THE CANCER LETTER

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CCIRC DISAPPROVES NCOG RENEWAL, BUT CARTER PLANS APPEAL TO NCAB; SETBACK FOR NCI ON REGIONAL GROUPS

The Cancer Clinical Investigation Review Committee last week overrode the recommendation of its site visit team and disapproved renewal of the Northern California Oncology Group. Unless that decision is overturned, a distinct possibility, it would be a devastating blow to NCI's plan to encourage formation of new regional groups and once again leave a large area of the Far West without reasonable access to clinical trials.

NCOG Chairman Stephen Carter told *The Cancer Letter* that he has

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In Brief

LITTLE DOUBT THAT DEVITA, FREDRICKSON WILL KEEP THEIR JOBS; NEW DCT PROJECTS MAY NOT BE FUNDED

DESPITE SECRETARY Richard Schweiker's refusal last week to comment on the tenure of NCI Director Vincent DeVita and NIH Director Donald Fredrickson (*The Cancer Letter,* Feb. 27), there is little doubt that both will be retained. Schweiker apparently does not want to reveal decisions on key health personnel until his assistant secretary for health is on board. Sources have told *The Cancer Letter* that Schweiker privately agrees there is no logical or valid reason for replacing either DeVita or Fredrickson. . . . **NEW INITIATIVES** approved by NCI's Div. of Cancer Treatment Board of Scientific Counselors at its meeting last October will not be funded in the 1981 fiscal year unless the division gets more money than currently available. Those included new studies in hyperthermia, intraoperative radiotherapy, correlation of the tumor stem cell assay with treatment results, and calorimetry. "They are out at the moment, but we still hope to fund them," DCT Acting Director Saul Schepartz said. Board member Enrico Mihich suggested that existing studies might be cut back to provide funds for the new programs. "I would not like for ongoing commitments to be curtailed or taxed to make room for new initiatives. I personally would not like to have my grants reduced. But that would be one way to make room for new initiatives," Mihich said. DeVita agreed that might be possible but said it would have to be an NIH policy. "The feeling now is not to do it," he said. . . . **WASHINGTON POST** reporters Jonathan Neumann and Ted Gup, who have been assigned by that paper to do an extensive study of the Cancer Program, won the national reporting prize in the annual George Polk Awards in Journalism for a five part series on fraud and waste in government contracting. . . . **DOROTHY MACFARLANE** is back on the job as executive secretary of the Cancer Clinical Investigation Review Committee after giving birth to Andrew Edward in January.

NCI STAFF REACTION: SHOULD SAME CRITERIA JUDGE REGIONAL GROUPS?

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officially requested Div. of Cancer Treatment Acting Director Saul Schepartz to appeal the CCIRC action to the National Cancer Advisory Board.

In a similar situation three years ago, the CCIRC disapproved renewal of the Gynecologic Oncology Group after the site visit team had recommended approval. A minority report of the CCIRC also recommended approval, and the group asked the NCAB for a special action. The NCAB accepted the minority report and returned the GOG grant application to the CCIRC for budget recommendations. GOG was funded and is still operating.

Carter indicated he would follow a similar route. CCIRC members supporting NCOG's renewal are in the process of writing a minority report.

Another precedent exists with the Southeastern Cancer Study Group, which was disapproved by the CCIRC a few years ago. An appeal to the NCAB resulted in the Board's demand that the CCIRC rereview the group. That was done, and the group was renewed and is still in operation.

Carter said that if the NCAB asks for rereview instead of accepting the minority report, he would request that the new review be done by an ad hoc committee rather than the CCIRC, which he feels is dominated by members of existing national groups. Some members of existing groups have bitterly opposed adding new groups, especially those regionally organized, which they contend would dilute NCI's available funds for cooperative groups.

The DCT Board of Scientific Counselors has approved the concept of supporting at least three new regional groups this year and earmarked $1.5 million for that purpose.

The major reason for the CCIRC's disapproval of NCOG, sources told ***The Cancer Letter,*** was because it was felt that the group attempted too many protocols rather than trying to achieve well with a smaller number. One critic said it was because NCOG had too many "me too" studies.

