THE CANCER LETTER

Vol. 12 No. 25
June 20, 1986

Subscription $150 year North America
$175 year elsewhere

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Impact Of DRGs On Clinical Research Less Than First Feared, Speakers Tell NIH Directors Meeting

Although little hard data is in yet, the impact of Medicare's prospective payment system and DRGs on clinical research does not seem to be as great as many people feared,
(Continued to page 2)

In Brief

Calabresi Named DCT Board Chairman; NCI Gets $5 Million Gift For Intramural Breast Cancer Work

PAUL CALABRESI, chairman of medicine at Brown Univ., is the new chairman of the Board of Scientific Counselors of NCI's Div. of Cancer Treatment. He replaces Samuel Wells, who has completed a four year term on the board, the last two as chairman. Calabresi has been a member of the board since 1982. . . . **LEONARD ABRAMSON** family of Philadelphia will give NCI $1 million a year for the next five years to support breast cancer reserch in the intramural program. The money will support projects now ongoing in DCT and the Div. of Cancer Biology & Diagnosis. Mark Lippman, chief of the Medical Breast Cancer Section, will head the working group that is carrying out research on oncogene expression in breast cancer cells, growth factors regulating breast cancer growth, and the genetics and biochemistry of drug resistance in breast cancer. . . . **CITY OF HOPE** "has done such a remarkable job in improving its animal care facilities" that NIH has lifted the suspension of funds supporting lab animal research there, NCI Director Vincent DeVita said recently. NIH also lifted a similar suspension at Columbia Univ. . . . **NCI AND NIH** advisory group and study section members will be delighted to learn than the per diem rate for the Bethesda area will go up July 1 from the present $75 a day to $112 a day. The maximum for hotels is $79, and $33 for meals. . . . **STEPHEN O'BRIEN**, chief of the Genetics Section in the Laaboratory of Viral Carcinogenes is, has been named chief of the lab by Div. of Cancer Etiology Director Richard Adamson. O'Brien has been acting chief of the lab for several months . . . . **JACK ROTH**, who has been head of thoracic surgery at NCI, has been appointed chairman of the Dept. of Thoracic Surgery at M.D. Anderson Hospital. . . . **HENRY PITOT**, director of the Univ. of Wisconsin McArdle Laboratory, has received a $1 million grant from the American Cancer Society for basic research on cause and prevention of cancer.

Study Needed To Assess Impact Of DRGs, HMOs, PPOs On Centers

(Continued from page 1)
according to a number of speakers at the NIH Directors Advisory Committee meeting.

Discussing the impact of DRGs on General Clinical Research Centers, Betty Pickett, director of NIH's Div. of Research Resources, said, "To date, we have no hard facts on the DRGs' impact on the centers since there has been so far no truly systematic research on the issue." NIH does, however, have "some suggestive bits of preliminary information" on the participation in studies by persons 60 and older. Between the years 1979 and 1985, the number of patients admitted in this age group increased 28 percent. One third of all patients admitted to the centers have been category B patients, those admitted for diagnosis and treatment with established medical techniques, but who also participate in research protocols. Routine care is paid for by third party providers, with ancillary costs such as extra tests and extra hospital days paid for by investigator research funds or by the GCRCs. From 1982 to 1985, there has been a 17 percent decline noted in category B admission days, while patient days for category A patients (those admitted solely for research, including normal controls) increased very little. Outpatient visits rose more than 30 percent in the same period. Pickett suggested that the decline in category B patient days could be attributed to many factors, possibly including DRGs, increased use of health maintenance organizations, changes in research emphasis, and an increase in technologies that can be carried out in outpatient centers.

A preliminary retrospective self study conducted by one center in late 1984 found no apparent adverse financial effect of DRGS on the reimbursement of category B patients. The pilot study analyzed changes in net income that would have occurred if DRGs had been in place instead of the then actual payment mechanisms. The method actually found that net income would have been higher with DRGs. The extension of the pilot study to three other centers had mixed results, with two of the three centers looking essentially like the first one studied, she reported. The fourth center, one that had significantly longer patient days, however, showed a huge projected loss, which was so large that it would have outweighed the combined excess of the other centers, according to Pickett.

