THE CANCER LETTER

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Taxol Approved By FDA For Ovarian Cancer; Bristol Sets Price Tier In Line With Platinum

Taxol, the anticancer drug made from the bark of the Pacific yew tree, was approved last week by the Food & Drug Administration for the treatment of refractory ovarian cancer.

Immediately following the news of the approval, taxol's sponsor, Bristol-Myers Squibb Co., announced the price schedule for the drug.

The approval was consistent with the unanimous recommendation by the agency's Oncologic Drugs Advisory Committee (**The Cancer Letter**, Nov. 20). The average price of a cycle of taxol, including shipments of the drug at no charge to NCI clinical trials and the indigent assistance

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In Brief

Antman, Chabner Vie For ASCO President-Elect; Irwin Krakoff Is 1993 Karnofsky Lecturer

ASCO NOMINEES: Karen Antman of Dana-Farber Cancer Institute, and **Bruce Chabner**, director of NCI's Div. of Cancer Treatment, have been nominated for president-elect of the American Society of Clinical Oncology. ASCO members will receive their ballots later this month to vote before the May meeting in Orlando, FL. Chairman of the nominating committee is **Philip Pizzo** of NCI. . . . **IRWIN KRAKOFF**, head of the Div. of Medicine and chairman of the Dept. of Medical Oncology at M.D. Anderson Cancer Center, was selected to deliver the 28th Karnofsky lecture at the ASCO meeting. He was cited for his extensive research on anticancer agents and chemoprevention. **Michael Friedman** of NCI is chairman of ASCO's Program Committee. . . . ASCO's Special Awards committee, chaired by **Nancy Kemeny**, selected the following awards winners: **James Holland**, Mount Sinai Hospital, for the society's Distinguished Service Award; **C. Everett Koop**, former Surgeon General, for the Public Service Award; and **Grace Powers Monaco**, founding member of the Candlelighters Childhood Cancer Foundation, for the Special Recognition Award. . . . **THELMA DUNN**, a retired NCI official, died at 92 of congestive heart failure Dec. 31 in Lynchburg, VA. She headed the carcinogenics branch of NCI's pathology laboratory until 1970. . . . **REORGANIZATION** in NCI's Div. of Cancer Etiology formed two branches and three sections in the Epidemiology & Biostatistics Program: Genetic Epidemiology Branch; Viral Epidemiology Branch, Viral Studies Section and AIDS and Cancer Section; and Nutritional Epidemiology Section. . . . NCI's **Div. of Cancer Treatment** established the Laboratory of Leukocyte Biology in the Biological Response Modifiers Program and the Solid Tumor Section in the Pediatric Branch.

FDA Okays Taxol For Ovarian Cancer; Bristol Sets Average Price At $695

(Continued from page 1)

programs, will be $695.25. At the highest level of the pricing tier, the wholesale list price, a cycle of taxol will cost $986.18.

These numbers appear to be in line with the NCI position that taxol should be priced at a level comparable to that of cisplatin, another drug used to treat ovarian cancer.

The technology transfer contract between Bristol and NCI includes a "reasonable pricing" clause, and taxol may provide the test case that would sharpen the language of this vague contractual provision.

Rep. Ron Wyden (D-OR), a leading congressional critic of the agreement that produced taxol, was reserving judgment about the drug's price. "This is still an unresolved issue that bothers us," said a Wyden staff member.

On Jan. 25, Wyden will hold a hearing on the pricing of taxol as well as of future drugs that are likely to be developed through Collaborative Research and Development Agreements. Witnesses are expected to include NIH Director Bernadine Healy, NCI Div. of Cancer Treatment Director Bruce Chabner and Bristol's vice president, Zola Horovitz.

The Price Schedule

A 30 mg vial of taxol carries the wholesale price of $146.10;

The physician direct price is $140.26;

The Medicaid price, after rebate, is $123.16;

The Federal Supply Schedule price, after discount, is $108.11;

The Public Health Service price, after discount, is $123.16.

