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NCAB SETTLES PDQ CONTROVERSY; MORE CCOP AWARDS MAY BE MADE, CENTER GUIDELINE REVISIONS COMING

The National Cancer Advisory Board this week (1) settled a controversy over PDQ without pushing NCI Director Vincent DeVita into a position where he would have to disregard the Board's advice; (2) de-

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In Brief

MICHAEL BOYD NAMED NEW DTP DIRECTOR; SAUNDERS RETIRES; MICHAEL FRIEDMAN NEW CHIEF OF CIB

MICHAEL BOYD, chief of the Laboratory of Experimental Therapeutics & Metabolism in NCI's Div. of Cancer Treatment, will be the director of the Developmental Therapeutics Program effective Dec. 1. DCT Director Bruce Chabner announced Boyd's appointment last week, ending a year long national competition for the job, which includes heading NCI's Drug Development Program. John Driscoll, who has been acting director of DTP for three years, did not seek the permanent appointment and has returned to his position as deputy chief of the Laboratory of Medicinal Chemistry & Biology. John A.R. (Tony) Mead, DTP deputy director, will be acting director until Boyd takes over. . . . JOSEPH SAUNDERS, acting director of NCI's Office of International Affairs, has retired after 34 years of government service. Ihor Masnyk, director of the Extramural Research Program in the Div. of Cancer Biology & Diagnosis, is the acting director of OIA. . . . MICHAEL FRIEDMAN, medical oncologist at the Univ. of California (San Francisco), has been named chief of the Clinical Investigations Branch in DCT. The branch has responsibility for DCT's extramural clinical trials, including the cooperative groups. Edwin Jacobs, who has been acting branch chief, returns to his job as deputy branch chief. . . . SYLVIA MARSONI has been appointed deputy chief of the Investigational Drug Branch. . . . FRANCIS MAHONEY is acting director of DCT's Radiation Research Program while a search goes on for David Pistenmaa's successor. Pistenmaa announced earlier this year he would go into private practice Oct. 1. . . . SUSAN HUBBARD is chief of the Scientific Information Branch and ROBERT ESTERHAY is chief of the Computer Communications Branch, both in the reorganized OIA. . . . GREGORY CURT has been named special assistant to the DCT director.

cided against making any further efforts at this time to influence the final regulations on Diagnosis Related Group reimbursement; heard DeVita say that the door is still open for funding a few more of the Community Clinical Oncology Program applications to fill in some geographical blanks; and also heard from DeVita that the Div. of Resources, Centers & Community Activities once again had started revising the guidelines for cancer center core grants.

PDQ (Protocol Data Query) is the new system which enables physicians to obtain information on state of the art treatment options and treatment research protocols. PDQ-1 has been in operation for about a year but includes only a small amount of the information envisioned for it by DeVita and its chief instigator, Richard Bloch, member of the NCAB. Bloch told the Board that his concept of PDQ is that it would contain all the information needed "so that the next person who gets cancer will have the best chance for cure."

Bloch and his wife, Annette, contributed a major portion of the money NCI used to buy and renovate a building adjacent to the NIH campus which houses PDQ, the rest of the International Cancer Research Data Bank, the "Journal of NCI," "Cancer Treatment Reports," and "Cancer Treatment Symposia." The building is named the R.A. Bloch International Cancer Information Center. Other major contributors were Mr. and Mrs. Kenneth Jonsson, Alan Kay, Mr. and Mrs. Abe Pollin, Mr. and Mrs. Allan Sheehan, and the Wald Foundation. The building was dedicated in ceremonies Oct. 2.

