THE CANCER LETTER

Vol. 9 No. 5
Feb. 4, 1983

Subscription $125 year North America
$150 year elsewhere

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PRESIDENT ASKS $989.3 MILLION FOR NCI, BUT MISTAKE IN GRANT ALLOCATIONS MAY LEAD TO ADDITIONAL MONEY

President Reagan's 1984 fiscal year budget for NCI, following the policy of freezing domestic spending at 1983 levels, seeks only a $5.7 million increase, to a total of $989.3 million in the request submitted to Congress Monday. In allocating that money to the various NCI budget mechanisms, Office of Management & Budget and/or HHS

(Continued to page 2)

In Brief

DURANT NEW PRESIDENT OF AACI, ULTMANN NAMED PRESIDENT-ELECT; FARBER CENTER GETS NEW NAME

JOHN DURANT, president of Fox Chase Cancer Center, assumed the presidency of the Assn. of American Cancer Institutes at the organization's meeting last week in Memphis. **JOHN ULTMANN**, director of the Univ. of Chicago Cancer Center, was named president-elect. New members of the board of directors are **ROBERT DAY**, Fred Hutchinson Cancer Center; **ROBERT HICKEY**, M. D. Anderson Hospital; **PETER MAGEE**, Fels Research Institute; and **PAUL MARKS**, Memorial Sloan-Kettering. . . . **SYDNEY FARBER** Cancer Institute is being renamed the Dana-Farber Cancer Institute following announcement that the Charles A. Dana Foundation will contribute a $10 million grant in support of the center's $38 million capital development program. It is the largest grant ever made by the foundation. The money will be given in two phases, as $5 million challenge grants, with the institute required to raise $5 million on a one for one basis and then $15 million on a one for three basis. The fund, projected to reach the $38 million in five years, will constitute an endowment to support strengthening of basic research and clinical programs, creation of new lab research programs and new initiatives in cancer treatment. . . . **ANNUAL MEETING** this year of the Assn. of Community Cancer Centers (Washington D.C., March 11-13) has the theme, "Clinical Research Issues in the Community." Speakers will include **PAUL CARBONE**, chairman of the Eastern Cooperative Oncology Group, and **LAWRENCE DAVIS**, associate chairman of the Radiation Therapy Oncology Group, who will talk about clinical research results from the group perspective; and **EMIL FREIREICH**, head of the Dept. of Developmental Therapeutics at M.D. Anderson-Univ. of Texas System Cancer Center, and **ALAN YAGODA**, acting chief of the Solid Tumor Service at Memorial Sloan-Kettering Cancer Center, who will discuss clinical research results from the centers' perspective. **JOHN YARBRO**, professor of medicine at the Univ. of Missouri, will discuss his plan for "Independent Clinical Research—An Alternative" at the Saturday luncheon. NCI Director **VINCENT DEVITA** will be the keynote speaker on Sunday.

GRANTS POOL FOR '84 SLASHED, BUT ADJUSTMENT COMING; '83 PLAN SET

(Continued from page 1)

officials—for reasons that are not yet clear—did not put enough into research projects to meet department and NIH goals on numbers of grants to be funded. The result:

"Discussions are under way in the Administration as to the appropriate level of funding of research project grants. An adjustment upward will be made," Donald Poppke, budget analyst for NIH in the Office of the Secretary, told ***The Cancer Letter.***

Poppke said, "It is not clear if additional resources" will be requested for NCI to bring research grants up to a more appropriate level or if that will be accomplished by transferring funds from other allocations. "I think that a request will be made for more money," he said.

The budget allocation has a total of slightly more than $378 million for research projects, compared with $393.3 million in 1983. The noncompeting grants pool, representing commitments over which NCI has little control, is up $5 million but the R01-P01 pool for new and competing renewals is down by $20 million.

That is a masssive reduction from a year that was not all that great to start with. NCI expects to fund only about 31 percent of new and competing renewals this year, and staff did not even want to speculate on how far that would drop if the new figure stands.