NCI's clinical supply, Treatment Referral Center and BMS Oncology Access Program will receive taxol at no charge. According to a company projection, on the average, the price of a vial will be about $103. At this level, the weighted average cost of a cycle of taxol will be $695.25.

At the highest level, the wholesale list price, a cycle of taxol therapy will cost $986.18, the company said.

FDA Action

FDA, acting on the ODAC recommendation, approved the dose of 135 mg/m2 24-hour infusion.

A large study in Europe and Canada is testing alternative dosage and administration schedules.

The agency's review time for the drug was five months, one of the fastest reviews ever for a cancer drug.

"We applaud the FDA for the speed with which it reviewed this New Drug Application," said Stephen Carter, senior vice president, Bristol-Myers Squibb Pharmaceutical Research Institute.

"This is consistent with the massive concentration of resources and effort that the NCI, our company and others have devoted to making taxol rapidly and widely available to cancer patients who may benefit from it," Carter said.

Clinical trials conducted by NCI at five centers around the country, and multi-center trials in Europe sponsored by Bristol-Myers, found that the agent, generic name paclitaxel, shrinks tumors by at least one-half in 20 to 30 percent of patients with refractory ovarian cancer, with responses lasting from five to nine months on average.

Taxol was associated with serious side effects including a decrease in white blood cells, hair loss and numbness of the fingers and toes.

Remarkable Accomplishment

"Taxol is a very important drug, and I am proud of NCI's role in bringing it to the public," NCI Director Samuel Broder said in a press release. "Taxol is not a cure, but it clearly can help many women with advanced ovarian cancer who have few other options."

Broder praised the Dept. of Agriculture's Forest Service, the Dept. of the Interior's Bureau of Land Management, and Bristol-Myers Squibb for cooperating with NCI to develop an adequate supply of the drug.

The collaborations were made possible by the Federal Technology Transfer Act of 1986.

Two years ago, NCI had enough taxol to treat only 500 women per year.

"At this time, no woman who medically needs Taxol will be denied the drug," Broder said at last month's meeting of the National Cancer Advisory Board. "I think this is a remarkable accomplishment."

Broder publicly thanked NCI's Div. of Cancer

THE CANCER LETTER

Editor: **Kirsten Boyd Goldberg**
Associate Editor: **Paul Goldberg**
Founder & Contributing Editor: **Jerry D. Boyd**

PO Box 15189, Washington, DC 20003
Tel: (202) 543-7665 Fax: (202) 543-6879

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Treatment and its Developmental Therapeutics Program for "phenomenal efforts in bringing this drug to a reality."

According to Bristol, later this year, sources other than yew bark will begin to be used in taxol production on a commercial scale, and by the end of 1995, yew bark will no longer be needed.

Eyes on Wyden

Wyden has insisted that Bristol provide NCI with a cost-based analysis of research, production and marketing costs for taxol before the drug's price could be judged "reasonable."

The company said it considers such data a trade secret and would not provide it. Both NCI and NIH have said that they have neither the mechanisms nor the expertise to evaluate such information.

Last month the Advisory Committee to the NIH Director was asked to make recommendations for interpreting the reasonable price clause in the boilerplate CRADA contract. (**Cancer Economics**, November and December 1992).

According to Wyden's correspondence with NCI and Bristol, the Congressman is likely to persist in his insistence on closer scrutiny of Bristol's books.

In a Dec. 14 letter to Richard Thompson, the company's vice president for government affairs, Wyden suggested that NCI assemble a panel of drug pricing experts to conduct what amounts to an audit of the price of taxol.

"This panel will work in the strictest confidence, analyzing the initial price for taxol suggested by Bristol-Myers on the basis of (1) development and marketing costs presented by Bristol-Myers, (2) an assessment of the likelihood of competing products and the specific timing of their market entry, and (3) assurance of a reasonable rate of return for Bristol-Myers investors. The last should consider the rate of return of other intensive research and development companies.

