THE CANCER LETTER
RESEARCH EDUCATION CONTROL

Vol. 5 No. 7

Feb. 16, 1979

Subscription $125.00 per year

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BILL PLANNED TO OKAY MEDICARE/MEDICAID PAYMENT FOR 100% OF OUTPATIENT ANTICANCER DRUG COSTS

Legislation will be introduced in Congress this year which will authorize Medicare and Medicaid reimbursement for 100% of the cost of certain specified anticancer drugs for outpatients.

The Social Security Act presently allows reimbursement of only 80% of the cost of drugs prescribed for outpatients. For most diseases, the

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In Brief

MAGUIRE WANTS FIVE ENVIRONMENTAL EXPERTS IN ADDITION TO THOSE ALREADY ON THE BOARD

CONGRESSMAN MAGUIRE'S interpretation of the Cancer Act amendment regarding appointees to the National Cancer Advisory Board was not exactly what was attributed to him by *The Cancer Letter* (Feb. 2). Maguire staff member Steve d'Arazien said the congressman did not agree that the three present members of the Board with expertise in environmental carcinogenesis—Henry Pitot, Philippe Shubik, Gerald Wogan—could be considered as three of the five required by the amendment. "We want five in addition to those," d'Arazien said, and indicated some should be experts in occupational cancer. The amendment specifically says, "Not less than five members must be knowledgeable in environmental carcinogenesis (including carcinogens involving occupational and dietary factors)." That most certainly could include Pitot, Shubik and Wogan, if the President (or HEW Secretary Joseph Califano) so decide. Another amendment requires "at least two members must be physicians primarily involved in treating cancer patients." Again, there are existing members who fit that description. However, the Assn. of Community Cancer Centers, which lobbied for that change, insists it should be someone in community practice or at least working full time in treating patients. ACCC members are pressing for appointment of their former president, Gale Katterhagen, Tacoma oncologist . . . . **WILLIAM HUTCHINSON**, director of the Fred Hutchinson Cancer Research Center, has been appointed president of the UICC Congress of 1982, which will be held in Seattle. The appointment was made by the USA National Committee of UICC. Other appointments included Edwin Mirand, Roswell Park Memorial Institute associate director and dean of the RPMI graduate division, secretary-general; Enrico Mihich, director of the RPMI Cancer Drug Center, national program chairman, with William Shingleton, director of the Duke Univ. Comprehensive Cancer Center as cochairman; Karl Hellstrom, Hutchinson center, chairman of the local organizing committee; Hutchinson and Mirand, chairman and cochairman of the committee of scientific advisors; Sen. Warren Magnuson, honorary president of the Congress; and NCI Director Arthur Upton and President-Emeritus R. Lee Clark of Univ. of Texas System Cancer Center, honorary vice presidents.

MEDICARE/MEDICAID CUTOFF THREATENED FOR PATIENTS ON RESEARCH PROTOCOLS

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other 20% does not impose hardships on either the patients or their physicians should the latter choose to absorb the costs. Some anticancer agents, most notably adriamycin, are so expensive that paying 20% causes real hardships for patients and precludes physicians from picking up the balance.

The result is that all too frequently when patients require the more expensive drugs, physicians hospitalize them and thus qualify them for 100% reimbursement of drug costs.

The American Society of Clinical Oncology took on the job of finding a solution to this problem last year and turned it over to the Society's Clinical Practices Committee, chaired by David Fischer.

A practicing oncologist as well as associate professor of clinical medicine at Yale, Fischer conducted a survey to find out how much the unnecessary hospitalization of cancer patients was costing third party payers, including the federal government, in Connecticut. He found that the cost was at least $250,000 a year. Blue Cross-Blue Shield conducted its own survey in the state and came up with an estimate of $500,000.

The amount the government would save on hospital admissions might equal or even exceed the extra cost of paying 100% of outpatient anticancer drug costs, Fischer said. He took that argument to Congressman William Cotter, a Connecticut Democrat and a member of the Ways & Means Committee which has jurisdiction over all Social Security legislation.

Cotter drafted a bill and sent it to HEW for comments. HEW is in the process of gathering cost information and will rely heavily on the Connecticut surveys.

The bill as drafted would provide for reimbursement of 100% of the costs of anticancer drugs to be named (by the HEW secretary or his designee). It would apply only to drugs administered in a physician's office under a physician's direction.

A Cotter aide told ***The Cancer Letter*** the bill would be introduced by late spring or early summer.

Another and potentially more serious problem involving Medicare/Medicaid reimbursement has surfaced—the refusal in a few isolated cases to pay for the hospital care of cancer patients entered on research protocols.

