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Moertel Criticizes Janssen Over Levamisole Price, Delivers Final Report On Intergroup Adjuvant Trial

Having demonstrated that 5FU-levamisole significantly improves the cure rate of Dukes C colon cancer patients, the Mayo Clinic's Charles Moertel went on to criticize the maker of levamisole at a plenary session of the American Society of Clinical Oncology annual meeting in San Diego last month.

American colon cancer patients pay $1,495 for a year's supply of the drug, compared to owners of American sheep, who pay approximately

(Continued to page 2)

In Brief

Seffrin's ACS Appointment Is Official; Liotta Selected As NIH Deputy; Strategic Plan Meetings

JOHN SEFFRIN was officially appointed executive vice president by the American Cancer Society Board of Directors at its meeting June 6 in Portland, OR. Seffrin, 48, will assume the post Aug. 10. Seffrin is chairman of the Dept. of Applied Health Science at Indiana Univ. He received a PhD from Purdue Univ. and a master's degree in health education from the Univ. of Illinois. He has been a volunteer with ACS since 1972 and served as its national chairman from 1989-91. Seffrin's appointment fills the position left vacant when **William Tipping** resigned last September. The executive VP directs a national staff of nearly 400 and reports directly to the national board. . . . **LANCE LIOTTA** has been selected as NIH Deputy Director for Intramural Research, NIH Director **Bernadine Healy** said last week. The appointment still requires confirmation by HHS Secretary **Louis Sullivan**. Liotta is chief of the Laboratory of Pathology in NCI's Div. of Cancer Biology, Diagnosis & Centers. . . . **EXECUTIVE OFFICER** is being sought by the Cancer & Leukemia Group B, located at Dartmouth-Hitchcock Medical Center. The full-time position would be ideal for a senior academic oncologist needing a change of scene or a young MD with subspecialty training eager to learn about large scale clinical trials administration, according to CALGB Chairman **Ross McIntyre**. Prospective candidates should submit a letter, curriculum vitae, and three references to McIntyre at 444 Mount Support Rd., Lebanon, NH 03766. . . . **NIH STRATEGIC PLAN** is still being planned. NIH will hold a meeting June 23-25 near Washington Dulles International Airport with 200 participants from the extramural community to consider the NIH strategic framework developed earlier this year; 11 panels will be convened representing the areas of science and policy in the plan. The NIH director will hold a retreat July 15-16 with institute directors and representatives from each of the 11 panels.

Moertel Criticizes Janssen For Cost Of Levamisole, 100 Times Vet Price

(Continued from page 1)

$14 a year for levamisole used for deworming, he said.

The veterinary levamisole and the human kind are "the same doggone levamisole, precisely the same drug," though the inert fillers are slightly different, Moertel said. "The only difference is the 100-fold difference in cost. I would hope the pharmaceutical company would realize this is totally beyond reason."

Moertel's comments were picked up by a number of lay media.

"Dr. Moertel feels the price difference between the veterinary and human use is unjustified," said Robert Kniffin, spokesman for Janssen Pharmaceutica, which markets levamisole under the trade name Ergamisole. "We have been aware of that, and we simply disagree. We think the price is fair and reasonable, and it is not an expensive therapy as measured against most other compounds used to treat cancer."

The price of Ergamisole reflects in part costly research and development "over decades," Kniffen said. Over a 25 year period, there were 1,400 studies involving 40,000 patients, including 400 studies in cancer involving 20,000 patients.

Kniffen said the company does "quibble" with Moertel on the cost of the drug. The average price for a year's therapy of Ergamisole is $1,250, he said, while the cost of the drug for deworming a horse three times a year is about $10 to $12. "There is a considerable discrepancy, but it's a function of what kind of animal, what kind of dose," Kniffin said.

Janssen licenses levamisole to American Cyanamid, which sells the product to Pitman-Moore, based in Illinois, which formulates veterinary medicines.

The disagreement over the cost of the drug notwithstanding, Moertel's "final report" on the intergroup study found that 5FU plus levamisole in addition to surgery reduced the rate of recurrence by 41 percent and reduced the mortality rate by 33 percent. The proportion of patients cured of colon cancer increased from 49 percent to 65 percent, Moertel said.