"At the conclusion of the panel's evaluation, NCI would report to the congressional committees with jurisdiction over NCI that the company had, or had not, adhered to the fair and reasonable pricing provisions of the taxol development agreement.

"Fundamental to the success of this proposal would be Bristol-Myers' agreement to provide basic data on development and marketing costs, as well as estimates of other important variables, such as the likelihood of development of competing products...

"I fully realize this proposal instructs federal agencies to embark into new territory. But I submit that it is fair and consistent with the terms of the agreement."

Bristol: Panel Not Feasible

In a response dated Dec. 29, the day taxol was approved and its priced announced, Thompson wrote that the panel Wyden suggested may not be feasible because of the need to work in strict confidence by qualified experts who would be obligated to protect both the interests of the taxpayers and the company.

The review would also constitute an unfair modification of the language of the CRADA Bristol and NCI signed nearly two years ago, Thompson wrote.

"Clearly, the taxol CRADA does not contemplate the pricing review process which you propose," he wrote.

"We would be pleased to suggest to you and your staff model pricing language for future CRADAs," the letter continued.

"It is our view that the need for flexibility exists for each individual CRADA, depending upon several key factors, including the existence--or lack--of intellectual property rights.

"Despite the lack of pricing guidance of the Technology Transfer Act which had made CRADAs possible, agencies such as NIH should attempt to write pricing language as specifically as they deem necessary.

"Then, if a potential commercial partner can be identified, the pricing clause would become a subject of negotiations before executing the agreement.

"This is exactly the process that occurred with the taxol CRADA. Additionally, we believe that there is one important way which assures fair pricing, and that is to foster healthy competition in the marketplace. This is precisely what NCI has done by signing CRADAs covering both taxol and taxotere."

Frank Rauscher Jr., Former Director Of NCI, Dead At 62 Of Heart Attack

Frank Rauscher Jr., the first NCI director appointed by the President under the National Cancer Act of 1971, died Dec. 31 in Nyack, NY, after a heart attack. He was 62 and lived in Weston, CT.

Rauscher went to work for NCI in 1959 in the Laboratory of Viral Oncology, where he discovered a mouse leukemia virus whose properties made laboratory studies in mice and rats faster and easier. The Rauscher leukemia virus still is widely used in research.

In 1964 he was appointed head of the Special Virus Cancer Program, and in 1967 became associate director for viral oncology. The viral oncology program eventually led to discoveries that form the basis of modern molecular genetics. From 1969 to

1972 he headed what is now the Div. of Cancer Etiology.

After the National Cancer Act became law in December 1971, providing NCI with special authorities above that of the other institutes in NIH, cancer program advocates felt the new effort should begin with a new leader.

Benno Schmidt, chairman of the President's Cancer Panel, created by the Act, submitted Rauscher's name to President Richard Nixon, who appointed Rauscher director of NCI on May 5, 1972.

Resigned For Financial Reasons

Rauscher was a respected administrator and effective advocate for the National Cancer Program. He charted the rapid expansion in the early years of the cancer program as NCI's budget climbed from $400 million to more than $800 million when he resigned in 1976.

He expanded programs in viral oncology and chemotherapy, as well as what he called "people programs" in cancer prevention and control and research training.

He made several important appointments, including Alan Rabson as director of the Div. of Cancer Biology, Diagnosis & Centers, Vincent DeVita as director of the Div. of Cancer Treatment, and Paul Van Nevel as director of the Office of Cancer Communications.

One of his administrative accomplishments was consolidating treatment activities in the Div. of Cancer Treatment by moving the cooperative groups, the Surgery and Radiation Therapy branches, and the NCI clinical director's position into the division.

"His major problem as NCI director was spending money fast enough," Rabson said.

However, Rauscher's own salary was capped at $37,800, since he was not a PHS commissioned officer and could not receive military pay bonuses. He was one of the lowest paid NCI executives.

With three children in college and two more to follow, Rauscher said he could no longer afford to work at the Institute.

