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FCRC CONTRACT WILL BE COMPETED IN FIVE PARTS, TWO OF THEM FOR SMALL BUSINESS; RFP AVAILABLE JULY 24

NCI has completed redesigning its contract for operation of Frederick Cancer Research Center, and the new RFP which will recompete the $20 million-plus program as five separate contracts will be available July 24, if contract officials remain on the schedule they have established. (Continued to page 2)

In Brief

CHABNER NAMED DCT ACTING DIRECTOR, SCHEPARTZ RETURNS TO DEPUTY JOB; GM WINNERS ANNOUNCED

BRUCE CHABNER has been named acting director of NCI's Div. of Cancer Treatment. He replaces **SAUL SCHEPARTZ**, "who for the past 18 months has served admirably" as acting director of the division, NCI Director Vincent DeVita said in announcing the change. Schepartz returns to his job as DCT deputy director. **ARTHUR LEVINE**, chief of the Pediatric Oncology Branch, replaces Chabner as acting director of the Clinical Oncology Program. Chabner previously had been chief of the Clinical Pharmacology Branch and is widely known for his work on the pharmacology of antitumor agents. DeVita said the change was made because of the "enormous workload" brought on by new programs with large clinical counterparts which made it necessary for Schepartz to return to his role in supervising the coordination of preclinical programs with each new clinical component. He also will resume his responsibility for operation of all DCT programs supported by contracts. . . . **WINNERS OF** the 1981 General Motors Cancer Research Foundation awards of $100,000 each were **E. DONNAL THOMAS**, director of medical oncology at Fred Hutchinson Cancer Research Center; **WALLACE ROWE**, chief of the Laboratory of Viral Diseases at the National Institute of Allergy & Infectious Diseases; **CESAR MILSTEIN**, molecular biologist in Cambridge, England; and **TAKASHI SUGIMURA**, director of the National Cancer Center Research Institute in Tokyo. Thomas was honored for his work in development of bone marrow transplantation; Rowe for his contributions in virology; Milstein for development of hybridoma technology; and Sugimura for leadership in identifying carcinogens in food. . . . **ARE CANCER** center core grants the best mechanism for supporting institutions engaged only in basic research? DeVita raised the question at the meeting of the Div. of Resources, Centers & Community Activities Board of Scientific Counselors, suggested that program projects or some other mechanisms might be better. A subcommittee chaired by **HARRY EAGLE** will meet July 14, NIH Bldg 31 Rm. 11A10, from 1-6 p.m. The meeting will be open. .

LITTON WILL COMPETE FOR THREE OF FIVE NEW CONTRACTS FOR OPERATION OF FCRC

(Continued from page 1)

Litton Bionetics Inc. has been the contractor for the GOCO (government owned, contractor operated) facility since 1972, when President Nixon decided to end the biological warfare operations at Ft. Detrick, Md., and turn most of the base over to NCI. The contract reached as much as $30 million a year but has been phased down to $25 million for the current year as NCI and NIH moved some intramural labs to FCRC and Litton's activities were scaled down somewhat.

NCI Director Vincent DeVita, with concurrence of the National Cancer Advisory Board, has decided that the contract would be recompeted at a 20 percent reduction, with half that amount to be put back in over the life of the five year contract to permit growth of meritorious programs.

Litton Bionetics won out over spirited competition in 1972, but when the contract was recompeted in 1977, there was no opposition. The new RFP will assure competition this time, with the contract split into five parts—research, operations and technical support, animal production, computer services and library services.

The last two will be small business set asides, removing Litton Bionetics from that part of the competition. Michael Hanna, FCRC director for the company, said Litton will compete vigorously for the other three. "We view the recompetition as a positive thing," Hanna said. "We are looking forward to it."

There are any number of organizations which could compete for the support and animal production contracts. NCI executives, who were dismayed by the lack of competition the last time, are confident that organizations with those capabilities will submit proposals.

The research portion of the contract may be another story. This accounts for almost half the total cost of the contract. Hanna has assembled an outstanding group of scientists whose work has impressed NCI boards of scientific counselors which have reviewed them, as well as the NCAB. A new contractor would have to agree to keep the team intact.

DeVita has suggested that a university or consortium of universities would be interested in competing for the research contract. Other for profit firms and the not for profit research institutions also might be more tempted this time to go up against Litton Bionetics for the research end of the operation.

