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FORD BUDGET GIVES NCI SAME AMOUNT AS FY 1977; CARTER PROBABLY WON'T ASK FOR ANY INCREASES

The Ford Administration went out of business this week leaving in the same way it came in, as far as its budget requests for NCI were concerned. Once again, the White House put an unreasonably low request

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In Brief

SHINGLETON TO HEAD AACI; SAUNDERS TO GET TWO MORE JOBS AT U. TEXAS MEDICAL BRANCH

WILLIAM SHINGLETON, director of the Duke Univ. Comprehensive Cancer Center, is the new president of the Assn. of American Cancer Centers. He succeeds Albert Owens Jr., director of the Johns Hopkins Univ. Oncology Center. Gordon Zubrod, director of the Florida Comprehensive Cancer Center, was elected vice president/president-elect at the AACI meeting in Houston last week. Shingleton, who is chairman of NCI's Cancer Control & Rehabilitation Advisory Committee, says he'll push for more cooperative programs "to prevent duplication and to allow easier comparison of results." Another high priority will be the computerized data base to be shared by all member centers, long an AACI project. . . . **PUBLICATIONS**: "DES Expsoure in Utero" and "Irradiation-Related Thyroid Cancer," published by the Div. of Cancer Control & Rehabilitation in the NCI Information for Physician Series. Write to the Office of Cancer Communications, NCI, Bethesda, Md. 20014. ACS has published its annual "Cancer Facts & Figures," loaded with information on incidence and death rates by cancer sites and by state, and on the Society's activities. Copies may be obtained from Division offices and ACS headquarters, 777 Third Ave., NYC 10017. . . . **J. PALMER SAUNDERS** retired 2½ years ago as director of NCI's Div. of Cancer Research Resources & Centers and has been keeping busy as dean of the Univ. of Texas Medical Branch School of Biomedical Sciences. His "retirement" hasn't been busy enough, however—He'll soon get two more jobs, as executive director of the cancer center there and as research coordinator for the entire medical branch. . . . **NEW STAFF** appointments announced by DCCR Director Diane Fink include: Wadie Elainey, who will head review and evaluation of the Community Based Cancer Programs in the Community Resources Development Branch; Andrew Hegyeli, program director for carcinogenesis, and Marsha Litwack, program director for prevention, in the Prevention Branch; Chauncey Bly, program director for pathology, John Lane, assistant program director for the Breast Cancer Detection Project, and Bob Bowser, program director for the Cervical Cancer Program, all in the Detection Branch; Richard Costlow, chief of the Detection Branch; Donald Buell, program director for oncology in the Treatment Branch; Wayne Hurst, executive secretary for the Grant Review Committee; and Ben Acton, special assistant to Fink.

NEW INITIATES, PROGRAMS WILL GET FUNDS ONLY WHEN OTHERS ARE ENDED

(Continued from page 1)

for cancer funds—$819 million for fiscal 1978, virtually the same amount appropriated by Congress for NCI in the current fiscal year.

Executives at NCI and elsewhere at NIH do not expect President Carter to add any to their budgets when he submits his own recommendations to Congress. Carter's staff has indicated those recommendations will be ready by mid-February.

Carter has made very little mention of biomedical research, and has placed emphasis on national health insurance as his major interest in the health field. The economy is his big concern right now, and it isn't likely that he'll go out of his way to add anything to Ford's NIH budget.

So once again, as it has since the National Cancer Act was adopted, Congress will have to take the lead in providing adequate funds for cancer research. The Ford request is less than a stand-still budget—it would represent a reduction in activities supported by NCI, considering inflation and mandatory increases in in-house expenses.

NCI is receiving $815 million in fiscal 1977. The Ford budget asks for the same amount, plus another $4 million earmarked as NCI's share of the cost of implementing the Toxic Substances Act. The Environmental Protection Agency has primary responsibility for that program. The Office of Management & Budget decided to encourage EPA to make use of NCI's carcinogenesis testing program rather than set up its own.

