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GRANTEES NOT IN DANGER OF LOSING COST-FREE BIOLOGICAL MATERIALS, BUT CAN'T HAVE CHEMICALS

It now appears that NCI grantees are not in any immediate danger of being deprived of NCI supplies biological materials, including test ani-

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In Brief

NCI SCIENTIST MAY RUN FOR CONGRESS; UPTON BACKS HEROIN FOR TERMINAL CANCER PATIENTS

REGIONAL MEETINGS on various aspects of community cancer programs are being conducted by the Assn. of Community Cancer Centers. Next one, cosponsored by the Fred Hutchinson Cancer Research Center and ACS, is scheduled Sept. 16-17 at Yakima, Wash. The program includes discussions of basic components of community hospital cancer programs, examples of some community programs, and hospice concepts. Contact Richard Zandstra at the Hutchinson center, 1124 Columbia, Seattle 98104. . . . **SECOND INTERNATIONAL** Conference on Integrated Cancer Management is scheduled Feb. 22-25 in Phoenix, sponsored by Good Samaritan Hospital Div. of Oncology and ACS-Arizona Div. The program includes sessions on treatment of gynecological, breast and colon cancer and lymphomas and leukemias. Program chairman is Robert Thoeny, Good Samaritan, P.O. Box 2989, Phoenix 85062. . . . **RICHARD ADAMSON**, chief of chemical pharmacology in NCI's Div. of Cancer Treatment, is thinking about running for Congress to give biomedical science and the National Cancer Program more support on Capitol Hill. His congressional district now is represented by moderate Republican Newton Steers, who may run for Maryland governor. Adamson is a Republican, says he can't talk much about running until the Hatch Act is repealed or modified or until he resigns from NIH. . . . **NATIONAL BLADDER** Cancer Conference proceedings have been published by *Cancer Research.* A limited number of copies are available; write to National Bladder Cancer Project, St. Vincent Hospital, Worcester, Mass. 01610. . . . **BREAST CANCER** mammography screening meeting Sept. 14-16 will be held at NIH's Masur Auditorium, in the Clinical Center, instead of the smaller Wilson Hall as previously announced. Meeting starts 8:30 each day. . . . **CONSTRUCTION SUBCOMMITTEE** of the National Cancer Advisory Board meeting Sept. 18 is closed (listed as open in ***The Cancer Letter*** Aug. 26 list of meetings). The NCAB Subcommittee on Environmental Carcinogenesis meeting Sept. 18, 7:30 p.m. in NIH Bldg 31 Room 6, is open. . . . **NCI DIRECTOR** Arthur Upton said on "Meet the Press" that he favored making available medically pure heroin to terminal patients for pain control; that NCI would survey patients who have used laetrile to determine if there is any basis for proceeding to clinical trials; and that he felt the proposed ban on saccharin was "good basic public policy."

SPECIFIC CONGRESSIONAL AUTHORITY NEEDED TO GIVE GRANTEES CHEMICALS

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mals, viruses, cell lines, antisera, or of therapeutic agents. But grantees still may not receive chemicals.

The Cancer Letter reported last week that HEW legal counsel had stopped NCI from distributing reference chemical carcinogens to grantees, ruling that the only legislative authority for distribution of chemicals was for contractors. NCI executives feared that this ruling could be applied to other materials, which would be a major blow to grantees who have long relied on availability of a variety of research materials and wrote up their grants accordingly.

NIH counsel Richard Riseberg assured *The Cancer Letter* that the exclusion of grantees was limited only to chemicals. Riseberg said that sufficient legislative authority exists for giving therapeutic and biologic agents to grantees. It was the lack of specific authority either in the Cancer Act or the Public Health Service Act for giving chemicals to grantees that was the basis for HEW counsel's interpretation which cut them off. The Cancer Act mentions only biologic and therapeutic agents.

Riseberg said in a memo to NCI that the basis for the conclusion was that the PHS Act contains specific provisions permitting distribution of penicillin and other antibiotic compounds to grantees, but does not mention chemicals.

For a number of years, Congress in appropriations bills included language listing chemicals as among the materials that could be given to grantees. That language has not appeared in recent appropriations bills, however.

