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CENTER DIRECTORS SOLIDLY OPPOSED TO CORE GRANT CHANGES, ASK UPTON, NCAB TO FIND OTHER SOLUTIONS

When the National Cancer Advisory Board approved "in principle" the NCI staff proposal for drastic changes in the cancer center core support grant guidelines, Board members suggested that the reaction of center directors be solicited before the new guidelines are adopted.

They got that reaction at Memphis last week: A resounding "No" on the questions of phasing out staff investigators' salaries from core grants and transferring costs of shared resources to individual grants and contracts. (Continued to page 2)

In Brief

KENNEDY SEEKING COMMENTS ON HSA REGULATIONS; SHIMKIN'S HISTORY OF CANCER NOW AVAILABLE

COMMENTS ON HSA regulations (PL 93-641) are being solicited by Sen. Edward Kennedy for his Health & Scientific Research Subcommittee. Send them to the subcommittee, Committee on Human Resources, Dirksen Senate Office Bldg, Room 4220, Washington, D.C. 20510. HSA (for Health Systems Agencies) regulations could add three to nine months in contract and grant review time; as it now stands, a substantial number of NCI programs could be affected. . . . **"CONTRARY TO NATURE,"** Michael Shimkin's history of cancer research "from Greco-Romans to Rauscher," is finally off the press. It's available from the U.S. Government Printing Office, Washington, D.C. 20402 (Stock No. 017 042 00128 5), at $12.75 per copy. In the prologue, Shimkin says, "Today cancer is among diseases aptly called by the ancients as tumors contrary to nature. Tomorrow it will be among the horrors of the past. Its conquest will be by man's intellect, using a disciplined yet unbridled method of imagining and thinking called scientific research". . . . **EMIL (TOM) FREI** and Georges Mathé were honored at the annual M.D. Anderson clinical conference this week. Frei, director of the Sidney Farber Cancer Institute, received the Jeffrey A. Gottlieb Memorial Award; Mathé, director of the Institute of Cancerology & Immunogenetics in Villejuif, France, received the Heath Memorial Award. Frei has played a major role in developing anticancer chemotherapy, and Mathé is often called the "father of immunotherapy". . . . **"1978 CANCER** Facts & Figures" is now available from the American Cancer Society. Incidence by disease sites broken down by states in the U.S. and by nations around the world is listed. Also included are a list of institutions which received ACS grants and fellowships in FY 1977, descriptions of ACS supported programs and types of grants, and how the Society's funds are spent. . . . **LYMPHOID LEUKEMIAS** workshop will be held at Cedars-Sinai Medical Center, Los Angeles, Jan. 20-21. Richard Gatti, director of pediatric hematology, oncology & immunology at UCLA, is chairman. Write to Lore Kahane, Cedars-Sinai, 8700 Beverly Blvd., Los Angeles 90048.

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1825 Conn Ave N.W. Room 315

2:00

SUPPORT FOR INVESTIGATORS' SALARIES, SHARED RESOURCES VITAL, DIRECTORS SAY

(Continued from page 1)

Representatives from most of the 64 centers which are supported by NCI core grants spent nearly an entire day pounding away at the proposed changes. The debate was effectively concluded when John Yarbro, director of the Missouri Cancer Programs and former Cancer Centers Program director for NCI, took the floor.

"I want to compliment Tom King (director of the Div. of Cancer Research Resources & Centers)," Yarbro said. "He wants our advice. There are many at NCI who do not want our advice. But Tom has a problem, and we've heard his suggested alternatives for handling that problem. I would like to know what this group's feeling is for those alternatives."

Yarbro asked for a show of hands in support of the proposed changes, and those against. Predictably, not a single hand was raised in support, and nearly everyone voted against them.

"Tom, we don't have a solution for you," Yarbro said. "But you can see that the group is not enthusiastic about your proposals. Do you think that with 64 institutions solidly opposed, it would be a good idea to implement them?"

Most NCI staff members were convinced that such an action would be difficult, although Bernard Keele, special assistant to acting Centers Program director William Walter argued with Yarbro:

"John, how many people were in favor of the present core grant guidelines when you phased them in?"