In its budget request to OMB, NCI had asked for $955 million. That would have permitted funding over 50% of approved competing (new and renewal) traditional grants, $25 million in construction, additional funds for centers but with no new core grants, and reasonable but modest increases in treatment, detection and diagnosis, and etiology research.

Cancer control would have received about $70 million under the NCI request, but the $819 million budget allows only $60.8 million, an increase of $734,000 over 1977 spending.

Traditional grants will be funded at the rate of about 33% of approved competing grants this year, with $52 million. The 1978 budget has nearly $59 million for the same category, which would fund 36% of approved grants. The budget adds $3.5 million for regular research grants; the rest of the extra amount going into competing grants would come from a reduction by that amount in non-competing grants (those which expire and are not recompeted).

NCI is still planning to take $10 million out of the 1977 construction budget and distribute it among several other programs. Traditional grants would get $3.5 million, which would lift the funding percentage a couple of points. The congressional appropriation committees must approve that reprogramming, however. NCI has submitted that request, and it is by no means certain the committees will approve. The new budget request has only $12 million for construction, down $10 million from the amount appropriated for this year.

If recent history can be used as a guide, the House will add about $10-15 million to the Administration's request, and the Senate will add another $100 million. The final compromise appropriation will be about $875-$890 million.

Even the full $955 million would not permit much growth in the Cancer Program but would only support a few new initiates in each research area and meet most (but not all) of the commitments to centers and cancer control.

It has become apparent that unless major increases in funds are obtained in the next two to three years, new programs, new projects, new centers, new research in all areas—and strong continued support of basic research—will be possible only when existing programs, projects, etc. can be phased out.

There is a variety of ways the budget can be dissected. Here's how NCI broke it down by mechanism (dollars in millions):

	1977		1978	
	No.	Amount	No.	Amount
Research Grants				
Regular:				
Non-competing	1,418	$110.1	1,205	$107.8
Competing	(583)	(52.1)	(605)	(57.9)
Renewal	263	26.1	257	27.9
New	320	19.9	348	22.9
Supplemental	(187)	6.2	(186)	7.0
Subtotal	2,001	162.3	1,810	165.8
Specials:				
Research centers	188	138.5	184	139.6
Task forces	158	14.3	151	14.3
Research careers	129	3.1	125	3.0
Clinical Education	85	9.0	77	9.0
Radiation development	19	4.1	17	4.0
CREGs	119	9.5	129	10.2
Subtotal	698	178.5	683	180.1
Total Research Grants	2,699	340.8	2,493	345.9
Training Programs				
Individual awards:				
Non-competing	146	1.6	207	3.0
Competing	(189)	(2.9)	(115)	(1.6)
New	189	2.1	115	1.6
Supplemental	(268)	.8	(- - -)	- - -
Subtotal	335	4.6	322	4.6
Institutional awards:				
Non-competing	112	15.4	88	13.6
Research and development contracts	976	222.8	963	221.3
Intramural research		79.9		84.8

Budget breakdown (continued)

	1977		1978	
	No.	Amount	No.	Amount
Direct operations		61.5		67.8
Program management		7.4		7.8
Cancer control		60.6		61.2
Construction		22.0		12.0
TOTAL		**$814.9**		**$818.9**

The figure of $165.8 million includes $28 million for the Clinical Cooperative Groups, which are getting $25 million this year.

Here's the summary by research programs:

Epidemiology	$ 31.2	$ 32.1
Carcinogenesis (Physical & Chemical)	103.0	112.0
Viral Oncology	98.8	97.8
Nutrition	7.4	7.6
Tumor Biology	61.2	62.0
Immunology	77.2	78.3
Diagnostic Research	28.1	28.4
Preclinical Treatment Research	108.2	106.2
Clinical Treatment Research	121.3	126.4
Rehabilitation Research	2.5	2.8
Total	**$639.0**	**$653.8**

Not included above are funds for resource development, with $104.2 million in the budget request, compared with $115.8 this year, and cancer control.

