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Conference Asks NCAB To Develop Guidelines For Clinical Alerts; Must Be Investigator-Initiated

The National Cancer Advisory Board should develop general guidelines for NCI to follow in deciding when and how to issue clinical alerts, a special conference recommended last week. The NCAB sponsored the unusual meeting of representatives from cooperative groups, cancer centers, individual investigators, American College of Surgeons, American

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In Brief

Six On NCAB Serve Out Terms, No Successors In Sight; DCBD Renamed With 'Centers' In Title

SIX NATIONAL Cancer Advisory Board members have served out their terms as of the board's meeting last week, but since President Bush has not appointed replacements, they remain on the board. The six received certificates of appreciation from NCI Director Samuel Broder last week, who said, "You are not free to go." They were: Board Chairman David Korn, Helene Brown, Roswell Boutwell, Gertrude Elion, Enrico Mihich and Louise Strong. Korn will continue as board chairman until a successor is named. There are two more vacancies on the board, that of Louis Gerstner, who resigned, and Louis Sullivan, who became HHS secretary. When will the total of eight vacancies be filled? The President is a year behind in reappointing members another advisory group, the President's Cancer Panel. . . . **NEW NAME** of NCI's Div. of Cancer Biology & Diagnosis reflects the recent move of the Cancer Centers Program to the division, which is now called the Div. of Cancer Biology, Diagnosis & Centers. . . . **EMIL FREIREICH** is working in the NCI director's office on an intergovernmental personnel assignment from M.D. Anderson Cancer Center until the end of June. He will assist on special projects. . . . **NCI STAFF** changes: **Lloyd Law,** chief of the Laboratory of Cell Biology in DCBD retired Dec. 30. **Michael Gottesman** has been appointed his successor. **James Phang** has been appointed chief of the Laboratory of Nutritional & Molecular Regulation, within the Cancer Prevention Research Program of the Div. of Cancer Prevention & Control. **Faina Shtern** was appointed chief of the Diagnostic Imaging Research Branch in the Div. of Cancer Treatment. **Patricia McCormick**, from the Center for Nursing Research, was appointed program director of the Cancer Centers Branch. The branch chief position is still open, an appointment is expected by mid-March. **Donald Henson**, of DCPC's Early Detection Branch, has been elected chairman of the American Joint Committee on Cancer. . . . **NIH DIRECTOR'S** Award was given to Barney Lepovetsky and Dorothy Grant of NCI's Office of Technology Development.

Panel Asks NCAB To Develop Rules For Clinical Alerts

(Continued from page 1)

Cancer Society, scientific journals, and trade and lay press, to discuss the controversy over NCI's issuance of two clinical alerts in the past two years and to attempt to set some ground rules for the future communication of research results.

The conference raised the larger issue of the right of patients and the public to know the results of government-sponsored research versus the right of investigators to the research data. The meeting also brought to light more information on the way the decisions were made to issue the first two clinical alerts, one on the adjuvant treatment of node negative breast cancer in 1988 and the second last October on the combination 5-FU/levamisole for the adjuvant treatment of Dukes C colon cancer.

Ultimate Responsibility To Patients

Conference participants struggled with questions such as, When is an alert necessary and who decides to issue one? Should that decision be made in public? For what types of studies should an alert be issued? and How is the information to be disseminated?

While some within NCI argued that the institute has a responsibility to inform the public about major research findings when they become known, without waiting for publication in scientific journals, others did not agree with that position.

"I think we have to start with the assumption that our ultimate responsibility is to patients." said Div. of Cancer Treatment Director Bruce Chabner. "It's not to publications, it's not to IRBs, it's not to statisticians or investigators or people who want to win prizes, it's the patients. It wouldn't really bother me in the long run to see the right to publish something compromised by the fact that the public is made aware of a very important finding and that it saved lives. But how does one determine at what point the rights of the investigator to hold on to the data should be compromised by the need to make that information public?"

However, there was disagreement over, as Robert Wittes, senior vice president for cancer research of Bristol-Myers Squibb Co., said, "When do you know (the results), and what do you do about it?"

Michael Friedman, associate director of NCI's Cancer Therapy Evaluation Program, pointed out that there is no formal bureaucratic structure to deal with those questions. There is no separate, non-NCI, non-investigator body to review data before dissemination, there is no formal agreement with a professional organization to distribute the information, and there is no uniform agreement with journal editors to release data after acceptance of a paper but prior to publication.