"It's true we had some opposition," Yarbro answered. "But you have succeeded where I failed. For the first time, you have unified the center directors."

The center directors drafted a statement to be forwarded to NCI Director Arthur Upton and the NCAB. It said:

"Severe financial constraints currently threaten the continuing development of cancer centers as a strong, productive national resource central to the past achievements and future development of the national cancer program. In response to those financial stringencies, changes in the cancer center guidelines have recently been suggested.

"It is the sense of the meeting of cancer center directors convened by NCI in Memphis that: Recognizing fully the current and prospective financial constraints in the NCI budget, the guideline changes proposed for cancer center core grants will be detrimental to the centers and to the National Cancer Program.

"1. The elimination of the salary of staff investigators from core grants will prejudice institutional commitment to cancer centers, will endanger the continuity of many of the centers and will make it difficult or impossible to recruit promising and talented young investigators into the program.

"2. The elimination within three years of funding for shared resources and services will result in a major loss of the efficiency now achieved by their pooling and centralization. It is unlikely that study sections for R01 and P01 grants will allow adequate individual support for animal facilities, biohazard facilities, glassware washing, media preparation and the many similar resources that are vital to the operation of a cancer center; while the fractionation of support for those services would result in reduced efficiency and greater total cost.

"3. Instead of implementing the proposed guideline changes, we recommend the thoughtful exploration of other mechanisms to meet the budgetary problems of NCI in general and of the centers program in particular, which would not endanger the stability, continuity and productivity of cancer centers. We believe these centers to be vital to the continuing development of the National Cancer Program.

"4. We strongly support the formation of a group advisory to the NCI director. Individual cancer center directors will gladly offer their counsel on these issues to appropriate NCI staff and advisory committees."

"Some of the centers representatives complained about Upton's absence from the meeting, feeling it was another opportunity missed to thoroughly impress on him the nature of their problems and of the importance of centers to the Cancer Program. The NCI director will make any final decisions relating to core grant changes, budgets and any other aspect of NCI support for centers.

Upton had to attend a meeting in London of the International Commission on Radiological Protection, a commitment he had made before going to NCI and one he felt he had to honor. King read a statement from Upton in which he said, "I would like to take this opportunity to reaffirm my steadfast support for the Cancer Centers Program. It is my conviction that this program should continue to receive major emphasis in the nation's cancer effort, as envisioned by Congress in the National Cancer Act. I am sure you realize that serious problems have arisen because of the small increases in the National Cancer Institute's budget during the last two years. These budgetary problems, however, do not diminish my commitment to the Cancer Centers Program.

"It is my belief that by working together it will be feasible for us to resolve the problems in a way that can assure the viability, stability, and continuing quality of our cancer centers. Our task for the immediate future is to address the problems together vigorously and without delay."

King also said that Upton had agreed to the formation of an outside advisory group "to help make the Cancer Centers Program a more integrating force in the National Cancer Program."

The short term goal of the group, King said, would be to take a look at the problems NCI is having with reviewing core grant applications and to consider the budgetary problems. It was the budget squeeze and growing difficulty with reviewing core grants that prompted King and his staff to come up with the guideline change proposals.

"This group's long term goal would be a continuing evaluation of the total Cancer Centers Program—its objectives, accomplishments, and potential," King said. "We are to discuss with Dr. Upton the names of individuals who might serve on such an advisory body and the reasons for their selection. We are considering the names of individuals who would represent comprehensive, clinical, nonclinical and consortia-type centers, as well as biomedical scientists and administrators from noncenter institutions."

That doesn't exactly fit with the Carter Administration's determination to reduce the number of advisory committees, an effort that has resulted in the elimination and consolidation of several NCI advisory groups. But King and his staff feel the Centers Program Advisory Committee (if that is what it will be called) can be set up without being officially chartered, perhaps as an ad hoc group of consultants.