The small business set asides for computer and library services will be competed only among firms which meet the government's definitions of small business. That varies, depending on the type of work to be done, and the limits—annual gross and number of employees—will be included in the RFP. NCI staff has determined that sufficient competition in those two areas exists to justify the set aside.

NCI's announcement of the impending RFP follows:

Proposals will be solicited under a single RFP of five parts for the conduct of research, management and operation of the FCRC for the period Sept. 26, 1982, through Sept. 25, 1987, with the possibility that up to five contracts may be awarded. The five RFP parts, which may be awarded as five separate contracts are: 1. Research contract. 2. Operations and technical support contract. 3. Animal production contract. 4. Computer services contract, and 5. Library services contract. The computer and library services contracts will be small business set asides. Negotiated level of effort cost type contracts are contemplated.

FCRC is presently operated under a single cost plus award fee/cost plus fixed fee contract with a current annual budget in excess of $25 million, exlusive of alteration/renovation of facilities which will be added to the operations and technical support contract during contract performance.

The FCRC facility consists of 70 buildings on 68.6 acres. Estimated date for RFP availability is July 24, 1981, with probable due date of proposals on or about Nov. 16, 1981. A preproposal conference, to include a facility inspection of FCRC, will be held approximately two weeks after the RFP is mailed.

The major functional activities of these five proposal areas include:

RESEARCH CONTRACT

This research shall be solicited and negotiated as a level of effort contract to include biological carcinogenesis, chemical carcinogenesis, cancer biology (including genetic engineering), and metastasis and treatment.

Under this research contract, the contractor will be required, for the first year, to furnish the level of effort as set forth in the RFP, and to deliver an annual technical progress report. A cost plus fixed fee contract is contemplated.

OPERATIONS AND TECHNICAL SUPPORT CONTRACT

This contract will provide for nearly all support necessary for the entire FCRC operation, both contractor and government, as well as the maintenance and upkeep of the FCRC buildings and grounds. Aside from certain mandatory corporate functions such as retirement, insurance, etc., concerns submitting proposals in this area will be required to structure them so that they will be virtually self subsistent under this contract from an overhead and resource standpoint. However, the provision of research animals, library services, and computer services may be furnished by the government through separate awards which may result from this RFP.

The RFP will stipulate both estimated level of effort and completion requirements, as applicable to

the various parts. All such level of effort and completion requirements will be based upon most current contract experience available.

Under this contract, the contractor will be required to perform the work and services set forth in the RFP workscope and to furnish the level of effort negotiated. Current staffing levels will be made a part of the RFP and provide a basis which offerors may use to prepare their proposals. The contract will also be required to furnish an annual report. A cost plus award fee contract is contemplated.

The Operations and Technical Support Contract will include business and administrative management, facilities maintenance and construction, support of NIH/NCI intramural research programs, fermentation program (pilot plant), environmental control and research, occupational health care, research services support including pathology and histotechnology, biological resources production, central laboratory services and animal health diagnostic service and quarantine; and animal holding.

ANIMAL PRODUCTION CONTRACT

The contractor shall be required to maintain a production capability for rodents including mice, rats and guinea pigs at a level of: (1) approximately 2,200 mouse cage equivalents as foundation colonies; (2) approximately 9,500 mouse cage equivalents as pedigreed expansion colonies, and (3) approximately 600 guinea pig cages.

A cost plus award fee, level of effort contract is contemplated. Monthly reports and an annual support report of the quantity, quality, and disposition of animals produced will be required.

COMPUTER SERVICES (Small business set aside)

The contractor shall be responsible for the operation of a comprehensive automated data processing facility in support of all FCRC operations.

The computer resources of the NIH Div. of Computer Research & Technology (DCRT) will be used for work of a scientific nature. For work of an administrative nature, the resources of the Management Information Systems Directorate (MISD), Ft. Detrick, shall be used. Access to these computer systems and data entry capability is provided by a currently existing Mohawk Data Sciences 2400 Remote Job and Data Entry Terminal. This terminal consists of a dedicated minicomputer driven operating system that can simultaneously communicate with a remote computer and provide local data entry capability. Associated with the equipment is a high speed printer (600 lines/minute), a tape drive, a large capacity disk, a console CRT, and four data entry terminals.