Vincent DeVita, physician in chief at Memorial Sloan-Kettering Cancer Center and former NCI director, argued that the NCAB is the proper forum for discussing clinical alerts, but that any discussion of whether to issue an alert should be conducted in an open meeting. He noted that some data from the levamisole study was discussed at a closed NCAB meeting early last year. (**The Cancer Letter**, June 9, 1989). "If you decide not to do something, then the decision should be made in public so that people have a chance to hear why," he said.

The federal Committee Practices Act allows closed meetings in only two circumstances, for discussion of the President's budget before it is released and discussion of the qualifications of individual grantees, not data, DeVita said.

Friedman and Chabner argued against making the decision in an open meeting, since that would release the information whether or not an alert is issued.

"The issue is when do we have enough confidence in something so we can have an impact on the public?" Friedman said.

"But you have to discuss it in public," DeVita insisted. When the breast cancer data were made available, "we didn't say we couldn't release that data, but we said we could discuss it with the NCAB, and we did discuss it in a general way: Is this enough for us to inform the public? The NCAB said, we concur with informing the public.

"The clinical alert was not a method of informing the public, it was a method of warning the doctors that we were going to inform the public. I think the purpose of it has been confused," DeVita said.

Chabner said the investigator's right to his data, in

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this case, Charles Moertel of the Mayo Clinic, is what led to the closed session in the levamisole alert. "I think the investigator's right to his data should be infringed only when you have made the determination that the data is conclusive. There are dangers of carrying out the debate openly. If you say the government has a right to an investigator's data at any point and can disclose it and talk about it, then any investigator's data is liable to public disclosure."

Wittes suggested that data safety and monitoring committees should be the forum for releasing results, but others were opposed to that idea. "Those boards tell us when a study has reached certain milestones," Chabner said. "They don't tell us whether that's the right therapy for a patient with a disease. There are often other studies that have conflicting information or may even supersede that study. We need a broader cross-section of the nation's medical expertise to lend that opinion."

Chabner said the NCAB may not have "the necessary expertise in terms of clinical trials. Certain members on the board do, but many of the members have no real experience or understanding of the process of doing clinical trials or interpreting data. I think they should be consulted, but I'm not sure they should have the final advisory role. I think what's needed is a more expert group in clinical trials."

Whose Data Is It?

NCAB member Erwin Bettinghaus questioned Chabner's assumption that the data belongs to the investigator. "The basic data in most cases is the patient's record," he said.

Charles Coltman, director of the Southwest Oncology Group, cited SWOG policy from a contract with a biotechnology firm: "The sponsor recognizes that the data generated in sponsored clinical trials are the property of the Southwest Oncology Group."

"This clearly defines the relationship between the sponsor and the investigator," Coltman said.

Coltman argued that NCI cannot release research findings without the principal investigator's consent, because cooperative groups are awarded funds as a cooperative agreement. "This is an assistance mechanism for support of clinical trials which requires cooperation between the awardee and NCI," Coltman said. A paragraph of the cooperative agreement states that NCI will have access to all data "although they remain the property of the awardee institution," he said.

He also said it would be inappropriate for NCI to ask for changes in protocols based on interim results. "Only data monitoring committees have access to response, relapse or survival data. Only the DMC has a right to recommend changes in the clinical protocol or early stopping of a clinical protocol. NCI has a representative on each DMC. Our policy is to do interim analyses according to carefully laid out guidelines which preserve statistical error rates. If an extreme result appears in an interim analysis, early stopping rules will be applied. It then becomes the DMC's and group's responsibility to disseminate results quickly.

"Bypassing the peer review process has the potential for harm, since error in data presentation and interpretation are often found during this process," Coltman said. "What should be criteria for speedy review? Disease free survival does not always translate into survival benefit.

"The criteria for rapid review should be limited to those trials demonstrating a survival advantage upon final analysis. It should be the responsibility of the publishing industry to expedite peer review and early publication."

Clinical alerts should be disseminated to physicians on the NCI mailing list "to bring the publication to the notice of practicing community oncologists," Coltman said.