PDQ-2, which will be available soon to physicians through computer utility vendors, the American Medical Assn., and the National Library of Medicine, will include details of currently accepted best standard care for each type and stage of cancer, as selected by an editorial board of more than 300 physicians, most of them not NCI staff members, also will include lists of protocols, with it the names, addresses and phone numbers of the physicians associated with the protocols; identity and addresses of every comprehensive and clinical cancer center, American College of Surgeons Commission on Cancer approved hospitals, participating hospitals in the Community Clinical Oncology Program, and members of the American Assn. of Cancer Institutes and Assn. of Community Cancer Centers; names and addresses of physicians supported by NCI clinical trials including all cooperative group members; and all members of the American Society of Clinical Oncology, American Society of Hematology, American Society of Pediatric Hematology & Oncology, American Society of Therapeutic Radiologists & Oncology, Society of Gynecologic Oncology, and Society of Surgical Oncology.

It was the list of society memberships that caused the controversy with the NCAB. The Board's Committee on Cancer Control & the Community had recommended that membership lists not be included in PDQ. DeVita, who spent much of the past year selling the societies on the worth of PDQ and on allowing use of their membership roles, was not in a mood to back down. The 10,000 names had already been punched into the data base, the commitments had been made, and DeVita was convinced that PDQ would be significantly diminished if it did not offer users a selection of names of oncologists in each region of the country.

Why use the professional oncology societies? Membership criteria includes the requirement that a majority of the physician's time be spent in caring for cancer patients.

DeVita pointed out that if the membership lists are excluded, 80 percent of the names which would be in the system would be medical oncologists associated with the various protocols. "There's no such thing as a no name list. You can't put up some protocols and then say, 'Guess who's doing these,'" DeVita said.

DeVita acknowledged that there may be a few physicians who spend a majority of their time caring for cancer patients who do not belong to any of the societies. And he admitted that a number of highly qualified surgeons, who may not spend a majority of their time with cancer patients, may be excluded. He promised to work on finding ways of getting them into the system.

Board member Ed Calhoun, an Oklahoma surgeon, argued that the list would encourage "self referrals." After Bloch had commented that excluding the lists would mean "when someone from Walla Walla calls and asks for the name of a board certified medical oncologist, this Board is saying, 'We won't tell you,'" Calhoun said, "You can tell him to call the county medical society."

"Frankly," DeVita said, "I'm not prepared to tear this system down before we try it." DeVita rarely has rejected decisions by his

advisors, but it appeared he was prepared to do so this time.

Board member Morris Schrier came up with the suggestion that avoided the showdown. He suggested that NCI make available to vendors the various physician lists and permit them to offer them or not to their customers. Bloch added the caveat that all lists continue to be available through the NCI supported Cancer Information Service (accessed by phone rather than computer). Victor Braren, who had made the motion to remove the lists, said that amendment was acceptable to him, and the amended motion was passed unanimously.

It had been NCI's intention all along to allow vendors the option of offering any combination of services, including making available or not the membership lists.

The Board avoided taking any further action related to the DRG issue.

Gale Katterhagen, chairman of the Committee on Cancer Control & the Community, reported on the committee's action taken last June, when a statement was drafted urging the Health Care Finance Administration to permit exclusion of hospitals which place 25 or more cancer patients a year on research protocols and which are part of NCI supported programs. The statement was circulated to Board members by mail and approved by them.

Katterhagen noted in his report this week that HCFA had ignored the Board's appeal and that exclusions from DRG reimbursement regulations would be available only to Fox Chase Cancer Center and M.D. Anderson Hospital, under the proposed regulations.

Board member William Powers said that an analysis made at Detroit Medical Center found that "the amount of money is going to be a significant shortfall, and the institution will significantly reduce the number of patients going on protocols within one to two years."

DeVita had suggested previously that more information on costs and on DRG reimbursement schedules is needed before anyone will know if the new system will hurt clinical trials.

The problem will not be that the cost of clinical trials is not covered by DRG reimbursement, since NCI pays those costs which are incurred through requirements of the protocols, DeVita said, "but where the situation is that DRG payments do not provide enough money for standard care. . . Isolate the money required for standard care from research costs. Just be sure that the money they allow for standard care is enough."