The rationale for distinguishing between contractors, considered "collaborative" researchers, and grantees is that contract programs involve closer working relationships and include whatever the parties agree to. A grant is merely a means to help support someone with an idea which the government feels is worthy of pursuing. Grants are authorized by specific legislation which is intended to spell out the type of support to be made available and to limit it. HEW lawyers feel that in the absence of specific authority for certain types of grant support, in this case specific in kind contributions, that support cannot be made available.

NCI has established a chemical repository from which reference chemical carcinogens have been distributed to contractors, grantees, and other government agencies with whom NCI has interagency agreements. It was felt that by making available standard reference carcinogens, results from research conducted by a variety of investigators around the country would be more meaningful and easier to interpret. In fact, NCI hoped to offer the chemicals to all investigators with bonafide requirements for them, regardless of whether or not they are supported by NCI. However, HEW counsel previously ruled that it had to be limited to those receiving NCI support.

The latest ruling preventing grantees from receiving chemicals has been particularly embarrassing to NCI's Div. of Cancer Research Resources & Centers, which administers most grants. At a time when Congress and public interest groups are applying increasing pressure for carcinogenesis research, DCRRC has to tell grantees to find their own sources for reference chemicals. Not considering the financial burden this may place on grantees, it also removes the guarantee that they will be using the same standard chemicals that are used by NCI intramural scientists and contractors.

Complicating the problem somewhat is the fact that while DCRRC executives are telling grantees they can't have the chemicals, some enterprising staff members in the Div. of Cancer Cause & Prevention have made them available to certain grantees on the basis of "interagency agreements" (probably grantees at institutions with contracts with other government agencies). Other semilegal means to get around the HEW ruling are probably employed in some cases.

John Kalberer Jr., DCRRC program planning officer, emphasized that it is not NCI program directors or intramural scientists who are causing the problem. "We are all willing and anxious to make reference chemical carcinogens available to all worthy investigators regardless of the mechanism by which they are funded," Kalberer told *The Cancer Letter*. "The inequity of the situation is further proof that the law should be amended as quickly as possible, especially in light on Congress' request for new emphasis in the environmental carcinogenesis area."

One possible remedy would be an appeal to the controller goneral, who as head of the General Accounting Office, the congressional watchdog agency, frequently interprets legislative intent. Riseberg indicated that an opinion from the controller general in favor of grantees would be accepted by HEW.

GROUP B DRUGS AVAILABLE TO INDIVIDUAL INVESTIGATORS LISTED, CENTERS NAMED

Twenty three clinical cancer centers and all 19 comprehensive centers have been authorized to participate in NCI's new plan for distributing experimental anti cancer drugs to individual physicians, hospitals and other institutions which do not now receive them through NCI supported contracts and grants.

This is the plan approved by the Food & Drug Administration (*The Cancer Letter*, Aug. 26) for handling distribution of experimental drugs which NCI in the past has made available to physicians on a less organized basis for humanitarian purposes. The drugs are not available from any source other than NCI.

The new plan requires a greater degree of super-

vision, through the centers, than in the past. And it could lead to broad participation in clinical trials by individual physicians and investigators, or at least the generation of a broader data base on drugs being studied by Div. of Cancer Treatment contractors, the cooperative groups, and other NCI grantees. Drugs will be available at no cost to physicians, institutions or patients.

The centers will be involved in distribution of 19 (at present) drugs from NCI's "Group B" list—those are drugs which have been studied in some phase II trials and have been shown to be tolerated by patients at specific doses and schedules. Reasons for additional studies will usually, though not necessarily, be based on evidence on objective responses in previous trials.

Not all Group B drugs will be available for study. Excluded will be those in limited supply, those available from commercial drug firms, or those which DCT believes should not proceed to extensive trials for any number of scientific or economic reasons.

Following is a list of the 19 Group B drugs NCI will make available now (the list will be updated as other drugs are added or existing ones removed):

ICRF-19, Baker's antifol, methyl GAG, camptothecin, VM-26, VP-16, dianhydrogalactitol, 3TGdR diglycolaldehyde, cyclocytidine, cycloleucine, IV-melphalan, TMCA, azaserine, tubercidin, dibromodulcitol, streptonigrin, dibromomannitol and Yoshi 864.

