THE CANCER LETTER

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Vol. 5 No. 21

May 25, 1979

Subscription $125.00 per year

NCI REORGANIZATION TASK FORCES NEAR DECISIONS ON NEW DIVISIONS' MAKEUP; TERRY MAY BE CANDIDATE

The latest and what Director Arthur Upton said he hopes is the final stage in the reorganization of NCI should start shaping up this week when one of the two task forces which will recommend the makeup of

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In Brief

SUBCOMMITTEE ADDS $16-18 MILLION TO NCI BUDGET; UPTON MIGHT LEAVE IF BILL FAILS

HOUSE HEW Appropriations Subcommittee, meeting behind closed doors for the first time in recent years, reportedly added $16-18 million to the President's budget request of $937 million for NCI. It isn't much of an increase, especially with inflation, but it's better than the 5% cut Subcommittee Chairman William Natcher hinted might be imposed. Unless the full Appropriations Committee or House members in floor action reduce the figure (as could happen with a vote to slash everything 5% across the board), the $935-955 million probably would be the least NCI will get. The Senate usually increases cancer funds over the House amounts, but this year could be an exception. . . . **THE HOUSE** was scheduled to act this week on S. 869, which would ease the restrictions limiting employment of senior government execs who take jobs in industry and academia. The House has amended the bill approved by the Senate, and a conference will be necessary before it can be sent to the President. There is some urgency, since the restrictions in existing law will not apply to those who leave government before July 1. One of those watching the bill's progress closely is NCI Director Arthur Upton, who told ***The Cancer Letter*** last week that he would seriously consider leaving for a university job if it appears the new legislation will not pass. Unlike his civil service and PHS colleagues who have a certain degree of job security, Upton pointed out, "I serve at the pleasure of the President. He could decide at any time to get a new director. And we could possibly have a new President next year. I hope I've got quite a few years of work left in me, and I have to be able to take a position at a university if I leave here." . . . **EMIL (JAY) FREIREICH** was elected president-elect of the American Society of Clinical Oncology at the meeting in New Orleans last week. Freireich, M.D. Anderson, will succeed Charles Moertel, director of the Mayo Comprehensive Cancer Center, who took over as 1979-80 president from Albert Owens, director of the Johns-Hopkins Comprehensive Cancer Center. . . . **BAYARD CLARKSON**, Memorial Sloan-Kettering, was chosen vice president and president-elect by members of the American Assn. for Cancer Research. Paul Carbone, director of the Wisconsin Comprehensive Cancer Center, assumed the AACR presidency from Hugh Creech. . . . **GERALD MURPHY**, director of Roswell Park Memorial Institute, has picked up his sixth honorary degree, this time from St. John's Univ.

PREVENTION TASK FORCE REPORT READY SOON; DISAGREEMENT ON TOUGH DECISIONS

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the two new divisions starts to work. The other may wrap up its assignment next week.

William Terry, who is acting director of the soon to be phased out Div. of Cancer Control & Rehabilitation, heads the task force which will consider what programs should be included in the new Div. of Cancer Resources, Centers & Community Programs. Terry was out of the country when Upton initiated this move and only this week was able to get his task force organized (division directors had not approved the membership by press time).

Terry will be away for another week in June when he accompanies a delegation to the USSR, but he said he hopes the task force's recommendations will be ready to present to Upton by mid-June.

Robert Hoover, chief of the Environmental Studies Section of the Environmental Epidemiology Branch in the Div. of Cancer Cause & Prevention, heads the task force which will recommend to Upton what programs should be included in the new Div. of Cancer Prevention. Some of those would be existing prevention programs in the control division, others from DCCP and perhaps elsewhere.

Hoover's task force includes DCCP Director Gregory O'Conor, and John Mulvihill, Roberto Saffiotti, Michael Sporn and James Sontag of DCCP; Richard Costlow and Andrew Haggylei, DCCR; Richard Adamson, Div. of Cancer Treatment; Robert McIntire, Div. of Cancer Biology & Diagnosis; Marvin Schneiderman, Office of the Director; and John Bailar, JNCI.

Presumably, all of DCCR's present programs which do not go into the prevention division would remain with the centers and resources division, at least for the present. There had been some speculation that the Community Oncology Program, for one, might be transferred to DCT. That probably will not happen.

Upton said in his memo on the reorganization (***The Cancer Letter,*** May 4) that the resources, centers and community programs division might include those programs still based in the old Div. of Cancer Research Resources & Centers, which is supposed to be exclusively devoted to extramural program review—construction, organ sites and professional education. The Centers Program had already been removed and was operating out of Upton's office, with Terry as acting director.

