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NCI Faces Major Cuts On Gramm-Rudman Sequestration; Grants, Centers, Trials Slashed

NCI last week released projected budget figures for fiscal year 1990 based on the continuing resolution, minus the Gramm-Rudman sequester. NCI is operating "as if this is the budget we will have," NCI Director Samuel Broder told the Div. of Cancer Etiology Board of Scientific Counselors last week. "You can speculate about what Congress will do, but for now we must make funding decisions as if this is the budget we will have." Under the continuing resolution, which was extended to Nov. 15, NCI will get $1.652 billion, slightly less than the $1.664 billion

(Continued to page 2)

In Brief

Ruddon To Head Eppley Institute; Shapiro Elected ACR President; ACR Medalists Named

RAYMOND RUDDON, chairman of the pharmacology department at the Univ. of Michigan, has been named director of the Eppley Institute for Research in Cancer & Allied Diseases at Univ. of Nebraska Medical Center in Omaha. He has been a faculty member at Michigan for 20 years. Ruddon succeeds Edward Bresnick, who is now deputy director and chairman of pharmacology at Norris Cotton Cancer Center. . . . **JEROME SHAPIRO,** of Boston Univ., has been elected president of the American College of Radiology. Other new officers for 1990-91: Vice president, **Frank Hussey,** Lutheran General Hospital, Park Ridge, IL; chairman, **Lee Rogers,** Northwestern Univ.; vice chairman, **James Moorefield,** Sacramento Radiology Medical Group; secretary-treasurer, **Carl Bogardus,** Univ. of Oklahoma; council speaker, **Milton Gallant,** General Hospital Center, Passaic, NJ; council vice speaker, **Abner Landry,** Mercy Hospital, New Orleans. . . . **GOLD MEDAL** winners named by ACR for distinguished service are: **Kenneth Krabbenhoft,** of Birmingham, MI, secretary and executive director of the American Board of Radiology; **Jerome Wiot,** chairman of radiology at Univ. of Cincinnati Medical Center; and **Gerald Dodd,** head of diagnostic imaging at M.D. Anderson. . . . **ERNST WYNDER,** president and founder of the American Health Foundation, has received the first Nathan Pritiken Pioneer Award by the foundation. . . . **WILLIAM PLUNKETT,** professor medicine in the Dept. of Medical Oncology at Univ. of Texas M.D. Anderson, has been appointed to the Hubert and Olive Stringer Professorship in Medical Oncology. He is recognized for research in adult leukemia. . . . **DAVID GERSHENSON** has been appointed associate vice president for patient care at M.D. Anderson. Gershenson, a gynecology professor, will be responsible for overseeing a broad range of clinical activities, from referral through outpatient care.

Grants, Centers, Clinical Trials Slashed Under Gramm-Rudman Cut

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agreed on by the House and Senate conference committee. However, the Gramm-Rudman sequestration will cut $86.4 million from that figure, leaving a budget of $1.566 billion.

If Congress and the President work out an overall budget for the government this year, the sequestration will not be necessary.

The House last week failed to override President Bush's veto of the Labor-HHS-Education appropriations bill over federal funding of certain abortions. The veto, however, probably will not effect the dollar amount NCI will get. A new bill probably will include the same budget levels.

If Congress and the President cannot work out an overall budget for the government, the Gramm-Rudman cut "will have a great impact on every element of NCI," Broder said.

Because the limited funding might cause new investigators to lose out on some awards, the institute will attempt to develop "some type of policy to give some break to new RO1 applicants," Broder said. He also said NCI is "looking at the entire grants portfolio" to see if policy changes are necessary in light of the budget.

Under the current budget situation--the continuing resolution minus the Gramm-Rudman cut, research project grants (R01s, PO1s) will receive $724.5 million. That figure is up very slightly from $723 million in FY 1989.

Cancer centers will receive $96 million, down from $101 million in 1989.

Cooperative clinical research, $56.6 million, down from $60 million in 1989. Research career program, $7.9 million, up from $7.6 million in 1989. Cancer education, $1.9 million, down from $2.9 million in 1989. Other grants, $77 million, down from $82.7 million in 1989.

National Research Service Awards will receive $34.2 million under the continuing resolution, up slightly from $33 million in 1989.

