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THE CANCER LETTER

Vol. 7 No. 4

Jan. 23, 1981

Subscription $125.00 per year

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CARTER IN LAST BUDGET ASKS FOUR PERCENT INCREASE FOR NCI, BUT THEN SEEKS $13.5 MILLION RESCISSION

The Carter Administration's last budget request unveiled last week, for the 1982 fiscal year which starts next Oct. 1, included a modest four percent increase for NCI, to a total of $1.04176 billion—that's one billion, 41 million 760 thousand. Not much of an increase but a little better than Carter's previous stand pat budgets for the Cancer Program. And then, while offering a few crumbs with one hand, the

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In Brief

SENATE HEALTH SUBCOMMITTEE LINEUP COMPLETED; GAO CALLS FOR MORE IONIZING RADIATION STUDIES

NEW LINEUP for the Senate Health Appropriations Subcommittee: Harrison Schmitt of New Mexico is the new chairman, as previously reported. Other Republicans are Mark Hatfield of Oregon (who is chairman of the parent Appropriations Committee), Lowell Weicker of Connecticut, Ted Stevens of Alaska (all returning senators and all but Stevens previous subcommittee members) and new GOP senators Mark Andrews of North Dakota, James Abnor of South Dakota and Arlen Specter of Pennsylvania. All Democrats on the subcommittee are holdover members—William Proxmire of Wisconsin, who is the ranking minority member; Robert Byrd of West Virginia, Ernest Hollings of South Carolina, Thomas Eagleton of Missouri, Lawton Chiles of Florida, Quentin Burdick of North Dakota, and Daniel Inouye of Hawaii. . . . **TED KENNEDY'S** Health Subcommittee was eliminated in the reorganization of the Labor & Human Resources Committee, with the full committee responsible for writing health legislation. Orrin Hatch of Utah is the committee chairman. House subcommittees are not yet organized. . . . **NATIONAL CANCER** Advisory Board ad hoc subcommittee on nutrition will discuss the NCI Diet, Nutrition & Cancer Program at a meeting Jan. 29, Bldg. 31 Room 11A10, starting at 9 a.m. . . . **GAO REPORT** on problems in assessing cancer risks of low level ionizing radiation exposure has been published and is available from: U.S. General Accounting Office, Document Handling & Information Services Facility, P.O. Box 6015, Gaithersburg, Md. 20760; phone requests are accepted—202-275-6241. First five copies are free, additional copies are $3.25 each. GAO recommended that Congress enact legislation giving statutory authority to an interagency committee to coordinate federal research on health effects of ionizing radiation exposure. The agency suggested that increased priority be given to study of mechanisms of cancer induction through cellular and molecular studies and other fundamental research, and called for more epidemiological and animal studies.

CENTER RENEWALS WILL BE LUCKY TO GET SEVEN PERCENT INCREASES IN 1981, 1982

(Continued from page 1)

White House took away with the other, submitting a rescission request to Congress that would cut $13.5 million from NCI's 1981 appropriation.

The fate of these maneuvers by the outgoing Administration will be in the hands of President Reagan and the new Congress. Rumors have been circulating that Reagan will cut Carter's 1982 budget request by two to five percent; if upheld by Congress that could leave NCI at the $1 billion level for the third straight year.

The rescission request is up to Congress, although Reagan could withdraw or modify it. It must be approved by both houses of Congress within 45 days after the request is submitted. Disapproval or failure to act by either house kills the request.

In the past, no rescission involving NCI funds has been approved by Congress. With Republicans now in control of the Senate and a marked conservative tendency growing in the House, coupled with the continuing national economic problems, Congress no longer may be counted upon as automatically disapproving Cancer Program budget cuts.

Here's how the $13.5 million rescission will be applied if it goes through:

Cancer Centers–$1,596,000, from the present 1981 total of $70,035,000 for exploratory and core grants.

Organ Site Program–$500,000 cut from $15,300,000.

Cooperative Groups–$888,000, cut from $35,459,000.

Training programs–$2,559,000, cut from $26,628,000.

Contracts–$3,522,000, cut from $205,130,000.

Intramural research–$1 million, cut from $162,824,000.

Cancer Control–$2 million, cut from $56,553,000.

Construction–$1,500,000, cut from $3,500,000.

