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HOUSE PASSES CANCER ACT RENEWAL WITH PROVISION PERMITTING NCI TO REINSTATE TRAINING PROGRAM

A provision that would permit NCI to fully restore the research training grant and fellowship program without regard to objections from HEW or the Office of Management & Budget was included in the bill extending the National Cancer Program for another three years passed by the House 390-1.

Debate on the bill did not touch on the training issue. And a letter from HEW Secretary Caspar Weinberger which Chairman Staggers of the Commerce Committee placed in the record did not include the training provision among his objections. In fact, it probably was overlooked by both opponents and proponents of efforts to force the Administration to revive the old training grants program.

The intent of the House is clear, however. The committee report includes this statement:

"The legislation originally provided to NCI (The National Cancer Act of 1971) authorizes the conduct of training for individuals con-

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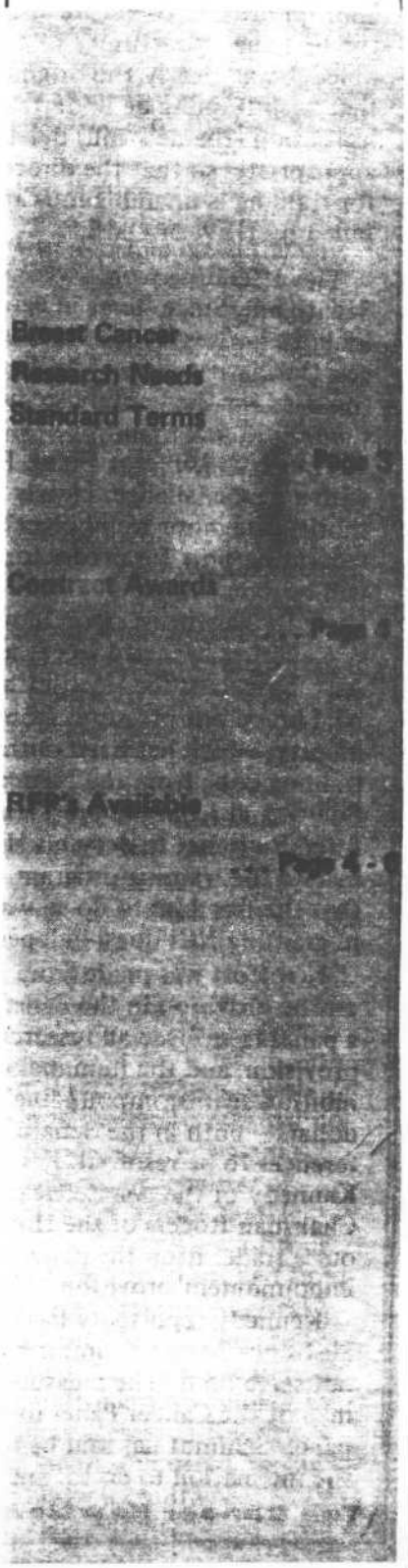
In Brief

HEW OPPOSES RESEARCH CONTRACT PEER REVIEW; CONGRESSMAN BLASTS INADEQUATE GRANT FUNDS

QUOTES: "Ours is the only responsibility in the country for drug development (in the cancer field). The pharmaceutical houses are not seriously involved in developing new anticancer drugs" -- Gordon Zubrod, NCI Cancer Treatment director . . . "**THINKING** ahead 10 - 15 years we'll have biochemical tests to determine if a woman has breast cancer without discernible symptoms. We also could have a process to reverse cell transformation" – Paul Carbone, chairman of the Breast Cancer Task Force treatment committee . . . . "**EVERYONE** (of the nine cooperative groups studying lung cancer treatment) tries to do his protocol just enough differently to make comparability difficult" – Oleg Selawry, coordinator for the National Lung Cancer Program . . . . "**I'M** not sure some of these studies (drug treatment of GI cancer) are worthwhile. We've seen so many negative results. Let's forget the rehash of these older drugs" – Bayard Clarkson, Sloan-Kettering, member of NCI Cancer Treatment Advisory Committee . . . . "**WE** oppose provisions which would require scientific peer review of contracts. It would be unwise to adopt in their totality grant review procedures for research contracts" – HEW Secretary Weinberger . . . . "**IT** is startling to note that the National Cancer Institute has reported that they are able to fund only one half of the scientifically approved cancer research projects which they received. This is a shameful record, for which we cannot blame the Cancer Institute. The blame must fall on Congress" -- Congressman Gus Yatron (D.-Pa) . . . .