Finally, here's how it breaks down by activity:

Research:		
Cause and Prevention	$215.8	$223.6
Detection & Diagnosis	48.9	49.4
Treatment	259.2	117.7
Resource Development:		
Cancer Centers Support	59.5	59.8
Research Manpower	33.5	31.6
Construction	22.9	12.9
Cancer Control:	60.1	60.8

KEY HEARINGS SCHEDULED ON CANCER ACT RENEWAL, APPROPRIATIONS BILLS

Four congressional subcommittees will be holding hearings during the next two to three months on two bills that will have both immediate and long-term effects on the National Cancer Program.

Renewal of the National Cancer Act will be the subject of hearings before the House Subcommittee on Public Health & Environment, chaired by Rep. Paul Rogers (D.-Fla.), and the Senate Subcommittee on Health, chaired by Sen. Edward Kennedy (D.-Mass.). Rogers has tentatively scheduled his hearings for early February; Kennedy has not yet determined when he'll start.

The Senate Labor-HEW Appropriations Subcommittee, chaired by Sen. Warren Magnuson (D.-Wash.), plans to start its hearings on the Labor-HEW appropriations bill, which will include NCI, in late February or early March. The House Labor-HEW Appropriations Subcommittee, chaired by Rep. Daniel Flood (D.-Pa.), plans to start the last week in March or the first week in April.

A successor to Harley Dirks, the long-time staff director of the Magnuson subcommittee, will be named by the end of January. Dirks resigned last year.

The subcommittees all permit a limited number of public witnesses to appear at the hearings and make statements regarding their respective bills. Here's how those interested in appearing should go about obtaining permission:

Kennedy subcommittee—Write to Kennedy at the subcommittee, Room 4226 Dirksen Office Building, Washington D.C. 20510.

Rogers Subcommittee—Call the subcommittee, 202-225-4952.

Magnuson Subcommittee—Write to Magnuson at the subcommittee, Room 1108 Dirksen Office Building, Washington D.C. 20510.

Flood Subcommittee—Write to Flood at the subcommittee, Capitol Room H 164, Washington D.C. 20215.

Include in the letters the subject on which the statement is to be made and the witness' qualifications to discuss that subject.

Most congressional committees ask that copies of the statement, including supporting documents if any, be available prior to the hearing. The complete statement will go into the printed record of the hearing, and the witness is encouraged to give a brief summary of the statement in his oral presentation.

NEW MEXICO COMMUNITY BASED PROGRAM WILL ATTEMPT TO COVER ENTIRE STATE

The two contractos awarded so far by NCI's Div. of Cancer Control & Rehabilitation for implementation of Community Based Cancer Programs offer an extreme contrast in the definition of "community."

Detroit, with the Michigan Cancer Foundation as the lead agency, is the epitome of an urban area with the massive problems that afflect most large U.S. cities. This $21.5 million program is limited to three counties of the Detroit Metropolitan Area (***The Cancer Letter,*** Jan. 14).

The Univ. of New Mexico Cancer Research & Treatment Center, with its $13.7 million contract ($6.8 million of which will come from NCI), includes the entire state as the area in which it will attempt to improve the detection, diagnosis, prevention and treatment of cancer through a coordinated effort by a variety of cooperating agencies.

New Mexico's problems in cancer control include the widely scattered health facilities typical of a rural area, and thousands of people living in remote areas with little or no access to those facilities.

A major part of the Detroit program will be aimed

at the urban poor, predominantly black. New Mexico will focus its attention on the rural poor, largely Mexican-American and Indian.

Morton Kligerman is the director of the program at the Univ of New Mexico Cancer Research & Treatment Center in Albuquerque. The State Health Dept. is a subcontractor, and the Medical Society of New Mexico has agreed to work with Kligerman on a voluntary patient referral system. Other groups collaborating in this program are the New Mexico Div. of the American Cancer Society, the New Mexico Health Education Coalition and the Southwest Health Care Corp.