Warning that the method had "critical methodological pitfalls," Pickett said it should not be extrapolated. "It does underline the need for a very careful prospective design which would deal with a broad sample of centers" and confront the impact of DRGs, as well as HMOS, IPAs and PPOs on the availability of patients for study, and examine shifts from category B to category A patients. NIH will provide $87 million in the current fiscal year to fund 78 CGRCs with about 600 dedicated research beds.

Noting that there is little published evidence that DRGs have influenced the pace of clinical research, Frank Moody cited a recent audit conducted by the Conjoint Council for Surgical Research that found research by surgeons in a very bad state. "It would be nice if we could blame the DRGs for this situation, but the downslide started about a decade ago, possibly catalyzed by the financial rewards of clinical practice," he said. Moody, chairman of surgery at The Univ. of Texas Health Science Center at Houston, said, "the most immediate problem that DRGs posed for clinical research in our hospital was the perception that Medicare would deny payment for the hospitalization of patients who were considered by them to be research subjects." The concern has not been realized when proper documentation has been provided that the patient was admitted for treatment of a defined illness with a specific therapy, he said. Restraints on admission and length of stay "will clearly have a profound effect" on some clinical research, he said, adding that "there no longer will be an opportunity for 'bootlegging' a data base upon which to evaluate a new idea." DRG reimbursement "is only one of a number of approaches to financing health care that may impact in a negative way on clinical research," he said, citing HMOs as a force that will keep patients away from academic medical centers.

Outgoing American Hospital Assn. President J. Alexander McMahon also noted the impact of factors other than DRGs on clinical research. The myth that "DRGs are the major impact in the world today" is wrong, he asserted. "I put first the increase in the number of physicians and the concomitant change in physician practices," including increased out patient services, enrollment in HMOs and other selective insurance programs, and co-insurance.

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Arnold Relman also cited the adverse impact of increased numbers of physicians. "The real cost problem is that we're producing too many specialized, high technology, hospital oriented physicians and we're putting them into a system which until now has rewarded what they do on a piecemeal basis, and until we change that, we're not going to solve the problem." Noting that the mix of specialists and primary care physicians has to be changed, he said "legally we can't do it without a government mandate" and urged the medical community to support such initiatives.

Relman also stressed the need for technology assessment. "We've got to argue as persuasively as we can that the government and the other third party payers will get more than their money's worth back by their support of technology assessment. He also called for a greater emphasis on ambulatory services and preventive medicine.

NIH "must continue to give a high priority to the GCRCs," he said. "It must not allow the GCRC program to lapse--that's absolutely essential." Most of what needs to be done, however, has to be done by government and by communities.

"In the short run, we're going to have to revise fee systems so that they provide more appropriate incentives for economically efficient delivery of health care," he said.

Relman also urged state and federal support for the 400 major teaching hospitals in the U.S. "Although they constitute only 6 percent or so of all the acute general hospitals, they take care of about 18 percent of all hospital patients," he said. "They must be put in a functional position that makes sense. It does not make sense for teaching hospitals to be competing with community hospitals. The community hospitals can do what they do much more efficiently than the teaching hospitals."

Teaching hospitals "must not only be allowed to survive, ...[they] must be put at the apex of the network. That's going to require some state and federal support," he said. Some type of regulatory requirement will be needed "to make hospitals organize themselves into networks which will feed the appropriate kind of patients into the teaching hospitals. If there's got to be some closing of hospitals, it's got to be out there in the endlessly duplicated redundant community voluntary hospital system."

Challenging a prediction made earlier in the day by health consultant and forecaster Paul Ellwood, Relman said, "I do not believe that the final answer is going to be a competitive market oriented system of competing managed systems. I believe it's ultimately going to have to be replaced with some sort of comprehensive nationally financed plan which will pay the private sector for services with funds derived from federal and state tax revenues. My instinct is that we're going to wind up 10 or 20 years from now with a system" similar to Canada's. While acknowledging that "cost controls will inevitably be part of that plan," he emphasized that "there will always have to be special payments to teaching hospitals under some kind of formula that recognizes the necessity of supporting clinical research.