'Final Report' On Intergroup Study

An estimated 7,000 cancer deaths could be prevented each year if 5FU plus levamisole is offered to the more than 20,000 Americans found to have Dukes C colon cancer, Moertel said.

Three years ago, the halls of the Moscone Center in San Francisco during the ASCO meeting were abuzz with rumors that early results of the study were showing an advantage for the patients receiving adjuvant therapy.

There were behind the scenes discussions between those who advocated informing physicians and the public about the new 5FU-levamisole combination and those who argued that until all the data were in, a "clinical alert" by NCI would be premature.

Moertel insisted that more time would be required to determine whether the patients were being cured, or whether the treatment was simply delaying recurrence.

That fall, NCI held a press conference and issued a carefully worded "clinical update" discussing the adjuvant therapy's benefit.

"The information that we made available with the update is much stronger now than it was then," Moertel told **The Cancer Letter**. "We know this is not delayed recurrence. These people are not going to recur, so we have contributed to the cure rate."

The 929 patients entered onto the study have now been followed for a median of five and a half years after surgery. "Essentially, all cancer recurrences have occurred and well over 90 percent of all deaths due to cancer," Moertel said.

The data for Dukes B_2 patients remain equivocal. "We will never be able to show a significant survival advantage," since so many patients survive to that stage that an extraordinarily large study would be required, he said.

"However, about two-thirds have characteristics that put them at very high risk, and we will be looking at those," Moertel said. "We hope we will have that data soon." Those characteristics include perforating tumor to the wall of bowel, tumor that invades other organs in the vicinity of bowel, and aneuploid nuclear pattern.

"Currently we are entering patients like that on adjuvant trials," he said.

Alfred Cohen, discussant of Moertel's presentation,

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noted that three decades of clinical trials with other drugs were unsuccessful until the levamisole/5FU trials. "It has taken 30 years to reach this small, incremental clinical benefit," Cohen said. "These data clearly suggest that the standard of care has changed."

"It was an important presentation because there is little doubt that the benefits ascribed to 5FU/levamisole are real," said Michael Friedman, director of NCI's Cancer Therapy Evaluation Program. "We now have really solid evidence that we have something that works for colon cancer patients. It is still far from satisfactory."

Various combinations of 5FU, leucovorin, interferon, and levamisole are being tested in clinical trials, some of which have been closed and are awaiting analysis.

"It seems quite possible that one or more will be as good as or superior to levamisole," Friedman said.

Until data on other combinations are available, 5FU/levamisole "should certainly be considered the standard for the community, and for many of the protocols it is the standard to which others are being compared," Friedman said.

"Everyone is expecting the newer regimens will be better," NCI Director Samuel Broder told **The Cancer Letter** in between sessions at ASCO.

"We do know the combined 5FU-leucovorin added to survivorship of patients with metastatic disease," Moertel said. "Some people are using it as standard therapy. They should not. In fact they could detract from patient survival."

Moertel said it would be "a minimum of two years, and probably longer" before the data is in on the newer regimens. "Now that we've moved up the survival curves, you have to have more data."

Trials that have completed entry included an NCCTG/intergroup study with the National Cancer Institute of Canada and M.D. Anderson Cancer Center testing 5FU/levamisole versus 5FU, levamisole and leucovorin.

Another trial by the Eastern Cooperative Oncology Group is testing the NCCTG regimen, the Roswell Park regimen, and the three drug combination; the control arm is 5FU/levamisole.

"I'm really struck by the collegiality of the individuals working in large bowel cancer," CTEP's Friedman said. "It's a model of cooperation--there are a lot of intergroup studies now. There really have been changes over the past few years."

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Other ASCO plenary papers also reported long-anticipated results of trials involving aggressive adjuvant chemotherapy.:

▶Daniel Budman, North Shore Univ. Hospital, discussed Cancer & Leukemia Group B study 8541, a dose and dose intensity trial of cyclophosphamide, doxorubicin, and 5FU as adjuvant treatment of stage 2 node positive breast cancer. The study, with 1572 patients, found that three-year disease free survival improved from 50 percent to 92 percent with the highest dose of adjuvant therapy after radical mastectomy, while 84 percent of patients on the lower dose remained disease free.