Research and development contracts, $193.9 million, up from $187.3 million in 1989. Intramural research, $301 million, up from $294 million in 1989. Research management and support, $68.4 million, down from $72 million in 1989.

Cancer prevention and control, $70.4 million, down from $74 million in 1989.

The dismal budget situation generated some discussion at the DCE Board meeting. Board member Anna Barker asked DCE Director Richard Adamson, "How do you operate during this time?"

Equipment purchases have been restricted, but no staff cuts or hiring freezes have been necessary, Adamson said.

However, RFAs are "on hold until we see what the budget is, because there is such uncertainty," Adamson said.

The NCI Executive Committee currently is developing a percentile for funding of the first round of grant awards for FY 1990, Adamson said. Applications that miss out in the first round could be funded later if money becomes available, and the percentile also could be adjusted.

Continuing grants that are reaching the end of their award periods might be kept afloat for two to three months so there is no gap in funding, Adamson said.

Board member Lawrence Fischer said he thought is was not right to advertise RFAs and then withhold the funding for an undetermined amount of time.

"Those people (grant applicants) are welcome to exercise their free speech rights and send a message to the people who haven't given us a budget," Adamson said.

Other board members were concerned about keeping young investigators, both intramural and extramural, interested in cancer research during a difficult fiscal year.

Adamson said that beyond the FIRST Award mechanism for new investigators, the institute tries to address the problem through reviews by laboratory chiefs and division directors. It is also a subject that concerns the Executive Committee.

"We have to make sure we encourage new awardees," Adamson said. On the intramural side, he said, "I will make sure we don't lose young investigators because of the funding situation."

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DCE Board OKs New Virus Studies To Total $2.5 Million In First Year

Three new grant award programs to stimulate laboratory research in tumor viruses, including hepatocellular carcinoma and human T-cell viruses, received concept approval from the Div. of Cancer Etiology Board of Scientific Counselors at its meeting last week.

The board set aside a total of $2.5 million for first year funding for the programs, which will continue for five years.

The board approved concepts for recompetition of a contract for a biological materials repository, support services for epidemiologic studies and a study of radon exposure in Missouri.

The board also approved concepts for continuation of an interagency agreement with the Centers for Disease Control for a study of polybrominated biphenyls contamination of farms in Michigan, an interagency agreement with the Smithsonian Institution for operation of a tumor registry in lower animals, a cooperative agreement with the International Agency for Research on Cancer for publication of monographs on carcinogenic risks, and a new noncompetitive grant to the Karolinska Institute in Sweden for a study of thyroid cancer following exposure to I-131.

Concept statements and board discussion follow:

Viral oncogenesis and pathogenesis of hepatocellular carcinoma. Proposed first year funding of $1 million, five year grants.

The current emphasis of extramural research on human primary hepatocellular carcinoma (PHC) supported by the Biological Carcinogenesis Branch has centered on determining the role of hepatitis B virus in PHC etiology. PHC is responsible for 500,000 to 1 million deaths per year worldwide. Chronic carriage of HBV is involved in 75 to 90 percent of the cases of PHC. The likelihood that 200 to 300 million chronic HBV carriers worldwide will, without some novel prevention or intervention strategy, eventually die of liver cancer, furnishes strong impetus for new studies on etiologic mechanisms, pathogenesis, intervention strategies and prevention activities.

The thrust of this RFA concept is to stimulate research on the human hepatitis viruses associated with liver cancer (hepatitis B virus, non-A, non-B hepatitis virus, or HCV), environmental factors such as dietary aflatoxin and host factors (chromosomal fragility, immune response) to determine mechanisms involved in establishment of chronic infection, cell transformation and PHC.

Examples of research objectives would include the following: 1) development or use of sensitive and specific assays for blood borne NANBH to determine the possible role of this agent in PHC; 2) determination of the prevalence of HBV strains resistant to currently available vaccines and the role of genetic variation of HBV isolates in this process; 3) definition of the role of the HBV X gene in transformation; 4) systematic studies of co-carcinogenesis in the development of PHC in animal models of human cancer (the woodchuck); 5) determination, in transgenic animals, of the oncogenic potential of specific viral gene products; 6) determination of the possible role of cellular oncogenes or anti-oncogenes in PHC; 7) investigation of the role of chromosomal abnormalities in susceptibility to PHC; and 8) measurement of the host response to individual viral proteins with the goal of delineating the host response to different viral antigens in hepatitis associated sequelae.

