THE CANCER LETTER

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ETHICS COMMISSION REMAINS SPLIT ON COMPENSATION BUT TELLS STAFF TO DEVELOP PILOT PROGRAM PROPOSAL

The President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, although obviously divided and unable to reach a consensus, moved a step closer last week

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In Brief

SENATE SETS NCI RESCISION AT $14 MILLION; BALTIMORE PROGRAM CONVERSION TO CANCER CENTER WILL BE ASKED

SENATE HEALTH Appropriations Subcommittee marking up the rescision bill from FY 1981 appropriations agreed to a $14 million cut for NCI. The House Appropriations Committee previously had approved a $7.7 million rescision, both committees rejecting President Reagan's request for a $25 million cut in NCI spending for the fiscal year which ends next Sept. 30. The Senate Subcommittee directed that none of the $14 million cut could come out of cancer centers funding. . . . **NCI PROPOSAL** going to the National Cancer Advisory Board next week will recommend that the Baltimore Cancer Research Program be phased out as an NCI intramural program and be converted to a cancer center as part of the Univ. of Maryland. BCRP staff members are federal employees, in the Div. of Cancer Treatment, and DCT further supports the operation through a $4 million a year contract with the university for certain support services. Staff will have the option of remaining with NCI, in which case they would be transferred to Bethesda; transferring to other government agencies; or remaining with the new cancer center as university employees or faculty. Program Director Peter Wiernik, asked by ***The Cancer Letter*** how many would remain with the center, said, "All of us." The program now has 39 fulltime NCI employees. Nineteen would be shifted to the new center payroll in September, supported by an interim (P-50) grant. Ten others with time limited appointments will be phased out in FY 1982, the rest either opting to stay with the center or seeking reassignment some time later. As those employees go off the NCI rolls, their slots become available for use elsewhere in NCI. The center probably will have three years under the interim grant, after which it will have to compete for a regular cancer center support (core) grant. . . . **JEROME DECOSSE**, chief of surgery at Memorial Sloan-Kettering, was elected president of the Society of Surgical Oncology at the organization's annual meeting this week in Boston. **GERALD MURPHY**, director of Roswell Park Memorial Institute, was named president-elect. Other officers elected were **ROBERT McKENNA**, Univ. of Southern California, vice president; **CHARLES McBRIDE**, M.D. Anderson, secretary; and **ROBERT HUTTER**, St. Barnabas Hospital, treasurer.

ETHICS STAFF PROPOSALS GO BEYOND COMMISSION PILOT PROGRAM REQUEST

(Continued from page 1)

to approving a pilot program for compensation for research injuries.

The commission agreed, with only Mathilde Krim expressing adamant opposition, to a motion asking the staff to write a proposal for a pilot program for the commission's consideration at its September meeting.

The commission at its January meeting had reluctantly agreed to look at alternatives for a small pilot program as a feasibility test (*The Cancer Letter*, Jan. 16). That was approved by a 6-3 vote, after another motion to drop further consideration of a compensation program had been defeated by a 5-4 vote (two members were absent).

The commission staff went considerably beyond what had appeared to be the intent of the commission in its January action—the pilot program was to be limited to subjects participating in research conducted by the Public Health Service.

Instead, the staff submitted a 200 page "working draft" of a report which included details on three plans, none of which would be limited to PHS conducted research. The draft report includes summaries of presentations made to the commission (with one glaring omission), and is heavily weighted with arguments for a compensation program.

Of the three plans drawn up by the staff, one would include federally sponsored research—research supported by the federal government, such as NIH and NCI contract and grant supported clinical trials, as well as that conducted directly by federal agencies. The other two plans would be limited to "federally conducted" research, and thus include that performed by agencies other than PHS. The Dept. of Defense and Veterans Administration are two examples.

Following are summaries of the three plans:

Plan A—Federally conducted research, institutional review board approved, all biomedical, limited behavioral, nontherapeutic only.