The fifth largest state in area, with a population of slightly over one million, New Mexico has only 12 cities with more than 10,000 people. Approximately one-third of the population lives in the Albuquerque metropolitan area, the only city with more than 50,000 people. Nine of the 32 counties have fewer than two persons per square mile.

Median levels of education and per capita income are in the lowest 10th percentile of the 50 states. Roads in northern New Mexico and the Navajo Nation are sometimes impassable in winter. More than half of the counties have only one doctor per thousand or more population, and only five hospitals in the state have cancer programs approved by the American College of Surgeons.

Large cultural minorities of Spanish-Americans and Indians do not seek early medical attention for health problems, and their lifestyles are not seen as conducive to good nutritional and health practices. Large numbers of Indians and other persons in the low-income, rural population groups, at high risk for certain types of cancer, are currently served primarily by the U.S. Public Health Service.

For six years the New Mexico Tumor Registry has been collecting baseline data for the state through a cancer reporting system. The NMTR is a member of the NCI SEER Program (Surveillance, Epidemiology and End Results).

The Univ. of New Mexico Cancer Research & Treatment Center accepted its first patients in January 1975. It is now the central cancer facility for the entire state and has been designated as the coordinating agency for the statewide cancer control program. The center has already done extensive planning to reach the state's medical community through professional and technical assistance, education, and case referral mechanisms, which will preserve the integrity of the private practitioner-patient relationship yet provide patient access to the most current cancer management techniques.

For the Community-based Cancer Control Program, NCI funds the first year will be matched by the same amount from state and local agencies and the American Cancer Society.

Projects for public and professional education, detection, diagnosis, treatment, rehabilitation and continuing care will be coordinated in an attempt to achieve greater impact on many more people in the state than is produced by the current fragmented approach. Professional education will focus on pre-treatment evaluation and treatment. Treatment will remain the responsibility of the medical practitioners, institutions and health care facilities of New Mexico.

Target population groups in the first year of the project are those at higher than average risk for cancers of the breast, uterus (including cervix), and colon-rectum. People in these high-risk groups are all over 40 years of age—women in all ethnic and income groups for cancer of the breast; women also from all ethnic backgrounds but primarily those from minority, low-income groups for cancer of the uterus; women over 40 for cancer of the colon-rectum.

A 50-member New Mexico Community Based Cancer Control Board, geographically, ethnically and professionally representative of the various groups in the state with an interest in cancer control, has been established to ensure statewide participation and is responsible for planning the statewide program.

The New Mexico Div. of the American Cancer Society has several units in the state, with extensive public and professional participation. The New Mexico Health Education Coalition will provide both outreach and public health education functions during the first year of the program in a number of communities with diverse ethnic and cultural backgrounds, according to need and access to resources. These activities will serve as demonstration projects. In the following years of the program additional communities will be added. Staff members will assist other components of the program to gain entry into these communities and will aid in the development and dissemination of health education programs and materials aimed at target populations. They also will assist with professional and paraprofessional education.

The Southwest Health Care Corp. program is aimed mainly at rural populations served by its clinics, and urban populations served by St. Joseph Hospital and Presbyterian Hospital Center in Albuquerque and their affiliated hosptials in other communities.

METHODS OF IMPLEMENTATION

1. Public and Professional Education

The New Mexico Health Education Coalition program focuses mainly on rural Spanish-American and Indian populations not accessible or receptive to traditional health education programs.

The Southwest Health Care Corp. outreach program will give patient and staff education in clinics and four hospitals in Bernalillo, Tijeras Canyon, Carrizo, Estancia and South Valley.

The American Cancer Society education program is directed at urban populations of all ethnic groups, who are accessible through membership in civic, fraternal, service, church, business industrial or other types of organizations. During the first year of the program the ACS will send teams of a doctor, nurse

and layperson to give presentations on each cancer site in 24 communities.

2. Detection

ACS detection clinics will join with the NMCCP staff and with volunteer physicians, nurses and clerks, plus transportation, to be available to examine 30 patients daily once a month in eight locations throughout the state. It is anticipated that 2,880 individuals will be reached in the first year of operation.