Webster Cavanee, a new board member, said, "It's a perfect time for an RFA like this to stimulate research."

The concept was approved unanimously.

New approaches to understanding transformation by SV40 virus, polyomaviruses and adenoviruses. Proposed first year funding $750,000, five year grants.

Simian virus 40, mouse polyomavirus and adenovirus are DNA tumor viruses which are important model systems used in the study of virally induced tumors in susceptible animals and the transformation of cells in culture. The primary cause of these neoplastic events is the introduction into cells of viral transforming genes which encode viral oncoproteins. Unlike the oncogenes of acutely transforming retroviruses, these transforming viral genes do not have cellular homologues.

The transformation mechanism of these viruses is unknown, but recent evidence suggests that their transforming activity is mediated by interactions with cellular proteins. Support for this model comes form the discovery of strong binding interactions between the viral oncoproteins and cellular proto and anti-oncogene products. The first such association to be identified was the complex between middle T-antigen of polyomavirus and the product of the c-src proto-oncogene. More recently, the large T-antigens of SV40 and polyomavirus and the E1A protein of adenovirus were each shown to form complexes with the product of the retinoblastoma tumor suppressor gene.

The goal of this RFA concept is stimulation of research leading to an understanding of SV40, polyomavirus and adenovirus transformation of cells in terms of the cellular processes which are altered by viral oncoproteins. Functional studies of viral oncoprotein or cellular protein complexes will be encouraged.

Studies on the Rb, p53 and c-src interactions with oncoproteins will not be accepted since these associations are currently the subject of intense investigation.

Examples of studies that may be supported are: 1) investigations of the impact of viral oncoprotein or cellular protein complexes on elements of cellular physiology related to transformation such as, but not limited to, second messenger regulation, cell cycle control, transactivation of cellular protein synthesis and alteration of plasma membrane properties; 2) development and application of new approaches to understand the physiological activities of pertinent cellular proteins and second messenger molecules and assessment of the role of these processes in cellular transformation; 3) functional and structural characterization of cellular proteins which bind to viral oncoproteins; 4) development and application of new techniques and reagents to identify and characterize additional cellular proteins which bind to viral oncoproteins.

Janet Butel, who just finished her term on the board, presented a report on a workshop she chaired on retroviruses. The concept grew out of the research needs identified at the workshop. Alan Schreier, the project director, noted that investigators have "shied away" from these studies. "It's an important, but neglected area of research," he said.

The concept was approved unanimously.

Human T-cell lymphotropic viruses in human neoplasia. Proposed first year funding $800,000; five year grants. Approximately four to five awards.

At present, little is known about the viral and host factors involved in HTLV pathogenesis which result in cancer induction vs. those which result in neurotropic damage. An elucidation of the overall pathogenic mechanisms of HTLV is needed. The goals of this RFA concept are to stimulate research on the role of HTLV-1 like viruses in human neoplasia and other diseases with suspected retroviral etiology and the development of animal models to delineate the mechanisms of disease pathogenesis.

Studies will be invited in, but not limited to, the following areas of research: 1) systematic laboratory studies to define the possible retroviral etiology of diseases whose clinical features suggest a retroviral role, including diverse hematologic and solid tissue malignancies; 2) exploration, through laboratory studies, of HTLV-2 disease pathogenesis and its role in human cancer; 3) studies to address the basis for the differing pathogenic potentials of the HTLV isolates, i.e., molecular mechanisms for the leukemogenic vs. neurotropic behavior of the virus, including the comparison of the genomic sequences of HTLV isolates from leukemic patients, intravenous drug abusers and TSP patients, and comparison of virus target cell interactions or HTLV infections which result in neoplasia vs. those that result in neurotropic damage; 4) laboratory studies to determine the role of cofactors (genetic, viral, bacterial) in the triggering of disease expression associated specifically with HTLV-1 infections; 5) identification of host and viral factors responsible for the repressed state of HTLV-1 genome in vivo; 6) development of animal/tissue culture models of human lymphoproliferative and neurologic diseases, including the use of mutant retroviruses with altered pathogenic properties and transgenic mice.

