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P.O. Box 2370 Reston, Virginia 22090 Telephone 703-620-4646

First TIL Results: Four Patients, All Responded, One Complete; Panel Opens Reauthorization Drive

The first very early preliminary results from Steven Rosenberg's tumor infiltrating lymphocyte (TIL) phase 1 trial at the NIH Clinical Center became known last week when Rosenberg briefed Chairman Armand Hammer of the President's Cancer Panel on the study prior to the Panel's meeting. Responses have been seen in the first four patients to receive the new treatment, and one had a complete response.

(Continued to page 2)

In Brief

Lepovetsky Heads New NCI Office Of Technology Development; Temporary Now, Maybe Permanent

BARNEY LEPOVETSKY, who has been chief of the Cancer Training Branch in the Div. of Cancer Prevention & Control and its predecessors since the mid-1970s, is heading up NCI's new Office of Technology Development. It's a six month assignment, but if Lepovetsky and Director Vincent DeVita are satisfied with how it works out, it will probably be made permanent. The office will implement provisions of the Federal Technology Transfer Act passed by Congress last year. The act was intended to encourage collaboration of the private sector with government scientists and investigators supported by government grants and contracts in development of the fruits of their research. Scientists are allowed to receive a percentage of royalties and licensing fees from their inventions. In addition, their laboratories may get some of the proceeds, a marked departure from the past when royalties paid to the government went back to the Treasury. The extra money will not be deducted from the labs' budgets. Leopovetsky is uniquely qualified for the job of helping NCI staff and extramural investigators deal with such things as patents, licensing, and cooperative agreements with the private sector. He holds an MD as well as a doctor of law degree. . . . **BYPASS BUDGET:** Copies of the 1989 fiscal year bypass budget may be obtained from the NCI Financial Management Office, NIH Bldg 31 Rm 11A18, Bethesda, MD 20892, phone 301/496-5803. "New Publications" (**The Cancer Letter**, Nov. 13) incorrectly listed Mary Knipmeyer, legislative liaison officer, as the NCI contact for free copies. . . . **ARNOLD MITTELMAN**, who has retired as chief of surgical developmental oncology at Roswell Park Memorial Institute, will remain there as a special consultant to Director Thomas Tomasi.

Rosenberg Says TIL Results Too Early To Discuss; Panel Opens Renewal Drive

(Continued from page 1)

"Dr. Rosenberg is getting remarkable results with the new protocol," Hammer said at the Panel meeting. "He's had 100 percent success, four out of four patients having responded. One was a complete response, and three had marked reductions in their cancers."

Rosenberg, contacted later, declined to comment on the study, insisting that it is "very early, very preliminary, much too early to talk about." He said it would be several months before the study will be ready for publication.

So far, Rosenberg has been able to enter only one patient a month in the study, which uses cells from the patient's tumor that are cultured in vitro to develop lymphocytes capable of infiltrating solid tumors. Interleukin-2 is involved in the process. Animal studies, which Rosenberg has published and discussed in several forums, including a National Cancer Advisory Board meeting, have indicated that TIL is 50 to 100 times more potent than the LAK/-IL-2 treatment, also developed by Rosenberg.

Reauthorization Issues

Hammer's mention of the TIL study was an aside to the Panel's agenda, which was to discuss reauthorization of the National Cancer Act and hear reports from the NCI divisions. Hammer asked NCI for a detailed report on issues involved in reauthorization which the Panel can study, "make available to others and present our own views to Administration officials and Congress as we deem appropriate.

"We believe this to be highly relevant to the mandate given the Panel by the National Cancer Act, to review and oversee the National Cancer Program as operated by NCI and report directly to the President on any obstructions which we believe might affect the program," Hammer continued.

He asked that the report include a description of the special authorities granted NCI by the National Cancer Act, including those that were in the original Act but were dropped in subsequent renewals. "Should those authorities be restored? Are there new authorities needed in 1988 to guarantee our ability to pursue the highest quality National Cancer Program for the country? Are there any ongoing or anticipated problems that could be resolved through the next reauthorization?"

Hammer repeated the suggestion he had made to the National Cancer Advisory Board that cancer program advocates seek a five year reauthorization period instead of three years as in the past.

"While the Panel recognizes the importance of the reauthorization process," Hammer said, "we do wonder why it has to occur so often. It might very well be that everyone concerned could benefit substantially from a longer period between reauthorizations. Indeed, other parts of the National Institutes of Health are authorized until such time as Congress would see fit to terminate them. Perhaps this would be the most efficient method for the National Cancer Institute, as it would provide stability at a time when it is badly needed if we are to take full advantage of the important discoveries and advances which have taken place in the last several years.

"We have been concerned that there has been a gradual chipping away of the special authorities which made so many of these discoveries and advances possible, and we must make sure that the direction of the National Cancer Program is forward and positive and not backward and negative."

NCI Director Vincent DeVita said that "the very existence of the Panel" is one of the chief benefits of the National Cancer Act. The Panel "gives the Institute a place to speak its mind, to keep us from being swallowed up in the government."

Another benefit from the Act is the bypass budget, DeVita said, "one of the few vehicles in the government with which you can express what you can do" with the optimal amount of money.

"The people who framed the National Cancer Act were realistic in understanding how the bureaucracy works," DeVita continued. "It was a stroke of genius."

Some activities developed by NCI through the authorities in the Act "are now routine at NIH," DeVita said. These include the hiring for up to two years of expert consultants, permitting the Institute to use experienced and highly qualified individuals who might not otherwise be available; some of the training programs; and the extended grant, such as NCI's seven year Outstanding Investigator Grant awards.

"People involved in AIDS research are looking at the National Cancer Act as a model

for expediting research," DeVita said.

In response to Panel member William Longmire's question on how difficult it would be to get Congress to go along with a five year reauthorization, DeVita said that "five years is reasonable. My guess is that Congress is not ready to give us indefinite authorization."

DeVita warned the Panel not to "underestimate resistance" that might develop to renewal of the Act.

The Panel heard from three of the five NCI division directors in brief presentations on new developments in their programs and some problems they are facing. Div. of Extramural Activities Director Barbara Bynum and Div. of Cancer Prevention & Control Director Peter Greenwald were in Atlanta attending the National Conference on Black Awareness of Cancer.

Div. of Cancer Treatment Director Bruce Chabner cited "notable successes with new drugs," including deoxycoformycin which he said is so active in treatment of hairy cell leukemia that it "probably will be better than interferon," the current standard therapy for that disease.

Also, studies by Lawrence Einhorn at Indiana Univ. using ifosfomide to treat testicular cancer have found that it "is curative in patients who have failed other regimens," Chabner said.

DCT's differences with FDA over approval of anticancer drugs and biologicals were brought up by Chabner. "That's one of our most significant problems," he said. "There are some very good drugs that are not reaching patients. It is probably costing some lives."

DeVita added that if FDA applies the same rules it now uses for anticancer agents to LAK/IL-2, "we are years away from approval. We believe the criteria for approval should be when you see improvement in patients, not overall survival."

Chabner said that a draft document outlining NCI's proposed criteria for approval has been drawn up. He will ask the DCT Board of Scientific Counselors to go over it, "then we'll attempt to muster support from the oncology community." He said he has written to B.J. Kennedy, president of the American Society of Clinical Oncology, asking for the Society's support.

"There are some important drugs being held up for not very good reasons," Chabner said.

DeVita cited as another major new success in chemotherapy the clinical trial conducted at Memorial Sloan-Kettering Cancer Center by Alan Yagoda for treatment of bladder cancer. Yagoda, using a combination of methotrexate, velban, adriamycin and cisplatin (MVAC), has obtained excellent results "in a disease for which there is no good treatment," DeVita said. Included are some complete responses. "I'm very impressed when something gets a complete response. You only cure cancer when you get rid of all of it."

Maryann Roper, NCI acting deputy director, said that MSK is also using colony stimulating factor (CSF) with MVAC. CSF reduces significantly the degree of bone marrow suppression.

"If that holds up with other drugs, it will revolutionize chemotherapy," DeVita said.

Responding to Hammer's question on availability of CSF, Chabner said "that is one problem that can't be laid at the feet of FDA. The real problem is getting the cooperation of industry. Some of the patents are held very close to the best by companies inexperienced in drug development. They are mistrustfull of other institutions. It is causing significant delays in development of CSF."

Alan Rabson, director of the Div. of Cancer Biology & Diagnosis, mentioned one of his division's more notable successes in training young investigators:

"One of the responsibilities of our intramural program is training young people from various disciplines in basic sciences. A few years ago we had one who came here and worked in immunology. We kept him out of the clinic for two years, and he then went back and finished his surgery training. Later, he returned as chief of surgery. We're trying to find more Steve Rosenbergs."

Rabson said it is "a myth" that basic scientists don't care about clinical applications. "Most of them would like to be famous, which they could be if they found the cure for cancer. They are also humanitarians and feel they can make a contribution."

Some of the most excitement in DCBD has been in the new understanding of molecular genetics, Rabson said. An example is the genetic manipulation of monoclonal antibodies and an immunotoxin which eliminates unwanted features of each, making a highly specific antibody armed with an agent that will kill the cancer cell.

(Continued to page 7)

Cancer Letter, PR Firm Settle Out Of Court On Copyright Violation

The Cancer Letter Inc. and a New York public relations firm, Financial Relations Board Inc., have reached an out of court settlement on copyright violation charges. Terms of the settlement were not announced.

The Cancer Letter Inc. charged that Financial Relations Board had photocopied without permission a complete issue of **The Cancer Letter** and had distributed it to an undetermined number of recipients, through the mail and otherwise.

Theodore Pincus, chairman and managing partner of Financial Relations Board, acknowledged that as many as 10 copies of **The Cancer Letter** and its supplement, **Cancer Economics**, had been copied and distributed. That issue was dated Feb. 27, 1987, and it included the February issue of **Cancer Economics** which featured an article on in vitro treatment testing systems and companies involved in developing and marketing those systems.

One of those companies was Applied DNA Inc. of New York, which is developing the Rotman in vitro chemotherapy assay in partnership with Brown Univ. At that time, Applied DNA was a client of Financial Relations Board.

Applied DNA insisted that it had not asked the PR firm to photocopy the newsletter nor had any knowledge that it did. After notification by The Cancer Letter Inc. of the copyright violation, Applied DNA severed its relationship with Financial Relations Board.

"We always give permission for copying of single articles from our newsletters as long as appropriate credit is given," Jerry D. Boyd, president of The Cancer Letter Inc., said. "But we absolutely refuse to permit copying or reproducing by any means entire issues of any of our newsletters. We intend to vigorously defend our rights under the copyright laws, especially when those rights are violated for commercial purposes."

Violators of copyrights are not only subject to payment of damages of up to $50,000 for each violation, plus legal costs, but also to criminal penalties under certain circumstances. The copyright prohibits reproduction as well as storage in a retrieval system, recording, and transmission by any means, including electronic, without prior permission of the publisher.

