THE CANCER LETTER

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NCI PLANS TO FUND FY 1985 R01s, P01s WITH CUTS 2.9-3.8%

UNDER RECOMMENDED; GROUPS, CENTERS REDUCED 7-10%

The shape of NCI's "funding plan" for the 1985 fiscal year was made known last week when Director Vincent DeVita made his annual appearance before the House Labor-HHS Appropriations Subcommittee. Members of the subcommittee made it known they did not like

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In Brief

HAMMER APPOINTED TO NEW THREE YEAR TERM, STAYS AS PANEL CHAIRMAN; ACCC ELECTS YARBRO, MOORHEAD

ARMAND HAMMER announced last week at the meeting of the President's Cancer Panel in Birmingham that he had been informed by the White House he has been appointed to a new three year term on the Panel and will remain as its chairman. Still no word from the White House on appointments to the National Cancer Advisory Board. The terms of six members expired March 9.... **JOHN YARBRO**, professor of oncology at the Univ. of Missouri, became president of the Assn. of Community Cancer Centers last weekend at the association's annual meeting. He succeeds **WILLIAM DUGAN**, Indianapolis medical oncologist. **EDWARD MOORHEAD**, director of the Grand Rapids Clinical Oncology Program, was voted president elect.... **JOSEPH EARLY** (D.-Mass.), member of the House Labor-HHS Appropriations Subcommittee, after hearing NCI Director Vincent DeVita say that the booklet telling Americans how they can prevent cancer by modifying their diet and refraining from smoking is being distributed free: "I have 600,000 people in my district. Why wouldn't it be a good idea for me to get 600,000 copies, print across the bottom, 'How to decrease your chances of getting cancer,' print across the top, 'Reelect Joe Early,' and distribute them? Politicians are always looking for something to give out that people won't throw away".... **STANLEY COHEN** of Vanderbilt Univ., whose pioneering work in growth factors has paved the way for cell proliferation studies, received the Ernst W. Bertner Memorial Award last week from M.D. Anderson Hospital & Tumor Institute. **MARY ELLEN HARPER**, whose work led to the development of a technique for determining the precise chromosomal locations of specific genes, received the Wilson S. Stone Memorial Award. She is a staff fellow at NCI. Both awards were presented during M.D. Anderson's symposium on mediators in cell growth and differentiation.... **TEXAS HOUSE** Speaker Gib Lewis has established a legislative task force of citizens to help identify ways to "dramatically reduce the burden of cancer for Texans." James Dannenbaum, Houston engineering exectuve, will chair the panel of 51 which includes elected officials, representatives of voluntary organizations concerned with cancer, state agency officials, and others from throughout Texas.

NATCHER SUBCOMMITTEE OBJECTS TO CUTS PLANNED BY NCI IN PRESIDENT'S BUDGET

(Continued from page 1)

this "funding plan" any better than they did last year's.

"Funding plan" is NCI terminology for funding grants at less than their peer review recommended levels and using the money saved to support more grants. DeVita told the subcommittee that NCI was able to fund 100 additional laboratories in the 1983 fiscal year that way, by reducing grants an average of 15 percent from their recommended levels.

Last year, the subcommittee directed that NCI pay research grants at their full recommended levels and added enough money to the budget to cover the extra cost. NIH interpreted that directive to apply only to RO1 (traditional) and PO1 (program project) grants. Management of cancer centers and the clinical cooperative groups, who had to take substantial cuts from their recommended budgets, did not like that interpretation, and they have expressed their opinions to some of the subcommittee members.

Responding to questions from subcommittee members about intended funding levels for 1985, DeVita said that for RO1s and PO1s, the present plan is to reduce noncompeting grants by an average of 2.9 percent under their approved levels, and to cut competing grants 3.8 percent under approved levels.

DeVita did not mention the cuts for cooperative groups and cancer centers, other than to respond to a question from Subcommittee Chairman William Natcher (D.-Ky.) if he intended to fund them at "amounts recommended by peer review" with the answer, "No."

At present, the reduction planned for cooperative groups is seven to nine percent from recommended levels and for centers, nine to 10 percent, for both competing and noncompeting.