He resigned as NCI director on Nov. 1, 1976 after Congress failed to act on legislation to increase his salary and those of the other NIH institute directors.

Rauscher accepted the job of senior vice president for research at the American Cancer Society at twice his government salary, directing the Society's $30 million research budget (**The Cancer Letter,** Sept. 24, 1976).

At ACS, Rauscher developed innovative grant programs that the Society continues to use. He devised a program for rapid funding of hot new research ideas, the Research Development Program, which provides

Frank Rauscher Jr.

pilot funding to investigators within three months of acceptance.

'A Unique Scientific Administrator'

He also developed the Special Institutional Grants for cancer cause and prevention, which provided $1 million over five years to institutions to hire faculty and attract students to develop the field of carcinogenesis.

"We don't use it any more for training people in carcinogenesis because it worked," Rauscher's successor, John Laszlo, said to **The Cancer Letter.** The grants now are used to develop the fields of nutrition and cancer, and psychosocial and behavioral research.

It was through Rauscher's leadership that ACS volunteers raised $2 million to bring interferon to the U.S. for testing in clinical trials.

"I saw him as a unique scientific administrator," Laszlo said. "He was never formally trained to be an administrator; he was a scientist first and an administrator second.

"He was so gifted in being able to articulate difficult scientific concepts into lay terms," Laszlo said. In his travels for ACS, Laszlo said he often meets people who say they were moved by Rauscher's explanations of science.

"He saw science as a tool to help people, and in that way he was a very idealistic man," Laszlo said.

Since 1988, Rauscher had been executive director of the Thermal Insulation Manufacturers' Assn. in Stamford, CT, where he directed research on noncarcinogenic thermal insulation materials to replace asbestos.

Rauscher was a native of Hellertown, PA, and graduated from Moravian College in Bethlehem, PA. He received a doctorate in virology from Rutgers Univ.

In 1968, Rauscher received the Arthur S. Flemming

Award for outstanding federal executives for his research linking cancer to viruses.

Survivors include his wife, Margaret; three sons, David, of Westport, CT, Frank III, of Princeton, NJ, and Michael, of Ridgefield, CT; two daughters, Mary and Megan, both of Westport; his father, Frank Sr., a brother, Kenneth, and a sister, Lois Grigoruk, all of Hellertown; and two grandchildren.

HHS Final Report Says Gallo Committed Scientific Misconduct

The HHS Office of Research Integrity has found that NCI's Robert Gallo committed scientific misconduct in the discovery of the AIDS virus.

The HHS report, the final step in a three-year investigation, reverses the conclusions of an NIH investigation which earlier this year cleared Gallo of misconduct.

The new report said Gallo had intentionally misled colleages to gain credit for himself and to diminish credit for Luc Montagnier, his French competitor.

According to the HHS report, Gallo "falsely reported" a fact in the 1984 paper in "Science" magazine in which he described isolating HIV, and that the false statement had "impeded potential AIDS research progress" by diverting researchers from work with the French.

In the 1984 paper, Gallo wrote that the French virus, LAV, "has not been transmitted to a permanently growing cell line for true isolation and therefore has been difficult to obtain in quantity." Gallo has said the the sentence meant that the virus was hard to grow, not that he had failed to grow it. The HHS report said that in that sentence, Gallo intentionally misled colleagues.

The HHS report also charged misconduct by former Gallo colleague Mikulas Popovic, who carried out the crucial experiments. The report said Popovic's infractions were "relatively minor" and "should not preclude his employment as a scientist."

Gallo said he was not guilty and would appeal the decision to a judicial board within the department.

"After reviewing everything I and my colleagues have ever published on the discovery of the AIDS virus and the development of the AIDS blood test, the Office of Research Integrity could only take issue with a few trivial mistakes and a single sentence written by me," Gallo said in a statement to reporters.