Bernard Fisher, chairman of the National Surgical Adjuvant Breast & Bowel Project, said that a "major unethical thing to do" is to report data and continue a trial. "A trial needs to be concluded before you disclose what happened. Concluding a trial relates to stopping rules which are established a priori. We establish how many patients it will take to get what kinds of results. Many times we stop a trial when we have reached those endpoints, but we don't have the data yet because there are not enough events. On the other hand if you stop a trial and analyze the data, there's no reason for not disclosing the data. Yes, you want mature data, 10 or 15 years or whatever, but I don't think that is realistic in today's world."

When the data relating to the breast cancer clinical alert became available, he said, the investigators were notified before the information was made public, and the investigators informed the patients. Only three patients decided to go off the control arm of the study.

Fisher reviewed the time it took from submission to publication of 14 papers written by NSABP investigators from 1985 to 1989. The journals involved were the "New England Journal," "Journal of the American Medical Association," "Journal of Clinical Oncology," "JNCI," "Lancet," and "Annals of Internal Medicine."

The average time from submission to first reply was four months. From the first reply to resubmission,

after investigators made the corrections requested, was only two to three weeks. The average time from resubmission to acceptance was two weeks. The average time from acceptance to publication was three months.

All together, the average time from submission of a paper to its publication was eight to nine months, and the time ranged from five to 11 months.

It took seven months to receive a reply to one paper that was sent to a journal. It came back with criticisms, which were answered in two weeks, Fisher said. The whole process to publish that paper took 13 months.

The papers that related to the breast cancer clinical alert were kept in peer review for five months after the alert was issued, then it took another four to five months for publication.

"Obviously, there is a need for more rapid publication of articles of significance," Fisher said.

Fisher argued that there is little difference between review of an article by a journal and peer review of an abstract for presentation at a scientific meeting. "The NCI update was peer reviewed within NCI, so what's wrong with that?" he asked.

"Why might people be unhappy about alerts? The commonest excuse that is given is that clinicians don't have time to see the full data set. I find most of the people I know read the abstracts of the papers, not the data set," Fisher said. The problem occurs, he said, when the press asks experts around the country for comments when a major finding is published, and those experts have not read the paper. "And then they make knee jerk comments which get in the press and this creates some confusion," he said.

Fisher said he was "convinced" that the editorials that accompany papers in most journals influence the clinician more than the paper itself.

Marvin Zelen, professor of biostatistics at Harvard, suggested that NCI use the "Journal of the National Cancer Institute" for "fast track" publication of important research. Clinical alerts, or updates, could be sent out at the same time as the publication.

'Shrill Voices'

Moertel said he agreed to the clinical update on levamisole when in became clear, last September, that the trial had reached the previously agreed upon stopping point. He opposed doing an update any earlier, he said.

"If we abandon scientific principles and yield to the loud and sometimes very shrill voices of the moment, I think we offer precious little to our cancer and AIDS patients today and a disservice to our patients of tomorrow," Moertel said.

Moertel showed data from several trials that demonstrated large survival improvements upon interim analysis, but later turned out not to have a survival advantage. "Many randomized controlled studies have had serious quality problems with 10, 15, 20 percent or more patients lost to analysis. With the raft of studies taking place today, it's inevitable that some studies will come out positive just by chance alone," he said.

"When I presented the interim analysis of the 5-FU/levamisole study a year ago, there was a large amount of unreported data. In one of the participating groups, over 30 percent of their patient reports were late. Biostatistical rules (related to early stopping of a study) should be incorporated into every protocol before the fact, and then these rules should be followed."

Saul Rosenberg, Stanford Univ., was one of a few who argued there is no place for clinical alerts. "I do not accept that NCI has the mission or the responsibility to protect the public from morbidity or deaths from cancer," he said. "There is no justification for bypassing the time honored system of peer review and publication. There just aren't the advances in cancer that justify that."

He said NCI should "back off" from clinical alerts and not pressure journals to review papers quickly. "It's the time itself that protects" from erroneous data, he said.

DeVita argued that Rosenberg's position has led to the uneven dissemination of information. Those on the inside know about the results and can better serve their patients or family members, while those on the outside cannot. "As (NCI Deputy Director) Maryann Roper said, it amounts to insider trading," DeVita said. Roper made the comment last year at a congressional "summit" on mammography (**The Cancer Letter,** Sept. 29, 1989).

DeVita suggested setting up a fast track to review trials that could be identified in advance, such as large, multicenter studies.