FDA Advisory Committee To Consider NDAs On Novantrone, High Dose MTX

The Food & Drug Administration's Oncologic Drugs Advisory Committee will consider two important new drug applications at its meeting Dec. 7-8, the first meeting of the committee since NCI and FDA officials debated their differences over drug approval policy (**The Cancer Letter**, Oct. 9).

The meeting will be held in FDA's headquarters, the Parklawn Building, in Rockville, MD, Conference Rooms D and E. It will start at 9 a.m. Dec. 7, 8 a.m. Dec. 8. The entire meeting is open.

Both NDAs are sponsored by Lederle Laboratories. One, which will be discussed Dec. 7, is for novantrone, in combination with approved cytotoxic drugs for treatment of acute nonlymphocytic leukemia; and for use in advanced metastatic breast cancer.

The other NDA is for high dose methotrexate in combination with other cytotoxic drugs for adjuvant therapy of osteosarcoma, which will be considered Dec. 8.

The committee also will discuss during the first day of the meeting use of various new phase 2 single agents with unknown antitumor activity as initial treatment of extensive small cell lung cancer. On the second day, the committee will take up the matter of FDA requirements for approval of new drugs in treatment of ovarian cancer; an FDA advisory on investigational new drug safety reports; and treatment investigational new drug and sales regulations.

Among the issues which have concerned NCI is FDA's failure on occasion to heed the advice of the advisory committee, and its insistence that survival rather than demonstrated antitumor activity be the primary consideration in approving an NDA.

How Do You Build Centers Program? NCAB Invites Comments, Suggestions

"If we were building a Cancer Centers Program today, how would we do it?"

That was the challenge John Durant, chairman of the National Cancer Advisory Board's Committee on Cancer Centers, has presented to all those who care to comment on the state of the Centers Program.

A mailing to all NCI grantees, presidents of cancer related professional societies, public health agencies and deans of medical schools included the list of issues drawn up

by Durant and his committee last month (**The Cancer Letter**, Oct. 23). The issues are grouped in four categories: Reevaluation of the concept of cancer centers in the context of today's research climate; the meaning and special characteristics of comprehensiveness; logistics of the Centers Program; and funding and management issues for the Centers Program.

In an accompanying letter, Durant asked for responses to any or all of those issues and for any recommendations anyone cares to make. Responses may be submitted by anyone, whether or not grantees or members of the organizations included in the mailing. Durant's letter states:

"The National Cancer Advisory Board's Committee on Centers, of which I am chairman, has undertaken a comprehensive review of the Cancer Centers Program of the National Cancer Institute. We want to discover how we can increase the value of the Cancer Centers Program to the national cancer effort. Among the many issues debated is that of criteria for designation of a cancer center as "comprehensive." While this issue is central to the review, numerous other questions require resolution both at the conceptual level and managerial/logistical level. The most fundamental consideration is: If we were building a Cancer Centers Program today, how would we do it?

"At the time the Cancer Centers Program was initiated, after passage of the National Cancer Act more than 15 years ago [Ed. note: see below], many reasons were advanced for the establishment of the program. Congress and its advisors, acting with the advice of the Yarborough Commission, appeared to have several goals in mind. The report language accompanying the Act stated that 'Cancer centers can play a major role in the conquest of cancer effort by (1) performing fundamental research in the clinical and nonclinical disciplines; (2) serving as lead organizations in planned and coordinated major cancer (organ site) programs; (3) performing a particular segment of a major program component in which they have special competence; (4) providing specialized research and/or clinical capabilities; (5) serving as focal points for testing and evaluating outputs of the cancer research program efforts to medical practice.'

"Since passage of the Act in 1971, we have seen the successful establishment of an outstanding group of centers across the country. They have attracted leading investigators and supported major advances in basic and clinical research, and in training, and have played a key role in the achievements of the National Cancer Program. Now it is time to reassess the Centers Program, particularly in light of the broad statement of intent of Congress and of the program's goals for the Year 2000.

"What are the responsibilities of centers within their own institutions, locally, and nationally, and what are the responsibilities of the National Cancer Institute?

"The Committee on Cancer Centers has decided to invite information and opinions from all interested parties to assist in its deliberations. We want to give you the opportunity to take part in this process. A list of issues to consider has been developed and is enclosed with this letter. Under Section 2 we address the meaning of the comprehensiveness designation. The intent here is to give careful consideration to the characteristics beyond the conduct of basic and clinical research and research training that make a center comprehensive. In particular, we would like your thoughts on participation of cancer centers in national initiatives such as clinical trials, as well as in cancer prevention and control research and outreach programs. We recognize that, for the basic science centers, many of the issues raised are not relevant but those of you at basic science centers may still want to express your views on the issues.

"We are asking you and your colleagues to consider these issues and comment on as many as you can. We will use your responses to develop options on these issues. We plan to hold at least two workshops at which these options, input from various constituencies, and possible recommendations will be considered.

"If you know of anyone else who would be interested in commenting, we encourage you to distribute copies of this letter. Responses should be received no later than Jan. 1, 1988, and addressed to John R. Durant, M.D., c/o Prospect Associates, 1801 Rockville Pike, Suite 500, Rockville, MD 20852."

The complete list of issues appeared in **The Cancer Letter** Oct. 23.

Note: NCI's Cancer Centers Program existed prior to the National Cancer Act of 1971, although without the numbers, visibility and extent of financial support from NCI that developed as a result of the Act. The concept

of comprehensive centers grew out of the Act and language of the committee reports, with enthusiastic suppport and guidance from the NCAB.

ACS Modifies Guidelines For Pap Test Frequency: Physician Discretion

The American Cancer Society's Board of Directors has voted to modify the Society's checkup guidelines for detection of cervical cancer.

Robert Hutter, former national president and current chairman of the ACS National Advisory Committee on Cancer Prevention and Detection, submitted and obtained approval from the Board the committee's new recommendation that:

"All women who are or have been sexually active, or have reached age 18 years, have an annual Pap test and pelvic examination. After a woman haas had three or more consecutive satisfactory normal annual examinations, the Pap test may be performed less frequently at the discretion of her physician."

This is a change from the current ACS guidelines which recommend that after two initial normal annual examinations, the Pap test be performed at least every three years.

ACS has been examining a series of issues relating to the benefits of the Pap test including frequency of testing and age, Hutter noted.

"Several national health professional organizations have different recommendations for detecting cervical cancer and this situation may have confused some women," Hutter said. "Because of these differences, the committee had recommended that current scientific data on testing for cervical cancer be reviewed and that a workshop be held with the major organizations that offer guidance to the public and to health professionals."

Hutter reported that the review and the workshop, held in Annapolis last August, resulted in the development of an acceptable recommendation on testing which the organizations could consider.

The new ACS guidelines are nearly identical to those developed at the Annapolis workshop.

"The Society, the National Cancer Institute, the American College of Obstetricians & Gynecologists, and other organizations that participated in the Annapolis workshop are taking a look at their Pap test guidelines because all realize the importance of creating a common message for the public and the medical profession rather than disparate recommendations," Hutter said.

ACS reports that because of the routine use of the Pap test, the death rate from invasive cervical cancer has decreased by at least 70 percent over the last 40 years. However, 15-20 percent of American women do not have regular Pap tests and account for the majority of deaths from invasive cervical cancer.

The Society estimates that there will be 13,000 new cases of cervical cancer and 6,800 deaths in 1987.

Most Radiation Exposure From Natural Sources, New Report By NCRP Says

More than 80 percent of the radiation exposure of most Americans is from natural sources, with the radioactive gas, radon, which seeps into homes and other buildings accounting for the largest fraction of that amount, the National Council on Radiation Protection & Measurements said in its new report No. 93, "Ionizing Radiation Exposure of the Population of the United States."

The report, the most comprehensive review of the sources of radiation exposure in America ever undertaken, also said that medical X-rays and nuclear imaging procedures account for most of the manmade radiation exposures but the levels are smaller than formerly estimated.

Copies of Report No. 93 may be purchased for $15 from NCRP Publications, 7910 Woodmont Ave., Suite 1016, Bethesda, MD 20814.

The total annual exposure for Americans from all sources averages 3.6 milliSieverts on the metric scale or 360 millirem on the older scale, the report said. Of that amount, 3mSv or 300 mrem are accounted for by radon and other natural sources. These other sources include the radioactive spectrum of cosmic radiation from the sun and outer space, radioactive rocks and faint traces of radioactive materials found naturally in living creatures including humans. These natural sources have always been present.

The major change from previous estimates takes into account more accurate measurements of radon seepage into homes and buildings.

Americans as a whole are not currently exposed to levels of ionizing radiation which would justify public concerns or regulatory actions, the report concludes.

"Windows Of Opportunity": Rabson; Adamson Lists Human Cancer Viruses

(Continued from page 3)

"That is genetic engineering in its neatest form," Rabson said.

"In laboratories, we see windows of opportunity," Rabson continued. "We have a tremendous amount of cooperation with Bruce's people. Clinical oncology rounds have become exercises in molecular genetics.

Richard Adamson, director of the Div. of Cancer Etiology, said that recombinant DNA techniques have permitted identification of viruses that are associated with human cancer to a much greater extent than seemed possible a few years ago. He listed those presently known to be in that category as:

--DNA viruses. Human papillomaviruses, anogenital cancers; hepatitus B virus, liver cancer; Epstein-Barr virus, Burkitts lymphoma, nasopharyngeal carcinoma, B cell lymphomas, some head and neck tumors; human B lymphotropic virus (HBLV), Sjogren's syndrome, acute lymphotropic leukemia, lymphoproliferative disorders.

--RNA viruses. Human T cell leukemia virus (HTLV-1), acute T cell leukemia, tropical spastic paraparesis, B cell lymphoma, minor immune deficiency; HTLV-2, hairy cell leukemia, chronic T4 cell lymphoma, T cell chronic lymphocytic leukemia; human immunodeficiency virus (HIV), AIDS, CNS disease (indirect), enhancement of B cell lymphoma, Kaposi sarcoma, others; HIB-2, some immune deficiency; HTLV-5, mycosis fungoides, cutaneous T cell lymphoma.

Identification of a virus as an etiological agent will help in development of vaccines and also therapy, Adamson said.

One of the problems his division is facing in its AIDS vaccine work is finding suitable animal models, Adamson said. The Gibbon ape and chimpanzee, both in limited supply, are the only ones available now.

Paul Rambaut, deputy director of the Div. of Extramural Activities, is also the new Rambaut said U.S. scientists have been excluded from studies following survivors of the Chernobyl nuclear accident. Hammer, who had just returned from concluding a $6 billion trade agreement between the Soviets and his Occidental Petroleum firm, said he would speak with the appropriate officials who will accompany Chairman Gorbachev on his visit to Washington for the summit meeting next month.

NCI Advisory Group, Other Cancer Meetings For Dec., Jan., Future

Clinical Intervention with AIDS--Dec. 2-4, New York. Contact Lisa Griffin, Course Secretary, Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York 10021, phone 212/794-7019.