In its conclusion, the report asks NIH to submit a plan "to ensure accuracy in the recording and reporting of research" by the Laboratory of Tumor Cell Biology, which Gallo heads, and recommends that increased supervision be given to both scientists should they seek federal funds for research through another institution. The sanctions are to be in effect for three years.

Lawyers for the Institut Pasteur in France, which splits the royalties with the U.S. for the AIDS blood test, have asked HHS to turn over its portion of the royalties.

"It has been clear for more than a year that Dr. Gallo went to school on the Pasteur virus, and even Dr. Gallo himself now admits there was only one virus--Pasteur's," Robert Odle, an attorney for Pasteur, said in a statement last week.

"Pasteur intends to return immediately to the U.S. government and ask that it do the right thing," Odle said. "In view of Dr. Gallo's own admissions, and an official finding of scientific misconduct, it is incumbent upon the U.S. government to act without delay."

Gallo and Montagnier each earn about $100,000 a year from the royalties on the blood test.

NIH Director Bernadine Healy said in a statement that NIH had no involvement with the investigation since the now-defunct NIH Office of Scientific Integrity sent its report to HHS earlier this year.

IOM Panel To Advise On Spending Defense Dept's Breast Cancer Money

The National Academy of Sciences' prestigious Institute of Medicine has agreed to mediate the debate about how the Dept. of Defense should spend the $210 million breast cancer research money.

The U.S. Army Medical Research and Development Command, which has control of the funds, contracted with IOM to convene a committee and prepare a report providing specific advice on spending the two-year appropriation.

The committee is expected to recommend the number and subject matter of grant or contract solicitations, and the methods of solicitation.

The work of the committee is to be completed in 120 days, Joseph Cassells, IOM study director, said to **The Cancer Letter**. There will be three meetings, including at least one public hearing.

Some Anxiety Eased

The involvement of the IOM partly eased the anxiety within the cancer research community over the Army's new research mission.

"I was very pleased to hear that the Institute of Medicine has been brought into this," Paul Calabresi, chairman of the National Cancer Advisory Board, said at the board's recent meeting.

"As a member of the IOM, I would like to

participate and be sure that the money gets well spent."

The committee will consist of experts in basic and clinical research, breast cancer, research administration, public policy formulation, and bioethics.

Selections for the committee have not been made as of early this week, Cassells said.

"We're looking for people broadly experienced in the field of breast cancer research and epidemiology and other areas," he said. Some members may be selected from the ranks of the IOM, but "the determining factor is the expertise" of the individual, he said.

According to a summary of the project, "The IOM committee has been asked to provide an overview on breast cancer research and where investments are likely to pay off in advances in knowledge." Two specific areas to be addressed are "the preferred programmatic investment strategy for the funds and the peer review procedures which should be employed in its allocation."

The methods of solicitation may include Broad Agency Announcements to seek proposals in general subject areas, or Requests for Proposals for more narrowly defined subjects.

NCI News Roundup

Six Panels To Identify Progress In Cancer Research For NCI

NCI has formed six panels of experts in six areas of cancer research to help the Institute develop "measures of progress;" i.e. identify the most important accomplishments in cancer research over the past 10 years and the implications for the effect on cancer incidence and mortality.

The panels, chaired by members of NCI's four division Board of Scientific Counselors, will meet for a day and a half in Bethesda this month and next. The chairmen of the six panels will meet to consolidate their reviews. The cancer treatment panel has already met.

The idea for the review began under former planning officer Judy Whalen. When Whalen left NCI last year, the review was put on hold until new planning officer Cherie Nichols had settled into the job.

NCI Director Samuel Broder said the Institute will use the report of the six panels as part of a Congressionally mandated review of the National Cancer Program.

The six panels and their chairmen are:

Panel on Cancer Control--Helene Brown.

Panel on Diagnosis & Early Detection--Noel Warner.

Panel on Cancer Treatment--Paul Carbone.

Panel on Mechanisms of Cancer Induction & Progression: Endogenous & Environmental Exposures--James Felton.

Panel on Molecular Medicine--John Niederhuber.

