THE CANCER LETTER

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FDA Announces Plan To Reform Drug Approval, Hire Outside Experts To Handle Some Reviews

FDA last week announced plans to reform the drug approval process, including handing over review of some drugs to outside experts to eliminate the current backlog of applications. The plan drew praise from NCI, but was criticized by three prominent members of Congress who said the reform would weaken the agency. The changes were proposed

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In Brief

Walter Lawrence, Reginald Ho Lead ACS; Henderson To Leave Dana-Farber For UCSF

WALTER LAWRENCE, professor of surgery and director emeritus of the Massey Cancer Center at the Medical College of Virginia, succeeded **Gerald Dodd** as president of the American Cancer Society at the annual meeting of the Board of Directors last week in Atlanta. **Reginald Ho**, chief of the Dept. of Oncology and Hematology at Straub Hospital and clinical professor of medicine at Univ. of Hawaii School of Medicine, was elected vice president and president-elect. **Stanley Shmishkiss**, a national director at-large, was elected chairman of the board. **Denman Hammond** was elected chairman of the Medical and Scientific Committee of the board, succeeding **Irwin Fleming**. . . . **CRAIG HENDERSON** of Dana-Farber Cancer Center will assume the position of chief of medical oncology at the Univ. of California (San Francisco), which has been admitted to the **Cancer & Leukemia Group B** as a provisional member. Henderson will be the CALGB principal investigator and will continue as chairman of the group's Breast Cancer Committee. Henderson is also chairman of FDA's Oncologic Drugs Advisory Committee. . . . **"20TH ANNIVERSARY** Symposium: Past Accomplishments, Future Goals," to mark the 20th anniversary of the National Cancer Act, is scheduled for Nov. 26, 8 a.m.-4:30 p.m. in Masur Auditorium of the NIH Clinical Center. The event is sponsored by the National Cancer Advisory Board. . . . . **MARILYN QUAYLE** will give the keynote address at a luncheon hosted by NCI Director **Samuel Broder** next week to celebrate the 15th anniversary of NCI's toll-free Cancer Information Service (1-800-4-CANCER), which has reponded to more than four million inquiries from Americans about cancer cause and prevention, detection, treatment and rehabilitation. . . . **CANCER TEACH-IN** sponsored by Families Against Cancer, a Syracuse, NY-based advocacy group, and several other organizations, was held last week on Capitol Hill to formulate a national agenda for patient advocacy and present arguments in support of a vigorous national policy on cancer.

FDA Plan To Reform Drug Approval Praised By NCI, Booed By Lawmakers

(Continued from page 1)
at the request of President Bush by the Council on Competitiveness, chaired by Vice President Dan Quayle, according to an FDA statement. The Council's study was requested in October 1990 in response to findings by the President's Cancer Panel that improvement in drug development and approval could speed the availability of treatments for life-threatening diseases such as AIDS and cancer.

The report of the Council on Competitiveness said the FDA reforms include:

▶"Expansion of the drug review process, using non-government scientific experts under contract with FDA, to augment FDA reviewers and eliminate existing backlogs of drug applications. Reviews using this 'external review' process will be given a strict 180-day deadline for completion.

▶"FDA will make a deliberate effort to maximize a drug's potential for approval and take into account the risks to human life and health that may result from delay of new treatments.

▶"Promulgation of new rules to accelerate the approval of drugs for serious and life-threatening illnesses and conditions that lack satisfactory alternative therapy, through the use, where appropriate, of 'surrogate endpoints,' or other evidence that indicates that the drug is effective. In some cases use of this kind of evidence can allow new drugs to be made available months before they would normally be approved. Further study after approval would be required to confirm that the surrogate endpoint was in fact a valid indicator of the drug's effectiveness, while procedures for removing a drug which proves to be ineffective will be strengthened.

▶"A commitment to harmonize FDA's drug review standards with those of other industrialized nations. Currently, drug studies in animals and humans are sometimes duplicated for each country in which a drug is marketed. This would move the U.S. and other nations toward common testing procedures that would reduce such duplication and speed the approval of drugs worldwide. FDA has begun to accomplish this initiative through its lead role in negotiating common international standards at the recent Conference on Harmonization of Drug Approval Standards in Brussels.

▶"A series of management improvements proposed by FDA that will bring the agency's scientific review processes further into line with modern management practices. Drug applications are to be computerized by 1995, and new systems of monitoring the progress of drug reviews will be installed."

