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Improved NCI Relations With FDA Cited As Model For Government Accord, Lasagna Committee Says

Relations between NCI and the Food & Drug Administration have improved so dramatically in the year since the first meeting of the National Committee to Review Current Procedures for Approval of New Drugs for Cancer and AIDS that committee members are now citing interactions between the two agencies as a model for government coordination. The first meeting of the group commonly called the Lasagna Committee after it chairman, Louis Lasagna, was marked by

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In Brief

AACR Award Lectures Announced; Hungerford Honored For Philadelphia Chromosome Discovery

AWARD LECTURES at the American Assn. for Cancer Research annual meeting will be given by the following researchers: the Rosenthal Lecture will be given by Carlo Croce and the Cain Lecture by Albert von Wartburg and Hartmann Stahelin, on May 23; Clowes Lecture by Erkki Ruoslahti, followed by the presidential address by AACR President Harris Busch on May 24; and the Rhoads Lecture by Ronald Evans on May 25. For meeting information contact AACR, 215/440-9300. . . . **DAVID HUNGERFORD,** Fox Chase Cancer Center, will receive the first Lifetime Achievement Award presented by Eagles Fly for Leukemia, a nonprofit organization affiliated with the Philadelphia Eagles football team. Hungerford is being honored for his discovery of the Philadelphia chromosome, the first chromosomal abnormality linked with a specific cancer. . . . **ERNEST BORDEN** has been named director of the Cancer Center of the Medical College of Wisconsin. He will join the faculty Oct. 1. Borden is currently professor of oncology at Univ. of Wisconsin Clinical Sciences Center. . . . **MELVIN DEUTSCH,** Pittsburgh Cancer Institute and professor of radiation therapy at Univ. of Pittsburgh School of Medicine, has been selected the first Raul Mercado Professorship in Radiation Oncology, a new, $1 million endowed professorship established by University Radiotherapy Associates in conjuction with the radiation oncology department. . . . **ISAAC DJERASSI,** director of research oncology and hematology at Mercy Catholic Medical Center, Darby, PA, is the recipient of the first Edwin Cohn-De Laval Award. The award was presented last week at the Third International Congress of the World Apheresis Assn. in Amsterdam. Djerassi introduced platelet transfusions using apheresis technology and developed a method to collect white blood cells for treatment of leukemic or cancer patients with life threatening infections. He invented a means of mechanizing the process.

Improved NCI/FDA Relations Cited As Model For Interaction

(Continued from page 1)
often heated discussion between FDA and NCI officials about the approval process for new cancer drugs.

At its final meeting last week, committee members were lauding efforts made between the two and citing the NCI-FDA relationship as a model that should be used by the National Institute of Allergy & Infectious Diseases to better its relationship with FDA.

"There's a colossal irony here, which is that a year ago, I would have found it inconceivable that people would be saying that the NCI and FDA are models for collegiality, cordiality and synergistic interaction," commented Michael Friedman, head of NCI's Cancer Therapy Evaluation Program. "Does this irony escape everybody or is it just me that finds it colossally funny?

"In fact, it's true," he said. "In fact, there is a lot of good will, there is a lot of collegiality. This has been at the expense of a lot of hard work by a lot of people, but I don't think it is cosmetic, I don't think it is superficial. I think it's real. I think there is a lot for both groups to gain from these sort of interactions. I think it's obvious to both groups. There are some very large issues at stake here, and everyone recognizes those.

"If that's become at least one model for interaction, that's fine," he said. "It's important because it's good to move new agents along, to find new knowledge in an efficient way, to find better treatments for patients and that's what I think we are all committed to."

Stating that he was pleased "to see FDA and NCI moving closer together," Lasagna said he was troubled to hear that NIAID and FDA are not working well together.

The committee is drafting a report on its more than year-long inquiry into the approval process, which is tentatively scheduled to be available to the President's Cancer Panel in time for its next meeting, in June.

FDA officials took the opportunity to emphasize the importance of early dose response studies in drug development. Dose response studies should be among the first clinical trials to be conducted in humans, said Carl Peck, director of the FDA's Center for Drug Evaluation & Research.

"I think it's imperative to recognize that the dose response or something akin to it should be one of your first ones so that you can minimize the number of trials ... thereafter."