The concept was approved unanimously.

Repository for storage and distribution of biological research resources. Recompetition of a contract held by Microbiological Associates Inc. Total proposed award $1.96 million over five years, proposed first year award $354,350.

The Biological Carcinogenesis Branch is responsible for maintaining a coordinated program of research resources support to meet the needs of extramural investigators funded by the branch. A major component of the resource program is a facility for the centralized storage and distribution of biological reagents. Biological resources are made available to established investigators involved in cancer research.

The successful offeror will operate and maintain the BCB repository facility and provide a centralized location for storage of biological reagents. The contractor will receive, store, aliquot as necessary and inventory the reagents shipped to the BCB repository by other NCI contractors. The contractor will receive requests for reagents, ship materials, provide appropriate characterization data with each shipment and collect charges for materials and shipping and handling costs as directed by the NCI project officer.

The repository currently has a variety of tumor virus reagents available, including viruses from 65 different virus culture propagation combinations, antisera from over 200 different species, antigen, treatment combinations, and more than 230 monoclonal antibodies and associated reagents from avian and mammalian retroviruses. In addition, over 17,000 human sera specimens from donors with malignant and nonmalignant diseases, family members and normal individuals.

The contract will operate as part of the branch resources payback system, whereby the recipient pays a reasonable charge for the materials, plus the cost of shipping and handling. The contractor will maintain a computerized inventory system to provide a monthly status report on shipping and receiving activity and on current inventory stocks. The system will also provide fiscal information on invoices and receipts.

Wilma Verrato, the project officer for the repository, said operating costs will decrease when some unused materials are removed, including about 700 sera from baboons in an old U.S.-USSR primate study whose principal investigator was Soviet researcher Boris Lapin. The repository has not received any requests for the baboon sera in five years, Verrato said. Board member Myron Essex noted that records from the study seemed too inconsistent for investigators to rely on. The board concurred in shipping the materials, which fill one freezer, back to Lapin.

The concept was approved unanimously.

Case-control study of residential exposure to radon and lung cancer among nonsmoking women in Missouri. Proposed first year award, $320,340 for the competitive portion of this contract; two years. Current contractor is Survey Research Associates. The two noncompetitive portions of the contract are held by the U.S. Dept. of Energy.

The objective of this concept is to enlarge the current study of residential exposure to radon and lung cancer from 280 to 600 nonsmoking female lung cancer cases and from 560 to 1,400 population based controls. One reason for expanding the survey is that the level of radon in the homes is lower than anticipated. A larger sample size is required to compensate for the loss of statistical power. The current population based lung cancer study entered the field in January 1988. With a high level of residential stability in Missouri and a response rate of at least 85 percent, it will be possible to detect a relative risk of 1.5 with 80 percent power.

The contractor will provide additional support necessary to 1) collect radon dosimeters during the last two years of the current study; 2) supplement with more personnel the case ascertainment system of the Missouri Dept. of Health to make it more rapid; and 3) interview subjects and measure radon levels in all homes occupies during the past 30 years for 1,160 new study subjects. Radon measurements will be made in Missouri homes in which a study subject lived for at least six months during the past 30 years. Up to six homes per person will be sampled. Two alpha track etch detectors will be placed in each of the selected homes for one year. Plastic film detectors would be places on household glass in 100 homes. Cases will have their histologic material reviewed to validate the diagnosis of lung cancer by cell type and to exclude misclassification of metastatic disease.

Board member David Schottenfeld said the study is "well designed and includes a lot of features to address problems we've had in the past on long term dose studies." Project officer John Boice noted that EPA risk assessments of radon exposure were based on underground miners and translated into risks for homeowners, based on estimates of radon levels in homes which are probably too high.

The concept was approved unanimously.

Support services for epidemiologic studies. Recompetition of a contract held by Westat Inc., $8.5 million over five years, proposed first year award $1.57 million.

The objective of this concept is to provide services in support of field investigations conducted by the Environmental

Epidemiology Branch. These services include maintenance of coordination and liaison with those whose cooperation is needed, forms development, study subject selection, training of field personnel, supervision and management of field operations, interviewing/record abstraction, biologic specimen collection and processing, computerization and editing of data collected and quality control activities. The services would be provided for those investigations continuing from the current procurement as well as new investigations initiated over the next five years. The procurement will provide for flexibility such that priorities for the conduct of investigations can be altered quickly to ensure that high priority or emergent problems can be addressed in a timely manner.