A cut of $13.5 million may not seem like much when stacked up against the expected federal deficit of $60 billion this year. The impact on individual programs would be severe, however.

Even without the rescission, the 1981 cancer centers budget of $70 million will not fund competing renewals at peer review recommended levels. Those centers could expect to get, at best, a cost of living increase of about seven percent. With the rescission, they would get no increase at all.

The Carter 1982 budget request for centers is $75 million which would cover an increase of about seven percent for competing renewals, again not paying core grants at recommended levels.

Cooperative Group competing renewals also were due to be funded at substantially less than recommended levels (***The Cancer Letter,*** Jan. 2) with the $35.5 million budget. The proposed rescission probably would guarantee that those lower levels would prevail.

The 1982 request for Cooperative Groups is $38 million.

Cancer Control has undergone a severe reduction over the last two years, from a 1980 high of $66 million to the present level of $56.5 million. The 1982 request lists $57.6 million for control.

Construction grants, woefully underfunded for years despite a National Cancer Advisory Board mandate to allot at least $25 million a year to that category, were due to receive $3.5 million in 1981 without the $1.5 million rescission. The 1982 budget request for construction is $4 million.

Once again, investigator initiated research grants are protected from cuts. None of the rescission would come from that category. The 1981 budget has $351 million total for research grants (R01s and P01s), including $97 million for new and competing renewals. That would fund about 30 percent of the approved new and competing renewal grants. The 1982 budget of $369.8 million, including $106.3 million for new and competing renewals, also would fund about 30 percent of approved grants in those categories.

Program projects probably would be funded to priority scores of about 200 both years.

Training programs, always a favorite target of the White House Office of Management & Budget whatever the Administration, have been struggling with level or reduced budgets. The Clinical Education Program is due to receive $8 million in 1981 (not included in the $26.8 million listed previously for training) and escaped the rescission cut. However, funding would drop to $6 million under the 1982 budget request. Other training funds would rise to almost $30 million in 1982.

Reagan's 1982 budget revisions, and any alterations to the 1981 rescission requests, probably will be among the first items of business the new Administration will consider. The various subcommittees of the House Appropriations Committee will start hearings on FY 1982 late in February.

NTP CONCLUSION ON CARCINOGENICITY TO INCLUDE REPORTS ON OTHER TESTS

The National Toxicology Program Board of Scientific Counselors took on again an issue which has bothered NCI, NTP and their respective advisors since peer review by outside scientists was given a role in the interpretation of carcinogenesis bioassays–the relevance of the tests to human risk.

The NTP Board, meeting last week in Research Triangle Park, N.C., also took up the corollary question of whether statements on human risk which ac-

company the carcinogenesis test reports should take into consideration other reports appearing in the world literature on the same compounds or classes of compounds.

The answer to that question, Board members concluded after some debate, is that the broader view should be acknowledged in the reports. That reverses a policy established by NCI's Clearinghouse on Environmental Carcinogens when the Clearinghouse was established in the mid-1970s to advise on the Carcinogenesis Testing Program and review the bioassay reports.

Clearinghouse members had chaffed over the restriction which limited their statements on potential human risk strictly to the specific test results being reported. "That is not intellectually satisfying," grumbled Arnold Brown, who was chairman of the Clearinghouse during its four years of existence. But Clearinghouse members and NCI staff felt that the task of reviewing the world literature and incorporating those findings into the reports would have added an impossible burden to their jobs.

The Clearinghouse and NCI then were struggling to overcome the backlog of more than 200 test results, and they had enough to do just to consider and evaluate the NCI tests. The situation is more manageable now. The NTP Technical Review Committee will review only 10 reports at its meeting next month.

"We have to be cognizant of other studies," NTP Director David Rall told the Board. "I thought we all had agreed that the reports would be a good review of the toxicity of compounds. I thought that was what NTP was all about."

Norton Nelson, Board chairman, said, "We are faced with making a quality judgment that goes beyond the bioassay."

Rall suggested the reports could be in two parts, one limited to the bioassay and the other including a review of the literature, with updates.

James Huff, assistant to NTP Deputy Director John Moore, said, "We do review all the literature in respect to the carcinogenicity of that chemical or class of chemicals. Also the mutagenicity. In the summary, however, we say the conclusion is limited to that bioassay under the conditions of the test."

"That's not satisfactory," Rall said. "We can't say it is not carcinogenic in our test and not point out that all other tests so indicate."