"It's not a pleasure to reduce budgets, but the trade off was worth it," DeVita said. "There was no reduction of activities (funded by grants), just smaller increases (than those approved by study sections). "We were not strangling anyone."

"Do you agree with Dr. (James) Wyngaarden (NIH director who preceded DeVita before the subcommittee) that we should raise the percentage of approved grants that are funded to 45 or 50 percent?" Natcher asked. NCI, and NIH in general, will fund about 30 percent of approved competing grants in FY 1985 unless Congress adds money to the President's budget request.

"There is always the feeling that you take a risk of leaving some very good research unfunded, at any level, even 50 percent," DeVita answered.

"If you were to receive additional funds, would you prefer to use it to increase the number of grants; to increase funds for each grant; or to support other programs that otherwise would not be supported?" Natcher asked.

"All of the above," DeVita cracked. Then, more seriously, he added, "All really is the answer I would give," indicating that if Congress does give NCI more money and allows him to allocate it, he would spread it around by funding more grants at higher levels and would pick up a few new programs.

"Some people feel clinical research is being neglected because of the emphasis on basic research," Natcher said.

DeVita noted that the budget for cooperative groups had increased from $18 million in 1974, when he became director of the Div. of Cancer Treatment, to the present level of $46 million. He acknowledged, however, that the groups' budget has been level for several years and that "there is an element of truth in the criticism."

Natcher pointed out that DeVita last month told the Board of Scientific Counselors of the Div. of Cancer Treatment that he intended to "loosen up more money for clinical research." Natcher asked, "How do you plan to do that, doctor?"

DeVita responded that some grants probably will be renegotiated downward, and that there could be some changes within the groups that might free up some money. It was a vague answer, undoubtedly intended to circumvent the restriction Administration witnesses are always under at budget hearings, when they are under orders not to ask for more money than was included in the President's request. DeVita's statement at the DCT Board meeting made it clear that he intended to add money to the cooperative group budget, not just reshuffle a few dollars among the groups. It is also clear that the only way any significant amount of additional funds can be made available to the groups will be for Congress to increase NCI's appropriation and direct that some of the increase be used for that purpose.

Both Natcher and Louis Stokes (D.-Ohio) expressed concern about the fact that the 1985 budget indicates NCI's intention to support the same number of centers, 59, in 1985 as are being supported this year despite a cut of nearly $1 million in the budget for center core grants.

DeVita said that part of the difference might be accounted for by the fact that two new core grants will be awarded, replacing two which had been funded at higher levels. One of the new centers is in Nebraska, he said.

"Moneywise, and otherwise, what can we do to help you, what additional assistance can we give you, other than what is in the budget request?" Natcher asked.

Here, DeVita went into his smooth routine to avoid being accused of "budget busting" while still answering a question posed by a powerful congressman. Instead of asking that the subcommittee give NCI the amount it asked in the bypass budget ($88 million more than the President's budget), which would have brought a new director to NCI the next day, DeVita responded that congressmen could help by passing the word to their constituents that cancer is a preventable and treatable disease. "There is a great gap between what people think we can do and what we can do," he said.

More subcommittee questions and DeVita answers:

Natcher: "What evidence can you cite to prove that we are winning the war on cancer?"

DeVita: "National mortality figures from our SEER program. They show decreasing mortality which can be traced to development of new therapy. We're saving 30,000 lives a year as the result of our investment in the National Cancer Program."

Natcher (after recounting the history of NIH appropriations since the 1950s: "One day we asked Dr. (James) Shannon (former NIH director) if he could use a billion dollars (when the entire NIH budget was $400 million). He said no. We've come a long way, doctor. If we were to give you $100 million over the request, I don't know anyone who would object."

Silvio Conte (R.-Mass.), ranking Republican on the subcommittee: "There's been a great deal of attention given to chemicals, EDB and others. I would add the large number of fish with cancer caused by pollution. Are we winning the battle, or are we losing the war?"

DeVita: "We are winning. I don't want to minimize the problem of exposure to chemicals, but we think about four or five percent of all cancer is caused by chemical carcinogens. We're not sure that exposure is greater today than in the past. One thing we are sure of is that our ability to measure chemicals in the air, water, and workplace has been improved tremendously."

