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NCI To Press FDA For Quicker Drug Approval, Relaxation Of Survival Impact Requirement

"The present stance of the Food & Drug Administration serves to discourage both government and industry in their efforts to develop anticancer drugs, and needs to be debated publicly," Div. of Cancer Treatment Director Bruce Chabner

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In Brief

Tom Hall Named CMMI VP For Clinical Affairs; Rabson, Fauci Named To Institute Of Medicine

THOMAS HALL, director of the Univ. of Hawaii cancer control program, has been appointed vice president for clinical affairs of the Center for Molecular Medicine & Immunology, a specialized cancer research center affiliated with the Univ. of Medicine & Dentistry of New Jersey. The appointment was announced by CMMI President David Goldenberg. . . . **EDWARD COPELAND** delivered the first Murray M. Copeland Distinguished Lecture at M.D. Anderson Hospital & Tumor Institute last week. Edward Copeland, chairman of surgery at the Univ. of Florida, is the nephew of the late Murray Copeland, who was a legend at MDA for his surgical skill, contributions to treatment of large bowel cancer and bone cancer, and his wit and sense of humor. He died in 1982. . . . **VINCENT DEVITA**, NCI director, and his boss, HHS Secretary Otis Bowen, received honorary doctor of science degrees earlier this month from New York Medical College . . . . **NEW MEMBERS** of the National Academy of Sciences Institute of Medicine include **Alan Rabson**, director of NCI's Div. of Cancer Biology & Diagnosis, and **Anthony Fauci**, director of the National Institute of Allergy & Infectious Diseases and the NIH AIDS coordinator. . . . **MICHAEL WALKER**, director of the Div. of Stroke & Trauma in the National Institute of Neurological & Communicative Disorders & Stroke, has received the Farber Award from the American Academy of Neurology for his contributions to neurooncology. Walker is editor of the "Journal of Neurooncology" and has been a leader in the design, implementation and analysis of brain tumor clinical trials. . . . **J.V. KLAVINS** has been elected president of the Interntional Academy of Tumor Marker Oncology. He is editor in chief of the "Journal of Tumor Marker Oncology". . . **PETER HUGHES**, executive vice president of Memorial Sloan-Kettering Cancer Center, has been named deputy provost and executive vice president of New York Univ. Medical Center.

Chabner Urges Public Debate On FDA Drug Approval Requirements

(Continued from page 1)
told his Board of Scientific Counselors at the Board's meeting earlier this month.

That stance, Chabner said, has led FDA to disregard the recommendations of its Oncologic Drugs Advisory Committee for approval of mitoxantrone and vindesine based on the agency's conclusion that evidence did not show either drug had had positive impacts on survival.

"It is our position that the ability to produce remissions in the absence of overall survival benefit should qualify drugs for approval," Chabner said.

That argument has been debated at FDA everytime a drug comes in with strong evidence of good response but without conclusive data that it improves survival. FDA staff members are divided on the issue, as is the clinical cancer research community.

Chabner said that he planned to invite FDA Commissioner Frank Young to the October meeting of the Board to discuss the issue.

Chabner's comments were made after he had described the situation regarding the new FDA policy for permitting distribution of experimental drugs to treat serious and life threatening diseases. "While the thrust of this proposal was aimed at anti-AIDS drugs, it inevitably will affect anticancer drugs," Chabner said. "We regard the major direction of this new policy, which defines circumstances under which experimental drugs could be released for treatment of individual patients, as being favorable, in that the so called reproposal would considerably loosen the restraints on distribution and use of experimental drugs for these specific patients (see **AIDS update**, June 5).

"However, the initial rule lacked a requirement for evidence of therapeutic efficacy, and this deficiency raised serious questions as to whether the rule would allow widespread use of ineffective, and possibly dangerous, drugs and would undercut the early clinical testing of drugs before efficacy could be established."

Chabner noted that after congressional hearings on the matter, "FDA significantly modified the proposal to require that for life threatening diseases, such as AIDS or cancer, experimental drugs would be approved for treatment IND use if reasonable evidence of efficacy is presented, if the sponsor is diligently pursuing clinical development through controlled trials, and if no alternative standard therapy exists. While we still have some residual concerns about the effect of this new rule on our ability to complete late phase 2 and phase 3 trials, we feel that the reproposal will have salutory effects on the approval process, in that it will allow more rapid entry of drugs into a status equivalent to Group C."