Huff noted that most of the chemicals going through the NTP bioassay have not been adequately tested previously.

Board member Mortimer Mendelsohn commented, "We're spending umpteen millions but are not presenting a complete report."

Moore noted that "the burden of work will increase dramatically for a number of compounds (to include a review of other tests). For some it is a non-issue."

An observer from the Environmental Protection Agency opposed including other test results in the bioassay reports. "I question if the peer review should be in the position of looking at other studies and determining if those studies and data are adequate," said Stephen Johnson, coordinator for chemical testing and science policy at EPA. He added that the regulatory agencies assess the validity of various studies in their deliberations on whether to take action against a chemical. Making a value judgment based on other studies without determining the validity of those studies is not appropriate nor helpful to the regulatory agencies, Johnson suggested.

Board members disagreed. "I thought that was the mandate to NTP, to do just that," said Curtis Harper. "I think we should review the value of a bioassay in relation to what's in the world literature," said Marjorie Horning.

"There seems to be a sense of the Board that the larger mandate applies to NTP," Nelson said. "We should include other tests, and perhaps epidemiological studies. I reject the position that this should be left to the regulatory agencies. I'm sure the regulators will continue to make their own value judgments and may reject ours. We still should continue to offer our own value judgments."

The Board also accepted the recommendation of its subcommittee, headed by Harper, to adopt the International Agency for Cancer Research concept of categorizing experimental results and establishing warning statements for potential human health hazards. Horning, Alice Whittemore, and Margaret Hitchcock were other members of the subcommittee. Their report stated:

"The subcommittee recognizes that several scientific, regulatory, and legislative agencies are now studying criteria for human hazard statements. Any attempt by NTP to develop new statements to be used with the cancer bioassay reports would perhaps contribute to potential confusion and fragmentation of these efforts. The subcommittee recommends that further efforts to develop new criteria for human hazard warnings be suspended until (a) there is a congressional directive to the NTP to develop such statements and/or (b) there is sufficient collaboration between the NTP and other interested agencies to facilitate a unified effort and provide a framework for international acceptance of such criteria.

"A. With respect to the Carcinogenesis Bioassay Technical Reports the subcommittee endorses the International Agency for Research on Cancer concept concerning extrapolation from experimental results in animals to humans: 'No adequate criteria are presently available to interpret experimental carcinogenicity data directly in terms of carcinogenic potential for humans. Nonetheless, utilizing data collected from appropriate tests in animals, positive extrapola-

tions to possible human risk can be approximated.' Using this guideline, the subcommittee recommends adoption of the definitions used by the IARC for experimental animal bioassay results.

"B. The IARC assessments of the strength of evidence for carcinogenicity from experimental animal studies divide into four categories—sufficient evidence, limited evidence, inadequate evidence, and negative evidence:

"1. Sufficient evidence of carcinogenicity indicates that there is an increased incidence of malignant tumors: (a) in multiple species or strains, or (b) in multiple experiments (preferably with different routes of administration or using different dose levels), or (c) to an unusual degree with regard to incidence, site or type of tumor, or precocity of onset. Additional evidence may be provided by data concerning dose-response effects, as well as information on mutagenicity or chemical structure.

"2. Limited evidence of carcinogenicity means that the data suggest a carcinogenic effect but are limited because: (a) the studies involve a single species, strain, or experiment; or (b) the experiments are restricted by inadequate dosage levels, inadequate duration of exposure to the agent, inadequate period of followup, poor survival, too few animals, or inadequate reporting; or (c) the neoplasms produced often occur spontaneously or are difficult to classify as malignant by histological criteria alone (e.g., lung and liver tumors in mice).

"3. Inadequate evidence indicates that because of major qualitative or quantitative limitations, the studies cannot be interpreted as showing either the presence or absence of a carcinogenic effect.

"4. Negative evidence means that within the limits of the tests used, the chemical is not carcinogenic.

"The categories sufficient evidence and limited evidence refer only to the strength of the experimental evidence that these chemicals are (or are not) carcinogenic and not to the extent of their carcinogenic activity or potency.

"For chemicals having 'sufficient evidence of carcinogenicity in animals,' the IARC makes the following statement: 'In the absence of adequate data on humans, it is reasonable, for practical purposes, to regard such chemicals (or the particular chemical name) as if they (it) presented a carcinogenic risk to humans.'

