THE CANCER LETTER

Vol. 19 No. 12
March 19, 1993

Price $225 Per Year US, Canada.
$250 Per Year Elsewhere

P.O. Box 15189 Washington, D.C. 20003 Telephone 202-543-7665

Healy Attacks Scripps-Sandoz Research Deal, Rep. Wyden Asks For HHS Investigation

NIH Director Bernadine Healy delivered a blistering surprise attack on a proposed technology transfer deal between Scripps Research Institute and Swiss-based Sandoz Pharmaceutical Co.

According to Healy, the proposed deal constitutes a violation of

(Continued to page 2)

In Brief

Roper To Resign From CDC; Clinton Nominates Phillip Lee For Asst. Secretary For Health

WILLIAM ROPER, director of the Centers for Disease Control and Prevention in Atlanta, announced he will resign June 30. Roper was in Washington last week for a meeting with HHS Secretary **Donna Shalala**. Roper, a pediatrician and former administrator of the Health Care Financing Administration, was appointed by President George Bush in 1990. Roper previously served on the Domestic Policy Council in the Bush White House. . . . **PRESIDENT CLINTON** made two nominations in the Dept. of Health & Human Services: **Phillip Lee**, a physician and director of the Institute of Health Policy Studies at Univ. of California at San Francisco, was nominated as assistant secretary for health. In that position, Lee will supervise the Public Health Service including NIH, CDC, and FDA. He was deputy assistant secretary for health and scientific affairs from 1965-69 in the Dept. of Health, Education & Welfare. **Kenneth Apfel**, legislative director to Sen. Bill Bradley (D-NJ), was nominated for assistant secretary for management and budget. Both nominations require Senate confirmation. . . . **VINCENT DEVITA**, former NCI director now at Memorial Sloan-Kettering, is likely to become the next director of the Yale Comprehensive Cancer Center, sources have confirmed. Current center director **Alan Sartorelli** will step down in June. . . . **CYNTHIA MILLER** has been appointed deputy executive director of the Oncology Nursing Society. Miller will continue as director of the Oncology Nursing Certification Corp. . . . . **CLARIFICATION:** The 80 potential anticancer agents identified in the past two years by NCI's revised drug screen (**The Cancer Letter,** Feb. 26) are still in preclinical testing and are not yet available for clinical research. The 48 agents identified through the AIDS-related lymphoma screen are undergoing secondary in vitro testing to determine which agents are the highest priority for testing in the SCID mouse model. Once tested in the mouse model, they will go to the Decision Network Committee, which will select the most promising agents for further development. . . . **'IN BRIEF'** continues to page 8.

Healy Attacks Scripps-Sandoz Deal, Rep. Wyden Seeks IG Investigation

(Continued from page 1)

federal technology transfer regulations, threatens academic freedom of Scripps scientists, excludes small businesses from dealing with Scripps and takes Scripps inventions off the institution's campus and, possibly, outside the US.

"I think it excludes our small businesses, it excludes our scientists," Healy said in testimony before the subcommittee on Regulation, Business Opportunities and Technology of the House Small Business Committee last week. "I also think this would be intolerable for the scientific community. I do not believe that the scientific community would work under these restrictions."

On March 15, four days after the hearing, the subcommittee issued a bipartisan appeal for the HHS Inspector General to investigate the deal. The letter, to Bryan Mitchell, of the Office of the Inspector General, was signed by Reps. Ron Wyden (D-OR), chairman of the subcommittee, and Larry Combest (R-TX), ranking minority member.

The outcome of the investigation is likely to affect similar agreements between federally funded research laboratories and for-profit pharmaceutical companies.

"It was as though she said to herself, I have three months left, and I will do what I believe in,'" said a committee staff member after watching Healy testify. Meanwhile, in the hallway, attorneys representing Scripps and Sandoz confronted Reid Adler, director of the NIH Office of Technology Transfer.

"I am shocked!" one of the attorneys shouted to Adler. Speaking to a reporter later in the day, attorney Allan Fox, of Fox, Bennett & Turner, said the attack on the deal "smacks of McCartyism."

"Fortunately, [Dr. Healy's] description of the arrangement is simply inaccurate," Ernest Beutler, chairman of the Dept. of Molecular Medicine at Scripps, testified at the hearing.

"Were it not, I would not choose to conduct my research and professional career at Scripps," said Beutler. Under questioning, Beutler said he did not have a working knowledge of the contract between Scripps and Sandoz.