TRAINING PROGRAM COULD BE REVIVED BY PROVISION IN CANCER ACT RENEWAL

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cerned with cancer and the use of training stipends, fellowships, and career awards for this purpose. The original legislation includes a provision that this training is to be undertaken 'where appropriate.' This provision has been interpreted by HEW as allowing them to find that such training is never appropriate and therefore as allowing them to deny the NCI the opportunity to conduct such training. Since it was clearly the original legislative intent that such training be undertaken, the proposed legislation (the new bill) deletes the phrase 'where appropriate' so that the director of NCI's authority for training is unambiguous and cannot be curtailed by HEW or OMB."

The offending words were also deleted in the Senate bill. Since items in agreement in bills passed by both houses are not subject to change by conferees, the clarification of NCI's authority will stick (no date for the conference had been set by press time).

Thus NCI Director Frank Rauscher will be faced with a new challenge: clearly he will have the authority to ignore Weinberger's determination to kill federal support for predoctoral research training; will he dare use the independence that Congress repeatedly has thrust upon him?

Rauscher has tried to get along with Weinberger, Asst. Secretary for Health Charles Edwards, and the NIH brass. but pressures from the scientific community, which has been outraged and dismayed by training cuts; from the National Cancer Advisory Board, and from the President's Cancer Panel may force Rauscher to defy his HEW superiors and reinstate the training program. There's no question that the freedom to do so was the intent of Congress in granting NCI quasi-independent status.

No effort was made from the House floor to tack on the provision in the Senate bill that would create a panel to oversee all research at NIH. The panel provision, and the item making permanent the prohibition against impounding of all health program dollars – both in the Senate bill – are the major differences to be resolved. It's possible that Chairman Kennedy of the Senate Health Subcommittee and Chairman Rogers of the House counterpart will work out a trade: drop the panel and retain the anti-impoundment provision.

Kennedy reportedly has cooled off on the panel idea since Benno Schmidt has made it clear he will not serve on it. The measure would require the chairman of the Cancer Panel to be a member of the NIH panel. Schmidt has said he has neither the time nor the inclination to do so, and does not feel it can be effective. Also, Schmidt has taken up the cause of trying to get more money for NIH without any special authority to do so, which is accomplishing at least part of what Kennedy hoped to achieve with the NIH panel.

Rogers has not been quite so eager as Kennedy to strip the President of authority to impound health appropriations. There's no doubt that the move would be popular with House members, however, given the current mood of Congress.

Weinberger reiterated his intention to seek a veto if the panel provision is left in. "A Presidential panel overseeing all biomedical research could well lead to loss of the priority which the Administration and the Congress both chose to give to cancer research programs," Weinberger said in his letter. "If a bill were sent to the President providing for such a panel, I would be compelled to recommend that the President veto the bill despite the Administration's strong support for an extension of the cancer research authority."

Interestingly enough, the veto threat was not applied to the anti-impoundment provision. Weinberger insisted that the President should have the discretion "to manage spending for overall budgetary purposes," but did not suggest the bill might be vetoed if it limits that discretion.

Weinberger also said he opposed "a requirement for OMB to make specific personnel allocations for NCI." Actually, the bill may not go quite that far. It authorizes the NCI director to submit an estimate of his personnel needs along with his budget estimate directly to OMB. "It is the committee's hope and intention that positions made available to NCI by the Appropriations Committees and by OMB will be made directly available to NCI by OMB," the committee report says.

In other words, NCI, Congress and OMB will decide how many positions will be allocated to NCI, not HEW. Weinberger's opposition is understandable, but again he did not threaten the veto.