"In the meantime, it is clear that clinical research and research training in the academic centers will require special appropriations since cost shifting is no longer acceptable, and it will be crucial for the [academic centers] to make an effective argument before the public, before the Congress, which persuades people of the need for public support, but reassures them that the real costs of clinical research and training can be identified and controlled."

Health Care Financing & Administration official Robert Wren told the meeting that the prospective payment system established for the first time, "a very clear statutory basis for Medicare payment for clinical research that heretofore had not been there." He noted that the Prospective Payment Advisory Commission has the authority to carry out or award grants or contracts for original research, including clinical research, where existing information is inadequate for the development of guidelines. "We have not done so yet, the commission has not yet asked us to fund such research, but that provision is now a part of our law," he said. A second way hospitals can use Medicare funds for clinical research is through cost savings under DRGs, he said. "Where they save a dollar under PPS, they retain the option to spend that dollar in whatever fashion they deem necessary... that can be for clinical research or teaching." Both Wren and National Capitol Area Blue Cross-Blue Shield VP for Health Care Finance Steven Sieverts said investigators may be underestimating the support available from both government and private third party payers in supporting clinical trials to determine the cost effectiveness of various treatments.

DCE Board OKs Breast Cancer Risk Study RFA, Kills Two Other Concepts

The Organ Systems Program's batting average slumped last week when the Board of Scientific Counselors of NCI's Div. of Cancer Etiology gave concept approval to only one of three presented to it by OSP working groups.

Since the revamped Organ Systems Program started submitting concept proposals for research the working groups had determined was needed to fill in gaps or stimulate new areas, NCI's BSCs had approved every one (**The Cancer Letter**, June 6). That string ended when the DCE board turned down concepts for an RFA (request for applications) to support case control studies of risk factors for pancreatic cancer, and for a program announcement for studies of factors affecting susceptibility of the breast to experimental carcinogensis.

The board did approve the concept for a $350,000 a year, three year assessment of breast cancer risk among women with proliferative benign breast disease. This will be supported through an RFA, which means the money will be set aside to fund two to three grants, provided that many clear peer review with fundable scores.

The concept, submitted by the Breast Cancer Working Group of the Organ Systems Program, was presented by Mary-Claire King, Univ. of California (Berkeley), a member of the working group.

The board made short work of the other concept brought in the the Breast Cancer group, presented by Elinor Spring-Mills, State Univ. of New York (Syracuse), who is chairman of the working group. Although it was presented as a program announcement which does not require set aside funds, the vote to disapprove was quick and decisive.

The concept would have supported animal studies to define details of the factors that determine baseline susceptibility of the mammary gland to experimental carcinogens, delineate factors that govern the emergence and disappearance of susceptibility to mammary carcinogenesis, explore mechanisms underlying changes in susceptibility, and investigate possible protection against carcinogenesis through imposed conditions.

"I would be embarrasssed to come out with a program announcement like this," board member George Vande Woude said. "There are many laboratories doing this work."

"We see this sort of project all the time coming in to NIH study sections," board member Peter Magee agreed.

Elizabeth Anderson, NCI staff coordinator for the Breast Cancer Working Group, argued that there are only three NIH grants in two labs which are involved in those kinds of studies. None were the interdisciplinary, collaborative type proposed in the concept.

The board was not convinced, and Vande Woude's motion to disapprove carried by a 9-3 vote.

The pancreatic cancer RFA did not go down as easily. Presented by Thomas Mack, Univ. of Southern California, a member of the Pancreatic Cancer Working Group, it would have set aside a total of $2.5 million to support two grants for five years. The studies would be looking for new hypotheses and reexamining previous leads on pancreatic cancer risk factors.

"There is a lot of this kind of work going on," board member Donald Davies said. Board member Lee Wattenberg added that the proposed concept "is expensive and highly repetitive. I feel that in the end it would only produce something that is marginally better than what is known now."

