THE CANCER LETTER

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SEER PLACES SURVIVAL NOW AT LEAST AT 45 PERCENT, COULD BE AS HIGH AS 50 PERCENT FOR 1973-79 PATIENTS

Latest data from NCI's Surveillance, Epidemiology, and End Results (SEER) Program provide evidence which not only supports Vincent DeVita's recent statements that 45 percent of cancer patients are curable, but that survival is even better than that and may be as high as 50 percent.

The NCI director has been using the 45 percent figure in testimony

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In Brief

DRCCA BOARD SPLIT ON GUIDELINES FOR CCOP REMAINS UNRESOLVED; CHOP IMPLEMENTATION TALKS STARTING

NCI IS STARTING negotiations with the 23 Community Hospital Oncology Program contractors for the implementation phase of the program now that some are completing their planning. Donald Buell, program director for medical oncology and community activities in the Div. of Resources, Centers & Community Activities, said that "for the most part, they seem to be doing pretty well. They seem to be in better shape than the COPs were at a similar stage, probably because of the upfront effort." Buell said some of the 23 are struggling, but all have their guidelines set up, and "we don't anticipate losing any." Implementation will be for two years. . . . **MEANWHILE, THE SPLIT** on DRCCA's Board of Scientific Counselors over guidelines for the new Community Clinical Oncology Program (***The Cancer Letter***, Oct. 30) has not been resolved. DRCCA Director Peter Greenwald said the Board's Subcommittee on Community Activities would try to reach an agreement through either a conference phone call or a meeting prior to the next Board meeting in January. At issue is the determination of Assn. of Community Cancer Center representatives that community hospitals play the predominant role in the program vs. the view of the subcommittee chairman, Charles Moertel, that larger centers and cooperative groups be permitted to compete on equal terms. . . . **JANE HENNEY**, who had been special assistant for clinical affairs in the Div. of Cancer Treatment, is now acting deputy director of NCI. Henney, a medical oncologist, has been performing many of the tasks usually assigned to that office for several months. Director Vincent DeVita told the National Cancer Advisory Board Monday that Henney was his acting deputy. His nomination for permanent deputy director is awaiting action by HHS Secretary Richard Schweiker. . . . **ORRIN HATCH** (R.-Utah), chairman of the Senate Labor & Human Resources Committee, postponed hearings scheduled for this week on food safety law amendments until next year. One change Hatch is considering would soften the Delaney Amendment to permit regulation based on risks. Consumer activists are gearing up for a fight.

NEW SEER DATA ON PATIENTS DIAGNOSED FROM 1973-79 SHOW IMPROVED SURVIVAL

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before Congress and in interviews. He has been careful to say that that number represents patients who are "curable" rather than those who actually "survive."

The new SEER data relate more to survival, although DeVita still used the more cautious term. These data are based on patients diagnosed from 1973 through 1979. They reflect the continuing improvement in survival which was estimated in the late 1950s and early 1960s to be out one-third of cancer patients.

The optimistic 50 percent figure is based on assumptions that are open to challenge. DeVita acknowledged that in his statement presented at the National Cancer Advisory Board Monday:

"The National Cancer Institute closely monitors the survival experience of cancer patients. A summary report, published in 1976, showed that five year relative survival for white patients diagnosed between 1967 and 1973 was 41 percent. These statistics were based on followup analyses conducted at three hospital based cancer registries and one population based registry.

"Based on an exhaustive review of published reports from clinical trials and a review of the literature, I recently estimated that 45 percent of the 785,000 patients diagnosed with serious cancer in 1980 are curable. My estimate also was based on the assumption that physicians are now applying what we have learned in the past 10 years about the use of the combined treatments of surgery, radiation therapy, and chemotherapy.

"These curable patients include 219,850 with localized disease who are curable by surgery alone; approximately 90,000 patients curable as a result of radiation therapy and surgery; and 46,000 patients curable as a result of using chemotherapy alone or with surgery and/or radiation therapy. None of the figures include early skin or cervical cancers, which are nearly 100 percent curable.

"Now, for the first time, five year survival statistics from NCI's SEER Program are available for patients diagnosed since 1973. They confirm and exceed our recent estimate. The message is clear: patients with cancer are living longer now than ever before.