The reforms drew qualified praise from one NCI official who has criticized FDA in the past over the drug approval process. "If everything happens that they are talking about doing, it's good news," Bruce Chabner, director of NCI's Div. of Cancer Treatment, told **The Cancer Letter.** He said he supported the use of outside experts to help FDA review drugs, especially for approvals of drugs for secondary indications. "I really wish they would get outside experts that know about the disease and the drugs," he said.

In a letter to FDA Commissioner David Kessler, Sen. Edward Kennedy (D-MA), Rep. Henry Waxman (D-CA), and Rep. John Dingell (D-MI) endorsed the goal of the reform but said the plan to hire outside contractors to help review drug applications "would undermine the very purpose for which [FDA] was created and that it is uniquely qualified to fulfill--the protection of the American public from unsafe and ineffective drugs."

The congressmen asked FDA to delay the reform until Congress has the opportunity to evaluate the changes.

In response to the criticism, Kessler said the use of outside experts is a recognition of the fact that FDA cannot hire "every expert clinical pharmacologist" to conduct drug reviews. Far from weakening the agency, he said the reform would strengthen FDA's scientific expertise.

In 1988, the President's Cancer Panel established the National Committee to Review Current Procedures for Approval of New Drugs for Cancer & AIDS, which devoted more than a year to studying the issue. Also known as the Lasagna Committee after its chairman,

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Louis Lasagna of Tufts Univ., the committee made 20 recommendations for improving the drug approval process, one of which was the use of outside experts.

The use of outside experts was the most controversial provision of the proposed reforms. The other changes would institutionalize principles FDA has been using in review of drugs for AIDS.

Kessler pointed out that the recent approval of dideoxyinosine (DDI) for AIDS was made possible by the application of several innovative concepts recommended by the Council.

"DDI was approved in close cooperation with Canadian researchers working on the same project, and the decision was reached on the basis of surrogate endpoints, without waiting for the completion of the clinical trials," Kessler said.

To speed up the review, FDA had to act without long term efficacy and safety data that would only be known after a full clinical review, Kessler noted. However, he added, "confronted with a life-threatening disease and no other therapy, patients are willing to take risks and should be allowed to do so."

NCI's Chabner noted that cancer drug approvals also have improved recently. "Things are really moving faster than they used to. We really haven't in the past couple of years had any arguments with FDA on drug approval. We have drugs now that are going to get really quick approvals once the NDAs are filed, but may have other problems. For example, with taxol [the drug derived from bark of the yew tree], the problem is drug supply, not approval."

However, Chabner said he was "cautious" about greater reliance on foreign drug reviews. "The idea is that other countries review faster than we do, and we should depend on them. That's okay, but for a limited number of countries," he said. "I'd be willing to buy the conclusion of the drug review process in Canada or England, but in some countries a lot of worthless stuff gets approved." However, he praised the idea of more extensive use of clinical trials data from other countries.

The FDA reforms did not directly address what Chabner called NCI's "current headache," the off label use of approved cancer drugs.

In the statement released by FDA, Vice President Quayle said of the reforms, "Patients with serious and life-threatening diseases will benefit from earlier access to important new drugs, unnecessary regulatory burden will be eased and U.S. competitiveness will be strengthened."

"This administration puts the highest priority on ensuring a vigorous and responsive Food and Drug Administration," HHS Secretary Louis Sullivan said.

NCI Probably Would Fund 1,000 Or More Competing Grants In '92

President Bush had until Nov. 19 to decide whether to veto the Labor, HHS, Education appropriations bill passed by Congress that provides NCI with nearly a $2 billion budget and the largest increase for the Institute since 1976, $275 million.

As **The Cancer Letter** went to press this week, no action had been taken by the White House.

Also this week, NCI and NIH officials were negotiating exactly how NCI would allocate its increase. According to an NCI source, one point of contention is the number of competing grants the Institute proposes to fund in fiscal year 1992, which is well over 1,000. That would be the largest number of competing grants NCI has ever funded in one year.

However, that does not mean NCI will be able to fund all grants at the requested levels, the source said. With institution of the new rules for grant funding in the NIH financial management plan, mandated by Congress, NCI staff still must negotiate grant budgets downward individually, a process that has replaced across the board grant budget cuts.

Still, if the appropriations bill is not vetoed, or if the dollar amounts are not changed after a veto, and if other possible reductions that NIH and HHS can take out of NCI's budget are not too severe, FY 1992 will be a better than average year for competing grants, the NCI source said.

FDA Panel Urges Thorough Studies Of Long-Term Breast Implant Safety

FDA advisors last week recommended that silicone gel breast implants continue to remain on the market even though data are lacking on the safety of the devices and their impact on long term health. The panel urged the agency to require manufacturers to conduct larger and more thorough safety studies.