The principal activities can be classified as follows: 1) liaison, whereby the contractor assists in the coordination of multicenter studies and helps facilitate cooperation between NCI and its collaborators; 2) development of study materials, including questionnaires, abstract sheets, coding forms, manuals of field procedures and other documents; 3) identification of study subjects, including location of cancer patients and their relatives, selection of controls through such methods as random digit dialing and acquisition of appropriate study population rosters or files; 4) training of interviewers, abstractors and other field personnel; 5) field supervision and management; 6) interviewing of study subjects; 7) abstracting and coding relevant medical and other records; 8) obtaining biologic specimens, appropriately processing them and providing for laboratory tests on them by designated laboratories; 9) data reduction and processing, including editing and preparing information in a format suitable for computer analysis; and 10) quality control and standardization.

Robert Hoover, one of three project officers for support services contract, noted that the support services funding for the project is about one third less than in the past because the biostatistics portion of the Epidemiology & Biostatistics Program now has its own support contract.

"The quality of work in this program is always high," board chairman Hilary Koprowski said when a question was asked about quality control.

The concept was approved unanimously.

Blue Cross Envoy, Broder Skirmish On Group C Drug Reimbursement

A representative of the Blue Cross and Blue Shield Assn. and NCI Director Samuel Broder sharply disagreed last week over insurance coverage for NCI's Group C cancer drugs.

The confrontation took place at a meeting of the National Committee to Review Current Procedures for Approval of New Drugs for Cancer and AIDS.

The Blue Cross and Blue Shield Assn. is a national coordinating agency for the 73 autonomous Blue Cross and Blue Shield plans, which provides support services, including technology assessment and coverage information. Plans make their own coverage determinations.

The association currently recommends that its member plans should not pay for drugs that have not been approved by FDA for marketing, including Treatment Investigational New Drugs and NCI Group C drugs, according to David Tennenbaum, a representative from the association.

"To be considered eligible for coverage, there must be conclusive scientific evidence that use of a technology improves health outcomes, such as length of life, ability to function and quality of life. We wish to emphasize that the scientific evidence must be conclusive," he said.

"Treatment INDs and NCI Group C drugs are considered to be investigational because their efficacy has not been demonstrated sufficiently to warrant full FDA approval to market," Tennenbaum said. "Coverage of Treatment INDs and Group C drugs would be inconsistent with our principle of coverage for effective treatment."

The association is "especially concerned that parameters for the Treatment IND designation are shifting and seem to be a moving target," he said. "The regulations describe Treatment INDs as a bridge between the completion of phase 2 studies and the point of marketing approval. Yet ddI was recently given Treatment IND status on the basis of small phase 1 studies. The new, evolving concept of the parallel track and its relationship to the Treatment IND raises additional questions from a coverage perspective."

"Proposed coverage for Treatment INDs brings to the forefront the broader issue of coverage for all investigational technologies, drugs, treatments, procedures and devices."

Broder told Tennenbaum that NCI "takes strong exception to the idea that Group C is a vague regulatory mechanism." He noted that FDA's decision last May to place levamisole in combination with 5-FU for the treatment of colon cancer on the Group C list was based on a one third increase in overall survival demonstrated in two major randomized trials.

"You can't get any better than that," Broder said.

"We accept your argument and say that Group C and Treatment IND are in the same category (thus not eligible for coverage)," Tennebaum repeated.

"We strongly object to your statement, strongly and vigorously," Broder said. "There is no way I can say how strongly we object to that.... There's no scientific basis for that decision. This is an arbitrary decision."

"We are constantly faced with the dilemma of promising technology," Tennenbaum said. "I don't think we are insensitive. I don't think we are doing this solely on the basis of costs. You cannot expect the insurance industry to pay for all investigational costs."

Committee Chairman Louis Lasagna noted that,

"Blue Cross is tougher" than the Health Care Financing Administration, in that HCFA policy is to reimburse for Group C drugs.

