THE CANCER LETTER

Vol. 10 No. 41
Oct. 26, 1984

Subscription $150 year North America
$175 year elsewhere

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NCI PLANNING TO SWITCH DRUG DEVELOPMENT EMPHASIS FROM COMPOUND TO HUMAN CANCER ORIENTED STRATEGY

NCI's Div. of Cancer Treatment has proposed a major change in its Drug Screening Program which would switch emphasis from a compound oriented effort to a disease oriented strategy using human

(Continued to page 2)

In Brief

GREGORY CURT NOMINATED DCT DEPUTY; DCPC SEEKS OCCUPATIONAL CANCER, PREVENTION BRANCH CHIEFS

GREGORY CURT, who has been special assistant for clinical affairs to Div. of Cancer Treatment Director Bruce Chabner, has been nominated for the position of DCT deputy director. The official appointment has yet to be made by HHS Secretary Margaret Heckler, but Curt is now serving as acting deputy director. The deputy job has been vacant since Saul Schepartz left last June, although Arnold Welch has been working with Chabner in that capacity. Chabner said Welch would stay on as a special assistant and will be program director for the National Cooperative Drug Discovery Groups.... **TWO KEY** DCT staff departures: Edwin Jacobs, assistant chief of the Clinical Investigations Branch who served as acting chief for extended periods, leaves Oct. 26 to return to his native San Francisco. Jacobs left UCSF, where he headed medical oncology, in 1976 to join CIB, the branch which works with the clinical cooperative groups. Cathy Thomas, whose 31 years with NCI included a long stretch as secretary to Vincent DeVita before he became NCI director, retired earlier this month. She more recently has handled most of the management details of the DCT Board of Scientific Counselors.... **DIV. OF CANCER** Prevention & Control is attempting to recruit two branch chiefs— the Occupational Cancer Branch and Cancer Prevention Studies Branch. They are tenured positions and may be filled by medical officers or health scientist administrators at the GM-15 level. Salary ranges from $50,495 to $66,400, and physicians may be eligible for comparability pay up to $10,000 a year. Candidates must submit an SF-171 (personal qualifications statement), a CV and bibliography to NCI, Personnel Office, Bldg. 31 Rm. 3A32, Bethesda, Md. 20205, or phone Jerry Chambers or Janet Gregory, 301-496-6862.... **INDUSTRIAL MANEUVERS** related to the cancer field: Damon Biotech has acquired a majority interest in Biotherapy Systems Inc., a company founded by Ronald Levy, Richard Miller and Barnet Adelman to conduct research into and develop products for the diagnosis and treatment of cancer. Levy and Miller developed monoclonal antibodies for the treatment of B-cell lymphoma. Siemens Medical Systems has entered into a marketing agreement with BSD Medical Corp. for marketing and distribution of the BSD hyperthermia systems in the U.S. marketing and distribution of the

DCT, DCE Boards Angered When NCI Ignored In AIDS Money Amendment
... Page 6

DCT Board Okays 11 Concept Contract Recompetitions
... Page 3

NCI Advisory Group, Other Cancer Meetings
... Page 7

RFPs Available
... Page 8

DRUG DEVELOPMENT TO USE HUMAN TUMOR CELL LINES FROM MAJOR MALIGNANCIES

(Continued from page 1)
tumor cell lines from the major cancers such as lung, colon, breast, ovarian, CNS and melanoma.

The division's Board of Scientific Counselors last week expressed support for the new thrust; a committee of Board members will work with DCT in drawing up details.

Michael Boyd, DCT associate director and head of the Developmental Therapeutics Program, noted that the Board previously had approved a disease oriented in vitro screen using established cell lines when it went along with the staff's recommendation earlier this year to establish the Lung Cancer Drug Discovery Project. The program also has been using the Human Tumor Colony Forming Assay as a disease oriented in vitro screen since 1982.

Historically, the Drug Development Program from its inception through 1974 used the L1210 as the primary screen for thousands of candidate compounds each year. In 1975, the concept was introduced for initiating long range experiments in drug screening, leading to use starting in 1976 of the P388 prescreen and a panel of tumors to screen for agents missed by the L1210. A prospective study of animal/human correlations was initiated. In 1982, the tumor panel was modified.

Boyd reported to the Board last week these conclusions from those experiments:

*Tumor panel screening can identify agents that would have been missed by the L1210.

*The modified tumor panel will detect >90 per cent of the actives detected by the full original tumor panel.

*The majority of disease oriented phase 2 trials of agents selected by the tumor panel have not shown useful levels of clinical activity; there is no apparent correlation between efficacy in a preclinical model and clinical utility based on tumor type.