Under the Bayh-Dole Act of 1980 (P.L. 96-517), the law that authorizes technology transfers between federally funded laboratories and the private sector, the laboratories are not obligated to receive regulatory approval before entering into technology transfer deals.

Federal agencies, including NIH, can step in after a deal is made if an invention is not being developed effectively, to meet health or safety needs, or if a product intended for the US market is not being substantially manufactured in the U.S.

According to Healy, no federal agency has ever exercised these enforcement rights.

The Deal And Its Critics

The Scripps-Sandoz deal, yet to be finalized, would bring $300 million to Scripps over 10 years beginning in 1997. During the same period, Scripps is expected to receive about $1 billion in federal funds. The deal would give Sandoz commercial rights to research it would fund at Scripps.

According to attorneys for Scripps and Sandoz, the proposed deal is similar to the existing agreement between Scripps and Johnson & Johnson, which ends in 1997.

So far, no money has changed hands, and the option would expire July 1, unless Sandoz chooses to exercise it.

Last year, Scripps received $70 million, nearly 60 percent of its $120 million budget, from NIH.

The Scripps-Sandoz deal was announced last December, and a month later, it came to Wyden's attention. Wyden had just received an avalanche of national publicity resulting from his hearing on the pricing of the cancer drug taxol.

According to Capitol Hill sources, he first learned about the Scripps-Sandoz deal from letters and phone calls citing news stories in "The San Diego Union."

Seizing on the issue, Wyden fired off a letter to Healy.

"In essence, Scripps becomes a Sandoz laboratory," Wyden wrote in a letter dated Feb. 2. "And what is most troubling about this deal is the apparent fact that the government has raised no objection to the arrangement... It would seem that the federal

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

Subscription rate $225 per year North America, $250 elsewhere. ISSN 0096-3917. Published 48 times a year by The Cancer Letter Inc., also publisher of The Clinical Cancer Letter.

government does not even review these agreements."

The Scripps-Sandoz deal was a godsend to both Wyden and Healy. For Wyden, it presented an opportunity to stay on top of the issue of drug pricing. For Healy, it was a chance to return to the problem she confronted from the start of her tenure at NIH: the drafting of conflict of interest regulations for recipients of NIH grants.

More importantly, several observers said, at the time Healy received Wyden's letter, she was yet to be asked to resign. To strengthen her position, she needed an issue.

Days after receiving a letter from Wyden, NIH cited its audit authority to request the contracts for about 103 technology transfer deals nationwide.

"Although NIH has not required the submission of such information on a routine basis, it does have a right of access to that information, for the purpose of auditing and copying, under the [HHS regulations]," Healy wrote in a Feb. 9 letter to Scripps Director Richard Lerner. A copy of the letter was obtained by **The Cancer Letter.**

Sources said Healy and Wyden discussed the Scripps-Sandoz deal on several occasions, with Healy making it clear that she would be eager to appear at a hearing on the issue.

Meanwhile, Scripps, Sandoz and Johnson & Johnson were not as eager to cooperate with either Healy or Wyden.

Following their lawyers' advice, Scripps and Sandoz resisted the NIH request for a copy of the contract, arguing that NIH did not have the authority to demand it.

Finally, Scripps heeded the advice of the newly elected Rep. Lynn Schenk (D-CA) of San Diego. Sources said Schenk suggested that Scripps would fare better at a hearing held by Wyden's subcommittee than at a hearing chaired by Rep. John Dingell (D-MI), chairman of the Energy and Commerce Committee, which has oversight powers over NIH. Both Schenk and Wyden sit on Energy and Commerce.

At the same time, Scripps attorneys attempted to convince Wyden to delay the hearing until NIH collected and analyzed all the existing deals. That way the hearing would focus on the broad issues rather than make an example of the Scripps-Sandoz alliance, the attorneys argued.

"TSRI [Scripps] stands ready to cooperate with the subcommittee in its consideration of these issues," Fox wrote in a March 5 letter to Wyden."TSRI also intends to release the materials requested by NIH.

"In light of the present circumstances, however, TSRI respectfully would request that the subcommittee postpone the hearing until all relevant facts have been assembled and analyzed by NIH... TSRI believes that, once NIH evaluates all such agreements, the subcommittee could undertake a more comprehensive analysis of the public policy issues relating to them as a group."

A copy of the letter was obtained by **The Cancer Letter.**

Sources said the hearing would have probably been delayed if not for Healy's determination to appear as a witness. Sandoz and Johnson & Johnson submitted written statements for the record, and Scripps sent Beutler, a scientist, to testify.