Board member Peter Hutt suggested that there may be "confusion" about the Treatment IND and Group C. "These are extraordinarily narrow categories out of a much larger pool. There may be 200 to 300 Compassionate INDs and less than 20 Treatment INDs," Hutt said. "What FDA has done is provide you with a real definition of what you should pay for. I urge you to take another look at Treatment IND and Group C."

Hutt also argued that FDA approval "is never based on 'conclusive scientific evidence.' It is based statutorily on 'substantial' evidence."

Tennenbaum outlined the association's other recommendations on reimbursement issues.

Off label drug use: The association recently completed a review of the off label drug use issue. Off label indications should not be automatically excluded. "Off label drug uses will be evaluated to determine whether health outcome is improved," Tennenbaum said. Evidence for the evaluation will come from studies accepted for publication in peer reviewed journals and "possibly" from the three major drug compendia.

"We believe that our recommendation will meet many of the concerns of the oncology community over payment for cancer protocols," he said. "We are aware that combination chemotherapy with certain off label uses and off label uses of agents such as interferon have been questioned by insurers. Once these drugs are evaluated, most coverage problems will be resolved."

Clinical trials: "The plans contribute substantially to clinical trials through routine reimbursement. In most cases, investigational interventions are used in combination with noninvestigational services and are therefore reimbursed."

A survey conducted by the association found that BC/BS plans are paying most of the patient care costs associated with clinical trials, Tennenbaum said. Of the plans responding to the survey, 86 percent cover hospital services, 91 percent cover physician services, and 77 percent cover diagnostic studies for hospitalized patients receiving investigational therapy "if the primary reason for admission is to receive necessary medical care." Most of the plans responding to the survey also cover treatment of complications resulting from investigational treatment.

"We realize that insurance does not cover all the patient care costs associated with clinical trials," Tennenbaum said. "Nor can we expect insurance to pay all these costs. Ten years ago, NCI paid these patient care costs. As funds for research diminished, these costs were shifted to the private sector. But just as it is not realistic to expect that the government can assume the total burden, it is also not realistic to expect that insurers can assume the total burden."

However, Tennenbaum said, the Blues are "responsive" to the needs of desperately ill patients. "On a local basis, plans have developed mechanisms consistent with their contractual responsibilities, that provide access to promising investigational treatments."

One such mechanism is "case management," which permits coverage to be tailored to the individual needs of seriously ill patients. Other "innovative programs permit access to the most promising investigative treatments offered at the leading institutions in the plan's locality."

AIDS patients have gotten AZT and aerosolized pentamidine through case management while the drugs were still under Treatment IND, he said.

"Plans will approve promising investigational cancer treatments at specific major cancer treatment centers in their service area."

Members of the committee (commonly called the Lasagna committee after its chairman) also objected to the policy on investigational drugs and questioned the fairness of a health insurance system in which local coverage decisions can vary around the country.

"I would say this is a cost related issue," board member Samuel Hellman said. "I understand the Blues are under great pressure to hold down costs. It's better to admit that you are in a price bind and not to suggest that quality is the issue."

"We are truly concerned that we want to pay for things that work," Tennenbaum said.

Hutt said he was concerned that local decisions by the Blues could mean that "a drug that might be effective in San Francisco is ineffective in Toledo. That doesn't seem to be logical or fair."

Tennenbaum replied, "We are a decentralized system." Later, under more pressure from committee members, Tennenbaum said, "You will never get payers to give an across the board payment for all investigational treatment."

"This is really regressive," board member Thomas Merigan said. "Payments may be made in one state and not another. We need a national decision."

In September, the committee released a statement urging that Medicare cover drug and clinical care costs for investigational drugs received by persons enrolled in cancer and AIDS clinical trials (**The Cancer Letter**, Sept. 29, 1989).

The committee also advised that, "there is essentially no difference" between the Compassionate

IND or Treatment IND and NCI's Group C investigational drugs. "To treat these two classes differently is inconsistent and indefensible on any grounds. Both should be covered, along with the clinical care costs for drug recipients."

The committee also recommended reimbursement for off label use of approved drugs, and said that coverage should rely primarily on the medical compendia. A national commission should be set up to advise HHS and third party insurers on currently accepted medical technologies, the committee said.

Tennenbaum said the association would welcome the creation of a national commission to review reimbursement.

