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P.O. Box 2370 Reston, Virginia 22090 Telephone 703-620-4646

NCI Shakeup Possibilities Grow; Marc Lippman To Head Lombardi Center; DCT Could Lose CTEP

As if there weren't enough ferment already involving possible NCI organizational changes, Marc Lippman's appointment as the new director of the Lombardi Cancer Center at Georgetown Univ. and other new developments have further added to the shakeup possibilities. Most of the proposals

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In Brief

NCI Construction Authority To Continue Under Panel's Plan; NCAB Hearing In Philadelphia

EXISTING NIH construction authorities, including that of NCI, would **not** be superceded by the new authorization recommended by the panel of experts (**The Cancer Letter**, March 4). The panel's report specifically recommends that existing authorities be continued, a point not emphasized in **The Cancer Letter's** article. . . . **NATIONAL CANCER** Advisory Board's next public hearing will be April 19 in Philadelphia, at the College of Physicians. NCAB member John Durant, president of Fox Chase Cancer Center, will chair the hearing in which the public and health professionals will discuss cancer prevention and detection programs and needs of the community. Previous NCAB public hearings in Los Angeles, Atlanta and Miami have been considered big successess. . . . **CEIBA-GEIGY** annual award has gone to **Samuel Broder** and **Robert Gallo** of NCI and Luc Montaigne of the Pasteur Institute for their work on AIDS. . . . **FIVE YEAR**, $12.5 million contract from NCI's Office of Cancer Communications for editorial, phone answering and publications services was won again by the incumbent, Biospherics, which has had the contract since 1974. The company didn't know it, but no other firms went up against it this time. Don Mullins is the PI. . . . **NIH IS** establishing an "NIH Reviewers Reserve" (NRR) whose members will be available to supplement chartered scientific review committees as needed. NRR is intended primarily for use by the NIH Div. of Research Grants for its study sections but will also be available to individual institute committees, including NCI's. Executive secretaries may continue to bring in ad hoc special reviewers as needed, but those assigned from the NRR pool will be permitted to vote on and score grant applications; ad hoc reviewers may not. Nominations for the reserve will be made primarily from among retired members of chartered review committees.

DCE, DCPC Could Be Combined Into "Cause & Prevention" Divison

(Continued from page 1)

for change are meeting with strong opposition from one quarter or another, the most vocal of which has been the Div. of Cancer Etiology and its advisors who object to the prospect of losing the Epidemiology & Biostatistics Program to the Div. of Cancer Prevention & Control.

This latest of NCI's interminable reorganizations was touched off last year when Director Vincent DeVita decided to consider moving cancer centers out of DCPC, either into his office or into a new division. That move most likely would also include the other elements of the Centers & Community Oncology Program, which include the Community Clinical Oncology Program, the Research Facilities Branch, and the Organ Systems Program. It would probably also include the Cancer Training Branch.

That issue has still not been resolved. Then, DeVita told the National Cancer Advisory Board last month that he and his senior staff members were considering moving the the epidemiology program to DCPC so that it could be more involved in national networks, including reuniting it with SEER, which was moved to DCPC four years ago.

Because centers and the CCOPs are involved with the clinical cooperative groups, DeVita has toyed with the idea of bringing them together into the new organizational setup, whatever that might be. The groups are administered by the Cancer Therapy Evaluation Program in the Div. of Cancer Treatment. CTEP handles all of DCT's extramural clinical trials, and some NCI executives think those should all be under the same roof as centers and CCOPs. But take all extramural clinical trials away from DCT? In the mid-1970s, just after DeVita became director of that division, he won a long and sometimes bitter struggle to consolidate all treatment related activities in DCT, getting the groups away from what was until then the only division that could support extramural research with grants.

NCI Acting Deputy Director Maryann Roper told the DCT Board of Scientific Counselors two weeks ago that DeVita had decided against moving CTEP out of DCT. "That could be throwing out the baby with the bathwater. It could have a negative impact," Roper said.

However, DCT Director Bruce Chabner told **The Cancer Letter** this week that the issue was still open, and that CTEP could end up somewhere else.

Meanwhile, Roper revealed another intriguing possibility in discussing the various proposals with the DCE Board of Scientific Counselors. DCE and what would be left of DCPC after removing the Centers & Community Oncology Program could be "molded into one division," she said.