Fischer said his committee knows of only six such instances—three in New York, one each in Connecticut, Massachusetts and Georgia. Since the committee was not authorized by ASCO to pursue that problem, it hasn't taken any action. "It's hard to get excited about that," Fischer said.

Several cancer center directors were excited, however, when the matter was discussed at the recent meeting of the Assn. of American Cancer Institutes. "This would have a terrible impact on our ability to carry forward clinical research," said Albert Owens, director of the Johns Hopkins Oncology Center.

Barbara Sanford, Sidney Farber Cancer Center, where one of the Medicare refusals took place, said, "If this represents a serious effort on the part of Medicare, then we have a tremendous problem. If they are saying that when a patient is on a research protocol the hospital bill is not collectable, clinical research is in major difficulty. We're very concerned."

Denman Hammond, director of the Univ. of Southern California Cancer Center, said it would be a threat to AACI members and "to the National Cancer Program. I'm distressed." He suggested AACI develop a plan to deal with it, including enlisting the aid of consumer groups."

Charles Moertel, director of the Mayo Comprehensive Cancer Center, offered a cautionary note. "We ought to look to ourselves and make sure we're not augmenting the problem," Moertel said. "When patients are admitted to hospitals for pure research, such as an early phase 1 study, that's purely research, not care. Could we set some guidelines?"

AACI President Gordon Zubrod referred the issue to the task group headed by Alvin Mauer, medical director of St. Jude Children's Hospital.

Vincent DeVita, director of NCI's Div. of Cancer Treatment, agreed that it would be a serious problem if third party payers stop reimbursements for cancer patients on research protocols. He pointed out that any such effort probably would not reduce Medicare/Medicaid costs and might even increase them.

"The question involves hospital payments for any patient treated with a cancer investigational drug," DeVita said. "It ought to be recognized that if a patient doesn't get an experimental drug, he will be treated with an older drug and Medicare will pay anyway." NCI supplies investigational drugs at no cost to patients, investigators or insurance carriers.

DeVita said it appears that Medicare's concern is over patients who do not need treatment being placed on research protocols. That does not seem to be a reasonable concern considering the seriousness of the disease and the toxicity of the treatment.

Part of the problem may be due to a Social Security Administration determination that use of investigational drugs is pure research, without recognizing that since there is not enough "standard treatment" for cancer, the best hope many patients ahve is by being placed on research protocols.

The issue may be further scrambled by the "group C" drugs which NCI distributes to any qualified physician requesting them. Those are drugs which have been tested to the point where they should be on the market and thus no longer considered investigational. For a variety of reasons, no drug manufacturer has obtained FDA approval for marketing them, but they are still useful in many cases.

Unlike reimbursement for outpatient drugs, the issue of paying hospital costs of patients on research protocols may not need legislative correction. It could be a matter to be resolved administratively. DeVita has discussed the issue with NIH Director Donald Fredrickson. If a Medicare and Medicaid cutoff does become a widespread problem, they will take up the matter with the Social Security Administration and, if necessary, HEW Secretary Joseph Califano. The assistance of ASCO, AACI and other groups might then be helpful.

PITOT SUBCOMMITTEE DRAFTING REPORT ON BIOASSAY-HUMAN RISK RELATIONSHIP

The National Cancer Advisory Board's Subcommittee on Environmental Carcinogenesis will produce sometime this year a document that could have a profound impact on the regulation of carcinogenic substances and perhaps an equally significant effect on the direction of carcinogenic research.

The subcommittee, chaired by Henry Pitot, director of the McArdle Laboratory for Cancer Research, has produced the first draft of a document entitled, "The Relation of Bioassay Data on Chemicals to the Assessment of the Risk of Carcinogens for Humans under Conditions of Low Exposure."

The draft was compiled with the aid of 37 scientists, industry, labor and consumer representatives. After a critique by subcommittee members, it will be distributed more broadly for a general review before the subcommittee puts together a final document.

Benno Schmidt, chairman of the President's Cancer Panel, suggested more than a year ago that a state of the art assessment was needed on the relationship between bioassay data and human risk. The subcommittee agreed to take on the assignment, expanding on a topic covered only briefly in a massive earlier effort by the group when it was chaired by Philippe Shubik, the document "General Criteria for Assessing the Evidence for Carcinogenicity of Chemical Substances."

The 36-page draft document, supported by a 32-page bibliography, summarizes:

"The importance of relating actual risk estimates to the real human situation cannot be overemphasized. On the basis of such determinations, regulations governing such agents should be established in order to insure the safety of specific population groups on the one hand, while at the same time modifying such regulations for populations where the risk is truly relatively negligible."