Southwest Health Care Corp. clinics, with a doctor, nurse and health educator, will conduct one clinic per week in five locations (three rural, two urban). An estimated 3,525 individuals will be examined. Locations are the same as for the organization's public and professional education program.

Univ. of New Mexico Rural Detection Clinics will use specially trained paraprofessionals in a mobile clinic to reach underserved areas in four rural localities. Approximately 1,200 people will be examined.

Univ. of New Mexico Cancer Research & Treatment Center Detection Clinic for the medically indigent in Bernalillo County (Albuquerque) is expected to serve 2,500 persons.

New Mexico Health Dept. detection clinics will serve women not seen in family planning clinics in 31 counties (all except Bernalillo). An estimated 10,000 women will be examined the first year.

3. Treatment

Among the cancer services involving hospitals, efforts will be made to coordinate cancer management guidelines and referral networks for diagnosis and treatment. Hospitals will be encouraged to screen entering patients for cancers of the breast, uterus, and colon-rectum.

4. Rehabilitation

The ACS rehabilitation services will be available statewide to all cases as needed. The services include transportation, nursing care, counseling, equipment, Reach to Recovery for breast cancer patients, and ostomy assistance for colon-rectum patients.

Cancer Research & Treatment Center psychological rehabilitation, patient care and consultation will be available within commuting distance of CRTC (estimated patients–300). A training program to ensure that hospitals not within commuting distance will have these services eventually is planned.

The Indian Health Service, the National Health Service Corps, and HURA (Health Underserved Rural Area) centers are also involved in many of the above activities and will participate in professional and public education especially.

COMMITTEE NIXES FDA GUIDELINES FOR COMBINATIONS, OKAYS NDA POLICY

Food & Drug Administration staff won one and lost one with its Oncologic Drugs Advisory Committee last week.

Once again FDA failed to get the committee's approval of a plan to impose guidelines for clinical drug research. This time, R.S.K. Young, group leader for oncology, proposed guidelines for investigations with combinations of antitumor agents. The committee rejected FDA's claim that the guidelines are needed and expressed fears that they would add further to delays in approving investigational new drug applications.

The committee went along with Young's proposal to establish new efficacy standards for approval of new drug applications involving cytotoxic antineoplastic drugs. This was the result of the committee's action last year when it disapproved an NDA for methyl CCNU because of evidence that it did not prolong survival, although it did produce tumor shrinkage. Bristol, the drug's sponsor, objected on the grounds that tumor shrinkage in statistically significant numbers had been accepted in the past as sufficient evidence that a drug was beneficial, if not in terms of life prolongation at least as a palliative therapy.

The committee resisted last year when FDA asked for its support to establish guidelines for clinical testing of all anticancer drugs. After rewriting them several times to meet objections of committee members, NCI and others–without gaining much in support from the objectors–FDA has not pressed that issue.

But the issue of guidelines for testing of drug combinations has developed at FDA because of the increasing use of combinations in experimental chemotherapy. Investigators frequently use experimental drugs for which INDs had previously been obtained, in various combinations without bothering to secure new INDs for those combinations. FDA has been considering a requirement for a new IND for each new combination.

Young submitted to the committee a proposed set of guidelines for combination cancer chemotherapy. He labeled them as "draft" guidelines and insisted they were not to be considered anything but a "starting point for discussions." The proposal follows:

GUIDELINE: COMBINATION CANCER CHEMOTHERAPY (DRAFT)

"Much work in the field of clinical, experimental, cancer chemotherapy involves the testing of combinations of chemotherapeutic agents in order to devise drug regimens that will be safe and effective for a particular tumor. Although each agent in a particular combination may be approved for the particular disease (tumor) being studied, at the time it is proposed for study, the combination itself, and/or the dose of each agent comprising the combination, and/or the time interval at which each agent is administered is not generally recognized as safe and effective. The combination is by definition a 'new drug,' and subject to the new drug regulations (IND).