Conte: "Are you satisfied that we are doing enough?"

DeVita: "Yes. NCI developed carcinogenesis testing, which is now part of the National Toxicology Program in the National Institute of Environmental Health Sciences. We can't test all chemicals, but I'm pleased with what we are doing."

Stokes: "How effective has the Community Clinical Oncology Program been in improving the quality of cancer care?"

DeVita: "That was just funded, and we've only had about six months experience with it. I'll be able to tell you better how we're doing after another two and a half years, when they are being recompeted. I just had the pleasure of visiting one, (the new community cancer center) at Halifax Hospital, in Daytona Beach. I was very impressed."

Steny Hoyer (D.-Md.): "I note from your statement that there are CCOPs in 34 states. What about the other 16?"

DeVita: "Those 62 were all we could fund. Most of those who applied were institutions not experienced in applying for grants. We funded all we could, the best of the crop. We will compete that again. Our original target was to have 200 CCOPs. We will try to get to that number by 1990."

Stokes: "I see that you plan to establish a predoctoral research training program for nurse oncologists."

DeVita: "That is part of the Clinical Education Program. Nurses are farther along than surgeons in focusing on oncology. The Oncology Nursing Society now has 5,900 members. Its growth has been phenomenal."

Joseph Early (D.-Mass.): "I still don't understand how you can support the same number of centers with a $1 million cut."

DeVita: "There are 20 up for recompetition. The mix coming out of that may be different."

Early: "When they come up for recompetition, they don't get cheaper."

DeVita: "Sometimes they do."

Early: "It looks like all of them will get smaller, from this budget."

Conte: "I received a letter from Dr. Armand Hammer on the issue of applying the number of expert consultants you hire to your personnel levels. Has this had an effect on NCI?"

(Hammer, as chairman of the President's Cancer Panel, contacted Congress and the White House after DeVita had pointed out late last year that HHS was insisting on taking NCI's expert consultants out of the personnel ceiling, contrary to the express intent of the National Cancer Act, which created the authority for NCI, and later NIH, to hire outside the normal federal personnel process, experts for up to two years).

DeVita: "That was a policy change which was contrary to the National Cancer Act, and I am required to bring that sort of thing to the attention of the President's Cancer Panel. It (HHS policy) has caused us to lose a recruiting edge."

DOLE TO PUSH FOR "DRG 471," WITH NEW LEGISLATION IF NOT ADMINISTRATIVELY

Sen. Robert Dole (R.-Kan.), chairman of the Finance Committee which writes Medicare legislation, told the Assn. of Community Cancer Centers last weekend that he has not given up on his efforts to liberalize exemptions from the Diagnosis Related Group reimbursement system for clinical research. "If we can't find some relief administra-

tively, we will take the legislative approach," Dole said.

Dole addressed the 10th annual meeting of ACCC to accept its annual award made to someone who makes an outstanding contribution to quality patient care. Dole had pressed for the amendment to DRG legislation providing exemptions for institutions engaged in cancer research, an amendment the Health Care Finance Administration chose to interpret so narrowly that only a handful of large centers and no community centers qualify. Dole pressed HHS Secretary Margaret Heckler to liberalize that regulation, without success.

Dole revealed in his ACCC appearance that he had sent a new letter to Heckler, again pointing out that the DRG regulations did not go along with congressional intent and asking her to convene a meeting of representatives from HCFA, NIH, other appropriate agencies, and "major lay, professional and advisory groups, such as the National Cancer Advisory Board. I believe that our concerns can be systematically addressed and if necessary, a strategy for systematic data collection to assist in a resolution of this matter should be developed."

Dole continued in his address, "As it stands now, if only a few large institutions get an adjustment, I am concerned that relatively few cancer patients will have access to community based care. Research results from the National Cancer Institute will no longer be widely disseminated, and fewer patients will benefit from their application. Since passage of the National Cancer Act of 1971, the intent of Congress has been to disseminate the latest cancer treatment to communities. I intend to continue to see that this congressional intent is carried out through what has proven to be a most effective vehicle, the community cancer centers. I encourage you to continue to provide us with the information necessary to identify the legitimate differences between the costs of hospitals caring for patients under NCI protocols and those who do not."