"Pharmacokinetics and dynamics offer a rational framework for discovery of optimal dosing regimens," Peck said. "The use of this technology early in drug development can significantly reduce drug development time and costs."

FDA Office of Drug Evaluation Director Robert Temple also stressed the importance of early dose response studies. "It's terribly important to find these things up front," he said. Without dose response randomizing patients to several different doses, time may be wasted, he asserted.

Committee Member Gertrude Elion, however, questioned the emphasis on early dose response studies in trials of new agents for cancer and AIDS.

"I think we have to remember that when we're talking about cancer and AIDS drugs, we don't have quite the same latitude for looking at dose responses," she said. "In the first place, response often takes a long time before you can evaluate it. The other thing is that we have grown up with the concept that, in the case of cancer particularly, you use the maximum tolerated dose because you're never going to have a very large therapeutic index."

Such drugs should be given at doses that are efficacious, "even at the risk of some toxicity. You could of course take three different doses, only to find that the first two doses do nothing.

"I think that what you're saying is absolutely applicable to some of those pharmaceutical drugs. I'm not so sure that you can do a large dose finding study in the case of cancer or AIDS."

Temple countered that "the experience is that in AIDS that one could have. One didn't for AZT, but in retrospect, it's fairly clear that one might well have studied a lower dose and benefitted from that."

Ellen Cooper, head of FDA's Antiviral Drugs Div., asserted that in the case of nucleoside analogs, dose response studies seem to be "the very way to go. The likelihood is not that you won't find those lower doses are effective, but that you will find that they

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are as effective with less toxicity. It might not be true of all drug classes, but certainly if you don't look at it, you're not going to find out."

Lederle Labs Vice President Robert Desjardins also suggested that more data be obtained on investigational drugs in early stages of development.

"It is possible to obtain more data regarding the activity, mechanisms of action and potential toxicity of a drug and its metabolites in preclinical studies, which in conjunction with early clinical pharmacokinetic and metabolism data will lead to improved design of early phase 2 studies, and a reduced risk of error in the definitive studies of safety and efficacy later," he said.

Desjardins suggested that FDA "find a mechanism to facilitate the process of early entry into phase 1 and even phase 2 studies in man" and a way "to simplify requirements for the approval of early studies in small numbers of volunteer patients." Such studies could include early pharmacokinetics and pharmacodynamics.

FDA could even consider allowing such studies on "a preferred sponsor basis" among drug sponsors "who have demonstrated scientific excellence," he advised.

"It's important before we go into a full phase 1 or full phase 2 to know that some of the data that we've accumulated in the animal is relevant, otherwise we're right up a creek," Elion said. "We just don't know if this is a toxic or nontoxic drug that should be given orally or i.v. or whatever." She also urged that FDA allow early studies in small numbers of persons "to find out whether the metabolism and pharmacokinetics is at all like the animal models we've used, because if it's not we better find another animal model."

Temple said FDA regulations make it easy to conduct such early studies in patients with cancer. "The preclinical toxicology that you need to start a cancer drug actually does consist of just a few studies in mice," he said. "It's the LD10 in mice and then you go from there ... I think it should be fairly easy to get into."

"We don't believe that," Elion replied. "We don't feel confident doing that."

"But you could do that," Temple responded.

"Yes, but I don't think it saves time to go from an LD10 in mice into man without knowing the metabolism in mice, the metabolism in man," Elion said. "I think it's a waste of time."

Noting that FDA has been working with NCI on a project that would "allow more rapid dose escalation by matching up the area of the curve in mice and in man," Temple said, "my only point was that one can get into man for those purposes extremely readily with oncologic drugs, and perhaps with AIDS drugs.

"We've been thinking but not doing much about that general problem for all drugs for a long time," he said. "There is document under development that contemplates doing that on the basis of acute studies alone."

FDA officials used the opportunity to again emphasize the desirability of drug sponsors meeting with the agency early in the drug development process.

"There was a historical worry that if we helped shape the development, we'd be compromised, that we wouldn't be adequately critical, we wouldn't be able to disagree with anything later," Temple said.

"It's very costly to watch mistakes being made and not try to do something about it. A long time ago, we became willing to comment on a sponsor's development plan and specific protocols. We in general can't do that unless we're asked."