An effort by Congressman Jack Brinkley (D-Ga.) to double the authorizations and to extend the renewal time for five instead of three years was easily defeated.

The secretary's letter made no reference to his earlier opposition to the removal of the limit on number of comprehensive centers, not to his request that no specific authorization figures be included in the bill.

The debate on the Brinkley amendment did make it apparent, however, that the House will vote for just about any amount of money that Rogers requests for cancer (getting those amounts through the Appropriations Committee could be another matter).

Brinkley insisted that the number of approved but unfunded grant applications for cancer projects

demonstrates that the program needs more money. He brought a chart which showed $69 million of approved but unfunded projects for fiscal 1974.

Referring to cancer mortality statistics, Brinkley said "even in view of this staggering figure, this great loss of life in this country, the National Cancer Institute reports that they can fund only about half of the scientifically approved cancer research projects which they receive . . . I refer the members to this chart. These are approved but unfunded projects from the National Cancer Institute for one year. And remember, any one of these projects might well be the project which could produce a cure for cancer or a preventive treatment."

Brinkley quoted Solomon Garb, scientific director of the American Medical Center at Denver and cochairman of the Citizens' Committee for the Conquest of Cancer, as stating that the cancer program needs twice as much money as it is getting.

Brinkley wrapped up his argument with what he obviously felt was a shocker: Linus Pauling, Nobel prize winner and "one of this nation's most valuable resources," was denied a $37,000 grant to study possible cancer causes "because the funds are not available."

Brinkley cited American Cancer Society figures which support an appropriation of $988 million for 1975. The extra money could be spent this way: $151 million, research grants; $32 million, grants and contracts to 16 more comprehensive cancer centers; $10 million to support smaller centers; $27 million, training and fellowship grants; $3 million for 200 NCI staff additions; $9 million, cancer prevention research; $16 million, bladder, colon and other organ site task forces; $12 million, construction.

Staggers pointed out that NIH never funds all its approved grants, and Rogers mentioned that some of those projects on Brinkley's chart were duplicates of others that were funded. Staggers said he would approve of spending $100 billion this year if it "would insure we would cure this disease."

BREAST CANCER TREATMENT STUDIES NEED STANDARD DEFINITIONS -- CARBONE

Uniform definitions of basic standards of design must be developed to eliminate inconsistencies of results in breast cancer treatment research, Paul Carbone, chairman of the Breast Cancer Task Force Treatment Committee said in a presentation to the Cancer Treatment Advisory Committee.

"The ways that surgery, chemotherapy, and radiotherapy can be combined in a treatment approach for breast cancer are so manifold that it will be impossible to test more than a small fraction of all the combinations and sequences," Carbone said. "It is crucial that the data resulting from these and other studies contain enough comparability so that future studies can be rationally planned and patient resources utilized as efficiently as possible in the next generation of protocols.

"Unless all investigators come together to agree upon definitions of basic standards of design then the vicissitudes of performance will lead to inconsistencies of results, ending in continued protracted controversies about the optimal therapy for breast cancer."

Patients with initial diagnosis of breast carcinoma fall into one of two groups, Carbone pointed out – operable or inoperable. At present it is the operable broup which is the primary attack of surgical adjuvant chemotherapy.

"A critical question then is whether or not 'operability' for cure is consistently defined among the various studies. This in turn depends upon the patient eligibility factors in the protocols," Carbone said.

Critical to the five-year survival rate of breast cancer patients is the number of metastatic axillary nodes present at the time of mastectomy. When the axillary nodes are not involved, there is a 75-80% survival rate, and such patients are not included in any of these studies.

When one to three nodes are involved, the five-year survival rate becomes 62%. Two studies exclude this group, the exceptions being protocols of the NCI of Milan and the National Surgical Adjuvant Breast Project. When four or more nodes are involved with tumor, the five-year survival drops to 29%. This prognostically poor group is included in each of these trials.