Earlier in the four day meeting in Washington, ACCC members stormed Capitol Hill, enlisting congressional support for "DRG 471," a new category in the prospective payment system for clinical research which would permit Medicare payment for extra costs of patient care required in clinical trials, such as additional tests, measurements and supportive care. The usual reaction from most congressmen, ACCC members said, was that they thought they had addressed that situation with the amendment HCFA virtually ignored.

Michael Maher, who as a top HCFA official had played a major role in writing the DRG regulations, was on a panel at the ACCC meeting top discuss the program. Maher recently left government to join an accounting firm in Philadelphia. Also on the panel were Marilyn Koch, HCFA staff member; Jeffrey Wasserman, of Health Research & Educational Trust of New Jersey, who has made a study of that state's prospective payment system and compared it with the federal DRG system; and Lee Mortenson, ACCC executive director.

Maher and Koch defended their interpretation of the legislation and repeated HCFA's position that any extra costs entailed in clinical research should be paid for by NCI. Both insisted that HCFA intended to be flexible and permit adjustments, but only with solid information.

Mortenson challenged the contention that NIH or NCI should make up the differences for clinical research, contending that the cost would "rival NCI's total budget." He said there is "a growing case being made that DRGs will suppress innovation. Only cost effective innovations may be accepted."

All of the speakers agreed that considerably more information is needed on DRG impact on quality of care and on clinical research. ACCC is undertaking such a study, at an estimated cost of $325,000 a year. Delegate members of the Association are being asked to contribute $500 each to finance the study, and additional help will be sought from foundations if needed.

John Yarbro, who succeded William Dugan as ACCC president at the meeting, established as the goal of his year in office creation of DRG 471.

DRG 471, Yarbro said, would "provide that the reimbursement for care of any patient on an NIH approved clinical trial be made on a cost basis. There is nothing new in this. This is the way research patients are presently paid for. . . It would cost so very little and do so very much. Only a few of the many millions of patients each year are on clinical trials, so the cost would be minimal. If DRG 471 were restricted to NIH approved clinical trials there would remain a federal lever to prevent overutilization and the use of the DRG system would allow appropriate audit. NIH could serve as a guarantor against abuse. . . This is a problem of the entire biomedical community, not just those of us concerned with the welfare of the cancer patient. . . I call upon the members of ACC to work together to make DRG 471 a reality. . . It is likely that we will not be listened to. . . I do not really expect DRG 471 to happen. I just hope that it will. In any event it is such a worthwhile endeavor in which to spend our energies and such a worthwhile goal for our organization that we will, all of us, be better for having tried."

Yarbro said that some health providers still do not believe DRG implementation "is really going to happen. . . Others adamantly refuse to understand

that they will no longer be permitted to charge whatever the traffic will bear. Many who have come to understand this insist that it is unfair. Each person seems to have his own special notion about how to beat the system and some ideas remind me of the schemes dreamed up by compulsive gamblers to win at roulette... Make no mistake, competition will bring down costs."

Yarbro continued, "Let us consider the situation we have gotten ourselves into. We have too many doctors, too many medical schools, too many hospitals, and too many students in the pipeline on their way to making the situation even worse. Like bacteria in a log phase growth we are about to outgrow our nutrient broth. The amount of nutrient broth we will have available, of course, is determined by politicians, who got us into this mess in the first place by listening to us when we told them there was going to be a doctor shortage. We are costing our country too much and our politicians have called a halt."

DCE BOARD APPROVES RECOMPETITION OF HEALTH PLAN ENVIRONMENTAL STUDY

Among the concept approvals voted by the Board of Scientific Counselors of NCI's Div. of Cancer Etiology were recompetition of studies on environmental cancer utilizing prepaid health plans and a new mortality study of workers exposed to acrylonitrile. Other concepts approved, for grants and contracts, were reported last week in **The Cancer Letter.** The Board also gave concept approval to seven noncompetitive contract projects.

Studies on environmental cancer utilizing prepaid health plans--Present contractors are three Kaiser Research Institute groups in Portland, Ore., Oakland and Los Angeles which have been conducting the studies since 1981 costing from $172,000 to $290,000 a year each. Estimated first year cost following recompetition totals $663,087, with a four year cost of $2.8 million.