Plan B—Federally conducted, IRB approved, all biomedical, limited behavioral, nontherapeutic and limited therapeutic.

Plan C—Federally sponsored, IRB approved, all biomedical, limited behavioral, nontherapeutic only.

Eligibility for benefits would be the same for all three plans—subjects and injured fetuses only, for nontrivial bodily injuries.

Standards of conduct would be the same—nonfault system, exclusion for subject misconduct. Plans B and C would modify "exclusion," adding "limitation for subject misconduct."

Plans A and B would limit the time for making claims to within three years of discovery (of injury), with no outside limit from the time of research. Plan C would limit the time to within three years of discovery but would limit it to 10 years from time of research.

Benefits under Plans A and B would include medical care, death benefits, financial indemnities for lost wages and out of pocket costs. Plan A would have no upper limit on benefits, Plan B a $100,000 limit. Plan C benefits would be limited to medical care, death benefits, and limited financial indemnities, with a limit of $10,000.

All three would permit offsets for recoveries from collateral sources.

Plan A would foreclose all other prospects of compensation (lawsuits) while Plans B and C would permit the subject to choose between the benefits in the program or access to tort recovery.

Plan A would limit resolution of disputes to administrative action, with no judicial review. Plans B and C would provide for arbitration, with virtually no judicial review.

Benefits paid under Plan A would be financed by the government through direct appropriations; for Plan B, direct approrpations or research funds; and for Plan C, by the government through institutional costs allowable under federal grants and contracts.

The plans are not mutually exclusive. Features of one could be incorporated into another, and the commission could recommend that either Plan A or Plan B or a combination of the two could be implemented along with Plan C.

Of the 10 members of the commission present, five appeared to be either leaning toward or solidly in favor of an eventual recommendation that a compensation program be adopted. They are Renee Fox, Univ. of Pennsylvania sociologist; Albert Jonsen, chairman of bioethics for the five Univ. of California schools of medicine; Donald Medearis, chief of children's service at Massachusetts General Hospital and professor of pediatrics at Harvard; Charles Walker, Nashville physician; and Carolyn Williams, faculty member in the Dept. of Epidemiology at the Univ. of North Carolina.

The other five, although agreeing that injured subjects should be assured of receiving compensation as a moral obligation, seemed more influenced by previous arguments that there is no public demand for a program (it was initiated by former HHS Secretary Patricia Harris in response to a suggestion by a department task force); that what little information is available indicates the number of research injuries is small; that determining whether an injury was a result of the protocol or the illness could be very difficult; that any program could lead to development of another expensive bureaucracy and might generate a problem where none exists.

Those leaning away from approval of a compensation program include the commission chairman, Morris Abram, New York attorney and former presi-

dent of Brandeis Univ.; Mario Garcia-Palmieri, former Puerto Rican secretary of health and currently professor and head of the Dept. of Medicine at the Univ. of Puerto Rico; Krim, associate member of the Sloan-Kettering Institute for Cancer Research and co-director of its interferon evaluation program; Arno Motulsky, professor at the Univ. of Washington School of Medicine and director of the university's Center for Inherited Diseases and of the Genetics Clinic; and Anne Scitovsky, chief of the Health Economics Div. at Palo Alto Medical Research Foundation.

Frances Graham, professor of psychology and pediatrics at the Univ. of Wisconsin, was not present at the meeting.

Scitovsky objected to the extent of all three plans. "I thought we had agreed in January that we should try to come up with a recommendation for a pilot program. These plans are carefully thought out. They are more comprehensive than what we had in mind. Plan A (and Plan B) would include all federally conducted biomedical research. What I had in mind was that some programs should be tried in a small number of institutions or a small number of large projects."

"I favor a more extensive plan," Medearis said. "I favor Plan B. Part of the trial has to address the problem of therapeutics research. I would like to have federally sponsored research also included but I feel that if limited to federally conducted research, it would have a better chance of being approved."

