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"HOP" MAY INCLUDE 100-200 HOSPITALS, FUNDED AT TOTAL OF $10 MILLION A YEAR, SHOULD START IN FY 1982: DEVITA

NCI's new effort to involve community physicians in clinical research has been in a gradually accelerating state of evolution since Director Vincent DeVita suggested last March that a followup to the Community Hospital Oncology Program might be a good vehicle to reach that goal.

The Assn. of Community Cancer Centers endorsed the idea and formed a Clinical Research Committee to pursue it. DeVita, who said at the time he had no clear idea of how the program would shape up,

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In Brief

CONSTRUCTION GRANT APPLICATIONS DUE OCT. 1 FOR FUNDING IN FY 1982; BACKLOG CLEARED OUT

NEW LIFE given to NCI construction grants demands that grant applications be submitted by Oct. 1 or the increased money which probably will be available in the 1982 fiscal year will be spent on something else. The entire backlog of approved, unfunded construction grants was cleared up, possibly with one exception, with the extra $1 million in 1981 the program received (***The Cancer Letter***, May 29). Although an estimated $300 million in construction needs exist, applications stopped flowing in when the money dried up. The message: Get to work on those applications immediately and send them in before Oct. 1. For assistance, call Donald Fox, chief of the Research Facilities Branch, 301-427-8804. . . . **GLORIA HEPPNER** has been appointed acting scientific director of the Michigan Cancer Foundation by Director Michael Brennan. She replaces Marvin Rich, who will leave next month to become director of the American Medical and Cancer Research Center in Denver. Heppner also is deputy associate director for research at the Comprehensive Cancer Center of Metropolitan Detroit. **NOEL ROSE**, chairman of the Dept. of Immunology & Microbiology at Wayne State Univ., was named by Brennan as acting associate director for research of the comprehensive center, filling another position vacated by Rich. . . . **JOHN HIGGINSON** will take a position with Universities Associated for Research & Education in Pathology, in Washington D.C., when he leaves his job for the past 15 years as director of the International Agency for Research on Cancer. He will be responsible for building a collaborative program on environmental health in 15 U.S. universities. . . . **CATHOLIC UNIV.** (Washington D.C.) School of Nursing has initiated a new curriculum in cancer nursing which leads to a master of science in nursing degree. The university is one of only 11 institutions in the country with graduate education in oncology nursing. The program's coordinators are Caroline Bagley and Ann Schreier.

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DEVITA SAYS GROUP C COULD BE CHANGED TO GIVE HOPs EXCLUSIVE DRUGS RIGHTS

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has been discussing it with his staff and others and now is beginning to see some details emerge, as related to the Div. of Centers, Resources & Community Activities Board of Scientific Counselors June 4:

- DeVita referred to the embryo concept as a "Hospital Oncology Program," thus, unintentionally perhaps, assigning it the acronym "HOP"—the logical successor to CHOP and its predecessor, COP (Community Oncology Program). Until someone comes up with a better name, HOP it will be.
- DeVita guessed that HOP would include from 100 to 200 hospitals as the number required to achieve good geographic coverage along with cancer centers, regional cooperative groups, and existing community oncology programs.
- "Do you have a ballpark estimate on the budget that would be required?" Board member Charles Moertel asked. DeVita said he was "willing to guess, and I could be off as much as 30 percent either way. I would estimate about $10 million."
- The 23 present CHOP contractors, or at least some of them, would be logical contenders for HOP support, as the 3½ year CHOP contracts expire. So would the original seven COPs.
- Commenting that some community physicians he's talked with seem more interested in resources "and the exclusivity of resources" than in dollar support, DeVita said he would consider revamping the system through which NCI distributes investigational drugs. "That would please FDA no end. They have always been uneasy about Group C distribution (which makes available certain investigational drugs at no cost to physicians who are not necessarily participating in clinical trials).
- HOP contractors, as well as other groups involved in clinical treatment trials, also should be considered for the clinical testing of chemoprevention agents.

NCI executives and DRCCA Board members agreed that it probably would not be possible to design one system for community participation in clinical trials which would be suitable for every community.

"This is terribly important," DRCCA Acting Director William Terry said. "We may be establishing the system for the next decade for clinical research and cancer control. It may be a model for all of NIH."

Terry said one approach could be the national Cooperative Group outreach program, in which his division supports several groups in extending their protocols to communities.