What made the big cut in extramural funds seem even worse is the projected increase for intramural research of $6.7 million. That's a combination which could bring on a march on Washington.

The additional money for the intramural program will be necessary to cover mandatory within-grade pay increases, the lifting of salary ceilings for those in the higher pay brackets, and other increases in overhead costs charged against the program, Poppke said. It does not represent any significant growth in the intramural program.

NCI executives refused to discuss the situation lest they be accused of "budget busting," a crime in Washington worse even than not swearing allegiance to the Redskins.

It appears that OMB or the department settled on the $989.3 million figure for NCI, and when they covered the various mandatory increases and untouchable commitments, the grants pool received only what was left. The rush to get the budget to Congress did not leave time to rectify the problem.

Since HHS is committed to the policy of funding 5,000 competing grants a year at NIH, and since NCI represents about one fourth of NIH, the department has to put more money in the grants pool, one way or another.

It's not as if NCI was already getting more than its share of any increases. In fact, it is business as usual—shaft NCI, with a percentage increase less than one third that of the NIH average. The budget request for NIH totaled $4.077 billion, an increase of $73 million over 1983. That amounts to a 1.8 percent increase, compared with NCI's .5 percent.

Hearings on the budget proposals by Senate and House appropriations committees will start later this month. Congress seldom accepts the Administration's figures for NCI, either the total or the program allocations. It could be a different situation this year, with great pressures being exerted on Congress to hold down the massive budget deficit.

As it stands now, those programs scheduled for increases, in addition to those mentioned, are:

- Clinical education, up $2 million.
- Cooperative groups, up $2.1 million.
- Cancer control, up $4 million.
- Research and development contracts, up $4.8 million.
- Cancer centers core grants, up $1 million.

Reductions other than in the grants pool would include training, down $1.6 million, and construction, down $1 million.

Meanwhile, back in the current fiscal year, the budget picture cleared up when Director Vincent DeVita told the National Cancer Advisory Board Monday how the Institute proposed to spend the $40 million it will receive this year over the amount received in 1982. The Board's Committee on Planning & Budget considered the proposals Monday night and recommended one major change. The full Board was scheduled to act on the proposals, the 1983 "funding plan," Wednesday.

The funding plan approved by the Board last October called for a 20 percent reduction from recommended levels for all competing grants. After Congress approved the final 1983 total for NCI of $983 million, DeVita and his staff decided to apply some of the extra money toward softening those reductions.

NCI recommended in the new funding plan that the reduction from recommended levels for competing R01 grants be held to 10 percent rather than 20. The 20 percent reduction for P01s would remain.

Several Board members objected. Maureen Henderson said the plan would be perceived as discriminating against program projects, especially at a time when the review of P01s is being modified in a manner which will result in smaller grants. "It will look like a double cut for them," she said. "There's great concern in the scientific community about the change in review of P01s. The 20 percent cut, while R01s are being cut only 10 percent, will send further signals that P01s are out of favor."

"There is a danger in sending the wrong signal," DeVita agreed.

National Cancer Institute Budget Mechanism

	1982 Actual	1983 Estimate	1984 Estimate
Research grants			
Research projects:			
Noncompeting	$257,256	$280,248	$285,262
Administrative supplemental	7,250	6,325	6,473
Competing			
Renewal	50,069	58,677	50,836
New	48,130	47,997	35,488
Supplemental	86	—	—
Subtotal, competing	98,285	106,674	86,324
Subtotal, research projects	362,791	393,247	378,059
Research centers:			
Core grants	75,447	77,021	78,000
Other research:			
Research career program	4,921	5,473	5,627
Cancer task forces	13,945	11,710	12,000
Clinical education program	4,614	6,000	8,000
Cooperative clinical research	38,808	42,294	44,322
Minority biomedical support	1,977	2,014	2,512
Other research	3,392	3,680	3,808
Subtotal, other research	67,657	71,171	76,269
Total, research grants	505,895	541,439	532,328
Training	22,374	25,061	23,470
Research and development contracts	135,659	129,437	134,225
Intramural research	168,181	173,860	180,557
Direct operations	38,416	40,979	42,591
Program management	12,825	13,800	13,942
Cancer control	55,192	56,000	60,040
Construction	4,493	3,000	2,110
TOTAL	$943,035	$983,576	$989,263

(Dollars in Thousands)

DeVita suggested that the reduction from recommended levels could be established at 15 percent for both R01s and P01s, although "that will not allow us to go down and fund more grants."