Temple said FDA does have adequate staff to respond to sponsors' requests for comments on development plans.

"We don't consider ourselves more knowledgeable about the basic disease processes than anybody else," he said. "We are to a degree, though, specialists in how to demonstrate things and without sounding immodest, I think in general we're better at that than the people we encounter, probably because it's most of what we do. We can contribute and do regularly contribute ... to the improvement of study designs, to suggest approaches that possibly haven't been thought of. I think we make important contributions. We put interest in dose response back on the map."

Committee members, however, asserted that some sponsors may not seek FDA's advice on drug development and study design because they believe such advice is tantamount to requirements.

Noting that sponsors do not want to affront FDA, member Emil Frei said companies would do what the regulatory agency suggested.

Noting complaints at previous meetings by NCI Div. of Cancer Treatment Director Bruce Chabner that FDA tries to micromanage drug development, member Peter Hutt said, "the problem is drawing that fine line between being overbearing in FDA's advice. That's the way it's often viewed on the other side of the table, as contrasted with trying to be extremely helpful and forthcoming.

"Once FDA gives advice, the people on the other side view that as an absolute requirement, no matter how well you try to put it in any other way," he said. "That came out at our first meeting. NCI and NIAID both regard your 'advice' as mandatory requirements that they cannot avoid."

"We clearly have a different experience in viewing

the outcome of our giving advice," Peck said. "It's impressive how often our advice is just blatantly ignored. I think there are a lot of bold individuals out there who are tough enough not to accept our advice.

"We represent it as being voluntarily available and not binding," he said. "Our experience with some is that they will ignore good advice, push forward with mediocre science and go to the White House or lawsuits, or though premature public announcements."

Lederle's Desjardins praised "the willingness of FDA to meet regularly with sponsors in the early stages of the drug development process.

"In my own experience, these meetings have quite often contributed to the scientific excellence of the process," he said.

"There's a key element absolutely essential for success in the process that sometimes gets lost or forgotten in all the rhetoric about regulations and the politics of new drug development, and that's scientific excellence," he said.

"Increased emphasis on scientific excellence in the early stages of the process will reduce the risk of error, accelerate the later stages, including the review and approval at FDA," he said. "In essence, a little more time and investment early can save a great deal of time later. False starts and changes of direction in the later stages are extremely costly in time and resources.

"Unfortunately, the pursuit of new drug development has often taken what I call the ramrod approach ... there's extreme pressure in this approach to 'get into man' as quickly as possible, and a determination to keep costs to a minimum until there is evidence of efficacy in man."

Richard Gams, senior director of medical research for Adria Labs, said he believes the major delay in the drug approval process for cancer "is the time taken to recruit significant number of patients to clinical trials to reach accrual goals." Such delays could in part be caused by the burden of paperwork required of physicians participating in studies of investigational drugs, he suggested.

"I actually don't believe that in my experience with FDA that they are overbearing," said Daniel Hoth, director of the AIDS Div. at NIAID. "I think the problem is the unequal power relationship can lead to an inordinate degree of acceptance of things. In fact, there are wimps out there."

Cooper said her staff was told "in a moment of candor" by a pharmaceutical company representative "that they are told not to tell us anything or provide information unless they're asked for it. That certainly is something that is not conducive to candid discussion."

"We're convincible," Temple said. "It happens all the time. There's plenty of room for modification.

"This isn't a war that goes on," he said. "It's a bunch of people trying to get the best possible data under difficult circumstances. Cancer and AIDS are hard to study because you can't do usually the kinds of trials that give the clearest answer" such as placebo controlled studies.

Hoth urged an increased willingness on the part of drug sponsors to express themselves to FDA. "Many sponsors will go into a meeting, view it as an adversarial relationship and basically craft the meeting to get a certain result, which creates a lack of free exchange," he said. "It's naive to think we'll ever get away from that because certainly there are those who are trying to manipulate the system purely for commercial gain, but there is a group of very responsible scientifically oriented sponsors, and I would encourage them to express themselves even more fully."

Hoth also called for an increased willingness to innovate in drug development, such as conducting the blood level directed studies suggested by Peck. "We'd like to do that in our area." He endorsed the concept of making it easier to go into phase 1 studies in humans "so that there can be a quicker movement between ideas in the laboratory, piloting them in phase 1 trial, going back into the lab, and having more control at the phase 1/2 interface.