*The Human Tumor Colony Forming Assay screen detects new actives missed by the P388 in vivo or in vitro.

*Clinical activity of HTCFA screened actives is as yet unknown.

*Technical, logistical, and cost considerations make large scale, disease oriented screening with the HTCFA difficult to achieve.

Boyd suggested these as possible reasons for difficulties in clinical testing of drug candidates that result from compound-oriented screening:

—There is no basis for detection/selection of drug candidates with disease specific activity in relevant preclinical systems.

—Current phase 1 trials generally are not specifically disease oriented, i.e. trials generally are done in highly heterogeneous patient populations.

—Phase 2 trials are typically conducted in a broad variety of tumor types selected empirically.

—Conclusive results concerning critical target populations are very slow to achieve.

About 1,000 compounds are anticipated entering the HTCFA screen, 70 are expected to show some activity and be considered based on further selection criteria, 20 are expected to undergo formulation and toxicology, with 10 entered into clinical trials.

Boyd said that the proposed new disease oriented strategy would run 10,000 compounds a year through a screening panel of human tumor cell lines (15-20 lines each) from lung, colon, breast, ovarian, CNS and melanoma. He listed as potential advantages of in vitro screening with cell lines:

—Extensive availability of well characterized cell lines with widely divergent morphological, biochemical, metabolic and growth features.

—Relative simplicity; they are amenable to large scale screening.

—Sensitivity; screening is possible on very small amounts of synthetic or natural products.

—Reproducibility; potential for determination of selectivity, thus amenable to disease oriented screening.

Compounds showing high selectivity for specific tumor types would be selected for high priority development to clinical trials. This would include comprehensive preclinical pharmacology studies in two species incorporated within preclinical toxicology studies. Specific disease oriented phase 1/2 trials in appropriate populations would follow.

Compounds with nonselective activity would undergo further evaluations in tumor panels or other in vivo animal models.

Here's how comparative costs for the screens break down:

*P388 prescreen—10,000 compounds a year, screening cost per compound, $256.

*Tumor panel—200 compounds a year, $10,787 per compound.

*HTCFA—300 compounds a year, $2,373 per compound.

*Disease oriented cell line panels (six panels, 90 cell lines total)—10,000 compounds a year, $300 per compound.

Boyd suggested a schedule for implementing the new screen, already started in 1984 with the Lung Cancer Drug Discovery Project, to extend into 1987 before it is fully developed. Large scale screening for the LCDDP would begin in 1985, with 10,000 compounds being screened and model development work

starting for ovarian, CNS and colon models. In 1986, screening models for lung, ovarian, CNS and colon would be at a screening level of 10,000 compounds a year. Model development work would be initiated for breast tumors and melanoma. The full, 90 cell line, six tumor system would be operating at a capacity of 10,000 compounds a year in 1987.

"What we really need is a general idea from you," DCT Director Bruce Chabner said to the Board. "Are you sold enough to encourage us to go ahead and continue to explore this idea? We won't commit any money immediately. The important question is, How do we develop compounds found active? How much in vivo screening should we do? Should we go to clinical trials immediately? Do you think this is sufficiently attractive to pursue?"

"I think we answered that when we approved the lung cancer project," Board member Carol Portlock said.

"We think we'll have the answers soon on the tumor panel," Chabner said. "We feel it is not useful. As we phase that out, we will phase this one in."

"I take it the Board's answer is yes, go ahead," Board Chairman Samuel Wells said. He named Portlock, Susan Horwitz and James Goldie as the Board's representatives on an ad hoc committee to assist in designing the new program.

DCT BOARD GIVES CONCEPT APPROVAL TO RECOMPETITION OF 11 CONTRACTS

The Board of Scientific Counselors of NCI's Div. of Cancer Treatment gave concept approval to the recompetition of 11 contract supported projects with an estimated total annual cost of $5.5 million at the Board's meeting last week. Ten of the recompetitions are in the Developmental Therapeutics (Drug Development) Program.

Concept proposals, with staff descriptions of the projects, follow:

Title: Literature surveillance of natural products. Recompetition of the contract now held by Univ. of Illinois. Estimated annual cost, $110,000, three years. Staff description:

Over 5,000 natural products structures from microbial, plant, and animal sources are reported in the literature each year. A significant per cent of these compounds represent novel structure types which could provide new leads for development of antitumor agents. This is particularly important in the natural products area since natural products provide highly unusual chemical structures which represent entirely new classes of compounds for anticancer screening. To conduct such a search with a limited staff could cover only a small fraction of the available literature. It is clear that a more extensive search program by an institution properly staffed and adequately equipped is necessary for adequate literature coverage.