Harold Amos, member of the President's Cancer Panel, suggested that R01 grantees in general had accommodated themselves to the 20 percent reduction and that the scientific community would prefer to see the reduction stay in place in order to fund a greater number of grants. The committee agreed to the 15-15 reduction, however.

DeVita pointed out that funding R01 competing renewals at 85 percent of the recommended level would amount to an average increase of 17 percent over current levels. The average increase recommended by study sections was 37 percent.

Funding P01s at 85 percent of recommended levels would give the average competing renewal an increase of 11 percent over current levels.

"There is the danger that cutting from recommended levels will become permanent," DeVita said. "I feel there is merit in the recommended levels. Study sections work very hard on grant budgets."

Reducing the cuts from 20 to 15 percent would require about $6 million. The rest of the extra $40 million would be spent by:

—Restoring the $15 million cut from indirect costs, as decreed by Congress.

—Putting an extra $12.5 million into grants, to fund an additional 77. The priority score payline for P01s would be raised from 170 to 178; for R01s, it would remain at about 172.

—Adding $3 million for National Research Service Awards.

—Adding $1.7 million to the Organ Systems Program to fund the 23 additional 1982 grants as directed by the NCAB (*The Cancer Letter*, Dec. 3).

—Adding $800,000 for program management.

—Adding $1 million for construction (some for construction grants, the rest for construction and renovation on campus and at Frederick Cancer Research Facility).

The remaining elements of the 1983 funding plan approved by the Board in October remain in place—no competing renewal recommended for an increase will receive less than the current level; grant dollars will be allocated by program, and program directors, with the division director's concurrence, can approve a 10 percent variance on funding levels for individual grants; contract funds will be reduced by five percent; and intramural research will be limited to a four percent growth over the 1982 base.

NCAB COMMITTEE REACHES CONSENSUS ON ORGAN SYSTEMS; DEVITA AGREES

The National Cancer Advisory Board's Committee on the Organ Systems Program struggled through a Saturday night-Sunday session this week and eventually came up with a framework for the program which appeared to be acceptable to most committee members and to NCI Director Vincent DeVita.

The committee's recommendation, which was scheduled to be presented to the full NCAB Wednesday, essentially would keep intact the four existing off campus projects—National Bladder Cancer Project, National Prostatic Cancer Project, National Large Bowel Cancer Project, National Pancreatic Cancer Project—but with major modifications; establish the Breast Cancer Task Force as a fifth such project; remove responsibility for review of grants from the first four and transfer that to the NIH Div. of Research Grants and NCI Div. of Extramural Activities; create a new off campus (away from NIH) headquarters which would have certain undefined responsibility for the entire program.

The new recommendation does not significantly change the Board's recommendation of last May, except in the matter of establishing a continued role for the working cadre of the four national projects. Under the former recommendation, the four projects would be combined into two and the fate of the working cadre was left unclear.

Under the new recommendation, the working groups—including the breast cancer task force and any new site specific group which may be established —will monitor all NCI grants in their respective areas of interest, not just those which the groups have been initiating and reviewing. They will be charged with identifying areas of need; carrying out communications efforts through newsletters, workshops, and other methods; and developing initiatives to meet research needs through RFAs, RFPs, and program announcements; and then recommending those initiatives for concept approval to the appropriate NCI divisional board of scientific counselors.

The headquarters will be established by a grant awarded after competition through an RFA to be issued by NCI. The principal investigator will be designated the chairman, and a committee will be appointed to advise him. The five individual projects and their working groups will be responsible to the headquarters but they may have their own headquarters located elsewhere.

One of the primary functions of the main headquarters will be to develop criteria both for initiating and terminating groups along with the responsibility for carrying out those decisions.