"There are a lot of drugs that are moving into clinical trial in Europe that couldn't make it here because of that," he said.

Hoth also called for adequate numbers of scientific staff at FDA. "One of the reasons that I think that the AIDS group at FDA has done a very good job at moving things through is the number of scientific staff," he said. "Compared to the staffing levels of the oncology group four or five years ago, the staffing levels in AIDS are so much higher that they're simply able to move things through faster."

"Staff is critical," Temple agreed. "They are closer to what they need than a lot of places, and their turn-around time reflects that." Both the AIDS and cancer review groups "are more in command of their total net workload than a number of other places, and that's because they've had adequate ceilings to do it, and they've always been able to find people to do it."

"The result is extremely important," Hoth said. "I would wonder if there is a lesson here for other areas of drug development."

Hoth also called for more distinction between scientific advice provided by FDA staff and agency regulations. "Many of the staff want to give scientific

advice and that becomes confused in the sponsor's mind as rules and regulations."

Members also discussed the need to develop standardized forms for use in drug development protocols. Sandra Gotzkowsky, clinical supervisor for the Clinical Research Center, called for standardization of protocols, case history and report forms. She cited tremendous variations in forms such as those for medical histories or specific medical tests. Forms for EKG reports, for example, may range from whether it was normal or abnormal to as many as 200 questions.

Lasagna queried participants about efforts to standardize forms.

"A lot of effort has been put into standardization," Leighton replied. Although standardization can be used in some areas, such as adverse event reports, or forms for certain tests, items that apply to a particular drug are not candidates for standardization, he said.

"I think there is always a tendency to ask more questions than you really need," he said. "Between companies, I think virtually nothing has been done and that's an area worth exploring."

"This is the nuts and bolts of our day to day operation," said Jan Drayer, vice president of a contract research house, noting that forms such as physical histories could be standardized.

"In one study that we are currently doing, it takes one [records administrator] six hours to source document and review the first visit of a patient with AIDS. I think that that is unacceptable," he said. "I think it is not a proper use of the limited research time that we all have."

"A lot of the stuff that's collected, especially the deeply distant history, is probably not usable," said Temple. Many times data that is important to be collected, such as blood pressure history, and responses to previous treatment for hypertension are not available, "yet you probably have all kinds of garbage about how much they weighed when they were born."

Levamisole/5-FU Could Save $226 M In 1990 If Fully Adopted, Report Says

An NCI economist has suggested that adjuvant therapy of colon cancer with levamisole and 5-FU would save more than $226 million in 1990 alone by extending patients' lives if the treatment is fully adopted for the eligible population.

Martin Brown, an economist in the Applied Research Branch of the Div. of Cancer Prevention & Control, presented an economic analysis of the treatment this week at an NIH consensus conference on colon/rectal cancer. The conference was scheduled to continue through Wednesday, and a draft of the panel's recommendations will be reported in next week's issue of **The Cancer Letter.**

NCI produced the cost benefit analysis at the request of the NIH Office of Science Policy and Legislation, which periodically asks for such information, Brown said.

Brown estimated that the cost of development of levamisole/5-FU for the treatment of Dukes C colon cancer was approximately $10.8 million. This investment would yield a return of $226.6 million in just one year, 1990, assuming full adoption of the treatment.

"This return includes the economic value of life years, imputed by wage earnings, that are saved as a result of the treatment," Brown wrote in a paper presented at the conference.

Brown also estimated the cost effectiveness of the treatment, or the economic cost incurred to gain a year of life. The number of life years gained per patient through the use of levamisole/5-FU is estimated at 2.37. The actual cost of a course of treatment is $4,220, but if the value of lost work time due to treatment is included the total cost is $4,775. Thus, the cost effectiveness is $2,014 per life year gained.

"This is a very favorable cost effectiveness ratio. By way of comparison, the cost effectiveness of screening for cervical cancer with triennial pap smears has been estimated at $14,300 per life year gained, and the cost effectiveness of coronary bypass surgery has been estimated to range from $5,660 per life year gained for left main disease to $44,100 per life year gained for one-vessel disease," Brown wrote.