The draft document makes a strong case for the direct relationship between selected whole animal bioassay data, quantitatively and qualitatively, and the risk of carcinogenesis in humans. Citing the report of the Meselson Committee (NAS, 1975): "The risk of carcinogenesis in the human may be seen from the small sample of a qualitative and quantitative comparison of carcinogenesis in animals and the human. The known human carcinogens are also carcinogens in animal tests with only one or two possible exceptions and many of the human carcinogens were first identified by cancer tests in animals.

"However, the quantitative relation is much more uncertain and, given the need to set priority for regulation and the improbability of removing all carcinogens from the environment, must be a matter of the highest research priority."

The draft discusses problems involved with extrapolation and determining human exposure.

1. Mathematical and Probabilistic Estimates of Human Risk

"A. Dose-response and threshold extrapolation to humans. Despite the difficulties in the establishment of whole animal bioassays and screening procedures and in the interpretation and evaluation of data obtained from such tests, extrapolations from this data to relatively safe dosages and estimates of tumor probabilities in humans still must be performed. As Gaylor and Shapiro have pointed out 'there is no choice but to extrapolate' (1978). The problem then becomes one of determining the optimal extrapolation from the test data obtained to risk of the agent to the human species. Many procedures have been proposed for such extrapolation in a variety of ways. Freireich, et al. (1966) suggested that interspecies extrapolations for toxicity may be performed on a surface area basis. Mantel and Schneiderman (1975) have also suggested a similar sort of calculation in extrapolation between species.

"Such may be clearly possible where humans are exposed to doses comparable to those given to animals. The difficulty in extrapolation lies primarily in the low dose range and the question of a threshold of an agent for the exposed human population. As Gaylor and Shapiro (1978) have pointed out in most instances it is impossible to determine whether mathematical models (vida infra) which describe a dose-response relationship in the experimental situation will be applicable to the human situation at exposures which only demonstrate effects in a very small or even zero proportion of the test animals. Hoel (1978) has also pointed out that estimating effects of agents at low dose levels, from information from the high dose bioassay which is so commonly employed in most whole animal situations, may lead to inaccuracies. This inaccuracy could be in either direction: underestimating risk at low doses in those cases where there is intercurrent toxicity and/or the multiple hit effect, and overestimating risk in cases where the shape of the dose response curve is concave.

"One of the results of extrapolation from whole animal bioassays to the human situation is the designation of 'safety factors.' Such factors comprise the dose level of an agent which may be permitted in the environment and is considered safe to the human population. A number of proposals have been utilized which result in 'safe' doses varying by approximately

six orders of magnitude. One common practice is to divide observed experimental 'no effect' levels by 100 and set this as the 'safe' level. Weil (1972) has suggested the use of a safety factor of 5,000 predicated at the lowest experimental effect level while the original publication of Mantel and Bryan (1961) assumed a dose of 'virtual safety' to be 10^{-8}. The pros and cons of these varying safety levels have been previously discussed. Still one must remember that there is no defined way to demonstrate absolute safety of an agent on the basis of statistical conclusions from test data.

"The statistical analysis of whole animal test data (vida supra) have employed a number of mathematical models. . . . None of these models can prove or disprove the existence of a threshold of response and none can be verified on the basis of biological argument. However, they have clearly found usefulness in data evaluation and also have been utilized to some extent in extrapolation of experimental data to the human situation. One of the more commonly employed techniques is that of the Mantel-Bryan procedure (1961) and its more recent modification (Mantel et al., 1975). This procedure uses the probit model and is relatively conservative in its estimation of safe dosage at higher and relatively non-conservative at lower doses.

"Although the Meselson Committee attempted to relate dose response effects of several carcinogens in humans and test animals, the committee pointed out that comprable dose-response relationships in animal tests and human experience occurred with three compounds, benzidine, chlornaphazine and cigarette smoke while for three other compounds animals appeared to be more sensitive than humans although the human data is too crude for a definitive analysis. Cranmer has attempted to relate some of their data to the determination of risk factors utilizing mathematical models as described above (Cranmer, 1977). In this study the difference between the observed effects in the human and experimental animal in relation to 'safe' levels as predicted from the mathematical models clearly differ by many orders of magnitude in the case of diethylstilbesterol, alfatoxin B_1 and DDT.

"B. Extrapolation of short-term test data to humans. As might be expected even greater difficulties may be found in the extrapolation of screening test data to humans. However, if one makes the initial assumption that such extrapolation will be largely at a qualitative level rather than the quantitative determination of safety levels and quantified risk in the human, then such extrapolation is made more easy. Meselson and Russell (1977) have reported an approximate correlation between mutagenic and carcinogenic potencies of about a dozen chemicals. While others have taken exception to this (Ashley and Styles, 1978).