The changes in the core grant guidelines proposed by King were:

A. Increase the emphasis on developmental funding.

B. Phase out over time the funding of staff investigators' salaries.

C. Fund shared resources only during their developmental stages.

D. Limit the number of core grants to one per institution, although permitting those programs supported now by more than one to continue without disruption for the present.

E. Increase the core grant period of performance from a maximum of three to five years.

There was little argument and practically no discussion over proposals A, D and E. But dropping support for staff investigators' salaries and requiring centers with shared resources to charge back those costs to users would be a devastating blow to many centers, according to opinions expressed at the meeting.

One criticism frquently expressed of the Centers Program and core grant support of investigators' salaries was that this permitted some centers to maintain on their staffs scientists who could not compete on their own for individual (R01) and program project (P01) grants. However, center directors pointed out that existing guidelines require that those receiving support from core must be working on peer reviewed, approved and funded projects. Those grants frequently do not provide for investigators' salaries, and that is where core support comes in, when institutions are unable to pick them up with their own or other resources.

A sampling of comments by the center representatives and some responses from NCI staff:

Mahlon Hoagland, Worcester Foundation—Our small core grant has allowed us to attract some of the best basic research investigators. Sixty per cent of the grant pays professional salaries. It has allowed most of them to get their own grants, and part of their salaries are on those grants. To force us to put all salaries on R01s is not feasible.

King—I'm hearing you say that your institution does not have the wherewithal to pick up the difference. Bob Good at Sloan Kettering Institute has the same situation. It's not related to bigness.

Norton Nelson, NYU Medical Center—We're trying to recruit a bright young man who has tenure at a state university. If I'm forced to ask him to come in and provide his own salary, he'll stay at the state university, continue teaching 90% of the time and be lost to research.

Harry Eagle, Albert Einstein—These proposals concentrate on staff investigators and ignore the unrealistic high percentage of core supporting center administrative staff. Those centers that have created a hierarchy of generals and colonels would not be affected. Those with privates and sergeants who do the work would be wiped out.

Keele—It's been charged that centers are in a competitive, privileged position by being able to pay all or part of an investigator's salary, since that permits him to go to a study section with a smaller grant request.

Eagle—We should be able to pay salaries of investigators, in whole or in part, for those who can't mobilize their own for a variety of reasons.

Keele—That's a terrible argument, a deadly argument, that core should pay for someone who can't get funded any other way.

Steven Silverberg, Colorado Regional Cancer Center—The suggested guidelines include the statement that one aim is to increase the emphasis on centerness. How do you increase centerness when you decrease money for shared resources? Long term support for salaries and shared resources possibly may induce a department chairman to give up some of his clout, make it to his advantage to participate in a center.

Keele—The center director would still have money to develop shared resources. He would have a developmental fund to support individuals new to the center or working on a new project. The only thing he would lose is long term salary support, and components within his center would have to help pay for shared resources.

Jacques Fresco, Princeton—NCI seems to have ruled out the possibility of increasing quality requirement as a means to distribute a smaller amount of money to fewer institutions. Research dollars should go where you get the best return. Rather, NCI is ready to make decisions to hurt all of us to

keep more of us in business.

King—It's not as easy as it appears. At some institutions you're dealing with 20-30 people. You just don't categorize all 20-30 as either wheat or chaff. It would be disruptive to say, this is the line, below which we won't go.

Fresco—I've been on site visits. There are places where, under the umbrella of a few good people, less qualified people survive. We should devise some mechanism in which institutions can be forced to weed them out.

William Roberson, chief of NCI's Cancer Centers Branch—This is coming into play in the review process. Review is getting more critical. Several core grants have been disapproved, some approved but not funded. Some good core grants will be phased out in the next year or two because they don't measure up as well as their competitors.

Hilary Koprowski, Wistar Institute—The ink is not yet dry on the old guidelines (adopted in March, 1976). We just went through these convulsions, and it's happening again. None of us is using his core grant for slush funds for people who can't get other support. Remove support for shared resources, and it will increase costs, not decrease them. We should not worry about closing some cancer centers (withdrawing support from those with lower priority scores to make more money available to the survivors). Perhaps some should be closed.