Proposed 'Ground Rules'

Most of the participants agreed that NCI's second clinical update, on levamisole, was more successful than the first alert on breast cancer, mainly because NCI sought input from and sent the update out to a wider range of interested parties, especially surgeons.

The participants also agreed that the choice of the word "update," used for the levamisole alert, was a better term than the word "alert." They suggested NCI abandon the word "alert" because it sounds as if the institute were attempting to mandate a change in standard medical practice. "They do come down like

edicts," said George Blumenschein, of the Arlington (TX) Cancer Center.

Zelen, who said he was not in favor of alerts, but acknowledged the "the clinical facts of life," proposed the following "ground rules" for issuing clinical updates that the conference participants agreed to pass on to the NCAB:

▸The investigator should initiate discussion about whether to issue an update.

▸The research results should have the potential to affect a large number of patients between the time the update is issued and the time of publication.

▸There should be an understanding that NCI will try to arrange expedited peer review of the data, based on one or more scientific papers.

▸If the outcome of the peer review process is positive, NCI and the investigators will write a clinical update.

▸Before the update is released, all patients and physicians involved in the studies should be notified in advance of the update.

While at the end of the meeting there was still disagreement over many major points, "there was more convergence of views that I thought possible," said NCAB Chairman David Korn.

He said the NCAB will discuss the issue at its next meeting, in May.

Next week: DeVita asks, "Why weren't the levamisole results released earlier?" Moertel, Friedman, Chabner and others provide more details on the deliberations to release the levamisole update.

Report On Burton's IAT Due In June; NCI Could Be More Open, OTA Says

The Office of Technology Assessment is scheduled to release a report in June on unconventional cancer treatments that will examine Immuno-augmentative Therapy as a "case study" of an unproven treatment.

Roger Herdman, assistant director of the Health & Life Sciences Div. of OTA, appeared before the National Cancer Advisory Board last week to inform the board about the upcoming study. Immuno-augmentative Therapy, or IAT, was developed by Lawrence Burton, a zoologist by training, who founded a clinic in the Bahamas to offer the therapy to patients willing to pay a reported $10,000 per treatment cycle for the unproven therapy.

The major controversy surrounding the clinic is the efficacy of the therapy, involving blood products. It has not been formally evaluated nor have any clinical results been published in a peer reviewed journal. Yet Burton's supporters include many members of Congress. Rep. Gary Ackerman (D-NY) has taken a leading role in the effort, Herdman said.

The OTA study was requested by Rep. John Dingell (D-MI), chairman of the House Committee on Energy & Commerce. Another 37 members of the House and three members of the Senate requested that OTA examine the evidence of the efficacy of IAT and develop a protocol to evaluate IAT. The study was begun in January 1987.

Herdman riled NCI Director Samuel Broder and NCAB members with the suggestion that NCI had not done all it could to offer Burton a chance to test his therapy. Yet, Herdman repeatedly acknowledged that NCI had offered to review Burton's best cases, in which tumor regression can be documented, and for which tissue diagnosis, good records and follow up, x-rays, scans and other data are available.

On paper, OTA has taken the same position as NCI in the matter. In a letter describing OTA's position, Herdman wrote that OTA agrees with NCI that an assessment should begin with a best case review. In addition, he wrote, "in order to enable consideration of federal support for an evaluation, Dr. Burton is obliged to submit data for a Drug Master File for an IND. In doing so, he is obliged to make a complete disclosure of the preparative process for his treatment materials." The letter noted that Burton and his associates have not been helpful. "Dr. Burton cannot reasonably expect this process to move forward without his personal commitment, engagement and effort."

Broder noted that NCI arranged with a non-government employee to go to Freeport for a consultation, but Burton rebuffed the offer. "The opportunity to review the best cases has been offered," he said.

Yet, Herdman said the effort "hasn't been persuasive on Capitol Hill."

Burton's clinic was closed by the Bahamian government in July 1985 following reports that serum produced there was contaminated with HIV and hepatitis B. The clinic reopened in early 1986 reportedly on the condition that the clinic will screen blood products for hepatitis B and HIV, (**The Cancer Letter,** March 28, 1986).

A 1984 analysis by NCI found that materials submitted by the family of a deceased IAT patient were dilute blood proteins, the major component of which was albumin. None of the materials were electrophoretically pure and all fractions were devoid of the four compounds described by Burton as being essential to activity, according to an article published in the "Journal of the American Medical Assn."