The disapproval interrupted Carter's string of successes after he left NCI as DCT deputy director about six years ago. He developed the Northern California Cancer Program, overcoming what had been an impossibly contentious situation in the Bay Area and organizing universities, medical schools, community hospitals and other entities into a consortium cancer center. He then put NCOG together, a network of university and community physicians in communities throughout Northern California and Northwestern Nevada. It was the prototype regional cooperative group which filled in the gap left by the demise of the Western Cancer Study Group.

NCI staff reaction was that "this will force us to think about what the objectives ought to be of regional groups and the criteria for reviewing them," as one DCT executive said. "The CCIRC has a single standard of review, applying the same yardstick to regional groups that it uses for the national groups. Shouldn't there be some consideration given to a group in its formative years which allows for deficiencies? If a group continues to show improvement, that should be taken into consideration. Once it has plateaued, then think about applying the same yardstick. We should think about how many years that would take, to reach that point.

"The groups, for their part, need to be introspective on their strengths and not try to be all things to all people."

The next big test for a regional group will come soon. The North Central Cancer Treatment Group, sponsored by the Mayo Comprehensive Cancer Center, also is up for renewal this year. Its site visit is scheduled for May 14-15, and the review will be conducted by CCIRC at its June 22 meeting.

"We are watching that with interest," the DCT executive said. "One negative experience does not disprove a theory or concept. Assessment of the regional concept is still an open question."

FREI REPLACES HOLLAND AS CHAIRMAN OF CALGB; HOOGSTRATEN LEAVES SWOG

The two most outspoken, colorful and controversial Cooperative Group chairmen are leaving the scene.

James Holland decided not to run for reelection as chairman of Cancer & Acute Leukemia Group B after 15 years of leading that group. Emil (Tom) Frei, director of the Sidney Farber Cancer Center, was elected as the new chairman. Frei was the original chairman of the group, helping to organize it while he was at NCI.

Barth Hoogstraten, who was just reelected as chairman of the Southwest Oncology Group, has decided to resign "to give new direction to my career." He has headed SWOG for the last eight and a half years. The election to replace him has not yet been held.

CCIRC TRYING TO DEVELOP GUIDELINES TO REVIEW COOPERATIVE GROUP BUDGETS

The Cooperative Groups, with more than 4,000 individual investigators, 742 participating institutions and a total budget in excess of $35 million, are on hard times. So are most other NCI supported programs, with the institute's budget declining again in constant dollars for the sixth consecutive year and due to do so again in FY 1982. But the groups feel particularly strapped.

NCI has doubled money supporting the groups since they were transferred from the old grants divi-

sion to the Div. of Cancer Treatment in 1975. Several groups were phased out, and their money redistributed to the survivors, further increasing their funding.

The extra money did not bring affluence to the groups, however. Along with the increased support went a mandate to emphasize multimodality clinical trials, which substantially increased costs. The groups are still trying to deal with the impact of those additional costs.

Rising costs are reflected in increased budget requests submitted along with renewal applications to the Cancer Clinical Investigation Review Committee. In this year's round of renewals, the CCIRC has reduced those requests substantially. The groups could live with those levels, but because of the overall NCI budget restriction, DCT has announced that, for now, it appears the groups will be funded at only 70 percent of the CCIRC recommended levels.

Review of Cooperative Group budgets by the CCIRC has been one of the more controversial developments arising from the move into multimodality studies. NCI staff, group chairmen and CCIRC members agree that some changes may be necessary.

The CCIRC has established an ad hoc working group on budget guidelines. It is chaired by Hugh Davis, chief of the Div. of Hematology/Oncology at Henry Ford Hospital and a member of the Southwest Oncology Group. Other members, their disciplines and group affiliations are Laurence Baker, medical oncology, SWOG; Alfred Bartolucci, biostatistics, Southeastern Cancer Study Group; John Bennett, medical oncology, Eastern Cooperative Oncology Group; William Donegan, surgical oncology, National Surgical Adjuvant Breast & Bowel Project; Arvin Glicksman, radiation oncology, Cancer & Acute Leukemia Group B; Richard Kempson, pathology, Norhtern California Oncology Group; and Sanford Leikin, pediatric oncology, Children's Cancer Study Group.

Dorothy Macfarlane, CCIRC executive secretary, wrote to Davis last December that the working group's charge would be "to investigate how budget recommendations for Cooperative Group grant applications have been made and to make recommendations on how we can assure consistency and logic in these recommendations."

