $44 million to $31 million."

Board member David Goldman said that he supports the concept because "it takes drugs we don't know anything about and investigates them. It's a logical interface. On the other hand, I don't think you should screen analogs that we know a lot about and give them to a group like this."

"The objective is to give us some initial information on a compound, to help us decide whether to go ahead or drop it," DCT Director Bruce Chabner said. "Usually, the information we get leads to dropping it."

"This is an important screen," Board member Gertrude Elion said. "The important thing is to find out the class, then ask someone to follow up."

Board member Ephraim Racker suggested that the compounds could be made available to the scientific community, on a voluntary basis, for analysis. "On a voluntary basis, it would take 10 times as long," Driscoll said.

"I don't think so. You could get an answer from us in a week, if the compound falls in an area we're working in," Racker said.

"That's the trouble. We can't always determine that," Driscoll said.

Goldman asked if the work could be done by DCT inhouse. Chabner said that although DCT staff does include people with expertise in many of the areas involved, "We're not sure they would be willing to put down what they're doing to work on this. It is not the type of work that is rewarded by site visitors."

The Board conditioned approval of the concept on submission at the next meeting of responses to the concerns expressed, particularly the prospect of doing the work inhouse.

In vivo screening of materials from European sources. Present contractor is Institut Jules Bordet. Estimated first year award, $200,000, five years.

Approximately 3,000 compounds (99.7% from Europe) were screened last year under this contract. This represents about 25 percent of input of new materials to the in vivo prescreen. About 20 percent of the materials tested in the DCT preclinical tumor panel screens were initially screened under this contract. The estimated first year cost is six percent of the total cost for all in vivo screening contracts. All DCT preclinical in vivo animal tumor models are used and strict conformance to DCT protocols is maintained. The testing level of 11,000 L1210 equivalent tests per year is purposefully low relative to testing levels at U.S. contractors, but the cost per test of about $18 is the lowest among in vivo screening contractors. The express purpose of this continental European contract is to encourage European sources to submit materials for NCI screening and, to this point, NCI maintains a liaison office in Institut Jules Bordet. This office serves as an ongoing, day to day contact and liaison between Western Europe and the United States and deserves a large share of the credit for encouraging the large input of European compounds to our program. The progressive increase in the percentage of compounds screened under the Jules Bordet screening contract from European sources reflects the confidence of the European suppliers in the ability of our European contractor.

The European suppliers receive their results rapidly and can visit the contractor to discuss the data. There is little question that the willingness of European chemical and pharmaceutical companies to submit compounds to the NCI program stems, in large measure, from their ability to interface with our European screening contractor in contrast to the alternative of dealing with NCI across the ocean. The project is cost sharing de facto inasmuch as NCI pays for direct labor and materials. Institut Jules Bordet facilities and collaboration of other scientists (and technicians when required) are not charged to the contract. Reimbursable costs do not include overhead, G&A, or fees.

Inasmuch as the value of this contract is contingent on the contractor's proximity and professional relationship to European sources of materials for screening, we are recommending advertising the project within Western continental Europe and that competition be restricted to that geographical area.

Development and production of solid oral dosage forms. Present contractor is Roxane Laboratories. EStimated first year award, $79,000, five years.

Roxane Laboratories is the principal contractor for the manufacture of oral tablet and hard gelatin capsule dosage forms of chemotherapy drugs. During the last contract period, the contractor produced a total of over 1.1 million solid oral dosage units. This represented over 12,600 individual bottles shipped to NCI for subsequent redistribution. The drugs manufactured consisted primarily of hexamethylmelamine 50 and 100 mg capsules and semustine (methyl CCNU) 10, 50, and 100 mg capsules to support NCI's Group C distribution program. In addition, dibromodulcitol 50 and 100 mg tablets were made for use in clinical trials.

Other products that the contractor has manufactured previously, and will probably provide in the future, include ICRF-159 50 and 100 mg tablets, methotrexate 50 mg tablets, and other infrequent or one time products. Tablet and

hard gelatin capsule manufacture are processes that generate substantial amounts of extraneous product dust. Therefore, the contractor has extensive and complete containment procedures and facilities, including separate HEPA filtered air handling, dedicated manufacturing equipment in an isolation room, plus special protective personnel suits with independent air supply and communication. These precautions serve to protect both the personnel and the environment from contamination with the toxic and/or carcinogenic chemotherapy drugs.

The Pharmaceutical Resources Branch plans to recompete this project with no major changes in the workscope or level of effort. The contractor is required to have special manufacturing facilities for the handling of cytotoxic agents.