One of the primary goals of the Environmental Epidemiology Branch is to evaluate rapidly hypotheses concerning potential environmental causes of cancer. These hypotheses may arise from clinical observations, epidemiologic studies, or from laboratory experimentation. A relatively rapid way to accomplish this for some environmental exposures would be to utilize already recorded information in a prepaid health plan on large groups of patients with a particular cancer and a comparable series of persons without the disease. This sort of record linkage capability is taking on increasing importance, since it involves review of already recorded information and therefore avoids many of the problems associated with issues of privacy and confidentiality. Because of the nature of prepaid health plan records, the primary hypotheses that can be tested involved those associated with the use of therapeutic drugs, clinical conditions, surgical procedures, radiologic procedures, occupation, location of residence and exposures that are highly correlated with one of these variables. Utilizing longitudinally recorded information concerning demographic and specific exposure characteristics of cases, and controls representative of the group from which the cases are drawn, is a valuable way to determine whether a more extensive study is required.

A secondary type of investigation that is appropriately done within these prepaid health plans is the hypothesis generating type of investigation, utilizing the same approaches outlined for testing hypotheses. Here, also, because a substantial amount of specific information has already been recorded for substantial numbers of cases and controls, these resources provide a cost efficient way of exploring variables for associations that can then be tested in other populations.

Finally, in some large prepaid health plans in existence for many years, several data banks and other resources have been developed for a wide variety of reasons (e.g., multiphasic screening, serum banks, computerized pharmacy files, data from other ad hoc studies). Exploration of plans for such epidemiologic resources can result in the identification of opportunities to test current hypotheses with respect to environmental carcinogenesis.

Over the last two and a half years, the Branch has collaborated with large large prepaid health plans that have been in existence for 20 or more years. As outlined below, a number of studies have been conducted which illustrate both the utility of the approach and the flexibility to test important etiologic hypotheses.

Progress to date: In a study of over 300 breast cancer cases and 600 controls from the Portland Kaiser Plan, an excess risk of breast cancer was noted among long term users of menopausal estrogens (JNCI 1981, 67:815-820). This risk was substantially higher among women who had had a prior oophorectomy than among women with natural menopause. To followup on these findings, comparable investigations in two other plans were initiated and have thus far resulted in approximately 600 case control pairs for women with a natural menopause and approximately 200 cases and 400 controls among women with a bilateral oophorectomy. The data are currently being analyzed and some preliminary

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Funding levels associated with contract concepts are preliminary staff estimates for purposes of discussion and planning. Actual funding of any contract is determined based upon proposals submitted in response to RFPs and detailed negotiations. Endorsement of a project concept may not necessarily result in issuance of a contract. Funding levels of contracts may be altered due to unanticipated budgetary changes. Multiple contract awards also might be made. Organizations interested in submitting proposals to implement approved contract concepts are cautioned to carefully read any resulting RFP and not to assign undue weight to the staff estimates. Notice of availability of the

RFPs will appear in The Cancer Letter. Dollar estimates listed with RFA concepts (grants or cooperative agreements) are the amounts NCI plans to set aside to support those projects. Those amounts also are subject to budget changes, and final awards will depend on amounts approved by peer review and availability of funds.

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findings are available (Cancer, in press). A large hypothesis generating study of ovarian cancer was also initiated pooling the resources of two health plans. A total of 500 ovarian cancer cases and 600 controls were identified and information concerning prior drug use, all prior gynecologic conditions and surgery, demographic vehicles, and various exposures were abstracted from the charts. Analyses of these data are also currently under way.