Wattenberg's motion to refer the concept to the board's Epidemiology Committee for further consideration was approved 8-5, but some of the opposition to the motion came from members who felt it should be disapproved immediately. "I don't think it should go back to the committee. It should be disapproved now," Edward Bresnick said.

"The sense of the board is that this is not the time for this study," board member Noel Weiss commented.

Compared to the breast cancer benign breast disease risk factor concept the board had just approved, "this is not valid," Vande Woude said. "That was a well defined project. They knew what they were looking for. Here, you're not sure what you're looking for."

The committee met briefly the next day and concluded that there was no testable hypothesis on which to base a large scale study. In reporting back to the full board, the committee recommended that no further action be taken on the concept. When the board accepted the committee's report, the concept was dead.

The board gave concept approval to the recompetition of three resource projects involving five contracts totaling almost $5 million over multiple years. Summaries of the approved concepts follow:

Assessment of breast cancer risk among women with proliferative benign breast disease. Two or three three-year grants, with first year funding estimated at $350,000. To be competed through an RFA.

Women with benign breast disease are widely reported at increased risk of developing breast cancer; prediction of an individual's risk is more difficult. Breast biopsy specimens range from normal breast in varying physiologic states to changes approximating carcinoma in situ. It is not surprising that breast cancer risk appears not to be uniformly distributed among women with benign disease and that there is inconsistency in the literature concerning the degree of such risk.

A recent study found that among women biopsied for benign disease, breast cancer risk is concentrated in women with proliferative lesions, particularly with atypical proliferative lesions. This risk is significantly increased when proliferative disease is combined with the presence of certain epidemiologic risk factors. In a large sample of over 10,000 women having benign breast biopsies, 30% contained proliferative disease. In 3,303 women followed for a median of 17 years (1,925 with proliferative disease), women with proliferative disease without atypia had about a two fold increased risk of breast cancer compared with women without any proliferative disease, while women with atypical hyperplasia were at 5.3 times greater risk; such atypia was found in only 3.6% of all biopsies.

Although family history of breast cancer in a first degree relative had little effect on cancer risk in women without proliferative disease, women with atypia plus such a family history had a cancer risk 11 times that of women without either proliferative disease or a family history of breast cancer. No appreciable increase in breast cancer risk was found for women with cysts who did not have a family history of breast cancer, but in women with such a history, cysts were associated with a two fold higher risk. Calcification observed in mammography was also associated with elevated cancer risk in women with proliferative disease; in contrast, calcification was of no significance in women with nonproliferative lesions. This study, by Dupont and Page, thus strongly suggests that the majority (70%) of women who undergo benign breast biopsy are not at increased cancer risk, and that the small minority who are can be defined by particular histopathologic parameters.

A further paper has provided etailed definitions of atypical lobular and atypical ductal hyperplasias, both of which are associated with similar levels of increased cancer risk. Assessing cancer risk in different types of benign lesions is complicated by differences in histologic criteria among different investigators. Page's histological classification scheme is related to those of others, as are his criteria for atypical hyperplasia and for carcinoma in situ. His system differs primarily in defining atypia so as to recognize lesions that have some, but not all, characteristics of carcinoma in situ; these rare, atypical lesions are thus separated from the usual hyperplasias. A recent consensus development meeting sponsored by the College of American Pathologists considered the entire question of the histopathologic classification of various subcategories of benign breast disease, with particular reference to risk of subsequent breast cancer development, and arrived at consensus on parameters for classification and for designation of appropriate subcategories by pathologists. Their consensus includes the recent classifications by Page.

Because the findings of the Page-Dupont study have thus far been restricted to only one cohort of women, it is now essential to validate the results in other populations. It is also important to extend these initial findings by including in further studies the evaluation of additional epidemiologic risk factors for breast cancer, with the aim of attaining the most definitive preduction of risk. Among the large group of women having benign breast biopsies, it would be extremely valuable to be able to distinguish with fair certainty between those women who are at essentially no increased risk of subsequent breast cancer and those who have a very substantially elevated risk. It might then be possible to tailor strategies for surveillance, or studies on possible interventions, for a very small subset of women pinpointed as being at highest risk, or for a somewhat larger subset at moderately elevated risk. Equally important, the majority of biopsied women could be informed with a much larger measure of confidence, that their particular benign breast lesion very likely signifies no increased risk at all.