FDA's general and plastic surgery devices advisory group discussed premarket approval applications for implants manufactured by Dow Corning Wright, McGhan Medical Corp., Mentor Corp., and Bioplasty Inc. at a meeting Nov. 12-14. In addition to considering data submitted by the manufacturers, the panel heard testimony from women who had received the implants, health advocacy groups, and professional societies. FDA Commissioner David Kessler will make a final decision whether to allow the implants to remain on the market on Jan. 6, but he is expected to adhere to the panel's recommendation.

Breast implants never had been approved by FDA

because they were already being sold in 1976 when the agency was given authority to regulate medical devices. FDA said it was concerned about hardening of the tissue surrounding the implant, interference with mammography, and rupture of the implant or leakage of silicone gel, which has been suggested as a cause of certain autoimmune diseases. FDA asked manufacturers to submit data to prove the silicone implants are safe, and said it will seek similar data from makers of saline-filled breast implants.

After a preliminary review earlier this year, FDA decided that three manufacturers did not submit sufficient information to permit a full review. Those firms have taken their products off the market.

An estimated 2 million women have had breast implants over the last 25 years, 80 percent for breast augmentation, and 20 percent for breast reconstruction following mastectomy, according to the American Cancer Society, which testified at the meeting.

ACS issued a position statement saying that the Society "ACS does not believe that it would be in the best interest of cancer patients if silicone breast implants were summarily removed from the market at this time. The Society agrees that more research needs to be done to determine the long term safety and efficacy of breast implants for breast reconstruction patients. . . . ACS believes that breast implants should continue to be made available as an option in cancer rehabilitation."

In contrast, Public Citizen, the Washington-based consumer group, urged FDA in 1988 to ban the devices based on "evidence of a variety of clearly demonstrated safety problems, including concerns about cancer and reports of autoimmune diseases such as rheumatoid arthritis and scleroderma.

NCI is planning a study of cancer risk in women with breast augmentation (see following story in this issue).

The advisory panel members urged FDA to require the manufactures to produce more detailed studies as quickly as possible on the rate of rupture, the amount of silicone that leaks, the long term effects of chronic seepage, and how the implants affect results of mammograms.

DCE Plans Study Of Cancer Risk In Women With Breast Augmentation

NCI's Div. of Cancer Etiology plans to conduct a study of cancer risk in women with breast augmentation, including the risk in women with silicone gel implants versus those with other types of implants.

The study, estimated to cost $2.1 million over four years, would be conducted by a contractor. DCE's Board of Scientific Counselors approved the study in concept at its recent meeting, but said the proposed sample size of 9,000 women should be increased to take into account the rather low relative risk. The board also allowed for an appropriate increase in funding, and, if necessary, an increase in the length of the study.

Following is the concept statement:

Cancer risk in women with augmentation mammaplasty. Proposed total award $2.1 million, first year award $500,000, four years. Project officers are Louise Brinton and Robert Hoover.

Although an estimated 2 million women in the U.S. have undergone augmentation mammaplasty, there has been little epidemiologic investigation of the long term effects associated with the procedure. For some time, there has been concern regarding the effects of such implants on the immune system, particularly given anecdotal reports of an increased risk of certain connective disorders, including scleroderma, systemic lupus erythematosus, rheumatoid arthritis and Sjogren's syndrome. Also under suspicion has been a possible delay in the diagnosis of breast cancer, since augmentation mammaplasty has been reported to be associated with a decreased ability to detect breast lesions, both on clinical examination and with mammography.

Questions concerning potential carcinogenicity of breast implants were raised by an industry based bioassay of silicone gel which revealed a 50 percent attack rate of soft tissue sarcomas at the site of implantation in rodents. Suggestions of a carcinogenic hazard were recently heightened by reports that the polyurethane foam coating that envelopes the silicone gel, the breast implant, may dissolve and produce the chemical 2,4-diamino toluene (TDA). This chemical has been linked to increased rates of breast and hepatocellular carcinomas in rats and mice and possibly also lymphomas and sarcomas in mice. Effects of this chemical in humans are unknown, but the finding of TDA in the breast milk of women with polyurethane foam coated breast implants has raised further interest in long term effects.

The uncertainties surrounding these potential adverse side effects of silicone breast implants is a specific concern of the Senate Appropriations Committee, which called upon NCI "to develop a strategy for conducting longitudinal studies on women on the various types of silicone breast implants" in the 1992 appropriations bill.