Two years ago, an intriguing observation emerged from several prospective heart disease studies. Namely, the risks of malignancy in general, and particularly colon and lung cancer, were substantially higher among men with low serum cholesterol. This has been followed up in two ways. First, an analysis of cancer incidence among 162,000 men and women who took part in a multiphasic health examination in one health plan between 1964 and 1972 has been completed. In addition, utilizing data from another plan, 240 cases of colon cancer and 480 controls with prior cholesterol determinations have undergone detailed chart review and abstraction for cholesterol readings, other potential risk factors, therapeutic drug usage, location and stage of disease, and survival. A similar investigation of lung cancer cases has just been initiated in the same plan. Overall in the multiphasic cohort data set, the risk of malignancy was inversely related to the level of serum cholesterol. This was most promin- ent among males for lung, colon, and prostate cancer. The relationships were diminished somewhat when control was applied for potential confounding factors. Finally, investigation of these risks by interval from cholesterol determination indicated that the risks were elevated only for the several years following the determination itself. This suggests that the low cholesterol reading may be related to some aspects of the preclinical cancer state, rather than an etiologic factor. These issues are being pursued in a more analytic manner with the case control data set described.

One year ago a prominent publication reported that alcohol consumption may be a risk factor for breast cancer. Again, utilizing data from the multiphasic health examination within one health plan, the relationship between prior alcohol consumption and subsequent breast cancer risk was evaluated. Initially, a strong positive association with evidence of dose response was noted, but control for potential confounding factors reduced the risks markedly, and abolished the dose response relationship. There remained a statistically significant 40 percent elevation among those women who averaged three or more alcoholic drinks per day compared to nondrinkers. Within the last year also, a relationship found between cigarette smoking and lower luteal phase estrogen levels led to the hypothesis that smoking may have a protective effect on breast cancer incidence. Utilizing data from the multiphasic screening exam, no reduced risk was noted for smokers overall, and a more detailed analysis incorporating breast cancer risk factors confirms this finding. In order to test the hypotheses that the level of serum vitamin A may be inversely related to the risk of lung cancer, 156 cases of lung cancer were identified among persons who had participated in the multiphasic screening exams and had serum frozen and stored. The sera for these cases and 312 controls matched to the cases on age, sex, race, and smoking habit are currently being analyzed for serum retinol.

Because of an interest in time trends for site specific malignancy and a concern that these trends be related to changing demographic profiles, cancer incidence data from one prepaid health plan over a 20 year period are currently under analysis and being related to specific demographic and exposure information routinely obtained on a 10 percent sample of the population over the same period.

In one plan an active program of mammography has been conducted for a number of years. Utilizing information on 2,000 such women who filled out a form recording breast cancer risk factors and who were asymptomatic at the time of exam, the relationship between parenchymal patterns and risks of developing breast cancer was investigated, as well as the relationship between various parencymal patterns and breast cancer risk factors. A high risk parenchymal pattern is associated with an approximately three fold excess risk of subsequent breast cancer and this level of predictability persists for at least five years. In addition, most breast cancer risk factors appear also to be risk factors for high risk parenchymal patterns.

These types of studies are also useful in evaluating the relation between drug exposures during pregnancy and the risk of subsequent malformations or cancer in offspring. To evaluate the possibilities for such studies, an investigation of the relationship between hormonal exposures (oral contraceptives, hormonal pregnancy tests, and others) and the risk of limb reduction defects is being conducted with 70 cases and three controls per case.

A cursory evaluation was done of the charts of 224 patients with cervical cancer and a similar number of controls from one plan, to determine the risk associated with prior venereal conditions diagnosed within the plan. Relative risks of three fold were noted for a variety of venereal disorders, including genital herpes, with no particular condition showing any more prominent risks.

Prepaid plans with unit records also provide a special opportunity to evaluate the risks of malignancy in relation to diagnostic radiation. Controversy over the potential level of excess risk exists for leukemias, lymphomas and multiple myeloma. To address these concerns we abstracted the diagnostic radiology records of 663 adult patients who subsequently developed leukemia, 339 patients with nonHodgkin's lymphoma, and 254 cases of multiple myeloma and compared these to data for over

1,500 controls. Dosimetry estimates for each procedure were provided by the Radiation Studies Section and the data from two plans are currently under analysis. Efforts are now being made to include the third plan in this study in order to obtain more stability in the disease specific, dose response relationships currently being seen.

Finally, a complex protocol has been developed to investigate the relationships suggested between specific subtypes of benign breast disease, hormonal exposures including oral contraceptives and menopausal estrogens, and subsequent risk of breast cancer. This study is now being initiated within one plan.