Advanced Cancer in Later Years: A Nursing Challenge --Dec. 3, Ruth Taylor Geriatric & Rehabilitation Institute, Westchester County Medical Center, Hawthorne, NY. Contact Sr. Patricia Sheridan, Coordinator, Continuing Professional Education, Calvary Hospital, 1740 Eastchester Rd., Bronx, NY 10461, phone 212/863-6900.

Cancer Therapy Program Project Review Committee--Dec. 3-4, Chevy Chase Holiday Inn, open Dec. 3 8-8:30 a.m.

Cancer Preclinical Program Project Review Committee--Dec. 3, Bethesda Holiday Inn, open 8:30-8:45 a.m.

Cancer Clinical Investigation Review Committee--Dec. 3-4, Omni Shoreham Hotel, Washington DC, open Dec. 3 8:30-9 a.m.

National Cancer Advisory Board Committee on Organ Systems Programs--Dec. 3, Linden Hill Hotel, Bethesda, 8:30 a.m.-5 p.m., open.

Patient Care Evaluation--Dec. 3-4, Adam's Mark Hotel, St. Louis. Hospital cancer program component sponsored by the National Tumor Registrars Assn. Also scheduled for March 4-5 in Philadelphia. Contact NTRA Headquarters, 104 Wilmot Rd., Suite 201, Deerfield, IL 60015, phone 312/940-8800.

Cancer Center Support Review Committee--Dec. 4, Hyatt Regency Hotel, Bethesda, open 10 a.m.-3:30 p.m.

Clinical Cancer Program Project Review Committee--Dec. 4, Howard Johnson Inn, Crystal City, VA, open 12-12:30 p.m.

Societa Italiana di Chirurgia Oncologica--Dec. 5-8, Genova. Contact Dr. Fausto Badelino, Chief, Div. of Surgical Oncology, Istituto Tumori Genova, V. Benedetto XV, 10, 16132 Genova, Italy.

Human Rights, Government Roles & the Environment--Dec. 6-8, Annapolis, MD. Sponsored by Collegium Ramazzini, Workplace Health Fund, OSHA/Environmental Network and the Univ. of Maryland Center for Philosophy and Public Policy. Contact Workplace Health Fund, 815 16th St. NW, Washington, DC 20006, phone

p.m., open.

Interferons and Tumor Necrosis Factors Advances in Clinical ~Research--Dec. 9, Brussels. Contact D. Eeckhoudt, Executive Secretary, EORTC Data Center, Boulevard de Waterloo 125, 1000 Brussels, Belgium.

Radiation and Cancer Risk--Dec. 9-10, Oslo. Contact Norwegian Cancer Society, Huitfeldtsgt. 49, 0253 Oslo 2, Norway.

Regulation of Proliferation and Differentiation in Normal and Neoplastic Cells--Dec. 10-11, Westin Hotel, Boston. 10th annual Bristol-Myers Symposium on Cancer Research. Contact Nancy Taussig, Bristol-Myers, 345 Park Ave., New York 10154, phone 212/546-4337.

Clinical Aspects of HIV Infection--Dec. 10-11, Brussels. Contact D. Eeckhoudt, EORTC Data Center, Blvd. de Waterloo 125, 1000 Brussels, Belgium.

10th Annual San Antonio Breast Cancer Symposium--Dec. 11-12, San Antonio. Contact Terri Coltman, RN, Cancer Therapy & Research Center, 4450 Medical Dr., San Antionio, TX 78229.

Cancer Management Course--Dec. 11-12, Nashville. Contact William Johnston, MD, FACS, Cancer Dept., American College of Surgeons, 55 E. Erie St., Chicago 60611, phone 312/664-4050.

Second Tokyo Symposium on Prostate Cancer--Dec. 11-12, Tokyo. Contact Dr. Hidetoshi Yamanaka, Dept. of Urology, School of Medicine, Gunma Univ., Maebashi, Gunma-ken 371, Japan.

Annual Symposium on Carcinological General Surgery --Dec. 11-12, Villejuif, France. Contact N. Chassaing, Dept. of General Surgery, Institute Gustave-Roussy, 39, rue C.-Desmoulins, 94805 Villejuif Cedex, France.

Women's Health Trial Ad Hoc Committee--Dec. 15-16, NIH Bldg 31 Rm 4A48,8:30 a.m..

Div. of Cancer Prevention & Control Board of Scientific Counselors Committee on Prevention--Jan. 6, time and place to be announced.

DCPC Board of Scientific Counselors Committee on Centers & Community Oncology--Jan. 6, NIH Bldg 31 Rm 7, 7 p.m., open.

DCPC Board of Scientific Counselors--Jan. 7-8, NIH Bldg 31 Rm 10, 8:30 a.m. both days, open.

Third International Conference on Prevention of Human Cancer: Chemoprevention--Jan. 12-15, Arizona Health Sciences Center, Tucson. Contact Mary Humphrey, Conference Coordinator, Arizona Cancer Center, Tucson 85724, phone 602/626-2276.

Biological and Molecular Aspects of Atrial Peptides--Jan. 17-23, Steamboat Springs, CO. Contact UCLA Symposia, 103 Molecular Biology Institute, UCLA, Los Angeles 90025.

Occupational Health in the 1990s: Developing A Platform for Disease Prevention--Jan. 21-23, Washington DC. Contact Ellen Marks, Conference Coordinator, New York Academy of Sciences, 2 East 63rd St., New York 10021, phone 212/838-0230.

Transitional Cell Carcinoma of the Urinary Tract--Jan. 23-24, New Hyde Park, NY. Contact Ann Boehme, CMP Associate Director for Continuing Education, Long Island Jewish Medical Center, New Hyde Park 11042, phone 718/470-8650.

Mechanisms and Consequences of DNA Damage Processing--Jan. 24-31, Taos, NM. Contact UCLA Symposia, 103 Molecular Biology Institute, UCLA, Los Angeles 90025.

Symposium Annuel d'Oncologie Pediatrique--Jan. 25, Paris. Contact L. Saint Ainge, Organisation des Reunions Scientifiques, Institut Gustave-Roussy, 39, rue C. Desmoulins, 94805 Villlejuif Cedex, France.

Session de Formation a l'Activite Pluridisciplinaire en Oncologie--Jan. 25-30, Toulouse, France. Contact Le Centre Claudius Regaud, 20-24, rue du Pont Saint-Pierre, 31052 Toulouse Cedex, France.

Care of the Patient with Cancer--Jan. 27-29, London. Contact Institute of Oncology Marie Curie Memorial Foundation, 28 Belgrave Square, ,London SW1X 8QG, UK.

Management of Hematologic Malignancies--Jan. 30, Cleveland. Contact Barbara Guy, PhD, Assistant to the Director, R. Livingston Ireland Cancer Center, Univ. Hospitals of Cleveland/Case Western Reserve Univ., 2074 Abington Rd, Cleveland, OH 44106, phone 216/844-7856.

Technological Advances in Vaccine Development--Jan. 30-Feb. 6, Park City, UT. Contact UCLA Symposia, 103 Molecular Biology Institute, UCLA, Los Angeles 90025.

B Cell Development--Jan. 31-Feb. 7, Taos, NM. Contact UCLA Symposia, 103 Molecular Biology Institute, UCLA, Los Angeles 90025.

FUTURE MEETINGS

American Society of Preventive Oncology--March 14-15, Hyatt Hotel, Bethesda. Annual meeting. Biochemical markers of colorectal cancer, recently completed etiologic studies of colorectal neoplasms, issues and recommendations in the early detection of colorectal cancer, strengths and limitations of methodologic approaches to study of diet and cancer, and priorities and barriers in cancer prevention and control. Contact Richard Love MD, ASPO, 1300 University Ave., 7C, Madison, WI 53706, phone 608/263-6919.

Fundamental Tumor Registry Operations--April 6-8 in Princeton, NJ; May 22-24 in Seattle; Sept. 7-9 in Mobile, AL; and Sept. 28-30 in Chesterfield, MO. American College of Surgeons Cancer Dept. 1988 schedule of tumor registry programs. Contact ACOS, Cancer Dept., 55 E. Erie St., Chicago 60611, phone 312/664-4050.

13th Annual Mental Health Conference--April 21-22, Houston. Sponsored by M.D. Anderson Dept. of Pediatrics. Contact Office of Conference Services, HMB Box 131, MDA, 1515 Holcombe Blvd., Houston 77030, phone 713/792-2222.

American Society of Clinical Oncology--May 22-24, New Orleans. 24th annual meeting. The cancer education program, chaired by Bruce Peterson, will be held May 22; the scientific program, chaired by Clara Bloomfield, will be held May 23-24. The annual joint session with AACR will be held may 25. Deadline for abstracts is Dec. 1. Contact ASCO Headquarters, 435 N. Michigan Ave., Suite 1717, Chicago 60611, phone 313/644-0828.

Clinical Aspects of Hyperthermia--June 12-17, Sheraton University Center, Durham, NC. Contact Sandy Huskins, Duke Univ. Medical Center, Box 3085, Durham, NC 27710, phone 919/684-4384.

Fourth International Symposium on Selenium in Biology and Medicine--July 18-20, Univ. of Tubingen, West Germany. Contact Dr. A. Wendel, Physiologisch-Chemisches Institute der Universitat, Hoppe-Seyler-Strabe 4, D-7400 Tubingen, West Germany; or Dr. O. Levander, USDA Agricultural Research Service, Human Nutrition Research Center, Beltsville, MD 20705, phone 301/344-2504.

NCI/EORTC Symposium on New Drugs in Cancer Therapy --March 8-10, 1989, Free Univ., Amsterdam. Contact EORTC New Drug Development Office, Free Univ. Hospital, PO Box 7057, 1007 MB Amsterdam, The Netherlands.

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

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Cancer Economics

Report Calls MRI Scans Money Loser, Suggests New Reimbursement Method

Health care providers on the average lose $177 on each magnetic resonance imaging scan performed on outpatient basis and reimbursed through Medicare, a Washington consulting group has found.

According to a November 1987 report by Medical Technology and Practice Patterns Institute Inc.:

--An average operating cost per MRI scan is $355, variable cost is $26 and capital cost is $249. This adds up to $651.

--The Health Care Financing Administration model for Medicare Part B payment methodology estimated the average MRI cost per case at $474, about $177 less than the MTPPI estimated average cost.

--One implication of the difference in these cost models is that a single MRI provider with a 30 percent Medicare caseload would lose about $80,000 a year on MRI service.

--For the universe of 400 outpatient sites providing 400 Medicare scans a year, this translates into a total loss of $21 million.

--The capital intensity of MRI services compared to the average of all other services is six times greater.

The purpose of the institute's two year study involving 19 hospitals was to measure the impact of Medicare policy on the adoption, diffusion and use of MRI in the outpatient setting.

The sample included only MRIs operating in hospital settings and did not include free-standing and mobile units.