The contractor shall be required to support a total of 28 low speed terminals located in the computer center and in several of the laboratory buildings.

The contractor shall also be required to support an HP 3354B Laboratory Data System located in the computer center. The system consists of an HP 2100 computer, a disk drive, a paper tape reader, and a line printer.

The contractor shall also provide statistical services including the design of experiments, the development of sampling plans, the analysis of data, and the development of mathematical models. Extensive use is made of a comprehensive statistical computing library at DCRT, including SAS, BMDP, SPSS, and MLAB.

A cost plus award fee, level of effort contract is contemplated. An annual report of work performed will be required.

LIBRARY SERVICES (Small business set aside)

The contractor shall be responsible for operation of an existing on site scientific library facility in support of all FCRC operations.

Resources that are currently available include 4,800 square feet of space, a 14,000 volume collection, 461 journal subscriptions, and various computer terminals. In addition there are five branch libraries in research buildings.

A cost plus award fee, level of effort contract is contemplated. An annual report of work performed will be required.

All research effort and support services described above will be performed at the Frederick Cancer Research Center, with all facilities, including buildings and equipment, to be furnished by the government.

Firms interested in competing for all or parts of the procurement described above must submit a written request to obtain a copy of the RFP to: Ronald Defelice, Contracting Officer, National Cancer Institute, Bldg. 427, Room 11, Frederick Cancer Research Center, Frederick, Md. 21701; telephone 301-663-7148.

DCT BOARD APPROVES CONCEPTS OF EIGHT BIOLOGICAL RESPONSE MODIFIERS RFAs

The Board of Scientific Counselors of NCI's Div. of Cancer Treatment has approved the concept of eight requests for applications (RFAs) which earmark a total of $5.1 million for new grants in the Biological Response Modifiers Program.

The Board rejected two other RFAs proposed by the BRMP staff and also turned down a cooperative agreement RFA for development of new treatments for gastrointestinal cancer.

Publication of RFAs requires that a specific sum of money be allotted to fund grants they generate. Those grant applications compete only against each other and not those in the regular R01-P01 pools. This would permit NCI to fund grants which score above the payline for R01-P01s, if that would help stimulate research in an underdeveloped area.

Board members were uneasy about establishing favored categories which could allow funding some grants of less quality than others which might go unfunded.

DCT Deputy Director Saul Schepartz pointed out

that the National Cancer Advisory Board has gone along with a deviation of up to 20 points when program staff felt it was necessary to fund a grant which helped fill a need. The DCT Board agreed with that policy and recommended that all RFA stimulated grants in the division be funded at the same payline as NCI R01s with the 20 point deviation at program staff's discretion.

Board members were particularly interested in RFAs for monoclonal antibody research proposed by BRMP Director Robert Oldham and his staff, adding $500,000 to $1.5 million earmarked for monoclonal antibody in cancer therapy. The Board also approved an RFA for monoclonal antibody in animal tumor models, although trimming the earmark from $1.5 million to $1 million.

RFAs approved by the Board, all to be announced during the summer with awards to be made July 1, 1982. Funds earmarked probably will cover multiple awards:

Monoclonal antibody is cancer therapy. Proposed first year award, $2 million.

Monoclonal antibodies provide a chemically and immunologically homogeneous reagent of defined specificity. They can be obtained in quantities necessary for therapeutic evaluation in man either as a means of selectively eliminating tumor populations directly or indirectly by eliminating or inactivating suppressor cellular components of the immune system.

Studies to be proposed should evaluate the therapeutic effectiveness of monoclonal antibody administration in man. Monoclonal antibodies directed against specific antigens expressed on human tumor cells or on lymphoid cells suppressing an effective antitumor immune response may be evaluated alone or coupled with drugs, toxins, or radioisotopes to determine the pharmacokinetics, clinical toxicity, potential efficacy as anticancer agents, and maximum tolerated dose that can be administered parentally. Parameters to be monitored following administration of monoclonal antibody preparations as therapeutic agents will be degree and specificity of binding to target cells, fate of antibody bound tumor cells, modulation of target antigen, and alterations in circulating tumor cells and tumor antigen.

Monoclonal antibody in animal tumor models. Proposed first year award, $1 million.