▶Richard Fisher, Loyola Medical Center, discussed preliminary results of Southwest Oncology Group study 8516 (later intergroup 0067), a phase 3 comparison of CHOP vs. mBACOD vs. ProMACE CytaBOM vs. MACOP-B in patients with intermediate or high grade non-Hodgkin's lymphoma. The study found thus far that the new "third generation" regimens were no more effective than the standard CHOP regimen in improving overall survival rate or response rate in 1138 patients. Fatal toxicities were more common with the newer regimens.

▶Robert Mayer, Dana-Farber Cancer Institute, discussed another CALGB study, a phase 3 comparative evaluation of intensive postremission therapy with different dose schedules of ara-C in adults with acute myeloid leukemia. Initial results of the study in 1085 patients found that high doses of ara-C significantly prolong remission for AML patients aged 40 to 60. Nearly half the patients in that age group had continuous complete remission for more than three years, while patients over age 60 experienced the same remission rate as seen with conventional therapy.

Congress Okays NIH Reauthorization, Allows NCI An Additional $472 Million

The long-awaited legislation reauthorizing the National Institutes of Health would authorize an additional $472 million over the President's $2.01 billion proposal for NCI in fiscal 1993.

The legislation, which cleared the Senate in an 85-12 vote June 4, would direct NCI to spent $325 million on breast cancer programs, $75 million on ovarian and other gynecological cancers, and $72 million on prostate cancer.

The President is expected to veto the measure, and the House, which approved the measure 260-148 on May 28, does not have the votes to override the veto.

Considering that 28 of the President's consecutive vetoes have been upheld, NIH is likely to continue functioning without authorizing legislation.

Moreover, congressional generosity with authorization does not always translate into actual

appropriations.

As cancer program advocates plot strategy for last minute maneuvers on the budget, their mood seems to fall someplace between glum and uncertain.

"I think we may be looking at the President's budget as the best case scenario," said one of the players. "Of course, this is also what we were told last year," said another.

NCI Could Lose $2 Mil. In Recision

In addition, a recision of the FY 1992 budget could well be a harbinger of a lean year to come. NCI stands to lose approximately $2 million to $2.5 million from its fiscal 1992 budget under a recision approved by a House and Senate conference committee in an action unrelated to NIH reauthorization.

If enacted and signed by the President, the recision would make three major cuts in the budget for the current fiscal year. It would:

▶Rescind one half of one percent of FY92 funds that were to become available on Sept. 30 for all of HHS. NCI's share of that amount is estimated at $500,000.

▶Rescind $7 million from the Public Health Service for salaries and benefits, and $7.5 million for program evaluation. NCI could expect to lose about $1.5 million to $2 million under these cuts.

The impact on NIH could amount to an $8 million to $10 million decrease in FY92 funding, if the recision is enacted. The conference committee also recommended reducing the National Science Foundation's budget by $2 million.

The committee also specified that HHS should not reallocate funds among agencies unless approved through "normal reprogramming procedures"--that is, by the appropriations committees.

Fetal Tissue, Not Cancer

Until now, the President opposed the NIH reauthorization bill for reasons that had to do with abortion, not cancer. According to George Bush and other opponents, the reauthorization's provision that lifts the ban on fetal tissue research, would give women justification for choosing abortion. The President's current plan is to set up a "bank" of fetal tissue from miscarriages and tubal pregnancies.

Now, with the reauthorization bill calling for additional funding for NCI, the White House is likely to have another reason to oppose the measure, observers say.

To a member of Congress, a vote on reauthorization has meant having to choose between the wrath of "pro-lifers" and the wrath of breast cancer activists.

Last Friday, Rep. Chris Smith (R-NJ) proposed separating NCI from NIH reauthorization. The bill, HR 2507, was sent to the House Energy and Commerce Committee last Friday. Smith had voted against NIH reauthorization.

Cancer Control or NCI Control?

The prospect of a veto notwithstanding, the reauthorization bill is indicative of what NCI's legislative mandate would be regardless of the outcome of the White House-Capitol Hill clash over budget and fetal tissue research.