Another analysis found HIV antibodies in eight of 18 products from the clinic. The Centers For Disease Control isolated HIV from one of the samples.

Herdman said OTA had "serious concerns" about the finding of HIV and hepatitis B. However, he said more current reports on the content of the blood products given to Burton's patients or the efficacy of the therapy do not exist.

'Help Them Bring Evidence'

Despite the Burton case, NCI should do more to help those with unproven treatments to prepare data for testing, Herdman said. "We haven't been impressed that NCI has not carried out a study of these treatments. What we're suggesting is that you try to think through whether it's worth paying any attention at all to them, and help them bring some evidence to you. They need help in understanding what data is necessary."

DCT Director Bruce Chabner took exception to Herdman's implication that NCI is closed to unconventional therapies. "We have an extensive natural products branch. The one requirement is that people have to tell us where the product came from and, if it is given to patients, it has to be in a pure form."

"OTA is not suggesting that anyone be injected with an agent that may be unsafe," Herdman replied. "We don't disagree at all. But I have to disagree about how open NCI is. I think there's room for improvement."

NCAB member Helene Brown said she understood that Burton was now accepting AIDS patients. "It's very difficult for us to separate scientific method and some other routine. OTA is not looking to NCI to have two types of scientific methods, is it?"

"We're not suggesting two types of science," Herdman said. "It's very difficult for conventional scientists to look at a treatment like Burton's. My clients (members of Congress) would ask you to take another look at it."

NCAB member John Durant objected to that statement. "The implication is we have some sort of disease we as scientists need to get over, by insisting on certain standards that Congress has formalized in the form of FDA regulations--but I'm not sure I'm sick."

"We don't want to leave the impression that NCI has all the answers," Broder said to Herdman. "We're very happy to be taught and we want people to bring ideas to us. I hope you will help us to identify what we can do to explain our mission." Broder said the appeal of unproven treatments indicate a need to "educate the public that cancer is not an immediate death sentence."

Herdman said the OTA report will be circulated for review and invited the board to submit comments.

NCAB members Erwin Bettinghaus and Dorothy Cantor suggested that NCI write a letter on its efforts to deal with Burton and submit it to OTA as an appendix to the report.

"It strikes me that NCI has gone well beyond what I would have done if a student came to me with this," said Bettinghaus.

FDA Advisors OK Levamisole, Conditional New Tamoxifen Use

The Food & Drug Administration's Oncologic Drugs Advisory Committee has unanimously recommended approval of the new drug application for levamisole in combination with 5-FU for adjuvant treatment of Duke's C colon cancer.

The committee's action was taken at its meeting last week when it also recommended unanimously, but with a number of caveats, approval of tamoxifen for treatment of node negative breast cancer.

In still another action, the committee gave FDA the go-ahead to approve an NDA for idarubicin in treatment of acute nonlymphocytic leukemia. No formal vote was taken on this NDA; instead, the committee agreed with FDA's suggestion that it withhold approval until it could review data presented last week but not included in the application.

The committee's approval of levamisole was based on the strong evidence of its effectiveness with 5-FU which was provided by the North Central Cancer Treatment Group study and the larger confirmatory intergroup study. That evidence had been convincing enough to prompt the investigators and NCI to issue a clinical update last year, and to warrant adding levamisole to the Group C list.

The drug has been available free through the Group C mechanism to physicians for adjuvant treatment of Duke's C colon cancer since last May.

If FDA accepts the committee's recommendation and approves levamisole for marketing as a prescription drug, it will be removed from the Group C list.

FDA approval is not assured, however, although the agency usually follows the committee's advice. FDA staff members indicated they were not convinced that the combination's effectiveness was due to levamisole. They suggested that the benefit could be related to 5-FU alone, and contended that no modern clinical trial had tested it for efficacy as a single agent in the treatment of Duke's C colon cancer following curative resection.

Charles Moertel, NCCTG chairman who headed

both that study and the intergroup trial, presented a long list of studies in which 5-FU was undeniably ineffective as a single agent. But FDA statisticians presented figures which they said held out the possibility that it could be active. They inferred, without overtly insisting, that an additional study should be undertaken testing 5-FU/levamisole and possibly other combinations, with 5-FU alone as one arm.