"I agree with Anne," Garcia-Palmieri said. "The message is that the draft document goes for a broader program than we agreed upon." He also objected to portions of the opening chapter which attempted to relate public concerns aroused over the Three Mile Island and Love Canal problems to concerns over biomedical research. "That emphasizes certain negative aspects of research might might hurt the image of biomedical research," Garcia-Palmieri said. "Whatever recommendation we make should make it clear that the money to support a compensation program is additional money given to the agency. If it applies to NIH, the money should not come from research funds."

"I've been bothered by a lack of accurate data," Motulsky said. "From the information we have at the Univ. of Washington, the problem is minimal. I am bothered by the prospect that this will grow into a new agency, and take a lot of money, in days of very limited money. Ethically, perhaps there is some need. But realistically, it is not practical. We should emphasize data gathering. Newspaper accounts of stories such as Three Mile Island, Love Canal, and atomic testing in Utah, have excited people, but there are very few documented injuries."

Motulsky objected to a statement in the draft that the U.S. "has become a nation of guinea pigs."

Medearis insisted that "we won't get any information until we have a plan. It isn't necessary to get more information to get started. I feel a sense of moral obligation." He argued that behavioral research should be included, along with therapeutic and non-therapeutic biomedical research, and pressed for including compensation for lost wages. "I would recommend a line item appropriation, even if it comes from research funds."

Fox said she did not agree that the draft report emphasizes the negative aspects of research. "There is a tremendous amount of anxiety about possible harm from research in general, and biomedical research in particular."

"Does Three Mile Island and Love Canal have anything to do with research?" Abram asked.

"That's a literal argument," Fox said. "This has to do with the entire climate."

"The problem has been enlarged and inflated far beyond proper proportions," Scitovsky said. "We have heard no demand, there is no pressure. There may be a need for compensation in a few cases, but we don't need a program for them. By dragging in Love Canal, you are confusing the issue. I don't think we need to spend hours and hours of time on this. We should be ready to finish the subject today."

Jonsen suggested that the report should point out that "we are dealing exclusively with research conducted ethically and in an ethical enterprise." Unethical research, such as that conducted years ago at Tuskeegee in which the subjects did not know they were being experimented upon, would be excluded. Victims of such research could seek compensation through the courts, or as in the case of Tuskeegee, from Congress.

"Some philosophers contend that moral principle overrides all practical considerations," Jonsen said. "I don't think so. Some are overriding, some not. We're on the borderline between the two."

"We're talking as if the choice were between compensation or no compensation," Scitovsky said. "That's not true. There are methods for compensation available now."

Medearis said he wanted to see more details on the three plans. "I am interested in how the arbitration system works, how therapeutic research is defined. "We've heard from every investigator who is interested in this, and all have said there is no need to do anything, that they provide care (if injuries occur). They do something, put themselves up front, and they make the decisions on whether injuries have occurred."

"I feel strongly about the moral obligation," Walker said. "Things do go on over which someone should have some control."

"I feel uneasy about opening up Pandora's box," Motulsky said, referring to difficulties in sorting out treatment caused injuries and the natural course of

disease in cancer research. "There are all sorts of new things being done in cancer research."

Krim argued that there is a basic contradiction between whether government has a duty to compensate and at the same time require informed consent. "Either an individual takes himself into hand and makes a decision and accepts the risk, or he is not capable of making decisions. Systems of compensation in effect now have relied on the responsibility of physicians, and patients are being compensated.

"My overriding reaction," Krim continued, "is that the document does not reflect accurately the information we received, which overwhelmingly told us to be careful. The problem is not a serious one, there is no great injustice being done, and the program could create a quagmire of bureaucratic problems. I feel strongly there is a moral obligation, an ethical one. But we have other ethical obligations we don't fulfill because of practical considerations, and I don't see anything wrong with admitting it."