This is a competitive contract involving surveillance of literature in the natural products area for new and novel compounds which may have potential activity as chemotherapeutic agents against human cancers. The contractor searches through periodicals and provides the Natural Products Branch (1) with listings of new chemical structures found in plants, animals and microorganisms; (2) abstracts and reprints of pertinent articles; (3) lists of many biological properties of these compounds, including antitumor activities, thus providing DTP staff with information that is necessary for selecting and acquiring new and promising compounds that may show anticancer activities. The current contractor is well equipped and adequately staffed to perform thorough searches of the literature in the natural products field. The literature available to the contractor is extensive and comprehensive and the coverage of the field has been excellent.

As natural products are excellent sources for new and unusual compounds, they can provide NCI with many entirely different classes of compounds than those now being used clinically. A continuation of this project is essential for a continuous supply of new agents for testing against tumors. This contract has been extremely valuable to the acquisition program of the Natural Products Branch.

Title: Large scale isolation of antitumor agents from natural sources. Recompetition of a task order contract held by Polysciences, with an estimated annual cost of $200,000, for three years.

Major objectives of this contract are to isolate highly purified bulk drugs from plant and animal materials in large quantities sufficient to meet NCI needs for compounds in clinical trials and advanced preclinical development, and to develop suitable processes for large scale isolations.

During the 15 month period from the inception of this contract in April 1983 to June 1984, the following tasks have been accomplished: (1) extraction, solvent partitions and chromotography of 700 gallons of dolabella, 275 pounds of psorospermum and 1,200 pounds of sesbania pods for final isolation by other groups; (2) isolation of 25 g. of pancratistatin from 130 kg of plant for formulation and toxicology studies; (3) isolation of baccharins B-1, B-2 and B-4 from 4,000 pounds of plant material for tumor panel evaluation; (4) development of a greatly improved procedure for the isolation of camptothecin for analog development; (5) completion of the initial extraction, solvent separation and preliminary chromatography on 8,000 pounds of taxus bark to produce taxol for clinical trials.

The contractor will be required to supply NCI with highly purified compounds isolated from plant and marine animal sources. The major task will be to produce bulk drugs for clinical trials and for advanced developmental work including pharmaceutics and toxicology in quantities from several grams to several kilograms depending on the potency of the compounds NCI needs. Each major assignment will require workup of from several hundred pounds up to 20,000 pounds of plant or animal material. Antici-

pated major projects will include isolations of taxol (in clinical trials), phyllanthoside (in preclinical development), camptothecin (for prodrug synthesis) and pancratistatin (in preclinical development). There are several other pure compounds in tumor panel testing which have good potential to become candidates for advanced development and which will require pilot plant scale isolation if they become preclinical candidates. Pilot plant assignments are regularly reviewed and are subject to change depending on the priority needs of the DTP program for bulk drugs from plant or marine animal sources. In addition to preparing bulk drugs for clinical and advanced preclinical use, the contractor will also be required to isolate smaller quantities of compounds for tumor panel testing and to perform extractions and partial purification of leads in those cases where large amounts of raw material need to be processed to get enough of the active fractions for final chemical isolation and identification of the active constituents.

Title: New fermentation, antineoplastic drug acquisition, evaluation, development and screening. Recompetition of two contracts presently held by Bristol Laboratories and Warner-Lambert, at an estimated total cost of $1,378,200 a year for three years.

This recompetition is for two major fermentation contracts to obtain novel antineoplastic agents. A multitude of different organisms (actinomycetes, yeast, and bacteria) are evaluated for their ability to produce various compounds with varied biological activities. These compounds are isolated and evaluated in the NCI in vivo screens. The prescreens, media, environmental conditions, etc., are changed periodically to maximize the chance of producing and isolating new compounds of interest. In addition, varied isolation techniques to obtain different organisms are being used.

Bristol has isolated and submitted seven in vivo active compounds of novel structure type during the first 18 months of the current contracts while Warner-Lambert has submitted 15 compounds during the same period. One compound from Warner-Lambert, phosphotrienin, has entered toxicology studies and another recently passed Decision Network point 2A and is undergoing formulation and analytical studies. Much of the most recent effort at Bristol has been concentrated on development of production methods and preformulation work on two promising leads which are likely to become Decision Network 2A candidates in the next year. The emphasis on both contracts has been entirely directed toward discovery of new structure types with antitumor activity and the majority of the compounds submitted are sufficiently unusual chemotypes to be considered as new classes of lead compounds.