This call for further study reflects the paucity of available data on long term effects of augmentation mammaplasty. Most studies evaluating breast cancer risk have lacked systematic case ascertainment and estimates of expected risk. In addition, the devices evaluated were for the most part markedly different in design and material from those currently in use.

The only large scale study is that conducted by Deapen et al (Past. Reonstr. Surg. 1986; 77:361-367) in which 3,111 women receiving mammaplasty from 35 plastic surgeons in the Los Angeles area were followed for a median of 6.3 years. Although the nine cases of breast cancer observed were close to the number expected based on local incidence rates, more cases than expected were seen in older women and those with longer periods of follow up.

Unfortunately, only scant information on possible disease covariates was available, limiting the ability to evaluate observed

relationships. In addition, the majority of operations were performed during 1970-79 so that the issue of the effect of implanted polyurethane coatings could not be evaluated. Thus, further follow up of a similar cohort of women is needed, with particular attention given to effects of specific types of implants.

Objective of this project is to assemble a large cohort of women with augmentation mammaplasty in order to assess the long term health effects of this procedure, particularly as related to specific implanted products.

A retrospective cohort study of approximately 9,000 women is planned. It is anticipated that these women will be recruited from several large reconstructive and plastic surgery practices, possibly in several diverse areas. The beginning phase of the project will include a feasibility study to assess the capabilities of assembling and following a cohort of the size required for this study.

Included in this phase will be an assessment of whether further follow up of previously assembled cohorts should be considered. Should the project prove feasible, a cohort will be identified and records at the collaborating practices reviewed to obtain information on the particulars of the surgery.

Information to be abstracted will include identifying information on potential study subjects, date of the surgery, the age of the woman at the time of implant, type of implant, immediate complications, and any known information on longer term complications.

In addition, any available information on potential confounding variables will be obtained, including the woman's history with respect to reproductive events, medical surveillance (e.g., frequency of breast examinations), and medical conditions before and after the implant.

Following the identification of the cohort, a questionnaire will be developed and sent to the study subjects. This questionnaire will request information from the subjects on perceived complications of the implant, history of breast examinations and mammograms, frequency of breast self examination, development of diseases of interest (e.g., age at menarche, age at first birth, age and type of menopause, family medical history, immune alterations).

The contractor for this investigation will assist in the identification of surgeons and practices that would be willing to participate in having their records on patients reviewed. Following identification of the study cohort, the contractor will, with input from NCI investigators, develop a medical record abstraction form and a patient questionnaire. The contractor will abstract records for the required information. Initial information on subject location will be subjected to intensive tracing efforts to obtain updated information.

Questionnaires will then be sent to subjects and, if necessary, telephone follow up pursued. Any reports of breast procedures (biopsies and mastectomies) or cancer development subsequent to the breast implant will be verified through retrieval of pertinent medical records. Copies of death certificates will also be obtained for any deaths occurring among study subjects.

Because of difficulties in comparing this population to an external standard, an internal comparison cohort will also be assembled. This will consist of approximately 3,000 women receiving operations from the same plastic surgery practices as the breast augmentation patients.

This comparison group will consist of women undergoing a variety of procedures, such as blepharoplasty, rhinoplasty and abdominoplasty. Attempts will be made to assemble a cohort of similar ages and operation dates as the breast implant patients. Records of these patients will be abstracted and follow up pursued in the same manner as for the mammaplasty patients.

Sample size calculations involved 1) an estimate that 25 percent of the cohort will have had polyurethane coated implants, the majority between 1980-85, 2) the assumption that data are available on other types of implants since 1970, 3) an average estimated age at implant of 31 years, and 4) power of 0.90 and a one-sided alpha level of 0.05.

Given these assumptions, a cohort of approximately 9,000 women will be required to detect a relative risk of 1.9 for breast cancer among women with polyurethane coated implants versus women with other types of implants (approximately 85 cases of breast cancer are expected).

Although attempts will be made to oversample women having the polyurethane coated implant more than 10 years ago, the power to detect risks among those with greater than 10 years of follow up will be considerably less. Greater power will be achieved in evaluating whether breast cancer incidence in the entire cohort is elevated after 10 years of follow up.

Namely, comparisons with an external standard (population incidence rates) will yield a minimum detectable relative risk of 1.3 for ever having had an implant. The minimum detectable relative risk for implants occurring more than 10 years prior to the development of breast cancer is 1.4.

DCE Advisors Ok Recompetition Of Technical Support Contracts

Advisors to NCI's Div. of Cancer Etiology have given concept approval to recompetition of four competitive contracts that provide the division with various support services, animal facilities, and support for epidemiologic field studies.