Terry told ***The Cancer Letter*** this week that his task force will seriously consider whether construction, organ sites and education programs properly belong in the division with centers and the nonprevention control elements. It is possible they could end up in other divisions or in Upton's office, but that isn't likely. They certainly will not remain in DCRRC (or the Div. of Extramural Activities, the proposed new name), since Upton is committed to separation of program from review.

Determining which parts of DCCP should be split out and placed in the prevention division could be a much more difficult and controversial task. Hoover put his task force to work right away; he agreed that decisions were not made without considerable argument.

Hoover's task force was to meet one more time to develop final recommendations, and submit its report to Upton next week. Hoover said the "tough decisions" probably would not be a consensus but would be presented on the basis of majority votes as a series of options.

Hoover did not mention specific programs considered for the move. Earlier speculation included as candidates parts or all of the two epidemiology branches—clinical and environmental; Field Studies & Statistics; the Biometry Branch; certainly the Carcinogenesis Testing Program but not the Carcinogenesis Research Program; Smoking & Health; and perhaps even Sporn's chemoprevention effort, which includes support for a clinical trial in addition to basic research and resource development.

Some have speculated that those programs which are primarily application of prevention methods would go to the new division, leaving DCCP with the research programs.

If that philosophy were to be applied, it could also affect the Div. of Cancer Biology & Diagnosis. The Breast Cancer Program, housed in that division, could join the other organ site programs in the new centers and resources division, although it is administered by NCI staff while the other organ site efforts are administered through grantees.

That would leave DCBD and DCCP essentially with basic research responsibilities, both intramural and extramural—DCBD with biochemistry, molecular biology, pathophysiology, theoretical biology, immunology, metabolism and pathology; DCCP with carcinogenesis, experimental pathology, chemistry, metabolism and toxicology, and of course, viral oncology.

"Much of the basic research in those two divisions overlap or is closely related," one NCI executive said. "There is really no reason why, with the removal of the programs involving application, those two divisions should not be merged."

That apparently was not in Upton's mind when he initiated this latest reorganization, but it could be an option the task forces will consider.

Meanwhile, speculation has been growing about who will be the directors of the two new divisions. Search committees are being formed. Addressing a session of the American Assn. for Cancer Research annual meeting last week, Upton said the task forces and search committees "would be grateful for your suggestions."

standstill budget in constant dollars since 1975.

The 1981 budget proposal fully reflects for the first time the impact of the reorganization aimed at increasing support for investigator initiated grants while reducing support for research contracts.

The $954 million NCI estimated it will get for FY 1980 would provide $51.6 million for traditional competing grants, permitting funding of 46% of approved renewals and only 23% of approved new grants. For 1981, the request is for $102 million, permitting funding of 57% of approved renewals and 40% of approved new grants. The 1980 figures are still subject to congressional manipulation, as demonstrated by the House HEW Appropriations Subcommittee actions (see above).

Here's how NCI justified its 1981 request:

I. Research

A. Epidemiology—Increase of 41 positions and $9,472,000 over the 1980 estimate of 167 positions and $41,872,000. Assistance will be continued for research and regulatory agencies concerned with epidemiologic studies of cancers relating to environmental agents. Studies of cancer in the workplace will be expanded, for example, mortality studies of rubber and beryllium workers and printers. Efforts will be expanded to identify the effects of low level radiation including the effect on patients who receive radiation treatment. Studies will be initiated to monitor the risk to new cancers resulting from the administration of therapeutic agents. Information will be obtained from examinations of NCI-sponsored treatment trials. The occurrence of cancer will be studied in selected patients, including children, because the peculiarities of the cases offer clues to the possible causes of cancers. Relationships between breast cancer and genetic markers will be examined for the purpose of identifying individuals at high risk to this disease. Studies of familial risk patterns will be expanded.

B. Carcinogenesis (physical and chemical)—Increase of 20 positions and $35,232,000 over the 1980 estimate of 284 positions and $125,264,000. As part of the National Toxicology Program large scale, multiyear animal bioassays will be expanded so that 75 new chemicals can be put on test in 1981. Research will be expanded to study carcinogens and mutagens in water and air pollutants and estimate exposures to each chemical agents. Research will be expanded concerning prospective studies of smoker profiles to identify persons at high risk to tobacco-related diseases and evaluate pharmacologic and behavioral approaches toward smoking cessation/reduction/prevention. Research will be expanded to assess the effect of smoking cessation on the potential for reversibility of bronchial dysplasia. It is theorized that intervention programs such as cessation of smoking may facilitate regression of premalignant lesions. Studies to develop biochemical and morphological markers for the detection of early responses to carcinogens by target cells will be expanded.