NIH general counsel Robert Lanman received a copy of the 100-plus-page contract in the evening of March 8. The packet also contained the agreement between Scripps and Johnson & Johnson.

Less than two days later, on the morning of March 11, Healy told Wyden's subcommittee that she was not impressed by what she had read.

Healy's Criticism

Healy said the deal gives Sandoz two seats on the Scripps board of trustees as well as control over the scientific council and constitutes an "extraordinary intrusion into the daily scientific activities of a public institution."

Other problems outlined by Healy included:

▶ **The potential for conflict of interest.**

"There is a provision for individual scientists who get personal financial return for their participation under this agreement," Healy said.

"One has to raise the question as to whether or not there might not be a potential for conflict of interest, particularly when some of the scientists who are working on a clinical research project are in fact getting consulting arrangements from Sandoz.

"We have been concerned at the NIH and the scientific community that in the area of clinical trials it is important that scientists not stand to gain personally from the products of their research, particularly if it involves human subjects.

"It's a problem if research results are directly correlating to personal gain for the scientist who is generating those research results that could create a perception of a conflict of interest."

▶ **The potential for Sandoz benefiting from research supported by NIH.**

"There are some provisions within that contract which appear to give Sandoz the rights to NIH supported research in human pharmacology and clinical trials," Healy said.

"The Sandoz relationship is so extremely tightly

coupled to the institution is that a joint committee is established which oversees research, which includes the development of protocols..."

▶The deal is inconsistent with the Bayh-Dole Act.

"There are a number of concerns that we raise with regard to Bayh-Dole, particularly the policy objectives of Bayh-Dole," Healy said.

"The policy objectives, clearly, are competitiveness, free enterprise, giving preference to small businesses, and involve giving preference to American industry, and generation of American jobs.

"I think that if one looks at the contract in the context of these policy objectives, you see that broad options are being granted on all research performed by NIH money. Without Sandoz directly funding necessarily these projects.

"The limiting of small business preference by having an exclusive relationship with Sandoz on virtually all research that will be done for the next 10 to 20 years, small businesses are basically forbidden even access to Scripps. There are clauses where public companies including small businesses cannot even have access to the campus, they cannot collaborate with Scripps scientists. There is a monopolistic tone not only toward the inventions and future inventions, the future ideas, but also to all the scientists at Scripps.

"Scripps has also these form agreements with existing companies, most of them small businesses, and under this agreement, when these agreements expire, Sandoz has a say as to whether or not these agreements could be renewed and has the right of review.

▶ The potential that manufacturing may be done outside the U.S.

"I am also concerned that the clause on US manufacturing under the contract might violate the intent of Bayh-Dole," Healy said. "Specifically, it says that Sandoz understands that it must substantially manufacture in the US, but it adds the clause, 'as long as it is commercially feasible.'

"That clause does not belong in Bayh-Dole. In fact, the commercial feasibility clause as it appears in Bayh-Dole, relates to the NIH grantee looking at a field of people who are licensed to develop technology and the grantee looks for someone in the US who can license and manufacture that technology.

"Only if they find out that there is no company in the US to develop it, then they look outside.

"In this agreement, they have taken this commercial feasibility clause and moved it upfront and said that if Sandoz decides that it is not commercially feasible to manufacture in the US, that that is an exception, and in addition Scripps agrees to help Sandoz in this contract to use all its legal efforts to get a waiver from the agencies so it does not have to manufacture in the US."

▶ A threat to academic freedom.

"In essence [the agreement] says that Sandoz can assume the research of a Scripps scientist and take it out of Scripps and move it to their facilities anywhere in the world, theoretically, including to Switzerland, and that the Scripps scientist cannot seek funding to continue that research," Healy said.

"That seems to be not only against Bayh-Dole, but also a disregard for academic freedom in the rights of scientists to pursue their own ideas."

Letter to Inspector General

In a letter requesting the Inspector General's investigation, Wyden and Combest asked for an audit of the 130 patents issued to Scripps during the past 10 years, to determine the level of federal support involved in each application.

Citing a 1992 report by the General Accounting Office, Wyden and Combest wrote that "private research institutions receiving federal support generally [are] less likely to credit federal grants, and more likely to credit corporate support in their applications.

"It is unclear what--if any--ownership NIH and the taxpayer will have over technologies and discoveries from [Scripps]," the letter said. "Under the terms of the agreement, how will ownership be established?"

Other questions included:

▶ "What should be the disposition of licenses on [Scripps] technologies transferred to the company and then not commercialized?