"The Ames system detects almost all the organic chemicals suspected as human carcinogens (McCann and Ames, 1977). On the other hand, some other test systems do not appear to be as valid as the Ames system, but the better ones detect most of these same carcinogens and there is a strong correlation between mutagenicity and carcinogenicity as well, Sobels has also commented extensively on the problems associated with the extrapolation from screening test to human situations (1977).

2. Exposure Patterns in Human Populations

"As has been clearly pointed out by Kolbye (1976) any basis for the estimate of human risk must take into account the geographical and social differences in the patterns of cancer mortality and morbidity throughout this country and throughout the world. It is clearly of much greater concern to populations exposed to a particular agent, that the agent is a strong, weak, or noncarcinogen. Furthermore, it is apparent from epidemiologic and social studies that even when specific carcinogens for the human are demonstrated either by epidemiologic means or by animal or screening test data, little if any societal regulation or change may occur with respect to that knowledge. Certainly the results with smoking in this country is an excellent example of this latter statement.

"The recent volume edited by Fraumeni (1975) has described a variety of specific population groups which are at greater risk for cancer than the average individual. Furthermore, the interrelationships between environmental agents become of major significance in our studies of the epidemiology of human cancer and its relationship to bioassay data (Falk, 1976). Such considerations emphasize the importance of the natural history of carcinogenesis and the two stage concept, in particular, becomes extremely important in the real world of the human species. The promoting action of ethanol in smoking populations and the combined effects of smoking and asbestos exposure are only two of such examples. Furthermore, as pointed out in Fraumeni's book the genetic background of specific individuals and groups of individuals can be extremely significant factors in the incidence of cancer and the susceptibility to cancer from a variety of environmental agents. Therefore, it is not sufficient merely to determine qualitatively and quantitatively which agents pose an actual and potential human risk but also which combinations of agents may pose even greater risks and which specific groups of the population due to peculiar genetics, environmental, occupational or other reasons may be most susceptible to agents shown to be carcinogenic by bioassay data.

"A. Risk estimate based on data evaluation of the human situation with respect to the agent. The specific quantitative risks for six human carcinogens have been described above as reported by the Meselson Committee. In addition, Cranmer has made certain statistical considerations in the case of those humans

exposed to DDT (Cranmer, 1977). Unfortunately we can do little more than attempt to point out a relationship between environmental components and an apparent alteration in the risk of cancer induction. Wynder and his associates (1978) have pointed out on the basis of epidemiologic studies that increased intake of saturated fat in the human diet leads to a significant increase in the risk of colon and gastric cancer. Areas with high incidences of liver cancer may be associated with a high intake of aflatoxin as well as an increased evidence of infection with hepatitis B virus (Shank, 1977; Blumberg et al. 1975). Miller (1978) has suggested that the relatively high incidence of cancer seen in childhood may be the result in part of an interaction of genetic influences with various known carcinogenic agents. Tuyons et al. (1977) have re-emphasized the relation of alcohol and tobacco in the etiology of human esophageal cancer and claims a dose response for both agents, their effects being additive."

The draft document includes discussion on:

- Human bioassay data from epidemiologic studies—A list of chemicals or mixtures of chemicals associated with increased incidences of cancer in humans, as compiled by the International Agency for Research on Cancer. Due to extended lag periods between exposure and clinical occurrence of cancer, "it is only under exceptional circumstances that it is possible to identify the causal agent solely by epidemiologic studies."
- Comparative dose response characteristics—Limited data "suggest that the cumulative dose required per kg body weight for tumor induction in the human and experimental animals are of the same order and magnitude."
- Metabolism of putative carcinogens in humans or other primates—"The data indicate that the pathways utilized by the human are similar to if not identical with those in lower animals. . . . That polycyclic hydrocarbons are metabolized in human tissues in manners similar to those observed in rodents has been documented in several studies. . . . The evidence to date suggests that metabolism of xenobiotics is likely to be similar in the human and other animals, but differences in the rates of various reactions between experimental animals and humans should be expected."
- Bioassay methodologies, data generated, and limitations of application—"Although the production of neoplasia in animals at a statistically higher level than in controls has been considered indicative of carcinogenicity, modern concepts of the natural history of neoplastic development require that this simplistic evaluation of the data must be reconsidered. Experimental format, routes of administration, genetic variation in metabolism and specific test systems affect interpretation of results."
- Initiating agents and promoting agents—"An agent—chemical, physical, or biological—capable of directly altering the native molecular structure of the genetic component (DNA) of the cell is an initiating agent. . . . An agent that alters the expression of genetic information of the cell is a promoting agent."
- Interaction of chemical and viral oncogenesis—"There is now considerable evidence that in a number of rodent strains and in cells derived from such strains, treatment with chemical carcinogens enhances the appearance of endogenous viruses. . . . The importance of carefully choosing the animal species in the bioassay to prevent a secondary interaction of the host with the virus, which in itself may lead to cancer, must be emphasized."