Objectives of the project are (a) to assess in different cohorts of women the risk of breast cancer associated with particular, histologically defined categories of proliferative benign breast disease; (b) to correlate mammographic patterns with histologic parameters associated with high risk; (c) to evaluate the interactio9n between histopathologic diagnosis and various, specific epidemiologic risk factor for breast cancer in predicting overall risk.

This project requires a cohort of women who have been biopsied for breast disease, on whom are available biopsy slides for review and at least five years of followup information. Mammographic information at diagnosis would be a valuable adjunct and should be obtained if at all possible. Epidemiologic information could have also been collected at the time of biopsy or could be obtained retrospectively.

Questions that could be aasked include:

1. Can the histopathologic categories identified in the recent work as predictive of breast cancer risk be consistently identified by other pathologists in other populations of women, and do they have the same prognostic value in such populations?

2. Can additional histopathologic or clinical information improve the precision of risk assessment?

3. Do particular mammographic patterns correlate with the histopathologic categories considered to be indicative of high risk of breast cancer?

4. Does family history of breast cancer in a first degree relative interact with histopathologic diagnosis to influence risk in the same way in other populations?

5. Do other epidemiologic risk factors likewise interact with histopathologic parameters predictive of highest risk, and can they augment the accuracy of risk prediction? Are any such epidemiologic patterns suggestive of underlying mechanisms of increased risk?

6. Can other aspects suggestive of mechanisms such as immunologic parameters be correlated with histologic parameters predictive of risk?

It is estimated that the proposed study would require at least 200 breast cancer cases with prior biopsy information and at least an equivalent number of biopsied cancer free women. Such a study could be carried out on a single large cohort. However, collaborative investigations should also be feasible and are encouraged, to facilitate comparable methodology, including the essential pathology review, and to increase sample sizes. Cohorts of potentially great interest include those collected as a result of earlier studies on benign breast disease stimulated by NCI's Breast Cancer Program, and cohorts accrued in breast cancer screening programs, e.g., the large number of biopsied women in the Breast Cancer Detection Demonstration Project. Others may be available in large hospitals or elsewhere.

"What would happen if we don't do this study?"

Vande Woude asked. "Isn't it likely that someone will pick up on this and do it on his own?"

If no one did, "women will continue to be told that if they have benign breast disease, they are at two to three fold increased risk for breast cancer," King said. "There is an enormous number of women being operated on unnecessarily. No one else out there seems willing to do this. The scientific fun isn't there. This is a confirmative study, and no one wants to do it without guaranteed money."

"When I read Dr. (David) Page's article, which I thought had a lot of pizzaz, my first impression was that someone should try to confirm it," Bresnick said.

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CONCEPT REVIEW FIGURES ARE ESTIMATES ONLY; RFPS, RFAS ARE NOT YET AVAILABLE FROM NCI

The dollar estimates with each concept review brought before the various boards of scientific counselors are not intended to represent maximum or exact amounts which will be spent on those projects. They are intended only as guides for board members to help in determining the value of the projects in relation to resources available to the entire program or division. Responses should be based on the workscope and description of goals and methods included in the RFPs (contracts) and RFAs (grants and cooperative agreements). Availability of RFPs and RFAs will be announced the the Institute is ready to release them.

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Synthesis of selected chemical carcinogen standards and chemopreventive agents. Recompetition of two contracts, held by Eagle-Picher (Chemsyn) and SRI International. Estimated first year award is $450,000 with a total estimate of almost $2.5 million over five years. NCI estimates it will recoup about 30% of that amount through its payback system.

These contracts provide DEC's Chemical & Physical Carcinogenesis Branch with selected chemical carcinogen standards for distribution through its Chemical Carcinogen Reference Standard Repository. Availability of these chemical resources is well known by scientists in chemical carcinogenesis research around the world and by a wide spectrum of government agencies. The chemical repository is cited as the source of specialized carcinogen standards in many scientific publications and is advertised widely with other resources offered by DCE each year.