That would get epidemiology together again with SEER and with the application missions remaining in DCPC, without bringing down the wrath of DCE staff and Board members. Roper observed at that meeting how determined the opposition was.

DCE's epidemiology program, headed by Joseph Fraumeni, "is one of the best in the world, certainly in cancer," Roper said. "But there are some concerns that it needs to be involved with the national network, and with centers." She added that no deadline had been established for making a decision on a move, and "whatever decision is made will not be made in a closet."

DCE Director Richard Adamson said that "the thrust of this program is the etiology of cancer. Many of the studies in the program are multidisciplinary incorporating a laboratory component. Obviously such studies must involve interaction with either the Biological or Chemical and Physical Carcinogenesis Programs. The presence of the Epidemiology & Biostatistics Program within DCE facilitates the administrative aspects of scientific interactions in cancer etiology, including shifting resources so that high priority projects receive necessary support. Various etiologic leads from all three DCE programs are already communicated to the Div. of Cancer Prevention & Control, the Office of the Surgeon General, the NCAB, Congress and the regulatory agencies and do have a major impact on cancer prevention and control."

Adamson touched on what is probably the most important factor in the location of programs in a bureaucracy.

"Sometimes collaborations just don't happen. They have to be forced a bit. As the division director over both (epidemiologists and lab scientists), I can do that."

Board member Allan Conney stressed the importance of collaboration of epidemiologists with basic scientists. "I think it is in the best interests of the country to have epidemiology in this division. I am very much opposed to moving it."

"It would be very disruptive," Board member Alice Whittemore said. "What are the advantages of a move?"

"Epidemiology is in the middle, with research on one side and SEER on the other," Roper said. "We need better identification of what's coming out of SEER." SEER is Surveillance, Epidemiology & End Results, the nationwide collection of incidence and survival data through a contract supported network of tumor registries.

Roper argued that "the relationships with basic scientists are there, they are cemented and would not be broken" by a move.

Board member Anna Barker said that in previous years, epidemiology had been "adrift. Now, it is just the opposite. It has a scientific orientation in cause and prevention." Moving the program elsewhere "could cause it to go adrift again."

"Under the present arrangement with epidemiology in this division, it has been very responsive to national needs," Board member Peter Magee said. "I am very much opposed to a move."

After Maureen O'Berg and Pelayo Correa expressed their opposition, Chairman Hilary Koprowski asked, "Do any members of the Board favor a move?" Not one did, and Koprowski told Roper, "You can take that as your message."

"I will take the message home," Roper said. "It distresses me that DCE is insular, that you feel if the program is moved, that is the end of collaboration, that collaboration can't go across division lines."

That argument can be turned around, of course. If interdivision collaboration is easy, why bother making the move?

"We do cross division boundaries," Adamson insisted. "We do bring issues to the attention of DCPC."

NCI is viewing the impending move of Lippman to Georgetown as not losing one of its brightest stars but rather gaining a new constellation in the Institute's universe.

Lippman is chief of the Medical Breast Cancer Section, in the Medicine Branch of DCT's intramural Clinical Oncology Program. The impact he has made, as one of the world's premier breast cancer scientists, far transcends the role of a section chief.

Georgetown has been searching for a director of the Vincent Lombardi Cancer Research Center since its founding director, John Potter, stepped down last July. The university has been negotiating with Lippman for about six months; they concluded an agreement last week.

"NCI is a fabulous place to work, but it is not a university," Lippman said in an interview with **The Cancer Letter** this week. "This is a tremendous opportunity for me, with the likelihood that we can put together a neat program at Georgetown."

The Lombardi center was founded in 1970, named for the famed football coach who was treated there for colon cancer that year and who died there. Soon after NCI initiated its program of recognizing centers as comprehensive cancer centers, Lombardi and Howard Univ. won such recognition jointly. They collaborated on some outreach programs, but that ended when NCI ended its support for center based outreach efforts. In recent years, with the departure of several key scientists, Lombardi's output has declined.

Lippman intends to turn that around, starting with a double edged effort that NCI welcomes on the one hand, and is opposing on the other.

Lippman, DeVita and Chabner all talked enthusiastically of developing a close collaboration between NCI and Lombardi, and DeVita also included Howard in that effort. That collaboration could include faculty appointments at the universities for some NCI staff members, and use of NIH facilities by Lombardi and Howard investigators.