The initial meeting, which was held last month, would be limited "to remedies which the CCIRC can implement immediately," Macfarlane said. "Obviously, there are more philosophic issues concerning Cooperative Group funding which could be addressed (e.g., should the review group deal with budget recommendations at all; should NCI fund groups rather than institutions, etc.). However, these are changes which would require a higher authority than the CCIRC to be implemented. Whether we should approach these issues, and perhaps make recommendations to DCT staff, is a question which might be addressed by this group at a later date, if its members choose to do so."

DCT staff, CCIRC members and site visitors developed a list of suggestions for improving Cooperative Group grant review which Macfarlane passed on to the working group. "These are only possibilities, given to stimulate your thinking along these lines," she said. "They are not meant to represent an entire range of options, nor are all of them necessarily feasible." Those suggestions were:

I. Assuring Consistency

A. Limit scope of individual institutional applications to patient accrual activities only, then recommend funding on cost per patient basis, or cost per patient plus some factor added for scientific activities (e.g., give rating of 1-10 and on this basis increase cost per patient figure by perhaps 5 percent for minimal scientific activity, 25 percent for maximal).

In this case, funding for committees, resource laboratories, headquarters and statistical offices would still be reviewed individually, and would require separate grant applications.

B. If a cost per patient basis is used, should this be broken down by modality involvement (e.g., more for chemotherapy/radiotherapy protocol patient than for a chemotherapy alone case)?

C. Should factors other than patient accrual and scientific contributions be involved if guidelines are developed for institutional applications (e.g., geographic cost differences, private vs. state-funded institutions, etc.)?

D. Should reviewers arrive at total budget figures by methods such as those mentioned above, then adjust budget request line by line to conform to this figure, or should total alone be given and investigator allowed to rebudget?

E. Would it be helpful to appoint a CCIRC member other than the site visit chairman to monitor consistency of budget recommendations at time of budget review session of site visit?

II. Time Considerations

Example: During the recent review of a major cooperative group, 15 site visitors spent eight hours discussing institutional applications (three work-weeks of professional time). At the CCIRC meeting, 20 members spent an additional four hours making budget recommendations on these applications (two work-weeks) for a total of five 40-hour work-weeks of professional time to complete these recommendations. Is this a time-effective method of review?

A. Is it necessary to look at the budget request line by line? Could this be reduced to category by category (e.g. $40,000 recommended for personnel, $2,000 for supplies, etc.) or total value of institution-

al member's participation recommendations?

B. If line by line method is judged to be useful, should guidelines be set (e.g., one data manager per 100 entries, one nurse oncologist per 100 entries, etc.)?

III. Budget-Priority Score Relationship

A. The priority score rating should be a measure of the scientific value of the grant proposal, regardless of the cost of carrying out the project. Recently, members of the CCIRC who thought recommended budgets were too high have nearly threatened to sabotage the approval of the application by giving it a low priority score if budget recommendations were not lowered. How can we avoid this situation in the future?

B. Would it be helpful to give each cooperative group as a whole a "priority score" as it is reviewed, so that low priority groups might be dropped entirely if money is tight?

IV. Impact of Conversion to Cooperative Agreements on Funding of Cooperative Groups

Will this new mechanism allow NCI staff more authority to adjust review committee recommendations, either initially or at interim funding years? (Should be addressed by NCI program staff.)

CCIRC Chairman Joseph Simone opened last week's meeting of the committee with a statement which could be considered a response to IIIA (above), as well as to those Cooperative Group members who feel their budget requests were slashed to accommodate NCI's current fiscal crisis.

"Our role and responsibility is to judge the science of applications, not to adjust to the budget of NCI," Simone said. "It would be a dangerous precedent for us to give priority scores and judge the merit of applications based on what we think the NCI budget problems are."

Davis reported on the first meeting of the budget working group and summarized the discussion. (Note: the following is Davis' interpretation of the discussion and had not been reviewed by the working group. Davis emphasized that further, extensive discussions would be required before development of guidelines could proceed, and he welcomed suggestions from others, including Cooperative Group chairmen):

Defining the Problem(s)

The problems of budget review and setting of priority scores of institutions need little repetition: They include:

1. Severe time constraints for site visit teams and the CCIRC.
2. Inconsistency of priority scores recommended by the CCIRC, particularly in regard to interpreting the recommendations of the site visit team.
3. Lack of existing guidelines for site visitors and the CCIRC for reviewing budgets and recommending levels appropriate to the scientific contributions of the group.
4. Equitable funding for modalities.
5. Realistic funding for operations offices, statistical offices and institutions in the areas of equipment, supplies, copying costs, telephone, postage, travel, etc.