It is intended that this contract will continue to evaluate new organisms using varied prescreens and environmental conditions to obtain novel antineoplastic agents and to continue the development of promising leads.

DCT Director Bruce Chabner said that, depending on the response to the RFP, "we might fund only one contract this time."

Title: Synthesis of congeners and prodrugs. Recompetition of three contracts held by the Univ. of Alabama, George Tech, and State Univ. of New York. Total estimated annual cost $550,000, five years.

Prior to initiation of this project in Sept. 1982, no mechanism existed that allowed for synthesis work that was necessary to advance novel but flawed lead compounds possessing poor solubility, stability and/or narrow spectrum activity to DN2 level (an activity level that is required of compounds that are presented to the Drug Development Committee). The objective of this contract was to fill this gap since neither acquisition nor resynthesis was geared toward such targeted drug synthesis. The three congener and prodrug synthesis contracts have demonstrated their utility in accomplishing the stated goals, i.e. to synthesize compounds with improved stability, solubility and/or wider spectrum of activity necessary for advancement to DN2 level. The diverse nature of the targeted compounds demanded a wide spectrum of chemical expertise such as neterocyclic-, sugar-, and coordination chemistry. A variety of approaches was brought to bear in this highly targeted drug design effort: Topliss Strategy, Craig Plots, and in one selected case, Hansch QSAR; isosteric and heteratomic substitution were employed in improving biological activity. The advantages of enzymatic vs. chemical degradation of prodrugs were explored.

The project has been highly productive: (1) NSC 363,812, a platinum complex related to carboxyphthalato platinum has passed DN2 level because of its attractive solubility (0.6%), outstanding stability (t 90> 90 hours) and its excellent activity against a subline of L1210 resistant to cisplatin (ILS > 200 with 30 day survivors). Additional leads have been developed: (2) NSC 361,456 a congener of the pyridinyl diazohydroxide NSC 159,159, has demonstrated DN2 level activity in four tumor panel test systems. In contrast to its parent, it possesses good stability, solubility and can be easily purified; (3) several water soluble prodrugs of mitindomide have been prepared. The most promising, NSC 373,529, will be presented to the Decision Network in the coming months. This derivative retains the activity against both the s.c. and i.p. implanted L1210, and in contrast to mitindomide, it does not require the addition of a base for formulation. Additional series are at various stages of development. Thus, a new lead related to isopropylpyrrolizi, NSC 278,214, has emerged as a viable candidate and replacement for the insoluble and unstable parent compound.

We plan to continue this project since it has been successful in overcoming the stated obstacles and in delivering novel DN2 candidates. Furthermore, we propose to expand the scope of this drug design strategy by utilizing three dimensional molecular modeling, i.e. preferred confirmation studies, comparison of molecular shapes, and computation of molecular properties.

Title: Evaluation of cogeners and purified natural products. Recompetition of a contract held by Southern Research Institute. Estimated annual cost, $310,000, three years.

This contract utilizes a variety of murine leukemia and solid tumor models to evaluate the antitumor activity of congeners of new lead antitumor agents. Structure activity studies are conducted under well controlled experimental conditions in order to guide future synthetic efforts and identify the most promising members of a class for further development. Among the new congener series, emphasis is placed on the testing of prodrugs and other rationally designed congeners synthesized under contracts monitored by the Drug Synthesis & Chemistry Branch. The parent compound for each series has demonstrated antitumor activity, but usually for reasons of solubility or stability, or perhaps limited activity and therefore has a poor prognosis for clinical development. In addition, other special studies are conducted to answer specific questions which arise during the course of a drug's development. These secondary evaluation studies often use the same assays used for primary screening, but the experimental protocols are custom designed depending on the known characteristics of the compoound or compound class. Also, purified natural products isolated under contract to the Natural Products Branch are tested on this contract. These products usually require special handling and nonprotocol vehicles for administration.