Abram used food stamps as an example of how a program started with good intentions, "to feed hungry people," grew into a massive welfare system. "Once you have a plan in place, other people will say that you cannot have it in just one institution and not in others, nor can you just have it cover therapeutic research and not nontherapeutic. How can you justify between government conducted and government sponsored research, and research not having any government connection? Once we make an intervention, 20 years from now it can have consequences unknown."

Alexander Capron, executive director of the commission, agreed to incorporate criticisms from commission members into a rewrite of the report. "We need to be much more explicit about the nature of the experiment and its scope," he said. He did not agree that a system of compensation would create more opportunities for litigation. He noted a "remarkable absence" of litigation in workmen's compensation because of specific limits against it. As for the prospects of expansion, he said "there are a number of major program experiments which have not led to expansion," and mentioned the negative income tax as one.

Scitovsky still disagreed. "The tenor of this report is, this is a pilot program that will be phased into a broad program. It gives the impression that what the commission wants is a compensation program to be gradually phased in. That is not what the commission wanted. . . . My personal feeling at this stage is that there is no basis even for a pilot program. It is a trivial problem in relation to other issues."

"I feel strongly that all therapeutic research should be excluded," Motulsky said. "That involves mostly cancer patients, or others with serious disease."

Abram drew an example of a patient with a tumor for which daunorubicin was the only drug of choice. "The disease is fatal. You know daunorubicin affects the heart, that so many units per weight and age forms the outer limit. It is administered with full consent well below the limit. The tumor disappears but the patient develops a cardiac problem. Are you saying the patient should be compensated?"

"My answer is no," Medearis said. "That would be clearly within the expected outcome."

"That would not be compensated under any of the plans here," Capron said.

Medearis offered another example. "In leukemia, you may get 90 percent remission with one treatment, and in an effort to reach 100 percent, you add a new agent that has an unpredicted terrible outcome. That is therapeutic research and ought to be compensated."

Krim insisted that "we have exaggerated the importance of this issue. I'm against even a demonstration program. Informed consent relieves us to a large extent from an obligation to compensate."

Jonsen referred to the "very negative evaluation of the insurance feasibility" related to the commission in January by George Bernstein, a lawyer specializing in insurance who had been hired by the commission to advise it. Bernstein told the commission to drop it. "In fairness, that should be in the report," Jonsen said.

Capron responded in all seriousness that Bernstein's comments had been omitted because they "were based on speculation."

If everything based on speculation had been exempted, there would have been no report, there would be no issue, and the commission would not have spent a major part of its $2 million budget during the past year worrying about a problem that does not exist.

Abram said at the end of the meeting that, "I did n o t vote, it was not necessary that I do, but if I had I probably would have voted with the majority. But I want to associate myself strongly with Dr. Krim's comments."

Abram and the others worried about dangers of a compensation program appear influenced enough by arguments on the ethics to stay with the decision for a pilot program. Those arguments were summarized by the staff in the draft report:

"Although the evidence consistently suggests that the incidence of serious injury is small, nonetheless, it is clear that at least some subjects sustain injuries as a result of their participation in federally funded or regulated research. For them, as for those who invite them to undertake risks on behalf of society, the question of compensation is real and of immediate importance. Furthermore, it is clear from the studies of the Quincy and Univ. of Washington programs that compensation can be paid without overburdening the research enterprise. Finally, a functioning compensation program—even on a pilot basis—seems the most

likely means of meeting the very real need for more data on research subjects and their injuries."

What does not seem likely, considering the present mood of Congress and current occupant of the White House, is that any new, potentially expensive social program with practically no constituency working for it will ever see the light of day.

EINHORN SEES RESULTS COMING SIMILAR TO SUCCESSES IN TESTICULAR CANCER

"Some anihilists grudgingly admit that we may have done well in treating hematologic malignancies with chemotherapy but not with solid tumors. Testicular cancer is a solid tumor. If we can identify active agents and put them together in tests, perhaps we can achieve similar results with small cell lung cancer and other solid tumors in the 1980s."