Moertel presented details from the intergroup analysis for the first time in support of the NDA. That analysis will be published in the "New England Journal" this month.

Janssen Research Foundation is the sponsor of levamisole, which was given the trade name, Ergamisole.

The NDA for tamoxifen was for an additional indication, node negative breast cancer. The hormonal agent, which the sponsor, ICI Pharmaceuticals, has named Nolvadex, had on previous submissions obtained approval for treatment of advanced breast cancer in postmenopausal patients, for use in combinations for treatment of stage 2 breast cancer in postmenopausal patients, as a single agent for treatment of stage 2 breast cancer in postmenopausal patients, and for advanced breast cancer in treatment of premenopausal patients.

Bernard Fisher, chairman of the National Surgical Adjuvant Breast & Bowel Project, presented details of NSABP study B-14, which found that disease free survival can be improved significantly by treating node negative patients with tamoxifen. Michael Baum, King's Hospital and Royal Cancer Hospital, London, described results of the NATO multicenter study in Europe which also found tamoxifen effective in treating node negative patients.

FDA staff pointed out that the NATO study did not include premenopausal patients and therefore could not confirm NSABP's finding of effectiveness in that group; and that NSABP had not yet demonstrated overall survival in pre or postmenopausal patients and thus could not confirm NATO's finding of significant survival.

The committee stopped short of recommending approval of tamoxifen for all node negative breast cancer, suggesting that physicians should have the discretion of prescribing it for various subgroups which appear to be at high risk for recurrence. The committee did say that it should not be given to node negative patients with tumors less than 1 cm; five year survival in that group is more than 95 percent.

Idarubicin, an analog of daunorubicin, was proposed for treatment of ANLL in combination with ara-C by the sponsor, Adria Laboratories. Idarubicin, which Adria has given the trade name, Idamycin, was compared in combination with ara-C against daunorubicin and ara-C. Results for idarubicin were at least as good and perhaps better, investigators reported.

Construction Money In Budget Is All Earmarked For Frederick

The $1,479,000 shown in the President's FY 1991 budget as construction money for NCI is not for extramural grants. Instead, it is intended for renovations and repairs at Frederick Cancer Research Facility.

The only extramural construction money which might be available is the $15 million NIH has this year, earmarked for AIDS facilities. NCI Director Samuel Broder said that he intends "to compete for our share" of the AIDS construction funds.

More followup on the FY 1991 President's budget:

▸The increase of $3.7 million in the $201.8 million research contracts budget is entirely for NCI AIDS activities, as is a large portion of the entire contracts budget. Of the 5.9 percent increase in the intramural research budget, about 3 percent is for cancer activities, the rest for AIDS. Much of it will go for salary increases, very little for growth. The 5.5 percent increase in the research management and support line is for increased NIH overhead.

▸The budget for National Research Service awards remains exactly the same as in 1990, $35,793,000. Broder said that would support about 1,400 trainees.

▸The total NIH budget recommended by the White House is $7.852 billion, up from $7.516 billion this year. That is a 4.5 percent increase.

NCI's total increase amounted to 3.9 percent; of that, 3.6 percent is for cancer, the rest for AIDS. The NIH AIDS budget increased 7 percent, which represents a tapering off of the huge increases seen in the last few years.

The total NIH AIDS research budget for 1991 was recommended at $800,164,000, an increase of $56.6 million.

Six More Reported In Funding Range Of CCOP 3 Recompetition

The priority scores of six more Community Clinical Oncology Programs which are probably in the funding range for "CCOP 3" have been reported to **The Cancer Letter**, bringing to 37 those identified as successful in this recompetition (see last week's issue and the Jan.

26 issue).

NCI had not determined the payline or a funding plan for the program as of last week. Those added to the list of CCOPs that scored better than 232, the payline in the previous recompetition are:

Southeast Cancer Control Consortium CCOP, Winston-Salem, NC, Charles Spurr, PI; Medical Center of Delaware CCOP, Irving Berkowitz, PI; Kalamazoo CCOP, MI, Phillip Stott, PI; Indianapolis CCOP, William Dugan, PI; Marshfield Medical Research Foundation CCOP, Tarit Banerjee, PI; Southern Nevada Cancer Research Foundation CCOP, John Ellerton, PI.

CCOPs in the probable funding range that should be on this list and were not reported in previous issues are invited to call **The Cancer Letter** at 202/543-7665.