The committee agreed to leave the matter of review of organ systems grants along the lines of its previous recommendation.

Individual investigator initiated grants will go to DRG for review by an appropriate study section, while the group clinical research and program project grants will be reviewed within NCI by DEA committees. The committee added a requirement for NCI staff to develop referral guidelines.

Program participants who have argued that their targeted grants would not get a fair shake from DRG study sections had their worst fears confirmed by results of the first round of project grants sent to DRG. Of 34 applications, 29 were approved but only three and perhaps four were in the funding range. (***The Cancer Letter*** article last week said only three or four were approved. That would have been a worse blow in prestige, but the end result is the same.)

By contrast, in the last three cycles of grants reviewed by the four project working cadre, 121 of 148 applications were approved, and 42 were funded.

In the last three cycles of breast cancer grants reviewed by DRG, 116 of 135 were approved, and 32 were funded.

The determination that only three of the present grants would be funded was based on a priority score payline of 172. If that line is lifted to 180, a fourth grant would be paid.

DeVita said at the committee meeting that NCAB members can do something about study section scoring. "When those grants come before you, you can fund beyond the payline if you think that is warranted."

DeVita later told ***The Cancer Letter*** that if DRG review did not prove satisfactory, he would consider moving all organ systems review to DEA.

The committee went along with DeVita's request not to allocate a fixed amount of money for organ systems grants. The four existing projects have $11.7 million this year, while the breast cancer program has $12 million.

"You're in the perfect position to determine how much money can go in this, in determining how far down the line to pay grants," DeVita said. "Fixing a line item does not allow flexibility for new initiatives."

If there is an inclination on the part of Board members to seek a line item to assure continuance of the program, "you don't need it," DeVita said. "You've sent the message that you're interested in organ systems grants. It will be heard."

Board member Victor Breren said, "I would accept Vince's position on the budget with this addition, that NCI continue to fund the Organ Systems Program on relatively the same level of viability it has now."

"That is acceptable," DeVita said. "I've already agreed to that."

"Do you consider these recommendations fair and

reasonable?" Committee Chairman William Powers asked.

"Yes," DeVita answered.

DeVita said the RFA for the headquarters grant would be issued in the near future, soon enough to permit review and award at the October meeting of the NCAB.

"DECADE OF CANCER CONTROL"—BRESLOW; DRCCA PLANNING EFFORTS DESCRIBED

Lester Breslow, chairman of the Board of Scientific Counselors of NCI's Div. of Resources, Centers & Community Activities, has suggested that the 1980s be the "Decade of Cancer Control, in the same sense that the 1970s constituted the Decade of Discovery."

At the Board's recent meeting, Breslow explained, "What that means is that we reached a new high level of discovery in the 1970s, a level that must be maintained and enhanced, probably through the next several decades, and that we can in the 1980s establish cancer control as a coherent enterprise also to be maintained and enhanced in the decades ahead."

Breslow suggested four principal "thrusts" for DRCCA—some of which were already in place before the Board came into existence—establish cancer centers; mobilize community resources against cancer, a significant contribution to which he said is the new Community Clinical Oncology Program; development of cancer control research directed both to prevention and management, with the new Cancer Control Research Unit and Cancer Control Science Programs coming into place; and a "fourth and as yet not well developed but much needed thrust to develop personnel for cancer prevention and control."

Although substantial funds have been spent on training laboratory and clinical scientists, training of epidemiologists "has languished," Breslow said. "There have been some NCI endeavors but nowhere near what appears needed. I hope we can have a presentation and discussion of that matter at the next meeting of our Board."

DRCCA Director Peter Greenwald described planning efforts undertaken by the division.