Development and production of parenteral dosage forms. Present contractor is Yamanouchi Pharmaceutical Co. Estimated first year award, $250,000, five years.

This project was designed to provide additional capacity and backup capabilities to DCT's major contractor for large scale parenteral manufacture. Yamanouchi has performed extremely well completing all projects assigned with no batch failures. They ha ve resolved difficult formulation problems such as improving the purity and freeze drying quality of indicine N-oxide. They have identified and corrected problems with other drugs including hydroxyurea and bromodeoxyuridine. All production reports from this contractor have been flawless and in suitable form for FDA submission. They have been thoroughly inspected by FDA with no cited deviations from United States current good manufacturing practices. Such inspections are very thorough and the lack of major citations is very unusual.

The Pharmaceutical Resources Branch plans to recompete this project with no major changes in the workscope or level of effort.

Computer substructure searches. Present contractor is Maxima Corp. Estimated first year award, $69,000, three years.

The contractor has performed a variety of full and substructure chemical searches as well as nomenclature searches in response to DCT requests. During this past year, the contractor processed approximately 1,000 such queries. The majority of these searches (80 percent) were against the NCI structural database. About half of the queries involved detailed substructure searching to identify chemical compounds for followup testing and task order/congener synthesis. Other searches involved published literature databases such as Darc/Questel, Dialog and the National Library of Medicine's databases. Searches of these systems provide DCT staff rapid access to citations relevant to our work areas. The Synthesis Projects require these searches as do the resynthesis and acqusition projects.

There will be a continuing significant need for high volume computerized chemical searches such as those mentioned above to support various segments of our program. Searches of the published literature databases, e.g. Darc/Questel, will be used to assemble facts (e.g. physical properties, known biological activities, toxicities) relevant to new candidates for the tumor panel and compounds presented to the Drug Evaluation Committee. In addition, the new to be formed National Cooperative Drug Discovery Groups will require full structure and substructure searches of the NCI database.

This contract has been set aside for a small business, and will be recompeted within the 8(a) Minority Business Set Aside Program.

Collection, storage, quality assurance and distribution of biologic response modifiers. Present contractors are Meloy Laboratories and Litton Bionetics Inc. Estimated first year award on the Meloy recompetition is $125,000, and on the Litton Bionetics recompetition, $200,000, both for five years.

The Biological Response Modifers Program has the responsibility for preclinical and early clinical evaluation and development of a wide variety of biological response modifiers with potential for cancer therapy. An important aspect of this responsibility is the procurement, quality assurance, control and distribution of various biological repsonse modifiers to qualified preclincal and clinical investigators. The present contracts provide for an efficient integrated program designed to facilitate BRM development and responsibilities and are divided between two tasks:

Task A: Purpose of this contract is to provide effective inventory, quality assurance, control confirmation and distribution of BRMs. The contractor is responsible for receipt, dispensing, storage, distribution and inventory control of biologic agents. Quality assurance control evaluation involves specific assays for sterility, pyrogenicity, endotoxin levels, general safety testing and preclinical studies related to safe dose and route of administration. All testing conforms to FDA specifications for biologic development and are in compliance with government regulations for human use products. The contractor also has the responsibility for development of master files and investigational new drug applications on biologics developed in the BRMP and in cooperation with extramural organizations.

Task B. Purpose of this contract is to confirm the stated properties of BRM preparations. Studies are carried out to to evaluate and verify the potential of each BRM to reduce tumor growth in in vivo animal tumor models to augment immunizing capability in animal tumor models, to evaluate effectiveness and mechanisms of each biological reponse modifier by in vitro tests, to determine a biologically effective time and dose of administration and a nontoxic biologically effective dose.

Accomplishments to Date:

Task A. Currently, this contract provides for storage and distribution of approximately 30 different biologics in quantities ranging from two or three to 4,000 vials for a given biologic. This contract has performed general safety, pyrogenicity, endotoxin, mycoplasma, bacterial, viral and dosage testing on three monoclonal antibody preparations in preparation for clinical evaluation. The contract has also provided capability in the analysis and collection of information in preparation of master files and IND applications on monoclonal antibody for submission to FDA for clinical trial approval.