DeVita said whatever plan or plans are developed should be firmed up by this fall, "so that in the spring we can issue some instrument. We would have to move along quickly." The DRCCA Board, which must give concept approval to any plan before RFPs or RFAs can be issued, will meet Oct. 22-23; that presumably would be the final deadline for getting the program started this year.

DeVita emphasized that any new program would have the "quid pro quo"—"In return for minimal support that allows them to do the things they think are important, in return they will commit certain numbers of patients to national studies. They will take part in exciting programs, including chemoprevention."

Board member Ernst Wynder asked if behavioral scientists and educators would be excluded. "We will not exclude anybody," DeVita answered.

Terry said he thought it would be difficult to implement October Board concepts in the 1982 fiscal year, but DeVita said, "We can do it."

Board Chairman Stephen Carter said that the program "must be related to cancer control if cancer control funding is used."

"That always comes up in discussions with community doctors," DeVita said. "They reply that they're prepared to treat some in the community, send some away, put others on local protocols."

Carter said that one of the major problems with the national Cooperative Group outreach program is that it does not relate to a cancer control strategy in a defined population.

Board member Charles Cobau, a Toledo medical oncologist and a past president of the ACCC, said, "It is difficult for me to come to grips with the global issues involved. The response to community participation in clinical trials has been very positive among ACCC members. But ACCC membership is a self selected component of community oncologists. A sizeable proportion of the membership is already involved in clinical research. They are sympathetic to arguments about the need to unfreeze halfway technology."

Cobau said an example is adjuvant chemotherapy for breast cancer, "which is universal among community oncologists. Scientifically, it is halfway technology, but for the next decade, the majority of patients will be treated with CMF and its variants, and it will be difficult to get back into clinical research."

Cobau noted that Bernard Fisher, chairman of the National Surgical Adjuvant Breast & Bowel Project, and Paul Carbone, chairman of the Eastern Cooperative Oncology Group, have said that one third of their patients are now provided by the outreach contract through communities. "This contribution is the tip of the iceberg. Thousands of patients who would be desirable for clinical research protocols are out there and are not included.

"Not all community physicians respond the same," Cobau continued. "It will not be possible to develop

a single strategy that will appeal to a majority of them. DRCCA should be investigating various ways, and channel those dollars into various programs."

Cobau said that in Toledo, where 10-12 oncologists are in private practice, "there are only three who actively place patients on protocols. The rest are intellectually content to use halfway technology. They are content with curing 90 percent of Hodgkin's disease patients, and if an occasional Hodgkin's patient dies, that's okay with them. They find participation in protocol studies is time consuming and deprives them of certain freedoms in practicing medicine. They look at a patient and say, "That's a CAF, or CMF patient, and I'll be damned if I'll let anyone tell me which is best. They don't approach it scientifically. They are resistant, if not opposed, to participating in clinical trials.

"What can we do about it?" Cobau asked. "First, we could cast aside the traditional idea of protocols. You could never get those seven in my community to participate in standard cooperative group protocols. You can't buy them, you can't seduce them. Second, we need a way to get information from a study and still permit oncologists freedom in treating their patients. Prerandomization has been talked down by most of us, but maybe if we permitted a physician to place a patient on one protocol or another, that might be the best way.

"One innovative approach I'm suggesting is to reduce the number of questions we require the oncologist to ask."

Moertel, who chairs the Board's Clinical Trials Subcommittee, agreed that "we have to adapt models to the needs of different areas. But to develop a model that compromises science to the need for getting more people is a waste of time and money and accomplishes nothing."

Moertel said physicians in the Dakotas and other areas covered by the North Central Cancer Treatment Group, a regional cooperative group organized by the Mayo Clinic, "are eager and anxious to participate in cancer control programs, epidemiology, and meaningful clinical trials, and they do have a sense of science. They participate in developing protocols. It is a pretty successful program.

"I thoroughly agree with Dr. Cobau's comments on forms. The number of questions is absurd. Page after page of silly data. . . . I disagree with Charley on trying to get 75 percent in. If they're not motivated, you won't get good science, and we don't need all those patients. There is only a limited number of questions to be asked."

Cobau disagreed to some extent. "If we cut out 80 percent of the patients, we would cut out 80 percent of rare tumors. Very few acute leukemias go on protocols. Most go to oncologist-hemotologists who are not interested in clinical research. Same with Hodgkin's disease."