The draft document discusses the relative merits of various test systems for assessing carcinogenicity and notes that "it is now clear that a battery of short term tests is a valuable new toxicological tool that complements animal cancer tests and human epidemiology. The unique advantage of short term tests is that they are being used by industry for screening thousands of chemicals in the development of useful products and that they are being used by thousands of laboratories for screening the large number of complex mixtures in the environment. In addition, the ability to use human autopsy tissue for activation of human cells in vitro in the tests, or to detect mutagens in human body fluids, provides additional information that (often in conjunction with a whole animal bioassay) helps to strengthen the case for relevance to humans."

FEDERAL HOSPITALS PROVIDING CANCER CARE SHOULD SHARE RADIOTHERAPY: GAO

The General Accounting Office concluded after a survey of cancer treatment conducted in federal hospitals that there are "opportunities for improving how radiation therapy is provided to beneficiaries and for reducing federal health care costs through interagency sharing."

The survey was undertaken at the request of the House Appropriations Committee. It looked at cancer treatment in hospitals operated by the Dept. of Defense, Veterans Administration and Public Health Service.

GAO noted that there are 45 radiation therapy facilities in federal hospitals. Thirty-six of them did not meet the existing utilization standards of about 6,000 treatments per unit per year, as established by DOD and HEW. Eight of the 36 provided less than half that number.

VA had established a utilization standard of about 2,850 treatments a year for a radiation therapy unit. "However, because it was considerably lower than that of Defense or HEW and far below the capability of a radiation therapy unit, GAO did not use VA's standard for evaluating utilization," the report said.

GAO said there are 23 geographic locations in the U.S. which have a high potential for sharing federal radiation therapy facilities. Facilities in 20 of those

locations were underused; at each of those locations there were other federal hospitals without radiation therapy facilities.

DOD, VA and PHS all plan to either establish new radiotherapy units or modernize ones at 34 locations by 1985, at an estimated cost of $16 million.

"Because considerable opportunity exists to provide radiation therapy more efficiently through interagency sharing, GAO recommends that the heads of these agencies direct the Federal Health Resources Sharing Committee to evaluate the sharing potential at the 23 locations before additional or upgraded radiation therapy capability is acquired by the federal agencies," the report said.

"Neither VA or PHS had any written policies specifically directed toward providing cancer care. Defense issued an instruction in 1967 containing policy guidance for providing cancer care in the military; however, little attention has apprently been given to it over the years and cancer care has evolved on a decentralized basis without the influence of the policy guidance.

"Cancer care is available more extensively in the military hospital system than recently characterized to Congress by Defense (the 1967 order said that where feasible, cancer patients should be treated in a single facility with a coordinated staff and a complete diagnostic and therapeutic capability; that proposals for new cancer treatment centers could be submitted only when the number of cancer cases amounted to at least 200 a year; each service should develop plans for the treatment and referral of cancer patients, develop common definitions, uniform diagnostic criteria, and comparable epidemiological data and make maximum use of all capabilities through interservice planning of professional services)."

DOD told Congress last year that the military's cancer treatment effort was confined to 15 major military medical centers. However, GAO said, "while a considerable part of Defense's combined surgery, chemotherapy, and radiation therapy capabilities are located at these 15 medical centers, these capabilities are also available at other medical facilities. Surgery, the most common cancer treatment method, was available at virtually every military hospital in the U.S."

DOD also had told Congress that certain medical staff required to provide cancer care were available at the 15 medical centers identified as cancer treatment facilities. GAO found, however, "that not all of the types of physician specialists identified by Defense were available at each of the 15 medical centers. In addition, certain other types of cancer specialists—considered important for providing good cancer care by the National Cancer Institute—were not identified by Defense and were not available at many of the 15 medical centers. However, a few of these types were available at other hospitals."

The report said that since there is a strong interdependence between cancer patient care and physician training, cancer care should continue to be provided in the military health care system. Further, "GAO found nothing inappropriate with the overall process in Defense of providing cancer treatment at lower level military hospitals when the necessary capabilities are available and referring individuals that could not be treated to other military hospitals with greater capabilities or to the civilian sector."