Task B. This contract has developed in vivo antitumor assays using 3-methylcholanthrene induced fibrosarcoma (Meth A), Lewis lung and Maloney murine leukemia virus induced leukemia tumors, in vitro B-cell assays to measure augmentation of antibody response, and in vitro assays to measure biological activity of various lymphokine/cytokine preparations. Using these assays the contract has evaluated antitumor potential of maleic anhydride-divinyl either, muramyl dipeptide, azimexon, and carbetimer. The contract has also evaluated preparations of macrophage activating factor, colony stimulating factor, interleukin 2 (T-cell growth factor) and interleukin using specific in vitro biologic assays for potency.

Future Plans:

Task A. The contract must: (1) Develop an inventory system for the receipt, storage and distribution of biologicals and tumor cell lines indicating source, description, required storage condition, storage location, restriction, if any, on disposition and uses, how dispensed, who received and to whom and date of shipment, with documentation that product was received. Aseptic facilities should be provided to dispense both solid and liquid reagents into aliquots and to label vials and other containers. (2) Assay preparations of biological response modifiers for microbiologic agents by performing tests for fungal, bacterial, mycoplasma and cytopathic viral contaminants; perform tests to determine pyrogenicity and

endotoxin levels; carry out general safety testing and preclinical evaluations of safe dosage regimen and route of administration; assay preparations for protein and antibody concentration composition when relevant. All testing should conform to FDA specificiations. (3) Provide capability to analyze and collate information in the proper format for submission of relevant master file and IND applications to FDA for clinical study approval.

Task B. The contract should continue to develop basic test procedures for: (1) Determination of the antitumor property of biological response modifiers using two to three selected in vitro passaged tumors for transplantations to mice; (2) determination of adjuvanticity measured by the in vivo induction of tumor specific immunity using the same two-three transplantable tumors; (3) assays for tumor cytotoxicity and/or cytostasis when the biolotical response modifier is incubated with in vitro grown tumor cell lines, either in the presence or absence of defined lymphoid or macrophage cell populations; (4) assays for the effect of biological repsonse modifiers on the in vitro induction of antitumor cytotoxic lymphoid cells andYor for the effect of biological response modifiers on susceptibility of tumor cells to lysis by cytotoxic cells; (5) assays for lymphokines/cytokines using relevant in vitro biological assays; (6) assays of antibody mediated, tumor cell binding and complement and lymphoid cell dependent tumor cell lysis; (7) assays of antibody binding to discrete subpopulations of mouse or human lymphoid cells and determinations of altered lymphoid cells function in blastogenic and cytotoxic assays; (8) activation of macrophage mediated tumor cell lysis and cytostasis; and (9) augmentation of antibody response with B-cell assays.

Provision, maintenance and transfer of tumored laboratory animal models for investigation. Present contractor is Litton Bionetics Inc. Estimated first year award, $336,000, five years.

The small laboratory animal maintenance contract with Litton Bionetics was established to provide facilities to house and carry out manipulations on small laboratory animals including mice, rats, hamsters, and rabbits. An average of seven senior investigators has utilized the facility at all times for the performance of an average of 15 simultaneous experimental tasks or projects.

Many of the tasks provided by the contractor involve holding of normal animals prior to experimental manipulation at NIH. The contractor provides transportation of the necessary animals between the contract facility and NIH on a daily basis. The contractor staff provides housing, watering, and feeding of the animals. In addition, animals which have been experimentally manipulated are observed by the contractor's staff who perform mortality checks and record data as necessary. The staff has the responsibility of notifying individual investigators when experimental animals have expired, are sick or have changed in their status.

The contractor has provided animal rooms which meet government regulations for the containment of hazardous substances. The containment rooms are used for carcinogenesis experiments where animals are exposed to actual or potential carcinogens for the induction of experimental tumors. There are no containment facilities in the Clinical Center which would permit carcinogenesis experiments on small animals to be carried out without exposure to personnel to hazardous chemical substances. The contractor's animal rooms also provide for the safe holding of animals treated with radioactive compounds which can be potentially hazardous to personnel involved in the animals' care.

The capacity to house animals treated with hazardous substances continues to be essential. Contractor support personnel will be required to monitor the health of experimental animals and to record data. Expected average housing needs include 5,000 mice, 100 rats, 1,000 hamsters, 25 rabbits. Changes in the interests of the individual laboratories may require changes in the proportions of various laboratory animals housed. The contractor, in conjunction with the project officer, must be flexible in determing the proportions and absolute numbers of animals to be housed at any particular time within a pre-established ceiling of total capacity.

Planning and conference support service. Present contractor is JWK International Corp. Estimated first year award, $350,000, five years.

This contract has served as a resource to the entire division to meet various planning and conference support needs. As these requirements arise on a sporadic basis, the use of a contract is the most expeditious and cost effective method of procuring these services.