The cost of adjuvant treatment is modest when compared to the total five-year treatment cost for Dukes C colon cancer, which ranges from $30,000 to $50,000, Brown said.

The total cost of treating all potentially eligible patients with levamisole/5-FU in 1990 would be about $94 million, with a gain of about 53,000 life years. In contrast, the total cancer treatment bill for these patients without the new treatment would be approximately $35 billion, Brown estimated.

In his paper, Brown noted that there are some uncertainties to this analysis, as in any economic analysis of cancer treatment:

--The cost of development of $10.8 million should be factored into the cost for treating each patient who derives benefit from the development. However, this amount is small compared with the total annual treatment cost, so it would not have a large effect on the cost effectiveness outcome.

--The eligible population and number of life years gained is based on the published results of the North Central Cancer Treatment Group controlled clinical trial. Results of more recent studies, still unpublished, may provide evidence of more favorable results.

--It is unrealistic to apply results of a controlled clinical trial to the general population. The median age of subjects in the NCCTG trial was 61, while the median age of patients with Dukes C colon cancer in the general population is closer to 70. It is possible that the survival benefit of the treatment is lower for older patients and that a higher percentage of older patients are not good candidates for treatment because of more frequent comorbidities.

--In calculating life years gained, it was assumed that a cancer survivor has the same life expectancy as a person from the general population of the same age. This is likely to be an optimistic assumption because the burden of severe morbidity probably reduces life expectancy.

--Full adoption of the treatment was assumed as well as treatment quality at least as good as that provided in the clinical trial. It is likely that the adoption of the treatment will take a few years and that it will never be administered to 100 percent of Dukes C patients.

This is true both because some patients who should receive the treatment on clinical grounds will not receive it for other reasons, such as refusal or lack of awareness, and because other patients cannot receive it for practical reasons. Brown estimated that a plausible range of adoption for the treatment is 50 to 80 percent, two years after the October 1989 NCI clinical update.

--In the calculations, not all conceivable costs, or offsets to costs, were taken into account. For example, the reduction in recurrence rates due to levamisole/5-FU will result in two types of additional savings. First, there will be less treatment of recurrent cases. Second, individuals spared recurrence will lose fewer productive days of work. On the other hand, many of the older individuals who live longer because of the treatment will, consequently, consume more transfer payments, such as Social Security benefits. Although not a cost from the individual perspective, many economists would assert that this consideration should enter into any social cost effectiveness calculation that is geared to policy analysis.

In addition, future economic analyses of levamisole/5-FU may have to consider that another treatment, leucovorin/5-FU, also may prove effective, Brown said. Leucovorin is more expensive than levamisole, but its cost has fallen in the past two years and may drop further if it were to come into widespread use. The next step would be to calculate cost effectiveness by examining the marginal cost per life year gained by using leucovorin rather than levamisole, Brown said.

Lasker VP Urges Senate Committee To Support FY 1991 Bypass Budget

An official with the Albert and Mary Lasker Foundation told a Senate committee that it should fully fund the FY 1991 bypass budget, which would provide NCI $2.4 billion, $716 million more than that requested in President's budget.

Alice Fordyce, executive vice president of the Lasker Foundation and vice president of the U.S. Coordinating Council for Cancer Research, made the statement recently before the Senate Labor, HHS, Education Appropriations Committee.

"This year the National Cancer Advisory Board has sent to the President the FY 1991 bypass budget, a needs budget, for NCI, of $2.4 billion," Fordyce told the committee. "The CCCR supports this level of funding and urges you and your colleagues to approve this request."

Fordyce said that without the extra $716 million provided in the bypass budget:

"--Fewer research grants will be funded in FY 1991 than were funded in FY 1990 and only 27 percent of approved grants will be funded at all.

"--Downward negotiations of 20 percent for competing grants and 4 percent for noncompeting grants will be necessary.

"In this funding climate, it is virtually impossible for NCI to commit dollars to crucial international research efforts. But we live in an age of international competitiveness. In order to really maintain our crucial international leadership, Congress will have to support NCI's major research programs. Already, Japan, West Germany and France commit a greater percentage of their GNP to biomedical research than we do in the United States.

"The Cold War is over. We are entering into a time when we must move away from hug defense programs and move towards the goal of a healthier nation and world.