"SEER registries collect information on the occurrence of cancer and the survival experience of patients from a large, population based sample of the United States population. The new statistics show that 46 percent of white patients diagnosed with cancer from 1973 through 1979 are curable. When all races and sexes are combined, the figure is 45 percent. These data are conservative. A more optimistic calculation, based on the same data, results in a 50 percent five year survival for white patients and 49 percent for both races. Complete five year followup is available at present only for patients diagnosed in 1973 and 1974, and only for all cancer sites combined, so these figures are preliminary.

"The lower figure of 46 percent is considered conservative because patients who have not been followed for the full five years or who could not be located to check on their status were assumed to have the same survival experience as those who were actually observed for the full five years. To the extent that the survival experience of cancer patients continued to improve for patients diagnosed since 1975, these numbers may underestimate the probability of five year survival for patients being diagnosed today. In addition, the higher figure of 50 percent assumes that the unlocated patients are all alive. A great proportion of unlocated patients can be expected to be alive, because patients who are free of disease after several years are less likely to have their status recorded regularly by a tumor registry.

"Unfortunately, it takes years to know how new therapies will affect the long term survival of patients. For the past decade, we have been more successful in treating cancer patients than we thought, because of the lag time between diagnosis and therapy and five year followup.

"Because of the improvement in survival rates, an estimated additional 320,000 patients diagnosed with serious cancers in the years from 1973 through 1981 will survive their disease at least five years. I believe these gains are real, and that they are due to the progress we have made in the treatment of cancer since 1970. In coming months, we expect to have more updated information on survival from the SEER Program. This will include more detail on the types of cancer that have shown improvement, and detailed information for black patients.

"Five year relative survival is defined as the probability of escaping death due to cancer for five years following diagnosis. The rates are calculated using an actuarial, or life-table, method and therefore include information on patients under observation for less than five years. Except for cancers of the breast, prostate, and kidney, five year survival is a reliable, though not absolute, indicator of the probability of cure in cancer patients. Of patients diagnosed from 1950-1954 and followed by NCI for 20 years, 85 percent who lived for five years after a diagnosis of cancer achieved a 20-year survival from their disease," DeVita's statement concluded.

The 1967-73 data were compiled in 1976 in Cancer Patient Survival Report No. 5, which included complete five year followup on patients diagnosed through 1968. Those data were contributed by the California Tumor Registry in Berkeley, the Connecticut Tumor Registry, and two teaching hos-

pitals—the State Univ. of Iowa Hospital, and Charity Hospital of Louisiana in New Orleans. Only the Connecticut Tumor Registry is population based—examining the cancer experience of all patients diagnosed in a specific geographic area.

Report No. 5 found that five year survival for whites was 41 percent and 40 percent for all races combined.

The 1981 SEER data statistics, showing five year survival at 46 percent for whites and 45 percent for all races were contributed by population based registries in Connecticut, New Mexico, Utah, Hawaii, Atlanta, Detroit, and Seattle-Puget Sound.

There are skeptics (or realists, perhaps) who contend that comparing mid to late 1970s five year survival with that of the 1960s and early 70s is not really comparing apples with apples. The remarkable phenomenon being observed with many cancers of earlier detection and diagnosis may be the basis for some unfounded optimism, the skeptics say. A breast cancer patient found with the disease two years earlier in 1979, by mammography, by more enlightened use of self examination, or whatever, naturally will live two years longer *from diagnosis* than she would have in 1969 diagnosed at a stage two years later.

Stage by stage comparisons also may be deceptive. Staging has become more precise and better defined, and some patients who earlier would have been considered borderline stage 1 are being classified stage 2, thus improving the survival statistics of both groups.

NCAB member William Powers disagreed with the assumption in DeVita's report that patients lost to followup may be assumed to be alive. "I have found that one of the reasons patients don't come back for followup is that they are dead," Powers said.

DeVita insisted that "the data are all there in the final figures." He said that he agreed 50 percent survival may be high, but that 46 percent probably is low. "I will wager that before we get the 1980 data, it will be at 50 percent."