Group C drugs are those which have been thoroughly investigated and found useful against certain forms of cancer. In most cases, all studies required for an NDA (new drug application) have been completed which would be necessary for FDA approval for marketing but which for a variety of reasons have not secured that approval. Neither NCI nor FDA is as concerned about close monitoring of these drugs as they are the Group B drugs.

Group C drugs will be made available to individual physicians and institutions directly, without going through the clinical or comprehensive centers. Those drugs and the indications are:

Azacytidine—refractory AML; L-asparaginase (E. coli)—ALL; daunomycin—AML and ALL; streptozotocin—islet cell carcinoma of pancreas, carcinoid; MeCCNU—carcinoma of colon and stomach, melanoma; hexamethylmelamine—carcinoma of ovary; and cis-platinum (II)—non-seminomatous carcinoma of testis, carcinoma of ovary.

Group C drugs are for use under the terms of common protocols which specify the disease indications. Any investigational protocol designed to evaluate the effects of these drugs on diseases not specified in the guidelines is considered to be a study of the drug under Group B conditions.

In other words, Group C drugs may be used under the protocol guidelines, without the reporting requirements of Group B drugs. They also will be available at no cost. But physicians or investigators who desire to try a Group C drug for some other disease must work through the centers, following the procedures for Group B drugs.

Center directors have the option of working with individual investigators, not affiliated with their centers or with member institutions of their centers, if they so desire. The centers may choose to distribute the drugs only to their own or affiliated investigators.

In the latter case, if the center with geographic responsibility for a given area chooses not to work with independent investigators, NCI will consider other alternatives to make drugs available to the independents in those areas.

The centers are in the process of responding to NCI on the program, and when those centers that will work with independents are identified, ***The Cancer Letter*** will publish the list.

The centers will be required to maintain files of protocols, patient consent forms, institutional review committee approvals, the form FD 1573 required for each investigator, and annual progress reports. Files of patient data flow sheets will be maintained either by the center or the investigator for at least two years after an NDA has been approved. The cancer center director must monitor the study at least annually and have documentation of such monitoring. This may consist of actual data review, presentation of data by investigators, or on site inspection of study results and performance.

For each drug studied through the center, separate reports containing the annual progress reports for each approved protocol for that drug will be submitted to NCI. The due date for each annual report shall be March 30, and four copies of the annual report for each drug studied will be sent to NCI.

The annual progress reports for protocols will be prepared by the investigator. It should consist, at least, of an analysis of the number and characteristics of the patients entered, the number of courses, the type of response seen, the toxicity parameter results, conclusions and future plans. Each report should contain a concise summary table of results.

The annual report submitted by the director will contain the annual progress reports and include at least an evaluation of the protocol studies. An integrated summary of results would be desirable.

Reports to be made by affiliated investigators to NCI include adverse drug reactions and alarming findings, which should be reported immediately; and when a protocol has been terminated or modified by amendment, the investigator shall notify the cancer center director and NCI immediately.

Following are the centers authorized to participate in the program, and their directors:

Georgetown Univ./Howard Univ. Comprehensive Cancer Center—includes Vincent Lombardi Cancer Research Center, John F. Potter; and Howard Univ.

College of Medicine, Jack E. White; Florida Comprehensive Cancer Center, C. Gordon Zubrod; Emory Univ. Cancer Center, Charles Huguley Jr.; Univ. of Hawaii at Manoa, Lawrence Piette.

Univ. of Alabama Comprehensive Cancer Center, John Durant; Univ. of Southern California/LAC Comprehensive Cancer Center, G. Denman Hammond; UCLA Comprehensive Cancer Center, Richard J. Steckel; Northern California Cancer Program, Stephen Carter; Colorado Regional Comprehensive Cancer Center, Steven Silverberg; Yale Univ. Comprehensive Cancer Center, Jack Cole.

Illinois Cancer Council, Jan Steiner, director—includes Northwestern Univ. Cancer Center, Nathaniel Berlin, Univ. of Chicago Cancer Research Center, John Ultmann, and Rush Cancer Center, Frank Hendrickson.

Mid-America Cancer Center Program, James Lowman; Johns Hopkins Comprehensive Cancer Center, Albert Owens Jr.; Sidney Farber Comprehensive Cancer Center, Emil Frei III; Boston Univ. Cancer Research Center, Sidney Cooperband.