"These definitions should be incorporated routinely into the foreword of each Carcinogenesis Bioassay Technical Report.

"C. Offered in the foreward to each Carcinogenesis Bioassay Technical Report is the statement, 'A negative result, in which the test animals do not have a greater incidence of cancer than control animals, does not necessarily mean that a test chemical is not a carcinogen inasmuch as the experiments are conducted under a limited set of circumstances. A positive result demonstrates that a test chemical is carcinogenic for animals under the conditions of the test and indicates that exposure to the chemical could pose a potential risk to humans. The actual determination of the risk to humans from chemicals found to be carcinogenic in animals requires a wider analysis which extends beyond the purview of this study.'

"The subcommittee recommends that this generalized statement continue to appear in each report.

"D. The subcommittee recommends that the summary and discussion/conclusion sections contain a standard and limited statement selected from the following list that is patterned after those defined by the IARC:

"1. Based on these bioassay data, chemical X exhibited sufficient evidence of carcinogenicity. NTP considers, therefore, that chemical X should be regarded as presenting a carcinogenic risk to humans.

"2. Based on these bioassay data, chemical X exhibited limited evidence of carcinogenicity. NTP considers, therefore, that in the absence of other data, no evaluation can be made about the potential carcinogenicity for humans of chemical X.

"3. Based on these bioassay data, chemical X exhibited inadequate evidence of carcinogenicity. NTP considers, therefore, that in the absence of other data, no evaluation can be made about the potential carcinogenicity for humans of chemical X.

"4. Based on these bioassay data, chemical X exhibited negative evidence of carcinogenicity. NTP advises the following statement of caution: A negative result, in which the test animals do not have a greater incidence of cancer than control animals, does not necessarily mean that chemical X is not a carcinogen, inasmuch as the experiments are conducted under a limited set of circumstances."

Gary Williams, of the American Health Foundation, a consultant to the Technical Review Committee, said the IARC definitions "are a source of amusement and befuddlement. What is meant by 'limited evidence' or 'sufficient evidence'? You never see unanimity on IARC panels. Carcinogenesis experts are frequently outvoted on the panels by epidemiologists and mutagenesis experts. You are imposing a difficult task on your peer reviewers."

Whittemore was critical of paragraph C in the IARC definition which "allows for the possibility of error with false negatives but not with false positives."

"We're a health agency," Rall responded. He objected to using the word 'could' in the sentence, "A positive result demonstrates that a test chemical is carcinogenic for animals under the conditions of the test and indicates that exposure to the chemical could pose a potential risk to humans."

"I think we should change 'could' to 'likely to,' Rall said. "The purpose of this program is not to report on carcinogenic threats to other mice and rats."

Nelson said, "I have heard those arguments (against the IARC definitions) before and am aware of them. It is true that several qualifiers state exactly what Dr. Whittemore said. Also, there is no unanimity on IARC panels. They merely represent the current point of view subject to revision. However, I think there is something to be gained in using the international terminology."

Rall asked Moore if the IARC format, as well as the literature search to include other applicable tests, could be included in the reports to be reviewed Feb. 18 by the Technical Review Committee. Moore answered, "Possibly."

NTP BOARD APPROVES SIX NEW CONTRACT SUPPORTED PROJECTS, TABLES ANOTHER

The National Toxicology Program Board of Scientific Counselors gave concept approval to six new projects which will be implemented with contracts and tabled one other at the Board's meeting last week.

Projects approved by the Board, which will be developed into requests for proposals and competed through the contract award process, were:

• Study on the potential hazard from chemically induced transmitted gene mutations using the morphological specific locus method in mice.

The proposed studies are designed to investigate the chemical induction of heritable mutations in mouse germ cells. Objectives include:

1. To test five environmentally significant chemicals for mutagenicity using the mouse morphological specific locus assay. Data from these tests will be used in the determination of human genetic risk estimations.

2. To conduct an in depth study of chemical induced mutation processes in mammalian germ cells, will be used to investigate a variety of variables including dose response, germ cell stage sensitivity, sex differences, and age effects. Molecular dosimetry studies will be conducted using radioactively labeled ENU.