It also will include joint efforts to continue the breast cancer research funded by the five year, $1 million a year grant from the Abramson family of Philadelphia. That grant had been turned over to Lippman to establish the program. Much of the equipment purchased with that money will go with Lippman, possibly with other NCI equipment which he said will probably be valueless to anyone else. "Vince has been terrific about that," Lippman said. The Abramson funding will complete its second year July 1, when the family will conduct a review of the program. Their approval will be required to implement joint NCI-Lombardi use of the funds.

The other side of the NCI-Lippman relationship is his efforts to take with him many of the people who have been working him. "There are some excellent people who will go with me," Lippman said.

"While I wish him the best, I'm going to try like hell to keep everyone here," Chabner responded. "I hope we have a good relation-

ship with Marc. He's a terrific researcher and will be a tremendous asset to the university. It is nice that he will still be in town. It will almost be like he never left. But right now, we're fighting over the same people. When that competition is over, I hope we can settle into a good relationship."

DeVita objected to inferences in the "Washington Post" that Lippman's departure, and that of other NIH scientists, was due primarily to the salary gap. "One reason people leave is because we have only a limited number of senior staff positions we can offer them," DeVita said.

Lippman agreed that his primary motivation was the opportunity to develop a first rate cancer research and treatment center, with a strong commitment from the university for the resources that will require. However, "it would be silly to say that money is not important. I have one kid in college, another who soon will be there, and two more coming along."

Lippman has a powerful recruiting tool in going after his NCI colleagues. "I can offer to double the salary of some of the people here who are making $45,000 a year." Just as important, he said, is the flexibility and freedom of the university environment, more space, and other perks.

WHT Participants Get "Phase Out" Help; Future Dietary Studies Planned

As NCI winds down its funding for the Women's Health Trial, it is "helping participants make a smooth transition out of the trial and is planning future efforts to clarify the link between diet and cancer," according to an Institute news release.

The 1,760 women who were enrolled in the three WHT centers will be given the opportunity to participate in special phase out interviews and will receive information materials to help them maintain a low fat diet if they wish to do so. They also will be asked to give blood samples that will be stored for future laboratory study.

NCI intends to design future dietary studies and will continue support of research to identify biochemical tests of dietary fat intake to aid future studies of dietary fat modification.

"NCI is committed to improving the understanding of fat's role in breast cancer risk," said Peter Greenwald, director of the Div. of Cancer Prevention & Control. "Nevertheless, there is enough information and sufficient scientific agreement to substantiate the need to reduce dietary fat, as recommended in NCI's dietary guidelines."

The WHT was a multi-institutional study of a low fat diet in healthy women 45-69 years old who were at increased risk for breast cancer. Fully implemented, it would have involved 32,000 women at 20 or more centers, with eight to 10 years followup and costing more than $90 million.

The primary hypothesis being tested was whether a low fat diet (20 percent of calories from fat) compared to the customary American diet (40 percent calories from fat) would cut in half after 10 years the incidence of breast cancer among those at increased risk.

Because of doubts about dietary compliance, monitoring and other aspects of the study, a "vanguard" group at the three centers was enrolled and monitored to determine the feasibility. Although the investigators demonstrated conclusively that compliance had been achieved, NCI and its advisors decided not proceed with the full trial. That decision was based on a number of factors, including disagreement over whether fat alone or in combination with calories is the critical factor in promoting breast cancer, and laci of a biochemical marker to assure adherence.

DCE Board Approves Concepts For HPV Model Grants, Leukemia Etiology

A new grant supported program for development of animal models for human papillomavirus associated neoplastic diseases was given concept approval by the Div. of Cancer Etiology Board of Scientific Counselors at its recent meeting.

A total of $1 million will be set aside for first year funding of the grants expected to be generated by the request for applications.

The Board also approved on a split vote the concept of a contract for the etiology of childhood leukemia. DCE staff estimated the four year contract would cost $2.8 million.

The Board approved recompetition of four contracts which total nearly $9 million according to staff estimates. Five million dollars of that was estimated for the contract for occupational studies support services, now performed by Westat Inc.

The concept statements follow:

Animal models for human papillomavirus associated neoplastic diseases. Five year grants, estimated total of first year awards, $1 million.