"Reaching the level of commitment which is recommended in the bypass budget of $2.4 billion is a challenge which must be accepted. This budget would allow for: expansion of the vaccine development effort, full funding of a 50 percent award rate, full funding of noncompeting research grants, and seriously addressing the needs of the

minority and over 65 populations.

"If this committee will approve funding of the $2.4 billion (bypass) budget for these programs, many scientific and technological breakthroughs which will have international consequence could be achieved, and millions of lives could be saved."

ONS Meeting To Highlight Progress By Nurses; Brown To Give Keynote

Helene Brown, director of community applications of research at Jonsson Comprehensive Cancer Center at Univ. of California (Los Angeles), will give the keynote address at the 15th Annual Congress of the Oncology Nursing Society, to be held May 16-19 in Washington.

Brown's address is titled "Cancer Control Tomorrow." She is a member of the National Cancer Advisory Board.

An estimated 5,000 oncology nurses will attend the meeting, which will focus on the progress made by oncology nurses in the past 15 years.

The meeting will begin with 22 pre-congress sessions May 15 and 16, including a visit by nurses to their legislators on Capitol Hill. That visit is scheduled for 12:30 p.m. on May 16.

During the main session, there will be two major lectures, scheduled for May 17. Richard Wells, director of the Marie Curie Rehabilitation Centre at the Royal Marsden Hospital in London will give the Mara Morgensen Flaherty Memorial Lecture. His topic will be the importance of cancer rehabilitation.

Karen Hassey, nurse specialist at Beth Israel Hospital in Boston, will deliver the ONS/Schering Clinical Lecture. The title of her lecture is "The Enduring Seasons of Survival."

In addition, there will be three symposia on May 20 jointly planned and presented by ONS and the American Society of Clinical Oncology. The symposia topics are metastatic breast cancer, infusional therapy and bone marrow transplantation.

The first ONS Public Service Award will be presented to Sen. Edward Kennedy (D-MA) for his support of nursing, oncology and health care issues, and his son, Edward Kennedy Jr., for his dedication to rehabilitation.

On-site registration for the meeting is available. For more information contact ONS, 1016 Greentree Rd., Pittsburgh, PA 15220, phone 412/921-7373.

Certification Examination May 16

The Oncology Nursing Certification Corp. will offer the 1990 Oncology Nursing Certification Examination on May 16 in conjunction with the ONS annual meeting. An estimated 1,500 nurses are scheduled to sit for exam.

The examination also will be offered Sept. 22 in New York City, Atlanta, Chicago, Dallas, Denver and Los Angeles. Reporting times and exact location will be printed on the admission ticket.

Certification is open to nurses who have and RN license current at the time of application and examination, two and a half years experience as an RN within the last five years, and a minimum of 1,000 hours of oncology nursing practice within the last two and a half years. Nursing experience may be in the areas of nursing administration, education, clinical practice or research.

The certification examination is aimed at testing general oncology nursing knowledge. The Educational Testing Services of Princeton, NJ, developed the test under contract with the ONCC. Items for inclusion in the examination are based on the core curriculum developed by the ONS Core Curriculum Task Force.

Nurses eligible for renewal may take the exam on either May 16 or Sept. 22. If there is no test center within 100 miles of the city in which a nurse wants to be tested, that nurse may request that an additional center be established.

Cost of the examination is $175 for ONS members, $250 for nonmembers. Renewal fees are $125 for ONS members, $200 for nonmembers.

For more information contact the ONCC, 1016 Greentree Rd., Pittsburgh, PA 15220-3125, phone 412/921-8597.

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-CN-95165-38

Title: ASSIST cancer prevention

Deadline: Approximately Sept. 25

American Stop Smoking Intervention Study for Cancer Prevention (ASSIST). The goal of this acquisition is to apply a specific set of proven, state of the art smoking prevention and control interventions developed in randomized research trials throughout approximately 20 demonstration sites. These sites will form the framework through which to implement and institutionalize these intervention strategies in order to reduce smoking prevalence. This framework will comprise a coalition of community and state level organizations and agencies which have

the capacity and/or the mandate to reach smokers and youth at risk of becoming smokers.