The compounds to be prepared are either not available from commercial chemical supply houses or are not available in sufficient purity to be used as standards.

The contractors selected from this recompetition will have two major responsibilities: resynthesis of PAH derivatives (by established procedures) for the restocking of the repository as necessary; and synthesis or purification of selected chemical carcinogens, chemopreventive agents and certain of their metabolites or derivatives.

The derivatives most frequently requiring resynthesis include epoxides, dihydrodiols, phenols, quinones, and diolepoxides. Compounds requiring resynthesis will be flagged by the computer generated inventory reported by the repository and assignment will be made to the particular contractor's laboratory which will have responsibility for preparing derivatives by resynthesis. The assignment of parent hydrocarbons will be designated in the contractor's workscope and will be based on the interest, experience, and capability of the selected contractor.

In addition to the resynthesis work, the contractor will have primary synthesis and/or purification responibility for various classes of carcinogenic, mutagenic or suspect compounds and chemopreventive agents. These classes may include, among others, nitrosamines, nitrosamides, polynuclear aromatic hydrocarbons, heterocyclic PAHs, aflatoxin metabolites, fecapentaenes, food mutagens, steroid derivatives, retinoids, antioxidants, and various compounds with ^{3}H or ^{14}C labeling.

Preparation of chemopreventive compounds has been included for the first time under the workscope of these contracts. In the past, CPCB had several contracts for the preparation of labeled retinoid derivatives and analogues. There are now several commercial sources for those of major interest, so this contract now will focus on potential chemopreventive agents that are not available commercially.

It is estimated that 2 1/2 to 3 1/2 man years (per year, per contractor) of effort will be necessary to conduct the work. The incumbent contractors together with the other synthesis contractors and the repository operate under a payback system. It is estimated that the full first year award will be necessary to have "up front" money to initiate the work. In future years, two through five, it is anticipated that funds from the payback will offset the requested funding by approximately 30% ($745,960).

In general, relatively complex multistep syntheses are required, and many of the compounds and synthetic intermediates are relatively unstable, necessitating a high level of skill and experience for their synthesis and isolation in the pure state. For these reasons and because of the hazard and expense of handling large quantities of carcinogenic compounds, it is necessary to conduct initial exploratory syntheses on quite a small scale, generally employing only sufficient amounts of intermediates to determine by NMR, HPLC or other appropriate analytical techniques whether and to what extent desired reactions have taken place. Numerous repetitions are frequently required to (a) find a suitable reagent to effect selectively a desired transformation; (b) develop optimum conditions with respect to temperature, solvent, stoichiometry, pH, etc; and (c) devise satisfactory analytical and workup procedures for the isolation and characterization of these often unstable compounds in pure state. Numerous techniques for this purpose have been developed during the course of previous studies, and when compounds require resynthesis the procedures from previous experience are utilized. It should be noted, however, that the developmental work does not always yield a marketable product and therefore full cost recovery through payback will never be completely achievable. Characterized unlabeled compounds will be shipped to the NCI repository according to shipping protocols established by the project officer. Distribution to the research community will be handled by the repository contractor for all unlabeled compounds and will be on a payback system. Labeled compounds will be subdivided and shipped on a payback system to investigators in the scientific community by the synthesis contractor as instructed by the project officer.

Resource to support the chemical, economic and biological information needs of DCE and to provide chemical process, production and economic information as support to the International Agency for Research on Cancer. Recompetition of a contract held by Tracor Jitco Inc. Three years, starting in October, 1987. Estimated first year cost, $475,000; total over three years, $1.425 million.

This contract is a mechanism for the development of information in environmental and occupational cancer. The project consists of four major tasks:

Task 1 supports NCI's Chemical Selection Working Group in selecting and nominating chemicals for carcinogenicity bioassay. NCI has been and will continue to be the primary source for nomination of candidate chemicals to the National Toxicology Program. During the past five years, NTP received 105 nominations

of chemicals for carcinogenicity testing, of which 75 were nominated by NCI. Of those, 30 are proceeding through the NTP selection process; the remaining 45 have received some degree of testing by NTP, and 23 are in or programmed for carcinogenicity testing. As part of the current contract, one class study has been completed, one is in progress, and several are under consideration.