"What proportion of the 80 percent is necessary to meet our goals, effectively maintain clinical trials and also do technology transfer?" Board member Leonard Derogatis asked. "Maybe we only need 15 percent."

"That's a fallacy," Cobau said. "Charley Moertel is successful in capturing a defined population. In my area, we need to capture all of them. We can't do a cancer control project any other way."

"It's a hopeless task if they are not enthusiastic," Moertel said. "Recalcitrant doctors won't spend time on forms and other tasks."

"If I understand Dr. Cobau correctly," Board member Peter Greenwald said, "it seems a large number of community oncologists are not practicing optimal cancer care."

"That's a critical issue," Carter said. "For any tumor, at any stage, a certain percentage can be treated successfully with existing technology. A goal of cancer control is to assure that patients at least receive that therapy. Clinical research accomplishes that, or offers patients new therapy that may be better. That's the beauty of it. There are 11 new drugs going into clinical trials this year, and nine more are in toxicology studies. We have radiosensitizers, and possibly soon will have monoclonal antibodies. The potential is there. The community oncologist has to have enough trust in the program to occasionally refer to centers. Community oncologists may be more willing to participate if they feel they are full partners."

Terry commented that "where effective relationships have been established, referral patterns improve." He suggested that it is not necessary to have 100 percent participation. "Physicians who choose not to participate may be 70 percent in one community, 15 percent in another. Even if we could get 20-30 percent, if we do the job right, they will be change agents."

Rose Kushner, member of the National Cancer Advisory Board who sat in on the meeting, commented that breast cancer patients "go to whichever oncologist the surgeon recommends for adjuvant chemotherapy."

"That's a terribly important point," Moertel said. "We (at Mayo) are determined not to give any adjuvant appointments unless the surgeon is included. If we have surgeons convinced this is the right thing to do, it doesn't matter what the oncologist down the block thinks. The surgeon will refer to the oncologist he thinks is doing the right thing."

ROBERT DAY TO SUCCEED HUTCHINSON AS CANCER CENTER DIRECTOR JULY 1

Robert Day, dean of the School of Public Health at the Univ. of Washington for the past 10 years, will succeed William Hutchinson as director of the Fred Hutchinson Cancer Research Center July 1.

Hutchinson will remain as chairman of the center's Board of Trustees and will confine his activities to planning and development.

Day, 50, received his MD degree from the Univ. of Chicago, an MPH from the Univ. of California (Berkeley) in epidemiology, and a PhD from Berkeley. He has been at the Univ. of Washington since 1968 when he joined the School of Medicine staff as head of the Div. of Health Services in the Dept. of Preventive Medicine. He was an associate clinical professor of pediatrics at UC (San Francisco) in 1967 after two years as chief of the California state Bureau of Maternal & Child Health and another as deputy director of public health for the state.

Day has been a member of the cancer center's Board of Trustees since 1978.

Hutchinson, who will be 72 in September, is the brother of the late baseball player, manager, and Seattle native for whom the center was named. Fred Hutchinson died of cancer in 1964 at age 45.

Bill Hutchinson, a surgeon, was a member of the National Panel of Consultants on the Conquest of Cancer whose work led to passage of the National Cancer Act of 1971. He became president and director of the cancer center in 1972, and shortly after it was named as one of the NCI-recognized comprehensive cancer centers.

Hutchinson is president of the 13th International Cancer Congress which will be held in Seattle in September 1982.

SEER GETS CONCEPT APPROVAL FOR THREE MORE YEARS, BUT WITH SEVERAL CHANGES

NCI's SEER Program (Surveillance, Epidemiology and End Results) was given concept approval for another three years by the Div. of Cancer Cause & Prevention Board of Scientific Counselors on the recommendation of a Board subcommittee which was assigned last year to review the program.

The Board's approval carried with it some restrictions which SEER contractors and NCI Field Studies & Statistics staff may find difficult to live with, and certain activities will be severely restricted or eliminated.

NCI may now enter into noncompetitive negotiations with the 10 present SEER contractors and will start searching for an 11th which probably will come from one of five metropolitan areas with concentrated populations of blacks and hispanics.

Board Chairman Seymour Jablon chaired the review subcommittee and presents its report.