"It is not at all obvious what constitutes an efficient level of MRI operation," the report said.

When HCFA derived its MRI cost model in February, 1986, it based its estimates on an operating year of 250 days, and a throughput of eight patients a day, which adds up to 2,000 patients a year.

(Continued to page 2)

ADNA Tools Up For 100,000 Assays; Competitor Sells 1,500 In 1987

In preparation for commercializing its in vitro chemosensitivity assays, Applied DNA Systems Inc. of New York has leased a 10,000 square foot facility in Providence, RI, company officials said.

The firm, one of four involved in development and marketing of in vitro chemosensitivity tests, plans to start commercial sales of its Rotman In Vitro Chemosensitivity Assay (RIVCA) in the first quarter of 1988.

Addressing the shareholders Nov. 2, Donald Bachman, Applied DNA's chairman and chief operating officer, said the plan is to process 10,000 assays in 1988 and 100,000 in 1989.

These projections significantly exceed actual sales of Applied DNA's leading competitor, International Clinical Laboratories of Nashville, TN.

ICL, which started marketing a different type of an in vitro test in January, has sold 1,500 so far. Another competitor, Earl-Clay Laboratories of Novato, CA, has sold kits to test "100 to 200 patients," according to the company president.

AntiCancer Inc. of San Diego, another firm developing a chemosensitivity assay, is determined not to market the test until it is

(Continued to page 7)

HCFA MRI Cost Model Results In Lower Reimbursement, Report Says

(Continued from page 1)

The HCFA estimate of capital costs assumed a six year useful life of facilities and equipment, and a 10 percent interest rate for the financing of 55 percent of capital expenditures.

"The HCFA projection of throughput is based upon an idealized number, which may or may not conform to actual hospital experience," the MTPPI report said.

By surveying MRI utilization and costs at 19 hospitals, the study found the average throughput of 1,862 MRI scans a year.

Using the HCFA model, the study estimated cost per scan at $507. Actual costs reported by the 19 hospitals averaged $651.

Making the situation still more complicated, Medicare carrier guidelines of July 1987 suggest that a carrier "determine costs of a scan based on its judgment on what should be minimum throughput levels; i.e. even if actual throughput levels are lower."

This guideline is based on the assumption that greater utilization of an MRI scanner necessarily leads to lowering of costs per scan, the report said.

"These Medicare payment incentives may reward providers who increase throughput in order to recoup operating expenses, even through lower levels of throughput were warranted by their case mix and patient volume," the report said.

"Providers which were operating at lower throughput levels because of greater efficiency and discrimination in utilizing lower cost hospital resources, such as CT scans in place of MRI, would now be given a payment incentive to increase the volume of a costlier hospital resource.

"Although Medicare reimbursement carriers are also instructed to use the Medicare allowance for the least expensive item or service which meets the patient's medical needs, it appears likely that because precise clinical indications for the use of MRI scans or CT scans are still forthcoming, providers still exercise a significant degree of discretion and exhibit practice variations in their choice of modalities.

"These suggestions [by HCFA] to base payment on an idealized efficiency level could tend to promote higher MRI utilization, regardless of the clinical needs or the patient suitability of substitution of other hospital resources."

Analyzing MRI costs at 19 hospitals, NTPPI found that there may be a level of utilization after which further increases in utilization actually add to operating costs per scan.

The sample showed that the highest costs per scan were not always associated with the lowest throughput.

NTPPI broke its sample into three groups:

--Group I, consisting of five hospitals, performing fewer than 1,500 scans a year reported total operating costs of $380 per scan and total capital costs of $199 per scan.

--Group II, seven hospitals that perform more than 1,500 but fewer than 2,100 scans had the operating costs of $446 and capital costs of $257 per case.

--Group III, seven hospitals that perform more than 2,100 scans had operating costs of $323 and capital cost of $95 per case.

"Instead of the expected outcome, this analysis demonstrated that the institutions operating at a level of 1,500 to 2,100 scans per year had the highest total costs per case of the three subgroups, greater than the institutions operating below 1,500 scans per year," the report said.

MRIs on Wheels

According to the American College of Radiology, 549 MRI scanners were in operation in the U.S. as of August, 1987. Of them, 400 were located outside hospitals.

By comparison, in June 1986, ACR reported that 314 MRI scanners were in operation.

Though the number of scanners increased, the proportion of hospital based units remained virtually unchanged.

--Mobile sites increased in number about 250 percent over the previous year, and increased in their share of the market from 14 percent to 27.5 percent.

--The number of freestanding sites increased 35 percent over 1986, but the proportion of the freestanding sites dropped from 59 percent to 45 percent.

--Of the 151 mobile MRI units reported to be serving hospitals in 1987, 144 were characterized as superconducting, with the majority falling in the range of the .6 Tesla and smaller magnet size.

--Of the 250 freestanding sites, 193 were described as superconducting magnets, 22 were described as resistive and 34 were described as permanent.

--The majority of magnets purchased for

freestanding sites was also .6 Tesla field strength and smaller, but about a third of purchased magnet sizes were greater than 1.5 Tesla.

The report outlined potential hazards of MRI use in outpatient settings:

--The lack of access to life support teams and intensive care units for emergency patients.

--The absence of alternative imaging procedures in the outpatient setting which may provide cheaper and more appropriate modes of diagnosis.

--The lost opportunities for teaching medical students and fellows and for consultation with colleagues.

--The increased chances of fostering what the report called "a corporate attitude" by the structuring of for profit MRI centers and of physician entrepreneurship.

There is little background or understanding of the cost, volume and quality tradeoffs for new medical technologies, the report said.

"Therefore, a reasonable approach is to steer a neutral course and neither unduly inhibit nor encourage the diffusion and provision of services.

"Optimally, payment rates should be based upon the existing data base of health care provider experience with costs and utilization, and should evolve with changes in practice patterns and input prices.

"The primary focus of a public policy intended to support and safeguard the provision of care to a constituency of beneficiaries should be on gathering and analyzing the information as best as possible, and on aligning payment incentives and support with current clinical practices for delivering quality care."

The report is available from MTPPI, 2233 Wisconsin Ave., NW, Suite 302, Washington, D.C., 20007. 202/333-8841. The price is $51.50.

Triton, UCLA Patent Oncogene Cancer Management Methods

Triton Biosciences Inc. and the Univ. of California (Los Angeles) earlier this month received a patent for methods and compositions for detecting and treating cancers, the company announced.

Included are:

--Methods for evaluating the probability of cellular malignancy by using nucleic acid probes or antibodies to identify elevated levels of genetic material (messenger RNA) or oncogene proteins associated with certain cancers.

--Antibodies specific for the proteins produced by human oncogenes such as c-myc, c-fos, c-ras (Ha), c-ras (Ki), c-fes, c-myb and c-src.

--Novel peptides defining epitopic sites (areas that permit attachment of certain antibodies on proteins produced by oncogenes.

--Methods for treating cancers through the use of antibodies to oncogene proteins.

Triton, a biotechnology subsidiary of Shell Oil Co., and UCLA were issued patent, U.S. 4,699,877.

The patent results from an invention made in research sponsored by Triton and conducted at UCLA laboratories by Martin Cline and Dennis Slamon.

Through an agreement with the regents of the University of California, Triton was granted worldwide exclusive license to the patent rights and technology derived from this research.

Besides the U.S. patent, the license includes also patents applied for in 27 countries and issued in Spain, Greece, Australia and New Zealand.

"Triton has a team of 95 research and development people concentrating on the diagnosis and treatment of cancer and other serious diseases," said Richard Love, Triton president.

"This patent will clearly strengthen the company position," he said.

Triton is continuing to fund Slamon's study of a specific oncogene, called HER-2 and c-erbB-2. This work involves investigation into whether elevated levels of the oncogene would be a prognostic indicator for certain cancers, including breast cancer.

In another development, Triton has agreed to provide Franklin, TN, based Biotherapeutics Inc. its other product, betaseron, a genetically engineered derivative of human interferon beta.

Under the agreement, Triton will provide betaseron to Biotherapeutics for physicians treating cancer patients who meet strict medical eligibility criteria regarding the type of malignancy involved and its potential response to betaseron treatment.

Betaseron is in advanced stages of development by Triton, under general partnership with Cetus Corp.

It has been tested on more than 1,300

patients and shown activity in cancers of the kidneys and lungs, brain tumors, pediatric cancers and the AIDS related Kaposi's sarcoma.

Triton was founded by Shell in 1983.

It is focused on the development, manufacture and marketing of diagnostic and pharmaceutical products for cancer and other life threatening diseases.

Xoma, Hoffmann-LaRoche to Test Monoclonal Antibodies, Interleukin-2

Xoma Corp. of Berkeley, CA (OTC: XOMA) and Hoffmann-LaRoche Inc. of Nutley, NJ, announced this month that they will collaborate on testing combinations of Xoma's monoclonal antibody products with Hoffmann-LaRoche's interleukin-2 therapy of cancer.

Clinical trials will be conducted at the Univ. of Texas M.D. Anderson Hospital & Tumor Institute.

The joint project's objective is to evaluate the two new approaches for their combined effectiveness in treating patients with widely spread cancer, officials of the companies said.

Malignant melanoma will be the first type of cancer to be evaluated. Patrick Scannon, Xoma president, said the cancer was chosen because both of the companies' products are known to have biologic activity against the melanoma tumors.

Additional cancer types may be added to the joint testing program at a later date, the firms said. If the therapy is effective, the firms will negotiate further business arrangements.

Xoma reported financial results for the third quarter of 1987 that showed a $3.6 million loss, compared with a $3.5 million loss during the same period last year.

Expenditures were primarily due to expanded human clinical trials, company officials said. During the third quarter, Xoma completed a combined phase 1 and 2 human clinical trials of the XomaZyme-H65 product for the treatment of bone marrow graft against host disease. The company also expanded human clinical trials of Xomen-E5, for treatment of septic shock.

Xoma posted revenues of $1 million during the quarter, primarily from contract research. No revenues were reported during the quarter last year.

For the first nine months of 1987, Xoma recorded a net loss of $11.6 million, compared with $42.4 million in 1986. Last year's loss included a $32 million charge for acquisition of the technology and rights of an affiliated research and development partnership.

As of Sept. 30, the firm reported a cash balance of $62.6 million and stockholders' equity of $37.6 million.

FINANCIAL

Genentech Patents New Techniques For Producing Hormones, Proteins

Genentech Inc. of South San Francisco this month secured a patent covering the firm's techniques for transplanting foreign genes into microbal hosts for the production of proteins and hormones, the company announced.

According to industry obesrvers, the broad nature of the patent may mean most of the firm's competitors will need to be licensed by Genentech, and pay royalties on their products.

The patent does not list specific products, but describes classes of products which include most of the fruits of the industry.

Genentech officials said the firm intends to make licensing decisions on a case by case basis, and will wait for other firms to make the first move. The customary royalty rate for nonexclusive licenses of this type are from .5 percent to 1 percent of sales.