During the past 16 months since this contract was awarded, contract studies have identified several congeners with greater potential for clinical development than the lead compounds. Illustrative of ongoing studies is the anthrapyrazole series, the testing of which was initiated under a preceding contract with similar workscope. At least 30 of more than 100 congeners synthesized demonstrated a %T/C greater than 200 with one or more cures in the P388 leukemia model. A number were identified for additional testing and finally one, NSC 349,174, was selected for development based on its wide spectrum of significant activity against both i.p. and s.c. implanted tumors, following both i.p. and i.v. treatment. The anthrapyrazoles are an excellent example of how coordination of synthesis, initial testing, selection and detailed evaluation can optimize a primary screening discovery to produce a highly effective agent in experimental models. Other current projects have resulted in the selection of (1) NSC 363812D, a platinum complex that retained good activity against the subline of L1210 resistant to cisplatin. Unlike carboxyphthalato 1,2-diaminocyclohexane platinum, this complex has sufficient solubility and stability for formulation development and was selected for further development by the DN committee in March 1984; (2) NSC 361456D and 369035D, two congeners of NSC 159159, which, compared to the parent compound, demonstrate greater activity in initial screening and greater stability. Although NSC 159159 had demonstrated activity in a number of tumor systems, its instability had prevented its further development. Once additional screening data have been accumulated, one of the congeners will be presented as a candidate for development to clinical trial; (3) NSC 373529D, a water soluble congener of mitindomide which retains activity against both the i.p. and s.c. implanted L1210 leukemia. The congener will be presented to the DN committee as a replacement for mitindomide, the development of which was delayed due to concern over the formulated form of the drug. Other new series of antitumor agents are under active evaluation, but most cannot be discussed because of confidential agreements with suppliers. Examples of secondary evaluations conducted under this contract to facilitate the development of drugs to clinical trial include comparison of bulk drug with its experimental formulation, testing of compounds against i.c. implanted tumors and reversal of activity by natural metabolites.

Plans are to continue this valuable resource for the drug development program at the same level of effort. The contract provides both the flexibility necessary to custom design protocols to meet requirements of individual agents and overcome development problems, and the well controlled testing procedures needed in drug development to maximize the potential of lead compounds identified in the general screening program.

Title: Production of bulk chemicals and drugs. Recompetition of a contract held by Monsanto Research Corp. Estimated annual cost, $725,000, three years.

This is a service project for developing existing or new processes, procedures, and techniques for the preparation, and the large scale production of compounds not readily available from the original supplier or commercial sources in the quality and/or quantities needed by the program. The materials assigned for preparation and isolation are needed for experimental and clinical use. Assignment of materials for preparation will originate with the Pharmaceutical Resources Branch and involve a wide variety of materials. The major portion of the project will be devoted to the preparation of kilogram quantities of materials requiring pilot plant facilities. All materials prepared will be fully characterized and will be of high purity. Solubility and stability studies and cost data will be provided upon request.

This contractor developed the government patented, new and improved procedure for the large scale preparation of high purity methotrexate and during the past year prepared 45 Kg at substantial savings to the government. An additional 45 Kg are being prepared and will be available in the near future. The contractor also developed a new, practical procedure for the large scale preparation of high quality homofolic acid, the starting material for emofolin, and prepared over 20 Kg of the material. The contractor also recently prepared multikilogram quantities of methyl G, ICRF-187 and indicine N-oxide. Additional synthesis of ICRF-187 is in progress.

This resource contract will continue to be utilized for the development of existing and/or new processes, procedures and techniques for the prepar-

ation of chemical substances and the large scale (kilogram quantities) production of compounds needed by the program that are not readily available from the original supplier or commercial sources in the quality and/or quantity required. The materials to be assigned for preparation and isolation are needed for preclinical and clinical studies. The major portion of the project will be devoted to the preparation of kilogram quantities of materials. All materials prepared will be fully characterized and will be of high purity.

Title: Preparation of radiolabeled materials. Recompetition of contracts held by Research Triangle Institute and SRI International. Estimated annual cost, $500,000, three years.

This service project is devoted to the procurement, either by synthesis or from commercial sources, of radiolabeled materials needed and requested by various areas of DCT. The compounds scheduled for preparation are not available from commercial sources and involve a wide variety of structures. Materials that are available commercially are also obtained by the contractors, checked for purity, and repurified, if necessary. The contractors also handle the storage and distribution at the direction of the project officer, and perform necessary analytical work for labeled materials.

All radiolabeled materials, whether to be prepared or obtained from commercial sources, are assigned by the Pharmaceutical Resources Branch upon request from other NCI investigators and/or NCI contractors. The materials are used primarily in preclinical pharmacological and toxicological studies, and clinical investigations. All requests for labeled materials are reviewed by proper authorities prior to assignment to the contractors. Only materials that have passed DN2A or beyond are considered for radiolabeling.

During the past year, 15 labeled compounds were prepared, five were obtained from commercial sources and 150 shipments of labeled substances were made during the same period. A wide variety of labeled compounds were prepared including 14C labeled adriamycin, daunorubicin, HMBA, WR-2721, ara-AC, and 3H labeled ara-AC and tiazofurin.

This resource project will continue to be used for the preparation of radiolabeled compounds not readily available from commercial sources. A wide variety of compounds of varying structures will be prepared and the amount of radioactivity will vary in quantity and specific activity according to the intended use and in accord with safe handling procedures.