Human tissues in organ and cell culture for study of the effects of carcinogens on human target cells will be established, with emphasis placed on interaction between cells and chemical carcinogens of occupational significance. Research will be initiated to develop short term tests to identify simultaneously the mutagenic and carcinogenic potential of environmental agents. Investigations will continue on factors (hormonal, chemical, etc.) that moderate the development of cancer resulting in its suppression or elimination. The role of dietary, nutritional and hormonal factors on the mechanisms of inhibition of cell proliferation will be defined. Studies of natural factors which inhibit or counteract the formation of certain carcinogenic compounds (N-nitroso) will be expanded. Studies will continue on possible tumor promoters that are natural products of the environment (such as sunlight, pollens, other allergens) and act as cofactors with carcinogens and growth promoters. Attempts will continue to determine whether certain combinations of agents modify, increase or decrease their carcinogenic potential.

C. Biological Carcinogenesis—Increase of 7 positions and $12,400,000 over the 1980 estimate of 299 positions and $103,714,000. Interaction (recombination) between cellular and viral genes in the development of sarcoma inducing viruses will be further investigated. These studies can lead to the basic understanding of the process of carcinogenesis. Gene products (specific proteins elicited by these genes) may be useful agents in diagnosis, prevention and treatment of cancer. Research efforts to identify factors of a biological, chemical or physical nature which interact to induce cell transformation will be expanded. Environmental factors such as tumor promoting agents will be studied to determine whether they can interact during the latent herpes virus infections to produce transformation of cells to malignancy. Identification of human herpes virus-specified proteins (glycoproteins) which interact with lymphocytes will be sought. Such information will be helpful in development of diagnostic and prognostic aids for a variety of syndromes caused by this group of viruses. Association of Epstein-Barr virus with human lymphomas and nasopharyngeal carcinomas will be pursued; the usefulness of these viruses as markers for early detection and prognosis will be examined.

Studies of interferon inhibition of virus activation will be expanded. Renal transplant patients treated with interferon show a reduction in tumor development and frequency of cytomegalovirus-induced disease. A vaccine for mice will be developed that will provide long lasting protection against occurrence of mammary tumors as a model for prevention of human breast tumors. Large amounts of specific DNA fragments will be generated by the new technique of molecular cloning, thus permitting DNA sequencing, defining specific regions which control or promote neoplastic transformation.

NCI 1981 PRELIMINARY BUDGET BY MECHANISM (IN THOUSANDS)	1970 ACTUAL		1971 ACTUAL		1972 ACTUAL		1973 ACTUAL		1974 ACTUAL	
	DOLLARS	PERCENT OF TOTAL	DOLLARS	PERCENT OF TOTAL	DOLLARS	PERCENT OF TOTAL	DOLLARS	PERCENT OF TOTAL	DOLLARS	PERCENT OF TOTAL
Group I—Investigator Initiated										
Regular Research Grants	$ 39,576	29.1	$44,133	24.2	$59,207	18.9	$ 73,412	21.1	$ 99,415	[illegible]
Clinical Cooperative Groups	6,112	4.5	7,013	3.9	10,102	3.2	12,791	3.7	16,196	3.5
Program Projects	21,021	15.4	30,205	16.6	38,415	12.2	52,008	14.9	71,997	15.6
Radiation Development Program	—	—	—	—	—	—	—	—	—	—
Clinical Education Program	—	—	—	—	—	—	—	—	—	—
Research Career Program	1,919	1.4	2,012	1.1	2,026	.7	1,818	.5	1,673	.4
Fellowships and Training	12,465	9.1	12,560	6.9	18,395	5.9	13,888	4.0	23,562	5.1
Organ Site	—	—	—	—	638	.2	3,950	1.1	10,007	2.2
Cancer Centers—Core Support	4,554	3.4	6,174	3.4	10,090	3.2	13,002	3.7	17,575	3.8
Subtotal	85,647	62.9	102,097	56.1	138,873	44.3	170,869	49.0	240,425	52.1
Group II—Co-Initiated										
Cancer Res. Emphasis Grants (CREG)	—	—	—	—	—	—	—	—	—	—
Research Contracts	15,240	11.2	26,047	14.3	43,302	13.8	57,187	16.4	89,964	19.5
Subtotal	15,240	11.2	26,047	14.3	43,302	13.8	57,187	16.4	89,964	19.5
Group III—NCI/NCP Initiated										
Resource Contracts	29,737	21.9	46,445	25.5	66,694	21.3	68,838	19.8	77,365	16.7
Interagency Agreements	4,727	3.4	5,704	3.1	12,053	3.8	10,136	2.9	13,031	2.8
Subtotal	34,464	25.3	52,149	28.6	78,747	25.1	78,974	22.7	90,396	19.5
Group IV—Other Resources										
Planning Grants	769	.6	1,889	1.0	1,698	.5	2,500	.7	2,880	.6
CCPDS	—	—	—	—	—	—	—	—	—	—
Construction Grants	—	—	—	—	47,004	15.0	34,737	10.0	31,692	6.9
Construction Contracts	—	—	—	—	3,999	1.3	4,067	1.2	6,398	1.4
Subtotal	769	.6	1,889	1.0	52,701	16.8	41,304	11.9	40,970	8.9
Total	136,120	100.0	182,182	100.0	313,623	100.0	348,334	100.0	461,755	100.0
Percent of Total NCI Budget		77.8		80.3		84.2		81.9		79.5
In-House Research	18,625	10.7	20,594	9.1	25,696	6.9	33,032	7.8	40,364	6.9
Management & Support	20,178	11.5	24,176	10.6	33,246	8.9	39,072	9.2	46,169	7.9
(NIH Management Fund)	(9,455)	(5.4)	(10,917)	(4.8)	(12,910)	(3.5)	(15,194)	(3.6)	(16,754)	(2.9)
Cancer Control (Grants & Contracts)	—	—	—	—	—	—	4,969	1.1	32,826	5.7
Subtotal	38,803	22.2	44,770	19.7	58,942	15.8	77,073	18.1	119,359	20.5
Total NCI	**$174,923**	**100.0**	**$226,952**	**100.0**	**$372,565**	**100.0**	**$425,407**	**100.0**	**$581,114**	[illegible]