Studies are proposed to evaluate the therapeutic efficacy of monoclonal antibody administration in animal tumor models. Currently available monoclonal antibodies directed against specific antigens expressed on tumor cells or on lymphoid cells suppressing an effective antitumor response may be evaluated either alone or coupled with drugs, toxins, or isotopes for in vivo antitumor properties. Therapeutic potential of these antibodies will be evaluated in the treatment of transplanted, induced, and spontaneous animal tumors. Studies will examine such parameters as: effects of passive administration of antibody or antibody conjugates on survival and cure rate; difference in ability of antibody of different isotope to mediate antitumor effects; antibody half-life and tissue distribution, degree and specificity of antibody binding to tumor cells, in vivo and in vitro fate of tumor cells, modulation of tumor cell antigens, optimal dose schedule and short- and long-term toxicity.

Therapeutic efficacy of adoptively transferred lymphoid subpopulations in tumor bearing hosts. Proposed first year award, $150,000 (cut by the Board from the staff's request of $250,000).

In vivo inoculation of defined subpopulations of lymphoid cells, and antigen presenting cells, in tumor bearing animals may provide an effective form of adoptive immunotherapy and biological response modification.

Studies to be proposed should investigate the capacity of adoptively transferred lymphoid and/or macrophage cells to achieve antitumor immunity. Several approaches may be tried including (1) the use of normal cells, especially lymphoid cells which may favorably regulate the immune response; (2) the use of antigen presenting cells; (3) the use of lymphoid cells specifically presensitized against tumor associated transplantation antigens either in vitro or in vivo. Methods which enable enrichment or selective proliferation of the therapeutically active cell subpopulation should be investigated, as should mixed combinations of various classes of immune cells. Therapeutic effects of these subpopulations should be assessed in animals bearing spontaneous, induced, or transplanted tumors.

Immunogenicity of purified tumor associated antigens. Proposed first year award, $750,000.

Methods of immunization need to be developed to evoke effective in vivo antitumor immunity using purified tumor associated antigens as immunogens.

Biochemical isolation of tumor associated antigens is possible using monoclonal antibodies. There is considerable uncertainty, however, how best to administer purified antigens in vivo to evoke effective antitumor immunity. Certain antigens may facilitate and others may inhibit tumor growth and metastases. The proposed studies should investigate this issue in both normal and tumor bearing animals using biochemically purified antigens as therapeutic agents. Preference will be given to nonviral tumor associated antigens on recently derived spontaneous or chemically induced fully syngeneic tumors although consideration will be given to viral coded tumor antigens and even normal cell surface alloantigens as model antigens. The use of various immunization schedules and adjuvants and detailed monitoring of the host cellular and humoral immune responses will be required. These studies must be directed toward optimizing the therapeutic effect of these antigens in vivo.

Animal tumor models for antipeptide factor and maturation factor therapy. Proposed first year award, $300,000 (staff had requested $150,000).

Low molecular weight peptide growth factors which promote cell division and anchorage independent growth of normal and transformed human cells in vitro and which may be required for tumor growth in vivo have been recently identified and characterized. In order to assess the potential therapeutic efficacy of agents which specifically block these growth factors, suitable animal tumor models need to be developed. In addition, other peptide growth factors and certain other substances have been shown to induce maturation (terminal differentiation) of human tumor cells in vitro. Animal tumor models are also required to assess these substances as potential anticancer agents.

Studies are proposed in which a transplanted or spontaneous animal tumor will be developed to determine the therapeutic efficacy of anticancer agents which act by specifically blocking the actions of specific peptide growth factors. These factors might include both normal and tumor cell products. The animal tumor must be shown to be responsive in vitro to a peptide growth factor (for example epidermal growth factor) and the agent being tested must have been shown to specifically block this same factor. In similar fashion an animal tumor model will be developed which can demonstrate the anticancer activity of maturation factors which are capable of inducing terminal differentiation of various transformed cell lines in vitro. Examples of cell lines previously shown to be responsive to such agents include PC-12 pheochromocytoma

cells and HL-60, Kg-1, and K 562 myeloid leukemia cells. Transplantable tumors of these or similar cell lines might form the basis of a suitable animal tumor model.

Therapeutic use of lymphokines in cancer. Proposed first year award, $250,000.

Administration of lymphokines that can selectively activate or suppress certain components of the immune system may produce a beneficial antitumor effect in vivo.