SEER contractors operate population based cancer registries, with the primary mission of estimating cancer incidence and patient survival in the U.S. The 10 contractors cover five entire states, four large metropolitan areas and Puerto Rico, which combined account for about 10 percent of the U.S. population with reasonable geographic representation. Blacks and hispanics have been underrepresented, which the addition of the 11th registry is designed to correct.

All new cases of cancer are identified among residents of each of the registry areas and information is abstracted from hospital records, pathology laboratories, radiation treatment centers and death certificates. Vital status is determined annually for all the active patients in the registry through active follow-up. Copies of updated computer tapes representing the entire registry file are sent to NCI annually for analysis.

Data derived from this program are used to describe cancer incidence in the U.S. annually, to assess trends in incidence, to identify unusual changes for specific forms of cancer, to detect differences in cancer incidence between geographic areas, between population subgroups, between ethnic groups, etc., and to serve as a basis for epidemiologic studies. The SEER Program provides a mechanism for carrying out large scale case-control studies to test specific etiologic hypotheses as well as a basis for linkage with data on "exposure" cohorts to estimate the probability of occurrence of specific cancers in relation to suspected risk factors.

The patient followup data are used for a number of purposes as an aid in clinical research. They are used to estimate patient survival from specific forms of cancer on a population base, to assess trends in survival over time, to analyze the relationship between a number of variables and extent of disease at diagnosis, to measure outcome in relation to extent of disease, to study the variation in survival among population subgroups, etc.

The SEER Program also serves as a basis for a large number of epidemiologic studies in the area in which the registries are located. Such research is encouraged, but when additional funds are needed, they are derived from other sources.

The staff request was for $10.5 million a year, but the Board trimmed that by $500,000, contending that changes it was recommending would reduce costs.

Jablon's subcommittee recommendations were:

1. The SEER Program should be continued. The interest of the public (and Congress) demands that incidence data be available but, beyond that, the monitoring of the possible effects of environmental factors, the effective planning of expensive case-finding programs, the promotion of preventive measures, and development of therapies, demand reasonably good, current information on the changing incidence of disease. This requires population-based registries which, at relatively small additional cost, can serve to assess survival and time changes in survival and serve as a basis for etiological studies.

2. Every registry included in the program should provide a population-based estimate of cancer incidence.

3. The total population included in the SEER areas need not be a faithful reflection of the U.S. population in terms of race, ethnicity, urban-rural composition or any other factor of interest. Race has been identified as an important risk factor for cancer. The SEER Program is an appropriate mechanism for study of this factor, and areas with large minority populations should be well represented in the total sample in order to permit accurate estimates of incidence for these populations.

4. The SEER program should attempt to take advantage of existing, population-based tumor registries that are not now part of the program. Some existing registries, although they may exist in a state already represented, cover large populations, and include ethnic or racial groups not otherwise well represented in the existing SEER registries. It seems likely that the provision of relatively small amounts of supplementary funds would enable these registries to join the SEER program at least for the measurement and analysis of cancer incidence.

5. Extent of Disease (EOD) should be coded at each registry at least in a summary way according to a uniform format. A hierarchical EOD code will enable more detailed coding to be collapsed easily into less detailed format. At some registries physician interest is such that survival analysis appears to be one of the most important aspects of the registry operations; such registries should be allowed to use the most detailed EOD coding that can be supported adequately by the kinds of medical records which become available routinely.

6. A test should be made promptly of the completeness of mortality clearance utilizing the National Death Index in addition to searching area vital statistics files. Especially for the less common cancer sites, it will be useful to have survival data from as many of the registries as possible. If search of area vital statistics files, supplemented by use of the National Death Index, can identify at least 95 percent of the deaths that occur in a cohort, the costs and difficulties associated wtih active followup can be avoided for those registries in which mortality clearance is effective.

7. Reviews of SEER contracts for scientific merit must be coordinated. The SEER program cannot achieve its goals of measuring the incidence of cancer in the nation and important subgroups, and assessing time changes in incidence without program continuity. Each registry must be judged in terms of its relation to the entire program, not merely in terms of its own achievements.

8. The wider use of SEER should be encouraged. Information should be available on such matters as the proportion of diagnoses in stage 1, the proportion of deaths in given time, the proportions treated in various ways, as by chemotherapy or other modalities, and other questions of interst. Better coordination is needed with the NCI Div. of Resources, Centers & Community Activities, and Div. of Cancer Treatment in order to explore the potential for further use of SEER in these areas.