The patent's impact may hinge on whether it covers newer biotechnology "factories" of mammalian cell cultures, as well as yeast and bacteria. The patent does not specifically address mammalian cell cultures, which are used to produce many of the industry's new products, including Genentech's clot dissolving drug TPA.

The patent's claims were made in 1979, and it has been issued in 20 other countries. Keichi Itakura and Arthur Riggs of the City of Hope in Los Angeles are named as co-inventors.

The two researchers carried out their work under Genentech sponsorship.

Scientific Leasing Inc. of Farmington, CN, (American Stock Exchange: SG and SG-A) announced the repurchase of $4 million of its 8.25 percent convertible subordinated debentures due 2003. The firm will realize from the repurchase an extraordinary book after tax gain of $772,065, or 25 cents per share on a primary and fully diluted basis.

The firm said the redeemed debentures will be used to meet the annual sinking fund requirement of $1.875 million in 1993, 1994 and part of 1995.

Otisville BioPharm Inc. of Otisville, NY (NASDAQ: OBPI) has signed a letter of intent to transfer the assets of its Rosanin Division to **Fluoromed Pharmaceutical Inc.** in exchange for 10 percent of Fluoromed's common stock.

The Rosanin Division holds the rights to a patented method for creating microemulsions, and a license agreement relating to fluorosurfactants. The division is developing second generation technologies for synthesizing fluorosurfactants and for creating improved emulsion methods for use in a synthetic oxygen carrier.

Fluoromed is conducting phase 2 human clinical trials for its first application of perfluoroctylbromide emulsions, as a contrast agent for the early detection of cancer in the liver and spleen, and for imaging the vascular system.

Duane Roth, president of Otisville BioPharm, said the firm's objective has been to develop Rosanin "to the point where the division could enter into a joint venture with a company involved in first generation emulsions."

Salick Health Care Inc. of Beverly Hills, CA (NASDAQ: SHCI) reported net income of $3.273 million for its fourth quarter and fiscal year ended Aug. 31.

Net income rose 29 percent from last year, from $2.535 million. Total revenues rose 21 percent to $25.74 million from $21.229 million last year.

Fourth quarter net income increased 28 percent to $967,000, from $755,000 in the prior period. Total revenues for the period increased 21 percent, to $7.555 million from $6.238 million.

Company officials attributed the record results to the strong performance of its Cedars-Sinai Comprehensive Cancer Center in Los Angeles and expanded dialysis operations.

Intermagnetics General Corp. of Guilderland, NY (NASDAQ: INMA) and **Diasonics Inc.** of South San Francisco have extended their agreement under which Intermagnetics supplies Diasonics with magnets for magnetic resonance imaging systems. The value of the new transaction, which calls for deliveries through the end of 1988, exceeds $8.5 million, according to Intermagnetics officials.

Immunex Corp. of Seattle, WA, announced that **Immunology Ventures,** its joint venture with **Eastman Kodak Co.,** has sold marketing and development rights to interleukin-4 to Kodak's **Eastman Pharmaceuticals Div.**

Under the terms of the joint venture, Eastman will conduct human testing of IL-4, which it plans to begin in early next year. Eastman will be responsible for product marketing and Immunology Ventures retains manufacturing rights and will receive royalties on sales of IL-4.

The profits of Immunology Ventures, formed two years ago, are shared by Immunex and Eastman Pharmaceuticals.

Aspen Systems Corp. of Rockville has received a $4.5 million contract to establish a National AIDS Information Clearinghouse.

The contract was awarded by the Center for Disease Control in Atlanta. Aspen is an information management company which specializes in establishing libraries, data bases for businesses and federal agencies.

The clearinghouse is to distribute government publications about the disease and make referrals for additional information. Under the contract, the company must also maintain an on line data base for use by state and local officials involved in combatting the disease.

DRUGS/EQUIPMENT

Lifecodes Leukemia Assay Called "Powerful Aid in Diagnosis"

Lifecodes Corp. of Vahalla, NY, has introduced a "powerful aid in the diagnosis of chronic myeloid leukemia (CML)," according to a study in the November issue of Cancer Genetics and Cytogenetics.

The test, called Breakpoint Cluster Region analysis, employs gene probe analysis and is more specific than cytogenic screening, according to Peter Benn, director of Lifecode's clinical laboratory and author of the report.

The BCR assay is processed in the company's laboratory in Vahalla. The fee is $275. Processing takes eight days, according to a spokesman.

CML is associated with a specific genetic marker, the Philadelphia chromosome, which is the product of the rearrangement of chromosomes 9 and 22. However, in 5 percent of the cases, the Philadelphia chromosome is absent, resulting in false negative findings.

The Lifecodes test identifies specific rearrangements in the breakpoint cluster region of chromosome 22, enabling a positive diagnosis in patients who have the disease but do not exhibit the Philadelphia chromosome, Benn said.

There are several other advantages to the test, Benn said. It can be used to analyze nonmitotic cells--cells that are not dividing--which is important for patients undergoing chemotherapy.

The analysis can be carried out on blood samples rather than bone marrow. Also, the BCR test can identify a malignant cell population of 2 percent or less.

More information is available from the company, (800)-LIFECODES.

T Cell Sciences Inc. of Cambridge, MA (NASDAQ: TCEL) announced the release of the Cellfree T8 test kit, the newest addition to its Cellfree line of immunoassays.

The kit is the first commercially available enzyme immunoassay to quantitate soluble T8/CD8 in serum, plasma or culture supernatants.

Levels of the protein may serve as as an index of suppressor/cytotoxic cell activity in both disseminated and localized immune reactions. The kit is for research use only.

The kit is priced at $485 if purchased separately. Each kit gives 96 determination. Processing is done by physicians.

The test kit will reduce the need for "complicated and time consuming techniques currently employed," the company said. The test also may be a more reliable index of T8/CD8+ cell activation than commonly used bioassays.

Dianon Systems Inc. of Stratford, CT, has developed a prostate cancer biopsy kit to be used by physicians.

According to the company, the Dyanacite TM Fine Needle Biopsy System includes a novel fixative that allows transport of prostate biopsy specimens without loss of diagnostic quality.

The fee for the kit and its processing is $185.

The biopsy is transported to a central laboratory specializing in the cytology of prostate cancer. For more information contact Diane DeCrow, the company's clinical program program administrator, Stratford, CT, 06497-7124.

Nikon Inc. of Garden City, NY, has introduced a CFN 1X Plan Achromat objective. The new objective has uses in a variety of disciplines for low power observations and photomicrography, including pathology, dermatopathology, neuroanatomy and histology.

The instrument provides total field flatness, enabling use with binocular and trinocular body tubes. In combination with Nikon's low power condenser and an FX camera system, the objective provides highly corrected Koehler-illuminated low power images with actual magnifications on film down to 2X.

Carl Zeiss Inc. of Thornwood, NJ, announced the availability of a new interactive image analysis system, called the Videoplan Morphometric Workstation.

The system includes a high precision digitizer tablet, a microcomputer, a high resolution color video monitor and a portable keyboard. The user can work with live video images as well as photographs. The system automatically prints out the contours of traced structures.

A 50 megabyte hard disk drive and high-density floppy disk drive are included. Software includes programs for measurement, data evaluation, data management, file management, help functions and word processing. To assist users, the company publishes a biannual image analysis newsletter, ZIPS: Zeiss Image Processor Systems, available without charge.

PEOPLE

Biotherapeutics Appoints Six To Scientific Advisory Board

Biotherapeutics Inc. of Franklin, TN (NASDAQ: NMS) has appointed a six member scientific advisory board to advise the firm's management on research and development programs relating to the biotherapy of cancer.

The board members are **Norman Klinman** of La Jolla, CA, **Carelton Steward** of Los Alamos National Laboratory, **E. Gregory MacEwen** of the Univ. of Wisconsin, **Jan Vilcek** of New York Univ. Medical Center, **Katsuyuki Haranaka** of the Institute of Medical Science, Univ. of Tokyo; and **Roland Mertelsmann** of Johannes Gutenberg Univ. in Mainze, Germany.

The company also has appointed **William Ramsey** chief operating officer. He joined Biotherapeutics in April of this year as executive vice president for operations and administration. From 1982 to 1987, he held

several positions with **Baxter Travenol Laboratories.**

Howard Willson has joined **Repligen Corp.** of Cambridge, MA, as chief operating officer. He previously was with **Bristol-Myers Company** as president of the Mead Johnson Nutritional Group.

Willson joined Bristol-Myers in 1983 as vice president for business development. Prior to Bristol, he held a variety of positions in seven years at **Abbott Laboratories.**

Cytogen Corp. of Princeton, NJ, announced the promotion of **Thomas McKearn** to the position of senior vice president, scientific affairs. He was instrumental in the formation of the firm in 1980, and as vice president of research and development, was the company's first employee. He remains as Cytogen's chief scientific officer, and in his new position will be responsible for all research, development and medical activities.

Cytogen also announced the promotion of **John Rodwell** to the newly created position of vice president, discovery research. He will be responsible for both chemical and biological research activities for new technology. He came to Cytogen in 1981 and is co-inventor of the company's proprietary carbohydrate linking technology system.

Four Firms Vying for In Vitro Chemosensitivity Assay Market

(Continued from page 1)
proven effective in clinical trials involving hundreds patients, said Robert Hoffman, company president.

The market for in vitro testing, depending on who is doing the projections, is estimated at $150 to $600 million by the end of the decade.

Skeptics say the existent assays may be more accurate in predicting when a treatment will not work than when it will. If the test indicates no response, patients would be spared the discomfort of unsuccessful chemotherapy.

In a report dated Oct. 16, just three days before the sharp drop in the stock market, Nicholas Lawrence & Co., a Red Bank, NJ, investment firm made this projection:

"We think ADNA stock could sell for a minimum of $35 per share two years out if the company meets our earnings traget for 1989."

Addressing the short run problem, ADNA's board has voted to extend the exercise date for its Class B warrants from Nov. 10 to Feb. 8, 1988. Exercise rights remain unchanged: each warrant entitles the holder to purchase of ADNA stock at $4.

Bachmann said the firm expects to retail its assay for about $1,000 per application. The distribution would be handled directly or through one or more marketing partners, he said. RIVCA is owned jointly by ADNA and Brown Univ.

RIVCA, ADNA's lead product, is being tested at Johns Hopkins Univ., Milton S. Hershey Medical Center, Univ. of California (Irvine), Univ. of Chicago, Rhode Island Hospital and Massachusetts General Hospital.

"The final step of the clinical protocol, that of demonstrating the correlation of in vitro and actual results, is now in progress and showing extremely favorable results," Bachmann said.

Getting Reimbursed

"It's been a good year," said Ronald Baker, vice president for oncology services at International Clinical Laboratories.

"We've got the assay in over 250 hospitals," Baker said. "We've done our job and convinced people that our technology works."

Data collected in the firm's clinical studies is expected to be published in the December issue of the "Journal of Clinical Oncology", Baker said. The firm charges $750 to test each tumor's response to 12 drugs.