The project will also provide for obtaining radiolabeled materials from commercial sources. Materials so obtained will be checked for radiopurity and homogeneity.

DTP staff had asked for Board approval of an estimated budget of $315,000 a year. But Board memeber Alan Rosenthal said, "With the expansion of programs needing radiolabeled material, I'm concerned about the budget not being big enough."

"We're not entirely comfortable with this either," Boyd said. "We may have to come back for more."

"How many compounds do you get for $315,000?" Rosenthal asked. "Not many," Boyd responded.

"Do you want us to change the amount?" Chabner asked. "Make it $500,000?"

The motion to approve the concept included raising the figure to $500,000 a year, and it passed without dissent.

(Remaining concepts approved by the Board will appear next week in **The Cancer Letter**).

AMENDMENT ADDS MONEY FOR AIDS AT OTHER AGENCIES, BUT NOT FOR NCI

Members of two NCI boards of scientific counselors were incensed last week when they learned that a last minute addition to the HHS appropriations bill added $11.2 million for AIDS programs, not one cent of which will go to the one agency which has done the most in combatting the problem—namely, NCI.

Sen. Alan Cranston (D.-Calif.) authored the amendment and directed that the extra money go to the Center for Disease Control, the National Institue for Allergies & Infectious Diseases, and the Alcohol, Drug Abuse & Mental Health Administration.

NCI plans to spend $26.8 million on AIDS related research, including development of diagnostic kits and vaccines, made possible by the magnificent work of NCI's Robert Gallo and his colleagues. All of that money will come out of NCI's 1985 research budget, "redistributed" from other programs.

The Div. of Cancer Treatment and Div. of Cancer Etiology Boards of Scientific Counselors both unanimously approved resolutions calling on Congress to add money to NCI's FY 1985 budget for AIDS research.

"I can't conceive that further research on AIDS won't also contribute to cancer research," Paul Calabresi, member of the DCT Board, said. "I would like for the Board to go on record calling for addtional resources for NCI to permit continued AIDS research without hurting the rest of the program."

"The seminal work on AIDS has been done at NCI," Board member Dani Bolognesi said. "No one else is as qualified to continue it."

"No one else is capable of doing the drug development," DCT Director Bruce Chabner added.

Chabner and Clinical Oncology Program Director Samuel Broder, whose intramural program has treated about 200 AIDS patients at the NIH Clinical Center, complained about the serious problem NCI and NIH are facing with the growing shortage of nurses at the Clinical Center. The government personnel freeze and limits on the number

of positions allocated to NIH have reduced the nursing staff to the point where "we can't asking the fine nurses who serve in our wards to do more than is humanly possible," Broder said.

The Board's resolution also called attention to the shortage of nurses and technicians.

Hilary Koprowski, member of the DEC Board, said that leaving NCI out of the AIDS funding in the Cranston amendment "is a scandal." Koprowski and other members drafted a letter requesting additional money for NCI which the Board approved unanimously.

Signs of a power struggle within NCI over the AIDS related programs surfaced at both Board meetings last week. Chabner told his Board, "Contrary to what appeared in The Cancer Letter, intramural AIDS research will remain in this division."

He was referring to an item in the Oct. 5 issue which was based on the report of the AIDS subcommittee. The Cancer Letter said, "... The new associate director for biological carcinogenesis in the Div. of Cancer Etiology now being recruited... will have primary responsibility for both intramural and extramural AIDS research." The subcommittee report said, "The key individual who will shoulder both the intra and extramural efforts will be the new associate director in DCE."

Chabner also told his Board there had been discussions about moving Gallo from DCT to DCE, where most NCI virology work has been located. Chabner left no doubt he opposed that move and indicated Gallo would remain in DCT. However, DCE Director Richard Adamson told his Board that he would reopen the Gallo issue when his new AD is on board. "In my opinion, Dr. Gallo belongs in this division," Adamson said.

NCI ADVISORY GROUP, OTHER CANCER MEETINGS FOR NOV., DEC., FUTURE

Leukemia Society Annual Symposium—Nov. 2, Alameda Plaza Hotel, Kansas City, Mo. Contact Jan Johnston, Univ. of Kansas Medical Center, 39th & Rainbow Blvd., Kansas City, Kan. 66103, phone 913-588-4480.

Advances in Hematology—Nov. 2, Boston. Second William B. Castle Symposium. Contact Dr. Andrew Schafer, Hematology Div., Brigham & Women's Hospital, 75 Francis St., Boston 02115, phone 617-732-5840.