9. A cost accounting of each element of the program at each registry is required. The allocation of each contract for administration, collection of incidence data, epidemiology, and survival should be carefully evaluated.

10. Only minimum core support for epidemiology studies should be included in the contracts. In general extra costs required for locally initiated studies of epidemiology should be obtained through grant applications for specific projects. However, SEER registries should be expected normally to participate in large-scale NCI-sponsored cooperative epidemiologi studies.

Jablon's motion to approve included these caveats:

- The program be limited to $10 million a year.
- Reduce the amount of active followup.
- Hold extent of disease coding to the minimum.
- Advise contractors that support for locally initiated research (usually epidemiology studies triggered by data turned up in the program) would have to come from other than SEER funds.
- A cost accounting system be implemented.

Cutting back on active followup probably can be accomplished without impairing SEER's effectiveness only if the new National Death Index being developed by the National Center for Health Statistics is workable. NCI staff has its doubts.

Funds for the Index have been cut, and an appeal was made to NCI for support. A test is being made to determine if the system can work before NCI commits any money to it. The major problem involves restrictions against release of names of cancer victims; the solution might require legislation in the states covered by SEER.

Large registries in Los Angeles and the state of New York are not SEER contractors, and the committee suggested they might be brought in at comparatively little cost. The New York registry probably would not fit in and is not interested anyway. FSS staff feels the Los Angeles registry could be brought in with some modifications.

Other possibilities for the 11th SEER registry include Miami, New York City, the state of Texas or portions of it, and Chicago.

The 10 existing SEER contractors are California State Dept of Health, Connecticut State Dept. of Health, Michigan Cancer Foundation, Research Corp. of Hawaii, Univ. of Iowa, Univ. of New Mexico, Fred Hutchinson Cancer Research Center, Emory Univ., Puerto Rico Dept. of Health, and Utah Cancer Registry. The program also has contracts with the Univ. of California (San Francisco) for training, and Yale Univ. for computer support.

Members of the Board's ad hoc review committee

were, in addition to Jablon who is a member of the Board and director of medical followup for the National Academy of Sciences-National Research Council, were Lawrence Garfinkel, vice president for epidemiology and statistics at the American Cancer Society; Leon Gordis, chairman of the Dept. of Epidemiology at Johns Hopkins Univ.; George Hutchison, professor of epidemiology at Harvard Univ.; and C.F. Starmer, professor of computer science at Duke Univ.

DCCP BOARD APPROVES CONCEPT OF SEVEN RECOMPETITIONS, DENIES TWO OTHERS

The Board of Scientific Counselors of NCI's Div. of Cancer Cause & Prevention gave concept approval to seven additional contract supported projects for recompetition (see last week's issue of ***The Cancer Letter*** for others) and disapproved two others, both projects NCI supports for work done by other government agencies.

Concepts approved for recompetition follow.

Inter and intraspecies identification of cell cultures. Estimated first year cost, $160,000 on a three year contract. Present contractor is Children's Hospital of Michigan. The narrative explanation of the program:

Many experimental techniques in virology, immunology, cell biology and biochemistry require the precise duplication of cells or mixtures of cells, with the result that cell identification services are of critical importance. This project concerns a research support service facility for the inter- and intraspecies identification of cells in culture which are used in cancer research. The present incumbent, Children's Hospital, is a world renowned facility for the identification of cell cultures. The extensive use and informal exchange of cell cultures among researchers has resulted in a major problem of frequent erroneous or mislabeled cell lines. Through its cytogenetic, immunofluorescent and isozyme testing services and expertise in cell identification, the laboratory serves to monitor the proper identification of cell lines used in cancer and biomedical research. A recently completed user survey indicated a continuing need for this project.

The Board's approval was conditioned on phasing the project into the division's new payback system (***The Cancer Letter***, June 5). From 85 to 90 percent of the users are extramural.