OMB CUTTING NCI 12 PERCENT FOR FY 82 UNTIL FINAL BUDGET HAS BEEN ADOPTED

The impact of the 12 percent cut in the 1982 fiscal year budget demanded by President Reagan was beginning to sink in this week when NCI was required to implement the cut by announcing that:

- Noncompeting grant renewals will be renegotiated, with grantees required to submit new budgets 12 percent less than originally negotiated.
- No new awards will be made.
- Competing renewals will be funded at the preceding year's level.
- No supplements will be made to grants, although a few exceptions will be permitted.
- These restrictions will apply to all grants—R01s, P01s, and cancer center core grants—except research training and career development, which will be funded at recommended levels. They will remain in effect until a final budget has been approved by Congress and the President.

NCI Director Vincent DeVita passed that bit of bad news along to the National Cancer Advisory Board this week. Orders to make those budget reductions came from the White House Office of Management & Budget, and "we have no choice but to go ahead with those instructions," DeVita said.

The sad saga of the 1982 budget began with the Carter Administration budget request of $1.040 billion (one billion, 40 million), which Reagan pared to $1.025 billion. That still would have been $25 million more than NCI was supposed to have received in 1981, with a congressional appropriation of just a few dollars less than $1 billion even. But Reagan pushed through a rescision, and NCI wound up 1981 with $989.3 million.

In the interval between Reagan's original budget and the end of the 1981 fiscal year, the economy worsened, taxes were cut, the deficit grew, and OMB panicked. The White House decided that the entire federal budget for the 1982 fiscal year which started Oct. 1 had to be cut back 12 percent. Congress had made a bad situation nearly intolerable by failing to push through the regular appropriations bills for the new fiscal year, so it had to get out an interim financing measure, a "continuing resolution," to keep the government going through Nov. 20. That measure held spending at the 1981 level (or the President's budget, whichever was lower) for those agencies which did not have a completed appropriations bill. That kept NCI at $989.3 million.

NCI could have struggled along with that amount without too many immediate problems, although if that turns out to be the final 1982 total it will severely impact the Cancer Program. But the situation is far worse than that.

The White House is holding to the 12 percent reduction, and Reagan's successful veto of the new continuing resolution, which would have extended into next June, made it more likely that a cut of that size eventually will be approved.

The second continuing resolution will expire Dec. 15. Anticipating that the President will succeed in getting his 12 percent or something like it, and aware that if the muddled situation went too far into the fiscal year with agencies permitted to spend at higher levels implementing the reduction might be impossible, OMB simply ordered everyone to comply with the reduction as if it were already in place.

For NCI, that means that, if the 12 percent cut holds for the entire year, it will receive $903 million. That would be $86 million less than the Cancer Program spending in 1981, and less even than in 1980.

The result could be disastrous for many of those who are making vital contributions to the Cancer

Program. No new grants; 12 percent reductions in existing budgets; competing renewals held to the previous year's budget; a payline cutoff at the 160 level—that adds up to top flight investigators losing their funding, a stifling of new ideas, a host of existing programs being dismantled, and momentum lost.

At the NCAB's October meeting, DeVita had asked members to help him decide where to apply the cuts if they had to be made. Harold Amos, who is also a member of the President's Cancer Panel, resisted, saying the Board should not only oppose as vociferously as it can any cuts but should refuse to have any part of applying them. "That makes us a party to actions which we know will set the Cancer Program back years," he said.

Board Chairman Henry Pitot had sent a telegram to the President objecting to any budget reduction, and Pitot said this week he had received "a cordial letter from a member of the President's staff" in response.

Amos pointed out that Congress still could salvage the situation. If a regular HHS appropriations bill is passed, it is possible it would be cut back enough for Reagan to accept and still not reduce NCI's funds so drastically. "In fact, Congress has been on our side," Amos said. "We have very strong support in Congress. Unless we come down on the side of not accepting cuts, it will weaken our case by jumping on the bandwagon for cuts. If cuts are imposed, we should have no part in allocating them."

DeVita had sent a questionnaire to each Board member asking for advice on how to apply any cuts. "There were only eight or nine responses (from the 18 member Board)," he said. "That means the rest are leaving it to the director and staff how cuts should be made."