Under the reauthorization bill, NCI is directed to:

▶Make a cancer control allocation equal to 75 percent of the amount recommended in the 1993 bypass budget.

According to the bill, the Institute ultimately would be required to allocate no less than 10 percent of its budget on cancer control.

Under the 1992 budget, cancer control accounts for $106 million. This is slated to be reduced by $15 million under the President's budget proposal.

▶Form an inter-institute task force to coordinate relevant research in breast, ovarian and prostate cancer throughout NIH.

▶Spend an additional $472 million on breast, ovarian and prostate cancer programs in FY93.

▶Establish six "research and demonstration" centers for basic, clinical, epidemiological, psychological, prevention and treatment research in breast, ovarian and prostate cancer.

According to NCI sources, this is likely to be implemented through an expansion of the Specialized Programs of Research Excellence, which will award three P50 grants each in breast, prostate and lung cancer research this September.

▶NCI Director is to submit detailed plans for the programs to the President's Cancer Panel and NIH director by Feb. 1, 1993.

Outlining prevention and control for prostate cancer, Congress directed NCI to step up "research on the role of prostate specific antigen for the screening and early detection of prostate cancer."

In another provision, the director of the Centers for Disease Control was instructed to establish a national program of cancer registries that would be part of an attempt to determine the factors for the breast cancer mortality rates in certain states. CDC also would be responsible for establishing a prostate cancer prevention program.

Under the reauthorization bill, NIH is directed to establish an Office of Research on Women's Health. In fact, NIH had set up such an office two years ago when criticism first arose of equal representation in clinical trials. NCI officials noted that women make up more than half of research subjects in NCI trials.

NCAB's AIDS Committee To Hold June 24 Forum For Gallo Statement

The AIDS Committee of the National Cancer Advisory Board will hold an open forum on June 24 for NCI Laboratory of Tumor Cell Biology Chief Robert Gallo to discuss "issues raised over the past several years about his laboratory's role in the discovery of HIV-1, the AIDS virus," NCI has announced.

The talk will be followed by a question and answer session in which Gallo will answer questions submitted in writing prior to the meeting, as well as questions from the Board, the President's Cancer Panel, and the Div. of Cancer Etiology Board of Scientific Counselors.

The meeting will be held Wednesday, June 24, 2-4 p.m., NIH Bldg. 31 Conference Room 6.

Questions may be submitted in writing by June 17 to Barbara Bynum, Director, NCI Div. of Extramural Activities, NIH Bldg. 31 Rm 10A03, Bethesda, MD 20892; phone 301/496-5147. Questions will be accepted at the discretion of the AIDS Committee Chairman, Howard Temin of the McArdle Laboratory.

Bynum told **The Cancer Letter** that NCAB Chairman Paul Calabresi asked Temin to organize the meeting to provide Gallo the opportunity to speak publicly about the NIH investigation of his laboratory, in an open forum.

OSI Inquiry Clears Gallo

The NIH Office of Scientific Integrity has completed its final report on the two-and-a-half year long investigation of Gallo and his laboratory. The report is under review by Assistant Secretary of Health James Mason, who is expected to sign it. Until then, NIH is not releasing the report, but copies have been obtained by the press and the information has been confirmed by NIH Director Bernadine Healy in statements to reporters.

The OSI report clears Gallo of scientific misconduct for the methods he used in conducting and reporting the key experiments that led to the development of the blood test for HIV. However, a critique of that report written by an outside advisory panel finds fault with some of OSI's conclusions.

Here is a summary of OSI's conclusions, and the conclusions of the panel of eight scientists nominated by the National Academy of Sciences to monitor the investigation, led by Yale biochemist Frederic Richards:

▶OSI: There is no evidence that Gallo "stole" the virus provided to him by Luc Montagnier of the Pasteur Institute. Gallo has maintained that he had no motive to steal the French virus because he had other viral isolates in his lab. The Richards panel agreed.

▶OSI: Gallo's behavior in the months leading up to the key papers (published in "Science" in 1984) was "less than collegial" and "self-serving," but did not constitute misconduct. The Richards panel was more critical, accusing Gallo of "intellectual appropriation" of the French virus and "essentially immoral" behavior for not making certain cell lines available to other scientists. Gallo said he did send cell lines to dozens of labs, with a requirement that the labs not publish papers without his prior approval. That requirement was in force for only three months, he said.