D. Nutrition—Increase of 4 positions, $6,816,000 over 1980 estimate of 10 positions, $16,136,000. Studies will be increased on dietary factors associated with carcinogenesis including relationship of mutagen/carcinogen excretion to tumor development; evaluation of cooking/processing methods relating to formation of mutagens/carcinogens; and influence of environmental stresses on nutrient requirements. Studies will be focused on changes in dietary habits in migrant populations whose movement from one area to another may be associated with changes in cancer incidence. Studies will be expanded on substances such as selenium, fibers, etc. which may be of potential value in tumor inhibition/regression. Studies of certain foods (e.g. cruciferous plants such as cabbage, kale, broccoli, etc.) which may be associated with the inhibition of carcinogenesis will be initiated. Total parenteral nutrition in randomized clinical trials will expand from small cell carcinoma of the lung to malignant lymphomas and testicular cancer. Studies of metabolic aspects of cancer and cachexia caused by various types of malignancies will be pursued, to enhance understanding of loss of appetite in cancer patients and the pathophysiology of weight loss in cancer patients.

E. Tumor Biology—Increase of 15 positions and $12,303,000 over 1980 estimate of 280 positions, $81,158,000. Emphasis will continue on basic molecular and cellular research to determine the differences between normal and cancer cells with attempts to prevent or reverse the malignant change. Changes in cancer cell surface membranes, which contribute to altered communication with other cells, will be studied. Continuing research on regulatory controls of the cell cycle during cell proliferation will be expanded. Cell culture models suitable for studies of the occurrence of neoplasia will be developed. Efforts will be made to determine the chromosomes and specific genes involved in tumor growth and progression. Studies of the mechanism of bone resorption in breast cancer, and methods to inhibit it, will be expanded. Investigation of the possible role of epithelial-stromal interactions in infiltrating ductal carcinoma of the breast will continue. Research on interaction of estrogens with progesterone and the effect on growth of mammary tissue and breast cancer will be expanded.

Because of the importance of energy-producing and biosynthetic metabolic processes to dividing cells, regulatory factors in these processes will be studied. There is evidence suggesting aberrant gene expression in tumors; the gain or loss of factors contributing to regulation of gene expression in neoplastic cells will be studied at the level of chromosome structure, RNA