GAO recommended that Defense make every effort to assign cancer specialists to those medical centers it considers to be cancer treatment facilities because "that is where the more difficult cancer cases will probably be referred."

The report noted five geographic areas where at least two federal agencies have radiotherapy facilities —San Francisco, Washington D.C., New York City, Chicago and Philadelphia. San Francisco and Washington have four federal megavoltage facilities.

The Army, Navy, Air Force and VA have radiotherapy facilities in the San Francisco area. During 1977, the Army facility provided 6,086 patient treatments and was the only one in that area which exceeded the economic utilization standard. Each of the others provided between 3,000 and 4,000 treatments.

The Army, Navy, Air Force and VA also have radiation therapy facilities in Washington. Only the Navy exceeded 6,000 patient treatments per unit during 1977. The Army had two megavoltage units in its facility—a linear accelerator and a cobalt 60 unit. They provided about 9,600 treatments, 2,400 below the standard for two units. The VA and Air Force facilities provided about 3,500 and 1,700 patient treatments, respectively.

NCI CONTRACT AWARDS

Title: Comparative leukemia and sarcoma viral studies, continuation
Contractor: Univ. of California (Davis), $426,000.

Title: Holding facility to support intramural research on RNA viruses, continuation
Contractor: Flow Laboratories, $61,512.

Title: Development of short courses on principles of biohazard and injury control, continuation
Contractor: Univ. of Minnesota, $99,323.

ADJUVANT CHEMOTHERAPY CONFERENCE COULD BE LIVELY, CONTROVERSIAL

One of the more significant and perhaps controversial conferences of the year dealing with the treatment of cancer is the Second International Conference on the Adjuvant Therapy of Cancer in Tucson March 28-31.

A number of the world's leading clinical cancer scientists are on the program which will conclude with a summary and overview session chaired by Charles Moertel of Mayo and Emil Freireich of M.D.

Anderson. Moertel and Freireich have sharply differing views of how clinical research should be conducted, and neither is reluctant to express those views.

A prospective Moertel-Freireich confrontation would not be the only lively aspect of that final session. A panel discussion will include Gianni Bonadonna, National Cancer Institute of Italy; Derek Crowther, Univ. of Manchester; Vincent DeVita, director of NCI's Div. of Cancer Treatment; Bernard Fisher, Univ. of Pittsburgh and chairman of the Primary Breast Cancer Therapy Group; Emil Frei, director of the Sidney Farber Cancer Center; Georges Mathe, director of the Institute of Cancerology in Paris; Donald Morton, UCLA; Charles Wilson, Univ. of California-San Francisco; and Freireich and Moertel.

John Ultmann, director of the Cancer Research Center at the Univ. of Chicago, will present a summary of the conference.

DeVita will chair the opening session which will present scientific considerations for adjuvant therapy. This session will include:

Frank Schabel, Southern Research Institute, recent studies with surgical adjuvant chemotherapy or immunotherapy in metastatic solid tumors of mice. V.C. Jordan, Bern, effectiveness of long term tamoxifen treatment in a laboratory model for adjuvant hormone therapy of breast cancer. Sydney Salmon, Univ. of Arizona-Tucson, human tumor stem cells and adjuvant therapy. Bruce Chabner, NCI, pharmacologic considerations in adjuvant chemotherapy. J.C. Allegra, Bethesda, association between steroid hormone receptor status and disease free interval in breast cancer. B. Lambert, Stockholm, genetic toxicity by cancer chemotherapy. W. Schreml, Germany, hematotoxicity of adjuvant chemotherapy regimens. George Blumenschein, Houston, tumor burden killed by adriamycin-combination therapy in metastatic breast cancer. Mathe, systemic immunotherapy of cancer minimal residual disease. Freireich, methods of design and evaluation of adjuvant trials.

Frei will chair a session on hematologic malignancies which will include:

Saul Rosenberg, Stanford, a 10 year analysis of the randomized Stanford trials of the use of adjuvant MOPP (nitrogen mustard, vincristine, procarbazine, prednisone) in the radiation management of Hodgkin's disease. E.M. Wolin, Stanford, a randomized comparison of PAVe (procarbazine, alkeran, vinblastine) and MOP (same as MOPP except without prednisone) as adjuvant chemotherapy for Hodgkin's disease. C.A. Coltman, San Antonio, patterns of relapse in localized (stage 1 and 2) Hodgkin's disease following extended field radiotherapy vs. involved field radiotherapy plus MOPP. R.T. Hoppe, Stanford, treatment of stage 1A, 2A Hodgkin's disease. Bonadonna, radiotherapy vs. RT plus chemotherapy in stage 1-2 non-Hodgkin's lymphomas–5 year results. T. Miller, Tucson, chemotherapy of localized histiocytic lymphoma. Stephen Jones, Univ. of Arizona, adjuvant use of BCG in the non-Hodgkin's lymphomas. DeVita, changing concepts in the management of lymphoma. Mathe, comparison of sequential chemotherapy-immunotherapy protocols in acute lymphoid leukemia. J.A. Russel, Canada, immunotherapy of acute myelogenous leukemia.