▶Discrepancies between published data and lab notebooks and other documents. Twelve allegations did not fit the definition of misconduct, the OSI report said. Four other allegations were determined to be misconduct, but the blame for them was placed on Gallo associate Mikulas Popovic, the first author on the "Science" paper. The Richards panel questioned why blame was assigned to Popovic and not his boss on two of the allegations.

In responses to the allegations, published in "Science," May 8, Gallo and Popovic asserted that the four discrepancies were either editorial error or misunderstanding of terms Popovic used, such as the notation "ND" for "not finished, or not done properly."

▶Recommended sanctions. OSI proposed three sanctions for Popovic: that he be prohibited from serving on any PHS advisory committee for three years, that with any grant or contract application he submits in the next three years he should submit a certification as to the reliability of the proposed research and procedures for monitoring his work, and any PHS agency considering funding him during that time be advised of the misconduct finding.

No sanctions were recommended for Gallo, since the investigation did not make any misconduct finding.

In a letter to Mason transmitting the report, NIH Director Bernadine Healy recommended leniency toward Popovic, saying that language difficulties and adequate supervision were extenuating circumstances. She also wrote that "other problems" relating to Gallo's management of his laboratory "are being addressed by me and others within NIH."

A remaining issue is whether the investigation, report, and sanctions will satisfy congressional watchdogs such as Rep. John Dingell (D-MI), who already has said he believes NIH cannot adequately investigate its own scientists. He has threatened to hold new hearings. In addition, there are two other investigations of Gallo still ongoing, by the HHS Inspector General and the General Accounting Office, examining whether Gallo made false statements regarding the patent for the HIV blood test.

NCAB Decides To Phase Out 7-Year Outstanding Investigator Grants

NCI's Outstanding Investigator Grant mechanism should be phased out as soon as possible to make more funds available for regular R01 grants, the National Cancer Advisory Board decided at its meeting last month.

Currently active OIG awards will be allowed to run their course, and the moratorium on new (type 1) awards will continue. However, NCI accepted amended type 1 applications for the June 1 deadline just past. Those applications will be reviewed at the NCAB meeting next January.

The OIG is a seven-year award for an experienced investigator to conduct long term "high risk" projects. The awards were begun in 1985 when the prevailing trend at NIH was toward longer term awards.

Under financial restraints imposed by Congress and affirmed by NIH, the average length of awards within the institutes cannot exceed 4 years. NCI found that the renewal rates of OIGs were not as high as R01 renewal rates; that led the Institute to impose a moratorium on new applications pending NCAB discussion (**The Cancer Letter**, May 1).

The Board's Planning & Budget Committee considered three options proposed by an internal NCI working group: retain the current OIG, modify the OIG but change it to require an additional 20 percent time-and-effort commitment by the awardee, or eliminate the OIG entirely.

The committee's discussion centered around what it considered the basic problems of the OIG considering the budgetary climate: its length, confusion over whether it supports investigators or projects, duplication with the MERIT award (Method to Extend Research In Time), and the relatively large proportion of the grants budget that NCI spends on OIGs (approximately 7.8 percent of the total RPG budget, or $62,000 in FY91).

If the OIG were retained and the Institute granted two new awards each year, assuming 5 percent inflationary increases, the program would cost $64,000 in FY94 and $79,000 in FY99, the working group found. Under the second option, the cost would fall, but the committee said restricting the award to investigators with records of accomplishment would not necessarily support the most innovative research.

The committee recommended phase-out of the OIG, and that option was unanimously approved by the Board. Current OIG commitments run through FY99, at which time NCI will spend only $12,500 on the final year of the awards.

NCAB To Screen 'Total Research Support'

The Planning & Budget Committee also recommended, and the NCAB approved, a plan to screen investigators whose grant applications would put their total NIH research support above $750,000.

The additional review will allow the NCAB to identify well-funded investigators and consider whether to recommend them for funding. "Is it cost effective to have single labs getting more than $750,000?" committee member Howard Temin asked. The plan would help the NCAB gather that information. "We may not need to do this in two years," he said.