According to the firm's study of 71 patients, LifeTrac can successfuly grow tumors in 83 percent of the cases.

When tumor sensitivity to chemotherapy was indicated in vitro, in 76 percent of the cases sensitivity also was observed in vivo.

When no response was indicated in vitro, in 94 percent of the cases none was found in vivo.

Neither Blue Cross/Blue Shield nor Medicaid have ruled on medical necessity of in vitro tests. ICL has compiled a list of insurance companies that have at least once reimbursed for in vitro tests.

In the past eight months, about 50 physicians have contacted ICL with questions about reimbursement, Baker said.

The firm assisted them in writing letters to insurance companies, and in more than half the cases reimbursement was obtained.

Another firm, Earl-Clay Laboratories, is the only firm to package the test into a kit.

The kit, called Ultraclone OncoScreening System, is sold to laboratories. Each kit, which allows the testing of response to one drug, is sold to physicians for $30 to $35, Lovins said.

The marketing is in conjunction with Soma Laboratories of Romeo, MI. The marketing is done with a caveat: the test is not to be used in diagnosis.

Earlier this year, Earl-Clay signed a licensing agreement with SmithKline, giving the company exclusive rights to use the product in commercial reference laboratories.

Biotherapeutics holds exclusive rights to use the assay in the custom tailored experimental care market. The agreement does not restrict Biotherapeutics from using other in vitro assays.

Earl-Clay also plans to help hospitals and groups of physicians to set up cloning laboratories, but, Lovins said, "We have not addressed that market yet. It will be another 12 months before we get into that area."

According to Lovins, trials are being conducted at the Arlington Cancer Treatment Center in Texas and Massachusetts General Hospital.

Earl-Clay was formed in 1983 and went public two years later, closing the offering in April 1986, raising $1.1 million.

Testing Chemotherapy Agents

AntiCancer Inc. is conducting clinical trialswith its assay. "We are carrying out retrospective and prospective clinical trials," said Hoffman. "We are also testing new agents for very important biotechnology and pharmaceutical companies."

He declined to name the pharmaceutical and biotechnology companies involved.

So far 300 patients have been involved in clinical trials, Hoffman said. However, it is too early to set the price of the assay or predict the date of its introduction on the market, he added. "It's too speculative. We consider clinical trials to be of paramount importance."

AntiCancer's assay analyzes one gram solid tumor biopsies. The goal is to maintain the tumors in their native state in vitro, said Hoffman. The assay doesn't introduce the artifact of cell disaggregation, doesn't separate normal stroma from tumor tissue and doesn't use dyes which purport to identify live cells. Such dyes may actually identify the viable enzyme systems of nonviable cell.

Hoffman said the test "won't be cheap, you won't be able to package it into a kit and it will take more than a few days to perform."

Hoffman said his firm has received a number of offers from venture capital firms. He turns down those offers, staying within the limits of the NCI's Small Business Innovation Research grants program and has some private investor financing as well as a private contractual arrangement to test antineoplastic agents in development.

ADNA Diversifying

Applied DNA, in an attempt to broaden its product range, purchased convertible debentures in Oxyrase Inc of Ashland, OH, which owns a nontoxic antioxidant.

ADNA has an option to purchase additional Oxyrase shares through Dec. 30, 1988, which would bring the in Oxyrase to 22.7 percent.

Under the agreement, ADNA had a right of first refusal to join Oxyrase on a 50/50 basis to commercialize its technology for all applications except foods.

Antioxydents could be used to replace carcinogenic compounds currently employed to remove oxidation from boiler water in fossil fuel and atomic power plants.

Plans have been approved by Oxyrase to establish a research and production lab facility in Oak Ridge, TN. The first joint venture proposal is expected to be submitted to ADNA's scientific advisory board in December.

ADNA is also continuing studies of recombinant collagenese for wound healing and treatment of slipped disks. The studies are being done under a contract with American Biogenetic Sciences Inc., a privately held genetic engineering firm based at Notre Dame Univ.

ADNA has $6 million in cash, which Backmann said, is "sufficient to fund all existing programs an allow consideration of new technology investments as well."

Expansion could also be enhanced through the exercise of all Class B warrants, which would provide the firm with about $6.8 million.

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Editor: Paul B. Goldberg
Associate Editor: Jerry D. Boyd

The Cancer Letter, Inc., PO Box 2370
Reston, VA 22090, Phone 703-620-4646

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AIDS update

News • Policy • Research

Proposed "ASAP" Expedited Review For AIDS Applications Outlined

A proposed expedited review system for AIDS related research applications will attempt to reduce to six months the time between the announcement of an RFP or RFA and the award of grants.

The proposed changes were developed in response to legislation introduced by Sen. Edward Kennedy that would require final decisions on AIDS related research applications to be made within six months after the publication of a solicitation.

NIH draft plans for the expedited review process were outlined to members of the NIH Director's Advisory Committee by Katherine Bick, deputy director for extramural research. The plans for the "Accelerated Solicitation to Award Process" were developed by a special committee established to review ways to streamline the NIH review process, and are still under review by NIH.

NIH will probably reduce to 45 days the time between the publishing of an announcement and the application deadline. The agency is legally permitted to allow only 30 days from the time of an announcement to the application deadline, but is attempting to streamline its internal procedures instead of placing additional pressures on extramural researchers.

Although all AIDS related applications will continue to be received within the Division of Research Grants, NIH plans to develop a "specific and unique" address to which AIDS applications will be sent. Unsolicited responses should be identified as AIDS related applications on their cover sheets in order to speed the review process.

A key element of the plan will call for applicants to receive prior approval from their institutional review boards and the necessary waivers for research involving humans and animals from the Office of Protection From Research Risks. NIH currently

(Continued to page 2)

HTLV-1 Screening Recommended For Certain Parts Of The U.S.--Gallo

HTLV-1 blood screening should be required testing in certain portions of the United States, Robert Gallo told the National Cancer Advisory Board. Gallo is chief of the Laboratory of Tumor Cell Biology within NCI's Developmental Therapeutics Program.

"I do believe that the leukemia virus should be required blood testing in portions of the United States," he said. Although emphasizing that he did not want to "sensationalize" the issue, he noted that "in parts of the United States, it's a relatively common infection in some groups."

Gallo cited Hawaiian investigators who believe that in Hawaii, "HTLV-1 may be more important to have as a routine test than the HIV test." Hawaii has a large number of immigrants from Okinawa, "who have a very high rate of infection."

Studies looking at "the serology in islands where the Japanese soldiers were compared to the nearby islands where they weren't" have found "an enormous difference" in HTLV-1 infection rates, Gallo said. "If you argue that that must mean that it wasn't there at all prior to World War 2, then you see that very fast, a lot of these people in some of these islands are now infected, so it must have happened fairly rapidly.

"Whether, or how fast, this is happening in the United States, I can't say. We don't have enough data."

(Continued to page 5)

Applicants May Need To Submit 30 To 40 Copies For Review

(Continued from page 1)
allows a 60 day grace period for such approvals.

Bick emphasized the need for applications to be complete and accurate in all details because "there will not be time" for many traditional prereview activities.

NIH will also try to speed reviews of grant applications by asking applicants to submit "sufficient copies" of their applications for the review process. Bick told **AIDS update** that applicants would probably be asked to submit 30 to 40 copies of their application.

Before NIH can ask for the additional copies, however, the agency will need to receive clearance from the Office of Management & Budget since the application forms are subject to the federal paperwork reduction act.

NIH does not expect many site visits to be possible under the proposed accelerated review process, and will try to request extensions beyond the six month time limit in order to conduct necessary site visits.

NIH expects to receive approximately 800 AIDS related applications this year, double the number received last year.

In establishing the proposed accelerated review system, NIH has sought to preserve the quality of dual peer review, as well as animal and human subject safeguards.

Many steps in the current review process will need to be parallel versus serial processes in order to meet the shortened timetable, Bick said. For example, it will be necessary to form technical review groups while applications are still being received. Applications would likely be "triaged" by peer review committees.

Bick acknowledged that the proposed changes will have a significant impact on both NIH's internal operations and external researchers.

NIH is also considering publishing "presolicitation" announcements that would contain broad outlines of concepts passed by institute advisory groups prior to the release of a formal RFA. The announcements would emphasize that they signify only the intention of issuing an RFA or RFP.

NIH is also considering setting fixed grant receipt dates approximately four months before advisory council meetings. Bick hopes that all investigator initiated applications and RO1 responses to RFAs would be assigned to a single chartered review committee with a number of subcommittees.

Bick described the possibility of creating an "AIDS flexi study section" that would be composed of 50 to 75 members with expertise in different disciplines. The flexible structure would allow for interchange of members within subcommittees. She suggested that the same type of committee could be used for contract proposals.

Institute directed reviews should use chartered review committees as much as possible. Routine mail balloting "is not desirable," and advisory councils may need to meet more than three times a year. An alternative already undertaken by NIAID and NCI is the creation of council AIDS subcommittees.

Under the ASAP process, many more processes would go on concomitantly, she said. The expedited review process will require additional personnel, provided for in the Kennedy legislation. Bick also suggested that each institute will need a person to coordinate AIDS reviews. NIH will also need to update its computers, but the bulk of the burden "must be carried out by humans."

Under a proposed ASAP review timetable, letters of intent would be expected five weeks after an RFP was announced. In the 10 week period in which applications were being received and processed, a peer evaluation group would be organized.

The initial review group would be expected to meet the 15th week after the solicitation, with summary statements and further processing of applications to be carried on in the next 10 weeks. Institute advisory councils or boards would review the applications and select awards by the 25th week after solicitation. Awards would be made in the 26th week after the initial solicitation.

The average time from solicitation to grant award is currently nine months for an RFA and 11 to 12 months for an RFP.

"I was listening to this with an increasing sense of dread," National Cancer Advisory Board Chairman David Korn said. "I wonder if three months difference is going to matter to anyone."

NIH Director James Wyngaarden, however, said that many awards require more than nine months. "When the existing system was put into place about 30 years ago, the pace of science was much slower," he said. Today, "a

wait of nine to 10 months on an application may mean the work may be done by someone else."

Wyngaarden told the meeting that NIH is using the potential mandate to accelerate review as an opportunity to look at the entire NIH review system.

"It seems an appropriate question to raise just because of the pace of science" today, he said. NIH is "looking at the whole system to see if can be accelerated."

Even if the Kennedy legislation is not enacted, NIH will continue to look at ways to expedite the review process, Bick said.

Daniel Hoth Named Acting Head Of NIAID's AIDS Program

Daniel Hoth, former chief of the Investigational Drug Branch in the Cancer Therapy Evaluation Program within NCI's Div. of Cancer Therapy, is the new acting director of the AIDS Program for the National Institute of Allergy & Infectious Disease.

Hoth, who also served as acting director of the Cancer Therapy Evaluation Program for several months before the appointment of Robert Wittes to the job, officially assumed his new duties at NIAID last month.