"Task forces have been set up with appropriate representation from other divisions, in order to develop planning proposals in five areas: 1) chemoprevention; 2) diet, nutrition and cancer; 3) detection and diagnosis; 4) smoking; and 5) a series of workshops leading to a conference aimed at setting national cancer control objectives. . . . In planning, we generally are using the (Louis) Carrese convergence technique. This describes research judged necessary to achieve program objectives sequentially ordered by stages, with decision points controlling movement from stage to stage. The planning itself is an extensive effort. For example, just in the chemoprevention program alone we have spent 24 full or part days thinking through the logic of the program. Our thought is to review the plan with several concentric rings of advisors. . . . The full chemoprevention plan will be discussed first with our Prevention Committee and brought to this Board in May. Finally, since the plan will involve new resource allocations, it will go to the National Cancer Advisory Board.

"The following characteristics of these plans should be emphasized:

"1. This type of program planning is done to identify what research must be done in order to achieve the purpose of the program. We are taking an organizational initiative; many of the scientific initiatives in the program will come from the scientific community. A plan provides for wide participation by expert advisors, flexibility, and an ability to adapt to new findings.

"2. New funding may not be required for some aspects of the plan as we are not starting from scratch. A major aspect is the identification and tracking of research important to the program. Much of this research will be investigator initiated. Some may be of a nature or scope that requires a large amount of NCI organizational effort.

"3. An analogy may be made between planning for cancer control and designing an individual R01 study, which in a sense is an individual research plan. In aiming for a national impact on incidence, morbidity, and mortality using leads derived from basic or clinical research knowledge, we need a plan just as any individual investigator would need to state the aims and methods for a single study. Admittedly, the cancer control plan may be much more complex and include within it many individual scientific initiatives.

"4. An instructive example may come from our chemoprevention program. It is an example of one way in which the plan is utilized.

"a. In chemoprevention, we first surveyed ongoing research to see what was going on in the scientific community regardless of the institution, mechanism, or source of funding.

"b. On Jan. 14, 1982, this Board approved a request for applications entitled "The Role of Natural Inhibitors in the Prevention of Cancer." This invited investigator initiated research in a broad area related to chemoprevention—both observational and human intervention trials were within the scope of the RFA.

"c. We are now requesting approval of a concept for a modified RFA based on research that we believe likely to be conducted as a result of the RFA noted in "b" above (*The Cancer Letter*, Jan. 28). The new one will limit its focus to human intervention trials and exclude studies of skin cancer. Thus, at this point, we are still encouraging investigator initiated research directly related to program aims. Investigators with other interests still have open to them the

R01 grant pool, but it would not be funded as part of this program.

"d. Finally, there may be times when, in consultation with our advisors, we know exactly what must be done and shall seek ways to do this in the most efficient manner. The determination, of course, will be made through processes involving the country's best experts regardless of their institution, and some of these processes are yet to be developed. An example of an efficient way to follow through on a clear lead may be the master contract concept.

"We hope to bring the diet, nutrition and cancer plan to our Board's Prevention Committee prior to bringing it to the full Board of Scientific Counselors in October 1983. Smoking and cancer planning are on a similar schedule, although the approach differs slightly.

"Regarding cancer detection, based on the report of Dr. (Barbara) Hulka's committee, we have begun development of a research plan. The formal plan shall be presented to our Prevention Committee and come to the January 1984 Board."

DRCCA Deputy Director Joseph Cullen said that a national conference on objectives of cancer control would be held next October to help update the goals of the division. NCI's original Cancer Control Program was based on recommendations which came from the Columbia conference held about eight years ago.

The October conference will be followed by a second one on applications, which Cullen said would be scheduled for April 1984, in Washington, to which 3-4,000 health care professionals will be invited.

Other comments made during the Board meeting:

Ernst Wynder, member of the Board—"I'm impressed by the esprit de corps of this division, and the enthusiasm. This is the Vince Lombardi of the Cancer Institute. . . . Application means how you get it to where the action is. Smoking prevention is not high on the priority of any school administrator or principal I've seen."

Jerome Yates, director of the Centers & Community Oncology Program—"On the issue of comprehensiveness and what that means. There is a requirement in the guidelines for (recognition as a) comprehensive cancer center for control activities. There are mixed feelings about the value of (being officially recognized by NCI as) a comprehensive center. (The Board's Committee on Centers & Community Activities) concluded we should not tamper with those comprehensive guidelines but should interpret them more freely."