Studies to be proposed should evaluate the therapeutic value of defined lymphokines in antitumor immunity. It is proposed that currently available lymphokines purified to near homogeneity be used in both in vivo and in vitro studies to evaluate and monitor specific effects on the various cellular components of the antitumor response. A further stage of analysis will involve testing the therapeutic efficacy of various lymphokine preparations in transplantable and spontaneous animal tumor models. Investigators may restrict their study to a single lymphokine or may wish to perform comparative studies on various lymphokines. A goal of the studies should be to provide information relevant to the choice of a lymohokine(s) for preliminary clinical testing and the type(s) of tumor host relationship most amenable to effective biological modification using lymphokines.

The Board approved two more RFAs but asked that they be combined, suggesting that some of the others might also be combined. The two were:

Therapeutic approaches to lymphokine dependent lymphoid malignancies.

In vivo administration of specific lymphokines or in some cases inhibitors of lymphokine production may produce a beneficial therapeutic result by selectively retarding the proliferation and/or promoting the maturation of certain lymphoid malignancies.

Studies to be proposed should investigate therapeutic benefits resulting from in vivo administration of lymphokine or inhibitors of lymphokine production to retard proliferation and promote maturation of lymphoid tumors. Studies are proposed to screen various lymphokines for their effects on the growth and maturation of human lymphoid malignancies cultured in vitro. These studies would be extended to determine the potential therapeutic benefit of in vivo attempt at arresting tumor growth and/or promoting maturation of lymphoid tumors using exogenously administered lymphokines or inhibitors of lymphokine production.

Sensitized T-cell lines in adoptive immunotherapy.

T-lymphocyte cell lines sensitized against tumor associated antigens may be generally beneficial in adoptive transfer of immunity to certain types of cancer.

Studies to be proposed should determine optimal conditions for obtaining positive therapeutic effects when T-lymphocyte clones are sensitized in vitro to tumor associated antigens (TAA) and transferred to tumor bearing experimental animals. Techniques will be developed for sequential culture of TAA sensitized lymphocytes using T-cell growth factor, optimizing primary sensitization to various TAA in vitro, analyzing and monitoring therapeutic effectiveness of sensitized lymphocytes in various animal tumor models using monoclonal antibodies to identify the lymphocyte effector cell subpopulation involved in adoptive immunity to TAA, enhanding and optimizing therapeutic effect by altering dose and schedule of administration of sensitized lymphocytes.

Staff had proposed $150,000 for the lymphokine RFA and $400,000 for the T-cells RFA. In combining the two, the Board added $100,000 for a total of $650,000.

The Board rejected RFAs for immunotherapy directed against organ specific antigens, with estimated first year total of $200,000; and therapeutic efficacy of alloimmunization in tumor bearing hosts, $150,000.

The proposed cooperative agreement for new treatments for GI cancer would have funded pilot studies for development of new chemotherapy or combined modality treatments, possibly including biological response modifiers.

John MacDonald, director of the Cancer Therapy Evaluation Program, said, "There isn't a lot of developmental work going on in GI cancer." Board member Walter Lawrence agreed. "It seems to me this is where we ought to stimulate people. There is a need. GI cancer is at a standstill," Lawrence said.

But other Board members suggested that the Cooperative Groups should be encouraged to develop GI cancer studies, and most of them felt that pilot studies should be funded through the R01 route. Several suggested that the field might be stimulated with a program announcement, which does not carry with it an earmarked sum of money and which would encourage investigators to submit grant applications through the regular process. No action was taken on that suggestion, however.

FDA COMMITTEE OKs AMSA FOR GROUP C, FAILS AGAIN TO APPROVE ESTRAMUSTINE

The Food & Drug Administration Oncologic Drugs Advisory Committee last week:

- Approved M-AMSA for Group C distribution by NCI for treatment of refractory acute leukemia.
- Tabled NCI's request to add radiotherapy induced nausea and vomiting refractory to standard antiemetic agents as a Group C indication for THC.
- Failed once again to approve an NDA for estramustine for treatment of metastatic and/or progressive carcinoma of the prostate.
- Approved addition of advanced bladder cancer as an indication in the NDA for cisplatinum.

NCI's Group C distribution system makes available at no charge agents proven in clinical studies to be useful in the treatment of cancer but which, for various reasons, have not been approved for marketing by FDA through the new drug application process. Except for THC, Group C drugs are sent to any physician requesting them who has filed Form 1573 with NCI (THC is distributed only through registered and cooperating hospital pharmacies).