Other third party payers also would support the commission, said David Plocher, vice president for medical services of the Prudential Insurance Co. of America. Plocher addressed the committee on behalf of the Health Insurance Assn. of America.

HIAA established the following voluntary guidelines for its 320 member companies:

Off label use: Insurers should consider initially the three compendia. (American Hospital Formulary Service Drug Information, American Medical Assn. Drug Evaluations and U.S. Pharmacopeia Drug Information.) If a determination cannot be made, a literature search should be conducted.

Investigational drugs: Treatment INDs and Group C drugs should not be considered ineligible for coverage on the grounds that they are experimental. Each agent should be evaluated to determine its demonstrated benefit.

Coverage of patient care costs depends on the treatment, the guidelines said.

Modifying the drug regimen with an experimental drug: When an unapproved drug is used in combination with two or three other drugs, insurers should consider coverage for the hospital stay and the regimen, but exclude payment for the unapproved drug.

Monotherapy with an unapproved drug: Hospital expenses should be ineligible for coverage, unless the patient's severity of illness, even without the drug treatment, would otherwise require hospitalization. the unapproved drug should be ineligible for coverage.

HIAA also recommended that FDA be encouraged to continue expediting its approval process for Treatment INDS, but "without compromising standards for safety and efficacy."

Roy Schwarz of the American Medical Assn. told the committee that AMA "supports every word in your statement" released in September.

Schwarz also said AMA is concerned about the recent decision of the Blue Cross and Blue Shield Assn. to change the term "investigational" in its contracts to "not eligible" (**Cancer Economics**, October 1989).

Lee Mortenson, executive director of the Assn. of Community Cancer Centers, told the committee that a survey of ACCC members found that physicians are spending more time trying to obtain reimbursement than they were three years ago.

Sixty percent said they were experiencing greater difficulty in the last 12 months obtaining reimbursement for previously reimbursed cancer therapies, while 25 percent said they were having some difficulty. Another 15 percent said they have had no difficulty.

Asked what reasons insurers were citing for denying claims, 66 percent said the drug was not indicated on the FDA label, 43 percent said the chemotherapy was experimental, and 23 percent said claims were denied because the drug was given in combination.

The survey asked physicians to provide examples of the types of denials they were receiving. Among them were: leucovorin and 5-FU, infusion therapy, interferon, pumps, bone marrow transplants, vincristine in breast cancer, MOPP and a range of other "everyday drugs with everyday indications," Mortenson said.

"A larger percentage of the denials are for drugs which are on the FDA label for an indication," he said.

Physicians are spending on the average more than four hours a week trying to get coverage for patients on denied claims, and all together, more than 23 staff hours per week are being spent on denied claims, the survey found.

Mortenson suggested that the President could recommend use of the three medical compendia for federally sponsored HMOs, and health plans for military and federal employees. "This would be an important example," he said.

The next meeting of the Lasagna committee is Nov. 9. The December 7 meeting of the committee, which was to be closed, now is open in order to hear more testimony. The committee expects to submit a report to the President's Cancer Panel early next year.

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-05605-56
Title: Resource for human esophageal tissue and cells from donors with epidemiological profiles
Deadline: Approximately Dec. 18

The Laboratory of Human Carcinogenesis in NCI's Div. of Cancer Etiology is recompeting an ongoing project that is currently being performed by the Univ. of Maryland (Baltimore).

NCI has a requirement for a contract collecting normal appearing and neoplastic human esophageal tissue and cells at the time of surgery (cancer and noncancer donors) at immediate autopsy (noncancer donors); and for culturing and storing stocks of epithelial and fibroblastic cells from the esophagus. The offeror must provide approval of the institutional committee for the protection of human subjects; routinely obtain informed donor consent; obtain an epidemiological profile of the donors employing trained interviewers; use proven methods for collecting, culturing and transporting of viable specimens to NIH, within two hours of collection (approximately 40 cases per year); and characterize the functional and pathological status of the tissue by histochemical and immunological methods and by light and electron microscopy.