Emphasis on line by line budget review without guidelines for realistic overall ceilings, leads to gross deviations in funding similar institutions.

Discussion and Recommendations to the CCIRC

1. Time constraints: This problem is serious in view of the crowded schedules of reviewers. It was recommended that the CCIRC consider extending by one-half day the time allotted for site visits and CCIRC meetings.

2. Inconsistency of priority scores:

a. Following the vote on a group there should be an open discussion of the merit of the group and its ranking compared to other clinical trials groups. An informal priority should be arrived at (in numbers) to help the CCIRC set individual institution priority scores, i.e.: Group WXYZ has been reviewed, found meritorious and recommended for approval for four years. A discussion ensues giving an informal priority in numbers, i.e., "this group rates a 1.2, a 1.8, a 2.5, etc." The subsequent scores of the institutions should reflect this overall consensus. Institutions deemed good should receive scores equal or better than the informal group score. Weak institutions should receive higher (worse) scores or be disapproved.

b. Differing opinions on institutions should receive some discussion before voting, i.e.: Institution X is recommended at a high or high moderate level by the site visit team. Objections? Differences of opinion? The point is to verbalize before voting so additional material can be included in the summary statement. The vote itself is "secret" and should be.

c. The site visit terms should be unambiguous and agreed upon by the CCIRC before voting—"High," "High Moderate," "Moderate," "Low," should have an unmistakable meaning to all. The actual pay line varies so broad guidelines only can be given but the CCIRC needs definitions. A suggested glossary might be as follows:

High = 1.0 - 1.5; High Moderate = 1.5 - 2.0; Moderate = 2.0 - 2.3; Low = above 2.3.

d. Priority scores and budget recommendations should be separated, insofar as is possible; budget differences should be thrashed out before the vote or alternatively the priority vote should occur before the budget vote. Committee members should have the time to fully discuss all aspects of a grant before voting a score.

e. The committee should keep in mind the elements of an institutional score within a group.

1) The overall merit of the group.

2) Ranking of that institution in the group by the group itself.

3) CCIRC estimate of its ranking in the group.

4) Number of institutions the group needs for optimum performance.

5) Institutional characteristics, case accrual, scientific leadership, publications, etc.

3. Guidelines for budget review of institutions:

A number of methods for reviewing institutional budgets is in practice. These include cost/patient, cost/patient and rewards for less tangible items such as scientific leadership, judgments based on the reviewers' own personal and institutional experiences and when in despair simply recommending last year's level plus C.O.L.

The Cooperative Group institution's major product is an evaluable patient and a completed published clinical trial. Thus, it is hard to avoid using case accrual as a major factor in arriving at a recommended budget. Furthermore, the institution is in a better position than the reviewer to know its needs. These factors would argue for the development of an overall formula to develop minima and maxima. Line by line review could still be used to exclude non-allowable costs and arrive at the final recommendation.

The development of a formula could be based on dollar costs/evaluable patient or a credit point system could be developed which could be translated into dollars using a dollar amount per credit point.

Dr. Baker illustrated the simplest formula based on his personal experience and using a fixed dollar amount. Let us assume: A single modality patient = $500; a multimodality patient = $1300.

Let us assume these are eligible patients and at least partially evaluable. Institution X enters 200 eligible patients; 100 are single modality, e.g. chemoRx or radiotherapy: 100 x $500 = $50,000; 100 are multimodality: 100 x $1300 = $130,000.

Thus the institution's base would be $180,000. This would cover all the basics, personnel, supplies, travel and other expenses.

The next question is the "bonus" for scientific leadership including institutional authorship of protocols, abstracts and manuscripts, committee memberships and chairmanships, etc.