Panel on Cancer Prevention--Alfred Haynes.

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NCI Director Samuel Broder has asked the National Cancer Advisory Board for its advice on three major issues this year:

--Training and retention of clinical investigators.

--The "philosophy and policies of the Institute dealing with program project grants in comparison to the traditional investigator initiated R01 grant."

--The NCI bypass budget for fiscal 1995. At this time of year, NCI begins to develop the bypass budget for the fiscal year two years in advance of the current fiscal year.

As he has at recent meetings since breast cancer advocates successfully lobbied for more money for breast cancer research, Broder discussed with the NCAB his concern over how the bypass budget is used.

"For example, a specific component of the bypass budget can be pulled out irrespective of the fact that it is a total document," Broder said at the board's meeting last month. "When that happens there can be significant problems. In effect, it is making a use of the bypass that is not intended.

"Let's say there is a request for a certain type of activity against the bypass line, but the total bypass isn't provided, then the document is being used in a way that really isn't reflecting the way it was put together," he said. "We will need your help as to how to clarify that use."

Board member Sydney Salmon noted, "The issue is that the earmarking is done on the basis of the bypass budget and, in fact, reduces the Institute's flexibility without providing adequate funds for other programs. It is doing potentially some harm rather than good."

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President's Cancer Panel has written to NIH Director Bernadine Healy to express concern about the advisory committee to the NIH Office for the Study of Alternative Medical Practices.

"The members of the panel are writing to Dr. Healy with the concern about the confusion that [the committee] might bring with respect to proven therapies being confused with some therapies that are unproven," Panel Chairman Harold Freeman said to the National Cancer Advisory Board.

• • •

NCI and National Institute of Neurology Diseases and Stroke scientists last month injected a thymidine kinase containing vector producing cells into a brain tumor in a patient at the NIH Clinical Center. It is the first clinical trial to test whether gene therapy has a role in malignant brain tumors.

Edward Oldfield of NINDS and Michael Blaese of NCI are collaborating on the project, with former NCI scientist Kenneth Culver. Culver now is director of clinical research at Genetic Therapy Inc. of Gaithersburg, MD. The NIH Recombinant DNA Advisory Committee gave approval to test the treatment in five patients.

About 35,000 Americans develop brain tumors or have metastatic lesions in the brain from other cancer sites.

"Metastatic disease to the brain may be the dominant cause of death, or in some cases may be the thing that separates a patient from cure," NCI Director Samuel Broder said to the NCAB last month. "There are examples in lung cancer where a primary solitary brain mass is the dominant issue and were that addressed, the patient might have a substantial prolongation of survival. That is also true in other diseases" such as breast cancer.

The treatment approach being tested "will stimulate new avenues of research into the process of tumor regulation," Broder said.

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NCI's Extramural Grants Program is 55 years old. The first NCI grant was awarded in November 1937, to Lewis Fieger at Howard Univ. for the study of carcinogen synthesis in structure activity.

Fieger received $27,500 for the four-year grant.

The first progress report noted that, "The transfer of funds occurred too late in the spring for us to tap this source of financial support to a great extent during this academic year."

"I think it is a way of saying, 'Thank you for the grant, but we got a lot done before you gave us the money,'" NCI Director Samuel Broder said in recounting the grant's history to the NCAB recently.

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"Women's Health, Occupation and Cancer" is the title of a conference NCI's Div. of Cancer Etiology is planning for this November.

Topics for the meeting may include gender specific differences in cancer risks and methodologic issues associated with occupational cancer risks. Suggestions for the conference may be directed to DCE Director Richard Adamson, Bldg. 31 Rm 11A03, Bethesda, MD 20892, phone 301/496-6618.

RFPs Available

Requests for proposals described here pertain to contracts planned for award by the National Cancer Institute unless otherwise noted. Address requests for NCI RFPs, citing the RFP number, to the individual named, the Executive Plaza South room number shown, National Cancer Institute, Bethesda MD 20892. Proposals may be hand delivered to the Executive Plaza South Building, 6130 Executive Blvd., Rockville MD.