Specific requirements include:

Task 1. Chemical testing. Chemicals chosen by NTP will be tested using the seven locus morphological specific locus assays according to the following general protocol:

a) Test chemicals will be administered to young adult male mice. Data from both spermatogonial and post-spermatogonial cell stages will be obtained.

b) Each chemical test will require one or two doses, the decision to be made by the following criteria. The first exposure level chosen will be the highest that can be tolerated without toxic effects, provided any temporary sterility that may be induced is of only moderate duration. If results under these conditions are clearly negative, and if it is determined histologically that there is no extensive spermatogonial killing, the experiment will be terminated. If results are positive or inconclusive at the chosen sample size, or if there was extensive spermatogonial killing, a lower exposure level will be tested.

c) Each test will be planned for the production of 12,000 offspring from treated spermatogonia. It may be possible to terminate the experiment before this total is reached if the experimental rate is significantly higher than the control rate. If, after 12,000 offspring have been scored, the result is not significantly positive or negative by the criteria proposed in the EPA Gene-tox Report on the specific locus assay, the experiment will be continued until 18,000 offspring are obtained. This experimental size is designed to exclude a five-fold increase in mutation rate.

d) Historical control data will be used in evaluating test results; however, small contemporary controls will be run with all tests. The size of these control groups will be determined later as will the size of solvent control groups when necessary.

Task 2. In depth study of chemical mutagenesis in mammalian germ cells. ENU has recently been found to be extremely effective at inducing heritable mutations in mouse spermatogonial cells. The high frequency of mutants recovered in the specific locus assay after ENU treatment will allow for quantitative comparisons of the effects of a number of variables.

a) A dose response curve will be investigated by determining mutation rates in spermatogonial cells at 100, 50, and 25 mg/kg ENU. Information is currently available for a dose of 250 mg/kg.

b) Molecular dosimetry studies will be conducted using ENU tritium labeled in the ethyl group. Ethylation of DNA will be determined in oocytes as well as in the spermatogonia and later male germ cell stages.

c) The relative sensitivity of all male germ cell stages to mutation induction and killing will be determined at a dose of 250 mg/kg.

d) The relative sensitivity to mutation induction and killing by ENU of oocytes in various stages of development will be investigated.

e) The effects of fractionated low doses of ENU will be investigated in spermatogonia at doses of 10 mg/kg x 10 weeks.

f) Age effects will be investigated by comparing spermatogonial mutation rates in male mice treated at ages ranging from 4 to 20 weeks.

• Investigation of modification of salmonella to test chemicals which may be metabolized by mutagens under reductive conditions.

The standard protocols using in vitro metabolic activation for mutagenesis studies assume that aerobic metabolism is sufficient for the activation of all pro mutagens. However, many substances such as azo-containing dyes may be metabolized to active mutagens by only reductive pathways. These pathways occur in the mammalian liver in situ and in the mammalian gut thorugh the action of the normal gut flora. Therefore, azo-containing chemicals metabolized to mutagens in vivo may appear to be non-mutagenic when tested using the standard aerobic metabolic activation protocols.

NTP currently is investigating the pharmacokinetics and carcinogenicity of a number of azo-containing dyes. The regulatory agencies requesting pharmacokinetic and carcinogenic data on these dyes have also requested salmonella mutagenicity data on the dye and dye metabolites.

Objectives include:

1. To develop a protocol or series of protocols which will provide reductive metabolism in a slamonella mutagenesis test.

2. Test a series of chemicals that are known to undergo reductive metabolism in vivo using the protocol(s) developed in Objective 1.

3. Test a series of metabolites of the chemicals tested in Objective 2 using standard oxidative as well as reductive metabolic activation procedures.

• Development and validation of a multiple endpoint mutation system in cultured mammalian cells.

The two major types of effects of concern in genetic toxicology are gene and chromosome mutations. Both gene and chromosome mutations are of interest because they both can produce human genetic disease. Genotoxic chemicals usually induce both types of effects, however the extent to which

chemicals will induce only gene mutations or chromosome mutations is not predictable at this time.

Typically, induction of gene mutations in mammalian cells is detected in a number of different cell lines and the induction of chromosome mutations is usually detected using the same or different cell lines in laboratories specializing in cytogenetics. As a result, it is difficult to determine the relative frequencies induced and the effective doses. Yet, a comparison between gene and chromosome mutations as a function of chemical dose is needed as a reference when moving from results obtained with cells in culture to predicted effects in treated animals. Such an extrapolation is necessary when only one type of mutagenic effect can be measured in vitro but one wants to estimate the sum of both effects.