Board member Maureen Henderson moved to table the committee's DRG report and end further discussion on it. The motion carried 11-2 with Calhoun and Powers opposed and Rose Kushner abstaining.

In his report to the Board, DeVita mentioned that four new CCOP awards had been made, above the 59 previously announced, to provide coverage of areas of the country without easy access to other CCOPS or cancer centers. "We are still looking for additional ones out of the pool of unfunded applications to fill in additional geographic blanks," he said.

NCI previously had indicated that no further awards above the 62 existing ones (the Evansville, Ind. CCOP, one of the 59, having since withdrawn from the program) would be made from this round. Asked later to expand on his statement, DeVita told The Cancer Letter that more awards would be made if there is enough money left of the $10 million set aside for the program to fund them. That would be from the $10 million committed from FY 1984 money, not from funds not spent from the original commitment in 1983.

"It looks as if Congress is tying our hands (on spending money appropriated above the budget request), so we won't have the flexibility of adding more money to the program," DeVita said.

Additional awards would come from those unfunded applications in the first round, DeVita said. "Also, we could put out another RFA." That probably would not be done until at least FY 1985, however.

One of three major issues which DeVita said will be brought to the NCAB during the 1984 fiscal year will be the revision of cancer center core grant guidelines. Cancer center executives might be forgiven for groaning, "What? Not again!" The guidelines were revised in 1976 but had barely been implemented when NCI staff proposed in 1977 that drastic new revisions be made. That issue was fought over for the next five years and through the administrations of three NCI directors before it was resolved.

DeVita said the new revisions would address such issues as the number of centers which NCI should support and their geographic dis-

tribution. DRCCA Director Peter Greenwald and his staff are working on revisions now and will present them to that division's Board of Scientific Counselors. That Board's version then would go to the NCAB, DeVita said.

The centers might look somewhat more favorably on this round of revisions, DeVita hinted. One of the major gripes of cancer center directors is that they feel they need more flexibility in how they spend their NCI money. Flexibility is one of the major considerations in the revisions, DeVita said.

Two other major issues which will go to the Board this year, DeVita said, are the question of stabilization of grants at the 5,000 (competing) level for NIH ("We need stability of grants but other programs of high priority need stability also," DeVita said); and the Institute of Medicine's study of the organization of NIH which includes looking at the issue of categorical vs. non categorical research. "We are the categorical of categorical institutes," DeVita said. "We can't afford to ignore this. . . We see a lot of signs that some people would like to squeeze NCI back into the bureaucracy."

SENATE GIVES NCI MORE MONEY, FEWER STRINGS; FULL GRANTS FUNDING ASSURED

The Senate Appropriations Committee offerred fewer strings and more money to NCI than the House, in the Labor-HHS appropriations bill it reported out last week.

As reported, the bill adds $98.1 million to the Administration's request for NCI, and $17.2 million more than approved by the House.

The Senate went along with the House in directing major portions of the increase to fund grants at close to full recommended levels and to paying full indirect costs.

"That means we will not have a funding plan, to stretch dollars to pay more grants," Director Vincent DeVita told the National Cancer Advisory Board.

But it also means that the grants which are funded will be healthier. DeVita and others had said during this past year that many grants have been cut to the bone and further cuts may not be possible.

Surprisingly, DeVita said, most investigators he has talked with during the past year or two have gone along with the cuts from recommended levels, as long as the money was going to pay more grants.

NCI had projected at the start of FY 1983 that it would be able to fund 790 competing grants, but by stretching the money made possible by cutting all grants 15 percent, 888 grants were funded. Incidentally, the payline for RO1 grants in the just completed 1983 fiscal year was 175, and 178 for PO1s. Thirty three percent of approved grants were funded. The payline in 1982 was 185, but the same percentage was funded, pointing out the continuing compression of priority scores as study sections try to get what they consider high priority grants funded with more liberal scoring.