Leo Buscher, chief of NCI's Grants Administration Branch—One advantage of the charge back system for shared resources would be to spread to a broader base. Other NIH institutes make use of some of those resources, but do not support them.

King—A lot of other people are benefitting from centers.

Fresco—That's an illogical statement. Other agencies and other NIH institutes support research relevant to cancer. They're picking up some of your costs.

King—You could say the intent of the Cancer Act was to put centers in a privileged position. Centers were intended to be different.

Eagle—Then what's all the shouting about?

King—We don't have enough money.

Robert Good, Sloan Kettering Institute—You've made very well the point that we've got a problem. I'm not sure that change means progress. Each center has different problems. To change the guidelines on shared resources and staff salaries could harm some, not affect others. At Sloan Kettering, shared laboratories are crucial. We try to provide some stability. The shared labs make more efficient use of R01 and P01 grants. Without shared resources, I don't know how can you have a center. I'm concerned about the frequency of changing guidelines. We start working and developing under one set, then they are changed in a year. The fiscal picture isn't changing as much as the guidelines. The idea that we can go in for R01s and P01s to make up the deficiency is a pipe dream.

Yarbro—Having said what I did about the guideline proposals, I will say that I believe there are too many staff salaries on core. You have to cut back, brutally in some cases. There are too many shared resources that ought not to be there. You have put your finger on two elements that should be cut back. But I don't agree with the rigidity of the proposals.

Charles Moertel, Mayo Clinic—Shared resources are cost effective at our institution and add to the cost effectiveness and productivity of our R01s and P01s. If we do badly, cut us off on peer review on the basis they are not cost effective. Let us have the opportunity to defend shared resources after three years. If they are cost effective and if we can't work out a pay back system, then continue funding them through the core.

Palmer Saunders, Univ. of Texas at Galveston—No one here can appreciate Tom King's dilemma better than I. I'm glad he's there and I'm here (Saunders was King's predecessor as director of DCRRC). The Centers Program was never designed as a program in competition with other programs. It was designed for a specific purpose, to get institutions involved in interdisciplinary treatment of cancer. Core support was to provide the glue to adhere the various parts together. Once you remove this incentive, many institutions will slip back into their old vertical type organization.

King told the group that budgetary limits would eventually force NCI to one of two other alternatives, if the core grant changes are not adopted, or if some other solution is not found. One would be to make across the board cuts in funds going to all centers with core grants, at less than the current levels; the other would be to fund only the most "meritorious"—those with the highest priority scores, phasing out the rest.

There is another alternative, and the centers representatives discussed it among themselves and with NCI staff between sessions: Put greater pressures on Congress for more money.

NCI can't do much lobbying for appropriations increases, other than in submitting its formal budget requests and defending them. But cancer center directors can, and they appeared ready—for the first time—to work up an organized effort in presenting the case for their own needs and the Cancer Program in general.

One of the problems in this regard, King said, was that as the budget approached a billion dollars, more people took notice and increasing criticism was generated.

"If a billion dollars bothers anyone, you can start saying a thousand million," said R. Lee Clark, Univ. of Texas System Cancer Center. "No one in this room will disagree that we can justify a billion or more right now. Maybe we should get the total figure up to where we could buy two bombers with it."

NCAB TO HEAR CENTER DIRECTORS' REACTION, OTHER REPORTS NOV. 14-16

The National Cancer Advisory Board will hear King's report on the reaction of center directors to the proposals when it meets next week (Nov. 14-16). That report is scheduled for 2:45 p.m. Nov. 15.

The Subcommittee on Centers will meet in closed session on the morning of Nov. 14, to consider reports of the Board site visits to comprehensive centers. The guideline proposals, which the subcommittee approved in September, will not be on the agenda.

Other subcommittees will meet Monday morning, and the Subcommittee on Environmental Carcinogenesis will meet Sunday evening, Nov. 13. That meeting and the session of the Subcommittee on Planning & Budget, 10:30 a.m. Monday, are open.