Cervical cancer is a common malignancy among women in the U.S. and the most common form of cancer affecting women in developing countries. Recent evidence strongly supports an etiological role for human papilloma viruses (HPVs) in anogenital malignancies including cervical carcinoma. Approximately 80% of the dysplastic or cancerous lesions of the cervix and vulva have been demonstrated to contain DNA from specific HPV types. Metastases from cervical tumors also contain HPV DNA of the same type as the primary tumor. Several established cell lines derived from cervical carcinomas (e.g., the HeLa cell line) have HPV DNA integrated into their genomes. Recent laboratory studies have shown that HPV DNA can transform cells in culture. Specific transforming genes have been identified. Animal papillomavirus model systems (e.g., rabbits and cattle) are also known where initially benign viral lesions (warts, papillomas, or condylomas) undergo malignant conversion with relatively high frequency.

Since the application of recombinant DNA technology to the papillomavirus field in the last decade, the molecular characterization of human and animal papillomaviruses has proceeded rapidly. Over 50HPV types have been described. Twelve HPV types associated with anogenital lesions have been identified, the genomes of some of them have been sequenced and a number of important viral proteins have been expressed in bacteria. Thus, the stage may be set to begin the development of vaccines and immunotherapies. In order to assess the potential for such developments, a workshop on the prospects for human papillomavirus vaccines and immunotherapies was held last September. Drs. Hilary Koprowski and King Holmes served as chairmen. The workshop consensus was that HPV vaccines could have an important role in preventing HPV disease and, consequently, their associated malignant sequelae. However, the systematic development of such vaccines and associated immunotherapies is currently hindered by two factors: lack of knowledge of how the host immune system responds to such infections and the lack of appropriate animal models for the development and testing of candidate vaccines and immunotherapies. The workshop participants strongly advocated the development of new animal models and the more vigorous investigation of known animal models to address these issues.

In the area of intracellular and immune mechanisms, animal models can provide a detailed understanding of the way papillomavirus associated dysplasias usually progress to a certain level and then either stabilize or regress at high frequency. Further progression to malignancy apparently occurs in only a small proportion of infected individuals. This progression/regression profile has been well documented in both human cervical dysplasias and in the cottontail rabbit papillomas. Preliminary data suggest that, in humans, progression to malignancy is associated with cofactors, e.g., other viral infections and smoking. Regressions are associated with an infiltration of immunocompetent cells (lymphocytes and Langerhans' cells) into the lesions. However, it is not known how this cell mediated immune response is initiated. Specific cytotoxic T-lymphocytes have not yet been isolated. Humoral antibodies to HPV virions have been detected in 46% of genital cancer patients, but the role of these antibodies in dysplastic tissue progression or regression is not known. An understanding of the natural mechanisms of progression/regression in animal models of papillomavirus associated lesions, particularly the identification of the viral or cellular epitopes involved in the process, will be especially helpful in developing new diagnostic aids, rational approaches to vaccines and new types of immunotherapy.

The scope of this RFA includes both animal and human papillomaviruses in animal models. Collaborative projects which include molecular, immunological and pathological aspects will be encouraged. Examples of studies (which are not all encompassing) are (1) identification and characterization of animal papillomavirus host systems whose disease pattern is similar to the progression/regression profile seen in oncogenic human disease; (2) identification and characterization of animal models which can be infected with human papillomaviruses; (3) characterization of the mechanism of progression/regression of lesions to carcinoma with particular emphasis on intracellular mechanisms and the participation of the humoral or cellular immune response; (4) identification of specific viral or cellular antigens (epitopes) which mediate the host immune response; (5) development of specific antibodies or the establishment of cytotoxic T-lymphocyte lines specific for HPV associated dysplastic or carcinomatous cells; (6) development of prototype animal/human vaccines which can protect animal models from viral challenge; (7) development of procedures to facilitate the regression of dysplastic or malignant lesions via immunotherapeutic or chemotherapeutic approaches.

Alan Schreier is the program director.

Etiology of childhood leukemia. Multiple four year contracts are anticipated involving the collaboration of several centers. The estimated cost for the first year is $810,000, total cost $2.8 million.