"We should remain unalterably opposed to cuts," Board member Rose Kushner said. "They just launched a new submarine, one that cost $1.4 billion without its 24 warheads. One billion is not too much for cancer."

Frederick Seitz, who is chairman of the Board's Planning & Budget Subcommittee, has taken the position that the NCAB should go along with whatever the Administration requests. "We're here to serve the President," he said. "I don't know if we should be unalterably opposed to cuts. NIH survived cuts of 15 percent in the past. I agree with the President, that inflation is our worst enemy."

Seitz suggested that Board members who cannot bring themselves to accept the budget reductions should consider resigning.

Pitot said he was "dismayed" by the fact that only half of the members responded to the request for allocation advice.

"I refused to participate and I called to say so," Amos said. "In the first place, it could not be done well by mail without discussions. Secondly, I oppose the cuts and refuse to participate in the process of making them. I also don't agree that in a participatory democracy, if you don't agree with someone's harebrained idea, you should resign."

Armand Hammer, chairman of the President's Cancer Panel, said he would continue to oppose the 12 percent cut in NCI's budget, "or any cut. If this country were to suffer 420,000 casualties in a military action, the people would demand that we do something about it."

"LOCAL UNIVERSITY" WILL COMPETE FOR PART OF FREDERICK CONTRACT

A "local university" will compete for the research contract at the Frederick Cancer Research Facility and possibly for the other two major contracts offered in the recompetition, the National Cancer Advisory Board was told this week.

Peter Fischinger, NCI associate director with responsibility for overseeing FCRF (now called a "facility" rather than a "center"), did not identify the university. Johns Hopkins Univ. was the only academic institution to send representatives to the preproposal conference, however.

Fischinger said the incumbent, Litton Bionetics Inc., was preparing to compete for all three major contracts. The two in addition to research are operations and technical support and animal production. At least one other company will compete for the support contract and possibly for all three, and several companies have indicated they will compete for the support contract only, Fischinger said.

The two small business set asides, for operation of the library and for computer services, are certain to draw competing proposals.

The deadline for proposals has been extended to Dec. 14.

This will be the second time the Frederick contract has been recompeted since LBI won the initial five year award in 1972. The recompetition in 1977 was on the same basis as the first time, with everything in one package. Other organizations felt it would be impossible to compete against LBI, and NCI had to accept the embarrassing, and somewhat humiliating, situation in which it had no choice but award the contract to Litton.

Splitting the job into five separate contracts was specifically intended to stimulate some competition this time around, and that appears to have succeeded.

Fischinger said that some potential competitors still felt it was not worth the trouble to go up against Litton and have "bowed out." It is a problem always faced in competing a GOCO (government owned, contractor operated) contract, he said. Complaints heard are, "We don't get enough information, the incumbent has a lot of information we don't have," and "the incumbent is favored," Fischinger said.

"Historically, that is true," Fischinger said. Incum-

bents at other GOCO facilities almost always win recompetitions.

NCI Director Vincent DeVita said, "The competition will be complicated. We are setting precedents for GOCO competition."

NCI has tried very hard to make it possible for other organizations to compete, including a provision in the RFP that new proposals could include suggestions for research not presently being done at FCRF. Litton scientists are engaged primarily in a basic cancer biology research program as well as physical and biological carcinogenesis.

LBI's proposal, of course, will include the present scientific staff. Proposals of others may assume that the Litton scientists would switch to the successful proposer. To make that a feasible alternative and help make the competition more fair, Litton has agreed that any employees who do change to a new contractor may take their pension benefits with them.

NUTRITION, DISEASE ORIENTED CONTRACTS SHOULD GET AX FIRST, DCT BOARD SAYS

The Board of Scientific Counselors of NCI's Div. of Cancer Treatment has recommended that budget cuts be applied selectively if necessary and that nutrition research and disease oriented contracts be the first to feel the ax.

DCT Acting Director Bruce Chabner told the National Cancer Advisory Board this week that a survey of his Board gave those two items the lowest priority. Drug development and the Biological Response Modifiers Program received the highest priority and should be spared cuts, if possible, the survey determined.

DCT's intramural programs, the cooperative groups, and radiation research were in the middle, Chabner said. The DCT Board suggested those areas should suffer only average cuts, if any have to be made.