A trial run of the review was conducted for the closed session of the May NCAB meeting, but no grants fell within the parameters, said Stephen Hazen, chief of the Extramural Financial Data Branch.

This is how the review will work: About three weeks prior to the NCAB meeting, NCI staff will run a computer check to identify grant applications which, if funded, would bring an investigator's support over $500,000 including all current NIH research project grant support to that individual as principal investigator. Then the program director responsible for the grant will review the application to determine whether the grant would bring the investigator's personal research support over $750,000. For example, an individual could be named a principal investigator on a program project grant, but he or she personally would only be principal investigator on one or two subprojects within a P01.

The applications that remain would be listed in the Board's special actions book under the title "Special Consideration of Total Research Support," and Board members could ask program directors to discuss the application in terms of the total research support for that individual.

Limitation on Program Project Grants?

The NCAB also considered a motion to limit the program project grant mechanism (P01) to clinical and translational research only, not to be used to support basic research studies. The motion was tabled to allow NCI staff time to gather data on the types of research supported by the P01.

"Our division uses the P01 mechanism to support research in all of its programs," Div. of Cancer Etiology Director Richard Adamson said to his Board of Scientific Counselors a week after the NCAB meeting. "The research involved ranges from extremely basic investigations of fundamental processes through translational-type science to actual clinical studies."

In DCE, the Biological program has 18 grants supporting 90 investigators, the Chemical program has

16 grants supporting 88 investigators, the Epidemiology program has 10 grants supporting 47 investigators, and the Radiation program has two grants supporting 10 investigators, Adamson said.

"The program project grant has a number of attributes which make it attractive for supporting cancer research," Adamson said. "It provides a focus for diverse talents and interests of several investigators who might otherwise not interact with one another. Another key aspect is the different types of core support provided to the participating investigators. . . The 46 [DCE] P01s contain 75 distinct core units. Another important focus of the P01 mechanism not fully appreciated is that it provides a critical mass of investigators who provide training opportunities in cancer research for individuals that do not pursue more formalized approaches to training. This mechanism also promotes the effective use and sharing of resources produced under the grant or by associated collaborating laboratories.

"Since we do not know which studies will result in the next major advance, it is important for us to continue to fund the best science, whether basic, translational, or clinical, and to be prepared to advance the relevant discoveries which that research results into the cancer patient as soon as possible," Adamson said.

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-CM-37818-28

Title: Screening for agents against the Human Immunodeficiency Virus
Deadline: Approximately July 27

NCI's Div. of Cancer Treatment, Developmental Therapeutics Program, Antiviral Evaluations Branch, is seeking an organization to provide assistance in the primary screening of experimental agents utilizing the HTLV-III/LAV (human AIDS virus). An organization is sought which will supply the necessary equipment, personnel, and facilities to conduct screening on the scale of 20,000 tests per year. The tasks will include maintaining and expanding one or more cell lines and the virus necessary to infect these cells, the preparation of experimental agents for testing, and the collection and submission of data. The project will primarily involve cell culture, although approximately 20 percent of the work will involve in vitro detailed agent testing, and less than 10 percent of the work will involve in vivo testing with murine leukemia virus.

It is anticipated that one cost-reimbursement contract, completion form, will be awarded. This contract is planned to be incrementally funded over a five year period. This is a recompetition of a contract held by Southern Research Institute.

Because of the nature of work involving live HIV, offerors must show evidence at the time of the best and final offer that P-3 level biocontainment facilities are available for use on this project. This project requires that the following restriction be applied: "NCI signs legally binding agreements with certain suppliers (often pharmaceutical or chemical companies) which state that all information on compounds submitted by the supplier will be held confidential. The successful offeror will be expected to test such commercially confidential agents. NCI believes that the compounds cannot be sent to potential competitors of the supplier, and thus pharmaceutical and chemical companies must be excluded from the competition."

Contract specialist: Carolyn Barker
RCB Executive Plaza South Rm 603
301/496-8620

Program Announcement

PA-92-81

Title: **Surgical oncology**

Application Receipt Dates: June 1, Oct. 1, Feb. 1

NCI's Div. of Cancer Treatment (NCI) is seeking applications for investigator-initiated research grants concerned with research in surgical oncology. The Principal Investigator must be a surgeon. This Program Announcement is designed to promote and develop a strong cadre of academic surgeons involved in clinical research.