1975 ACTUAL		1976 ACTUAL		1977 ACTUAL		1978 ACTUAL		1979 ESTIMATE		1980 ESTIMATE		1981 ESTIMATE	
LLARS	PERCENT OF TOTAL	DOLLARS	PERCENT OF TOTAL	DOLLARS	PERCENT OF TOTAL	DOLLARS	PERCENT OF TOTAL	DOLLARS	PERCENT OF TOTAL	DOLLARS	PERCENT OF TOTAL	DOLLARS	PERCENT OF TOTAL
12,2	20.9	$129,021	22.4	$139,156	22.8	$158,186	24.5	$178,207	26.0	$193,749	28.0	$ 253,152	30.1
19,213	3.6	23,263	4.0	27,121	4.4	29,774	4.6	31,215	4.6	32,500	4.7	38,050	4.5
83,468	15.5	77,805	13.5	81,211	13.3	85,373	13.2	91,634	13.4	91,634	13.2	108,568	12.9
4,005	.7	3,836	.7	3,245	.5	3,215	.5	2,475	.4	4,075	.6	3,712	.4
5,033	.9	7,698	1.3	8,996	1.5	9,952	1.5	10,904	1.6	10,904	1.6	12,500	1.5
2,806	.5	3,243	.6	3,507	.6	4,399	.7	4,283	.6	4,283	.6	4,900	.6
23,104	4.3	18,160	3.1	19,791	3.3	20,129	3.1	20,129	2.9	20,410	3.0	23,000	2.7
11,167	2.1	14,090	2.5	14,711	2.4	16,194	2.5	17,261	2.5	17,261	2.5	20,700	2.5
30,096	5.6	47,803	8.3	55,132	9.1	60,348	9.4	62,994	9.2	62,994	9.1	72,500	8.6
91,150	54.1	324,919	56.4	352,870	57.9	387,570	60.0	419,102	61.2	437,810	63.3	537,082	63.8
—	—	2,577	.5	7,266	1.2	9,412	1.5	7,567	1.1	5,104	.7	1,501	.2
94,976	17.6	99,925	17.3	97,240	16.0	97,459	15.1	90,901	13.3	87,873	12.7	102,688	12.2
94,976	17.6	102,501	17.8	104,506	17.2	106,871	16.6	98,468	14.4	92,977	13.4	104,189	12.4
93,016	17.3	108,109	18.7	107,729	17.7	110,706	17.1	124,720	18.2	120,644	17.4	147,793	17.6
11,593	2.2	13,262	2.3	19,414	3.2	21,621	3.4	23,426	3.4	23,605	3.4	25,290	3.0
04,609	19.5	121,371	21.0	127,143	20.9	132,327	20.5	148,146	21.6	144,249	20.8	173,083	20.6
2,568	.4	2,803	.5	1,199	.2	632	.1	300		200		200	
—	—	—	—	1,434	.2	1,617	.2	1,820	.3	1,920	.3	2,200	.3
30,000	5.6	20,000	3.5	16,000	2.6	12,000	1.9	12,000	1.8	11,000	1.6	20,000	2.3
14,976	2.8	4,721	.8	5,992	1.0	4,544	.7	5,000	.7	4,000	.6	5,000	.6
47,544	8.8	27,524	4.8	24,625	4.0	18,793	2.9	19,120	2.8	17,120	2.5	27,400	3.2
38,279	100.0	576,315	100.0	609,144	100.0	645,561	100.0	684,836	100.0	692,156	100.0	841,754	100.0
	77.0		75.7		74.8		74.0		73.1		72.5		74.2
50,532	7.2	61,243	8.0	67,855	8.3	79,217	9.1	86,408	9.2	91,769	9.6	102,045	9.0
61,935	8.9	69,876	9.2	80,184	9.8	86,594	9.9	98,855	10.6	103,771	10.9	115,927	10.2
20,248)	(2.9)	(23,037)	(3.0)	(26,817)	(3.3)	(30,150)	(3.5)	(35,048)	(3.7)	(37,174)	(3.9)	(42,000)	(3.7)
48,574	6.9	54,016	7.1	57,774	7.1	60,997	7.0	66,578	7.1	66,304	7.0	75,274	6.6
61,041	23.0	185,135	24.3	205,813	25.2	226,808	26.0	251,841	26.9	261,844	27.5	293,246	25.8
99,3	100.0	$761,450	100.0	$814,957	100.0	$872,369	100.0	$936,677	100.0	$954,000	100.0	$1,135,000	100.0

synthesis and protein synthesis. Research will continue to define the nature and mechanism of action of the spectrum of as yet undefined nutritional, hormonal and protein factors in serum and plasma that influence the growth and differentiation of tumors.

F. Immunology–Increase of 7 positions and $13,160,000 over 1980 estimate of 136 positions, $83,037,000. Structure, synthesis and function of antibody molecules, which can be involved in killing tumor cells, will be studied to enhance understanding of immunoglobulin character and permit better use of these molecules in detection, diagnosis and therapy. Proliferation and differentiation of hematopoietic stem cells into mature cells of the immune system, providing information on the heterogeneity of the cell types involved, will be examined for the interactive relationships between leukocytes involved in an immune response. Studies on the identification, isolation and characterization of antigens on the surface of breast cancer cells will be emphasized. A recently discovered natural killer cell will be studied to determine its role in the natural history of tumors. In order to better understanding the immune process and to determine if modulation by control of soluble factors is possible, increased emphasis will be given the study of soluble mediators. Studies applying the technology of recombinant DNA, cell hybridization and production of temperature sensitive mutants to immunology will be done in order to speed the exploration and development of the field of host-tumor interactions. Tumor immunology studies which utilize spontaneous autochthonous tumors as experimental models will be conducted. These tumor models more closely resemble human disease than transplantable allogeneic tumor systems used previously. Studies will be conducted on the genetic control of immune responsiveness to determine whether certain individuals may be more susceptible to cancer because of their inherent inability to mount a protective response against a tumor.