Here's all the Senate committee had to say about earmarks:

"The committee has provided sufficient funds to enable the Institute to support research project grants close to full commitments for noncompeting grants and close to study section recommended levels for new and competing grants. This action will provide for the average NIH levels of support that prevailed prior to 1982.

"In addition, the committee has restored full funding for indirect costs of research, for research centers, and for other activities proposed for reduction by the April budget revision."

That would leave NCI some discretion on how to spend some of its windfall. The House earmarks left NCI with about $7 million in unallocated money, plus about $7 million more the House added for contracts without saying how it should be spent. The additional $17.2 million over the House figure added by the Senate was totally without earmarks. If the Senate's total figure for NCI were to prevail in the conference, NCI would have more than $30 million of new money with no strings, in addition to the money required for full funding of grants and for full indirect costs.

Both House and Senate leaders were hopeful that the conference to settle differences would be held this week, brought back to both bodies with quick approval of the final bill and sent to the President, if not by the end of this week, then early next week.

The Senate report was extremely critical of the Administration's handling of the NIH budget. "During the hearings on the revised budget it became clear that Institute directors were consulted little, if at all, by OMB about the advisability of making the cuts and were left to devise a financial plan they could not realistically defend. The committee definitely is not pleased with this approach to the NIH budget. The biomedical research

conducted at NIH, research aimed at killing and crippling diseases, is too important to be subjected to budget exercises that in the end must be overridden by Congress. Moreover, the effect on the biomedical research community is surely unsettling when year after year it is faced with the instabilities created by the budgeting process. The committee is deeply concerned that this roller-coaster approach will drive scientists from the field and discourage young people from entering it."

The report included considerable praise for many NCI programs, including SEER, PDQ, prevention, basic research, CCOPS, and centers. The report zeroed in on centers because of the threat posed by the OMB budget:

"The Cancer Centers Program is an integral part of the continuum from basic research through successful application of research results. The program is the primary vehicle through which this transmission of new knowledge has been achieved, and is also vital in the new efforts aimed at cancer control.

"The proposed fiscal year 1984 budget would have required the defunding of 16 of 20 cancer centers up for renewal. After examining this proposal, the committee has decided to provide sufficient funding for all those cancer centers up for renewal funding in the new fiscal year. The cancer centers have proved themselves over the years as a vital and integral part of the cancer research effort, and no diminution of support for them should take place."

NTP BOARD APPROVES CONCEPTS OF THREE COOPERATIVE AGREEMENTS, TWO CONTRACTS

The National Toxicology Program Board of Scientific Counselors last week gave concept approval for three new projects to be supported by cooperative agreements, including one aimed at finding out if the suspicion that corn oil used as a vehicle in about one third of NTP's toxicity studies caused pancreatic cancer in rats has any validity.

A positive finding on corn oil could call into question results of a significant number of NTP and NCI bioassays conducted over the past 10 years and undoubtedly would require using vehicles other than vegetable oils in future tests. It would also have profound regulatory implications for the food industry and the public in general.

The Board also gave concept approval for two contract supported projects, one new and the other a recompetition.

The three RFAs given concept approval for funding as cooperative agreements were:

Determine the biological nature of proliferative exocrine pancreatic lesions in F344 rats and the possible role of vegetable oil in promoting formation of these lesions. Total estimated first year funding, $280,000 for two four year awards. The staff's justification:

Objectives are to determine the biological nature of acinar pancreatic lesions in rats and the role of vegetable oil in their production.

In a recent two year NTP study, male F344 rats exposed to methylene chloride had an increased incidence of pancreatic acinar cell hyperplasia and acinar cell adenomas. This was of interest since methylene chloride is used to decaffinate coffee and coffee has been associated with carcinoma of the human pancreas by some investigators. However, the vehicle control (corn oil) male rats in this study also had a high incidence of proliferative acinar cell lesions of the pancreas, prompting a wider reviews.