Objectives include:

1. Develop and test a protocol that can be used to determine the frequencies of both gene and chromosome mutations in a cell line.
2. Determine the possibility of detecting other endpoints such as sister chromatid exchange, aneuploidy and DNA damage/repair in the same cell line.
3. Test a series of chemicals using the protocol developed.

• Determination of background levels of chromosome aberrations and sister chromatid exchanges in peripheral lymphocytes of humans.

Monitoring of peripheral lymphocyte samples for cytogenic end points offers a practical means of detecting exposures of individuals or populations to genotoxic agents. The technique has been used in connection with ionizing radiation exposures for many years, and has become widely accepted in the radiation industry. It has also been advocated, and to some extent applied, in connection with exposures to chemical agents. Unfortunately, some past attempts to determine chromosomal aberration frequencies in the peripheral lymphocytes of populations suspected of having been exposed to hazardous chemicals has raised serious questions about both the general utility of such cytogenic monitoring, and the exact form such tests should take in the future. The protocols for the few cytogenetic studies that have been performed on persons exposed to chemical agents (usually occupationally) have been varied, precluding cross comparison. They have also often been flawed in one respect or another, precluding definite conclusions as to whether the exposures led to significant increases in the observed levels of cytogenetic effects compared to a presumably non-exposed control.

It has become apparent that the development of a standard protocol for cytogenetic monitoring is badly needed, and that we lack the background information (with any protocol) on spontaneous frequencies, their variability, and the causes of this variability, that are required before we can design a proper cytogenetic study of populations possibly exposed to potential mutagens or carcinogens.

Objectives include:

1. To develop and validate a protocol by which the frequency of the chromosome aberrations and sister-chromatid exchanges (SCE) can be accurately and reproducibly determined in the lymphocytes of humans.
2. To use the protocol developed to determine the spontaneous frequencies of chromosome aberrations and SCE's in a normal unexposed population of humans.
3. To determine the variability in such spontaneous frequencies and, where possible, to define factors affecting variability.

• Evaluation of mouse (in vivo) cytogenetic and sister chromatid exchange endpoints for identification of carcinogens and mutagens.

Assays for induction of cytogenetic effects and sister chromatid exchange (SCE) represent two genotoxic test systems in which the methodology has been well developed and exists in many laboratories throughout the world. However, these assays have not been utilized very extensively to identify potential genotoxic agents. In part, this is due to the fact that they are relatively laborious and require a good degree of cognitive skill and experience. The use of cytogenetic techniques in the absence of strict controls and verification safeguards has led to controversy. The systems, however, offer a significant advantage in that the problems attendant to the use of exogenous metabolic activation systems are avoided, as are many of the other constraints which limit extrapolation between in vitro and in vivo test results. While the mechanisms of chromosome aberrations and SCE induction are not clearly understood, it is clear that they represent discreet genetic endpoints which are indicative of clastogenic genotoxicity. It is only through a systematic evaluation of the techniques, and a comparison with data obtained from other systems, that the relative value as a primary mammalian in vivo screening system can be actually determined.

NTP is seeking to identify at least two independent laboratories to engage in the development of a protocol and to test up to 50 coded compounds for ability to induce chromosome damage or sister chromatid exchange in bone marrow cells in mice and rats.

Objectives include:

1. To develop an experimental protocol for the determination of the frequency of chromosome aberrations and SCE's in the bone marrow of laboratory rodents.
2. To determine the utility of the protocol developed for detecting carcinogens and mutagens by testing a group of coded chemicals, selected by the NTP, in two independent laboratories.

• Validation of three prescreens to examine large numbers of agents for teratological effects.

The Board tabled the request by NTP staff to support establishment of a resource laboratory capable of monitoring the metabolizing capacity of S9 and other metabolizing systems.