Lawrence Einhorn's account of successes in treating testicular cancer and how those successes are beginning to be applied to other cancers, delivered as the Rosenthal Lecture at the American Assn. for Cancer Research meeting, was described by some as the refreshing highlight of the annual week-long AACR-ASCO get-together.

One decade ago, Einhorn pointed out, cure rates in testicular cancer were 90 percent for stage A, 40-50 percent for stage B, and only 5-10 percent for disseminated disease.

"In 1981, we now have 100 percent cures for stages A and B, and 70 percent–documented, world wide, for those with disseminated stage C disease."

Einhorn's group at Indiana Univ. pioneered the work which achieved those stunning results, reaching those levels with the addition of cis-platinum to vinblastine and bleomycin. They eventually found and recently reported (see ***The Clinical Cancer Letter,*** March 1981) that the combination is so effective in treating stage A and B relapses following primary treatment that its use as adjuvant therapy is unnecessary.

Einhorn also mentioned in the lecture other promising studies growing out of the testicular cancer work which were reported at ASCO:

• The Southeastern Cancer Study Group, in a trial headed by Einhorn, found that maintenance therapy is unnecessary in disseminated testicular cancer after either complete remission or surgical removal of residual or immature teratoma. The PVB combination was compared with one substituting adriamycin for vinblastine in induction therapy, and there was no difference between the two groups. Patients randomized to vinblastine maintenance received the drug every four weeks for 20 months. The relapse rate was nine percent for those receiving maintenance, seven percent for those without maintenance. Nineteen patients randomized to the maintenance group refused further treatment and none relapsed, leading Einhorn to remark, "They were smarter than we were." Seventy percent of all patients are alive and disease free at median followup of 16 months. Einhorn said that when testicular cancer patients go 12 months without relapse, they have a "99 plus percent chance of being cured."

• VP-16, used alone or in combination with other drugs, appears to be "extremely effective" in salvaging patients who have failed on other combinations, including PVB, in disseminated testicular cancer. "Next to platinum, VP-16 is the most effective single agent and is markedly synergistic with platinum," Einhorn said. Thirty-seven percent of 46 patients with refractory testicular cancer treated with VP-16 alone or in combination are alive with no evidence of disease at 12 to 38 months. "Prior to VP-16, we never had one year NED salvage," Einhorn said.

Einhorn's group now is working on what he called a "fourth generation" protocol "to compare VP-16 up front." VP-16 replaces vinblastine in a combination with platinum and bleomycin and compared with PVB. VP-16 is less toxic than vinblastine, and equal results would represent progress.

Einhorn said AMSA is another drug being tested for use as tertiary therapy after PVB and VP-16 for refractory testicular cancer and presently is in a phase 2 study.

• PVB will induce a substantial number of surgically proven complete responses in patients with advanced ovarian germ cell tumors. In a Gynecologic Oncology Group study, patients with stage 2, 3, 4, or recurrent ovarian cancer were treated with PVB after maximum cytoreductive surgery. Eleven patients were evaluable, and there were a total of 13 second look procedures, 10 negative and three positive. One patient with a negative second look relapsed and the other nine are disease free from three to 18½ months.

Emil (Tom) Frei III, physician in chief at Sidney Farber Cancer Institute and one of the early leaders in development of anticancer chemotherapy, referred to clinical cancer research as "an embattled species" in delivering the Karnofsky Lecture at ASCO.

Among the threats Frei mentioned are the decreasing number of academically oriented young men and women entering clinical investigation, and the falling proportion of MDs who are principal investigators on funded NIH grants. "The attractions of practice; the prestige associated with basic research; the incredible bureaucracy that has mushroomed around clinical research; the insecurities associated with a shrinking federal dollar; the information explosion–these are only some aspects of the battle."