G. Diagnostic Research–Increase of 11 positions, $6,875,000 over 1980 estimate of 162 positions and $35,623,000. Efforts will focus on the development and clinical evaluation of large area solid state x-ray imagers to facilitate digitilization and optimization of x-ray images as well as data transmission, storage and retrieval. Research will be done to develop improved contrast agents for computerized tomographic x-ray imaging of the liver, as well as new algorithms for reduction of x-ray dosage in computerized tomographic imaging. Studies to improve imaging of pancreatic cancer will be supported, as will a study of improved low x-ray dose screening techniques in mammography. Development of improved detector systems

for use in radioisotopic cancer diagnosis will be expanded. Development of improved systems for tumor imaging without ionizing radiation including dedicated systems for ultrasonic mammography and ultrasonic mammography and ultrasonic probes for use with endoscopes, as well as the use of contrast agents in ultrasonic diagnosis, will be supported. Research will be conducted on automation of thermographic image processing and interpretation using computerized pattern recognition techniques. Identification of breast cancer risk associated with chronic cystic mastopathy, in situ carcinoma and "precancerous" mammary hyperplasias will be studied. Development of new systems for automated cytology will be expanded. Identification and quantification of tumor markers in the circulation of patients with cancer, e.g., tumor associated antigens, hormones, enzymes, serum proteins, will be studied. Efforts will be expanded to develop hybrid cell lines which have monoclonal antibody production toward human tumor antigens for possible production of specific antibody which could be used for diagnosis, screening and localization of tumors. In vitro techniques which can quantify the cellular immune responsiveness in patients with cancer will be further developed to provide a means for prognostic evaluation and monitoring the patients' reaction to tumor.

H. Preclinical Treatment Research—Increase of 16 positions, $23,842,000 over 1980 estimate of 296 positions, $135,905,000. Investigator initiated studies will be undertaken on the biochemistry and mechanism of drug action; pharmacology of anticancer drugs; and in various areas of experimental therapeutics, including fundamental studies utilizing in vitro and in vivo tumor systems. In addition, fundamental research will continue on radioprotectors, hypoxic cell sensitizers, and research in cell kinetics. Within the National Organ Site Program, research will be undertaken using the murine model to evaluate intravesical and systemic chemotherapy of bladder cancer; to improve the screening models and techniques to evaluate chemotherapeutic agents for activity against experimentally induced cancers of the large bowel; and for the characterization of hormone receptors in normal, BPH, and cancerous prostate tissue.

With formation of analog committees and radiosensitizer programs, and development of second generation drugs and special projects including interferon and interferon inducers, additional effort is needed for product development and small scale production to facilitate more rapid completion of drug formulation and subsequent clinical studies. Increased support will be required to meet the increased analytical workload brought on by the new Federal Good Manufacturing Procedures and other regulatory requirements. Development of in vitro screens for synthetic agents and natural products using selective toxicity assays will receive additional funds. Studies will be carried out to develop and apply renal capsule models for testing human tumors. In vitro radiobiology studies will be undertaken including biological and pharmacological investigations into interaction of radiotherapy, heat, sensitizers and protectors. Special emphasis will be placed on mechanisms of repair following toxic insults to cells. Also, studies will be undertaken on interactions of radiotherapy, heat, sensitizers and protectors on normal tissue tolerance (especially kidneys, lung and spinal cord).

The drug development program will take advantage of several highly capable foreign sources by expanding its current acquisition capacity and research and development program in natural products. This would allow setting up of a similar relationship with Europe as currently exists between NCI and Japan, and for some expansion of the latter activity. Funds would be provided to develop a screen for biologic response modifiers and would involve the development and use of a series of in vitro and in vivo model systems for evaluation of agents for their potential as biologic modifiers. Isolation of a factor from PHA-stimulated lymphocyte conditioned medium has been described which stimulates the growth of human leukemic cells. Funds will be provided to secure this factor which, if available in large quantities, will be very useful in enhancing the establishment of cell lines from tissues from human leukemia patients. These cell lines could also be useful for studying effects of drugs used in the chemotherapy of leukemia. Many anticancer agents such as cis-platinum produce severe nausea and vomiting, often leading patients to refuse therapy of potentially lifesaving drugs and to become quite debilitated. Funds will be provided to study several anti-emetic drugs which are emerging and which could be evaluated in dog studies.