NTP Deputy Director John Moore presented a statement to the Board describing the concept of the animal bioassay process and asked for the Board's approval, which was given. The statement, as modified slightly by the Board:

1. Rats and mice and other small laboratory animals are appropriate species for evaluating carcinogenic and toxicologic properties of chemicals.
2. The toxicologic evaluation of chemicals is generally conducted through a sequence of experiments that involve acute (1-2 day) subacute (approximately 14 days) and subchronic (approximately 13 weeks [90 days]) exposure to a chemical substance(s). In addition to defining the general toxicologic properties of a chemical this sequence of toxicity studies is a reliable method for establishing the dose levels most appropriate for conducting chronic (lifetime or 2 year) bioassays.
3. The chronic (lifetime) rodent bioassay is the current preferred procedure for determining the carcinogenic potential of a chemical. The chronic bioassay also has utility for assessing delayed or age-dependent toxicities.

4. Chemical toxicity and carcinogenicity are investigated using animal bioassays through the collection and assessment of data on body weight, survival, chemical disposition, food consumption, and specific organ or tissue effects using the data gained from clinical chemistry, hematology, urinalysis, functional or behavioral, and gross and microscopic pathological examinations.

5. Proper performance and evaluation of animal bioassays require a knowledge of the purity, stability, and storage requirements of the test chemical(s); synthesis of the chemical(s) (if the needed amount or desired purity of the chemical is not available); homogeneity and stability of the chemical in the test vehicle; and adequate storage capabilities are needed to provide the quantity of material necessary for the bioassays as well as for other tests that may be required and to maintain samples for future use.

6. Centralized, controlled colonies of appropriate strains insure an adequate and continous supply of animals, having homogeneous genetic and health profiles. Veterinary medical procedures must be performed routinely to characterize the health status of animals prior to and during the animal bioassays.

7. The NTP must continue to develop and monitor practices that insure the health and safety of persons involved in the performance of animal bioassays that utilize chemicals of known or suspected toxicologic and carcinogenic potential.

ACCC ANNUAL MEETING FEATURES IMPACT OF NEW TECHNOLOGY ON CANCER CARE

The Seventh National Meeting of the Assn. of Community Cancer Centers March 6-8 in Washington will feature a program on "The Impact of New Technology on Community Cancer Care in the 1980s."

The program will include presentations on radiologic diagnosis and CAT scans by E. James Potchen, chairman of the Dept. of Radiology at Michigan State Univ.; chemotherapy, stem cell assay and bone marrow transplantation by Stephen Carter, director of the Northern California Cancer Program; radiotherapy, high LET radiation, radiation sensitizers and hyperthermia by Arvin Glicksman, chairman of the Div. of Radiation Oncology at Rhode Island Hospital; and biological response modifiers and interferon by Frank Rauscher, senior vice president for research of the American Cancer Society.

Herbert Kerman, ACCC president elect, will be moderator of the program.

ACCC President Robert Frelick will moderate another program on "Issues Affecting Community Cancer Care in the 1980s." Presentations will include the government's role by ACCC Executive Director Lee Mortenson; the community and clinical research by Edward Moorhead, project director of the Grand Rapids Community Oncology Program; financial and administrative considerations by David Johnson, president of Deaconess Hospital in Evansville, Ind.; oncology nursing by Donna Stover, director of the Midwest Oncology Program; and supportive care by Jimmie Holland, chief of psychiatry service at Memorial Sloan-Kettering Cancer Center.

NCI Director Vincent DeVita will address the meeting on "NCI'S Role in the Future of Community Cancer Care." John MacDonald, director of the Cancer Therapy Evaluation Program, will speak on "Community Involvement in Clinical Research."

J. Gale Katterhagen, former ACCC president and presently a member of the National Cancer Advisory Board, will be the luncheon speaker, with the topic "Challenges Facing Community Cancer Care in the 1980s."

Carter, who in addition to his NCCP position is chairman of the Northern California Oncology Group, will discuss organization and management of a regional cooperative group.

Workshops are scheduled on organization and financing of community cancer programs, oncology nursing, and supportive care for cancer patients. Abstracts sessions will be held on rehabilitation, continuing care and pain management for community cancer patients; innovations in community cancer nursing; and cancer control organizations and their impact on community cancer care.

The meeting will be held in the Hyatt Regency Hotel, starting with a congressional briefing March 6 followed immediately by visitations to members of Congress.

ACCC may be contacted at 4733 Bethesda Ave., Suite 410, Bethesda, Md. 20014. Phone 301-654-2033.