Frei noted that "under the leadership of B.J. Kennedy, medical oncology became recognized by the ABIM as a subspecialty of medicine in 1972. Since then the number of medical oncologists that have

been certified has increased linearly to 1,788 in 1979. That is one of the major accomplishments of the 1970s. The vast majority were superbly qualified and trained and have done an excellent job of bringing the best in this rapidly moving field to the bedside. I am proud to number myself among you. Why is there a problem?"

The current number of certified medical oncologists plus the surgeons and others doing medical oncology roughly is equivalent to the need, each treating in a major way about 100 patients a year, Frei said. Although more medical oncologists will be needed, he estimated "there will be an excess within five years and a glut by 10 years. Obviously this is a threat to the practicing medical oncologist per se. How will it affect our clinical investigator in cancer centers? There is good evidence that the number of referrals to some cancer centers over the past few years have diminished, with a relative increase in the number of patients with advanced disease. It is inevitable that this trend will increase with the increasing number of practicing clinical and medical oncologists."

Frei said negative feedback of an increasingly crowded field will help reduce the number of physicians going into medical oncology. "The marked reduction in NIH supported training and education grants, while it will have adverse effects in other areas, should help. A careful monitoring system for medical oncology requirements in various geographical areas, and as affected by predicted trends in health care delivery, should be developed."

Another issue is the relationship of the practicing medical oncologist to the cancer center, Frei said. "Cancer centers should and most do concern themselves in a major way with their relationship to practicing oncologists and are proud of that relationship. Oncology practitioners in turn should have an important relationship to the cancer center, which is noncondescending in either direction, and may participate in the development of new knowledge such as participation in clinical trials.

"On the other hand, the referring medical oncologist should have a sense of participation in that research and the patient should be referred back as soon as those clinical investigative activities that require the patient's presence at the cancer center are completed. . . .

"The next threat to clinical research is basic science. Basic biomedical science is much higher in the pecking order than clinical science in most institutions, and particularly at major academic centers. . . . The basic science community has persuaded itself and a good part of the academic community that clinical research generally, and clinical cancer research specifically, is largely descriptive, empirical, and derivative of basic science. . . . We have done a thoroughly inadequate job of persuading basic scientists—and to some extent science administrators, the public, and even ourselves—that clinical investigation is a science in its own right, full of dignity, challenge, and the opportunity for creativity—in short, an excellent career choice

"Another major and current threat is the funding situation. The funding of NIH and NCI is set finally by the political process. It is essential that the public and the politicians understand what a bargain they are getting for their cancer research dollar. . . .

"In subjects under the age of 45 there has been a greater than 20 percent decline in mortality from cancer over the past 15 years. The vectors started down 10-15 years ago and continue down. The incidence of cancer in these age groups has not changed during this time period. Therefore this decrease has resulted from improved treatment. This is supported by the fact that the turndown in these curves occurred following the introduction of curative treatment. More compelling are the mortality statistics for individual cancers where major progress in cancer treatment is known to have occurred. I would emphasize again that there has been no change in the incidence of these cancers and that the difference between 1967 and 1977 represents a trend, not an abberation. The 20-40 percent decline in Hodgkins, ALL, and non-Hodgkins lymphoma mortality is consistent with the development of curative treatment for these diseases 15-20 years ago. The decline in bone cancer, which is mainly OGS, is of interest in view of treatment controversies relating to that disease. Premenopausal breast cancer mortality has fallen, perhaps as a result of adjuvant chemotherapy, and curative treatment for advanced testis cancer has been introduced too recently to impact on national statistics up to 1977. . . .

"What is not sufficiently realized is that such improvements in treatment result in substantial savings of the federal dollar. This saving is based primarily on the much reduced cost of curing the patient with initial treatment as compared to the much greater medical cost incurred if the patient fails or relapses from initial treatment and finally succumbs several months to several years later. Dr. DeVita has calculated that the savings from these and related examples are substantial and exceed 50 percent of the current NCI budget.