NCI CONTRACT AWARDS

Title: Preparation and updating of clinical protocol summaries
Contractor: Informatics Inc., Rockville, Md., $99,850.

Title: Iso-antigenic typing of mouse strains, six month extension
Contractor: Northwestern Univ., $29,956.

Title: Maintenance of a feral mouse breeding colony
Contractor: Litton Bionetics, $275,832.

Title: Monographs on organic air pollutants
Contractor: SRI International, $221,460.

DCT BOARD APPROVES RECOMPETITION OF BRM PHASE 1/2 MASTER AGREEMENT

The Board of Scientific Counselors of NCI's Div. of Cancer Treatment gave concept approval last week to three projects, including recompetition of the master agreement in which 27 institutions have been available through task orders for phase 1 and 2 studies of biological response modifiers.

The master agreements with the 27 institutions were awarded for five years in 1980, but DCT decided that since that time, a number of additional institutions have developed the capability to do those studies. In order to add them to the list eligible to receive the task orders, the master agreement had to be recompeted.

Robert Oldham, director of the Biological Response Modifiers Program, told the Board that the system has been working well, although "it could be improved. . . . It's flexible, and it has enabled us to get a huge cadre of investigators in hand and it doesn't cost anything."

The master agreement does not cost anything, but the task orders do. DCT spent $2.6 million in FY 1980, $14,000 in 1981 (the 1980 studies carried over into 1981) and $1.2 million in 1982. A total of $2 million was earmarked for 1983, but Oldham said the amount would be less than that each year.

Staff narrative describing the program:

It is the intent of the Biological Resources Branch to establish the clinical efficacy of new biological response modifying agents under a master agreement by the use of quick reaction task order contracts awarded to competitively selected contractors from among those who successfully compete for the master agreement.

Master agreements are nonfunded contracts competitively reviewed and awarded to multiple contractors who, for this agreement, will have demonstrated clinical and laboratory expertise in the evaluation of biological response modifiers. Individual task orders will be awarded on a competitive basis only to institutions holding master agreements.

Under the currently operative master agreements, task orders have been awarded to study two thymosin preparations, maleic vinyl ether-2 (MVE-2), leukocyte and lymphoblastoid interferons, anti-T cell monoclonal antibodies and anti-suppressor T cell monoclonal antibodies.

The thymosin (fraction 5 and alpha 1) were found to be relatively nontoxic but their biological and antitumor activity was not striking. Some preliminary data suggests that thymosin fraction 5 may be of value in the treatment of renal cell carcinoma and alpha 1 may be of benefit as an adjuvant to radiotherapy in the treatment of patients with nonresectable non-small cell cancer of the lung. Phase 1 trials with MVE-2

did not demonstrate significant immune augmentation or antitumor activity at doses which were nontoxic. In phase 1 trials, the interferons had some antitumor efficacy in malignancies such as lymphoma and multiple myeloma and less commonly in solid tumors such as breast cancer and melanomas. Dose limiting toxicities of leukocyte and lymphoblastoid interferon have been determined.

Immunological monitoring has demonstrated variable augmentation of natural killer cell activity (which may be dose dependent), cell surface antigenic stimulation, and probably monocyte activation. Phase 2 trials with lymphoblastoid interferon are under way in patients with multiple myeloma, breast carcinoma, melanoma, colonic carcinoma, renal cell carcinoma, and non-oat cell lung cancer. Phase 1/2 trials with anti-T cell monoclonal antibodies in patients with T cell malignancies have just begun, as well as a phase 1 trial with antisuppressor T cell monoclonal antibody.

Other task orders presently being formulated under the existing master agreement include phase 1/2 trials of gamma interferon, beta interferon, azimexon (an agent which appears to enhance T cell mediated cytotoxicity) and antimelanoma monoclonal antibodies.

Under the proposed master agreement, task orders will be issued to study specific biologic response modifiers in phase 1/2 clinical trials in order to determine their toxicity, maximal tolerated dose, maximal biologically effective dose and potential antitumor activity.