"The Food & Drug Administration has had a per-

missive attitude with regard to investigational studies of combinations of cancer chemotherpeutic agents. There have been instances, however, where the rationale for a proposed investigational combination is dubious, or where the preclinical toxicology is insufficient to safely guide the clinical investigator, or where the design of the clinical protocol is insufficient to allow substantial evidence of the combination's safety and efficacy to be gathered. In all of these instances, the experimental subject is exposed to unnecessary risk, contrary to the intent of the Food, Drug & Cosmetic Act. In order to correct the present situation, investigational studies of combinations of chemotherapeutic agents will be subject to the new drug regulations (IND), and the following interim guidelines will apply:

"1. Rationale

There must be convincing clinical evidence of biological antitumor activity against the disease under consideration for each agent in the combination, OR

There must be a convincing and compelling preclinical rationale supported by scientific studies for the inclusion of each agent in the combination, OR

There must be substantial evidence showing that the combination is a safe and effective therapy for another human tumor.

"2. Toxicology

All combinations which include agents which may interfere with the catabolism of a cytotoxic agent in the combination must be the subject of preclinical studies which define relevant drug interactions.

"3. Plan of Investigation

All clinically untried combinations must start with a formal phase I study of the combination in order to determine the maximally tolerated (safe) dose of each agent when given in conjunction with other agents.

"4. Phase III protocols

Besides being designed to gather substantial evidence that a combination is a safe and effective therapy, phase III protocols should show that the combination to be finally recommended is superior, on the basis of effectiveness or safety or both, to any subset of agents in the combination."

Young admitted that the "matter of combinations was not well defined in the agency. The question has come up before with other diseases, although not often. It is more widespread in cancer investigations."

William Vodra, FDA associate chief counsel for drugs, said that the agency's policy in general has been to require that each element in a combination "contribute to the treatment and that the combination be safe and effective."

Vodra said that FDA "probably does not have jurisdiction over an investigator at M.D. Anderson or the Mayo Clinic who is doing research with drugs previously approved (those with approved NDAs and thus are available on the market). If he is using investigational drugs, then the new combination should be with an IND. Otherwise, he is violating his previous IND commitment."

Following is a summary of the discussion which ensued:

Charles Moertel, committee member from Mayo: The question is, should this come under regulator. I think it is a matter of a physician's judgment.

Vodra: FDA won't say he can't use drugs concomitantly, but let's identify them, so we'll know where we stand after the study is over.

Robert Talley, Henry Ford Hospital, consultant to the committee: Our institutional review committee will review the protocols of two or three combinations. The doses are varied, not fixed. The review committee approves the study, but at any time I might vary the doses. Who's responsible? The review committee looks at it every six months, and there might be 10 changes in doses. That's my responsibility.

Young: The committee could discuss what should be in the labeling. Somehow, we have to get into the labeling some information, that a single agent might not be the best therapy for a disease.

Melvin Krant, Tufts Univ., committee consultant: How regulatory is the package insert? If a physician ignores it, how effective is it in malpractice or other legal actions?

Vodra: It has no legal status permitting FDA to prosecute a physician. It might have some use with state licensing boards or in the civil courts in malpractice. I know of no case where a license was lifted on that basis. In malpractice, an injury must be demonstrated.

Krant: Contraindications are more of a constraint on a physician than what the drug can be used for, in malpractice cases. Package inserts seem to be more concerned with making the physician be aware of what not to do with the drugs, as opposed to the best way to use them.

Vodra: I would be concerned about telling doctors only to avoid this or that. That is the wrong use of package inserts.

Krant: But physicians seldome see the package inserts. Pharmacies seldom send them along. There are other mechanisms from which physicians learn about drugs.

Vodra: But the package insert is the basic monography from which detail men, advertising, journal reports are derived.

Krant: If a more complete product could be produced by the manufacturer and distributed widely, it could be educational. The constraint on the insert is that it must fit into a package. We could have a truly educational brochure or booklet, not require that it fit into a package.