Leukemia is the most common childhood cancer, accounting for about one third of malignancies in children under age 15 in western countries. Epidemiologic studies, however, have failed to identify any major risk factors. The only consistent association is with in utero exposure to x-rays, use of which has been steadily decreasing. Recently interest has centered on the possible role of electromagnetic low frequency radiation from residentially proximate high power electric lines and household appliances, although study results have been inconclusive and no clear biological mechanism is apparent. Because of the widespread and increasing exposure of the U.S. population to electromagnetic fields, the high public interest in this issue, and the conflicting epidemiologic study findings, further clarification of the relationship with childhood cancers, and the most common of these, childhood leukemia, is needed.

The staff of the Epidemiology & Biostatistics Program has had a long and varied interest in studies of childhood cancer, beginning in the 1960s with characterization of the association between Down's syndrome and childhood leukemia, and extending to the present with further examination of prenatal maternal pelvimetric x-ray exposure as a leukemogen. While many exposures have been linked with childhood leukemia, the proposed study will focus on three important areas that can be examined using the epidemiologic approach. Thse are residential low frequency electromagnetic radiation, parental occupation, and other childhood residential exposures.

Since 1979 five investigations have examined the relationship between electromagnetic field exposure and childhood cancer; two of these have specifically considered leukemia as a separate entity. Three of the studies showed significant associations for all childhood cancer (odds rations ranging from 1.3 to 3.0). Another also reported increased risk, although not statistically significant, for leukemia (odds rations of 1.9 and 1.4 for low and high power magnetic fields, respectively. Two of the investigations found no relationship. Only one of the five studies character-

ized exposure through in home electromagnetic field measurements.

Two large case control studies of childhood leukemia (the Oxford Childhood Cancer Study and the Tri-State Leukemia Study) were carried out more than 25 years ago, but in the past 10 years only a few studies of limited sample size have been reported. Maternal reproductive characteristics, various prenatal and pregnancy related factors were emphasized in these studies; none of the reported associations have been confirmed, however. A few reports have linked familial occurrence of leukemia, other cancers, and congenital disorders with childhood leukemia. Postnatal exposures, such as breastfeeding, viral and bacterial infections, immunizations, other medical conditions and treatments, have received little attention.

Parental occupation is a suspected risk factor in the occurrence of childhood leukemia and other childhood cancers, although results have been contradictory. Hydrocarbons and other chemicals as well as undefined exposures of motor vehicle operators have been implicated in some studies, but not consistently confirmed. Lack of comparability among studies, small sample sizes and methodologic problems (particularly the indirect method used to assess fathers' occupations) limit interpretation. However, the data suggest that this is a productive area for further study. Residential exposures (pesticides, solvents, incense) have been implicated in small studies; anecdotal reports have also raised concern about in home exposure to radon. These exposures may be causal or may confound the postulated relationship with low frequency electromagnetic radiation (e.g., spraying of poles carrying high power lines with herbicides) or with parental occupation (e.g., residential solvents rather than occupationally related solvents).

Preliminary data also suggest that the major childhood leukemia cell types (acute lymphocytic, the substantially less common acute nonlymphocytic, and the rare chronic myelocytic leukemia) may have different risk factor profiles. In addition there appears to be variation in age specific incidence, sex rations, and possibly etiologic factors among the four immunophenotypic classes of acute lymphocytic leukemia: T-ALL, common ALL, B-ALL and pre-B-ALL. Inconsistent results of previous studies may reflect lack of specificity of case definition and failure to examine potential leukemia exposure associations by specific leukemia biologic subgroup. Previous studies have also failed to examine the possible role of recall bias due to over reporting by case mothers compared with mothers of healthy children.

The main objectives are to examine the relationship between three major types of exposure (electromagnetic low frequency radiation, parental occupation, and childhood residential exposures) and specific biologic subgroups of childhood leukemia as designated by hisopathology, immunophenotyping, cytochemical, and cytogenetic tests. Other implicated postnatal and prenatal factors will be briefly inquired about to assess their potential confounding effects. The possible effects of recall bias due to over reporting by case mothers in comparison with mothers of healthy controls will also be examined.