The contractor has provided slides, graphics, and other logistical support for the division and for the DCT Board of Scientific Counselors. The contractor produced verbatim transcripts of important meetings as well as a summation of the proceedings. For example, meeting materials and proceedings of each meeting of the BSC were produced as were materials for program working meetings of the BRMP, the PROD (Previous Reviewed Old Drugs) series of meetings, and the more recent NCI Symposium on Drug Resistance. The contractor also provided services to staff to prepare for various meetings such as those regarding Kaposi's sarcoma. Materials for intramural site visits were reproduced by the contractor for distribution to members of the site visit team and the Board of Scientific Counselors.

It is anticipated that the contractor will continue to provide similar services in the future at approximately the same level of effort as in recent years. The Office of the Director and the Board of Scientific Counselors and its committees will continue to need support of both logistic and material nature for its many activities, such as regularly scheduled meetings, workshops and conferences.

This will be recompeted as a minority small business set aside.

The Board approved eight month extensions for three of the contractors working on application of a human tumor clonogenic assay to new drug screening—UCLA, Mayo and South Texas—and a five month extension for the other, the Univ. of Arizona. Extension of the first three will cost $554,200, while the Arizona extension will be at no cost.

The four will now have common expiration dates, in FY 1984. The Board held off concept approval for the recompetition of the four contracts, preferring to wait until the extensions provide more data on the results of the work so far. Staff had asked for recompetition, with the work scaled down somewhat, to about $680,000 a year total from the $900,000 it has been costing.

The process has found 14 active compounds out of 79 which had been inactive in the other DCT screens. Some Board members felt that was insufficient to justify continuing the project, and Elion moved for disapproval. The vote was seven to seven, so Chairman Samuel Hellman broke the tie, voting against the motion. A subsequent motion by Calabresi to turn down the concept at this time, pending submission of more data, was approved.

Noncompetitive renewal concepts were approved for:

- Partial support of the Institute of Laboratory Animal Resources, contractor National Academy of Sciences, $32,000 first year, five years.
- Antitumor prescreen studies and development, in vitro and in vivo, and a study of potential antitumor agents from marine and other unique sources, contractor Microbial Chemistry Research Foundation, $265,000, first year, three years.
- Supportive services in virology, immunology and tissue culture, contractor Biotech, $100,000, first year, 2½ years.