Vodra: Dr. (Richard) Crout (director of FDA's Bureau of Drugs) has suggested that we eliminate package inserts and develop a compendium for better education of physicians on the use of drugs.

Young: We have never actively encouraged the

filing of INDs for approved agents. But for investigational agents, that is different. I would like the committee to help define the issues. . . . As new agents are developed and their effects demonstrated, they usually go into combination studies. We would like to be sure they are properly developed for combination studies.

Moertel: Would you require a new IND to move each new drug into a combination study?

Young: Not necessarily. But we should look at what the requirements should be, to take it into a combination study.

Krant: It is arbitrary, if you separate drugs already on the market from new ones. Some new drugs have been extensively studied, and we know as much about them as we do about approved drugs.

Young: The difference is that marketed drugs have already been formally examined. Drugs not approved but extensively studied have not been formally examined. We're just asking for data, for some justification for the combination.

Moertel: For drugs to go into a combination study, it requires review by the institutional committee, by a science committee, by a clinical investigating committee at NCI, by the ethics committee, all made up of highly qualified people. The studies are planned and conducted by qualified investigators. Is it necessary to impose still another review?

Marion Finkel, associate director for new drug evaluation in the Bureau of Drugs: What we're dealing with are investigational drugs. The guidelines proposed by Dr. Young are reasonable.

Moertel: It is not so much the reasonableness of the guidelines. They're like ma and apple pie. But it is the question of how many times do you have to review, to make it a good review. . . . We already have some problems in the delay of INDs. If we put in some more review requirements, it is frightening. The cancer patient may have to pay the price.

Krant: You could have a phase I study with five agents, with endless combinations. It would be mind boggling to try to sort out which does what. Most combinations are empirical, with no scientific base. The end result is that people get better faster.

Richard McHugh, Univ. of Minnesota, committee member: Some kind of rationale must be involved.

Krant: No, as soon as a new drug is tested, someone says OK, let's try it in a combination. It has to have proven its worth somewhere.

Julian Ambrus, Roswell Park, committee consultant: With MOPP (the regimen which has proven so effective against Hodgkin's disease), if we had had to provide a scientific basis on each step, it would have taken 100 years.

Stanley Balcerzak, Ohio State Univ., committee member: Really, why do we need any guidelines?

Young: We need some standards. We've been getting some combination studies in which there is no documentation of a rationale.

Krant: The rationale may be found in Richard II. Shakespear said, 'desperate diseases require desperate remedies'."

Young: I hope we don't act out of desperation. . . We only want to make people think about their studies, to consider logical points for advancing a single agent into combination studies.

Moertel: So many things change, we're constantly in a state of flux. We're at the point where everything has to be stopped, to cross the t's and dot the i's.

Finkel: I think we can assure you that won't happen.

Krant: With all the peer review that goes on now, guidelines might more appropriately be used to determine who should be involved in clinical research with combination drugs, not what. We should restrict the individual practitioner, not the institutions as they are now operating with all the controls and peer review.

John Whitaker, Capital Medical Clinic, Austin, Texas, committee member: It is almost impossible to establish workable guidelines, and it involves the danger of causing further delays. It would affect NCI, Mayo and other institutions more than the private practitioner.

Moertel and Balcerzak voted for Whitaker's motion against establishing guidelines. McHugh abstained. Margaret Sullivan, M.D. Anderson, who was acting chairman in the absence of Michael Shimkin, did not vote. Committee members Bernard Fisher and Philip Schein were absent.

The committee had disapproved the NDA for methyl CCNU as single agent therapy for colo-rectal cancer. Moertel, who had conducted extensive studies with the drug and who cited other cooperative group studies, contended that although some tumor shrinkage was observed, survival had not been extended. The assumption that tumor shrinkage as least would "improve the quality of life", a standard previously considered by FDA, was not valid in this case because less toxic drugs were available that were just as effective, Moertel insisted.

Young prefaced his proposed guidelines for working that decision into the standards for NDA approval by pointing out the decision "departs from the efficacy standard set previously by FDA for anticancer drugs. The discussion and decision of the committee appears to be of interest to many parties. Although this agency has not formally set forth its efficacy standard for each drug class, it appears reasonable to establish guidelines for this one."