Dr. Baker proposes that up to 30 percent could be added to the base for these activities. Thus, the minimum he would recommend for our hypothetical institution is $180,000 and the maximum $180,000 + 30% = $234,000. If the institution asked for funds to be a reference laboratory or some other special activity, this could be reviewed on its own merits and either become a part of the 30 percent or added to it. Thus if our institution had a $180,000 base and $54,000 (30%) added recommendation for scientific leadership and in addition was a group reference for an X dollars reference laboratory, this amount could be added to the base + 30%.

Let us also assume institution Y was a small institution with superior scientific leadership felt by the group and the reviewers to be vital to the group's overall mission. They entered 50 patients total, 25 on multimodality studies and 25 on single modality studies. The base would be: 25 x $500 = $12,500; 25 x $1300 = $32,500; total base = $45,000.

They could conceivably receive up to $13,500 for scientific leadership and thus increase their award to $58,000.

This simple formula has the appeal of creating a performance base and allowing the reviewers the option of adding a bonus. Some thought the formula as too simple in view of the types of studies and patients in today's groups. Furthermore, the groups are frequently behind in determining eligibility and especially evaluability.

Dr. Bennett suggested a credit point system and the group felt that a credit point system should be developed by each cooperative group, suited to their experience and mix of studies. Some possible definitions and categories were mentioned.

1. Study patient evaluation characteristics
a. Patient entered on study
b. Patients entered and eligible
c. Patients entered, eligible and cancelled
d. Patients entered, eligible, treated per protocol, evaluable or partially evaluable. (Early deaths, lost to followup, drug stopped due to refusal or toxicity)
e. Patients who had significant protocol violations and were unevaluable
f. Fully evaluable patients.

COMMENTS: There is a time delay to a) determination of eligibility, b) determination of evaluability. This is especially complex when different types of studies and patients are considered. The fundable output should ideally be a fully or at least partially evaluable study patient.

Another way of adding precision (and complexity) is to look at the steps and modalities in a study and credit for an evaluable patient at each step and modality participation and come up with a matrix to arrive at the final credit point determination.

Some terms:

1) Single modality phase 2 or 3
a. Standard phase 2 solid tumor
b. Multiple steps hematology patient or complex study, e.g., entry – induction – consolidation – maintenance – followup (4 treatment steps).
2) Multimodality phase 3 or adjuvant
a. Pathology review–lab assessment, markers, etc.
b. Surgical participation
–quality control review
–actual surgical procedure
c. Radiotherapy including quality control.

Entries could be subdivided as follows:

1. Phase 2 solid tumor or hematology, single modality.
2. Phase 3 solid tumor, hematologic malignancy, single modality.
3. Adjuvant patients–surgery plus single modality.
4. Multimodality studies–chemotherapy and radiotherapy, surgery plus radiotherapy plus chemotherapy.

Immunotherapy would be considered equal to (used alone) or additive to other modalities.

In addition:

1) Registry credit–no special protocol treatment.
2) Special studies–markers, pharmacology, immunologic assessments, etc.

The subcommittee recommended that the Cooperative Groups concerned work out demonstration credit point scores using these and additional variables and provide input to the CCIRC so this can be further deliberated.

If the groups could derive such a credit point score before each review (for each institution) and continue their valuable input in ranking the institutions by their scientific contributions, this could facilitate the review and leave more time for the scientific assessment by the reviewers.

4. Modality funding requirements

A. Pathology. Dr. Kempson emphasized the necessity of restricting all modality funds especially in these trying budget times. The functions that should be awarded to institutions include:

1) Slide preparation, mailing–currently $25 case.
2) Reimbursement for professional time of quality control review.
3) Research activities for the group.

Groupwide activities and central pathology activities should be funded from the chairman's grant.

B. Surgery. The key is the time and effort of the institutional surgeon(s). A realistic approximation of professional commitment is necessary. The extra cost of protocol treatment is not that of surgery (surgeons work on a flat rate). The costs are that of followup, administration, conferences, meetings, etc.

Assume one new patient a week on study requiring a H+P, conference to explain study, a five-year followup, etc. Dr. Donegan calculated that this would require about .2 of a FTE with 52 patients/year. (This would also require the services of one FTE data manager.) Note, however, that in some groups and some institutions the surgeon serves as the primary oncologist and his time commitment includes surgery, chemotherapy, etc. (e.g. the NSABP, some ECOG and SEG institutions).