The DCE Board of Scientific Counselors, at its recent meeting, committed a total of $17.8 million to the concepts over four to five years. Following are the concept statements:

Technical and logistical support services for the Div. of Cancer Etiology. Recompetition of a contract held by Crosspaths Management Systems Inc. Proposed total award $3.115 million, first year award $575,000, five years.

Purpose of this contract is to assist the Div. of Cancer Etiology in logistics and management of activities within the program areas. These support services fall into two major areas: 1) document preparation and 2) conference and meeting management.

The first task area, document preparation, can be divided into two major categories: 1) preparation of documents describing past, current, and planned division programs or specific activities, and 2) preparation of handouts, slides, and other graphics for use in presentations to various organizations and groups. The intramural site visit books and the Board of Scientific Counselors books are typical of major documents which would be prepared using these support services. Within a fiscal year, the contractor normally provides three sets of BSC books, and three or four three-volume site visit books.

Under the second task area, conference and meeting management, the contractor will provide logistical support services for division conferences, meetings and workshops. In general, this will include providing assistance in site selection, preparation and distribution of invitations, agenda, and other pre and post-conference materials, hotel and air reservations, reimbursement of participant expenses, recording services, etc. This contract will function as a task order contract.

Provision of animal facilities and performance of routine experiments and tests. Recompetition of a contract held by Advanced BioScience Laboratories Inc. Proposed total award $4,254,735, first year award $770,000 (FY93), five years.

The Laboratory of Tumor Cell Biology is involved in several areas of research which require the use of non-human primates or small laboratory animals. These include 1) studies on the development of effective vaccines against HIV-1 and HIV-2 infection, 2) the development of effective antiviral therapies for HIV, 3) studies on viral and/or cellular gene products implicated in the pathogenesis of human retroviruses, including the neurological disease associated with HTLV-1 infection and 4) regulation of cell growth and differentiation or in the initiation or maintenance of neoplasia, including AIDS associated Kaposi's sarcoma and B-cell lymphoma.

Objective of this contract is to provide a well equipped and maintained animal facility with biohazard containment for small laboratory animals and up to 30 non-human primates and to provide an option to acquire and maintain an additional 20-25 non-human primates.

The contractor will purchase the animals and provide facilities for housing them, including biocontainment facilities for viral infected animals. The contractor will provide routine veterinary care, routine inoculations of virus and antigens, bleeding, surgical procedures, post-mortem examinations, routine blood chemistry tests, routine immunological testing, virus detection assays, histological examination of tissue and -70 degrees C storage of tissue. The contractor will also provide animals for the production of antisera to purified viral and cellular proteins and mice for hybridoma antibody production.

International epidemiologic surveys of human retroviruses. Recompetition of a contract held by Research Triangle Institute. Proposed total award $2.7 million, first year award $537,340 (FY93), five years.

The Epidemiology & Biostatistics Program, Viral Epidemiology Section, needs a mechanism to rapidly deploy field studies to pursue promising leads which are emerging with the discovery of new agents or their variants, and from the application of new techniques such as PCR amplification and in situ hybridization for more precise detection of oncogenic agents.

This project will undertake internationally focused epidemiologic surveys to define the occurrence of oncogenic viruses, particularly human retroviruses, in various populations, and to evaluate the nature and frequency of cancer related outcomes. These studies will include case-control, cross-sectional, and cohort designs. The project will also employ epidemiologic approaches in conjunction with state of the art laboratory techniques to clarify the role of transmissible agents in cancer, and to obtain suitable cellular and biologic materials for virus isolation and detection by PCR and in situ hybridization. In addition, tumor tissues and cell blocks will be obtained for testing by molecular epidemiologic techniques to evaluate for the coincidence of oncogenic agents (e.g., integrated retroviruses) and mutated cancer associated oncogenes or other abnormalities (e.g., aberrant p53 tumor suppressor gene).