A multicenter U.S. case control study is proposed. The preferred centers should consist of facilities where a majority of newly diagnosed cases are carefully defined (suing the FAB classification scheme, with immunophenotyping and other appropriate histopathologic, cytochemical and cytogenetic tests). Multiple awards are envisioned, including one for a coordinating center. A total of 1,000 leukemia cases will be sought, among whom 750-800 will have acute lymphocytic leukemia, and most of the remainder, acute nonlymphocytic leukemia. Given the rarity of childhood leukemia and the absence of identified differences in etiology for individuals 15-19 years old at diagnosis compared with cases under age 15, the upper limit of the age range for eligible cases will be age 20 to increase the case group sample size and so that age specific associations can be examined in detail. Diagnosis will be confirmed by a central pathology review board. To achieve the required sample size, incident cases will be selected both retrospectively (going back approximately two years) and prospectively (concurrent identification for approximately three years).

Both population controls (N=1,000) and hospital controls selected from a broad range of serious chronic conditions (N=200, comprising a sample to be selected from one or two centers) will be obtained. The second hospital control group will consist of children newly diagnosed with serious conditions from a number of disease categories, such as degenerative neurologic conditions, diabetes, severe and frequent asthma attacks, and/or congenital heart disease not diagnosed at birth. Conditions will be chosen that are often life threatening, require frequent hospitalizations, and have been diagnosed at a definite point in time, providing a reference point for the purpose of recalling past exposures. Because of the seriousness of such disorders, the parent is likely to dwell extensively upon prediagnostic events and exposures, thus diminishing the potential for recall bias.

Another methodologic approach used to evaluate the possible effects of recall bias will be independent interview of both parents. Although the mother will be the main source of information about most exposures, the father will also be interviewed to obtain information about his occupational history and medical history and to verify specific maternal exposures (such as smoking and alcohol) consumption during pregnancy). Similarly the mother will be asked about the father's smoking and medical history since marriage or coresidence. Verifiction of certain exposures, such as parental occupation, may be considered if feasible.

For all cases and both types of controls, information will be obtained about use of electric blankets and electrically heated waterbeds by the mother during her pregnancy with the case/control and postnatally by the child. The child's lifetime residential proximity to high power lines will be evaluated, by interview and by objective "blind" assessment (by a trained technician) of wire code configurations, characterized during visits to as many lifetime residences of cases and controls as possible. Physical measurements of electromagnetic low frequency radiation will be made inside the subject's residence at diagnosis/interview, measured under low power magnetic field (all appliances turned off) and high power magnetic field (all appliances turned on) conditions. Twenty four hour continuous measurements will also be attempted. The

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The dollar estimates with each concept brought before the various boards of scientific counselors or other advisory groups are not intended to represent maximum or exact amounts which will be spent on those projects. They are intended as guides for board members to help in determining the value of the projects in relation to the resources available to the entire program or division. In the case of RFAs, the amounts cited are the maximum that will be set aside to fund those particular grants, the final amount depending on NCI's budget and program priorities. Responses should be based on workscope and description of goals and methods included in the RFPs (contracts) or RFAs (grants and cooperative agreements). Availability of the RFPs and RFAs will be announced when NCI is ready to release them.

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measurements will be done in a similar fashion as performed in recent studies. While it is not feasible to measure electromagnetic low frequency radiation under high power magnetic field conditions within previous residences (since the relevant appliances will not be present), measurements can still be taken under low power magnetic field conditions in all previous residences to which the study staff is allowed access. Types and average use of household appliances will be inquired about. At the time that magnetic field measurements are made in each residence, a radon detector will be placed in the home and instructions given about how and when to mail it in.

Odds ratios will be calculated using standard methods. Summary relative risk estimates adjusted for known and suspected confounding variables will be determined using maximum likelihood procedures with 95 percent confidence intervals. T-tests will be used to test case control differences in continuous variables such as mean birth weight and parental age at subject's birth. Mantel's extension test will be used to test for trends (2 tailed) in risk related to exposures such as residential magnetic fields.

Assuming similar exposure percentages as reported in the recent study of childhood leukemia in Colorado (65%, 13%, 16% and 6%) for the four categories of magnetic field strength under low power conditions (0-0.65, 0.65-1.00, 1.00-2.50+ milligauss), a sample size of 1,000 cases and 1,000 controls would be sufficient to detect an increasing trend in the estimated relative risk from 1.0 to 1.5 with 90% power. A sample size of 800 cases and 800 controls would result in 80% power. For most of the other exposures being examined, the proportion of exposed controls is greater than 5%. Assuming that only 5% of controls are exposed to a particular agent, to detect an estimated relative risk of 1.8 with 90% power, a sample size of 850 each of cases and controls would be needed; for a relative risk of 2.0, a sample size of 700 each of cases and controls would be required.