Operation of a facility to hold and maintain nonhuman primates for cancer research. Estimated first year cost, $425,000 on a two year award. Present contractor is Litton Bionetics. The narrative:

An important aspect of studies of biological carcinogenesis involves studies utilizing nonhuman primates as experimental hosts for known or suspected oncogenic viruses. Existing facilities for the maintenance and holding of nonhuman primates are limited. With the exception of the Regional Primate Research Centers, animal facilities at most research institutions do not have the capability for housing nonhuman primates, and their personnel are not experienced in handling and monitoring the animals' day to day health. The availability of a facility that has the capability for housing nonhuman primates allows cancer researchers the opportunity to perform in vivo experiments involving nonhuman primates that may not be possible at their institutions.

This contract effort supports a biohazard containment area that houses 95 Macaca mulatta (rhesus), six M. fascicularis (cynomolgus), seven M. arctoides (stump-tailed macaque), three M. nemestrina (pigtailed macaque), ten Papio hamadryas or P. cynocephalus (baboons), 28 Aotus trivirgatus (owl monkeys, several types), four Saquinus oedipus (cotton-topped marmoset), six S. fuscicollis (white-lipped marmoset), six Saimiri sciureus (squirrel monkey), three Lagothrix lagothricha (woolly monkey), seven Hylobates lar (white-handed gibbon), and six Pan troglodytes (chimpanzees) for a total of 181 animals.

The area has a change room and shower facilities as well as capability for autoclaving all contaminated materials leaving this area. Twenty-nine special animal studies are active involving 11 different cancer researchers (one Russian, eight NCI intramural, two extramural). Each researcher performing experiments at the facility is responsible for developing the experimental protocols, obtaining the nonhuman primates for study, and assuring the orderly completion of the study. The contractor's professional and technical staff have the ability to administer oncogenic or potentially oncogenic materials to the prenatal, infant or adult monkeys and the capability to collect blood and other specimens from experimental animals. A diagnostic laboratory is maintained to monitor the animals' health. The branch plans to institute the payback system for this resource.

The Board rejected the staff's request to recompete the contract for three years and limited the award to two years. "We're coming to the end of this kind of research," Board member Brian Henderson said, referring to virus studies with the animals.

DCCP Acting Director Richard Adamson said requiring payment from intramural as well as extramural labs, as the new system will do for certain resources supplied by the division, should result in reduction of demand for the holding facility services. "We'll determine just how badly this is needed if they have to pay for it out of their intramural budget."

Marmoset colony for cancer research. Estimated first year cost, $300,000 on a three year contract. Present contractor is Rush-Presbyterian-St. Luke's Medical Center. The narrative:

Marmoset models of neoplastic disease, induced experimentally by animal tumor viruses, provide excellent systems for studying, in a primate, the pathogenesis of virus-induced tumors, specific virus-host cell interrelationships, and host immune responses to oncogenic viruses and/or virus-transformed cells. The high susceptibility of marmosets, especially cotton-topped marmosets (Saguinus oedipus) which are a rare endangered species, to oncogenic viruses and the availability of well characterized sarcoma, lymphoma and glioma marmoset models provide a system wherein human virus isolates can be evaluated for oncogenicity and be compared to the animal tumor virus models.

The continuation of this contract effort will be to maintain a productive breeding colony of cotton-topped marmosets and to a limited extent white-lipped marmosets (S. fuscicollis or S. nigricollis) so that appropriate numbers of these animals will be available for experimental use. The breeding colonies contain 70 cotton-topped and 50 white-lipped marmosets with an anticipated survival of approximately 28 and 22 offspring annually, respectively. In addition to the marmoset breeding efforts, technical expertise and a containment facility are also available for the performance of experimental studies. Presently 27 studies involving 19 investigators (16 extramural and three NCI intramural) are utilizing 123 marmosets.

Personnel available to this facility have the ability to provide a service function by administering oncogenic or poten-

tially oncogenic materials to the prenatal, infant or adult monkeys and to collect blood and other specimens from experimental animals. A diagnostic control laboratory is maintained as an integral part of the primate colony to monitor animals' health.

The branch plans to institute a partial payback system for this resource. Only the cost of the animal holding portion of the effort will be charged to the investigators involved.