PHYSICIAN DIRECTORS, ADMINISTRATORS CHOP TRAINING CONFERENCES PLANNED

Elm Services, Inc., the Bethesda health consulting firm, is offering training conferences for Community Hospital Oncology Program physician and administrative directors. The administrative directors' conference is scheduled for Feb. 9-15 and physician directors' conference Feb. 12-15, both in Washington.

The conferences are timed to permit attendees to attend the first CHOP contractors' meeting planned by NCI for Feb. 16.

The administrative directors course will include presentations on fundamentals of cancer; how to access cancer resources; state of the art discussions on oncology nursing, cancer rehabilitation and terminal care; how to develop and manage a CHOP data system; the basics of CHOP contract management; and methods of attaining self-sufficiency and funding strategy development.

The physician directors course will include dis-

cussions on development of common evaluation data sets; CHOP's political future and potentials for future funding; how to affect committee decision making processes; roles and responsibilities of physician directors; and progress in clinical research and state of the art cancer therapy.

The initial CHOP awards are 18-month planning contracts. Elm noted that 30 percent of the original Clinical Oncology Programs (also supported by NCI and now being completed) were not funded for implementation. NCI has estimated that between 15 and 40 percent of the CHOP planning contracts will not proceed to implementation. COP directors felt the primary cause of failures was lack of knowledge of cancer control, data systems, cancer treatment and rehabilitation, and contract management, according to Elm.

COP administrative and physician directors have pointed to a series of obstacles they faced which the conferences will address, Elm said. These include lack of familiarity with contract procedures and contract management; lack of knowledge about data systems, registries, computer utilization and applications to CHOP data and evaluation needs; lack of formal knowledge about and training in participatory decision making processes and techniques; lack of detailed information on evaluation and on the requirements of NCI type evaluations; lack of support from the medical staff, hospital administrators and the community sufficient to secure its future; lack of experience in formulation of a plan for continuation of the program after NCI funding ceases; lack of specific approaches to the development of patient management guidelines by committees.

Collaborating with Elm in presenting the conferences are the Clinical Oncology Programs at Grand Rapids and Indianapolis.

Contract Awards

TWO MORE CHOPs ANNOUNCED— SAVANNAH, LOS ANGELES; TOTAL 12

Two more Community Hospital Oncology Program contracts have been announced by NCI, bringing the total awarded so far to 12. NCI plans to support a total of 23.

The new awards went to Memorial Medical Center, Savannah, $106,685; and St. Vincent Medical Center, Los Angeles, $109,884.

Other contract awards by NCI:

Title: Four additional alteration/renovation/maintenance/upgrading projects necessary to support the research program being conducted at Frederick Cancer Research Center
Contractor: Litton Bionetics, $205,514.

Title: Pharmacology of antitumor agents
Contractor: Arthur D. Little Inc., $459,242.

Title: Prime contractor for performance of protocol toxicology studies
Contractor: Battelle Memorial Institute, Columbus, $6,750,464.

Title: Production of monospecific antibodies against tumor associated antigens, renewal
Contractor: University of California (San Diego), $73,166.

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. Some listings will show the phone number of the Contract Specialist who will respond to questions. Listings identify the respective sections of the Research Contracts Branch which are issuing the RFPs. Address requests to the Contracting Officer or Contract Specialist named, Research Contracts Branch, National Cancer Institute, Blair Building, 8300 Colesville Rd., Silver Spring, Md. 20910. Deadline date shown for each listing is the final day for receipt of the completed proposal unless otherwise indicated.

RFP NCI-CP-11014

Title: *Computer support for resources management*
Deadline: *Feb. 26*

This contract will include the design and development of new systems for management, collection, storage and distribution of resource material, and the encoding and entering of data to support the operation of existing systems and the production of reports on the data bases for various systems. The level of effort required is programmer/systems analyst, one man-year; computer programmers, two man-years; and data technicians, two man-years.

The contractor must be located within 35 miles of NIH off-campus Landow Building, 7910 Woodmont Ave., Bethesda, Md. 20205. In order to quality for this procurement, offerors must have gross earnings of $12 million or less over the last three years (average $4 million annually).

Contracting Officer: Elizabeth Osinski
Biological Carcinogenesis & Field Studies
301-427-8888

The Cancer Letter _Editor Jerry D. Boyd
Published fifty times a year by The Cancer Letter, Inc., P.O. Box 2370, Reston, Virginia 22090. Also publisher of The Clinical Cancer Letter.