Examination of the pancreas from nearly 1,000 male F344 rats receiving corn oil as control vehicle in two year NTP studies revealed an incidence of 12.6 percent pancreatic acinar cell hyperplasia, 4.9 percent acinar cell adenomas, and 0.27 percent carcinomas, while no carcinomas and less than one percent acinar cell adenomas were found in the over 1,000 untreated controls examined. Thus, the role of methylene choride and/or the corn oil vehicle could not be determined.

CONCEPT REVIEW FIGURES ARE ESTIMATES ONLY: RFPs, RFAs NOT YET AVAILABLE

The dollar estimates with each concept review brought before the various boards of scientific counselors are not intended to represent maximum or exact amounts which will be spent on those projects. They are intended only as guides for board members to help in determining the value of the projects in relation to resources available to the entire program or division. Responses should be based on the workscope and description of goals and methods included in the RFPs (contracts) and RFAs (grants and cooperative agreements). Availability of RFPs and RFAs will be announced when the Institute is ready to release them.

While NTP two year studies generally mimic the route of exposure for humans, nearly one third of the chemicals have been given by gavage in corn oil because of solubility or stability problems with the chemical. It is important to determine the role of the corn oil vehicle in the production of pancreatic acinar cell lesions and the biological nature of these lesions in the rat. This is necessary for the interpretation of NTP two year studies utilizing corn oil as a vehicle. Knowledge gained in the study of rat pancreatic cancer may have relevance for pancreatic cancer in man which ranks fourth in frequency among fatal cancers in the U.S. and appears to be increasing in frequency.

This initial approach will be to administer by gavage, on a long term basis, various levels of corn oil and other vegetable oils to establish basic background data that can be used if these oils serve as vehicles in NTP studies. During this period efforts will be devoted to developing short term assays for

detecting compounds that cause proliferation of the acinar pancreas.

As lesions are produced, the biological nature will be studied by correlating histological classification with transplantability. This will be used to develop a more precise classification for these lesions which then can be used for the NTP studies. The awardee will be expected to provide insight and offer suggestions for further studies as the results from the early studies become available. The awardee will also be expected to have expertise in cancer biology, rodent cancer classification and in pancreatic endocrine physiology. It is anticipated that some studies will be developed concerning the role of pancreatic tropohic hormones. The progress in this project will be analyzed annually and those discussions will serve as a basis for jointly planning the next series of experiments.

Gary Boorman of NTP's staff said that there is "some feeling that all studies done with corn oil vehicle are null and void. But looking at the studies, we found no differences in most."

"There is little question of the need for understanding the pathology of these lesions," Board member James Swenberg commented. "One third of our studies use corn oil gavage."

"There are no studies showing no lesions," NTP acting deputy director Gene McConnell said.

"If we're sure of that, one of the first things we should do is stop using corn oil," Board member Jerry Hook said.

Development of an in vitro system for the coincubation or coculture of isolated renal tubules and hepatocytes. Estimated first year award, $130,000, three years. Staff description:

The system will be developed from a variety of mammalian species, including humans. It will maintain physical separation of the different tissues but allow passage of low molecular weight solutes via the medium. The tissue isolation techniques will be adaptable to the use of fresh autopsy or biopsy material. If successful, this system will be used by NTP to study initiating events in chemical nephrotoxicity at the molecular and subcellular levels, and to enhance extrapolations from in vivo animal studies to potential human health effects.

Recent chronic study results from the NTP chemical testing program have associated nephrocarcinogenic or other chronic nephrotoxic effects with an increasing number of common synthetic chemicals, in particular halogenated aliphatic hydrocarbons (e.g. trichloroethylene). Because of sex and species differences in toxic response, however, and the relatively large doses used of necessity in the chronic studies, questions have been raised as to the relevancy of these data for predicting similar effects in humans. Clearly, an approach other than repeating standard chronic toxicity studies in rodents is needed to indicate the significance of these animal findings to human health effects.