With the exception of the number of axillary nodes, there do not appear to be any significant differences in these patient eligibility factors with the exception of tumor size, which has been shown to have an impact upon survival. The Mayo Clinic study has no exclusion for size, while all the others do when criteria for patient ineligibility are studies. All the other studies exclude patients with inflammatory, ulcerating lesions greater than 2 cm in diameter.

"As can be seen, there is general broad consistency in patient ineligibility criteria, although for no parameter are all four studies totally consistent either by omission of the criteria all together or actual differences in approach," Carbone said.

Carbone's remarks were based on review of four studies covering the range of NCI divisions and funding mechanisms. They were the National Surgical Adjuvant Breast Project and the Mayo Clinic, supported under contract of the Div. of Cancer Biology & Diagnosis; the two cooperative groups funded by grants from the Div. of Cancer Research Resources & Centers; and the NCI of Milan supported by the Div. of Cancer Treatment under a contract.

MAIL MIXUP CAUSES SOME COPIES TO GO ASTRAY; SEND FOR ISSUES YOU MISSED

Due to a breakdown in the mailing operation, some subscribers may not have received the May 3 issue of *The Cancer Newsletter*, issue no. 13. Notify us if you missed that or any other issue, and your copies will be sent immediately.

CONTRACT AWARDS

Title: Production of antineoplastic compounds using transformations and co-oxidation
Contractor: Bristol-Myers, $578,676

Title: Study of the operation of cancer chemotherapy laboratory facilities, drug distribution service, and genetic center for rodents
Contractor: Microbiological Associates, $25,850

Title: Study of the synthesis of derivatives of 3-fotmylrifamycin-SV
Contractor: Dow Chemical Co., $141,083

Title: Study of the resynthesis of drugs and chemicals
Contractor: Monsanto Research Corp., $52,687

Title: Construction, renovation, alteration, equipment installation at Frederick Cancer Research Center
Contractor: Litton Bionetics, $360,832 (modification)

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. Some listings will show the phone number of the Contract Specialist, who will respond to questions about the RFP. Contract Sections for the Cause & Prevention and Biology & Diagnosis Divisions are located at: NCI, Landow Bldg, NIH, Bethesda, Md. 20014; for the Treatment and Control Divisions at NCI, Blair Bldg., 8300 Colesville Rd., Silver Spring, Md. 20910. All requests for copies of RFPs should cite the RFP number. The deadline date shown for each listing is the final day for receipt of the completed proposal unless otherwise indicated.

RFP NCI-CM-53765

Title: *Primary and secondary screening, detailed drug evaluation and biochemical pharmacology, and applied research in experimental antitumor therapy*
Deadline: *June 19, 1974*

The NCI drug evaluation branch, Div. of Cancer Treatment, is seeking organizations with exceptional qualifications, professional scientific personnel, technical and supportive personnel, and physical facilities to conduct a comprehensive applied research project in experimental antitumor therapy.

Principal objectives of the project will be:

– Large scale primary and secondary screening of synthetic and natural products against transplantable rodent tumors aimed at the discovery of new and more effective antitumor drugs.

– Detailed evaluation in vivo of the antitumor activity of drugs that emerge as active from antitumor screens emphasizing the influence of treatment route and schedule and site of tumor implantation on activity.

– The evaluation of combinations of drugs and chemotherapy plus surgery.

– Studies of resistance and cross-resistance to therapy.

– Studies of the physiological disposition and metabolism of anti-tumor drugs and their relationship to therapeutic efficacy, toxicity, treatment route and schedule dependency including studies of drug interactions that may influence the efficacy of combination chemotherapy.

Candidate organizations must have the capability to conduct all segments of the project. Established methods will be used. The required minimum staffing level for this contract will be one supervisory senior professional, five senior professional, six junior professional, 21 technical, two reporting personnel plus supporting clerical and animal caretaking personnel. Requests for Proposal will be available on or after 15 May 74. The number of RFP's is limited to 50 and distribution will be made on a first come, first served basis, until the supply is exhausted.

RFP NCI-CM-53766

Title: *Basic research and development for immunochemotherapy studies in experimental tumor systems*
Deadline: *June 19, 1974*

The immunochemotherapy section, Div. of Cancer Treatment is seeking a contractor to conduct basic research and development of new biological systems for immunochemotherapy studies in experimental tumor systems relevant to clinical problems.