Studies in in vitro methodology for rapid assessment of target-organ toxicity will be initiated involving use of cell culture and other techniques which make use of cells from plants, aquatic species, reptiles and mammals as well as human cells and tissues. Research to develop in vitro systems for studying drug toxicity will be carried out. These systems are advantageous in that exact cellular doses are possible, target cells can be studied without systemic influences, and various types of normal and neoplastic cells from animals and humans can be grown under well defined conditions. A high pressure liquid chromatography laboratory will be established. This is essential to the study of drug interaction and clinical pharmacology research. Measurement of nucleotide pools, drug metabolites and other intracellular compounds can only be done with this technology.

Molecular cloning will be undertaken to isolate fragments of DNA which play a role in the ordered growth and differentiation of hematopoietic cells. Resources will permit the growth of cloning vectors necessary for isolation of such fragments of genetic material which may permit development of new

therapy for control of leukemias.

I. Clinical Treatment Research—Increase of 17 positions, $26,558,000 over 1980 estimate of 291 positions, $138,092,000. Studies will be expanded in various areas of clinical treatment research including clinical studies of new drugs, problems in surgical oncology, use of x-ray and other radiotherapy techniques, and the interaction of these and other treatment modalities. Basic studies will be undertaken in drug-drug interaction. Research will be undertaken to advance development of computer assisted automated techniques for identifying cells in urine which show changes reflecting the effects of therapy on bladder tumors; to test the effectiveness of other drug combinations known to have significant antitumor effects against experimental models of colon cancer; to develop multi-institutional studies to evaluate various means of early chemotherapeutic treatment of pancreatic cancer; to test adjuvant chemotherapy for carcinoma of the prostate in patients with positive pelvic or para-aortic lymph nodes, all within the National Organ Site Program.

Clinical controlled prospective studies on radiosensitizers and radioprotectors are planned in selected cancers such as those involving the esophagus and the brain. Studies will be conducted in locally advanced cervical cancer to evaluate local heat as adjunct to radiotherapy. Funds will be provided to develop a computerized diode system to directly monitor radiotherapy to irregular fields. In addition, a facility will be developed to study the effects of dose rate and fractionation in small cell carcinomas, Ewing's sarcoma and myeloma. Intramural radiotherapy studies are planned on careful dosimetry on gonadal dose received by several fields and correlation with fertility studies. Research into better shielding techniques is also involved.

Research will be conducted in radiation toxicology, including problems related to late effects of radiation (alone and with chemotherapy) on normal tissues of small animals, the development of large animal models for studying radiation toxicology, and studies on human organ radiation pathology.

(The remainder of NCI's budget justification for FY 1981 will appear in next week's ***Cancer Letter.****)*

RFPs AVAILABLE

Requests for proposal described here pertain to contracts planned for award by the National Cancer Institute, unless otherwise noted. Write to the Contracting Officer or Contract Specialist for copies of the RFP, citing the RFP number. Some listings will show the phone number of the Contract Specialist, who will respond to questions. Listings identify the respective sections of the Research Contracts Branch which are issuing the RFPs. Address requests to the contract officer or specialist named, NCI Research Contracts Branch, the appropriate section, as follows:
Biology & Diagnosis Section and Viral Oncology & Field Studies Section—Landow Building, Bethesda, Md. 20014; Control & Rehabilitation Section, Carcinogenesis Section, Treatment Section, Office of the Director Section—Blair Building, Silver Spring, Md. 20910.

Deadline date shown for each listing is the final day for receipt of the completed proposal unless otherwise indicated.

SOURCES SOUGHT

RFP NCI-CP-VO-91041-66

Title: *Oncogenic or potentially oncogenic viruses*
Deadline: *Approximately June 15 (for statement of capabilities)*

NCI is seeking organizations capable of producing, purifying, characterizing, and distributing antisera to oncogenic or potentially oncogenic viruses, viral antigens, and to immunoglobulins of selected animal species. This effort is a continuation of an ongoing contract effort. Interested organizations must have these capabilities.

1. The contractor must have the capability to isolate, purify, and characterize viral antigens and species immunoglobulins needed for production of antisera without detailed protocols from NCI. The types of immunogens to be used include murine, avian, feline, and primate viruses and immunoglobulins from cats, goats, guinea pigs, horses, hamsters, humans, mice, pigs, rabbits, and rats. Initial preparation of viruses will be supplied by the government.

2. Utilizing these immunogens, the contractor must have the ability and facilities necessary to immunize, bleed and process approximately 130 liters of immune sera on an annual basis. A number of these antisera must be produced both in conventional forms and as fluorescein conjugates. In addition, antisera from "tumored" rats and hamsters shall be produced. Immunogens to be utilized shall be selected by the NCI project officer.

3. The contractor must have facilities and staff to house approximately 400 hamsters, 500 rats, 25 pigs, 70 goats, and occasional donkeys or calves as needed. Animals are government-owned.