Preparation of antisera to oncogenic or potentially oncogenic viruses. Estimated first year cost, $400,000 on a three year contract. Present contractor is Becton-Dickinson & Co. The narrative:

Of major importance to the cancer biology research programs is a source of potent and specific antisera to viruses and their purified protein components. These antisera are used in a variety of experiments including: studies of virus induced protein synthesis and protein processing in which immunological probes are used to isolate proteins; identification of oncogenic viruses in cells and tissues; elucidating the functional role of viral proteins in transformation; comparing and contrasting proteins of similar molecular weight to determine relatedness; producing immunosorbent columns for protein purification; fluorescence microscopy and fluorescence activated cell sorting and immunoelectron microphotography. In addition, the effort provides secondary antibodies directed against the primary antisera which the contractor produces.

During the past year, 399 immunoreagent shipments were made to 249 investigators. A recently completed user survey indicated a continuing need for the project. The branch plans to institute a resource material payback system for this project.

Henderson suggested that with the payback, the cost could drop to $300,000 or even $200,000 a year. But Board member Charlotte Friend said, "There's still a real need for these things. Until we straighten out differences between components and the viruses, these are very important tools. I would recommend that we keep this open but watch for developments that could change demand."

Synthesis of kilogram amounts of retinoids for chemoprevention and toxicity studies. Estimated first year award, $290,000 on a three year contract. Present contractor is Southern Research Institute. The narrative:

Theoretically the best way to reduce cancer incidence involves reduction or elimination of human exposure to carcinogens, cocarcinogens, initiators and promoters. However, such a strategy is not always feasible. For this reason, the Chemical & Physical Carcinogenesis Branch supports a preclinical drug development program on anticarcinogenic agents in addition to basic preclinical research on the biological and chemical prevention of carcinogenesis. The objective of this program is the development of safe and effective pharmacological and physiological agents for prevention of development of cancer. In the retinoids area, studies proceed on the synthesis, bioassay, efficacy of inhibition of carcinogenesis in animal systems and toxicology of the most promising compounds. In addition, a resource project exists for the synthesis of retinoids in kilogram quantities in support of the animal sutdies on anticarcinogenesis and toxicology. This resource project is the subject of the proposed studies.

The basic objective of this project will be the synthesis of new retinoids, to be specified by NCI, at the one kilogram level, which will be used for testing in long term animal experiments for prevention of the development of cancer at various organ sites, including bladder, breast and pancreas. Retinoids in these larger quantities shall also be provided for toxicological evaluation, and occasionally in smaller quantities for preliminary pharmacokinetic studies. Retinoids shall be provided to ultimate users in all cases in a high state of purity with appropriate analytical documentation.

Smoker compensation and cigarette smoke yield. Estimated first year award, $140,000 on a two year contract, with the total project estimated cost $190,000. This will be a new project. The narrative:

As the tar and nicotine levels of cigarettes are reduced, smokers may alter their smoking behavior in an unconscious attempt to extract more of the pharmacologically active materials in the smoke. It is therefore possible that in addition to nicotine, the smoker may also increase the uptake of other constituents such as carbon monoxide, nitrogen oxides, hydrogen cyanide, etc.

Volunteer smokers would be provided with experimental cigarettes of known chemical composition which they would smoke for a trial period of 4-6 weeks each. Each cigarette type would deliver a specified smoke such as high nicotine, low tar; low nicotine, low tar, etc. On the first day of smoking, and at the end of the 4-6 week trial, the subjects would undergo dosimetric testing consisting of blood nicotine, carboxyhemoglobin and other selected measurements, such as nitrosamine, acetaldehyde and thiocynate levels pre- and post smoking as well as a test of puff profile (puff volume and rate) and respiratory measurements during smoking to quantify depth of inhalation and breath holding behavior by impedance pneumography or magnetometry.

Earlier similar studies have counted numbers of cigarettes smoked per day, or lengths of cigarettes smoked, with no data regarding actual uptake of smoke constituents by the smoker. A study of the type proposed would give data relative to amounts of specific materials which are extracted by smokers who inhale and exhale quickly, puff and hold their breath, etc.

The concept of a one-year noncompetitive renewal of the interagency agreement with the Office of Naval Research for development and characterization of cell substrates for use in cancer research was approved by the Board, but approval to recompete the project as a contract for three additional years, after the agreement with the Navy expires, was withheld.

The Navy work, performed at Oakland, has cost from $480,000 to $618,000 a year. The phase out year will be an estimated $200,000, and staff estimated the first year of the new contract would be $325,000.

The effort at Oakland is winding down because key people are leaving.