In his new job, Hoth has the responsibility of overseeing five branches and a 43 person staff. AIDS activities account for 37.7 percent of NIAID's budget.

Discussing the institute's AIDS Program at the first meeting of the new NIAID AIDS Research Committee, Hoth said "the most important initiative we have in this area" is an RFA for Programs of Excellence for Basic Research on AIDS (see RFAs Available). The new 30 member flexible committee met for the first time last week, and will be responsible for the review and approval of AIDS related concepts prepared by institute staff, as well as peer review of AIDS research applications.

The committee contains three subcommittees with eight to 12 members each in the areas of: basic virology, immunology and pathogenesis; epidemiology and technology transfer; and clinical applications, prevention and treatment. The basic virology subcommittee will be chaired by Donald Mosier of the Medical Biology Institute in La Jolla, Calif.; the epidemiology group by Seymour Grufferman of the Pittsburgh Cancer Institute; and the clinical subcommittee by Margaret Ann Fischl of the Univ. of Miami School of Medicine.

IOM Plans AIDS Drug And Vaccine Development Group

The Institute of Medicine/National Academy of Sciences is planning to establish a group to meet regularly on the subject of AIDS drug development and vaccine development, Roy Widdus, director of IOM's Div. of International Health, told the NIH Director's Advisory Committee.

The group plans to hold a workshop on vaccine development Dec. 14-15, and believes there is a need "for a regular forum to exchange views in a neutral environment," he said.

IOM continues to monitor AIDS research and activities since the publication of the landmark report "Confronting AIDS" in 1986.

The institute has an AIDS Activities Oversight Committee that continues the broad monitoring and assessment functions of the report committee that was chaired by David Baltimore and Sheldon Wolff.

IOM will release an update of the report in late spring or early summer of 1988.

Baltimore spoke to the committee on the role of basic undifferentiated research and perspectives on AIDS research management.

In addition to citing the need for further undirected, investigator initiated research in the areas of cellular immunology, general molecular biology and virology, Baltimore identified possible deficiencies related to basic undirected research in AIDS.

Because investigator initiated research may not hit on every angle related to AIDS, the scientific community must make sure that there are "no unfilled cracks" in AIDS related research, he said.

Baltimore also emphasized the need for direct coordination of applied research.

While noting that the responsibility for coordinating applied research belongs to the whole scientific community, he acknowledged that the responsibility "tends to fall' on NIH. "It is the government's responsibility that every lead identified by the scientific community is followed up," he said, adding that such an effort will require "very close cooperation between NIH, the external scientific community and industry."

Baltimore also cited the need for more obvious management of AIDS research, and the need for careful consideration of "where the research holes are, and how they can be filled."

One of the major problems facing AIDS

research centers around the need to upgrade research facilities and equipment. Noting that institutions working with the AIDS virus need to build P3 level containment facilities, he said no funds are available through the federal government to build such facilities. In addition, more primate centers are needed to facilitate necessary research in animal models.

Another major problem facing AIDS research concerns reagent distribution, he said, adding that all viral isolates should be available to all investigators who can use them effectively. He also noted that most investigators don't know how such isolates or viral proteins are made available.

Baltimore also said he was "a little amazed looking at the programs coming out of NIAID" because they tend to be "so elaborate," or difficult to respond to.

Such programs are very inhibitory "to someone who's interested in just getting their feet wet" in AIDS research, he said.

Baltimore also told the committee that he was "struck by the very important need for increased openness of process" and the need for more public information about NIH AIDS research programs.

"What's going on is not evident enough to either the scientific community or the general public."

Wolff, who cochaired the report committee with Baltimore, also offered some advice to the meeting.

He repeated the report's recommendation for $1 billion for AIDS education and public health activities and another $1 billion for research by 1990.

"That figure was not taken out of the air," he said, but was the result of "considerable consideration." Noting that the committee also stressed that the funds should be new money, he said he "personally would advocate even more money."

Wolff also cited the need for funding for research facilities, citing a "crying need for new instruments and equipment." The estimated cost for building a P3 level facility, for example, is approximately $750,000. AIDS research also requires a cell sorter, which costs more than $200,000.

He also predicted that more research nurses and at least 100 additional beds will be needed by General Clinical Research Centers to conduct AIDS research. Wolff suggested that shared institutional grants could offer some support.

Wolff also noted the need to attract young investigators to AIDS research, and the need to provide career training awards. As a former NIAID Advisory Council member, Wolff says, "I was always appalled and embarrassed by the small number of training slots" that were available through the institute.

HHS Blasts Congressional Plans To Subpoena Patient Data From FDA

Top HHS officials are blasting Congressional plans to subpoena patient records, including patient identifiers such as initials or patient names, from FDA, although Congressional sources say they have routinely received such information for more than 20 years.

Deputy Assistant Secretary for Health Lowell Harmison told the NIH Director's Advisory Committee that the move "probably represents one of the most fundamental issues where the Public Health Service as an institution has to take a firm stand. We cannot weaken under this process."

NIH Director James Wyngaarden also decried the action, stating that "confidentiality is vital to the carrying out of AIDS clinical trials."

The debate centers around a six to two vote by members of Rep. Ted Weiss' (D-NY) Human Resources & Intergovernmental Relations subcommittee to subpoena records on five drugs from the Food & Drug Administration. The subcommittee has oversight over FDA. None of the records sought contain information on AIDS drugs or AIDS patients.

According to a Congressional staffer, FDA has supplied Congressional oversight committees with "hundreds of thousands" of records including patient identifiers since the early 1960s, and as recently as August of this year. The records were not "leaked," but have been accompanied by official transmittal letters, he said.

Records that included patient names were accompanied by a letter noting that patient names were included and that if the records were to be released to the public, FDA would provide suitable (purged) copies of the records.

FDA and HHS policy on providing patient identifiers to Congress is somewhat murky. According to the Congressional staffer, FDA first put in writing the need to purge patient identifiers from records sent to Congress in an internal memo dated Sept. 1.

An HHS letter sent to Weiss in mid September, however, referred to a policy established regarding deletion of patient specific material in 1983. It specifically referred to a May 1983 letter from former HHS Secretary Margaret Heckler to Weiss that requested advance notice for document requests so they could be purged for trade secrets or "patient specific" material. The Congressional staffer said the letter referred to CDC records of AIDS cases, and has never been applied to FDA records.

Congress wants patient identifiers such as initials in order to verify the accuracy of records and to determine if a patient record being reviewed is a new patient or one previously reviewed, he said. It also wants to retain the right to examine original documents if necessary.

In addition, Congress wants to shorten the time required to receive records on experimental drugs from FDA. The agency often takes 190 days to supply copies of even unpurged records, the staffer charged. Such delays make it difficult for Congressional committees to perform their oversight functions, he said.

FDA refused to comment on any aspects of the debate. An HHS spokesperson declined comment because "the whole issue is under review by the department."

Although there have never been any reports of breaches of confidentiality by Congressional staff, HHS officials have expressed concern about the special need for patient confidentiality in AIDS clinical trials.

None of the five drugs being investigated are AIDS drugs. The committee is seeking adverse reaction reports on the drugs Merital, Versed, lovastatin, Suprol, and THA, an experimental drug for Alzheimer's. The subpoena is expected to be delivered Dec. 1.

The NIH Director's Advisory Committee unanimously passed a resolution stating its concern that "the breach of confidentiality will send shock waves throughout the AIDS research and patient communities, and will have enormous negative consequences for voluntary participation in research protocols." The action could also "significantly interrupt rapid progress being made in the nation's capacity to treat and manage this disease."

The resolution states that "the release of patient identifiers with patient records to the public is contrary to the currently employed medical and ethical standards of confidentiality and informed consent."

HHS officials agree that Congress does have the legal authority to subpoena the records. "Congress has the right to do this," Harmison said, "but in a personal sense, it is not an issue for lawyers.

"This is an issue for society, for physicians and for people to address because this simply undercuts the voluntary nature of research."

Harmison said HHS has "suggested providing records with numbers and all hosts of mechanisms to avoid the individual identifiers." The issue is "unfolding over five specific drugs, but that's only the crack in the dike and we cannot accept this process."

HTLV-1 May Be More Important In Neurological Disease Than Leukemia

(Continued from page 1)

Data from epidemiologic studies in the U.S. indicate varying rates of infection from the virus in different groups.

Persons may be doubly infected with HIV and either HTLV-1 or HTLV-2, but have not been found to be infected with both HTLV-1 and HTLV-2.

Among i.v. drug users in Queens, NY, for example, 41 percent are HIV positive; 34 percent have either HTLV-1 or 2 infection, and 17.8 percent have a double infection of HIV and either HTLV-1 or 2.

In a similar study in New Orleans, only one percent were HIV infected, but 34 percent were infected with HTLV-1 or 2. When the study is broken down into race, differences appear between the rate of infection between blacks and whites.

Among 136 blacks in the New Orleans study, none were infected with HIV, while 49.3 percent were infected with HTLV-1 or 2. Among 72 whites, 2.6 percent were HIV infected, 6.5 percent were infected with HTLV-1 or 2, and 1.3 percent were doubly infected with HIV and either HTLV-1 or 2.

Some investigators believe people can become triply infected with HIV-1 plus HIV-2 plus either HTLV-1 or HTLV-2, Gallo said. "We have never proven that you can develop an infection with both HTLV-1 and HTLV-2," however.

Div. of Cancer Etiology Director Richard Adamson told the meeting that NCI is working closely with the National Heart, Lung & Blood Institute, FDA and blood banks in order to

develop a standardized test for HTLV-1 screening.

Although only 1 percent of people infected by the leukemia virus have a lifetime risk of developing leukemia, the rate of neurological disease resulting from HTLV-1 infection is probably higher, Gallo said. In addition, "probably most people infected with it have at least some impairment of their immune function."

To date, there are three reported cases of people with profound immunodefic- iency infected only with HTLV-1, Gallo said, emphasizing the rarity of serious immune deficiency in persons infected with the virus.

Noting that "any human retrovirus infecting the T4 cell lymphocytes is capable of causing some immunodeficiency," Gallo said that "even the leukemia viruses have been associated with an increased incidence of opportunistic infections, and an increased incidence of bacterial infections.",

Recent epidemiologic data indicate HTLV-1 "may be more important as a neurological disease virus than as a leukemia virus."

Associated diseases include "tropical spastic paraparesis, called HTLV-1 associated myelopathy," he said. The virus could also be associated with encephalomyelopathy, and demyelination.

In addition, "there's a clinical and pathological inability in some cases to distinguish this disease from" the more common multiple sclerosis found in the U.S. and Europe.

"In a sense this disease is an multiple sclerosis disease, but one should not get the idea that multiple sclerosis in general is associated with HTLV-1 or even an HTLV-1 related virus," he said, adding that it may provide an important model for the study of MS.

Gallo also suggested that "maybe we should consider antiviral treatment not only for HIV, but for HTLV-1 infected people."