A system will be developed to maintain in vitro isolated renal tubules and hepatocytes in a functionally and metabolically active state for four to 24 hours, longer if possible. The system will physically separate the two tissue types with a selectively permeable barrier that allows free and rapid transfer of solutes below a molecular weight of 500 daltons, and essentially no passage of molecules greater than 2,000 daltons. A liquid medium simulating physiological conditions (e.g. plasma) will be employed to maintain cell viability and to facilitate metabolite transfer between the cells. If necessary, a medium pumping system may be used to assure metabolite distribution.

The techniques for hepatocyte and renal tubule isolation must be consistent with the maintenance of viability and normal cell function, and adaptable for tissues removed via biopsy or autopsy. The latter stipulation is to allow for the predicted use of tissues from humans and other primate species in addition to rodents. A method other than in situ perfusion will probably have to be used.

Once a satisfactory system has been developed, studies will be undertaken to elucidate the initial biochemical and functional events (relevant to cytotoxicity) resulting from select chemical exposures. Comparative studies will be performed to evaluate modifying factors such as chemical metabolism, species, sex, and chemical concentration (dose) on toxic response of the renal tubular cells. NTP will be guided in selecting test parameters by the results of its in vivo toxicity research and testing programs.

The award recipient should have access to basic laboratory equipment (e.g. centrifuges, spectrophotometers, balances), analytical equipment (e.g. liquid scintillation spectrometer, liquid chromatograph), and adequate animal facilities. Some attempts at identification and quantitation of parent chemical and metabolites are expected. Since many of the chemicals of interest are appreciably volatile,the developed system should be compatible with precise control of atmospheric conditions (non ambient). Finally, the award recipient must work in close cooperation with NTP staff as needed to corroborate and extend the experimental findings.

Development of methods to assess human metabolism of chemical xenobiotics. Estimated first year funding for each of one to three awards, $200,000, five years. Staff description:

Objective is to develop methodology for assessment of the capacity of human tissues to metabolize chemical xenobiotics and thereby assess the suitability of laboratory animals as models for human metabolism of chemicals. The number of awards will be dependent upon the merit of responses.

Results from studies of chemical disposition in animals are extrapolated to predict the fate of the chemicals of interest in humans. In all species, rates and routes of metabolism, most frequently hepatic metabolism, are primary determinants of chemical disposition. Hepatic metabolism of chemical xenobiotics may result in activation or deactivation of toxic properties and may vary considerably with species. Species dependent variations in chemical metabolism frequently account for variations in species sensitivity to chemical toxicity. Therefore, the validity of animal to human extrapolation is subject to question when it has not been confirmed that the animal model and humans handle the subject chemical in a similar manner.

The obvious need for better methods to predict the fate of xenobiotic chemicals in humans has been addressed by a number of

research efforts designed to assess the metabolism of these compounds by human liver. The most promising techniques have utilized isolated tissues which could be stored frozen and used over a period of time. The best sources of such tissues or enzymes have been tissue banks stocked with healthy human tissues resected in the course of surgery and/or very fresh autopsy tissue gained at the time of kidney transplants. Studies with such tissues offer a variety of opportunities to assess the capacity of humans to handle chemical xenobiotics. They not only facilitate extrapolation of laboratory data to man, but also permit an assessment of human variability with sex, age, genetic makeup and pre-exposure to environmental factors such as smoking and chemicals in the workplace.

Approach: First, it must be established that reproducible and reliable data on the metabolism of chemical xenobiotics can be obtained in vitro with human tissues. Second, a tissue bank must be established to permit reliable comparison of data obtained with human tissues over a period of time with a variety of chemicals. The history of each donor must be carefully recorded with particular emphasis on age, sex, pre-exposure to chemicals and known genetic defects in metabolic competence. Third, there must be a systematic approach to study the metabolism of chemical xenobiotics which have previously been or will be studied in laboratory animals under similar conditions to obtain comparable results. Fourth, the effect of sources of human variability should be assessed whenever possible. Fifth, the results of these studies will be used to assess the reliability of animal models as predictors of the fate of toxic or carcinogenic chemicals.