"Another threat to the clinical cancer investigator is the hematology/oncology issue. A major effort is under way to combine hematology and oncology in major academic and clinical centers. Medical oncology is in its adolescence, whereas hematology is a long established mature discipline. In most institutions hematologists are more powerful as of now in the academic structure and with no important exception that I am aware of, hematologists are selected to head up combined hematology/oncology divisions. We must beware. Many hematologists, certainly in the

past, have not been sympathetic to medical oncology. Medical oncology represents a much larger clinical and scientific challenge than does hematology, and we must persuade department chairmen that this reality must be given prime consideration in the structuring and allocation of resources to the clinical and research activities that comprise medical oncology."

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-CM-17371-19

Title: *Support services for extramural clinical trials*
Deadline: *June 15*

This procurement will be a 100 percent small business set aside. The small business size standard recommended for this procurement requires annual receipts not to exceed $2 million over the preceding three year period.

The objective of this effort is to obtain support for the Cancer Therapy Evaluation Program, Div. of Cancer Treatment, NCI. The support services shall provide for the monitoring, coordinating, preparing and maintaining of materials and reports. The service will serve as the organizational center for the disease oriented clinical research contract groups and unaffiliated contractors.

The offeror shall be required to have in depth knowledge and experience in cancer clinical research protocols, of the following nature: design (understanding, and capability to formulate protocols); protocol requirements (understanding of all items of history and physical exams, laboratory tests, treatments, evaluation criteria, response and toxicity criteria, etc.); patient data forms (capability to design and to monitor all data submitted). The offeror shall be required to furnish facilities adequate for operating this project such as adequate filing systems and office equipment for maintaining materials and records; adequate space for meetings of up to 15 participants.

The clinical trials for which this contract will support are highly sophisticated and complex and are now being performed by many of the foremost cancer research institutions in the country. The successful performance of the trials depends on the quality of knowledgeable and experienced operations and data support services.

This contract will be written on a "level of effort" basis. It is anticipated that the project will require approximately seven technical staff years per year. The contract is expected to be awarded for a five-year period.

Contract Specialist: Kristina Boyer
RCB Blair Bldg. Rm. 228
301-427-8737

RFP NCI-CP-FS-11023-65

Title: *Followup study of women evaluated for infertility*
Deadline: *June 15*

The Div. of Cancer Cause & Prevention of NCI, Environmental Epidemiology Branch, desires to contract with a long established hospital or large clinic which has evaluated, using extensive clinical tests, large numbers of women for infertility over a period of at least 45 years. This lengthy followup period is mandatory because there is often lack of knowledge concerning the latent period for carcinogenesis. This will be a collaborative one year research contract with joint analysis and evaluation of data between the contractor and NCI personnel. The initiation date is expected to be in September 1981.

The objective of this contract is to evaluate the long term effects of infertility and its associated treatment, with particular reference given to cancers of the breast, endometrium and ovary. Infertility is defined as at least a one year period during which attempted conception has been unsuccessful in women of normal childbearing age not practicing contraception, and pertains both to primary and secondary infertility. The study will compare cancer incidence and mortality among women with varying causes of infertility (including hormonal abnormalities in the female, structural defects in the female, and problems in the male), and will evaluate risks associated with various modalities of treatment. In order to minimize referral bias, analyses will concentrate on women whose disease rates can be related to an identifiable, discrete population.

Requirements for the potential contractor (medical facility)

1. Study Group. The hospital or clinic must have evaluated at least 10,000 women for infertility, with their records encompassing a period of at least 45 years and minimum followup being at least 15 years. At least 1,500-2,000 of these women should be all or a representative sample of patients for infertility from an identifiable population on whom cancer incidence and mortality is available.