Chabner indicated he agreed with his Board. "I don't have confidence in nutrition, and I do have in new drugs that are coming along. The intramural program is strong, but we can probably compensate by cutting weaker areas."

Chabner said that with a 12 percent cut, "we couldn't protect all the high priorities. We would lose some quite good program projects and R01s. At a 167 (priority score) cutoff, we would lose some very worthwhile activities. Contracts would go first, with the cooperative groups and intramural program both taking sizable cuts."

NCI Director Vincent DeVita pointed out that the three main contract supported efforts of the division were the neutron generators, clinical trials, and drug development.

Chabner and DCT Board Chairman Samuel Hellman described the division's various activities and role of its Board as part of the NCAB's annual program review. Chabner referred to the Board's action last October in dropping DCT contracts for acquisition of plants in the search for natural anticancer drugs.

"In 25 years, we have not obtained anything clinically useful from the contract program (to acquire plants)," Chabner said. "We felt it was better to put the $2.5 million a year into RFAs for grants. We haven't deemphasized plants completely. We get many voluntary submissions."

"I have received more mail on this than anything else recently," DeVita said. "Technology is increasing around the world, there are more people doing plant collections and submitting them voluntarily. We will still evaluate them."

NCAB member Sheldon Samuels suggested that the pharmaceutical industry should help support evaluation of new drugs. DeVita said that many compounds are submitted for evaluation by organizations other than pharmaceutical firms and have no commercial interest in them.

Chabner said the Biological Response Modifiers Program, which received $14 million in 1981 fiscal year, was scheduled to get $21 million in 1982. The additional funds would go into grants, more staff members to run the growing program, and phase 1 and 2 studies of interferon, thymosin, and monoclonal antibodies.

Board member Morris Schrier objected to a $300,000 a year contract for support of various DCT activities, workshops and meetings. "Wouldn't this be more economical to do by hiring your own personnel?"

"I'm not sure it would," DeVita answered, "but even if it were, we don't have that number of positions available. Considering the ebb and flow of the workload, contracts for this sort of work are not necessarily inefficient."

Samuels said he wanted to "associate myself with Morris' instinctive reaction to contracting for the appearance of saving money when there are no actual savings. You are seeing the reaction of people who have to defend the policy." Samuels has strongly opposed use of contracts to avoid hiring of permanent employees by the government.

"I don't agtee with you," DeVita said. "We have government regulations which make us justify use of contracts."

"There may be routine functions one day, with one program or at one institute, and one day somewhere else. There is no central facility at NIH which could provide those services. When you have to have a contract to answer the phone or duplicate papers, that is not efficient and no business is run that way."

Board member Rose Kushner asked if there was money in the clinical trials programs for nurse oncologists. Chabner noted that the cooperative groups, individual investigators and program projects all fre-

quently support nurse oncologists. Kushner suggested that a nurse oncologist be appointed to the DCT Board.

Board member William Powers suggested that a radiologist be appointed to the Board and was assured that one would be soon. "While we try to have experts from various areas, our Board has been very good about not voting their specialties," Hellman said. "We try to be more catholic. Whether that will be true in the face of a 12 percent cut remains to be seen."

Powers said the transfer of cooperative group support from grants to cooperative agreements "has caused a lot of reaction. I have received phone calls from people who are not receptive to cooperative agreements. I have three questions. When was the Board of Scientific Counselors involved in the change? Why are phase 1 and 2 studies not being moved to cooperative agreements (from contract support)? Is it possible to put these concerns on the agenda of a Board meeting?"

"The answer to the last question is yes," Hellman said. The decision to move to cooperative agreements was one of the suggestions that came out of the 1979 clinical trials review conducted by the DCT Board. "It was clearly discussed with the Board, although I can't remember that the decision was unanimous." Phase 1 and 2 studies require contract support because of the degree of coordination needed, Hellman said.

Other items brought up at the NCAB meeting included:

• Armand Hammer, chairman of the President's Cancer Panel, said that developments with hybridomas "are the most exciting thing before us" and announced that the Salk Institute, of which he is chairman of the board, will hold an international hybridoma seminar next March.