Lung Cancer—Nov. 2-3, Cincinnati. Third Cincinnati Cancer Conference. Contact Thomas O'Connor, Medical Staff Education, Bethesda Hospitals, 619 Oak St., Cincinnati 45206.

Cancer Nursing '84—A Developmental Approach—Nov. 5-6, Turner Auditorium, Johns Hopkins Medical Institutions. Contact Program Coordinator, Turner 22, 720 Rutland Ave., Baltimore 21205, phone 301-955-6046.

Cancer Education Review Committee--Nov. 5, NIH Bldg 31 Rm 4, open 8:30-10 a.m.

Div. of Cancer Biology & Diagnosis Board of Scientific Counselors--Nov. 7, NIH Bldg 31 Rm 6, 8:30 a.m., open.

Lung Cancer 1984—Nov. 7-9, Shamrock Hilton Hotel, Houston. Contact Office of Conference Services, Box 131, M.D. Anderson, 6723 Bertner Ave., Houston 77030, phone 713-792-2222.

Chemotherapy Foundation Symposium IV: Innovative Cancer Chemotherapy—Nov. 7-9, Barbizon Plaza Hotel, New York. Phone 212-650-6772.

Workshop on Monoclonal Antibodies and Breast Cancer—Nov. 8-9, San Francisco. Contact Dr. Roberto Ceriani, Bruce Lyon Memorial Research Lab., Children's Hospital Medical Center, Grove & 52nd St., Oakland, Calif. 94609.

Leukemia Society Regional Medical Symposium—Nov. 8-10, Hyatt Regency Hotel, New Orleans. Contact Leukemia Society of American, 800 Second Ave., New York 10017.

High Technology Route to Virus Vaccines—Nov. 8-10, Houston. Contact Dr. Daniel Watanabe, phone 800-231-6388 or 713-785-0532.

Practical Approaches to Oncology--Nov. 9, Holiday Inn, Fargo, N.D. Contact Medical Education, St. Luke's Hospital, 5th St. N. at Mills Ave., Fargo 58122, phone 701-280-5933.

President's Cancer Panel—Nov. 9, Cancer Center of Hawaii, Univ. of Hawaii at Manoa, Honolulu, 9 a.m.-4 p.m., open.

Safety Evaluation & Regulation of Chemicals--Nov. 13-16, Zurich. Contact F. Homburger M.D., Bio-Research Institute, 9 Commercial Ave., Cambridge, Mass. 02141, phone 617-864-8735.

1984 Urologic Tumor Symposium—Nov. 15-17, Memorial Sloan-Kettering Cancer Center, New York. Contact CME Conference Planning Office, C-180, MSKCC, 1275 York Ave., New York 10021, phone 212-794-6754.

Tumors of the Hand and Forearm—Nov. 15-17, New York. Contact American Society for Surgery of the Hand, 3025 S. Parker Rd., Suite 65, Aurora, Colo. 80014.

Cancer Preclinical Program Project Review Committee—Nov. 15-16, Linden Hill Hotel, Bethesda, Md., open Nov. 15 8:30-9:30 a.m.

Lymphoproliferative Diseases: Pathogenesis, Diagnosis, and Therapy—Nov. 16-17, Louis B. Mayer Auditorium, Univ. of Southern California, Los Angeles. Contact Betty Redmon, Coordinator, phone 213-224-7123.

Radiological Society of North America—Nov. 25-30, Washington D.C. Contact A. Swenson, Executive Director, 1415 W. 22nd St., Suite 1150, Oak Brook, Ill. 60521.

National Cancer Advisory Board—Nov. 26-28, NIH Bldg 31 Rm 6. Open all three days for annual program review.

Prevention & Detection of Cancer--Nov. 26-30, Vienna. Sixth international symposium. Contact Prevention & Detection of Cancer, AMEX POB No. 790459, Dallas, Texas 75379.

Clinical Cancer Program Project Review Committee—Nov. 29-30, Biscayne Bay Marriot Hotel, Miami. Open Nov. 29 8:30-10 a.m.