Group C is the category in which unapproved drugs with demonstrated efficacy may be given to patients who are not participating in formal clinical trials.

It is through a modification of the Group C rules that interleukin-2/lymphokine activated killer cell therapy was offered to clinical and comprehensive cancer centers. NCI obtained permission from FDA to do that, but not before "extended debate with FDA staff," Chabner said.

Chabner mentioned some "novel features" of the expanded IL-2/LAK study which includes $1 million in "seed money."

One of those features is a protocol comparing IL-2/LAK with IL-2 alone. Also, "an escape clause has been written into the plan in order to provide IL-2/LAK treatment for patients refusing randomization or who have no clinically followable disease. It is our hope that this plan will encourage the development of research programs related to biologicals, such as IL-2, and will specifically lead to innovative research protocols in addition to the Group C trial. We will provide $1 million in seed money for the development of laboratory facilities required for LAK cell production.

"I personally see this as an important step forward in broadening the experience with IL-2, in mobilizing the resources of the cancer centers for biological therapies, and in moving FDA to adopt a more facilitory stance in cancer clinical trials."

Bristol To Support Grants For Studies On Resistance To Antitumor Drugs

Bristol-Myers has agreed to underwrite a multimillion dollar program for investigating the biochemical and genetic basis of resistance to antitumor drugs, Div. of Cancer Treatment Director Bruce Chabner said at the Board of Scientific Counselors meeting.

The program is part of the deal Bristol made two years ago with the government, in

which the company received a five year extension of its license for cisplatinum in return for a commitment to spend at least $30 million to support research related to the compound.

It was at DCT's suggestion that Bristol agreed to spend part of that money on drug resistance studies, Chabner said. "While our understanding of the ways in which experimental tumors become resistant to various drugs has greatly expanded in recent years, the critical studies of drug resistance as it develops during clinical treatment remain to be done. This money will be released under a grant program to be administered by Bristol, which will shortly announce details. We regard this effort as extremely important to the general effort to develop new anticancer drugs, and we congratulate the Bristol-Myers company."

Chabner added that the exact amount to be committed by Bristol had not been determined, but it could be as much as $15 million. He expects that "several grants of $100,000 or more each" will be awarded, and that Bristol will oversee the competition.

In response to Board member Mark Groudine's question on how the applications will be evaluated, Robert Wittes, director of the Cancer Therapy Evaluation Program, said, "This discussion is a bit premature. We're still discussing the ground rules with Bristol. They will have peer review, and they are serious about high quality science."

Licensing, Royalties

Chabner mentioned the licensing agreement recently negotiated with Hoffman-LaRoche for dideoxycytidine (ddC) for treatment of AIDS. "This agent, discovered by Sam Broder (director of DCT's Clinical Oncology Program) last year to have anti-AIDS activity, has shown promising activity in restoring immunologic reactivity during phase 1 trials and is the first of a series of dd-nucleosides that will be licensed by the government," Chabner said. "A request for applications for ddA and ddI licensing has been issued, and the licensing process will be completed this fall. Other active compounds will be advertised for licensing later this year.

"I would like to add my personal view that DCT should undertake the earliest possible licensing of active compounds in order to expedite their clinical development. We intend to follow that policy for both AIDS and cancer drugs, but as part of the licensing agreements we will reserve the right to pursue government supported and directed trials, such as those ongoing in the AIDS treatment units and in our clinical cooperative groups, and we will require that the licensing firm provide drugs for these trials."

A new feature in government licensing agreements, Chabner commented, is payment of a portion of the royalties to individual government scientists under newly adopted regulations.

"That has vast implications," Board member Robert Schimke said.

"Like any academic institution, people here like to be rewarded for their discoveries," Chabner responded. "The government is allowing a certain portion of royalties to go to the laboratories. There is a limit on how much one can receive, $100,000 a year. It is not unrealistic that some will generate that much. The AIDS test is. AIDS drugs probably will. This is a new ballgame for government scientists, but one I think is similar to what is happening in universities."

Schimke said that the normal practice in universities is that one third goes to the individual, one third to the department and one third to the university.

Peter Fischinger, NCI deputy director, said "the AIDS test is out of the norm. One third of all royalties coming in is from the AIDS blood test."

Schimke said one of his main concerns about the issue is that, in universities, "battles over patents bring on a lack of communication" by scientists who are reluctant to publish their findings until the patent rights are secured. "I don't want my tax money supporting a federal employee who keeps his mouth shut about something that should be communicated."