"Our concern is that companies with exclusive rights may choose to 'sit' on valuable technologies because of competitive considerations not necessarily in the broader public interest.

▶ "Dr. Healy testified that this contract could restrict access to Scripps scientists by non-Scripps scientists, putting a wall to what is usually a collegial environment between researchers in non-Scripps institutions. Is that the case?

▶ "Could this agreement allow Sandoz to halt funding of a Scripps researcher in order to move his project to its Swiss headquarters?

▶ "Should Sandoz be allowed to hold [two] seats on the Scripps board of directors?

▶ "Should Sandoz be allowed to review and control outside consulting agreements for certain Scripps employees?

▶ "Should Scripps be required to help Sandoz apply

for a waiver to the Bayh-Dole Act for the transfer of technologies outside the U.S. for the purpose of manufacturing?

▶ "How much authority should Sandoz have to direct the research of this heavily publicly sponsored scientific institution?"

Conte Institute Plans Conference On Central, East Europe Clean-Up

A Massachusetts-based not-for-profit research institute is leading an international effort to document the human health effects of environmental contamination in Central and Eastern Europe.

"It is, unfortunately, a very large experiment," said Arthur Bloom, president of the Silvio Conte Institute for Environmental Health, Pittsfield, MA. "There is an opportunity for important basic science work to be done in these populations to answer questions that can't be answered anywhere else. You don't have these massive population exposures in this country that you have over there."

The Conte Institute is planning a meeting on "Human Health and the Environment in Eastern and Central Europe," April 12-15 in Prague, the Czech Republic. The meeting, sponsored by the March of Dimes Birth Defects Foundation and the National Institute of Environmental Health Sciences, will bring together scientists from Central and Eastern Europe with their U.S. and Western European colleagues to begin to set a scientific agenda to address the problem.

The most urgent scientific need in these countries is to document the effects of environmental contamination, particularly in cancer, birth defects and occupational health, and to coordinate research, Bloom said to **The Cancer Letter.**

The environmental contamination is placing economic pressure on these countries. For example, the Hungarian government estimates that air pollution costs $60 million a year in related health costs and work days lost. In Czechoslovakia the drinking water is considered toxic and is not recommended for infants. In areas of Central and Eastern Europe that have had the greatest concentration of heavy industry, statistics show the average life span is shorter by five to ten years than in comparable developed countries, according to the Conte Institute.

The goal of the meeting in Prague will be to begin the process of documenting the damage to public health and the environment, and discuss the planning and implementation of environmental clean-up. The 50 invited scientists also will identify opportunities for collaborative research and sharing of data across national boundaries.

The impact of pollution on disease, the genetic risks and their correlation with birth defects in future generations, the nature of industrial risks to workers, and the effects of radionuclide exposures from nuclear facilities in the region are some of the pressing scientific questions, Bloom said.

Bloom said he hopes the meeting will result in the establishment of a permanent scientific organization which will organize and implement environmental health research and "remediation" in Central and Eastern Europe.

"The idea is to come up with a set of priorities for research in the region, and to use that to raise money for implementation of research," Bloom said.

Information on the meeting may be obtained from the Conte Institute, 2 South St., Pittsfield, MA 01201, phone 413/499-6100.

Founded Following Love Canal

Bloom, an M.D. and an expert in genetics, founded the Institute five years ago to bring together scientists of all disciplines to discuss environmental health, focusing on genetics and neuroscience. His specialty is the genetic susceptibility to cancer, and he has published articles on the identification of individuals genetically at risk of cancer in the presence of environmental toxins.

As an officer in the Public Health Service, Bloom was a cytogeneticist in Hiroshima, Japan, from 1965-68 studying the genetic effects of the atomic bombings. Later, he was appointed to the staff of the Presidential Commission on the Accident at Three Mile Island in 1979, and was a consultant for the National Institute of Environmental Health Sciences at Love Canal in 1980. He was on the Board of Scientific Counselors of NIEHS from 1982-86.

Bloom said that after his experience with Three Mile Island and Love Canal, he felt there was a need for an independent institute that could serve as a "think tank" with high scientific standards, for the evaluation of data on the human health effects of environmental agents and dissemination of that information to other scientists, the public, and government.

He left his position as professor of genetics and pediatrics at Columbia Univ. to found the Environmental Health Institute (renamed the Conte Institute) in 1987. He is also professor of pediatrics at Univ. of Massachusetts Medical School and on the medical staff at the Berkshire Medical Center in Pittsfield and director of its genetics program.