Lawrence Einhorn, Indiana Univ., will chair a session on genitourinary tumors:

Einhorn, adjuvant therapy for stage 2 testicular cancer: Is it necessary? M.E. Scheulen, West Germany, combination chemotherapy and radiotherapy in stage 2 nonseminomatous testicular cancer. N. Javadpour, Bethesda, the role of markers in the staging of testicular cancer and implications for the design of adjuvant trials.

Frei will chair the session on osteosarcoma:

Frei, adjuvant chemotherapy for osteogenic sarcoma–problems, progress, prospects. W.K. Murphy, Houston, update on adjuvant chemotherapy in osteosarcoma of adults, a Southwest Oncology Group study. C. Jasmin, France, adjuvant therapy of osteogenic osteosarcoma–results of the EORTC Osteosarcoma Working Group. Franco Muggia, NCI, adjuvant vs. delayed treatment in osteogenic sarcoma.

Melvin Tefft, Rhode Island Hospital, will chair the session on childhood tumors:

Tefft, pediatric adjuvant trials–an overview. B. LeMevel, France, five year survival of Ewing's sarcoma patients treated by radiotherapy and adjuvant chemotherapy. D. Glaubiger, NCI, early results of current combined modality therapy trials in Ewing's sarcoma at NCI.

Wilson will chair the session on brain, head and neck and thyroid cancer:

M. Al-Sarraf, Detroit, adjuvant use of cis-platinum, oncovin and bleomycin prior to surgery and/or radiotherapy in advanced untreated epidermoid cancer of the head and neck. Brian Durie, Univ. of Arizona, multimodality treatment for high risk thyroid carcinoma. K. Malekar, Canada, feasibility of treatment of advanced head and neck cancer using split course radiotherapy and kinetically based cyclic combination chemotherapy. Wilson, adjuvant approaches to the treatment of malignant glial tumors. H.A. Gilbert, Los Angeles, combination chemotherapy and delayed split course radiation therapy in malignant gliomas.

Robert Young, NCI, will chair the session on gynecologic cancer:

Young, a strategy for effective management for early ovarian carcinoma. A.J. Dembo, Canada, improved survival following abdominopelvic irradiation in ovarian cancer patients with a completed pelvic operation. David Alberts, Univ. of Arizona, BCG as an adjuvant to adriamycin-cytoxan for advanced ovarian cancer–a SWOG study.

Morton will chair the session on melanoma and soft tissue sarcoma:

Morton, adjuvant therapy for sarcomas and melanomas. T. Cunningham, Albany, a controlled ECOG study of adjuvant therapy in patients with stage 1 and 2 malignant melanoma. F. Golomb, isolated perfusion as an adjunct to surgical therapy for primary melanoma of the extremities. A Patterson, Canada, adjuvant BCG immunotherapy after surgery for stage 1 malignant melanoma.

Robert Livingston, Univ. of Texas-San Antonio, will chair the session on lung carcinoma:

Livingston, combined modality treatment of non-small oat cell lung cancer. P. Wright, Seattle, preliminary results of combined surgery and adjuvant BCG plus levamisole immunotherapy for resectable lung cancer. P. Pouillart, France, nonspecific systemic immunotherapy with BCG in patients with resected bronchus carcinoma. R. Egan, Rochester, Minn., national adjuvant trials in completely resected non-small oat cell bronchogenic carcinoma.

Fisher will chair the session on breast cancer:

R. Nissen-Meyer, Norway, one short chemotherapy course in primary breast cancer–12 year follow in series 1 of the Scandanavian Adjuvant Chemotherapy Study Group. Fisher, breast cancer studies of the National Surgical Adjuvant Primary Breast Cancer Project. Bonadonna, CMF adjuvant chemotherapy in operable breast cancer. Crowther, adjuvant therapy for breast cancer in Britain. H.J. Senn, Switzerland, divergent effect of chemo-immunotherapy with LMF/BCG in node negative and node positive breast cancer. D. Tormey, Madison, Wisc., postoperative chemotherapy with and without immunotherapy for mammary carcinoma. H. Glucksberg, Seattle, adjuvant chemotherapy in stage 2 breast cancer. T. Wheeler, England, four drug combination following surgery for breast cancer. A. Buzdar, Houston, adjuvant therapy with 5-FU, adriamycin, cyclophosphamide, and BCG for stage 2 and 3 breast cancer–prolongation of disease free interval and survival. A. Wendt, Tucson, adjuvant treatment of breast cancer with adriamycin, cyclophosphamide with and without radiotherapy. Blumenschein, update on the adjuvant chemo-immunotherapy of stage 4 NED breast cancer. S. Williams, Indianapolis, adriamycin prophylaxis in high risk