Chabner noted that in drug discoveries, "if you share information without patenting it, the companies aren't interested."

"That's called greed," Schimke said.

Chabner disagreed and pointed out that for private industry to invest in product development, the product "needs to have commercial appeal."

Fischinger said the new rules haven't changed anything. "Intramural investigators are publishing as rapidly as possible. But now they file a patent application first. Also now, the government has a greater say so than before."

"I hope it doesn't get to this point here, but I know in universities, what is done in

laboratories sometimes is geared to getting some product patented," Schimke maintained.

Schimke said he understands the need for royalty payments to government scientists, especially with NIH salaries falling behind those in academia and industry. "You need to compete with what is going on at certain universities."

Chabner agreed. "It is very hard to keep creative people if they can't share in royalties."

DCT Board Okays Concept For New BRMP Master Agreement Contracts

The Div. of Cancer Treatment Board of Scientific Counselors has approved the concept of a new master agreement for custom products and services for the Biological Response Modifiers Program, with an estimated annual cost of $2.8 million. The master agreement, which will be negotiated after competition with a variety of contractors, will be for a five year period.

Master agreements will be awarded in nine areas. Under the master agreement system, potential contractors will be identified as capable of competing for awards in one or more of those areas. As needs arise, all those with capabilities in a particular area will be invited to submit competitive proposals, from which the providers will be selected.

The description of the program in the concept statement follows:

The Biological Response Modifiers Program requires a number of specialized products and services, which can be obtained from extramural contractors, in support of its research programs in cancer and the therapy of AIDS. BRMP needs sources for the production of monoclonal antibodies, immunoconjugates, chimeric antibodies, oligonucleotides, synthetic peptides and other novel molecules used in clinical and laboratory investigations. In addition, BRMP requires the extramural performance of selected assays and tests arising in support of NCI funded clinical and laboratory research. For example, human antimouse and anti-idiotype antibody assays will be required for monoclonal antibody trials but are not widely available, and could be acquired as a service from key laboratories. Finally, BRMP needs access to highly specialized existing animal models in order to answer specific questions arising from its cancer research and AIDS development.

These custom products and services must be obtained quickly and at the least cost, without compromising quality. Each of the proposed areas has been identified as a scientific or technical area in which BRMP requires a more rapid turnaround than the 18 months needed to compete and award individual contracts. The present BRMP contract mechanism employs a few contractors for such tasks. Greater efficiency and flexibility is anticipated from a master agreement order system for which there are a larger number of alternative sources and projects are broken down into smaller and better defined tasks.

The master agreement system is expected to be more efficient for several reasons: (1) prices will be lower due to greater competition for each task; (2) BRMP can choose from a more diverse selection of alternative technologies to find the best source for a given product or service; (3) time to completion will be reduced in a more competitive environment; and (4) each prospective contractor will only propose on the tasks for which that contractor is currently best suited, reducing internal inefficiencies within the individual contractor's operations, and hence further reducing costs to the government. It is anticipated that research and development will be required for certain of the tasks.

BRMP proposes to set up a system of master agreements to procure specialized products and services in support of its extramural and intramural research programs. Master agreements and requests for proposals will be issued to solicit contractors, i.e., companies and academic institutions, and further agreements will be sought at least annually, to maintain the widest possible base of prequalified sources.

BRMP intends to award master agreements in each of the following areas: (1) murine antibody production, clinical and laboratory grades; (2) chimeric antibody production, clinical and laboratory grades; (3) production of human monoclonal antibodies, clinical and laboratory grades; (4) production of immunoconjugates, laboratory and clinical grades; (5) production of oligonucleotides for laboratory research; (6) synthetic peptide and hybrid protein production for laboratory research; (7) specialized biochemical, serological, and cellular immune assays in support of clinical BRM research; (8) production of standards for selected lymphokines and other widely used laboratory biologicals; and (9) evaluation of biological response modifiers using existing animal models.

Additional master agreements in other areas of importance to the program will be submitted to the Board for individual approval, as the need arises. Actual orders for products and services will be awarded through funded master agreement order RFPs, for which only the master agreement holders will be eligibile to compete.