• Despite the discredited *Washington Post* articles and 20/20 TV program, "if you add everything up, press coverage overall has been fair and accurate," DeVita said. "NCI is the most scrutinized agency in government. We've been looked at upside down, head to toe and sideways. We've come out pretty well, I think."

• Board member Frederick Seitz said the NCAB "is grateful to Dr. DeVita and his staff for the eloquent and forthright way they handled all the criticism."

The Board Subcommittee on Board Activities & Agenda, meeting to develop agendas for the February and May meetings, decided that:

–Henry Kaplan of Stanford, one of the world's leading authorities on human hybridomas, would be invited to speak on that topic at the February meeting. Kaplan subsequently accepted the invitation and told Board Chairman Henry Pitot he will "tell it like it is, with the plusses and minuses."

–The Organ Site Subcommittee will meet prior to the February meeting to hear the report of the ad hoc committee which reviewed all four organ site projects last week. That meeting will be in closed session, but the subcommittee's report to the Board, which will include any recommendations coming out of the review, will be in open session.

–The February meeting will include a report from Board members Harold Amos and LaSalle Leffall on cancer and minorities, and a detailed report from the Nutrition Subcommittee by its chairman, Maureen Henderson.

Amos said the major emphasis of the May meeting will be on the review process.

Samuels decided to drop his recommendation that the NCAB scheduled regional meetings around the country. "I don't spot any support for that," he said. "I won't beat a dead horse."

NCI CONTRACT AWARDS

Title: Bioassay of triamterene and propantheline bromide

Contractor: International Research & Development Corp., $115,425.

NEW PUBLICATIONS

The following "Oncology Overview publications, selected abstracts on particular subjects compiled by the International Cancer Research Data Bank, are available from National Technical Information Service, 5285 Port Royal Rd., Springfield, Va. 22161. Order by title and publication number:

Radionuclide Bone Scans in the Diagnosis and Staging of Cancer, $6 North America, $12 foreign; Nitroheterocyclic Compounds as Hypoxic Cell Radiosensitizers, $4.50 North America, $9 foreign; Diagnosis and Treatment of Mycosis Fungoides, $5.25 North America, $10.50 foreign; Small Cell Carcinoma of the Lung, $6 North America, $12 foreign; Tumor Localization with Gallium, Radiolabeled Bleomycin, Thallium, Selenium, Carbon and Nitrogen Radionuclides, $6 North America, $12 foreign; and Carcinoembryonic Antigen (CEA) in the Clinical Diagnosis and Treatment of Colorectal Cancer, $6.50 North America, $13 foreign. North America in the above refers to U.S., Canada and Mexico, foreign encompasses all other countries.

"Surveillance, Epidemiology and End Results: Incidence and Mortality Data, 1973-1977," edited by John Young Jr., Constance Percy, and Ardyce Asire. A 1,082 page compilation of SEER Program findings prepared by the Demographic Analysis Section of NCI's Div. of Cancer Cause & Prevention. Order from Supt. of Documents, U.S. Government Printing Office, Washington D.C. 20402, using title and NCI Monograph No. 57, $23, hardback only.

"The International Cancer Patient Data Exchange System," UICC technical report series volume 58. A two year progress report. Order from Hans Huber

Publishers, Langgassstrasse 76, 3000 Bern 9, Switzerland, 62 Swiss francs.

"Nutrition and Metabolism in Cancer," an international workshop held in 1979 in Freiburg, edited by Reinhold Kluthe and Georg-Wilhelm Lohr. Thieme-Stratton Inc., 381 Park Ave. South, New York 10016, $19.95.

"Combination Antibiotic Therapy in the Compromised Host," edited by J. Klastersky and M. Staquet, $28.50; "Lymphokines and Thymic Hormones: Their Potential Utilization in Cancer Therapeutics," edited by Allan Goldstein and Michael Chirigos, $38; "Mediation of Cellular Immunity in Cancer by Immune Modifiers," edited by Michael Chirigos, Malcolm Mitchell, Michael Mastrangelo, and Mathilde Krim, $31.50; and "Clinical Interpretation and Practice of Cancer Chemotherapy," edited by Ezra Greenspan, $48 (tentative). Raven Press, 1140 Avenue of the Americas, New York 10036.