The current contract provides a flexible and responsive mechanism for surveys of human oncogenic and immunosuppressive viruses, especially retroviruses in relationship to cancer and AIDS. Hypotheses are developed by NCI scientists and possible sites for conducting the study are identified. Study sites are selected on the basis of suitability for addressing the scientific questions of interest based on the frequency of a disease or exposure of interest to provide a sample of sufficient size to address the hypothesis. As a prelude to protocol development, the contractor principal investigator, at the request of NCI scientists, may visit the site and obtain more information on the capabilities of the onsite collaborators, the availability of study subjects, and the adequacy of logistical infrastructure. Based on these data, a protocol is developed by NCI investigators and submitted for technical review by the EBP with subsequent clearance by NCI, contractor, and onsite institutional review boards and, where appropriate, by the Office of Management & Budget. Questionnaires and field manuals are developed by NCI scientists with careful attention to ensuring that suitable quality control procedures are developed and implemented. Funding for field studies is provided through subcontracts negotiated and monitored by the PI. With oversight by NCI scientists, the PI implements the study onsite and performs frequent site visits to ensure that expected deliverables are being collected according to the timetable of the study. Data are keyed by the contractor into computer files, and the project officer monitors the quality of information for analysis. Samples and data are shipped to NCI for further analysis. Laboratory testing is performed and results confirmed and reported to individuals where indicated with appropriate counselling. Analyses are undertaken by NCI scientists in collaboration with the PI and onsite collaborators from the host country with authorship reflecting the critical role of host country investigators in successfully implementing studies often under adverse circumstances. Based on the results, additional follow up studies may be developed to refine hypotheses and extend etiologic insights.

Support services for occupational studies. Recompetition of a contract held by Westat Inc. Proposed total award $7.8 million, first year award $1.6 million, four years.

This concept provides over 80 percent of the support for the occupational studies program. It supports research activities for over 20 scientists from the Epidemiology & Biostatistics Program. The current contract expires in January 1993.

NCI seeks the assistance of an organization highly experienced in providing technical support to all phases of data collection in occupational health studies including the design of data collection documents, hiring and training of interviewers and abstractors, collecting, keying, editing, updating, and coding data, tracing individuals, monitoring and estimating exposures in the workplace, collecting, processing, transporting, and analyzing biologic tissues and fluids, creating and manipulating data files, and developing and running analytic programs. National and international studies may be conducted in single or multiple locations. Selection of scientific methods for all projects and the analysis and interpretation of the data are the responsibilities of the professional staff of the EBP. The responsibility of the contractor is to provide a team of study managers, abstractors and interviewers, questionnaire specialists, computer programmers, coders and keyers, industrial hygienists, and other support personnel to complete assigned study tasks.

Support activities provided under the contract are of two general types. In some studies, the contractor is responsible for virtually all of the field activities needed to complete the study, from developing data collection instruments and manuals to performing analyses as directed by the NCI staff. This approach occurs when the study is conducted without outside collaborators, or when the collaborating institutions are unable to carry out these activities. In other studies, the contractor provides only selected support activities that cannot be accomplished by the locally based collaborators. These specialized tasks often include forms development, interviewer training, random digit dialing for control selection, and uncommon tracing activities; but in actuality support for any task may be provided, depending on the circumstances.

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 collection documents developed by the contractors are thoroughly reviewed by NCI staff. Regular discussions occur between contract personnel and NCI staff to monitor study progress and to change direction and priorities as necessary. Detailed monthly reports are reviewed by NCI investigators.

The budget estimate is based on 4 percent above that of the previously awarded contract, plus an additional $200,000 per year for industrial hygiene and biochemical monitoring activities. In the current contract $130,000 per year is budgeted for industrial hygiene and biologic monitoring support. With the growing opportunities and need for these activities in occupational studies, the current level of support has proven to be insufficient. An additional $200,000 per year is requested specifically for industrial hygiene and biologic monitoring components which are increasingly being incorporated into occupational studies. This additional support is requested for ongoing and planned biologic monitoring components in studies of workers exposed to benzene and benzidine dyes in China, herbicide applicators, embalmers, as well as studies of brain and stomach cancer and development of an industrial hygiene job exposure matrix for use in case-control studies.

The board also approved in concept recompetition of a contract with Research Triangle Institute for a study of retrovirus epidemiology in hemophiliacs; the concept will be published in an upcoming issue of **AIDS update.**

In addition, the board gave concept approval to a noncompetitive contract to the National Academy of Sciences for epidemiological studies of cancer among A-bomb survivors in Japan, for a total of $1.7 million over five years. The board also approved the addition of $190,000 to a contract with Westat Inc. for completion of a study of breast and other cancers following x-rays for scoliosis. The contract expires in next March and will not be recompeted.

The board also gave concept approval to four interagency agreements, one with the Environmental Protection Agency for collaborative research and three with the National Institute of Occupational Safety & Health for research on occupatioal carcinogenesis, coding death certificates and developing a computerized occupational exposure data base.

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 Executive Plaza South room number shown, National Cancer Institute, Bethesda MD 20892. Proposals may be hand delivered to the Executive Plaza South Building, 6130 Executive Blvd., Rockville MD. RFP announcements from other agencies will include the complete mailing address at the end of each.