Applications may be submitted by foreign and domestic, for-profit and non-profit organizations, public and private. Applications from minority individuals and women are encouraged. Applications from one or more institutions with established clinical, laboratory, and statistical resources are solicited. Foreign institutions are not eligible for the First Independent Research Support and Transition (FIRST) Award. The special eligibility criteria for the FIRST Award (R29) can be found in the Guidelines for FIRST Award, which may be obtained from the Grants Inquiries Office, Div. of Research Grants, NIH (301-496-7441).

Awards will be made as FIRST Awards (R29s), research project grants (R01s) and interactive R01s.

The treatment of cancer has evolved as multi-disciplinary effort involving, but not limited to, the disciplines of surgical oncology, medical oncology, pediatric oncology, and radiation oncology. The disciplines of medical oncology, pediatric oncology, and radiation oncology have developed strong cadres of academic investigators while academic development in surgical oncology has not kept pace. It is felt that surgical oncology is not keeping pace because of an insufficient number of surgical oncology research programs and an insufficient number of surgeons undertaking research related to cancer. Continued development of superior multi-disciplinary treatment of cancer is the long-range objective of the DCT and the attainment of the goal requires sufficient academic strength in investigative surgical oncology.

Examples of relevant studies include mechanisms of metastases, effect of surgery on tumor cell kinetics, and tumor host responses to surgery. Preclinical and clinical research is encompassed in this program. Categories include but, are not confined to: (1) pathophysiologic studies in laboratory models or in humans related to surgery and cancer; (2) laboratory and clinical studies that examine the biochemical, cytokinetic, immunological, and nutritional effects of cancer surgery; (3) therapeutic studies in which surgery or a surgical question is the primary treatment modality; (4) novel immunotherapy procedures such as assessment of specific lymphokines stimulated cells and autologous vaccines which require surgical input; (5) new surgical techniques relevant to staging or care of patients; (6) studies to identify prognostic factors relevant to the treatment of cancer patients; (7) surgical supportive care; (8) regional chemotherapy or hyperthermia or radiation in which a surgical approach to the treatment site is a major aspect of the procedure.

The aims of this initiative are (1) to promote academic research in surgical oncology and (2) to stimulate development of innovative surgical related clinical studies with laboratory correlations so as to foster the development of interactions between basic science laboratories and clinicians performing these clinical trials.

Inquiries may be directed to Dr. Roy Wu, Program Director, Cancer Therapy Evaluation Program, Div. of Cancer Treatment, NCI, Executive Plaza North Rm 734, Bethesda, MD 20892; phone 301/496-8866, fax 301/480-4663.

RFAs Available: AIDS Training

RFA TW-92-02

Title: **International training grants in epidemiology related to the Acquired Immunodeficiency Syndrome**

Letter of Intent Receipt Date: July 1

Application Receipt Date: Sept. 10

The Fogarty International Center at NIH invites applications to develop international training programs in epidemiology related to AIDS for foreign health scientists, clinicians, and allied health workers. This announcement is for the second five-year funding cycle. Both new and competing renewal applications for this program are welcome. A major goal of the program is to train scientists of other countries to deal effectively with the AIDS epidemic through epidemiologic research, clinical trials, and AIDS prevention research programs.

Major changes for the second five-year funding cycle include a shift in emphasis from short to long-term training and greater emphasis on advanced research training in-country. Applicants are encouraged to develop training programs that facilitate the conduct of future international vaccine and drug trials in an ethical and equitable manner. This program will continue to emphasize trainees from, and training activities in, the developing countries of Africa, Latin America and the Caribbean, and Asia and the Pacific region. The program will also accommodate trainees from, and training activities in, countries of Central and Eastern Europe and the former Soviet Union.

Eligible institutions must be a U.S., non-profit, private or public institution. Only one application will be allowed under this program from each U.S. institution. Grants will be made as international training grants in epidemiology (D43) for a total project period of five years.