The two concepts approved for contract supported projects were:

Chemistry support for toxicity testing at NIEHS. Estimated first year award, $300,000, three years. Staff description:

Objective is to provide routine chemistry support for all inhouse TRIP toxicity studies. It is planned to award a contract to a laboratory located within a one hour drive of NIEHS, or the contractor should demonstrate how efficient response times could be provided.

During late FY83 and into FY84, the Toxicology Research & Testing Program will be occupying new laboratory space. This will create a significant increase in the number of inhouse toxicity studies initiated at NIEHS. In the past, chemistry support for TRIP's inhouse studies has been limited and was provided on an intermittent basis through the contract for analytical chemistry services for the NTP with Midwest Research Institute in Kansas City, Mo. Problems relating to timely shipments, adequate local cold storage for large batches of dosage mixtures and difficulties in coordinating work schedules have occurred. Due to these problems, it has become necessary to procure this support from a contractor with the ability to respond to the needs of TRIP within an hour. Midwest not only does not have this capability at this time but is not able to handle the increase of tests under the current contract.

It is anticipated that there will be approximately 25 studies initiated each year which will require chemistry support. This support will include procurement of test chemical, bulk chemical identity and purity, assays, dose preparation and verification, routine tissue and body fluid analysis, etc. Analytical methods development for bulk chemical, chemical/vehicle and tissue and body fluid analysis will also be required.

Hook and Swenberg suggested that this work could better be done by NTP/NIEHS staff. C.W. Jameson of the Program Resources Branch said that limits on staff positions precluded that approach. "We don't think it the best use of our time and positions to develop a large chemical mixing facility," NTP and NIEHS Director David Rall added.

Animal research on inhalation toxicology of environmental chemicals. Estimated first year award, $1 million, five years. This is a re-competition ; Northrop is the present contractor. Staff description:

NTP is becoming increasingly involved in conducting tests of chemical toxicity (including carcinogenicity) by inhalation. Of approximately 243 chemicals for which complete reports were available by mid-1983, only three had been done by inhalation. Of 84 chronic tests in progress at that same time, 15 were by inhalation. Of 83 prechronic starts, seven were by inhalation. A program that sponsors this level of research activity in a very technically demanding area should also have an active research program ongoing in that area in order to preserve its credibility as sponsors and interpreters of that work.

Contract laboratories across the country are selected to be given chemicals for testing as the needs of the program arise. These laboratories conduct studies according to rigidly specified protocols and the results are interpreted and disseminated by program personnel. In contrast, the purpose of our onsite contract operation is to provide a research facility for studies in both inhalation technology and toxicology in support of the broader aims of the testing program. The development of the theory and practice of inhalation toxicology, in all of its aspects, has tended to lag behind other areas of toxicology. All of the requisite resources that would be necessary to build a program aimed at contributing to the solution of problems in inhalation toxicology are potentially available at NIEHS.

Two general goals may be defined: To conduct research in the inhalation toxicology of chemicals in small animals and to develop a computer monitoring and control system for a small animal inhalation facility. Research in inhalation toxicology may include the performance of chronic toxicity studies of gases or vapors yet to be identified, and chronic toxicity studies of solid aerosols (fibers) yet to be identified. Another example is experiments to test the hypothesis that certain characteristics of time varying concentration exposure profiles are determinants of the inhalation toxicity of chemicals.

The resources of the contractor operated inhalation research facility and of the smaller government operated unit have been combined in the past into an integrated program of research in inhalation toxicology at NIEHS. The inclusion of the smaller facility in the new contract will not change the general way in which the government research needs in inhalation toxicology are met. Each experiment can be viewed as a joint piece

of research involving the contractor and the government project officer who works in collaboration with other government scientists. Individual protocols are agreed upon through the use of formal protocol review meetings in which government scientists convey their needs to the contractor through the government project officer.