NCI ADVISORY GROUP, OTHER CANCER MEETINGS FOR JULY, AUGUST, FUTURE

7th International Congress of Radiation Research—July 3-8, Amsterdam. Contact Dr. Arthur Upton, Finance & Travel Committee, Institute of Environmental Medicine, NYU Medical Center, 550 First Ave., New York 10016.
11th International Symposium for Comparative Research on Leukemia and Related Diseases—July 3-8, Cambridge, England. Contact Dr. David Yohn, Secretary General, Suite 302, 410 W. 12th Ave., Columbus, Ohio 432210.
First International Symposium on Tumors of the Urinary Bladder—July 4-6, Intercontinental Hotel, Paris. Contact Saad Khoury, M.D., Clinique Urologique Hosplital de la Pitie, 83, Boulevard de 1'Hospital, 75634, Paris Cedex 13, France; or James Karr, PhD, Roswell Park Memorial Institute, 666 Elm St., Buffalo, N.Y. 14263.
Oncogenes and Cancer—First Terry Fox Cancer Research Conference. Contact the Conference Secretary, British Columbia Cancer Research Center, 601 W. 10th Ave., Vancouver, B.C. V5Z 1L3, Canada.
Standardization in the Production and Use of Monoclonal Antibodies—July 6-9, Paris. Contact M. Barme, Institut Pasteur, 25 rue du Roux, 75015 Paris, France.
5th World Conference on Smoking or Health—July 10-15, Winnipeg. Contact K. Baumgartner, Canadian Council on Smoking or Health, 725 Churchill Ave., Ottawa, Ontario K1Z 5G7.
3rd International Conference on Oxygen Radicals in Chemistry & Biology—July 10-15, Munich. Contact Kongresswesen der GSF, Ingolstadter Landstr. 1, 8042 Neuherberg/Post, Oberschleissheim, Federal Republic of Germany.
Cancer Regional Studies Review Committee—July 11-12, NIH Bldg 31 Rm 7, open July 11 8:30-9:30 a.m.
Laboratory Workshop on Affinity Electrophoresis of Glycoconjugates—July 13-15, Copenhagen. Contact Glycoconjugate Workshop, The Protein Lab, Sigurdsgade 34, DK-2200, Copenhagen N, Denmark.
Biometry & Epidemiology Contract Review Committee—July 14-15, NIH Bldg 31 Rm 4, open July 14 9-9:30 a.m.
NTP Panel on Chemical Carcinogenesis Testing & Evaluation—July 15, NIH Bldg 31 Rm 9. Subgroup on Data Requirements from Prechronic Studies.
Cancer Preclinical Program Project Review Committee—July 19-20, Bethesda Linden Hill Hotel, open July 19 9-10 a.m.
Predictive Drug Testing on Human Tumor Cells—July 20-22, Zurich. Contact Dr. V. Hoffman, Div. of Oncology, Univ. Hospital, 8091 Zurich, Switzerland.
International Conference on Head & Neck Cancer—July 22-27, Baltimore. Contact Program of Continuing Education, Univ. of Maryland School of Medicine, 10 S. Pine St., Baltimore 21201.
Clinical Cancer Program Project Review Committee—July 25-26, NIH Bldg 31 Rm 10, open July 25 8:30-10 a.m.
Cancer Centers Support Grant Review Committee—July 28-29, NIH Bldg 31 Rm 7, open July 28 8:30-9:30 a.m.
8th International Congress of Reproductive Immunology—July 31-Aug. 5, Oxford, England. Contact Dr. John Shubak-Sharpe, Dept. of Virology, Univ. of Glasgow, Glasgow G11 5JR,U.K.
American Society for Pharmacology & Experimental Therapeutics—Aug. 7-11, Philadelphia. Contact Dr. Warren S. Chernick, ASPET '83, Hahnemann Univ., Broad & Vine Streets, Philadelphia 19102.
Interagency Collaborative Group on Environmental Carcinogenesis—Aug. 10, NIH Bldg 31 Rm 4. Contact Dr. Herman Kraybill, phone 301-496-1625.
Oncology in 1983—Aug. 16-19, Norris Cotton Cancer Center, New Hampshire. Contact Jane Bassick, Projects Coordinator, NCCC, Dartmouth-Hitchcock Medical Center, Hanover, N.H. 03756, phone 603-646-5546.
Expanding the Capabilities of the Tumor Registry: A Collaborative Effort—Aug. 17-19, Tampa Marriott Hotel.1983 Florida Registry Workshop. Contact Florida Cancer Council, 1001 S. MacDill Ave., Tampa 33609, phone 813-253-0541.
2nd International Congress of Reproductive Immunology—Aug. 18-20, Kyoto, Japan.
Early Breast Cancer Detection/Nutrition & Cancer—Aug. 19, Denver. Contact Ms. Midge Cullis, Director of Professional Education, American Cancer Society, 1809 E. 18th Ave., Denver 80218.
5th International Congress of Immunology—Aug.21-27, Kyoto. Contact Japanese Society for Immunology, Inst. of Virus Research, Kyoto Univ., Kawaracho Shogoin, Sakyo-ku, Kyoto 606, Japan.
Viral Oncogenesis, Cellular Interactions, Cancer Biology, Immunology, Treatment—Aug. 22-26, New London, N.H. Contact Dr. Alexander Cruickshank, Gordon Research Conferences, Colby-Sawyer College, New London 03257, phone 603-526-2870.
13th International Conference of Chemotherapy—Aug. 28-Sept. 2, Vienna. Contact Prof. Dr. K. Karrer, President, Institute for Cancer Research, Univ. of Vienna, Borschkegasse 8a, A-1090, Vienna, Austria.
Radiolabeled Cellular Blood Elements: Achievements, Challenges, & Prospects—Aug. 29-Sept. 9, Maratea, Italy. Contact Prof. M.L. Thakur, Div. of Nuclear Medicine, Dept. of Radiation Therapy & Nuclear Medicine, Thomas Jefferson Univ. Hospital, 11th & Walnut Sts., Philadelphia 19107.
2nd International Conference on Gynecologic Cancer—Aug. 30-Sept. 2, Edinburgh, Scotland. Contact Dr. Paul Morrow, Women's Hospital, 1240 N. Mission Rd., L903, Los Angeles 90033, phone 213-226-3397.

FUTURE MEETINGS

Cancer Nursing: Changing Times—Nov. 7-8, Baltimore, Md. Johns Hopkins Medical Institutions continuing education course. Contact Program Coordinator, Turner 22, 720 Rutland Ave., Baltimore 21205, phone 301-955-6046.

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.