1. Murine antibody production: $500,000

Murine monoclonal antibodies provide one of the most significant tools for cancer research and therapy. In the course of BRMP sponsored research, these antibodies have been raised against a number of antigens on cancer cells, against growth factor receptors, oncogene products, lymphokines, and other molecules of potential importance in cancer research and therapeutics, as well as against proteins associated with HIV and HIV infected cells. The initial development of the antibody to the appropriate antigen and performance of early studies are appropriate tasks for research laboratories. Once the desired hybridoma clones exist, however, the task of production is usually most efficiently allocated to outside contractors. BRMP requires the capacity for production of murine monoclonal antibodies for both preclinical and clinical studies, starting from hybridoma clones to be provided by BRMP. Required amounts of a given antibody range from 100 mg to 50 g. In rare instances as much as 100 g may be required. An important capability of contractors who perform this service is the ability to scale up from small amounts of research grade material, through medium (1 gram) to large (50 grams) amounts of clinical grade material,

with minimal difficulty or delay. BRMP requires access to several different technologies for producing these antibodies, since no single technology is optimal for every antibody. This field is extremely rapidly changing, and turnaround time of 18 months, typical of contracts, are too slow. Thus, a master agreement mechanism is preferred in order to allow the most rapid turnaround and, at the same time, access to the largest number of qualified suppliers.

2. Chimeric antibody production: $250,000

Monoclonal antibodies of murine origin can be efficiently raised against a wide variety of antigens of great potential importance in cancer therapy and BRMP sponsored research into HIV infections. There are three major obstacles hindering utilization of these substances in clinical research. First, technological and cost problems still limit the current availability of clinical grade human monoclonal antibody. Second, the developlment of human antimouse antibodies restricts the clinical application of murine monoclonals. Third, murine antibodies mediate human immune responses variably, and often poorly.

Although human monoclonal antibodies would appear to be the best solution to the problems encountered with murine antibodies, human monoclonals are much more difficult to obtain than mouse antibodies, and are usually further limited by being of IgM class and having low affinity.

The Fc portion of the mouse immunoglobulin molecule is considered more antigenic than the Fab portion, and it is the Fc portion of the molecule which determines its effector function. Substitution of a human Fc portion for a mouse Fc portion in a mouse monoclonal antibody, therefore, would potentially reduce the undesirable antigenicity of a murine antibody and improve its capacity to mediate an antitumor response. A number of technological approaches can be taken to produce such hybrid molecules. Mouse-human monoclonal antibodies showing reasonable promise have already been produced in limited quantities.

BRMP requires the capacity for producing chimeric mouse-human antibodies in quantities ranging from 100 mg through 1 gram to 50 g, in both research and clinical grade, starting from a mouse hybridoma line producing the analogous murine antibody. Since this field is rapidly changing, turnaround times are required by BRMP to be much less than the 18 months characteristic of contracts. Also, there are various evolving technological approaches to the production of these chimeric antibodies, such as genetic engineering, chemical coupling, and possibly others. Therefore, a master agreement mechanism provides the preferred approach to producing these chimeric antibodies.

3. Human monoclonal antibody production: $200,000

Compared to murine monoclonal antibodies, human monoclonals are less antigenic and are better mediators of human immune responses. Technical problems remain in terms of availability, cost, antibody class, and affinity. This field is rapidly evolving and it is important for BRMP intramural and extramural investigators to be able to pursue research questions arising from these important new agents. A small number of human monoclonal antibodies have been produced and are entering clinical trials. As with murine monoclonal antibodies, isolation and identification of a desired clone is an appropriate research questions; producing large quantities of antibody, however, is not the best use of a research laboratory. The master agreement mechanism provides the ability to produce these antibodies with the speed and flexibility needed.

4. Production of immunoconjugates: $400,000

Immunoconjugates couple all, or a portion of a monoclonal antibody to another molecule, such as a toxin, radionuclide, chemotherapeutic agent, or biological response modifier, in order to achieve specific effects. Immunoconjugates have been used to image tumors, to kill target cells, or to trigger effector cell mechanisms in the neighborhood of their target antigen. They have potentially great utility in cancer diagnosis and therapeutics, as well as in therapeutic research relating to HIV infections. The field of immunoconjugates is rapidly changing and presents a mosaic of varying technologies for which the master agreement mechanism is preferable to standard contracting.