The full Board meeting will start at 1 p.m. Monday. Board member William Powers and Simon Kramer of Thomas Jefferson Univ. will further discuss their proposals for increased NCI support for radiotherapy research, first presented last May.

Other items on the agenda include a report on the cost of upgrading grantee and contractor biohazard and animal facilities by Harold Amos; report on cancer research in China by William Terry and Robert Miller; report of the Subcommittee on Environmental Carcinogenesis by Henry Pitot; report of the Subcommittee on Planning & Budget by Fred Seitz; report on a pathology toxicology manpower meeting by Richard Griesemer and an update on the NCI Bioassay Program by Griesemer; overview of the Breast Cancer Task Force by Pietro Gullino; overview of NCI's International Affairs Program by Gregory O'Conor, Vincent DeVita, John Ziegler and Gerald Bodey; discussions on automated cytology by Chester Herman and the International Cancer Research Data Bank by O'Conor; presentation on disorders of immuno-regulatory cells in cancer by Thomas Waldmann; and a report on the Epidemiology Program by Joseph Fraumeni.

UPTON TO CLEARINGHOUSE: BROADEN ROLE, CONSIDER ALL DATA IN RISK ASSESSMENT

NCI Director Arthur Upton agreed to an expansion of the role of the Clearinghouse on Environmental Carcinogens, encouraging its members to become in effect an advisory committee for NCI's Carcinogenesis Program and to broaden their approach to determining human risk from chemicals found to be carcinogenic in animals.

The full Clearinghouse met last week for the first time since its initial meeting a year ago. The issue that surfaced repeatedly during the year at meetings of the Data Evaluation/Risk Assessment Subgroup—whether the Clearinghouse should consider only test results from the Bioassay Program or should include other relevant data in assessing risk to humans—was again a major topic of concern.

The Clearinghouse also heard Richard Griesemer, director of the Carcinogenesis Testing Program, say that bioassay results which will be announced in a few weeks will show that five of the most widely used commercial chemicals in the environment are carcinogens. They are tetrachlorethyline, used in dry cleaning; 2,4-diaminoanisole sulfate (also known as 4-methoxy-m-phenylenediamine, 4-MMPD, or 4-MMPS) used in hair dye products; BDCP, used to control fruit pests; toxaphene, the most widely used insecticide in the world; and ethylene dichloride, an industrial intermediate solvent which may expose large numbers of workers.

"Don't limit your advice to the reports themselves," Upton said. "The problem of extrapolation from observations in animals at high doses to risk estimates to humans at low doses is difficult. We may not have all the scientific brainwork we need to enable us to accurately assess the risks. We need to determine what the facts are, and arrive at a reasonable assessment of risks. We may not have a firm estimate, but it would be useful even to just arrive at a range of estimates."

Expanding the Clearinghouse role to consider data other than that produced in specific Bioassay Program tests will involve a considerable increase in staff support. It also will increase the burden on Clearinghouse members.

Gerald Wogan, chairman of the Data Evaluation/-Risk Assessment Subgroup, reported that the group had approved a resolution restricting its review of chemicals strictly to the data in the NCI bioassay reports. Clearinghouse Chairman Arnold Brown commented that it was a question of how far to go and where to stop in gathering information to determine risk assessment.

"It would be more comfortable to bring a broad base of information together," Brown said. "However, we recall the nine month long intensive review of cyclamate data. It required the full or part time efforts of 30 NCI staff members, plus the outside consultants. It required a long time to compile and evaluate all the information available, but there seemed to be no middle way. So our decision now is to confine ourselves to the bioassay results. That does not please us, it is not fulfilling, but the alternative is not feasible."

Clearinghouse member Louise Strong suggested that the data gathering, from all sources, should be a function of an NCI staff working group. "Instead of feeding more and more chemicals through a cookbook, we should have someone put it all together to enumerate data elements to consider, and to compile them."

Griesemer said, "The program staff shares that view, and have reported it to the NCI director. But we don't want to make a unilateral decision on where to go. We need your advice."