Mayo Comprehensive Cancer Center, Charles Moertel; Missouri Cancer Programs, John Yarbro; Univ. of New Mexico Cancer Research & Treatment Center, Morton Kligerman.

Memorial Sloan-Kettering Comprehensive Cancer Center, Lewis Thomas, president—includes Sloan-Kettering Institute for Cancer Research, Robert Good, and Memorial Sloan-Kettering Cancer Center, Edward Beattie Jr.

Roswell Park Memorial Institute Comprehensive Cancer Center, Gerald Murphy; Albert Einstein College of Medicine Cancer Research Center, Harry Eagle; Hospital for Joint Diseases and Medical Center, New York City, Vincent Hollander; Columbia Univ. Cancer Research Center, Paul Marks; New York Univ. Clinical Cancer Center, H. Sherwood Lawrence; Univ. of Rochester Cancer Center, Robert Cooper Jr.

Duke Univ. Comprehensive Cancer Center, William Shingleton; Univ. of North Carolina Cancer Research Center, Joseph Pagano; Bowman Gray School of Medicine Oncology Research Center, Charles Spurr; Ohio State Univ. Comprehensive Cancer Center, David Yohn; The Cleveland Cancer Center, Arthur Flynn; Oklahoma Cancer Center, G. Bennett Humphrey.

Fox Chase/Univ. of Pennsylvania Comprehensive Cancer Center—includes Fox Chase Cancer Center, Timothy Talbot Jr., and Univ. of Pennsylvania Cancer Center, Richard Cooper.

Univ. of Puerto Rico Cancer Center, Enrique Perez-Santiago; Roger Williams General Hospital, Paul Calabresi; Memphis Regional Cancer Center, James Nickson; Univ. of Texas System Cancer Center, R. Lee Clark; Univ. of Texas Health Science Center, Eugene Frenkel; Univ. of Texas Medical Branch, William Levin.

Medical College of Virginia/Virginia Commonwealth Univ., Walter Lawrence Jr.; Fred Hutchinson Comprehensive Cancer Center, William Hutchinson; Univ. of Wisconsin Comprehensive Cancer Center, Harold Rusch; and Medical College of Wisconsin, Donald Pinkel.

FDA'S YOUNG STILL NOT HAPPY WITH PLAN FOR DISTRIBUTING GROUP B, C DRUGS

R.S.K. Young, group leader for oncology in the Food & Drug Administration, says he still has "some problems" with NCI's plan for distributing anticancer drugs to investigators and to physicians for humanitarian purposes.

It was Young who initiated the two year long series of problems between FDA, NCI and NCI-supported investigators with objections which resulted in the interruption of a number of clinical studies. The resulting confrontation and series of discussions between FDA and NCI led to the plan to distribute certain investigational drugs through cancer centers.

Vincent DeVita, director of NCI's Div. of Cancer Treatment, told ***The Cancer Letter*** (Aug. 26) that FDA had approved the plan for distributing drugs through centers. DeVita indicated that Richard Crout, director of FDA's Bureau of Drugs, had agreed to the plan.

If so, Crout did not tell this to Young, who is three levels under him in the FDA hierarchy. Young contacted ***The Cancer Letter*** after reading that DeVita had said "Young is no problem now." Crout was on vacation, Young said, and he had not been able to discuss it with him. "But as far as I know, we have not approved the plan for group B drugs. I still have some problems with it."

Included in those problems, Young said, was that it is not clear to him exactly what center directors will be required to do in monitoring investigators.

Young said the distribution plan for group C drugs also has not been completely settled. NCI would require only that physicians using those drugs report adverse reactions. Young said he would like to have more—patient identification, type of disease, dose schedule, any results observed.

TOBACCO COUNCIL AWARDS SEVEN NEW GRANTS FOR SMOKING RELATED RESEARCH

Studies on a marker substance that may indicate the presence of lung cancer and on smoking and pregnancy are among seven new grants announced by the Council for Tobacco Research-U.S.A. Inc.

Since it was established in 1954, the Council has provided more than $44 million for research by independent scientists into smoking and health. Grants are awarded following recommendations by a scientific advisory board currently consisting of 11 physicians and scientists.