In this presentation, Dr. Donegan also grappled with the problem of patient care costs. These are highly variable and relate to:

1) The procedures, tests for a given study.
2) Local variations in costs.
3) Availability of third party coverage.

Currently, the third party coverage is excellent for the most part and clinical trials are a bargain for NCI. If this were to change, there isn't enough money to begin to fund them. Furthermore, current levels of NCI supplied commercial drugs

could conceivably be reduced further compounding the problem.

C. Radiotherapy. Dr. Glicksman presented the need for adequate support of the radiotherapy chairman's budget, the quality control activities and a restricted budget. [Glicksman and Carlos Perez last year presented recommendations for radiotherapy budgets to CCIRC. Their report was included with Davis' report.]

The working group also discussed funding for operations and statistical offices and concluded that those areas are complex enough to merit a minisymposium to explore personnel requirements, supplies, travel, equipment and subcontracts.

(Simone later told *The Cancer Letter* that funding the groups at only 70 percent of recommended levels "will hurt them very much." It will reduce travel substantially and severely restrict statistical offices. However, he agreed that if NCI allows each group to apply its own reductions as it sees fit, the amount of damage to the program would be limited.)

SCHWEIKER FIGHTS OFF FURTHER CUTS, NCI GETS $1.026 BILLION IN 1982 BUDGET

Thanks to HHS Secretary Richard Schweiker's adamant stand against further cuts in NIH funds, the amount requested for NCI in President Reagan's 1982 fiscal year budget which will go to Congress next week will be $1.026 billion—an increase of about $26 million more than NCI originally was supposed to get for 1981, and anywhere from $41 to 50 million more than it will end up getting.

The $1 billion, 26 million will be a cut of $16 million from the 1982 budget submitted by the outgoing Carter Administration. It will not begin to keep up with even the modest inflation estimate of 9 percent predicted by NIH. But it is substantially more than some of the more pessimistic Cancer Program advocates had been expecting.

The total amount requested for NIH will be $3.763 billion, up $246 million over 1981. To keep that amount, Schweiker repeatedly had to fight off the onslaughts of David Stockman and the Office of Management & Budget. After originally settling on the NIH total, OMB came back again and told Schweiker it wanted to slash another $186 million. Schweiker refused to budge. Stockman's troops regrouped, then tried once more, this time demanding a $100 million cut. Schweiker held firm, and finally prevailed on Stockman to let the $3.763 billion figure stand.

NCI has been battling with NIH, HHS and OMB for more equitable distribution of increases and, when necessary, budget cuts. Despite getting the largest dollar increase (ostensibly) over 1981 of any of the institutes, the percentage increase was anything but fair.

The unfairness begins with the current (1981) year appropriations. Congress had approved, in the continuing resolution which is funding HHS, $998 million for NCI. Carter's rescission request cut that by $13.5 million, and Reagan has converted that to a deferral, allowing that cut to stand unless either house of Congress disapproves.

Every other NIH institute and division is being permitted an increase in 1981 spending over 1980, while NCI is taking a cut of $14.7 million (NCI's 1980 appropriation originally was $1 billion but it came out $999.2 million).

The Reagan budget for 1982 will show an increase of $41.8 million for NCI, which translates to a 4.2 percent increase. However, that would be only 2.7 percent over the amount voted by Congress.

In contrast, the increase for NIH overall is 6.9 percent, and 7 percent for the research institutes (excluding the Library of Medicine, office of director, and buildings and facilities).

The unfairness thus is compounded by the fact that the other institutes are getting a 7 percent increase over the amounts voted by Congress and which they are getting this year while NCI is getting only 2.7 percent over the amount voted by Congress for this year. And even after the 1981 cut which other institutes did not suffer, NCI's percentage increase is only a little more than half that of the others.

The $984.5 million also is not yet assured for NCI. Unless Congress approves a supplemental appropriations request for 1981 to cover the cost of federal pay raises, NCI will have to absorb about $8 million not covered by the $984.5 million, in effect cutting that much from available funds.

Contract Awards

TWO MORE CHOPS FUNDED BY NCI

Two more contracts have been awarded for NCI's Community Hospital Oncology Program—to the Methodist Hospital, Brooklyn, for $144,693; and St. Peter's Hospital, Albany, N.Y., for $107,973. This brings to 14 the number of CHOP contracts awarded to date; NCI plans to fund a total of 23.