Clearinghouse member Sheldon Samuels said, "That is precisely what we need—a working group to report back to the Clearinghouse on all physical and biological elements that could be used in risk assessment, with an evaluation of each form."

"You have defined the role of the Clearinghouse," Brown said.

Strong commented that the working group should direct itself to making tests more relevant to human risk, and more relevant to human exposure.

Strong said to Upton, "From a practical point of view, the review of other data would require staff time and is beyond the present capability of the Clearinghouse. The question is how to design studies to make them more appropriate for human risk assessment. Is that in the program's scope of research?"

"Yes," Upton replied. "The use of high and low susceptibility animals, the conditions under which certain metabolic actions occur, tests with promoting agents, repair capability—all are pertinent. It is important in the design of experiments to address those questions first.

"Is the question whether the Clearinghouse is free to offer advice to NCI on research questions? I assume Dr. Griesemer would welcome such advice," Upton said.

"They have not been reluctant to offer advice," Griesemer said. "It's more a question of being in a position to know what advice to offer."

"We were a little reluctant to do this," Brown said. "We weren't specifically asked for this type of advice. And we had plenty of other things to do."

"We need and welcome this advice," Upton said. "It would be a pity if a group such as this focused its attention only on experiments designed five years ago."

"I couldn't agree with you more," Brown said. "We long to sink our teeth into some of these issues." He suggested that the full Clearinghouse should meet more than once a year, in order to consider those issues and develop its advice.

David Clayson, chairman of the Chemical Selection Subgroup, reported that the group had recommended 40 chemicals to be tested, with varying priorities. Future issues facing the subgroup include, Clayson said:

- How should environmental mixtures be tested—technical grade (as it exists when exposed to humans) or pure? The subgroup feels the technical grade should be the one tested, but this needs further discussion with specific examples, Clayson said.
- What is the correct route for a test, and what is the correct species to be used?
- Tests should be designed to help understand trans species extrapolation, Clayson said.

Clayson said criteria for selection include the urgency sensed by the group, annual production, environmental occurrence, if it enters the water supply, any epidemiological information, previous animal tests, short term tests where available, relation to known carcinogens. "The factor we would really like to have is the degree of human exposure," Clayson said.

Back on the issue of risk assessment, Clearinghouse member Norton Nelson said, "We don't require clear signs" to reach a conclusion that a chemical is a threat to humans. "Only a faint signal is required. . . . We can only make the crudest kind of risk assessment for humans, although we have many of the pieces within reach—we have to determine the sensitivity of the target cell, the dose to the target cell. We are being frightfully behind times in not moving ahead on these fronts."

Asked by Brown to be more specific, Norton said that the sensitivity of target cells, in terms of dosage, can be determined in human tissue. "We're in shooting distance of being able to determine the responsitivity of the target molecule. I would put my money that it can be done in five years." It would be especially useful in assessing low level risks, "where we are totally helpless now."

Samuels said that NCI should be concerned only with the biological problem. "NCI should not worry about risks. The regulatory agencies look to NCI for risk assessment on biological problems. We don't want regulatory decisions to come from a scientific institution."

"That is an important point," Brown agreed. "No one here will disagree. But we do bring a pretty simple point of view to risk assessment consideration. I would like to see more precision. If you have to say yes or no, it is not intellectually fulfilling to stop there."

"It's not a good idea to play with words, yes or no," Samuels said. "But if there is a risk to one species, it is at least possible a risk to another species. What we need is the best possible description of the data. We can't solve social issues here."

"Nor will we try," Brown said.

"We're spending a lot of the taxpayers' money on this research," Clayson said. "It seems to me we need someone to say if there is a threat to man."

"Risk assessment should be done, not risk determination," Samuels said.

Griesemer reported that his staff is on schedule to complete clearing up the backlog of chemicals tested but not reported by mid-February. "The backlog is under control. We're looking ahead to future developments. You might call it the frontlog." These include 158 chemicals currently on test, with 76 more ready to go. Tests on 81 chemicals will be completed this year, and Griesemer said he would use the same system and staff to review, analyze and write reports on those tests as are being used on the backlog.