RFPs AVAILABLE

Requests for proposal described here pertain to contracts planned for award by the National Cancer Institute unless otherwise noted. NCI listings will show the phone number of the Contracting Officer or Contract Specialist who will respond to questions. Address requests for NCI RFPs, citing the RFP number, to the individual named, the Blair building room number shown, National Cancer Institute, NIH, Bethesda, MD. 20205. Proposals may be hand delivered to the Blair building, 8300 Colesville Rd., Silver Spring, Md., but the U.S. Postal Service will not deliver there. RFP announcements from other agencies will include the complete mailing address at the end of each.

RFP NCI-CM-47650-64

TITLE: Collection, storage and quality assurance and distribution of biological response modifiers

DEADLINE: Approximately Nov. 25

The National Cancer Institute is interested in establishing a contract to support the Biological Resources Branch Div. of Cancer Treatment, in achieving its goals of producing high quality biological response modifiers and in ensuring the sterility, safety and potency of biological response modifiers for clinical and preclinical investigations.

This support project involves two parts--Task A and Task B. Offerors may propose on Task A, Task B or both tasks.

Task A--(1) Provide facilities and develop a computerized inventory system for the acquisition, receipt, storage and distribution of biological reagents and tumor cell lines; (2) Perform appropriate assays for each BRM as requested by the project officer. These assays will involve a variety of in vivo and in vitro techniques. Mouse antibody production and intracerebral lymphocytic choriomenangitis test capability should be available. General safety test on biologics for clinical use in compliance with 21 CFR 610.11 is required.

Task B--Offerors will be requested to perform on an assigned basis and according to protocols assigned by the project officer certain tests and assays designed to confirm stated biologic properties of BRM preparations. It is essential that the FDA Good Laboratory Practice regulations pertaining to preclinical studies by strictly followed.

Because of the need of frequent communication between the principal investigator and the project officer, and the need for pickup of biologics from the BRMP, participation is limited to offerors who can perform within a 75 mile radius of the BRB, located at Frederick Cancer Research Facility, Frederick, Md.

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RFP NCI-CN-45166-46

TITLE: Efficacy studies of chemopreventive agents in animal models including synthesis, bioavailability and encapsulation studies

DEADLINE: Nov. 15

NCI's Div. of Resources, Centers & Community Activities is interested in establishing master agreement contracts for the above studies.

Objective of this study is the evaluation of efficacy of various designated chemopreventive agents at several dose levels in animal models and the refinement and improvement of animal test models for chemopreventive studies. Emphasis will be to take initial leads on candidate agents and expand the data base as to the spectrum of carcinogens, spectrum of target sites and range of species.

Candidate agents from natural sources or synthetic analogs have been evaluated for anticancer efficacy in various in vitro tests and in a limited number of in vivo studies. However, before a decision can be made as to their suitability for phase I clinical trials their efficacy must be evaluated in various animal models.

Agents to be investigated are potentially hazardous. The animal model system will also involve the use of carcinogens. Laboratory practices shall be employed which will keep any element of risk to personnel at an absolute minimum. Where indicated, tissue and compound handling must be performed in (at least) Class I laminar flow cabinets which must meet NIH specifications for work with carcinogen agents. Animal facilities are to be fully accredited by the American Assn. for Accreditation for Laboratory Animal Care. Incoming animals are to be held in quarantine to monitor health and condition prior to entrance into the experimental animal facility.

All laboratory and animal studies are to be conducted in facilities that are in full compliance with FDA Good Laboratory Practice Regulations.

It is estimated that up to 50 task orders per year will be issued pursuant to the award(s) of the master agreement contracts.

Equipment: Contractor must have all equipment necessary to accomplish the studies including but not limited to, animal racks and caging, hazardous chemical storage cabinets and refrigerators, pathology equipment such as microscopes and microtomes and miscellaneous laboratory equipment. The laboratory shall have or have access to appropriate terminal and computer facilities and equipment for data collection and storage.

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