RFP NCI-CP-40501-21

Title: Support services for biostatistical and analytical studies

Deadline: Approximately March 1

The Biostatistics Branch of NCI's Div. of Cancer Etiology solicits proposals for the recompetition of a contract performed by Westat Inc. which provides support services for biostatistical and analytical projects. The primary objectives are to support data collection activities for almost 20 projects. The contractor must be capable of providing support for a number of studies conducted simultaneously in widespread geographic regions of the U.S. and other countries, including the Peoples Republic of China. A critical capability of the contractor will be the ability to respond quickly to changes in priority and to supply support to urgent new efforts.

Types of support needed will vary, but may include: 1) study initiation and liaison, 2) preparations of study materials and procedures, 3) the hiring, training and supervision of abstractors, coders, interviewers, tracers and field supervisors, 4) data collection, 5) data preparation, 6) data processing, which shall include the design and organization of a computer system to efficiently record and maintain the data in a manner which best facilitates analysis, and 7) study monitoring, quality control and reporting.

Contract Specialist: Barbara Shadrick
RCB Executive Plaza South Rm 620
301/496-8611

RFA Available

RFA DK-93-21

Title: **Urology research centers**

Letter of Intent Receipt Date: March 8

Application Receipt Date: April 9

The National Institute of Diabetes and Digestive and Kidney Diseases invites investigators to submit research applications for the George M. O'Brien Research Centers Program. The emphases for this program are (1) to attract new scientific expertise to the study of the basic mechanisms of urological diseases and disorders; (2) to encourage multidisciplinary research focused on the causes of these diseases and disorders; and (3) to extend the development of innovative clinical and epidemiologic studies of the causes, therapy and possible prevention of urological diseases and disorders. It is anticipated that extensive collaboration will be required between individuals in the clinical and basic sciences. It is the express intent of the announcement to attract new investigators not currently active in this field and to explore new basic areas that may have clinical research applications. Individual institutions with both basic and clinical research capabilities are invited to apply. Interinstitutional collaborative research arrangements are encouraged.

The National Cancer Institute plans to provide support for this program in the area of prostate cancer.

Applications may be submitted by domestic for-profit and non-profit organizations, public and private. Foreign institutions are not eligible. Support will be through the NIH specialized center (P50) award. NCI and NIDDK expect to jointly award up to two center grants in fiscal 1993. Awards are for five years. Total

amount of funds is $1.5 million per year. No applicant may request more than $750,000 (including both direct and indirect costs) in total costs in the initial budget period. A standard escalation factor may be used for subsequent budget periods. The award date for these grants will be Sept. 30, 1993.

Inquiries regarding cancer related programmatic issues and requests for the RFA may be directed to: Dr. Andrew Chiarodo, Chief, Organ Systems Coordinating Branch, Centers, Training, and Resources Program, Div. of Cancer Biology, Diagnosis and Centers, NCI, Executive Plaza North, Suite 316, Bethesda, MD 20892, phone 301/496-8528.

Program Announcements

PAR-93-33

Title: **National Cancer Institute/Minority access to research careers summer training supplement**

Application Receipt Date: Feb. 1

The Comprehensive Minority Biomedical Program (CMBP) of the Div. of Extramural Activities, NCI, invites interested grantee institutions that have Minority Access to Research Careers grants to apply for CMBP support of MARC scholars interested in obtaining laboratory research experience at NCI.

All domestic institutions with active MARC research training grants are eligible to apply. A MARC honors training grant (T34) to the academic institution requesting support for a student will be administratively supplemented. The supplement will provide a subsistence of $300 per week ($3,000 for a maximum ten-week period), and round-trip transportation to NIH.

The Principal Investigator must submit a letter, countersigned by an authorizing official of the grantee institution, requesting support of a student for short-term laboratory training at the NCI.