5. Production of oligonucleotides: $250,000

Several important purposes can be accomplished by synthesis of selected oligonucleotides, in support of specific laboratory research goals: Synthesis of short segments of DNA that correspond to known protein sequences for the purpose of "fishing out" the entire gene from a complex mixture of many DNA species; measurement of messenger RNA using an oligonucleotide probe in situ or from purified RNA; production of a manmade mutation of a known cloned gene and expression of the modified gene allowing subsequent analysis of the function of the resulting protein; production of oligonucleotide additions to known genes, so that new restriction sites are generated which will then allow molecular engineering of the DNA molecule. All of the above approaches will produce products which will help the laboratories understand how oncogenes and their protein products may function to cause the malignant process, how normal cells function, and how abnormal processes may be reversed. These tasks are best dealt with in a master agreement mechanism, due to considerations of speed and flexibility.

6. Custom peptide and protein production: $300,000

Certain peptides and protein fragments are of great interest in cancer research. For example, laminin fragments appear to play a role in the process of metastasis. BRMP requires the ability to produce these entities from well defined gene segments or protein sequences. In addition, the ability to produce custom hybrid proteins would allow creation of novel molecules with properties of significant research and therapeutic interest. For example, the combination of a toxin with a growth factor may allow unique manipulations of the target cells bearing these receptors. Another example would be the coupling of two monoclonal antibodies to produce a bifunctional antibody. Such antibodies have been used to target cytotoxic T cells to tumor targets. The custom production of these new molecules would allow a wide range of new experiments and interventions. Rapid turnaround and flexibility to choose between a number of possible business and university sources argues strongly for a master agreement order mechanism for these innovative and interesting products.

7. Specialized assays in support of BRM clinical research: $235,000

As clinical trials become more complicated, certain assays in support of BRM research would best be centralized in laboratories with a recognized ability to perform the assay. Frequently, these laboratories are set up to support research in or production of particular BRMs. For example, anti-idiotype or human antimouse antibody assays are sometimes beyond the capability of otherwise flexible and capable university laboratories. BRMP needs the capability of funding these tests on a flexible and rapid basis to support its extramural clinical research. The master agreement mechanism is the preferred approach to this problem.

8. Production of standards: $200,000

One of the most successful extramural functions of the BRMP repository is the distribution of an interleukin-2 standard for comparisons of IL-2 activity determinations between different labora-

tories. As new lymphokines and other bioactive substances are developed, preclinical in vitro research can be advanced by the ready availability of purified standards. The existence of a standard may also be of use in clinical studies, as the IL-2 standard has shown. Sources vary for each new compound, and the need varies rapidly with time. BRMP has determined that a set of flexible master agreements would give it the capability to advance the field in this area.

9. Evaluation of compounds using existing animal models: $450,000

Animal modeling presents unique problems in BRM development, both in cancer research and therapeutic research in AIDS. The field has advanced to the point that complex multiple agent trials are often required. These models are frequently available at a small number of unique commercial and university laboratories reflecting the interests and expertise of their principal investigators. Selected questions of higher complexity can be addressed better by choosing the laboratory to fit the question, than by attempting to find or set up one laboratory which is capable of all sorts of animal models. Master agreements can provide the capability and speed to address these individual questions, while maintaining a highly competitive environment.

NCI Advisory Group, Other Cancer Meetings For July, August, Future

Medical Oncology--July 6-11, Pomerio Castle, Como, Italy. Postgraduate course. Contact Secretariat, European School of Oncology, Via Venezian 1, 20133 Milano, Italy.

Oncogenes--July 7-11, Hood College, Frederick, MD. Third annual meeting. Contact Margaret Fanning, Conference Coordinator, PRI, NCI-FCRF, PO Box B, Frederick 21701, phone 301/698-1089.

Argentine Congress of Clinical Oncology and Riverplate Oncology Meeting--July 7-Aug. 1, Buenos Aires. Contact Dr. Hugo Crego, Dr. Estevez Foundation, Paraguay 5190, (1425) Buenos Aires, Argentina.

Emerging Technologies and Issues in Cancer Management--July 9-10, Society Hill Sheraton, Philadelphia. Contact CDP Associates Inc., 404/391-9872.

Developing and Implementing Freestanding Cancer Centers: The Hospital Perspective--July 9-10, Grand Hyatt, New York. Contact American Hospital Assn., P.O. Box 98946, Chicago 60693, phone 312/280-6083.

Neurofibromatosis--July 13-15, NIH Masur Auditorium. Consensus development conference. Contact Barbara McChesney, Prospect Associates, Suite 500, 1801 Rockville Pke, Rockville, MD 20852, phone 301/468-6555.