RFP NCI-CP-33000-21
Title: Support services for occupational studies
Deadline: Approximately Nov. 21

The Occupational Studies Section, Environmental Epidemiology Branch, NCI, is seeking sources capable of performing the above named project. This is not a Request for Proposal and does not commit NCI to award a contract now or in the future. No RFP package is available at this time. We are only seeking information from offerors with the capabilities to perform the stated project. This is a 100 percent small business set-aside.

The contract will support data collection activities for 20-25 projects. The studies supported by this contract are designed by NCI investigators who also analyze and interpret study results. The contractor must be capable of providing support for a number of studies conducted simultaneously in widespread geographic regions of the U.S. and other countries (e.g., Turkey and China). A critical capability is to be able to respond quickly to changes in priority and to supply support to urgent new efforts.

The types of support to be provided by the contractor in the conduct of the studies include: study initiation and liaison, preparation of study materials and procedures, data collection, data preparation, computer programming and data processing, and study monitoring, quality control and reporting. These tasks may vary. Communication between the contractor and NCI will often be on a daily basis with regularly scheduled meetings to review and adjust procedures for assigning work. The contractor must be capable of performing random digit dialing. Personal computers shall be used wherever possible for data processing and manipulation. The NIH/DCRT computer facility (which has IBM computers) shall be accessed by remote terminals to be provided by the contractor on their own premises. Monitoring of a wide spectrum of workplace exposures shall be performed by an industrial hygienist certified by the American Board of Industrial Hygiene who has access to equipment and a laboratory certified by the American Industrial Hygiene Association.

The contractor shall provide monthly and annual technical reports, monthly budget reports and a final technical progress report. Other deliverables shall include computerized data, raw data and biologic specimens and industrial hygiene samples. The total estimated level of effort to be provided is 35,880 direct labor hours from persons with skill in questionnaire design, coding, industrial hygiene, abstracting and interviewing, computer programming, collecting of biologic tissues and in the managing of epidemiologic studies. The contract will be a cost reimbursement, level of effort type for a 48 month period. Award is anticipated by Feb. 1, 1993.

Evaluation criteria, in descending order of importance, shall be: 1) experience and capabilities of key personnel and 2) corporate experience in conducting and managing widespread multiple studies as described in the RFP. There will be two mandatory qualification criteria: 1) the contractor's accomplishment of the need for face to face meetings on a nearly daily basis and 2) the provision of the services of a senior industrial hygienist who must be certified by the ABIH and must have access to a laboratory accredited by the AIHA. Contract Specialist: Barbara Shadrick

RCB Executive Plaza South Rm 620
301/496-8611

RFP NCI-CN-25404-46
Title: Prostate, lung, colorectal and ovarian cancer screening trial: laboratory
Deadline: Approximately Jan. 20

NCI's Div. of Cancer Prevention & Control, Early Detection Branch, is interested in soliciting proposals from clinical

laboratories to carry out PSA assays for 37,000 men and CA 125 assays for 37,000 women screened annually four times. A total of 148,000 PSA and 148,000 CA 125 assays are projected over eight years of screening. In the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial, up to 15 screening centers will be established, each recruiting no less than 5,000 subjects and 5,000 controls. Frozen serum will be prepared by screening centers and shipped periodically for assay to the laboratory. NCI has selected the cancer sites and screening modalities. Screening centers, in cooperation with NCI, will develop screening logistics and diagnostic protocols.

Contract Specialist: Schuyler Eldridge
RCB Executive Plaza South Rm 635
301/496-8603

RFP NCI-CN-25406-41

Title: Science enrichment program

Deadline: Approximately Jan. 10

NCI's Div. of Cancer Prevention & Control, Cancer Control Science Program, is interested in soliciting proposals for conducting regional, summer resident "Science Enrichment Programs" for incoming tenth grade underrepresented minority and underserved youth who have a demonstrated interest in science and/or mathematics. The goals of this program are: 1) to encourage underrepresented minority and underserved youth to pursue professional careers in science or research, and 2) to broaden and enrich students' science, research, and sociocultural backgrounds. High schools collaborating with colleges and/or universities, colleges, universities, as well as cancer centers or schools of public health are some of the eligible offerors.

It is anticipated that multiple awards will be made, for a two-year period (with a two-year option clause) to be incrementally funded as a cost-reimbursement type contract. Two pre-proposal conferences are anticipated, one in Bethesda, MD, and the other location, dates and times for each will be specified in the RFP. Anticipated award date is mid-May 1992.