2. Records. Complete clinical, laboratory, and treatment records must be available for all of these women.

3. Comparison Groups. The contractor must have access to age, sex, race and time specific cancer incidence and mortality data for the county and state in which the hospital or clinic is located. This information should relate to the time period over which study subjects have been evaluated for infertility.

4. Availability. The study subjects from the identified population must have been closely followed by the hospital or clinic, thus assuring current knowledge of the vital status of at least 90 percent of the study cohort. In addition, the contractor must have the capability for followup of the referred patients. For deceased patients, copies of death certificates must be obtained, and for living patients, a current address must be ascertained. For living subjects, capabilities must be available for sending the mailed questionnaires within a short period of time, and for obtaining an acceptably high response rate for patients who have been located, e.g. 70-80 percent. The contractor should have experience in obtaining patient cooperation of this nature.

5. Personnel. The respondent should have a principal investigator (project director) for this contract who is a highly experienced physician, board certified in obstetrics and gynecology, with 15 to 20 years clinical experience in the treatment of infertility. He or she should be able to devote 10 to 25 percent time to this project (please specify exact percentage). A co-principal investigator should be a physician with formal training in epidemiology and at least five years research experience in epidemiologic research. He or she should be able to devote 10 to 25 percent time to this contract. Both physicians must have had at least five years experience in conducting research on human subjects and in analyzing and publishing results in leading reputable medical journals. A team of at least three trained abstractors must be immediately available, each of whom must have had at least one year of full time paid experience in abstracting medical records of the sort required for this study. A clerk typist will be needed for 50 percent time. No other personnel are to be designated for this contract.

Any organization which believes that it meets all of the necessary requirements to undertake this research, and desires to compete for the award, should provide information in sufficient detail for evaluation by an experienced review panel. This is not a request for proposal; however, organizations which desire to present their capabilities must follow the format given below so as to enable competitors to be equally evaluated. It is estimated that this may encompass a submission of between 10 and 25 doublespaced pages. All information should be clearly written and self-explanatory, addressing the headings provided and matching the organization's capabilities against the requirements in this announcement. The requirements described herein will not be modified, therefore organizations which do not meet all of the specifications will not be considered.

The table of contents should list the following: 1. Organizational qualifications (a) location, (b) description of facilities, including equipment, (c) relevant resources and experience of institution. 2. Project personnel and their qualifications (a) principal investigator (senior obstetrician/gynecologist), (b) co-principal investigator (physician epidemiologist), (c) abstractors.

In addition to written descriptions of all of these personnel, include a detailed curriculum vitae for only the principal investigator and physician-epidemiologist. Each curriculum vitae should list education including universities, dates of degrees, and major subjects. For each employment position, beginning with the current one, provide the title of the position, name and address of employer, description and details of duties, and name and telephone number of supervisor. Also provide a complete publication list, and list of honors and awards. No person can be committed for more than 100 percent of his or her time.

Do not include any financial or budget information at this time, as the statement of capabilities refers only to medical and technical capabilities. All items are subject to verification by NCI personnel. Do not include information which is not relevant to this particular procurement.

Fifteen copies of the statement of capabilities must be submitted to:

Contracting Officer: Sydney Jones
RCB Blair Bldg. Rm. 128A
301-427-8888

RFP 210-81-6106 (REH)

Title: *Dichloroethane: Drug interactions*
Deadline: *Approximately June 15*

The contractor will be required to conduct a carcinogenic and toxicologic assessment of rats exposed to 1,2-dichloroethane by the inhalation route with or without concomitant exposure to either ethanol or disulfiram. The contractor shall be required to use male or female Sprague-Dawley CD rats and must have documented experience in inhalation toxicology; as well as a board-certified pathologist with a minimum of five years of documentable experience in examining and interpreting lesions in experimental animals in carcinogen bioassay programs.

Contracting Officer
National Institute for Occupational Safety & Health
5600 Fishers Ln., Room 8-29
Rockville, Md. 20857

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