The project aims are as follows:

– Testing the influence exerted by humoral or cellular antibodies against tumor-associated antigens on the growth of autochthonous or transplanted tumors.

– Testing the effect of antitumor drugs and animal viruses on the immuni response of mice against tumor-associated antigens.

– Testing the effect in vivo and in vitro of established or new antitumor drugs on the antigenic properties of normal and tumor cells.

– Conducting basic and developmental investigations with spontaneous and induced primary tu-

mors in inbred of F_1 hybrid mice leading to the development of new assay systems for immunochemotherapy studies.

The required minimum staffing level for this project will be one supervisory professional, two senior professionals and six technical personnel. Requests for Proposal will be available on or after 15 May 74. The number of RFP's, limited to 50, distribution will be made on a first come, first served basis, until the supply is exhausted.

RFP NCI-CM-53767

Title: *Development of biological systems for screening and detailed evaluation of established and experimental antitumor drugs*

Deadline: *June 19, 1974*

Drug Research and Development Div. of Cancer Treatment is seeking a contractor with exceptional professional scientific qualifications, technical & supportive personnel and physical facilities to conduct basic research projects directed toward the development of biological systems for screening and detailed evaluation of established and experimental anti-tumor drugs.

The principal objectives of this contract will be to conduct basic studies to aid the DCT in:

– Development of new animal tumor systems with predictive value in selecting drugs which will be active in human solid tumors.

– Development and evaluation of in vivo and in vitro experimental systems for the detailed investigation of anti-tumor drugs developed in the DCT program.

– Development of cell lines resistant to antitumor drugs and basic investigation of cross-resistance and collateral sensitivity among antitumor drugs.

– Investigation of biological systems useful in the selection of effective combination chemotherapy or combined modality regimens.

– Basic research leading to the application of cytokinetic, biochemical and pharmacologic characteristics of experimental antitumor drugs to improve therapeutic response in animal tumor systems by the design of novel treatment schedules and effective combined drug or treatment modality approaches.

The required minimum staffing level for this contract will be one supervisory professional, two senior professionals and five technical personnel. Requests for proposal will be available on or about 15 May 74. RFP's limited to 50 and distribution will be made on a first come, first served basis until the supply is exhausted.

Contract Specialist (for preceding three RFP's):
Joseph Kerner
301-427-7470
Cancer Treatment

RFP NCI-CM-53745

Title: *Acquisition of chemicals and drugs for evaluation in cancer chemotherapy*

Deadline: *June 28, 1974*

NCI is seeking proposals from qualified contractors, not affiliated with chemical or pharmaceutical organizations, to provide support services related to the:

– Acquisition of chemical and drug samples from various sources for experimental testing as potential anti-tumor agents.

– Preparation of chemical and structural data for entry into an automated chemical information system.

– Control of samples pending chemical data processing, and disposition of samples.

– The generation of data for suppliers and management.

Support services will require combinations of technical and managerial skills to:

– Establish new sources of materials and maintain effective liaison with existing and potential new suppliers from industry, government, and non-industrial organizations with the objective of acquiring a minimum of approximately 30,000 samples of chemicals and drugs per year from the collection effort.

–Perform on-site collection of samples, including the preparation of data sheets containing the chemical structure, molecular formula and other data related to the samples collected.

– Receive up to 20,000 samples per year (with associated data sheets) submitted to NCI from other domestic and foreign suppliers, and prepare related data processing entry forms.

– Store the samples in freezers or refrigerators, as required, pending the processing of data and disposition of samples.

–Correlate various outputs of the data processing system with samples in temporary storage.

– Assure the completeness of documentation required to accompany samples and transfer these documents and samples to a storage and distribution contractor.

– Prepare cover letters reporting data to suppliers.

– Forward operation and management reports to NCI.