"It's obvious that this study is motivated by public concern about the increasing incidence of ALL," Board member William Benedict commented. "Conceptually, there is a problem. This was the most common childhood cancer 25-30 years ago, before the exposures we have now. There is a lot of ALL in countries without these exposures. I have trouble seeing how you will get meaningful data out of this."

Martha Linet, one of the DCE project officers for the study (with John Boice and Louise Brinton), said, "We've come a long way in 25 years. More information is available now on exposures. There is more insight into specific chromosomal abnormalities. That leads us to think the time is right for the fourth big study and the first in 25 years."

"What will this study do that the Oxford and Tri-State studies didn't do 25 years ago, other than looking at electromagnetic radiation?" Board member Alice Whittemore asked.

"Those studies were limited to prenatal exposure," Linet said. "These are at a different time in the child's life."

Board member Roy Shore suggested that an advisory panel be established to help determine assessment of exposures. DCE Director Richard Adamson agreed and added that in the past, "studies that have been done created more questions than answers."

Board member Allan Conney said he favored approving the study "if the epidemiology can be tied together closely enough to keep track of variables." He asked if benzyne exposure would be looked at, and Linet said it would.

"I worry about going into school houses and creating panic," Benedict said.

"That's an important point," Linet said. "The controls are the issue. Are parents with healthy children going to be upset?"

"My colleagues (on the Board) are not impressed," Chairman Hilary Koprowski said. He suggested that the vote be conditioned on establishment of an advisory panel, but four members still opposed the concept, with nine approving it.

Support services for occupational studies. Recompetition of the contract now held by Westat Inc.. Estimated first year award is $1.184 million, with a total estimate of $5 million over four years.

The objective of the occupational studies program of the Environmental Epidemiology Branch is to generate and test hypotheses concerning environmental determinants of cancer associated with the workplace, to strengthen the quantitative basis for risk estimation, and to provide insights into chemical and physical carcinogenesis. To meet national needs the Branch must have the capability of responding promptly to new developments or requests in the area of occupationally related cancer.

The method developed to address these needs was a support services contract with a survey research organization that could provide assistance for field activities conducted at the national level as needed. Since 1978, the Branch has received support for a major portion of its occupational research activities from such a contract. The Epidemiology & Biostatistics Program originally developed the concept of an omnibus survey research support contract to extend and maximize the research capabilities of a limited number of investigators. In this approach, the epidemiologic expertise of program members is efficiently utilized in the formulation and design of research areas and in the analysis and interpretation of the data. The actual data collection and associated activities are contracted out, with the NCI staff providing oversight, monitoring and quality control activities. The support services contracts provide managerial, technical and clerical support for epidemiologic field studies. Each contractor functions in a supporting role, carrying out specific tasks, and does not engage in independent research.

Study designs to be employed include cohort, case control and proportionate mortality or morbidity approaches depending upon study objectives and the availability of resources. Feasibility studies, pilot investigations, and exposure methodologic projects may also be conducted. All studies are thoroughly reviewed by senior staff as well as by interested parties such as other government agencies, labaor unions, companies and industrial organizations, professional societies, collaborating scientists, and special advisory panels, where appropriate. A protocol is developed for each study and, after Section and Branch evaluation, receives a formal written review by the Committee for the Technical Evaluation of Protocols in the E&B Program. A written response to each criticism is required for approval along with a revised protocol.

The contractor must be highly experienced in providing technical support for all phases of occupational health studies including the design of data collection documents; hiring and training of interviewers and abstractors; collecting, keying, editing, updating and recording data; tracing individuals; monitoring and estimating exposures in the workplace; collecting and transporting biologic tissues and fluids to be used for measures of occupational exposures; and creating and manipulating data files. The scientific methods for all projects are the responsibility of the professional staff of the Branch. The responsibility of the contractor is to provide a team of study managers, abstractors and interviewers, computer programmers, coders and keyers,

industrial hygienists, and other support personnel to complete assigned study tasks.

Support activities have been applied in one of two ways. In some studies, the contractor is responsible for virtually all of the field activities required to complete a study. This generally occurs when the study is conducted in areas, or with collaborating institutions, that have none of these capabilities. A second manner in which the contractor assists is by providing only selected types of support activities that cannot be accomplished by the locally based collaborators. These specialized tasks typically include forms development, interviewer training, or random digit dialing for control selection in areas where such activities are not often conducted. The Westat contract will terminate in January, 1989.