Task 2 provides support to IARC by submitting information contained in Section 1 (chemical and physical data) and section 2 (production, use, occurrence and analysis) of the IARC monographs.

Task 3 deals with the development and maintenance of data for the Chemical Carcinogenesis Research Information System (CCRIS). This is an evaluated and fully referenced data base, containing carcinogenicity, tumor promotion and mutagenicity test results. Data are derived from a series of citations, with and without abstracts, produced by two commercial sources which search pertinent data bases for articles dealing with carcinogens, mutagens and tumor promoters, and a special core set of sources, such as the class studies, NCI/NTP technical reports, IARC monographs, and results from the DCE in vitro testing program. Test results are reviewed by experts in carcinogenesis before being incorporated into the data base.

Task 4 has allowed NCI to conduct special studies and prepare reports on topics such as evaluation of carcinogenicity and mutagenicity of organic and inorganic contaminants in drinking water; inhibitors of chemical carcinogenesis; species to species comparison of metabolism, etc. Due to budgetary constraints during the current contract, no special reports have been developed. This taks also provides for review, editing and ultimately the publication in the open literature of those class studies prepared in Task 1 in support of the chemical selection process which are considered suitable for this purpose. In addition, bioassay report summaries are prepared on the NTP technical reports for inclusion in the bioassay report summaries handbook, which is available through the National Technical Information Service.

For Task 1, the chemical selection and nomination process will continue at the present rate, which will require the preparation of 30 summary sheets per year, for a total of 90 summary sheets for the three year period. Should NTP increase or decrease the number of chemicals they will be able to test for carcinogenicity, adjustments to the number of summary sheets may become necessary. Current plans are to conduct six class studies, two per contract year. Nominations to the DCE in vitro program are anticipated at the rate of 35-40 per year.

For Task 2, we anticipate providing to IARC for three working group meetings per year, for a total of nine meetings, the information required for Sections 1 and 2 of the IARC monographs. Based on past experience, this will involve 75-90 chemicals per year, or approximately 225-270 chemicals total.

In Task 3, the mechanism in place for CRISS will be continued. These sources will provide approximately 250-300 chemicals for evaluation and classification as carcinogens, mutagens or tumor promoters. Results of these evaluations will be incorporated into the CCRIS data base, as will be the results of testing up to 40 chemicals per year in the DCE in vitro program.

Efforts in Task 4 will be governed by budgetary considerations. With minimum funding, they will be limited to the preparation of bioassay summary reports at an anticipated rate of 20-25 per year, and review, editing and publication in the open literature of class studies conducted in support of the chemical selection process.

The proposed budget allocation by task is: Task 1, 44% ($210,000); Task 2, 38% ($180,000); Task 3, 14% ($70,000); task 4, 3% ($15,000).

Additional concepts approved by the DCE board, including those for new contracts in the Epidemiology & Biostatistics Program, will be reported next week in **The Cancer Letter.**

New Education Program To Fund CE, Prebaccalaureate, Summer Training

A peek at what the revamped Cancer Education Program will look like was offered in a letter from Div. of Cancer Prevention & Control Director Peter Greenwald to Sen. Wendell Ford in response to a query from the Kentucky Democrat.

The popular program, which has supported cancer curriculum development and implementation in medical schools for many years, was earmarked for extinction by the NCI Executive Committee earlier this year. However, the National Cancer Advisory Board, heeding pleas from the American Assn. for Cancer Education, asked NCI to continue the program in some form. NCI agreed, but determined that it would no longer support curriculum development and that its budget would be slashed considerably from the $4.7 million a year level it had been receiving.

Greenwald had written in a letter to AACE President George Hill that the program "will be phased down to support medical, dental and nursing student summer research activities . . . All the ongoing R25 grants (the program's official designation) which support student summer cancer research education should remain active through their approved project periods, but only for the purpose of supporting the above activities. Thus many of them will not be terminating until 1990. Of course, future year budgets will be adjusted downward to fund only that part of the grant which supports student summer cancer research education. In addition, competition for new awards in support of said student cancer research education should be possible after new guidelines have been published."