Other contract awards include:

Title: Evaluation of the carcinogenic risk of chemicals to humans and the survey of chemicals being tested for carcinogenicity.

Contractor: International Agency for Research on Cancer, Lyon, France, $496,467.

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 announ ments from other agencies reported here will include the c plete mailing address at the end of each.

RFP N01-CM-15758-50

Title: *Mammalian Cell Transformation*
Deadline: *April 23*

The National Toxicology Program organizes and conducts a comprehensive interagency testing and research program focused on determining potential human health hazards due to environmental exposures to chemicals. The cellular and genetic toxicology component of NTP supports these effects through the development of establishment of in vitro and short-term test systems with predictive value for potentially hazardous chemicals. In order to complement the in vivo carcinogenesis testing segment, the NTP is seeking contractors to engage in the application of in vitro mammalian cell transformation assays for detection of potentially carcinogenic chemicals.

This is a multi-task RFP and contractors may bid on individual tasks or the complete task group which consists of: 1) Syrian Hamster Embryo (SHE) cells, 2) SHE cells infected with simian adenovirus 7 (SA7), and 3) rat embryo cells infected with retrovirus (Rauscher leukemia virus, MLV). At least two independent contractors will be sought for each test system to verify protocols through the use of chemicals of known carcinogenic activity. One or more tasks of this RFP may be withdrawn if two equivalently qualified independent contractors for each task component cannot be identified. The contract will involve the testing of up to 50 coded known carcinogens and noncarcinogens, with and without exogenous metabolic activation in each system.

Contract Specialist: Dave Monk
RCB Blair Bldg Rm 2A01
301-427-8774

RFP NCI-CM-17398

Title: *Storage and distribution of clinical drugs*
Deadline: *Approximately April 6*

The Pharmaceutical Resources Branch of the Developmental Therapeutics Program, Div. of Cancer Treatment, NCI, is seeking a contractor to store and distribute formulated clinical drug products and keep adequate records of such distribution in support of the clinical programs of the DCT. The project will involve the receiving of drugs from various sources, storage of the products under specified conditions, repackaging and subsequent shipment to NCI-authorized investigators in the United States and many countries throughout the world, and the use of manual and computerized data processing systems for various recordkeeping and reporting functions.

The contractor selected must meet at least the following minimum requirements:

1. Be within a 35 mile radius of NIH in Bethesda, Md.

2. Provide at least 5,000 square feet total available floor space which shall include the following:

a) 3,750 square feet of controlled room temperature storage space

b) 2,600 cubic feet of refrigeration storage space

c) 1,300 cubic feet of freezer storage space

d) A Drug Enforcement Administration approved vault for storage of Schedule I substances providing at least 1,200 cubic feet of refrigeration storage and provision for the addition of freezer storage.

e) Meet all applicable FDA current good manufacturing practices regulations.

3. Obtain a DEA license for the storage and distribution of scheduled substances, including Schedule I, before the award of the contract.

4. All personnel must be bonded prior to performing on this contract.

Contract Specialist: Maria Decker
RCB Blair Bldg Rm 228
301-427-8737

RFP NCI-CM-17493

Title: *Establishment and monitoring of microorganisms in isolator foundation colonies*
Deadline: *April 17*

The Animal Genetics and Production Branch, Developmental Therapeutics Program, Div. of Cancer Treatment, NCI, is seeking organizations having capabilities, resources, and facilities for the establishment and monitoring of microorganisms in isolator foundation colonies. The scope of this effort will consist of three major service phases:

A. (1) The establishment and maintenance of a repository of those organisms needed in order to obtain the desired flora for optimum physiological performance in isolator maintained foundation colonies.

(2) Shipping the organisms in vitro to those animal suppliers who maintain isolator foundation colonies, where administration of organisms will be performed according to protocol supplied by the government.

(3) Receiving animals in vivo as scheduled by the government from the foundation colonies and (a) making certain that the desired flora are being maintained in all isolators; and (b) making certain that no undesired flora have infected animals from these isolators.

B. Monitoring submitted animals (from isolators) for mycoplasma pulmonis, four strains of mouse hepatitis virus, i.e., JHM, S, MHV-1, and A59, Sendai and MHV.