The master agreement seeks to identify, using strict evaluation criteria, those institutions which demonstrate clinical and laboratory expertise needed to carry out successfully those task orders which will be released under this master agreement. In addition to documenting their expertise and capabilities, respondents will be asked to prepare a response to three mock task orders, including developing a full clinical protocol and a plan for the laboratory monitoring of biological responses for each. The three mock task orders will be: 1) phase 1 evaluation of macrophage activating factor, 2) phase 1/2 evaluation of antimelanoma monoclonal antibody, and 3) phase 1 evaluation of gamma interferon.

Respondents will be judged in terms of their current capabilities, and expertise. Personnel will supply curricula vitae and bibliographies documenting ongoing capability to clinically and immunologically evaluate agents. Evidence defining a functioning laboratory unit with experience and the capability of performing most of the standard assays will be sought.

A number of biological response modifiers will be candidates for future study under the proposed master agreement. These include monoclonal antibodies directed against various tumor associated antigens (both as antibodies alone and later coupled with toxins, cytotoxic drugs and radioisotopes), macrophage activators such as macrophage activating factors (MAF) and muramyl dipeptide (MDP) encapsulated in liposomes and perhaps other lymphokines such as B cell growth factor, interleukin 2, and lymphotoxin, as they become available. Chemical and natural products, demonstrated to be immunomodulators in the Biological Response Modifiers Screening Program, will also be available to be studied by means of the task orders.

Board Chairman Samuel Hellman, Harvard; Dani Bolognesi, Duke; Philip DiSaia and Theodore Phillips, Univ. of California; and Paul Marks, Memorial Sloan-Kettering, left the meeting during the discussion and vote, since their respective institutions are participants in the master agreement.

The Board approved the concept of a one year feasibility study, at an estimated cost of $200,000, for the acquisition, quality assurance and distribution of biological response modifiers. It will be competed as a contract through issuance of an RFP, probably as a small business set aside.

Staff narrative:

BRMP has the responsibility for the development of preclinical and clinical biological response modifiers (BRM). To provide for the efficient development of BRM, it is important to have an integrated program in place for the acquisition, quality assurance and distribution of BRM for independent scientific investigations. Such a program would provide for acquisition of diverse BRM from qualified sources and for testing of BRM related to quality, efficacy, toxicity and relevant biological activity, thereby making generally available uniformly characterized, quality controlled products.

The original plan to establish an acquisition/distribution system was presented to the DCT Board of Scientific Counselors in June 1982. It was generally agreed that the proposed program was too large and lacking in specific details. The Board requested BRMP to provide more detailed information before establishing an acquisition/distribution system. On Aug. 31, 1982, BRMP sponsored a retreat consisting of BRMP staff, BRMP Decision Network Committee members and extramural scientists from industry and academia to discuss various aspects of an acquisition/distribution program for biologics. There was general agreement on the need for such a program to make available BRM for university and research institute studies.

The participants in the retreat raised several questions about the acquisition/distribution program which were thought to need clarification before a program could be established. Areas requiring clarification were: number of BRM available; number of anticipated requests for BRMs; the most effective means of operation/management; mechanisms of cost reimbursement to pay for BRM; levels of quality assurance and relevant testing required; cooperation by potential BRM suppliers; confidentiality in treatment of data on agents provided; and flow of information generated through testing and distribution. The proposed feasibility study will provide the BRMP with an understanding of specific extramural requirements and help define the most effective size and breadth for an acquisition/distribution program for biologics.

This initiative cannot be undertaken by NCI program staff because the program does not have sufficient staff to adequately conduct such a study.

The proposed contract will assess the requirments of the extramural community for BRM that have been characterized for quality, efficacy, toxicity and relevant tests for in vitro and in vivo biological activity. An assessment will also be made

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 work, scope 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.

of the most efficient organizational structure to manage the acquisition and distribution program. The areas of clarification noted above will each be addressed by the contractor.