The fact that M-AMSA, which can produce severe toxicities at higher doses, might be made available for use outside of controlled situations bothered some committee members. Brigid Leventhal pointed out that intolerable toxicity seems to occur at doses above 120 mg/m2 but that therapeutic benefit usually cannot be obtained at lower doses. However, "I don't find this alarming in the context of resistant AML," she said.

Silvia Marsoni, of NCI's Investigational Drugs Branch who presented the case for the drug, said that physicians requesting it usually would be hematologist/oncologists experienced in administering potent anticancer agents. Branch Chief Daniel Hoth, answering Leventhal's question on whether NCI screens requests and could send the drug only to physicians experienced in handling marrow aplasia, said that has not been done but could be for M-AMSA.

Leventhal's motion to approve the drug for the Group C list was approved unanimously, as was her motion to recommend a dose of 120 mg/m2 times five, with repeated courses as necessary and tolerated. Committee member David Alberts added that because of the possibility of cardiotoxicity, "Physicians have to make sure patients are in electrolyte balance and have reasonably good cardiac function." Monitoring is not necessary, he said.

The committee, which last year approved THC for Group C distribution as an antiemetic for cancer chemotherapy patients, decided to await results of ongoing THC-radiotherapy studies before broadening the Group C indication.

Hoth argued that other antiemetics had not been approved for a specific stimulus and pointed out that THC would still be limited to those patients refractory to standard antiemetics. But committee member Carol Portlock said that differences between radiotherapy and chemotherapy patients should be considered, especially since CNS toxicity is one of the major THC side effects. Leventhal suggested that the "vomiting trigger" might be different for the two modalities, but Alberts said, "It is probably prostaglandin release that triggers vomiting."

Committee member Walter Lawrence suggested that there are not very many patients for whom radiotherapy is not tolerable. "Radiotherapists disagree with you," Div. of Cancer Treatment Deputy Director Saul Schepartz said. "They've been making loud noises to us (requesting THC)."

Beth Strunk, the committee's consumer representative, said she had polled a number of radiotherapists in anticipation of the issue before the meeting, "and they all said this is needed."

"If there are so many radiotherapy patients vomiting, it should be easy to do the study," Leventhal commented. Lawrence's motion to table was approved 5-0, with Strunk abstaining.

Hoth, reporting on the status of THC distribution, said that 701 registered hospital pharmacies had expressed interest in handling the compound, 544 had been approved by the Drug Enforcement Administration or were in the process of being approved, and that 1,794 registered investigators are eligible to request the drug. Distribution has leveled off at 1,000 bottles a month, Hoth said.

The committee's action on estramustine was a tie vote, 3-3 (four members did not attend the meeting). Since committee actions are advisory only, FDA could approve the NDA or not.

John Burns, vice president for research of Hoffmann-La Roche, the drug's sponsor, said, "Roche feels a commitment to make this drug available in the United States. We proposed very restrictive labeling, and only for those unresponsive to other therapy. It is available around the world, and the U.S. is the only country where it isn't. We want to make this available to those for which there is no other therapy. Roche had done all it can. I don't know what else we could do."

Roche representatives argued that estramustine has been proven, in randomized controlled trials, to be at least equal to DES in treatment of prostatic cancer.

"In 1979 and 1980, the main issue was whether stable disease is a useful category in prostatic cancer, and whether the drug had efficacy," Portlock said. "I have the greatest difficulty in saying efficacy has been demonstrated. Safety, yes. But I am dissatisfied that we can't base it on objective criteria."

"There is an undercurrent here that all anticancer drugs must show objective responses," FDA staff member Robert Young commented. "That is not true. You can base a decision on pain relief."

"I have no trouble in buying stable disease as a parameter," Lawrence said. "Also, I have no trouble in saying that estramustine is equal to DES. My trouble is this: Should we go on approving more complex and expensive drugs that aren't any better? Adding mustine has not helped."

Roche representatives argued that mustine did add something to hormone therapy and that the data showed it. They added that it was unlikely estramustine would be used as initial therapy, since DES treatment costs "three cents a day. But when they fail, there is nothing else."