4. The contractor must have a system for accounting for the production and distribution of reagents as well as an inventory of all government-owned reagents. Such a system must be compatible with the IBM/370 computer system so that monthly status updates can be transmitted to NCI on computer tapes. It is anticipated that one tape shall be necessary for distribution information and one tape shall contain inventory information. Data transmitted must be in a format acceptable to NCI. The accountability shall include a listing of names, addresses, and categories of recipients (e.g. NCI or NIH contractor or grantee). Inventory information shall include information on types of antisera, lot number, date produced, cross reactions, amount, etc.

5. The contractor must have the ability to store and ship antisera to recipients in all parts of the world as authorized by the NCI project officer.

6. The contractor must have immediately available space and a workable plan to transfer and store 1,350 liters of previously produced government-owned antisera. Six government-owned freezers are available to

store these sera.

7. In the past year the contractor supplied 123 different types of reagents to 300 investigator recipients and made 533 reagent shipments.

Responses should not include cost or pricing information. Concise responses should be to the points mentioned above, and indicate facilities, experience, and capabilities for carrying out this work and should include descriptions of availability and qualifications of professional and technical personnel to work on the project. An RFP will be sent only to those organizations deemed qualified to carry out the project. Ten copies of the resume of experience must be submitted.

RFP NCI-CP-VO-91040-66

Title: *Distribution of avian myeloblastosis virus and avian myeloblastosis virus reverse transcriptase*

Deadline: *Approximately June 15 (for statement of capabilities)*

NCI is seeking organizations capable of carrying out the production, storage and worldwide distribution of the materials described above. Interested organizations must have these capabilities:

1. Procurement of susceptible chicks for the propagation of myeloblastic leukemia by AMV and inoculation, monitoring, and bleeding of approximately 400,000 chicks per year.

2. Production, harvesting and storage of approximately 640 grams of avian myeloblastosis virus per year. Distribution of 214 grams of virus shipped to 52 investigators.

3. Utilize residual virus to produce avian myeloblastosis virus reverse transcriptase (AMV-RT) in yields of 25,000 units per gram (wet weight) of AMV. Specific activity of 30,000-50,000 units per mg of protein. Approximately 5.5 million units produced a year. Final product must be essentially free of RNase.

4. Storage and shipment of AMV-RT as directed by the NCI project officer. A total of 553 shipments were made to 444 investigators in the past 12 months, including 421 domestic shipments, and 131 foreign shipments.

Responses should not include cost or pricing information. Concise responses to the points mentioned above are requested. Respondents should indicate their facilities, experience, and capabilities for carrying out this research and should include descriptions of availability and qualifications of professional and technical personnel to work on the project. An RFP will be sent only to those organizations deemed qualified to carry out the project. Ten copies of the resume of experience and capabilities must be submitted.

Contracting Officer for the two projects above: Clyde Williams
Viral Oncology & Field Studies
301-496-1781

RFP NCI-CP-VO-91029-55

Title: *Support services for the Laboratory of Tumor Viruses Genetics*

Deadline: *Approximately July 10*

NCI is seeking resource and testing support for intramural research in viral oncology. The contractor must have the ability to provide large quantities of purified and concentrated mammalian and avian RNA tumor viruses from lots of 2-60 liters as needed.

Capabilities must include the ability to purified proteins and nucleic acids from these viruses, from cells infected with these viruses and from uninfected control cells. The contractor must be able to perform defined biological, biochemical and immunological assays to qualitatively and quantitatively analyze various RNA tumor viruses and prepare the necessary reagents to accomplish this task. The growth, characterization and storage of selected mammalian cell lines must be performed and up to 8,000 liters of various media associated with these functions are to be supplied.

The contractor will grow up to 50 different cell lines at one time and at least 10 roller bottles per cell line shall be provided. Selected bacterial cultures must be propagated and processed as prescribed by the project officer. This effort will be successor to current Contract No. N01 CP 43236, being performed by Meloy Laboratories Inc.

Contracting Officer: Fred Shaw
Viral Oncology & Field Studies
301-496-1781

Amendment to RFP NCI-CP-FS-91034-65

Title: *Support services for occupational studies*

Deadline: *June 22*

This RFP has been amended to delete the 100% small business set aside requirement due to changes in the workscope which requires that the contractor have national capabilities and be able to perform many or all of the workscope efforts simultaneously. However, small businesses are encouraged to respond. It should also be noted that a mandatory requirement for small business subcontracting has been added.

Due to these changes, the due date for proposals has been extended to June 22.

Contracting Officer: Sydney M. Jones
Viral Oncology & Field Studies
301-496-1781

The Cancer Letter _Editor Jerry D. Boyd

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