International Congress of Radiation Research--July 19-24, Edinburgh. Contact Dr. Martin Fielden, Secretary General, 8th ICRR, MRC, Radiobiology Unit, Harwell, Didcot, Oxon, UK OX11 OAE.

Medical and Experimental Mammalian Genetics--July 20-31, Bar Harbor, Maine. Contact Dr. Victor McKusick, 292 Carnegie Bldg, Johns Hopkins Hospital, 600 N. Wolfe St., Baltimore, MD 21205, or Dr. Thomas Roderick, Training & Ed. Office, Jackson Laboratory, Bar Harbor 04609.

Spheroids in Cancer Research--July 26-28, Cambridge, UK. Third international conference. Contact Dr. Peter Twentyman, Clinical Oncology and Radiotherapeutics Unit, MRC Center, Hills Rd, Cambridge CB2 2GH, UK.

Oncology Nursing Seminar--July 27-28, Dallas. Sponsored by St. Paul Medical Center. Contact Mary Gerbracht, RN, 5909 Harry Hines Blvd., Dallas 75235, phone 214/879-2648.

DNA Tumor Virus--July 27-Aug. 1, Cambridge. Contact P. Latter, Imperial Cancer Research Fund, Lincoln's Inn Fields, London, WC2A 3PX, UK.

FDA Radiological Devices Panel--July 27, Center for Devices and Radiological Health, 12720 Twinbrook Parkway, Rockville, MD. Agenda includes reclassification petitions for magnetic resonance devices. Open 9 a.m.-5 p.m.

International Assn. of Cancer Registries--Aug. 5-7, Copenhagen. Annual scientific meeting. Contact Danish Cancer Registry, Landskronagade 66, 2100 Copenhagen, Denmark.

Cancer Therapeutic Program Project Review Committee --Aug. 11, Holliday Inn Crown Plaza, Rockville, MD, open 8-8:30 a.m.

Home Pain Management--Aug. 14, Clinic Inn, Cleveland. Contact Dept. of Continuing Education, Cleveland Clinic Educational Foundation, 9500 Euclid Ave. Rm TT3-301, Cleveland, OH 44106, phone (local) 444-5696, (Ohio) 800-762-8172, (elsewhere) 800-762-8173.

National Laryngectomee Rehabilitation--Aug. 27-29, Melbourne. Contact Australian Cancer Society, GPO Box 4708, Sydney, NSW, Australia.

International Society of Hematology--Aug. 28-Sept. 2, Milan. 22nd Congress. Contact Organizing Secretariat, Fondazione Giovanni Lorenzini, Via Monte Napoleone, 23 Milan 20121, Italy.

FUTURE MEETINGS

Towards 2000 III--Oncology Today--Sept. 15-16, Fox Chase Cancer Center, Philadelphia. Contact Peggy Conners or Janet Spause, Conference Coordinators, Fox Chase Cancer Center, 430A Rhawn St., Philadelphia 19111, phone 215/728-6900.

Enhancing Quality of Life: Oncology Social Work Strategies--Oct. 9-10, Lincoln Hotel, Tampa. Contact Nancy Elkins, LCSW, 813/972-8407.

Lasers in Medicine: Expanding Clinical Applications --Oct. 10, Alta Baates Hospital Auditorium, Berkeley. Contact Mary Grim, Medical Education Coordinator, Alta Bates Hospital, 3001 Colby St., Berkeley, CA 94705, phone 415/540-0337.

Progress in In Vitro Toxicology--Nov. 4-5, Baltimore. Sponsored by the Johns Hopkins Center for Alternatives to Animal Testing. Contact Jeanne Ryan, Program Coordinator, Office of Continuing Education, 720 Rutland Ave., Turner 22, Baltimore, MD 21205, phone 301/955-6046.

Genetic Mechanisms and Cancer--Nov. 8-11, Westin Galleria Hotel, Houston. 40th annual Symposium on Fundamental Cancer Research. Contact Office of Conference Services, M.D. Anderson Hospital & Tumor Institute, 1515 Holcombe Blvd., Houston, TX 77030, phone 713/792-2222.

Second Conference on Immunity to Cancer--Nov. 9-11, Williamsburg, VA. Contact Carole Kirby, Biological Response Modifiers Program, NCI, DCT, Frederick Cancer Research Facility, Bldg 567 Rm 138, Frederick, MD 21701.