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-05254-33
Title: Phase 1 studies of new chemopreventive agents
Deadline: Approximately March 30

The Chemoprevention Branch in NCI's Div. of Cancer Prevention & Control wishes to award master agreement contracts for phase 1 studies of new chemopreventive agents and to perform pharmacokinetic studies during these phase 1 studies.

The objective of these studies is to determine the parameters and characteristics of toxicity in humans, the safely delivered dose and the basic clinical pharmacokinetics of agents emerging from the NCI chemoprevention agent development program so subsequent phase 3 risk reduction trials can be designed. The master agreement holder shall develop and conduct the following studies:

Task 1: Phase 1 studies shall provide the parameters and characteristics of drug toxicity, the safely delivered dose and a recommended phase 2/3 dose. Phase 1 clinical studies with combinations of agents may be performed if agreed upon by the contractor and the project officer.

Task 2: Pharmacokinetic studies shall provide the parameters of drug absorption, blood concentration time profiles, distribution and excretion. Using classical and nonclassical modeling, the pharmacokinetic data shall be used to determine patterns of distribution, excretion, compartmentalization and enterohepatic recirculation, and to include identification as well as distribution and excretion of metabolites.

The master agreement shall certify a holder's qualification to compete for both tasks. For a given agent tested, qualifications to carry out both tasks must exist, although only task 2 may be required. It is estimated that investigators or institutions shall be deemed to be qualified via peer review and thus shall be included in the MA. A maximum of 10 master agreement orders including both tasks, requiring approximately 200 subjects shall be issued annually for studies on specific agents.

The purpose of this acquisition is to qualify additional contractors to an existing pool of master agreement holders. There are currently six qualified contractors in the pool. The period of performance of the master agreement pool runs through July 26, 1993, which would be the expiration date for new MA holders too.

Contracting Officer: Vernon Rainey
RCB Executive Plaza South Rm 635
301/496-8603

RFP NCI-CM-07351-30
Title: Operation of an animal diagnostic laboratory
Deadline: Approximately April 11

The Biological Testing Branch in NCI's Div. of Cancer Treatment is seeking organizations with the capabilities and facilities to monitor the health status on NCI animal production contracts.

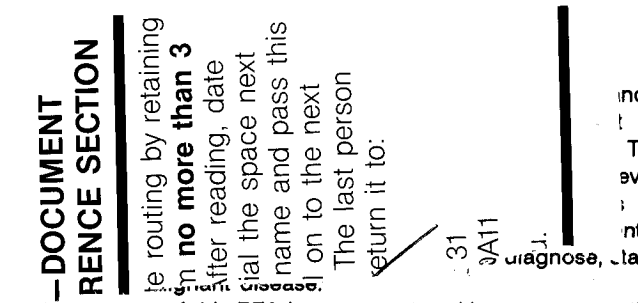
To be considered, each respondent must have existing diagnostic facilities and staff: 1) must be able to provide documentation of current experience in the successful performance of physical examination, 2) viral serology, 3) histopathology and 4) bacterial culturing on laboratory animals.

Approximately 1,000 animals, annually, sent at a rate of 20 per week will be provided to the diagnostic contractor at no cost. It is estimated that approximately 10,000 serological tests will be performed annually. It is anticipated that two contracts will be awarded for this effort at a period of 60 months per contractor.

This RFP is a recompetition of the "Operations of an animal diagnostic laboratory" contracts performed by the Univ. of Miami and the Univ. of Missouri.

Contract specialist: Elsa Carlton
RCB Executive Plaza South Rm 603
301/496-8620

RFAs Available



The purpose of this RFA is to support multicenter cooperative clinical trials to determine the most effective imaging procedures required to stage and monitor head and neck and musculoskeletal carcinomas. The successful applicants will join the ongoing cooperative agreement. This is a reissuance of RFA 88-CA-02. Sufficient numbers of patients including minorities and women must be available and committed to meaningful imaging trials.

Approximately $900,000 in total costs per year for four years will be committed to fund applications in response to this RFA. It is anticipated that six or possibly eight applications can be funded.

Request for copies of the complete RFA should be addressed to Dr. Matti Al-Aish, Acting Chief, Diagnostic Imaging Research Branch, Radiation Research Program, NCI, Executive Plaza North Suite 800, Bethesda, MD 20892.