breast cancer. Carlo Nervi, Italy, prolonged survival with post irradiation adjuvant chemotherapy in stage 4 breast cancer.

Moertel will chair the session on gastrointestinal tumors:

Moertel, gastrointestinal tumors. T. Taguchi, Japan, multihospital randomized study on adjuvant chemotherapy with futraful for gastric cancer. Theodore Grage, Univ. of Minnesota, adjuvant chemotherapy in large bowel cancer. F. Panettiere, Galveston, effectiveness of postoperative adjuvant therapy with methyl CCNU plus 5-FU with or without oral BCG in an attempt to prevent recurrence of Duke B2 or C colon cancer. Interim report of a continuing SWOG study. T. McPherson, Canada, adjuvant chemoimmunotherapy and immunotherapy in B2 or C colorectal cancer. B. Wassif, The Netherlands, contribution of preoperative radiotherapy in management of border operability carcinoma of rectum. H.R. Withers, Houston, post operative radiotherapy as an adjuvant to surgical resection of adenocarcinoma of the rectum and rectosigmoid.

For registration information contact Dorothy Baker, conference coordinator, Cancer Center Div., College of Medicine, Univ. of Arizona, Tucson 85724, phone 602-626-6044.

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 contract officer or specialist named, NCI Research Contracts Branch, the appropriate section, as follows:
Biology & Diagnosis Section and Viral Oncology & Field Studies Section—Landow Building, Bethesda, Md. 20014; Control & Rehabilitation Section, Carcinogenesis Section, Treatment Section, Office of the Director Section—Blair Building, Silver Spring, Md. 20910.
Deadline date shown for each listing is the final day for receipt of the completed proposal unless otherwise indicated.

RFP NO1-CN-95452-08

Title: *Breast Cancer Detection Demonstration Project: Interview contract*
Deadline: *Approximately April 10*

NCI intends to issue an RFP to obtain the services of organizations with demonstrated capability in conducting national multigeographical health surveys for the interview contract for the Breast Cancer Detection Demonstration Project.

The organization will institute a program to administer a comprehensive patient history (CPH) to women in 27 geographical locations across the U.S. over five years. The program will cover 7,500 women-approximately 2,500 of whom will have been identified as having breast cancer.

The contractor will be responsible for obtaining CPH by personal interview, coordinating with BCDDP project personnel and Div. of Cancer Control & Rehabilitation project officers all processes and procedures leading up to interviews, and reviewing CPH for completeness after conducting the interview.

Offerors will be evaluated on experience with designing and conducting national health surveys, experience and expertise of personnel, comprehension and understanding of the requirements, method of approach and commitment and offerors' resources and organizations.

The proposed procurement listed herein is 100% set aside for small business concerns.

Contract Specialist: Cynthia Hawley
Control & Rehabilitation
301-427-7984

RFP NO1-CN-95450-02

Title: *Health effects of carcinogenic exposure—a community demonstration project*
Deadline: *Approximately April 5*

NCI is seeking proposals for the development of a new program which will demonstrate and evaluate methods of dealing with exposure to a carcinogenic agent. This procurement is intended to demonstrate methods for incorporating management of the problem into the community's ongoing health care system. The main elements of the program are 1) the organization of the community, 2) the development of information and education programs for health professionals, exposed persons and the general public, and 3) the assurance of necessary quality control measures in medical intervention. It is anticipated that there may be multiple awards under the request for proposals.

Contracting Officer: James Cavanaugh
Control & Rehabilitation
301-427-7984

RFP NO1-CN-95453-02

Title: *Development of public health strategies for the individual, the professional, and the community for cancer prevention.*
Deadline: *Approximately April 10*

The Div. of Cancer Control of NCI is soliciting proposals for a project to (1) describe current intervention and control activities for several carcinogens and associated exposed groups and (2) discuss the role of the individual, the professional, and the community in cancer control and prevention. Expertise in public health, preventive medicine, epidemiology, education and the social sciences will be required.

Contract Specialist: Jacquelyn Carey
Control & Rehabilitation
301-427-7984

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.