C. Submit written reports indicating monitoring results to sender of samples (animal producer) and to the Contracting Officer as the tests are completed.

The accomplishments of this effort will require that the contractor receive animals from 27 identified isolators per week. Animals will be sent in germfree containers (prepaid). Two animals will be supplied from each isolator for a total of 54 animals per week or approximately 2,700 animals per year.

Contractor will monitor for the desired flora which presently consist of six organisms including the Schaedler 19X-Bacteroides, four oxygen intolerant fusiform shaped bacteria of the mouse cecum, lactobocillus acidophilus, lactobocillus salavarius, and a spirochete of the mouse cecum. Contractor will also report the presence of additional organisms observed while monitoring for the expected gut flora.

Contractor will maintain a repository of the desired organisms for associating gut flora in isolators and will supply them to breeding facilities upon request from the project officer.

Contractor will monitor one animal from each isolator submission (27 animals per week, approximately 1,350 animals per year) for mycoplasma pulmonis, four strains of mouse hepatitis virus, i.e. JHM, S, MHV-1, and A59, Sendai and MHV.

Respondents must demonstrate an understanding of the importance of and monitoring of microorganisms in isolator foundation colonies, the physical well being of "super clean" rodents and a keen awareness of recent developments in this field. The contractor must have the facilities and equipment for (1) the maintenance of a repository of microorganisms and (2) the receiving and monitoring of rodents for both aerobic and aerobic microorganisms. It is anticipated that an incrementally funded contract will be awarded for a period of five years.

Contracting Officer: Clyde Williams
RCB Blair Bldg Rm 228
301-427-8737

RFP N01-CM-15732-57

Title: *Production and isolation of type I and/or type II (immune) mouse cell interferon*

Deadline: *April 27*

The Biological Response Modifiers Program, Div. of Cancer Treatment, NCI, intends to investigate the basic mechanisms by which mouse interferons produce an antitumor effect to increase the therapeutic effectiveness of these agents in humans. Several diverse studies relating to interferon action will be carried out in the mouse system at the whole animal, tissue, cellular and molecular levels. These studies will require the acquisition of substantial quantities of type I and/or type II (immune) mouse interferon at a high degree of purity.

The BRMP seeks a contractor who can produce and isolate in the most efficient and cost effective manner possible, 10 billion units yearly of type I and/or type II mouse interferon at a minimum specific activity of 5×10^7 units per mg of protein. Due to the need for a large quantity of highly pure interferon, proposals in response to this solicitation are anticipated from organizations qualified to produce type I and/or type II mouse cell interferon by established animal cell culture technology and/or procedures relying on recent advances in recombinant DNA cloning techniques.

It is anticipated that initial awards will consist of master agreements and at least two task orders. As additional requirements arise, RFPs will be issued to all MA recipients eligible for the particular effort. The ensuing awards will also be task orders. Only those organizations who have received MAs will be eligible to compete for task order awards.

Contracting Officer: Damian Crane
RCB Blair Bldg Rm 2124
301-427-8764

RFP NCI-CM-17478

Title: *Development of plant tissue and cell culture fermentations as a source for antineoplastic agents*

Deadline: *April 20*

The Div. of Cancer Treatment, NCI, will make available to interested contractors a request for proposal concerning a project to determine the feasibility of plant cell fermentations and tissue culture as a source for antineoplastic agents. The contractor must provide and operate a plant cell fermentation laboratory and a chemical isolation laboratory.

It is planned that one contract will be awarded for a three year period of performance. To be considered for such a contract, candidates must show experience in plant cell tissue culture, fermentation (shake flask, stir jar), plant cell maintenance and selection, fermentation optimization, chemical natural products isolation, and purification of plant cell derived materials. It is anticipated that the level of effort during the three year period of the contract will be 3.0 staff years for year one, 2.8 staff years for year two and 2.6 staff years for year three.

Plants to be investigated will be assigned by NCI and NCI will provide living tissue of these plants to the contractor. The contractor will be required to develop conditions to grow the plants in tissue culture, assay for the presence of antineoplastic constituents, select superior cell lines, transfer cell lines to shake flasks and small fermentors, optimize fermentation conditions and isolate and characterize the antineoplastic principles produced.

Contracting Officer: John Palmieri
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