It is anticipated that cost reimbursement type contract will be awarded for a four year period. NCI shall consider proposals from all responsible sources. However, offerors must demonstrate in their technical proposal their ability to facilitate delivery of viable tissue and cell specimens to NCI in Bethesda within two hours of collection as a mandatory requirement of the RFP. Failure to demonstrate this element will result in the offeror's elimination from further consideration.
Contract Officer: Donna Winters
RCB Executive Plaza South Rm 620
301/496-8611

RFP NCI-CM-07318-41
Title: Clinical data management
Deadline: Dec. 6

The Clinical Oncology Program in NCI's Div. of Cancer Treatment is soliciting proposals from small business organizations for providing data management and data processing support relevant to clinical trials and design for identifying improved cancer therapies. This acquisition is under the direction of the Biostatistics & Data Management Section. The workscope includes the: 1) development and maintenance of computerized clinical databases; 2) retrieval of clinical and laboratory data on patients treated by NCI; and 3) provision of centralized support for operation of a statistical center as well as various routine and ad hoc reporting and retrieval requirements.

This is a recompetition of a project being performed by the Orkland Corp. This is a 100 percent small business set aside.

Prospective offerors should possess the capabilities necessary to: 1) enhance and maintain the Computer Data Registry database management system; 2) abstract data from medical records; 3) maintain various microcomputer databases in each of the branches of COP; 4) maintain databases for the multi-institution studies of the BDMS; 5) respond to reporting and data analysis needs; 6) maintain existing databases; 7) design, develop and operate new data collection systems and develop new retrieval programs; 8) provide comprehensive data management support for the special studies of the Surgery Branch; 9) prepare randomization and registration materials; 10) provide support in the areas of microcomputer programming, system design, development and maintenance, toxicity monitoring activities and comprehensive data management. The potential offeror will be required to meet with NIH personnel in Bethesda and to furnish a courier service between the corporate headquarters and various locations within the NIH facility.

It is anticipated that a cost reimbursement, incrementally funded type contract will be awarded as a result of the RFP for a period of 60 months, beginning approximately Oct. 1, 1990.
Contract Officer: J. Thomas Lewin
RCB Executive Plaza South Rm 603
301/496-8620

RFP NCI-CP-05620-56
Title: In vitro evaluation of chemical candidates for in vivo testing
Deadline: Dec. 21

This notice corrects the previous notice issued by NCI for this RFP under a 100 percent small business set aside for small business concerns with size standards of $3.5 million and standard industrial classification code of 8734. This RFP is reissued under the same project title but with a different small business size standard of 500 employees and standard industrial classification code of 8731. (Text of RFP, which remains unchanged, was published in The Cancer Letter, Oct. 27). All responsible sources meeting these criteria are encouraged to submit a proposal.
Contract Officer: Donna Winters
RCB Executive Plaza South Rm 620
301/496-8611

RFAs Available

RFA 90-CA-01
Title: Cooperative Human Tissue Network
Letter of Intent Receipt Date: Jan. 12
Application Receipt Date: April 25

The Diagnosis Research Program of NCI's Div. of Cancer Biology & Diagnosis invites applications for cooperative agreements from institutions for participation in the Cooperative Human Tissue Network. The network collects and distributes human tumor tissue and normal tissue for research. Basic and developmental studies in many areas of cancer research, including molecular biology, immunology and genetics, have been encouraged by improved access to tissue. NCI plans to expand the network from three institutions to four or five institutions for five years.

The network is not a tissue bank, but responds to investigator requests to meet existing tissue requirements on a current basis. Applicants may plan for limited storage of rare tumors that would otherwise not be available. Special consideration will be given to ensuring access to and nationwide distribution of rare pediatric tumor specimens.

Awards will be made as cooperative agreements, which create an assistance relationship with substantial involvement of NCI staff during the project. Although this project is provided for in the financial plans of NCI, the award of cooperative agreements is contingent on the availability of funds appropriated in fiscal year 1991.

Inclusion of women and minorities is encouraged. If they are excluded, reasons for this exclusion must be included in the application. This RFA is a one time solicitation.

A copy of the complete RFA describing eligibility criteria, the research goals and scope, the cooperative agreement mechanism, the review criteria and application procedures may be obtained from Dr. Roger Aamodt, Program Director for Pathology and Cytology, Diagnosis Program, DCBD, NCI, Executive Plaza South Rm 638, 6120 Executive Blvd., Rockville, MD 20892; phone 301/496-7147.