Work performed under the contract is carefully monitored by NCI investigators. All study activities are carefully documented. Forms, training manuals, visual and computer edits, and data flow documents developed by the contractor are thoroughly reviewed by NCI investigators. Regular discussions occur with contract personnel to evaluate study progress. Detailed monthly reports of projected activities are reviewed and critiqued by NCI investigators.

Aaron Blair is the project officer.

(Remaining concept statements approved by the Board will be published next week in **The Cancer Letter**).

RFPs Available

Requests for proposals 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 20892. 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-CB-85609-55
Title: Feral mouse breeding colony and attendant support services
Deadline: Approximately May 1

The Laboratory of Tumor Immunology & Biology of NCI's Div. of Cancer Biology & Diagnosis is seeking contract proposals for operation and maintenance of a feral mouse breeding colony. This project will provide the capability of maintaining pedigreed breeding colonies of feral mice from various geographical areas of the world, to test the effect of various biological (hormones and mouse mammary tumor virus) and provide a source of tumor tissue to define the organization and to test for the expression of tumor associated genes and retroviral genes.

Prospective offerors will be expected to provide documentation of experience in handling and care of feral mice, as the contract will require housing, feeding and maintenance of animals according to standards outlined in the "Guide for the Care and Use of Laboratory Animals" as published in the HHS publication No. (NIH No.) 86-23. The contractor shall maintain and breed a colony of mice that includes feral mice (Mus cervicolor popaeus, M. musculus and M. spretus), M.m. musculus XM. m. domesticus backcross mice and inbred M.m. domesticus strains.

Mice from these colonies are currently being utilized in the following experiments: (1) evaluation of the effect of exogenous biological (hormones and MMTV) and chemical carcinogens (administered separately and in concert) on the etiology of mammary gland neoplasia in MMTV negative mice; (2) introduction, by selective breeding, of single endogenous MMTV proviral genome into the genetic background of the MMTV negative mice. These mice will be used to determine the extent to which endogenous MMTV genome contribute to spontaneous and carcinogen induced mammary tumors; (3) identification and characterization of mammary tumor associated genetic loci; (4) evaluation of the extent to which the novel endogenous retroviral genes are involved in the development of mammary gland tumors; (5) study the genetic organization and evolution of endogenous retroviral genes in the genes Mus; as well as organizational rearrangements which are associated with tumor development.

This operation requires rapid exchange of reagents between the Laboratory of Tumor Immunology & Biology and the contract facility and frequent (several times per week) visits by NCI personnel to monitor and examine experimental mice to determine when mammary tumors are to be surgically removed from live mice for immediate shipment (in a viable form in some cases) back to the laboratory by the project officer. Offerors will thus need to demonstrate their ability to provide for rapid exchange of reagents between their facility and the NCI laboratory and to provide the project officer with rapid access to the mice several times a week.

The incumbent contractor is Hazleton Laboratories America Inc. A three year award is anticipated.
Contract Specialist: Mary McGarvey
RCB Blair Bldg Rm 114
301/427-8888

RFP NCI-CB-85608-61
Title: Facility for housing and preparing virus infected mice, genetically manipulated mice, and chimeric mice
Deadline: Approximately May 10

The Immunology Branch of NCI's Div. of Cancer Biology & Diagnosis is seeking contract proposals from small businesses for the operation of a facility for housing and preparing virus infected and chimeric mice.

The proposed project will house approximately 3,600 mice. Also, the contractor shall prepare and investigate the effect of the infectious virus, murine cytomegalovirus, in different mouse strains alone and in conjunction with or in series with other potential immunological insults and stimuli. Other responsibilities include research related services to perform: murine embryonic transfers into pseudopregnant female mice; preparation of bone marrow radiation chimeras using donor and/or recipient mice.

Offerors will be expected to provide documentation of experience in handling and care of mice, as the contract will require housing, feeding and maintenance of animals according to standards described in the "Guide for the Care and Use of Laboratory Animals."

The incumbent contractor is Bioqual Inc. A five year contract is anticipated.
Contract Specialist: C.H. Jackson
RCB Blair Bldg Rm 114
301/427-8888

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