Board member Louis Siminovitch asked for another concept review before the contract is recompeted. "Also, $325,000 (the amount staff had asked for the final year of the Navy agreement) is a lot of money. I'm not very enamored of this program anyway."

Board member Bernard Weinstein noted that the project serves "only 250 scientists. I would estimate $200,000 would be enough." He offered a motion to approve the one year extension, limited to $200,000 with no possibility of extension.

"I'll abstain," Board member Seymour Jablon said. "We're not a contract review body. It is not right for us to pull a figure out of the air. I don't know if that is valid."

"It's entirely within the purview of the Board to suggest figures," Adamson said. "If I don't think it's appropriate, I will say so. This Board does have cell line culture expertise."

"This sort of resource, when negotiated with the new vendor, should have the payback feature built in from the start," Henderson said.

Weinstein's motion was approved, with Jablon abstaining.

The two interagency agreements voted down by the Board were:

—Interactions of diet/nutrition and the use of genetically distinct animal strains in carcinogenesis studies, with the National Center for Toxicological Research (part of the Food & Drug Administration), at $250,000 a year.

—Toxicity of tobacco and smoke components and experimental tobacco, with the U.S. Dept. of Agriculture, at $80,000 a year.

"The past performance of NCTR has been terrible," Weinstein said. "It doesn't inspire confidence. We have our own resources, and extensive information is available. The Diet, Nutrition & Cancer Program should better spend its money on mechanisms of diet and carcinogenesis."

The motion to disapprove was unanimous, ending NCI's participation in a project that started in 1978.

The tobacco project performed by USDA with NCI money has been in existence since 1978. "Am I wrong, that the tobacco companies are very interested in developing less hazardous cigarettes and are devoting large resources to this kind of thing?" Jablon asked. When no one disagreed, Jablon moved disapproval "on the grounds that private industry already is putting a good deal of research into this area." The motion was approved, with two abstentions.

The Board first approved the concept for a three year contract to provide computer support services for family studies conducted by the Environmental Epidemiology Branch, at a cost of $250,000 a year. However, Board member Barry Pierce moved that the issue be reopened, and the Board subsequently voted to defer action to its September meeting.

Pierce and others expressed concern over whether this was the best way to provide computer services for the division's activities. Seymour Jablon suggested that a study be undertaken with the help of computer experts.

Joseph Fraumini, chief of the branch and director of the Field Studies & Statistics Program, said the existing contract for computer support "is being stretched to the limit." Adamson asked that the contract be approved for one year only while a study is undertaken, but the Board agreed with Pierce that delaying approval to September would not cause any hardship since the contract could not be awarded until the 1982 fiscal year anyway.

The Board approved the concept of a contract to study stomach and colon cancer incidence and mortality among Puerto Ricans in New York City, which has already been issued as an RFP and appeared in the May 22 issue of ***The Cancer Letter*** (RFP NCI-CP-FS-11024-65). Estimated first year cost is $75,000, with a total cost of $150,000.

The Board rejected the concept of doubling NCI's support for a health and nutrition survey being conducted by the National Center for Health Statistics. NCI is committed to $100,000 a year for three years, starting in FY 1981, and the proposal was to increase the total to $600,000 for the three years.

The study is the Health & Nutrition Examination Survey (HANES 1), with major support from the National Institute of Aging. Data were collected on the physical, psychological, biochemical, nutritional and medical characteristics of 25,000 persons between ages 1 and 74 during 1971-73. Followup studies are being made to link those detailed baseline data to health outcomes. Original plans called for following those 25 or older, but present funds will limit the study to those 45 and older. NCI's increased contribution was intended to restore the original plan.

"Most cancer occurs in people over 45," Henderson said. "I don't have much confidence in cohort studies such as this. Diets change. I can't justify spending this much." His motion to disapprove carried.

Approximately 300 deaths are likely to have occurred since the initial survey among 14,000 study subjects who were 25 or older in 1971. The number of cancer deaths would be small, but the ability to easily identify future deaths using the National Death Index appealed to DCCP epidemiologists.

NCI CONTRACT AWARDS

Title: Study of the clinical pharmacokinetics of cancer drugs
Contractor: Ohio State Univ., $340,198.

Title: Chemoprevention of cervical cancer
Contractors: Albert Einstin College of Medicine, $1,047,892; Univ. of Arizona, $428,499; and Georgetown Univ., $633,859.

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