Approximately $4,000,000 (total costs) will be allocated to this program in FY 1993, for an estimated ten awards. The total (direct and indirect) cost per grant for the first year may not exceed $600,000 for competing continuation applications and $400,000 for new programs.

The objectives are to train scientists, particularly from developing countries, to deal effectively with the AIDS epidemic through epidemiologic research, clinical trials, and AIDS prevention research. The program is intended to support collaborative research between U.S. and foreign scientists to enhance knowledge and skills in the epidemiology, diagnosis, and treatment of HIV/AIDS and to stimulate scientists from nations affected by AIDS to cooperate and share knowledge in combatting this global problem.

Emphasis will be on developing human resources in developing countries likely to be hosts of HIV/AIDS-related research and field trials of anti-HIV drugs, HIV vaccines, and other interventions. Specifically, the program is designed to:

--Increase expertise in epidemiology and laboratory components of AIDS-related epidemiologic research through short- and long-term training at U.S. institutions that may lead to MS and/or PhD degrees in epidemiology;

--Increase laboratory expertise of technical assistants in foreign countries who are engaged in epidemiological studies related to HIV/AIDS through in-country, short-term, didactical, and technical training; and

--Expand ongoing collaborative training and research in HIV/AIDS between U.S. and foreign scientists.

Inquiries may be directed to: Dr. Kenneth Bridbord, Chief, International Studies Branch, Fogarty International Center, NIH Bldg 31 Rm B2C32, Bethesda, MD 20892; phone 301/496-2516.

RFA TW-92-03

Title: **Special international postdoctoral research program in Acquired Immunodeficiency Syndrome**

Letter of Intent Receipt Date: July 1

Application Receipt Date: Sept. 10

The Fogarty International Center invites applications to develop multi-disciplinary postdoctoral fellowship programs in AIDS research for foreign and U.S. scientists. Funds will be awarded to encourage basic and population-based research in all biomedical and behavioral disciplines related to AIDS. This announcement is for the second five-year funding cycle for this program. Both new and competing applications are welcome.

Major changes for the second five-year funding cycle include a shift in emphasis from short to long-term training and greater emphasis on advanced research training in-country. Applicants are encouraged to develop training programs that facilitate the conduct of future international vaccine and drug trials in an ethical and equitable manner. This program will continue to emphasize trainees from, and training activities in, the developing countries of Africa, Latin America and the Caribbean, and Asia and the Pacific region. The program will also accommodate trainees from, and training activities in, countries of Central and Eastern Europe and the former Soviet Union.

Eligible institutions must be a U.S., non-profit, private or public institution. Only one application will be allowed under this program from each U.S. institution. Grants will be made as institutional research fellowship (T22) awards for a total project period of five years. Approximately $1,000,000 (total costs) will be allocated to this program in FY 1993, for an estimated four awards. The total (direct and indirect) cost per grant for the first year may not exceed $300,000 for continuing and $200,000 for new programs.

The objectives are (1) to support collaborative research between U.S. and foreign scientists who wish to enhance their knowledge and skills in the epidemiology, diagnosis, prevention, and treatment of HIV/AIDS and (2) to stimulate scientists from nations affected by AIDS to cooperate and to share research knowledge in combatting this global problem.

Under this award the program director will make the following types of training appointments to foreign and U.S. scientists:

--Postdoctoral research training conducted at U.S. institutions for foreign scientists varying from 3-24 months in duration. Postdoctoral scientists (MDs, PhDs) at all career levels are eligible for appointment. Training includes basic and clinical research in all biomedical and behavioral disciplines related to HIV/AIDS and is meant to enhance knowledge and skills in the epidemiology, diagnosis, prevention, and treatment of HIV/AIDS.

--Postdoctoral research training conducted at foreign institutions for U.S. scientists varying from 3-24 months duration. Scientists at all postdoctoral career levels are eligible for appointment to this type of training.

--Advanced in-country research training conducted at foreign institutions for selected, highly qualified foreign scientists under guidance of participating U.S. faculty, varying from 3-24 months duration.

Inquiries may be directed to: Dr. Kenneth Bridbord, Chief, International Studies Branch, Fogarty International Center, NIH Bldg 31 Rm B2C32, Bethesda, MD 20892; phone 301/496-2516.