One of AACE's primary arguments for retaining the program was the specific language in the renewal last year of the National Cancer Act mandating cancer education as one of NCI's activities. "We agree that under the terms of the new Act, NIH has an obligation to provide cancer education for students of the health professions," Greenwald continued in his letter to Hill, "but we believe that we are meeting that obligation through the summer cancer research

education program. We also agree with your tenet that cancer control requires the proper education of medical students."

In his letter to Sen. Ford, Greenwald said these elements would be added to the program:

*It will support cancer education programs for prebaccalaureate students.

*It will attempt to emphasize programs for minority students at the prebaccalaureate level.

*It will continue to support medical and dental students engaged in cancer education programs for up to three months in the "summer" programs (summer could be any three month period). Students will be paid $546 per month, plus their institutions will receive up to $125 per month per student.

*It will support continuing education efforts (related to cancer, of course) for health professions--MDs, DDSs, DOs, RNs--providing funds to cover per diem costs, tuition and fees.

"Those are striking changes in NCI policy," Hill told **The Cancer Letter**. "We have a large prebaccalaureate program in cancer here (New Jersey Medical School, where he is chief of the Div. of Surgical Oncology), and have had difficulty getting support for it."

The "new direction" as far as the addition of continuing education to the program is also welcome "at a time when continuing education programs are having difficulty attracting applicants," Hill said. Enrollment has dropped sharply in recent years, due primarily to the rising fees, which can be as high as $10 an hour, Hill noted.

Not so welcome was this information passed along by Greenwald: Allocations to existing R25 grants will be slashed by 47% from their negotiated levels. That may be hard to take, but half a grant is better than none, and none is what current R25s were going to get before the NCAB and AACE stepped in.

Greenwald was out of the country and not available for comment.

Barney Lepovetsky, also unavailable for comment by press time this week, plans to wrap up the final draft of the new guidelines this week. It then must be cleared by Greenwald, NCI Director Vincent DeVita and NIH.

Adamson Joins Counterattack On "Rip Van Bailar," Cites Research Advances

With the punch line, "Rip Van Bailar, please wake up," Richard Adamson, director of NCI's Div. of Cancer Etiology, joined the counterattack on the Harvard epidemiologists, John Bailar and Elaine Smith, authors of the article which contends that "35 years of intense effort (in cancer research) must be judged a qualified failure."

"Perhaps Dr. Bailar can be excused," Adamson said of his former NCI colleague, "but can Dr. Smith, who is from Iowa, with one of the highest literacy rates in the nation?"

Addressing his remarks to the DCE Board of Scientific Counselors, Adamson continued, "Apparently these authors have not read about the discovery of reverse transcriptase; the discovery of oncogenes and their controlling elements that can lead to cancer; identification of a human retrovirus which causes leukemia; identification of another human retrovirus which causes AIDS; determination of a possible etiologic role of Epstein-Barr virus in Burkitt's lymphoma and nasopharyngeal carcinoma; detection, isolation, characterization and partial sequencing of growth factors which cause the phenotypic transformation of cells; and advances in recombinant DNA technology impacting on the following areas:

"--Determination that DNA tumor viruses act as vectors for carrying transforming oncogenes.

"--Determination that RNA tumor viruses possess regulatory signals for activation of normal cellular oncogenes.

"--DNA sequencing technology which provided information on how oncogenic sequences are regulated.

"Apparently they have not read about the development of immunological probes to assess the interaction of carcinogens with DNA, the ability to transfer genetic material into the germ line of rodent species and observe its expression and function in the host animal, the use of monoclonal antibodies to measure and map tumor antigens, the discovery of tumor promoters and antipromoters and their mechanism of action."

The Cancer Letter _Editor Jerry D. Boyd Associate Editor Patricia Williams

Published forty-eight times a year by The Cancer Letter, Inc., P.O. Box 2370, Reston, Virginia 22090. Also publisher of The Clinical Cancer Letter.