Referring to the five chemicals which will be cited as carcinogens, Griesemer said, "The release of that data will create a whole new area of activities," in-

volving regulatory agencies, labor unions, industry, and consumer groups.

Mentioning NCI studies with development of short term tests, Griesemer said such tests would be applied to 200 chemicals in the animal test program "so we can come back and compare in vitro and in vivo results."

The Clearinghouse approved a resolution previously drafted by the Executive Subgroup calling on NCI to use the short term tests in selection of chemicals to be tested, test design, and evaluation of results. Only one change was made, deletion of the word "good" in describing correlation between in vitro and in vivo results. Some members objected to a statement implying any degree of comparability.

The resolution:

"During the past several years, a considerable research effort has been underway to develop and to validate short term assays for predicting the carcinogenicity of chemicals. NCI's in vitro program has taken a lead role in this important area of research. The below statement is intended for use by the Carcinogenesis Testing Program and is not formulated for regulatory guidance.

"Short term assays can be broadly divided into three major categories. Namely, those in which there is (1) induction of neoplastic transformation of mammalian cells in culture, (2) mutagenic or cytogenetic changes in microorganisms or mammalian cells, and (3) interactions between chemicals and target macrocells, e.g., unsheduled DNA synthesis. These assays are still in the process of being defined and evaluated in terms of their usefulness, reproducibility, and comparability to known in vivo carcinogenicity systems. Data thus far obtained indicate a correlation exists between in vitro and in vivo results, although no single assay is totally satisfactory for predicting the carcinogenic potential of all carcinogens tested. This does not detract from their usefulness since combinations of assays provide a higher level of reliability.

"Notwithstanding the limitations imposed by the current state of the art, there still appears to be an immediate, practical application for short term assays. At present, microbial mutagenicity assays offer a rapid and inexpensive approach to acquire information useful in selecting and ranking chemicals for long term carcinogen bioassay. The concomitant or sequential use of DNA repair and mammalian cell transformation systems should enhance the selection process. Results from these short term assays should eventually provide important information that may be useful in assisting in the evaluation of marginal data on carcinogenicity.

"It is recognized that short term assays are still in the process of evaluation. Further, it is acknowledged that short term assay data, by themselves, are inadequate to define the carcinogenicity or lack of carcinogenicity of a given chemical. Still, it is the sense of the Clearinghouse on Environmental Carcinogens that short term assays are sufficiently developed to provide information useful in the selection of chemicals for carcinogen bioassay and in their later evaluation. It, therefore, is recommended that the Carcinogenesis Testing Program take the necessary measures to integrate short term assays into the chemical selection and experimental design processes in a manner consistent with the tone and tenor of this resolution."

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. Some listings will show the phone number of the Contract Specialist, who will respond to questions. Listings identify the respective sections of the Research Contracts Branch which are issuing the RFPs. Their addresses, all followed by NIH, Bethesda, Md. 20014, are:
Biology & Diagnosis Section – Landow Building
Viral Oncology & Field Studies Section – Landow Building
Control & Rehabilitation Section – Blair Building
Carcinogenesis Section – Blair Building
Treatment Section – Blair Building
Office of the Director Section – Blair Building
Deadline date shown for each listing is the final day for receipt of the completed proposal unless otherwise indicated.

RFP NO1-CP-85601-56

Title: *Encapsulation of retinoids for administration in laboratory diets*

Deadline: *Jan. 13*

The basic objective of this project is the encapsulation of retinoids, with two primary goals. First the formulation used must give good protection of the retinoison from oxidation, moisture, light and bacterial decomposition. Second, the formulation used must allow good bioavailability of the retinoids in the gastrointestinal tract of rats, mice and hamsters. Sustained release formulations are not required.

A five year or greater effort is anticipated in the effective pursuit of this project. However, any contracts resulting from this RFP will be written for a three-year period. The estimated cost range for the three-year period is $206,960–$280,000.