American Radium Society--April 16-20, 1988, Four Seasons Hotel, Seattle. 70th annual meeting. Contact Suzanne Bohn, Administrative Director, American Radium Society, 1101 Market St., 14th Floor, Philadelphia, PA 19107, phone 215/574-3179.

Critical Issues in Tumor Microcirculation, Angiogenesis and Metastasis--June 13-17, 1988, Carnegie Mellon Univ., Pittsburgh. Contact Hilda Diamond, Aossiciate Director, Biomedical Engineering Program, Carnegie Mellon Univ., Pittsburgh, PA 15213, phone 412/268-2521.

Program Announcements

Title: Cancer education grants (R25)
Application receipt date: Oct. 1, Feb. 1, June 1

NCI announces the resumption of competition for cancer education grants (R25), but under new guide-

lines. Any institution wishing to compete should request a copy of the guidelines from the office listed below.

The new grant has three major aspects, namely:

1. Multiyear training in the interventive practice of chronic disease prevention and control (with a focus on cancer), such training to lead to a degree such as the doctor of public health.

2. Support for up to five years for the development of nutrition curricula for the aforementioned schools, again with an emphasis upon the prevention and control of chronic diseases, especially cancer.

3. Summer research experience support for students in schools of medicine, dentistry, nursing, public health and allied health.

An applicant may seek support for one or more of these three projects. Applications received by Oct. 1 shall be fundable on or about July 1, 1988. In that fiscal year (1988) it is anticipated that the program will have sufficient funds to support summer student activities at a reduced level; support up to three or four new training projects in disease prevention and control; and support up to seven nutrition curriculum projects.

Address inquiries to Program Director, Cancer Training Branch, CCSP, Div. of Cancer Prevention & Control, NCI, Blair Bldg Rm 428, Bethesda, MD 20892, phone 301/427-8866 or 427-8855.

Title: Research on the etiology and functional consequences of nonmalignant endocrine tumors

Application receipt date: See schedule in application kits

The National Institute of Diabetes & Digestive & Kidney Diseases invites investigator initiated research grant applications to advance understanding of the etiology and natural history of benign tumors of the thyroid, parathyroid, pituitary, adrenal and other endocrine glands.

Interdisciplinary approaches may be needed for this study with expertise required in several of the following areas: endocrinology, cell biology, histology, genetics, epidemiology, and peptide and/or steroid biochemistry.

Nonmalignant endocrine tumors are a widespread and important problem in endocrinology. These tumors occur particularly frequently in the thyroid, parathyroid, pituitary and adrenal glands. The etiology of these commonly occurring nonmalignant endocrine tumors is unknown. The long term functional consequences and the natural history of these tumors if left untreated are also unknown. It is unclear how often these tumors have sufficient endocrine function to produce clinically significant disease. Answers to questions about the etiology and functional consequences of benign endocrine tumors would shed light not only on appropriate strategies for their prevention or therapy but also on fundamental questions regarding regulation of cell growth and replication.

This solicitation is intended to stimulate research that will result in new understandings of the regulation of growth and proliferation of endocrine cells and of the pathogenesis of endocrine hyperplasia and nonmalignant neoplasia. It is also intended to stimulate investigation of the natural history and optimal clinical management of nonmalignant endocrine tumors.

For further information and copies of the complete announcement, contact NIDDKD, Div. of Diabetes, Endocrinology & Metabolic Diseases, Bldg 31 Rm 9A16, Bethesda, MD 20892, phone 301/496-7348. Applications must be submitted to the NIH Div. of Research grants.

RFP Deferred

RFP NCI-CM-87212-72, titled, Maintenance of the NCI Drug Information System (**The Cancer Letter**, May 15), has been deferred until further notice. All organizations which have already submitted requests for copies of the RFP need not request another. This RFP will not be released until a delegation of procurement authority clearance has been obtained for automatic data processing.

Surgery, Radiation Both Effective For Local Prostate Cancer, Panel Says

"Radical prostatectomy and radiation therapy are clearly effective forms of treatment in the attempt to cure tumors limited to the prostate, for appropriately selected patients," the NIH consensus conference on the management of clinically localized prostate cancer concluded last week.

The panel, chaired by Robert Livingston, head of the Div. of Oncology at the Univ. of Washington, heard two days of presentations addressing a variety of issues, then presented a draft of its conclusion and recommendations.