Contracting Officer: Susan Hoffman
RCB Executive Plaza South Rm 635
301/496-8603

RFP NCI-CO-21039

Title: Managing your child's eating problems during cancer treatments

Deadline: Approximately Dec. 4

Single award for a fixed price contract. Inspection of source materials will be on or about 11/28/91 at the National Institutes of Health, Bethesda, MD. Booklet. 36 page book with separate wraparound cover. Five color printing and varnish on outside covers; one color printing on inside covers; two color printing on text. 150,724 copies and films used in printing. Trim size 5-7/8" x 9-1/8", bind on the 9-1/8 dimension. 4-color process, PMS 100 yellow, PMS 155 tan and black. Solid inks, no builds allowed. Operations include printing, binding, trimming, separations, coating, packaging, mailing and shipping. Contractor furnish paper. Material furnished: 20 mechanicals mounted two up with tissue overlays. 1 reflective art illustration. Quality attributes level II for printing and finishing.

Contract Specialist: Charles Jackson
RCB Executive Plaza South Rm 620
301/496-8611

RFP NCI-CO-21050-61

Title: Clearing the air

Deadline: Approximately Dec. 27

Single award for a fixed price contract. Inspection of source materials will be on or about 12/19/91 at NIH, Bethesda, MD. Booklet. 24 page brochure with separate wraparound cover. Three color printing and six color printing on text. Varnish requried on outside covers. 1,200,723 brochures and films used in printing. Trim size, 4" x 9", bind on the 9" dimension. 4-color process, PMS 3255 aqua and PMS 2715 lavender. Solid inks, no builds allowed. Operations include printing, binding, trimming, separations, coating, packaging, mailing and shipping. Contractor furnish paper. Material furnished: 14 mechanicals with tissue overlays, artboard for gradations and a line illustration mounted on cover 1. Eight 35mm color transparencies and a sample for style only. Quality attributes level II for printing and finishing.

Contract Specialist: Charles Jackson
RCB Executive Plaza South Rm 620
301/496-8611

RFP NCI-CO-21054-61

Title: How to help your patients stop smoking

Deadline: Approximately Dec. 27

Single award for a fixed price contract. Inspection of source materials will be on or about 12/20/91 at NIH, Bethesda, MD. Booklet. Item 1: 112 page book with separate wraparound cover. Five color printing on cover and two color on text. Varnishing required. Item 2: Same as item 1 except 20 page book. Quantity: Item 1: 45,000 copies and films used in printing. Item 2: 45,000 copies and films used in printing. Trim size 8-1/2" x 11" for both items. Bind on the 11" dimension. Inks: PMS 417, 3262, 542, 257, 1785, 136 and black for both items. Covers 1 and 4 print a full bleed solid of PMS 417 and a mezzotint screen overprints in black. A silhouette halftone ko's on cover 1 and prints PMS 136. Binding: Item 1: Perfect bind text and wraparound cover: 1/4" hinge on covers: score on hinge and cover folds. Perforate pages 109-112. Vertical and horizontal perfs required. Item 2: Saddle wire stitch in two places and trim three sides. Score on cover fold. Type reverses to white on both cover and many areas knockout and print PMS 3262, PMS 1785, PMS 257, PMS 136 and PMS 417. Colors butt in many areas on cover 1. Operations include printing, binding, trimming, coating, packaging, mailing, and shipping. Contractor furnish paper. Material furnished: Item 1: 115 pieces of camera copy, one photo print and a sample for style only. Item 2: Pickup copy from item 1. Section G of the book. Cover mechanical. Quality attributes level II for printing and finishing.

Contract Specialist: Charles Jackson
RCB Executive Plaza South Rm 620
301/496-8611

RFP NCI-CO-21053-61

Title: Breast exams: What you should know

Deadline: Approximately Dec. 31

Single award for a fixed price contract. Inspection of source materials will be on or about 12/19/91 at NIH, Bethesda, MD. Booklet. 12 page brochure with separate wraparound cover. Three panel foldout which perforates on page 11. Outside covers print five colors. Inside covers print one color, text and foldout print 2 colors. 1,000,724 copies and films used in printing. Trim size, covers and pages 3-10 are 8" x 9", flat and fold to 4" x 9". Four color process, PMS 109 yellow and black. Solid inks, no builds allowed.

Operations include printing, binding, trimming, separations, coating, packaging, mailing, and shipping. Contractor furnish paper. Material furnished: 4 mechanicals with tissue and acetate separation. Art is a painting on paper. Art is scanable. Quality attributes level II for printing and finishing.

Contract Specialist: Charles Jackson
RCB Executive Plaza South Rm 620
301/496-8611