The general aim of this project continues to be the establishment of a collaborative research project which provides the Branch with a resource whose priorities could easily be manipulated to rapidly evaluate hypotheses about environmental causes of cancer by analysis of information from prepaid plans in existence many years and covering large groups of patients having particular cancers and comparable unaffected individuals. In addition, this resource can be used for exploratory studies to uncover previously unrecognized associations which deserve further study. Another objective has been to explore the unique opportunities for record linkage within these plans and thus utilize data collected for other purposes for epidemiologic assessments of cancer risk.

The main value of this resource is to provide a framework where emergent hypotheses can be evaluated relatively quickly. To some extent, the specific objectives for the next four years will depend upon the nature of these hypotheses as they emerge. However, currently the specific objectives we plan on pursuing the first year of the project would be 1) further expansion of the study of interrelationships between subtypes of benign breast disease, a variety of hormonal medications, and the risk of breast cancer; 2) detailed investigations of the hormone endometrial cancer relationship among subgroups not well studied in the past, including studies of various hormonal exposures among young patients and among those with advanced disease; 3) evaluation of the relationship between coffee consumption and pancreatic and other malignancies among populations for whom data on coffee drinking information has been previously collected; 4) based upon the current feasibility study of the investigation of drug exposures during pregnancy, further studies of potential teratogenesis and transplacental carcinogenesis will be pursued. Specifically, the suggestion that in utero and early life exposure to barbiturates may risk factors for childhood brain tumors will be investigated.

Robert Hoover is the project officer.

"Is the division thinking of the three Kaiser groups as the chosen institutions to carry on these studies?" Board member William Haenszel asked.

"You're right, these three have a competitive advantage," Hoover said. "Clearly, there is an advantage of incumbency. But the intent is to open it up to competition. Five plans competed last time. Kaiser won because they had both inpatients and outpatients, and had been in existence since the 1940s. That is important, because it gives more time for cancer to develop in their patients. As time goes on, that has been less of an advantage. There are more plans out there capable of doing cancer studies. I hope they respond to the RFP."

"Is it possible you may miss some environmental cancer associations because the prepaid plans miss lower income people?" Board member Dietrich Hoffmann asked.

"The plans mainly include middle class working groups," Hoover acknowledged. "They do include medicare and medicade patients, but not in numbers relative to the population."

The concept was approved unanimously.

Mortality study of workers exposed to acrylonitrile—Proposed first year award, $456,000; total project cost estimate, $998,000, three years. This will be a new competitive procurement.

Acrylonitrile is a synthetic organic chemical used in the manufacture of acrylic fibers, acrylonitrile butadiene styrene (ABS) and styrene acrylonitrile (SAN) resins, adiponitrile, nitrile elastomers, and other products. Principal exposure occurs among workers in acrylonitrile production and user industries. Over two billion pounds of acrylonitrile are produced annually and the National Institute for Occupational Safety & Health has estimated that 125,000 persons are potentially exposed to acrylonitrile in the workplace. Acrylonitrile is mutagenic in bacterial test systems and carcinogenic in rats following oral administration and inhalation, producing tumors of the brain, forestomach and Zymbal gland. Human exposure is known to result in acute toxic effects and there is limited epidemiologic evidence suggesting elevated cancer risk among acrylonitrile exposed workers. A number of studies implicate the lung as the principle cancer site, although the observed numbers are small. Excess cancers of the stomach and lymphatic system have also been reported, while other studies found no increased cancer risk or results were equivocal due to small population sizes and insufficient control for other exposures. None of the studies have adequately assessed the confounding effect of smoking habits on the cancer findings.

In response to the suggestive evidence of the human carcinogenicity of acrylonitrile, an eight member group of industry officials representing companies using or producing acrylonitrile met with NCI scientists to discuss the possibility of participating in an industrywide epidemiologic study. Results from an NCI survey of the acrylonitrile industry indicate that approximately 14,000 workers, employed between 1950 and 1970 in five companies comprising 11 facilities, are available for study. Because of the OSHA standard regulating acrylonitrile exposure levels in the workplace, detailed industrial hygiene monitoring data are expected to be available from all facilities beginning with 1977. The early monitoring data precede industry efforts to reduce acrylonitrile exposures, and should be representative of levels in earlier years.