Myelosuppressive Effects of Antineoplastic

Drugs—Nov. 29-30, Doral Beach Hotel, Miami Beach. International symposium preceding annual meeting of the American Society of Hematology. Contact Meniscus Health Care Communications, PO Box 30,000, Philadelphia 19103, phone 215-735-8450.
Biomolecular Events Underlying Cancer--Nov. 29, Roswell Park continuing education in oncology.
Limb Sparing Treatment of Adult Soft Tissue and Osteogenic Sarcomas--Dec. 3-5, NIH Masur Auditorium. NIH consensus conference.
Lung Cancer: Problems and What's New—Dec. 6, Roswell Park continuing education in oncology. Contact Gayle Bersani, RPMI, 666 Elm St., Buffalo 14263, phone 716-845-2339.
Seventh Annual San Antonio Breast Cancer Symposium—Dec. 7-8, San Antonio, Texas. Contact Terri Coltman, Cancer Therapy & Research Center, 4450 Medical Dr., San Antonio 78229, phone 512-690-0655.
Developmental Therapeutics Contract Review Committee—Dec. 10, NIH Bldg 31 Rm 9, open 8:30-9 a.m. ttee--Dec. 10, NIH Bldg 31 Rm 9, open 8:30-9
Smoking and the Workplace—Dec. 11-13, Washington D.C. Contact Society for Occupational & Environmental Health, 2021 K St. NW, Suite 305, Washington D.C. 20006, phone 202-737-5045.
Clinical Cancer Chemotherapy--Dec. 12-16, Delhi, India. Contact David Reed, UICC, 3 rue do Conseil-General, 1205 Geneva, Switzerland.

FUTURE MEETINGS Geneva, Switzerland. 3 rue do Conseil-

EORTC Symposium on Interferon in Cancer Therapy --Feb. 28, Brussels. Abstracts due by Dec. 15. Contact D. Eeckhoudt, EORTC Data Center, boulevard de Waterloo 125, 1000 Brussels, Belgium.
EORTC Symposium on Continuous Infusion Chemotherapy—March 1, Brussels. Abstracts due Dec. 15. Contact as above.
International Workshop on Chromosomes in Sold Tumors—March 3-5, Arizona Cancer Center, Tucson. Jeffrey Trent is program director; speakers include Mary Harper, Peter Nowell, Sydney Salmon, Avery Sandberg, Gordon Sato, J. Scheres, Jacqueline Whang-Peng, and Sandra Wolman. Contact Mary Humphrey, Conference Coordinator, Univ. of Arizona College of Medicine, Tucson 85724, phone 602-626-6044. Medicine, Tucson 85724, phone
Current Research: Springboards for the Future--March 21-22, Univ. of North Carolina, Chapel Hill. Ninth annual symposium marking the scientific dedication of the Lineberger Cancer Research Center. Speakers include Sidney Altman, Stanley Cohen, Carlo Croce, Walter Eckhardt, Robert Gallo, Elliot Kieff, Arnold Levine, Michael Oldstone, Phillip Sharp, and Robert Weinberg. Contact Pam Upchurch, Lineberger Cancer Research Center, UNC-CH, Chapel Hill 27514.
Society for Magnetic Resonance Imaging—March 22-26, Town & Country Hotel, San Diego. Third annual meeting. Deadline for abstracts is Dec. 4. Contact Secretariat, SMRI, 1340 Old Chain Bridge Rd., McLean, Va. 22101.
International Neutron Therapy Workshop: Brachy Vs. Beam Therapy—April 21-24, Hyatt Regency Hotel, Lexington, Ky. Contact Lawrence Beach, General Secretary, Radiation Therapy Oncology Center, Univ. of Kentucky Medical Center, Lexington 40536, phone 606-233-6489.
XIIth International Symposium for Comparative Research on Leukemia & Related Diseases—July 7-12, 1985, Hamburg Congress Centrum, West Germany. Contact Dr. David Yohn, Secretary General, Suite 302, 410 W. 12th Ave., Columbus, Ohio 43210, or Prof. Dr. Friedrich Deinhardt, Max von Pettenkofer Institut, Pettenkoferstrasse 9a, 8000 Munchen 2, Federal Republic of Germany.

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 NO1-CP-51004-74

Title: Resource for xenotransplantation and evaluation of human tissue and cells in athymic nude mice.
Deadline: Jan. 15

The Laboratory of Human Carcinogenesis of NCI's Div. of Cancer Etiology has a requirement for proposals to provide a barrier facility for breeding and experimental management of nude mice which will be given transplants of human tissues and cells. A pyrogen free, self sustaining unshared colony (600-800) of athymic mice is required as the source of the experimental recipients of the human tissues. The contractor should have proven capabilities for performing animal surgery, long term maintenance of experimental mice and preparation of tissues for high resolution microscopy.

The RFP contains a mandatory requirement that offerors must demonstrate in their proposal their ability to facilitate rapid pick up and transplantation of fresh tissues from NIH and its collaborators, most of whom are located within 50 miles of NIH. Litton Bionetics is the present contractor.
Contract Specialist: Odessa Henderson
RCB Blair Bldg Rm 119
301-427-8888

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.