"It is reasonable to approve a drug that is equal to another," Alberts said. "What bothers me is that we're basing a decision on the Wisconsin study, in which the dose was 3 mg a day. The VA study suggests that 1 mg can be cardiotoxic. Is this 25-30 percent incidence of congestive heart failure tolerable?"

Roche representatives said the incidence of heart failure was closer to 5 percent, "and if you treated the same population with adriamycin, you would get the same incidence."

"I think they've come quite close to demonstrating equality of treatment," Lawrence said. "It is unfair to ask them to go back and demonstrate more on objective/subjective response."

Committee Chairman Jack White, Lawrence and Portlock voted for approval; Leventhal, Alberts and Strunk against.

Portlock and Strunk had to leave the meeting to make plane connections just as Bristol started to present its case for adding advanced bladder cancer to

the cisplatinum NDA. Ann Greenstein, the committee's executive secretary, noted that this would leave the committee without a quorum and thus prevent a vote.

Bristol representatives objected strenuously, pointing out they had brought in investigators at considerable expense to make the presentation. Before the Bristol indignation could reach the explosion point, Lawrence suggested the committee "vote now and hear the presentation later," adding that he had already reviewed the material. The vote was taken, approval granted (5-0, with Leventhal abstaining), Portlock and Strunk made their planes, and Bristol reps—veterans of protracted debates on NDAs—flabbergasted but pleased.

NTP PANEL AGREES PBB IS CARCINOGENIC, TWO VARIETIES OF ASBESTOS ARE NOT

The National Toxicology Program Board of Scientific Counselors Peer Review Panel agreed with NTP staff conclusions that two compounds tested in the bioassay program were carcinogenic, including polybrominated biphenyl mixture (PBB) which was responsible for widespread environmental contamination and animal losses in Michigan.

The report accepted by the Panel at its June meeting concluded that "under the conditions of this bioassay," PBB (Firemaster FF-1) was carcinogenic in rats and mice of both sexes, inducing neoplastic nodules, hepatocellular carcinomas and cholangiocarcinomas in rats and hepatocellular carcinomas in mice. Other toxicities included porphyrogenic effects and hepatotoxicity.

Firemaster FF-1 is a flame retardant which inadvertently was substituted for a mineral food supplement for animals eight years ago in Michigan. Millions of animals died or were destroyed when the accident was discovered, but not before PBB found its way into human food supplies.

IARC criteria for human risk based on animal studies, although not yet accepted by the NTP Board, assigns a high degree of carcinogenic risk to man when a compound is determined to be a carcinogen in both sexes of a two species study.

The other compound the Panel agreed was carcinogenic in test animals was pentachloroethane, a solvent used primarily as an intermediate in the manufacture of tetrachloroethane. Processes have been developed which do not use pentachloroethane, and its annual production has declined to less than 5,000 pounds.

The bioassay report concludes that the substance was carcinogenic for male and female mice, causing increased incidences of hepatocellular carcinoma. It was not carcinogenic for rats of either sex but was nephrotoxic for male rats.

Two other compounds were determined by the program to have less convincing evidence of carcinogenicity, each producing tumors in only one sex of one species. 2-biphenylamine hydrochloride, a chemical intermediate used in the manufacture of C.K. Acid Red 15, produced angiosarcomas in female mice. Statistical evidence was incomplete for male mice possibly due to poor survival. It was not carcinogenic for rats. Allyl isothiocyanate, a flavoring agent, was carcinogenic in male rats, causing transitional cell papillomas of the urinary bladder. Evidence for associating it with subcutaneous fibrosarcomas in female rats was equivocal. It was not carcinogenic in mice.

Because the carcinogenicity of inhaled asbestos has been established and because of widespread exposure to the ingestion of asbestos, the program has undertaken studies to determine if ingestion leads to an increased incidence of tumors. The conclusion of reports on the first two tests to be completed: It does not.

Two varieties of asbestos—chrysotile and amosite—were tested in male and female Syrian golden hamsters. Neither produced significant increases in tumors. In fact, the report on amosite asbestos noted that both weight gain and survival seemed to be enhanced by asbestos ingestion. "A possible explanation for these observations may be that increased fiber content in the diet caused the increased weight gain and survival," the report said. "The increased fiber content in the diet may cause these effects, regardless of whether the fiber is organic or inorganic in composition."

Additional studies with asbestos, using other species, are being evaluated.