These data, combined with the collection of individual smoking information, will provide a unique opportunity to evaluate the association between occupational acrylonitrile exposure and cancer risk.

A contractor will be competitively selected to undertake all phases of data collection and management, vital statistics tracing, industrial hygiene monitoring, and pathology review for this project.

Objectives:

1. To determine the cancer mortality experience of workers exposed to acrylonitrile, and to make comparisons with the cancer mortality prevailing in the general U.S. population and in a subgroup of the study population having little or no acrylonitrile exposure.

2. To obtain sufficient exposure estimates to allow a thorough evaluation of dose response relationships for various causes of death. This may require industrial hygiene sampling of current acrylonitrile levels in the workplace, as well as obtaining data from monitoring done in the past.

3. To investigate the interaction of acrylonitrile exposure with host factors (e.g., age, race, sex) and smoking habits in relation to cancer mortality.

Methods: A retrospective cohort mortality study is planned. This approach is needed to identify specific types of cancer that may be related to acrylonitrile exposure, based on experimental and epidemiological observations. A minimum size of 7,000 exposed workers will allow detection of a 1.4 fold risk of lung cancer mortality, a 1.9 fold risk of stomach cancer mortality, and a 2.0 fold risk of brain cancer mortality with 80 percent power. However, it is expected that the total study population, including workers with little or no exposure, will likely reach 14,000 individuals.

Employment, medical and other appropriate records maintained by participating companies will will be abstracted for all study subjects. Information on use of tobacco will be gathered from a sample of active employees, next of kin decedents, and corporate medical records. Estimates of present and past workplace exposure levels to acrylonitrile will be developed from current and historical monitoring data supplemented with information regarding manufacturing process changes and personal protection practices. Intensity, frequency, and duration of acrylonitrile exposure will be assessed for each job within the various plants

Current vital status of study subjects will be determined and death certificates will be obtained for all decedents and coded by an experienced nosologist at NCI. Pathology specimens/slides for lung and brain cancer decedents will be obtained from hospitals, when available, and reviewed by a consultant pathologist. Data analyses will be conducted by NCI staff. Dose effects, disease latency, temporal aspects of exposure, and smoking interactions will be evaluated.

Barry Miller and Aaron Blair are the project officers.

Board member Carl Shy, informed that the study was being undertaken at the suggestion of industry, commented, "It is amazing that industry has come to scientists and asked them to do a study. It is even more amazing that they came to federal scientists."

Noncompetitive contract projects which received concept approval were:

Test of the usefulness of IRS occupation codes in determining mortality differentials through the Continuous Work History Sample maintained by the Social Security Administration. The work will be performed by the Internal Revenue Service at a total estimated cost of $350,000.

Nutrition intervention trial in Linxian, China. The Chinese Academy of Medical Sciences will carry out a randomized trial to evaluate the usefulness of multiple vitamin and mineral supplements in prevention of esophogeal cancer. DCE will contribute a total of $1.9 million over five years; the Div. of Cancer Prevention & Control also will contribute $350,000 a year.

International radiation study to evaluate the risks of radiation exposure in cervical cancer patients in Europe. This is a no cost extension of a contract with the International Agency for Research on Cancer which started in 1981.

Evaluation of carcinogenic risk of chemicals to humans. This will continue for five more years, at an estimated first year cost of $572,000, NCI's support for IARC publication of monographs on chemicals tested for carcinogenicity, identifying gaps in knowledge uncovered in preparation of the monographs, and publication of a compendium on chemicals tested for carcinogenicity.

Development of a national data base on body burden of toxic chemicals including carcinogens. This will continue for four more years collaboration with the Environmental Protection Agency on the project, at a total estimated cost of $1.2 million.

Etiology of tumors in bottom dwelling marine fish. This will be a new three year study by the National Oceanic & Atmospheric Administration at a total estimated cost of $690,800.

Breeding and production of 129/J and NFR mice; inoculation of viruses and cells; monitoring of animals; standard autopsies, including histopathology. This will continue for five more years the contract with the California Dept. of Health Services at a total estimated cost of $738,934.

The Cancer Letter _Editor Jerry D. Boyd

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