"Cancer: An Introduction," by William A. Creasey. An introductory text on principles of cancer biology and pharmacology for undergraduate and graduate students. Oxford Univ. Press, $18.95, $12.95 in paperback.

"Prenatal Diethylstilbestrol Exposure: Recommendations of the DESAD Project for the Identification and Management of Exposed Individuals," published by NCI's Office of Cancer Communications. Intended primarily for physicians. Free, from NCI, OCC, Bldg. 31 Rm. 10A21, Dept. SC, Bethesda, Md. 20205, phone 800-638-6694.

NTP BOARD GIVES CONCEPT APPROVAL TO RECOMPETITIONS, ONE NEW STUDY

The National Toxicology Program Board of Scientific Counselors has given concept approval to the recompetition of two contract supported projects and to a new study, to be funded through interagency agreements. The three contracts will cost an estimated $1 million a year.

The contracts to be recompeted are:

–Salmonella mutagenicity testing. Present contractors are Case Western Reserve Univ., EG&G Mason Research Institute, and SRI International. NTP proposes to award four contracts in December, 1982, for the testing of 1,600 samples for mutagenicity in salmonella. Each contractor will test 100 coded chemicals per year for four years, using a standardized protocol, at an estimated total cost each year of $480,000 in year one, $530,000 year two, $580,000 year three, and $640,000 year four.

Chemicals selected for testing in salmonella are those which have been tested or are on test for carcinogenicity by NTP, chemicals nominated for NTP toxicity and carcinogenicity testing by NTP or other government agencies, and chemicals of interest to the NTP because of structural or other considerations.

Results from salmonella testing are used to make decisions regarding further genetic testing of the chemicals. NTP's narrative justification:

The salmonella test has become widely accepted as a good indicator of a chemical's mutagenicity in higher organisms and carcinogenicity. It is capable of identifying chemicals that produce gene mutations but is not capable of detecting chemicals that produce other types of genetic damage. When performed using a standardized protocol, the test yields consistent and reproducible results within and between laboratories. If a chemical is mutagenic in salmonella there is a high probability that it will be carcinogenic in an adequately conducted rodent bioassay. However, if a chemical is not mutagenic its noncarcinogenicity is far from certain. If a chemical is not mutagenic in salmonella it is selected for testing in CHO cells for the ability to produce chromosome aberrations and sister chromatid exchanges (the present capability of this system in the NTP precludes testing all salmonella negative chemicals). Salmonella mutagens are tested in drosophila to determine whether they can affect the male germ cells and produce sex-linked recessive lethal mutations. In the future, nonmutagenic chemicals will also be tested for their ability to induce mitotic and/or meiotic nondisjunction.

The current size of the salmonella data base–over 425 unique chemicals representing over 550 salmonella tests–allows studies of inter- and intralaboratory reproducibility, structure-activity relationships and comparisons with other toxicological endpoints. By the end of the present contract period it is anticipated that data and results on over 700 unique chemicals will be in the salmonella data file, with 100-200 of these also tested in drosophila and/or CHO cells.

Continuation of the salmonella testing program will allow the NTP to increase the number of chemicals tested and will result in the formation of a unique and unparalleled data base which can be used by NTP personnel and other researchers for structure-activity studies, comparative mutagenicity studies and mutagenicity-carcinogenicity correlations. The individual data will be useful in making decisions on chemicals to be tested for carcinogenicity, mutagenicity or other toxicological endpoints and in the interpretation of carcinogenicity data. All results generated by this program will be published in the NTP Bulletin and in peer-reviewed scientific journals.