The report on the bioassay of stannous chloride, an inorganic tin compound used as a food preservative, a stabilizer for colors, perfumes and soaps, and a reducing agent in tin plating, concluded that the compound was not carcinogenic for rats or mice of either sex.

RFPs AVAILABLE

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

RFP NCI-CP-FS-11027-67

Title: *Case-control study of lymphoma and soft-tissue sarcoma: Association with herbicide exposure*

Deadline: *Aug. 14*

Certain herbicides and herbicide contaminants have been associated with teratogenesis, mutagenesis, and carcinogenesis in animal and bacterial experi-

ments. In addition, recent studies suggest that in persons exposed to herbicides the risk of cancer be increased five- to six-fold. The data suggest that phenoxyacetic acids and chlorophenols and/or their associated contaminants may be carcinogens which act on several body sites; possibly some unidentified factors are systematically biasing the studies. The heavy use of herbicides and the postulated high cancer risk associated with their exposure underscore the urgent need to conduct an independent epidemiological investigation of persons exposed to these agents.

The Environmental Epidemiology Branch, Field Studies & Statistics Program, Div. of Cancer Cause & Prevention, has planned a case-control study of persons with soft tissue sarcoma, non-Hodgkin's lymphoma, or Hodgkin's disease. Cases and controls, or their next of kin, will be interviewed by telephone to obtain occupational histories and other information which may be pertinent to the origin of these cancers. Particular attention will be paid to herbicide exposure. The RFP covers the data collection activities for the proposed case-control study. This will be a support or resource contract, with no independent research by the contractor although publications resulting from this study may recognize the contributions of key personnel of the contractor.

NCI would like to contract with an organization which is highly experienced in conducting all support phases of medical case-control studies. This includes: preparing data collection forms; selecting, tracing and interviewing study subjects; abstracting; coding, keying, and editing data; documenting procedures; and creating and manipulating data files. Experience limited to conducting nonmedical surveys will not be considered as meeting the basic requirements of this RFP.

The contract is expected to last two years. Funds for the second year will be identical to or less than the first year, by reduction of effort, not personnel salaries. It is anticipated that the contract will begin in September 1981, but the actual initiation date will depend on progress of the competitive procedures.

The overall objective of this contract will be to provide technical, managerial, and clerical support for a telephone interview study of persons with soft tissue sarcoma, non-Hodgkin's lymphoma, and Hodgkin's disease from areas of considerable herbicide use and appropriate controls, or their next of kin. The contractor will collect sufficient information to enable NCI to evaluate the role of herbicide exposure and other factors in the development of these diseases.

Personnel needed include 1) a principal investigator (10% of time) with at least three years experience in the conduct and management of medical case-control interview studies; in utilizing and evaluating medical questionnaires; in hiring and training interviewers; and in evaluating conduct and quality of interviewing and abstracting procedures. Minimum education is a master's degree with training in epidemiology or a related medical, social, or public health research field. 2) a field management specialist (100% of time) to supervise and be responsible for all data collection. Must have at least three years experience in hiring and training interviewers, and in coordinating and evaluating the conduct and quality of interviews and abstracting procedures. Education: bachelor:s degree with training in epidemiology or a related social or public health research field. 3) a computer programmer (50% of time in year 1, 20% in year 2), with three years experience in writing, debugging, and documenting computer programs in at least two computer languages.

No person named for this contract shall be employed for more than 100% of his/her time, i.e., not to exceed 40 hours per week, whether or not the project is funded by the government. All stated personnel qualifications are subject to verification by the government.

Contract Specialist: Camille Battle
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301-427-8888

RFP NIAID-OSD-82-8

Title: *Mouse leukemia virus research project*
Deadline: *Approximately Sept. 17*

The Laboratory of Viral Diseases of the Intramural Research Program of the National Institute of Allergy & Infectious Diseases has a requirement for a mouse leukemia virus research project. The function of the contract is to breed pedigreed hybrid mice, to test mice for the presence of murine leukemia virus by the XC tissue culture assay and to hold and examine mice infected with various murine leukemia viruses for occurrence of the disease. Potential offerors must have their facility within a 35 mile radius of the NIH, Bethesda, Md. campus location.

Requests for the RFP should include a self-addressed mailing label.

Chief, Contract Management Branch
NIH-NIAID
Westwood Bldg. Rm. 707
Attn: John Hamill
Bethesda, Md. 20205

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