The Board approved recompetition of master agreement contracts now held by SRI International and the Institute of Cancer Research for the synthesis and testing of radiosensitizing agents. A total of $1.8 million has been spent through those contracts from 1981-83 fiscal years, and Radiation Research Program Director David Pistenma estimated the 1984 cost could be as high as $800,000.

Staff narrative:

One of the major problems in the treatment of cancer is the presence of radioresistant hypoxic cells in the tumors which appear to be the primary cause of the failure of radiation therapy. A number of ways has been investigated to overcome the resistance of hypoxic tumor cells to radiation. The least expensive and most promising has been the use of radiosensitizing agents in conjunction with radiation therapy. The radiosensitizers which showed promise and were introduced into the clinic were representatives from the chemical class called nitroimidazoles. These agents have proved to be too toxic in man for clinical use. The search for new classes of radiosensitizers is a continuing effort and the current contractors are leaders in this area of research.

The current contractors have synthesized most of the 400 plus components they have evaluated to date. In the process, a better understanding of the relationship between molecular structure, physio-chemical parameters, and radiobiological activity was realized. Using this information, SR-2508, the optimal radiosensitizer of the nitroimidazole class, was developed and is being tested in the clinic. Other important leads have been uncovered which will ultimately result in the rational design and development of new, noval, non-nitro classes of radiosensitizers.

Using the principles and approaches learned from the systematic study of the nitroimidazoles and the non-nitro compounds investigated thus far, future efforts will be directed toward the development of other classes of radiosensitizers. Emphasis will be placed on the rational design and development of compounds without the nitro group as electron-effinic radiosensitizers, since non-nitro compounds appear to offer reduced toxicity.

The presently existing master agreement with its associated task orders has already demonstrated that this mechanism is most efficacious and prompt in determining the clinical efficacy and toxicity of biological response modifiers. The existing master agreement will expire Sept. 29, 1983 and therefore needs to be recompeted.

The Board approved the concept of renewing the interagency agreement with the Armed Forces Institute of Pathology for technical support for slide preparation in the testicular cancer intergroup study. The cost was estimated at $12,000 a year, for two years.

RFPs AVAILABLE

Requests for proposal described here pertain to contracts planned for award by the National Cancer Institute unless otherwise noted. Write to the Contracting Officer or Contract Specialist for copies of the RFP, citing the RFP number. NCI listings will show the phone number of the Contracting Officer or Contract Specialist who will respond to questions. Address requests for NCI RFPs to the individual named, the Blair building room number shown, National Cancer Institute, 8300 Colesville Rd., Silver Spring, Md. 20910. RFP announcements from other agencies reported here will include the complete mailing address at the end of each.

RFP NIH-ES-83-5

Title: *Study of chemical disposition in mammals*
Deadline: *Approximately March 28*

The National Toxicology Program, National Institute of Environmental Health Sciences is soliciting qualified sources having the capability to perform detailed chemical disposition studies on approximately six environmental contaminants or model compounds per year selected and supplied by NIEHS. Individual studies may vary in complexity from preliminary investigations of chemical absorption to detailed studies of all phases of chemical disposition and metabolism.

Most studies will be carried out in rats, although other laboratory rodents, dogs and/or primates may also be used. Offerors should possess demonstrated proficiency and experience in conducting chemical disposition studies.

Contract Specialist: Hollis Hawkins
NIEHS Procurement Office
P.O. Box 12874
Research Triangle Park, N.C.
27709

RFP NCI-CP-31018-78

Title: *Resource for transplacental carcinogenesis studies in primates*
Deadline: *March 31*

NCI has a requirement for animal facilities adequate to house 185 patas monkeys (erythrocebus patas). Individual and/or in harem breeding cages will be provided by the government to house these monkeys. The place of performance of this contract must be within a 70 mile radius of the Frederick Cancer Research Facility, Frederick, Md.

The contractor will administer carcinogens in accordance with protocols provided by NCI investigators. A rigid animal health surveillance program will be maintained and will include quarterly tuberculin tests, treatment with anthelminthics, body weights and collection of reference serum samples.

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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.