Since the contractor will have access to proprietary information on samples acquired by NCI, the contractor cannot be in a competitive position with current or potential domestic or foreign industrial donors of samples. Further, to maintain existing relationships with suppliers and to develop new suppliers, a senior member of the contractor's staff must be of sufficient professional stature to secure and maintain

the confidence of all such suppliers.

It is estimated that this project will require 12-technical man years of effort per year. All technical personnel should be available to the project 100% of their time. The technical personnel will include the following:

– A project leader (Ph.D or equivalent, trained in organic or medicinal chemistry) who can command confidence in the community of NCI suppliers and be capable of managing all operational aspects of this effort.

– Nine chemists with a minimum qualification of a B.S. in chemistry or equivalent, preferably with experience in chemical structuring conventions, and ability to develop chemical structures from chemical nomenclature.

– Two technicians, for non-structural input preparation, duplications and handling of chemical samples. In addition to the technical personnel, it is anticipated that one secretary and one clerk-typist will be required.

The project will require daily interaction between NCI staff and the contractor, and it will be necessary for the contractor to provide transportation between the two facilities. Therefore, the contractor must have facilities within a reasonably close driving radius of NIH facilities in Silver Spring, MD (the Blair Building), preferably within a 15-20 mile radius. The request for proposal (RFP) for this project will be issued on or about 22 May 74.

Contract Specialist: W.T. Harris
301-427-7470
Cancer Treatment

RFP NCI-43751

Title: *Operation of animal disease diagnostic laboratory*

Deadline: *May 30, 1974*

The animal procurement program of drug research and development division of Cancer Treatment (DCT), includes an animal disease diagnostic laboratory to monitor and control the quality of various species of rodents bred and produced by contractors of the mammalian genetics and animal production section. This service is made available to accredited suppliers of laboratory animals and laboratories which perform testing and research projects under contract with DCT. At the request of the project officer, these activities are performed for other program areas of the NCI and laboratories which perform collaborative studies with or of interest to NCI.

The major activities through the life of the contract may be summarized as follows:

Diagnostic services which include the operation of a salmonella spp. and pseudomonas spp. diagnostic effort for monitoring all rodent strains, stocks and species maintained and produced by MG & APS animal resources; monitoring of tumor stocks microbiologically, as required; provision of diagnostic services for unusual conditions; provision of assistance in control and prevention of epizootics.

Experimental investigations including the conduct of research on the nature, etiology, and prognosis of the diseases of laboratory animals.

The primary mission of the project is the operation of a salmonella spp. and pseudomonas spp. diagnostic laboratory. The contractor will be required to process 8,000 to 10,000 fecal specimens per year.

The contractor will be required to perform a limited number (500 - 1,000) of tests for mycoplasma, and ectromelia, polyoma, mouse hepatitis, lymphocytic choriomeningitis, reo 3, sendai, Theiler's GDVII, Toolan's H-1, SV-5, K, PVM and mouse adeno viruses.

Samples to be tested will include excreta, body fluids, tissues, tumors from frozen repositories, tumors in animals, and animals.

Selected animals and tumors may from time to time be tested for the presence or absence of Rauscher and Moloney leukemia viruses and the LDH virus. It is anticipated that not more than 500 tests for these viruses will be performed during a period of one year.

The contractor shall provide diagnostic services for unusual conditions which interfere with the orderly progress of an NCI-sponsored study or may be the beginning of a pathogenic condition in an animal colony. These diagnostic services shall include virological, parasitological and mycological studies.

The contractor will provide assistance in control and prevention of epizootics and enzootic situations.

The contractor will perform research studies in support of the DCT screening program. These studies will be directed towards the implications of microbiological contaminants in tumors and hosts.

Research activities shall not exceed 10-15% of the estimated effort. The service portion of this project is of prime importance. If all contract funds are expended on the diagnostic testing tasks for a particular contract period, research projects may not be funded, dependent upon funds available.

The period of performance of this contract shall be five years after the effective date of this contract unless the period of performance is extended by amendment of the contract.

Contract Specialist: Joseph Kerner
301-427-7470
Cancer Treatment

The Cancer Newsletter—*Editor* JERRY D. BOYD

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