Gallo also noted that reports of a fifth human lymphotropic retrovirus will be published by Italian investigators in an upcoming issue of "Science."

Noting the volume of discussion recently about HIV-2, Gallo said, "there's perhaps more about it in the newspaper than in the scientific literature." So far, the virus is more or less limited to Western Africa, and pilot studies in the U.S. and other countries "do not reveal a significant spread of this

"This does not mean that we can avoid looking at it, but it is not a cause for panic or overconcern at this moment."

The vast majority of persons infected with HIV-2 are healthy, although it is occasionally associated with serious immune deficiency.

"Although this virus and the AIDS virus are 50 percent related, we have to try to emphasize 'let's not take our eye off the ball. This [HIV-1] is the virus that is causing so much trouble.'

"I am not impressed by the data on HIV-2 related immune deficiency," he said. "I think this is overstated."

Discussing opportunities for therapeutic interventions against the AIDS virus, Gallo cited two characteristics of the HIV that differ from other human retroviruses. HIV differs in "the great amount of virus that is liberated in a short period of time when the T cell is reactivated" and in the virus' extremely tight binding of the envelope of the virus to the cell membrane receptor.

"The most peculiar characteristic of this virus is the envelope affinity for binding to the receptor of the CD4 component of the T4 molecule," he said. The "extremely tight binding of the gp120 to the CD4" molecule is a potential target for intervention.

Gallo noted that a number of investigators are trying "to block entry by using a soluble T4 molecule" made by rDNA technology or other means. The investigators use "specific regions of the T4 to bind to the virus in sucn soluble forms that the virus doesn't find its receptor on the cell membrane.

"On paper, that seems to be the most exciting approach to block infection."

Mentioning ongoing efforts to develop more effective and less toxic compounds to block reverse transcriptase, Gallo said, "there are many programs focusing on other related enzymes necessary in the virus life cycle.

"We suspect that in the future, maybe greater enhancement will occur upon interfering with the expression of the virus. The reason for this is because the genome of this virus contains extra genes that are essential to the virus life cycle" such as the TAT gene.

"This gene [TAT] is absolutely essential to the replication of the virus." Although "the exact function of all of these gene products," is not known, most of them are involved "in the fine tuning, the regulation of the RNA formation, lengthening and sub-

sequent translation, in other words the level of transcription and processing of the RNA.

"We believe that because TAT and TRS... are absolutely essential to the virus replication, and because there may not be exact analogs like them in normal cells, that interfering with their functions may be a selective way of blocking virus formation and may become important future sites for antiviral therapy."

Discussing infection of macrophage versus T cells, he said recent evidence "indicates that very, very minor changes in the genome of the envelope can produce major changes in the ability of a variant of the same strain of virus to infect the macrophage versus the T cell."

Describing "a remarkable result from the laboratory infected worker," Gallo said, "it took a lot of attempts to isolate the virus in this antibody positive person and the virus that was isolated seemed to be more macrophagetropic, so we said immediately, 'Aha! It can't be the laboratory virus the guy or gal was working with because those laboratory viruses the person was working with were grown with human T4 leukemic cell lines'...but apparently selection occurs.

"We think increasingly that this cell and its relatives are as important or more important than the infection of the T4 cell. One suspects that this cell is the earliest cell to be significantly infected--we suspect that it is an important reservoir for the virus because it doesn't get killed as easily as the T4 cell.

In addition, virus particles can be seen inside vesicles within the cell. "I don't know anybody who can prove those virus particles inside the macrophage aren't infectious, but they might be important in this area," he said.

"We argue that we need cellular immunity to kill virus infected cells when they express viral proteins, but what happens when you kill the macrophage? Unlike the T4 helper cell and other cells that get infected, the macrophage houses fully formed virus particles in vesicles and if you smash the macrophage and release those virus particles, you may actually promote more spread of the virus."

"It is likely that the macrophage brings the virus to the brain," but he is "not convinced of the importance of the multiplicity of cell types of the brain being infected."

Two New Presidential AIDS Panel Replacement Members Named

The White House has named two new members to its AIDS committee following last month's resignation of the panel's chairman and cochair. Beny Primm, a New York physician specializing in drug addiction treatment and Kristine Gebbie, Oregon's state health administrator, were named to the panel.

The two replace former chairman Eugene Mayberry and cochairman Woodrow Meyers, who resigned amidst reports of infighting on the panel and a lack of support from the administration.

Primm is a frequent speaker at conferences dealing with such issues as HIV testing and counseling for i.v. drug users.

In other AIDS advisory group news, NIH hopes to announce the members of its new NIH AIDS Advisory Committee in the near future.

Speaking before the NIH Director's Advisory Committee last week, Sen. Edward Kennedy (D-Mass.), who has introduced legislation that would create such a panel, appeared pleased with the plan.

"I look forward to carefully reviewing the names of those nominated by HHS to serve on this critically important committee," he said.

"Congress feels strongly about the 'experts' we recruit for this type of duty. AIDS represents an extremely complex biological--and public health--problem. In searching for the shortest path to successful results, we need the talents of those who are already 'up to speed' on the issues. "I'm sure you are aware of the concerns in this area about the Presidential Commission on the HIV Epidemic. The last thing we need is an attempt to politicize the scientific and medical assault on the problem of AIDS."

D4T Synthesis Credit Correction

The synthesis of the compound D4T (**AIDS update**, Sept. 18) was incorrectly credited.

D4T was synthesized by Tai-Shun Lin of Yale Univ. by the procedure published by J. Horowitz and colleagues at the Michigan Cancer Foundation. Horowitz was first to synthesize D4C, and Lin synthesized D4C by an alternative procedure published this year. Lin's synthesis of D4T and D4C was supported by an NCI grant to Yale pharmacology professor William Prusoff, but was evaluated both by the drug discovery group led by Andre Nahmias and the Bristol-Myers group.

RFAs Available

RFA 88-AI-01

Title: Programs of excellence for basic research on AIDS

Application receipt date: Feb. 17, 1988

The National Institute of Allergy & Infectious Diseases intends to make six to eight awards as a result of this RFA, with the starting date for the initial annual period to begin on or before September 1988. Award may be made for up to five years.

NIAID is inviting applications to establish "programs of excellence for basic research on AIDS" (PEBRA). The purpose of the RFA is to support basic research programs addressing questions on the pathogenesis of AIDS and its related opportunistic infections by using approaches from immunology, virology, cell biology or molecular biology. By increased understanding in these areas, more rational studies for the diagnosis, treatment and prevention of AIDS can also be designed.

The PEBRA program will be supported through the cooperative agreement assistance mechanism to encourage scientists and physicians with interests in AIDS research to participate in solving problems related to AIDS.

As envisioned, PEBRAs should have the capacity to generate new approaches and strategies to answer key questions leading to improved understanding of the processes of the immune system and infectious disease in AIDS. PEBRAs can be associated with AIDS, or they may be multidisciplinary in composition.

In addition, the PEBRA must facilitate creative interactive research activities between members of the group and not merely be a collection of individual RO1 applications. The degree of interaction can be, but should not be limited to: a) multidisciplinary research efforts; b) sharing of facilities and equipment; and c) seminars that involve all project leaders of a PEBRA.

NIAID has a broadly based contract and collaborative research portfolio related to virology and immunology. In addition, the AIDS program has initiated several cooperative multidisciplinary, multi-institutional research programs for AIDS. The National Cooperative Drug Discovery Groups for the Treatment of AIDS, the National Vaccine Development Groups and the AIDS Clinical Studies Groups are examples of these cooperative agreement programs. AIDS Program staff will interact with PEBRAs and other cooperative agreement programs to assist in the development of their research programs as they relate to AIDS and to facilitate the interactions between these cooperative agreement programs.

The PEBRAs will enable scientists in various fields of research to interact, with NIAID support, as a unit, to carry out the basic research essential for the realization of the PEBRA objectives. PEBRAs could be composed of scientists from academic, nonprofit and for-profit research institutions and commercial organizations.

When the applicant institution is outside the United States, awards will be limited to three years. Domestic applicants, including those with foreign components, may request funding for up to five years.

Requests for copies of the full RFA and further information may be directed to, and letters of intent may be sent to, Martin Padarathsingh, PhD, Chief, Pathogenesis Branch, AIDS Program, NIAID, NIH, Westwood Bldg, Rm 7A-04, Bethesda, MD 20892.

RFA 88-HD/MH-01

Title: Behavioral aspects of AIDS prevention in children and adolescents

Application receipt date: Feb. 12, 1988

The National Institute of Child Health & Human Development and the National Institute of Mental Health plan to make up to 10 awards through the RO1 mechanism in this area.

The two institutes are inviting research grant applications investigating selected topics addressing behavioral approaches to prevent AIDS in children and adolescents. Research is needed to learn how best to educate children and intervene in adolescent populations, who due to behavioral patterns (e.g. sexual activity and drug use) are at increased risk for exposure to and spread of HIV infection.

The RFA states that "until effective treatments and vaccines are developed, the prevention of AIDS is largely a behavioral issue. Therefore, research on prevention and/or intervention must focus on ways to reduce the likelihood of behaviors associated with the spread of the infection."

The institutes anticipate that new methods and approaches will be needed for learning how best to prevent AIDS in children and adolescents. New methods are required to assess behavioral change and modification as a consequence of intervention and education.

Developmentally appropriate teaching methods are needed to insure information provided is both understood and used to make decisions that will prevent exposure to the virus. Followup of infants, children and adolescents known to have been exposed to AIDS is needed to evaluate the consequences of exposure to their social and emotional development.

Applications are encouraged to carry out research on: a) developmentally appropriate educational approaches to teach AIDS related information to children of different ages; b) intervention methods for teaching high risk groups how to make decisions, resist peer pressure, and analyze the relationship between current behavior and future consequences; c) reliable and valid methods for measuring behavioral change resulting from intervention to prevent AIDS and d) the consequence of HIV exposure upon the social and emotional development of children and/or adolescents.

Applications should be submitted on PHS Form 398. The RFA label available in the 9/86 revision of application form 398 must be affixed to the bottom of the face page. Failure to use this label could result in delayed processing of the application such that it may not reach the review committee in time for review.

For further information or a copy of the full RFA, contact: Norman Krasnegor, PhD, Chief, or Sarah Friedman, PhD, Health Scientists Administrator, Human Learning & Behavior Branch, Center for Research for Mothers & Children, National Institute of Child Health & Human Development, Room 7C18, Landow Bldg, 7910 Woodmont Ave., Bethesda, MD 20892, phone 301/496-6591. Prospective applicants may also contact: Leonard Mitnick, PhD, Chief, Health & Behavior Branch, Div. of Basic Sciences, Room 11C06, Parklawn Bldg, 5600 Fishers Lane, Rockville, MD 20857,phone 301/443-4337.

AIDS Update

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Editor: Patricia Williams
Associate Editor: Jerry D. Boyd

P.O. Box 2370 Reston VA 22090

703-620-4646