Contracting Officer: M. Hamilton
Carcinogenesis
301-427-7574

RFP NCI-CM-87181

Title: *Synthesis of nucleosides as potential anticancer agents*

Deadline: *About Feb. 1*

The Drug Synthesis & Chemistry Branch of NCI is seeking organizations having capabilities, resources and facilities for the synthesis of unique nucleosides as potential anticancer agents. The objective is the rational design and synthesis of potential inhibitors of enzymes involved in the biosynthetic pathways to nucleic acid. Samples, greater than one gram, fully

characterized, will be prepared and submitted to the National Cancer Institute for antitumor evaluation.

The principal investigator should be trained in a branch of chemistry at the PhD level, from accredited schools and must be experienced in the synthesis of nucleosides for biochemical uses. He must be named and available to the project a minimum of 60% of his time. Except for the biologist (approximately 700 man hours), all other technical supporting personnel are required to be trained chemists. They must devote at least 50% and preferably 100% of their time to the project. It is also desirable to maintain collaborative studies in the nucleoside area between the synthesis group and at least one established group of biologists interested in the use of nucleosides in cancer therapy. Laboratories must be equipped with modern facilities for synthesis, analysis and preliminary testing of compounds. Library resources must be adequate.

It is anticipated that one contract of approximately four technical man years per year will be awarded for a period of three years.

Contracting Officer: John Palmieri
Cancer Treatment
301-427-8125

RFP NIH-ES-78-9

Title: *Chemical repository for mutagenicity screening*
Deadline: *Jan. 9*

Contract proposals are sought from organizations with the interest and capability to successfully conduct the studies proposed for this contract. NIEHS proposes the establishment of a chemical repository with an initial capacity of 200 chemicals and a growth rate of 200 new chemicals per year to a final capacity of 1,000 new compounds.

Chemical analysis of approximately 10% of the compounds will be required starting with year two.

Offerors should: (1) possess adequate facilities to include appropriate structures, organization, safety compliances and areas for receiving, handling, repacking, storage and shipping of chemicals; (2) evidence adequacy of operating procedures; and (3) commit personnel with experience and background adequate to the proposed studies. It is estimated that the contract will require five years to complete.

Research Contracts Branch
NIH Div. of Contracts & Grants
Bldg 31 Rm 2B47
Bethesda, Md. 20014
301-496-4487

RFP NIH-NIAID-DAB-78-5

Title: *Production of antisera to interferon*
Deadline: *Jan. 13*

Produce an estimated minimum of 300 one milliliter quantities each of antisera to mouse interferon, to human leucocyte interferon, to human fibroblast interferon and to human lymphoblastoid interferon which will be used as National Institutes of Health reference agents. In addition the contractor will prepare an estimate minimum quantity of 300 one milliliter vials of control globulins for each type of animal used in the immunization series.

Contract Management Branch
NIAID
NIH, Westwood Bldg, Rm 707
Bethesda, Md. 20014

CONTRACT AWARDS

Title: Study innovative techniques for passage of colonoscope into cecum
Contractor: Lahey Clinic Foundation Inc., $96,000.

Title: Survey of exposure to chemical carcinogens and recommended control and intervention programs (incremental increase)
Contractor: Stanford Research Institute, $305,446.

Title: Studies in a predictive transplantable animal mammary tumor model, continuation
Contractor: Mason Research Institute, $149,673.

Title: Investigation of estrogen binding and estrophile proteins in human breast cancer, continuation
Contractor: Worcester Foundation, $125,300.

Title: Rhesus monkey histocompatibility studies, continuation
Contractor: Litton Bionetics Inc., $161,215.

Title: Comparison of ceruloplasmin levels in cancer patients, normal controls and patients with non-malignant disease, continuation
Contractor: California State Univ. (Fullerton), $14,010.

Title: Mayo-NCI central serum-plasma bank for cancer detection test evaluation
Contractor: Mayo Foundation, $187,035.

Title: CEA and related tumor associated antigens in cancer patients
Contractor: Health Research Inc., $66,081.

Title: NCI sera bank facility for the Breast Cancer Task Force, continuation
Contractor: Mayo Foundation, $90,609.

—*Editor* JERRY D. BOYD

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