"Comparison across studies suggests that there is comparable 10 year survival with either form of management," the draft statement says. "What remains unclear is the relative merit of each in producing lifelong freedom from cancer recurrence. It is known that traditional radical prostatectomy can provide 15 year cancer free survival equivalent to that of a comparably aged control population. On the other hand, sufficient long term followup does not yet exist to permit a conclusion about the ability of radiation therapy to eradicate such cancer in an equivalent proportion of patients.

"After appropriate primary irradiation, the long term complication rate is now well defined and appears acceptable. The new approach to prostatectomy is clearly associated with a reduction in postoperative impotence. The true comparative incidence of impotence over time, however, awaits prospective evaluation. While impotence may result from the alteration of normal anatomy, the psychological considerations should not be overlooked. Sexual rehabilitation should address both medical and psychological needs.

"Information that a patient should have available when considering with his physician the choice of treatment includes:

1. Probability of cure, mortality, complications, and other side effects of radical prostatectomy and radiation therapy.

2. Risk of impotence and incontience for either treatment.

3. Psychosocial consequences of either choice.

4. Extent and risk of pretreatment staging assignment tests.

"As competing, noncancer related causes of death (e.g., cardiovascular disease) may be expected to decrease for men over the age of 50, the issue of cure will become more important in low stage disease. Properly designed and completed randomized trials that evaluate both disease control and quality of life after modern radiation therapy compared with radical prostatectomy are essential."

The panel offered suggestions for future research, clinically and basic. Clinical research needs include:

A. "Agree to uniform classification and schema for histologic and cytologic grading, disease staging and response criteria that are acceptable to health care professionals caring for patients with prostate cancer.

B. "Define the appropriate use of diagnostic imaging in staging prostate cancer patients through well designed, controlled comparison studies. The development of imaging methods to measure tumor volume could provide a noninvasive predictor of the aggressiveness of cancer.

C. "Encourage educational programs for lpathologists and cytologists in the diagnosis of prostate cancer with the purpose of increasing accuracy and uniformity.

D. "Assess the availability and quality of surgical treatment and initiate educational programs.

E. "Accept a uniform method for data reporting and statistical analyses that will allow meaningful comparisons of treatment results reported by various disciplines.

F. "Identify clinical and pathological prognostic variables. The identification of low and high risk features may allow the more appropriate selection of treatments for patients with clinically localized disease. Parameters to study may include morphologic predictors, the correlation of DNA flow cytometry, prostate specific antigen determination, and cytogenetics with disease outcome.

G. "Assess the clinical significance of positive postradiation biopsies, and identify ways to reduce the incidence of these positive biopsies.

H. "Assess the role of localized postoperative irradiation in patients with positive margins after radical prostatectomy.

I. "Assess in controlled trials the role of adjuvant hormonal therapy in patients with locally advanced disease after radical prostatectomy.

J. "Clarify the clinical significance and therapeutic implications of the extent of nodal involvement.

K. "Address the influence of treatment programs on the quality of life of patients and their loved ones. Identify appropriate psychosocial and psychosexual instruments and end points to assess quantitatively the effect of treatment in patients with both localized and metastatic disease. Study and implement innovative interventions to improve the psychological outcome.

L. "Agree upon a uniform clinical and pathological definition of stage A prostate cancer. Initiate studies to define the natural history of untreated stage A patients to help determine which patients may benefit from treatment."

Recommendations for basic research included:

A. "Encourage basic research to elucidate fundamental processes regulating normal prostate and prostate cancer growth and their impact on the natural history of the disease.

B. "Assess the diagnostic and therapeutic role of prostate cancer specific monoclonal antibodies."

Members of the panel were, in addition to Livingston, Alfred Bartolucci, Univ. of Alabama (Birmingham); Joshua Becker, State Univ. of New York (Brooklyn); William DeWolf, Harvard; John Ellis, New York Hospital-Cornell Medical Center; Anthony Engelbrecht, Stanford; Marc Garnick, Dana-Farber Cancer Institute; John Grayhack, Northwestern; Lance Heilbrun, Wayne State; James Jones, East Carolina Univ.; Shannon McGowan, John Muir Community Hospital and Cancer Center; Kent Osborne, Univ. of Texas Health Science Center (San Antonio); Joel Tepper, Harvard; and John Thornbury, Univ. of Rochester.

The conference was televised over the Hospital Satellite Network to 160 hospitals around the country. CME credit was available to attendees there and at NIH.

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

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