The RFP restricts competition to health departments in states or large metropolitan areas which have the capability to meet the government requirements in cooperation with a voluntary health agency. Twenty awards are anticipated for 6.5 year incrementally funded cost-reimbursement completion contracts.

Contracting Officer: Barbara Mercer
RCB Executive Plaza South Rm 635
301/496-8603

RFP NCI-CM-17509-14

Title: Synthesis of bulk chemicals and drugs for preclinical and clinical studies

Deadline: Approximately June 11

The Pharmaceutical Resources Branch of the Developmental Therapeutics Program in NCI's Div. of Cancer Treatment anticipates awarding two to three cost-reimbursement incrementally funded contracts for a period of five years beginning on or about March 31, 1991, to provide and operate a materials preparation laboratory for the development of existing or new processes, procedures and techniques for the preparation of compounds, and the synthesis of varying amounts of materials, not readily available from other sources in the quantity and/or quality needed by NCI for the preparation of anticancer drugs.

The successful offeror shall provide an operating large scale facility with at least one small (20-50 gallons) and one large (100 gallons or larger) glass-lined reactor, and the necessary supporting equipment and facilities.

Quantities of drugs requested will usually range from 50 grams to multikilograms. Process development for scale up and access to pilot plant equipment is essential. Specific assignment of the materials for preparation will be made by NCI and may include synthesis of all types of chemicals and drugs. Quality specifications will be determined by the PRB. All materials must be evaluated by the synthesis laboratory for identity and purity before being submitted to NCI.

The contractor's principal investigator should be trained in organic or medicinal chemistry, preferably at the PhD level, or equivalent in experience, and have extensive experience in chemical synthesis and synthetic process development.

At the time of submission of best and final offers, the offeror must be registered with the FDA as a manufacturer of bulk drugs and will have submitted a facilities Drug Master File to FDA.

Facilities shall meet FDA standards in accordance with the Current Good Manufacturing Practices, as well as be in compliance with applicable EPA and OSHA requirements and those of similar state and local agencies. Noncompliance with the above requirements shall render the proposal technically unacceptable without the consideration of award.

Two related RFPs are currently available. This RFP is nonrestricted, while RFP NCI-CM-17510-14 (see below) is a 100 percent small business set aside.Offerors who qualify as a small business are encouraged to submit proposals under both RFPs; however, not more than one award of the available two to three awards (under both RFPs) will be made to any single organization.

Contracting Officer: Dorothy Coleman
RCB Executive Plaza South Rm 603
301/496-8620

RFP NCI-CM-17610-14

Title: Synthesis of bulk chemicals and drugs for preclinical and clinical studies by small business

Deadline: Approximately June 11

The Pharmaceutical Resources Branch of the Developmental Therapeutics Program in NCI's Div. of Cancer Treatment anticipates awarding two to three cost-reimbursement incrementally funded contracts for a period of five years beginning on or about March 31, 1991, to provide and operate a materials preparation laboratory for the development of existing or new processes, procedures and techniques for the preparation of compounds, and the synthesis of varying amounts of materials, not readily available from other sources in the quantity and/or quality needed by NCI for the preparation of anticancer drugs.

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Offerors who qualify as a small business are encouraged to submit proposals under both RFPs; however, not more than one award of the available two to three awards (under both RFPs) will be made to any single offering organization.

Contracting Officer: Dorothy Coleman
RCB Executive Plaza South Rm 603
301/496-8620

RFP NCI-CN-05233-04

Title: Prostate, lung and colorectal cancer screening trial: Study coordinating and data management center

Deadline: Approximately June 25

NCI's Div. of Cancer Prevention & Control, Cancer Detection Branch, is interested in soliciting proposals from organizations for maintaining a study coordinating and data management center for the Prostate, Lung and Colorectal Cancer Screening Trial (PLC).

The purpose of the center is to develop and maintain systems and procedures for biomedical data management, study coordination, statistical analysis and report writing. The coordinating center must receive and process data from up to 10 screening centers in all phases of the proposed 16-year study, plus possess the ability to provide logistical support for meetings and other activities required by the project. It is anticipated that the coordinating center staff shall be required to interact with NCI project officers on a daily basis. Requests for this solicitation shall be made in writing and reference the RFP number above.

Contract Specialist: Christopher Myers
RCB Executive Plaza South Rm 635
301/496-8603