Research support has been given so far to 371 scientists in 247 medical schools, hospitals and research institutions. Grant recipients are responsible

for disclosing the results of their work and they have to date published 1,480 reports

Recipients of new grants, their institutions and the titles of their research projects:

Francois Booyse, Rush-Presbyterian-St. Luke's Medical Center, "In vivo and in vitro responses of endothelial cells and platelets to nicotine and extracts from standardized cigarette smoke condensates."

Elroy Cantrell, Texas College of Osteopathic Medicine, "Aryl hydrocarbon hydroxylase in single cells and subpopulations of human lymphocytes and other cells."

Linda Hall, Massachusetts Institute of Technology, "Hereditary alterations of nicotine sensitivity."

Abel Lajtha, Research Foundation for Mental Hygiene, Albany, N.Y., "The effect of nicotine and carbon monoxide on the transport of amino acids into brain and on protein metabolism."

Frank Manning, Women's Hospital, Los Angeles County-Univ. of Southern California Medical Center, "Fetal and maternal effects of cigarette smoking, nicotine injection and carbon monoxide inhalation in the pregnant rhesus monkey model."

Herbert Reynolds, Yale Univ. School of Medicine, "Bronchoalveolar lavage fluids in pulmonary carcinoma: secretory components of immunoglobulin A as a marker of neoplastic growth."

Thomas Stossel, Massachusetts General Hospital, "Functional anatomy of the pulmonary macrophage."

FDA ADOPTS AMENDMENT FOR DIAGNOSTIC X-RAY SYSTEMS PERFORMANCE STANDARDS

The final rule amending the performance standard for diagnostic x-ray systems and their major components has been adopted by FDA. The changes will be effective Nov. 1, 1977, for one section and Sept. 5, 1978 for another.

Announcement of adoption of the amendments appeared in the *Federal Register* Sept. 2, along with FDA's explanation of the changes, listing of comments received after the changes were proposed and the agency's response to the comments.

The new rule:

–Changes the applicability of the x-ray standard to include image receptor supports for mammographic x-ray systems and adds a definition of these comonents.

–Revises the x-ray field limitation and alignment requirements for mammographic x-ray systems and and attachments.

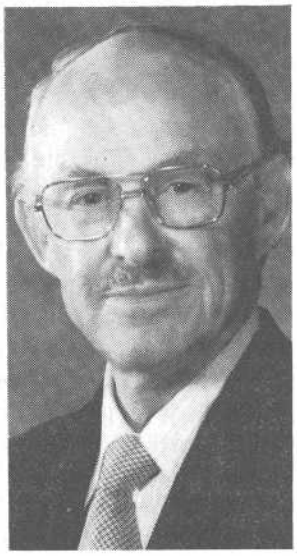
–Establishes a limit on the transmission of the x-ray beam through the image receptor support on mammographic x-ray systems.

–Allows alternative means for limiting and aligning the x-ray field for certain special purpose x-ray systems.

–Modifies the test method for measuring exposure reproducibility.

Further information may be obtained from Harvey Rudolph, FDA Bureau of Radiological Health, 5600 Fishers Ln., Rockville Md. 20857.

LEE CLARK TO RETIRE IN SIX MONTHS; TEXAS STARTS SEARCH FOR SUCCESSOR



R. Lee Clark

R. Lee Clark, who built M.D. Anderson Hospital into one of the world's foremost cancer treatment and research centers, will retire as president of the hospitals parent institution, the Univ. of Texas System Cancer Center, within the next six months.

In accepting reappointment as director for the fiscal year beginning Aug. 31, Clark informed the university's Board of Regents of his desire to retire. Clark underwent successful coronary bypass surgery earlier this year, and although he says he is feeling fine, looks as fit as ever and has resumed a full work schedule, he told the Regents that his physician has encouraged him to "slow down" a little.

The Regents have named a 16-member search committee, including five members of the MDA faculty, to look for a successor.

Clark intends to remain active at the center, with the title of president-emeritus.

Clark, 71, came to MDA in 1946 when it had 22 employees and a budget of $164,000. There are now 4,300 employees and the budget for the current fiscal year is $114 million. During that 31 years, Clark became one of the world's best known leaders in cancer research, taking a prominent role in development of the National Cancer Program and international cancer research activities.

He was a member of the commission appointed by the U.S. Senate whose recommendations led to the National Cancer Act, and he served as a member of the President's Cancer Panel from its inception in 1972 to this year. He is the current president of the American Cancer Society.