–Mouse lymphoma bioassay. Present contractors are SRI International and Litton Bionetics. NTP proposes to award two contracts each having the capacity for testing 50 chemicals a year. The priorities for testing will include those chemicals of direct interest to NTP as candidates for the long term carcinogenicity bioassay, data on chemicals required to complete the generation of the NTP data base, and chemicals which by virtue of their structure activity or other biological effects are useful in further validation of this system. Estimated cost is $500,000 a year for four years. The narrative:

A dual laboratory evaluation and validation of the mouse lymphoma mutagenesis system is now in the final year of a five-year effort initiated in 1976 through NCI's Carcinogenesis Testing Program and subsequently supported by NTP. This effort has resulted in the development of a standardized protocol and the definition of acceptability criteria for the data generated in this system and has generated both intra- and interlaboratory reproducibility of this assay. While only a relatively limited number of chemicals has been tested in this contract effort, the results have shown a high degree of correlation with the results of salmonella/mutagenicity and other muta-

genicity assays. In addition, results published from other laboratories indicate that the mouse lymphoma assay may be useful in detecting some types of potential mutagens which are not active in the salmonella assay system. The assay, therefore, may have its greatest use to the NTP in providing a supplemental mutagenesis assay system for chemicals which are ambiguous or negative in other systems or other available information are suspected to have mutagenic potential. Two other principal mammalian cell mutagenesis assay systems utilizing hamster cells (CHO and V79) have also been proposed for use in screening for potential mutagens. In addition to the fact that the program has developed a good deal of experience with the mouse lymphoma cell system, this assay has additional advantages of being a suspension assay with a lower expression time which allows the assay to bae run with less manpower and therefore a lower cost.

The new study approved by the Board will be an assay of chemicals for induction of heritable translocations in mice. It would make use of studies presently underway at the National Center for Toxicology Research and at SRI International, the latter supported by the Environmental Protection Agency. Cost to NTP would be $150,000 for the 1982 fiscal year and $175,000 for 1983.

RFPs AVAILABLE

Requests for proposal described here pertain to contracts planned for award by the National Cancer Institute unless otherwise noted. Write to the Contracting Officer or Contract Specialist for copies of the RFP, citing the RFP number. NCI listings will show the phone number of the Contracting Officer or Contract Specialist who will respond to questions. Address requests for NCI RFPs to the individual named, the Blair Building room number shown, National Cancer Institute, 8300 Colesville Rd., Silver Spring, Md. 20910. RFP announcements from other agencies reported here will include the complete mailing address at the end of each.

RFP NCI-CM-27513

Title: *Computerized literature surveillance of natural products*

Deadline: *Approximately Feb. 15, 1982*

NCI's Div. of Cancer Treatment is seeking sources to perform a project that requires surveillance of chemical, biological, and biomedical literature for natural products or extracts of natural products which may be of interest to NCI as potential anticancer agents by virtue of their chemical structures or reported biological activities.

The project will include both comprehensive surveillance of current literature and limited retrospective searches of past literature on compounds or organisms or plants of special interest. The current literature searches should give chemical taxonomic, geographic and pharmacological data. The address of the senior author is given.

Search capabilities must include the ability to: a) conduct substructure searches on a wide variety of natural products structures which entails access to a chemical data base which is searchable by chemical names and common names of compounds as well as structural fragments. b) identify biological sources of compounds of interest including nomenclatural synonyms of these sources, collection location, isolated yields and criteria of identity. c) search the literature for biological activities of natural products (both crude extracts and pure compounds) which may relate to anticancer activity. d) identify new natural product structures which appear in the literature and synthetic analogs of natural products. e) identify natural products of plant, microbial and animal origin.

All of the above data must be entered into a computer system for subsequent retrieval by any of the parameters involved including chemical structure or partial structure, biological activity, common and chemical names of compounds and sources organisms or synonyms thereof.

The principal investigator should be trained at the PhD level in organic, medicinal, or natural products chemistry or a closely related discipline and must be familar with natural products structures and chemical searches as well as having background and experience with biological activity preferably in the cancer area. The PI should also have at least two years' experience in working with computerized literature surveillance and retrieval.

The staff members to be used on the project must be trained at the bachelors level in either chemistry, library work, or computer programming. The mix of staff used on the project must encompass all of these areas.

Computer facilities must be adequate to perform searches as required by the scope of work. Retrieval of data must be available based on input of chemical names and common names of compounds, chemical structure fragments, names of organisms, and types of biological activity. The availability of the computer to the contract must be clearly defined.

A large library with extensive holdings in the areas of biology, chemistry, microbiology, pharmacology, biochemistry, and medicine is required for the project. The quantity of the journals and abstracting services available will be a major factor in evaluation of the proposals.

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