Here are the proposed guidelines:

"There will be two principal standards of efficacy for cytotoxic antineoplastic drugs. In terms of recommending the drug as a treatment for cancer, they will be:

"1. Unqualified indication: for drugs which cure, or control disease such that a patient can enjoy a relatively normal life, and life span.

"2. Palliative indication: for drugs which provide a statistically significant increase in survival, or in the quality of life (functional status) of a patient."

Whitaker argued that tumor shrinkage "probably does increase the quality of life" and noted that "there are a lot of drugs on the market that are worse than methyl CCNU."

"That's just the point." Balcerzak said. "We should stop releasing drugs that have no benefit."

Balcerzak, McHugh and Moertel voted to accept the guidelines, Whitaker against. Young then asked Ambrus to chair a subcommittee to "look into the quality of life," with Krant and Whitaker as members.

COMMITTEE APPROVES TAMOXIFEN NDA

The FDA Oncologic Drugs Advisory Committee recommended approval of the NDA for tamoxifen as palliative treatment for breast cancer in postmenopausal women after hearing a presentation by the drug's sponsor, ICI United States Inc.

Walter Lesky, senior physician for the firm, and John Patterson, medical advisor for affiliated Imperial Chemical Industries in the United Kingdom, presented data from studies of 1,100 breast cancer patients, 700 in Europe and 400 in the U.S. and Canada.

The first trials in Europe were reported in 1971, and studies were initiated in the U.S. in 1974.

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. Listings identify the respective sections of the Research Contracts Branch which are issuing the RFPs. Their addresses are:

Biology & Diagnosis Section—Landow Bldg
Viral Oncology & Field Studies Section—Landow Bldg
Control & Rehabilitation Section—Blair Bldg
Carcinogenesis Section—Blair Bldg
Treatment Section—Blair Bldg
Office of the Director Section—Blair Bldg

The Landow Bldg is located in downtown Bethesda, and the Blair Bldg in Silver Spring, Md., but the correct mailing address for both is the same as the NIH main campus, Bethesda, Md. 20014.

All requests for copies of the 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-CP-VO-71013-63

Title: *In Vitro transforming potential of MPMV*
Deadline: *March 30*

The Viral Oncology Program will make available to interested contractors a request for proposal to study the biological activity of Mason Pfizer monkey virus and to demonstrate whether the virus can cause in vitro cellular transformation in suitable cell culture systems. Candidate contractors must have the capability to develop and maintain cell lines for conducting transformation studies and demonstrate the ability to characterize in vitro transformation in the systems thus developed. In addition, the contractor must have the ability to utilize this information to study the events leading to cell transformation.

Contract Specialist: Jacque Labovitz
Viral Oncology
301-496-1781

RFP NCI-CM-77136

Title: *Statistical support for a cooperative group engaged in intensive studies and investigations on patients with gastrointestinal carcinomas*
Deadline: *Probably early April*

NCI will make available to interested offerors a request for proposal to provide statistical support and analysis for a cooperative group (11 institutions) accruing approximately 700 patients annually. Interested sources should have available to direct and perform the work, a senior biostatistician and trained computer personnel who are experienced in (a) sophisticated study designs for phase II and III, multidisciplinary therapeutic treatment programs on patients with gastrointestinal carcinomas, (b) setting up effective multifaceted computerized programs for clinical data and retrieval and interim and final evaluation of such data, (c) participating in the writing of protocols and publications, and (d) dealing effectively with physicians participating in group research studies.

Contract Specialist: C. Swift
Cancer Treatment
301-427-7463

SOLE SOURCE NEGOTIATIONS

Proposals are listed here for information purposes only. RFPs are not available.

Title: Development of laboratory animal virus diagnostic reagents and oepration of a service laboratory
Contractor: Microbiological Associates.

The Cancer Letter—*Editor* JERRY D. BOYD

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