The hospital announced three new appointments, effective Sept. 1. E.R. Gilley, who has been MDA's business manager since 1959, was named vice president for business affairs. Douglas Johnson, a surgeon at Anderson since 1968 specializing in treatment of urologic tumors, is head of the newly created Dept. of Urology. And Richard Martin, who joined Anderson in 1951, is head of the Dept. of Surgery. E.C. White retired earlier this year as head of the department for 28 years.

NIH SCHEDULES NATIONAL CONFERENCE ON CLINICAL TRIALS METHODOLOGY

NIH is sponsoring a national conference on clinical trials methodology Oct. 3-4 at the Masur Auditorium in the NIH Clinical Center.

NIH said the conference is "intended to bring together scientists involved in the design and conduct of clinical trials who come from a variety of disciplines and who work in a variety of disease areas. The program includes many of the complex and unresolved issues inherent in the conduct of clinical trials."

Program topics include "When and How to Stop A Clinical Trial," chaired by Curtis Meinert, Univ. of Maryland School of Medicine; "Who Will Be Effective as a Clinical Trials Investigator and What Are Adequate Incentives?" chaired by Robert Gordon, NIH; "Patient Recruitment: Problems and Solutions," chaired by Thaddeus Prout, Greater Baltimore Medical Center; "Quality Assurance of Clinical Data," chaired by O. Dale Williams, Univ. of North Carolina, and Fred Ederer, NIH; "Ethical Considerations in Clinical Trials," chaired by Robert Levine, Yale Univ. School of Medicine; and "Communications," chaired by Harold Roth, NIH.

No registration or notification of planned attendance is required. Individuals attending are responsible for their own travel costs and other expenses.

CONTRACT AWARDS

Title: In vitro study of interrelationships of host cell differentiation and oncogenic virus infections
Contractor: Sidney Farber Cancer Institute, $75,000.

Title: Immunological markers applicable to cytology automation
Contractor: Pennsylvania State Univ., $211,640.

Title: Epidemiology of benign breast disease
Contractor: UCLA, $511,850.

Title: Study of transformed mammary epithelial cells in vitro
Contractor: Univ. of Alabama, $378,500.

Title: Immunotherapy with in vitro lymphocyte sensitization
Contractor: Stanford Univ., $61,930.

Title: Immunotherapeutical trials with human tumors
Contractor: Fred Hutchinson Cancer Research Center, $77,413.

Title: Metabolism of carcinogenic compounds
Contractors: American Health Foundation, $64,211; and Southern Research Institute, $113,694.

Title: Breast Cancer Detection Demonstration Program, renewal
Contractor: University City Science Center, Philadelphia, $1,729,922.

Title: Validation and utilization of microbial mutagenesis systems as prescreens for chemical carcinogens, modification
Contractor: Inveresk Research International, Edinburgh, Scotland, $17,938.

Title: Detection and identification of mutagens in human body fluids
Contractor: Stanford Research Institute, $163,579.

Title: Studies of the mechanisms by which tumors avoid destruction by the immune system
Contractor: Univ. of Hawaii, $53,642.

Title: EPA/NCI special skin cancer epidemiology study
Contractor: Emory Univ., $123,469.

Title: Continue operation of Louisiana Tumor Registry
Contractor: Charity Hospital, New Orleans, $109,992.

Title: Incorporation of an alteration/renovation project as necessary for the performance of the cancer research program being conducted at the Frederick Cancer Research Center
Contractor: Litton Bionetics, $866,090.

Title: A study of exposure to chemical carcinogens and recommended control and intervention programs, renewal
Contractor: Stanford Research Institute, $61,090.

Title: Studies of mammalian cell transport system
Contractor: Johns Hopkins Univ., $61,559.

Title: Chemoimmunotherapy of acute myelocytic leukemia
Contractor: Mount Sinai School of Medicine, $70,309.

Title: Measurement of immunological reactivity to human cancer
Contractor: Litton Bionetics, $627,752.

Title: NCI sera bank facility for the Breast Cancer Task Force
Contractor: Mayo Foundation, $91,600.

Title: Immunological markers applicable to cytology automation
Contractor: Johns Hopkins Univ., $75,000.

The Cancer Letter —*Editor* JERRY D. BOYD

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