Direct inquiries to: Program Director, Comprehensive Minority Biomedical Program, Div. of Extramural Activities, NCI, Bldg 31, Room 10A04, Bethesda, MD 20892, phone 301/496-7344.

PA-93-31

Title: **Resistance to antivirals targeted to human immunodeficiency virus**

Application Receipt Dates: Jan 2, May 1, Sept 1

This Program Announcement is designed to stimulate research to:

1) elucidate mechanisms of HIV drug resistance, 2) determine the effects of viral drug resistance in lentivirus pathogenesis, 3) identify improved methods to screen for drug resistant HIV and animal lentivirus variants, and 4) design and evaluate novel therapies for treating or preventing drug resistance, utilizing in vitro and animal model systems as applicable.

Applications may be submitted by domestic, foreign, for-profit and non-profit organizations, public and private. This PA solicits R01 and R29 applications. The total project period will not exceed four years for domestic institutions and three years for foreign institutions.

The Developmental Therapeutics Branch, Basic Research and Development Program, Div. of AIDS, National Institute of Allergy and Infectious Diseases (NIAID) supports basic and applied research grants leading to the discovery of new therapies for the treatment of HIV infection and the opportunistic infections (OIs) associated with AIDS.

The following areas of research are particularly encouraged: --Elucidation of the basis for the apparent inability of cell-free assays to distinguish RT purified from AZT-resistant vs. AZT-sensitive isolates may shed additional light on this dilemma. This is contrasted by retention of the drug resistant phenotype in RT purified from NNRT-resistant HIV.

--Structure/function studies of drug resistant viral targets in the presence and absence of drug may also contribute to delineating the mechanisms by which genetic alterations result in loss of drug effect.

--The biological effects the genetic alterations conferring the resistant phenotype have on the properties of the virus in terms of its pathogenicity and capacity to accelerate or attenuate disease progression are not well studied. Information is also incomplete regarding the relationship between HIV variants capable of forming syncytium upon cocultivation of infected patient peripheral blood lymphocytes with MT-2 cells, viral drug resistance and clinical progression.

--The effect of drug resistance on viral transmission needs to be elucidated. If drug resistant HIV variants are transmitted, is the frequency comparable to that of their drug sensitive counterparts?

Phenotypic and genotypic detection of drug resistance: Sensitive and reproducible methods for (1) detection of drug resistant HIV mutants, including primary isolates within phenotypic mixtures and (2) quantitation of levels of drug resistance and proportion of resistant HIV variants are urgently needed to delineate the mechanism(s) and impact of resistance and to predict the efficacy of new therapies.

Methods for the expansion of primary HIV isolates to adequate titers with minimal selection for specific viral variant(s) are also critical.

Direct inquiries to: Dr. Roberta Black, Basic Research and Development Program, Div. of AIDS, National Institute of Allergy and Infectious Diseases, Solar Building, Room 2C12, Bethesda, MD 20892, phone 301/496-8197; fax 301/480-5703/402-3211.

World AIDS Foundation

The World AIDS Foundation announces its intent to support research and education relating to AIDS in the developing world. The goal of the WAF is to facilitate information exchange and assist developing countries in responding to the AIDS pandemic.

The WAF is particularly interested in projects that are catalytic and once in place could have a multiplicative effect. The WAF also is interested particularly in supporting applications that originate from developing countries and that emphasize collaboration between and among scientists from developed and developing countries. The main area of interest of the WAF is education for health professionals in developing countries, especially in-country training. This includes highly focused workshops that enhance the scientific process and transfer knowledge needed in the effort against HIV infection and AIDS.

The limit of a single funding request is $200,000. Applicants should submit concept letters for initial consideration. Following review, applicants may be invited to submit complete proposals. Deadline for receipt of concept letters is February 1.

Concept letters and inquiries may be directed to: World AIDS Foundation, Assistant Secretary for Health, c/o Director, Fogarty International Center, NIH, Bldg 31, Room B2C02, Bethesda, MD 20892, USA, fax 301/402-2056.