Most of the work of the Conte Institute is funded

by grants from NIEHS, which has provided $500,000 a year for the past five years. Other grant and contract support comes from the March of Dimes and Research Triangle Institute.

The institute now has a staff of eight besides Bloom and has programs in genetics, pharmacology/toxicology, neurosciences, population studies, and public and professional education. The institute supports more than 100 fellows in carcinogenesis and mutagenesis, genetics and reproduction, teratogenesis, epidemiology, biostatistics, dosimetry and neurobiology and neurotoxicity.

RFA Available

RFA AI-93-08

Title: **Collaborative mucosal immunology groups for AIDS vaccines**

Letter of Intent Receipt Date: April 15

Application Receipt Date: May 21

The Vaccine Research and Development Branch (VRDB) of the Div. of AIDS, National Institute of Allergy and Infectious Diseases, announces availability of an RFA for funding of new Collaborative Mucosal Immunology Groups (CMIGs) for AIDS vaccines. The purpose of this RFA is to invite research grant applications for collaborative projects from investigators pursuing research on mucosal immunity to Human Immunodeficiency Virus and/or Simian Immunodeficiency Virus (SIV) to participate in a network of CMIGs for AIDS vaccines.

NIAID wishes to encourage and expand research in the area of mucosal immunology to AIDS viruses, that will focus on: 1) design and development of novel recombinant vectors and/or AIDS vaccine formulations designed to induce regional mucosal immunity particularly in the female or male reproductive tracts and in the rectum (gut); 2) characterization of the components (T cells and antibodies) and their mechanism of action in the immune responses at mucosal surfaces, that are specific for HIV/SIV antigens; and 3) development of immunization strategies to prevent mucosal HIV infection and transmission.

The special feature of the collaborative project program is the concurrent submission of research grant applications by investigators who wish to collaborate on a common theme related to mucosal immunity to AIDS viruses, but do not require extensive shared physical resources or core functions to conduct their research. In order to be responsive to this RFA, a minimum of two research projects are required for a Collaborative Project Group. The common theme for any group should reflect a multidisciplinary approach in the areas of immunology and virology.

Investigators now participating in the National Cooperative Vaccine Development Group (NCVDG) that have pursued this area of research and new applicant groups are invited to apply. Applications from the private sector (e.g., vaccine, pharmaceutical, or biotechnological companies) are encouraged. Collaborative arrangements involving more than one institution are especially encouraged.

Support will be through individual research grants (R01) that are organized around a common theme into a collaborative project group. NIAID anticipates making three to five new awards to Collaborative Groups (6 to 15 R01 awards). NIAID has set aside $1.4 million (total costs) for the initial year of funding for this RFA.

The purpose of the CMIGs is to develop a network of focused, interdisciplinary, basic and preclinical research projects that will generate and evaluate novel strategies for eliciting protective immunity at mucosal sites of viral exposure. Applications are invited that seek to discover/design and develop vaccine strategies, animal models, methodologies, and assay reagents to study protective mucosal immunity to HIV (and SIV) in primates and/or humans. The following two general research areas are encouraged under this RFA:

--Development and use of animal models to explore novel strategies for vaccination and mucosal challenge with AIDS viruses.

--Development of assays, reagents and technology to evaluate specific, protective mucosal immune responses induced by AIDS vaccines in animals and human volunteers.

Examples of research areas of mucosal immunity for AIDS vaccines of high priority and that would be responsive to the RFA may include, but are not limited to, those listed below. These research topics are intended to provide a perspective on the scope of research. It is not required that all or any of them be included in a particular group of applications.

--Development and analysis of novel AIDS vaccine strategies, vectors, delivery systems, or adjuvant formulations that would stimulate protective mucosal immunity, particularly in the genital tract in primate models.

--Development of methods to evaluate mucosal immunity to lentiviruses in humans and primates.

--Identification and evaluation of functional antibody responses that might be effective in preventing HIV or SIV mucosal transmission. Analysis of the mechanism of action of antiviral IgA antibodies.

--Identification and characterization of mucosal cell-mediated immune responses (regional cytotoxic T lymphocytes (CTL) and helper T cells).

Direct inquiries and letter of intent to: Dr. Bonnie Mathieson, Div. of AIDS, NIAID, Solar Bldg Rm 2B04, 6003 Executive Blvd, Bethesda, MD 20892; Tel. 301/496-8200, fax 301/402-1506 or 301/480-5703.

Program Announcement

PA-93-063

Title: **Primary care and health care reform**

The Agency for Health Care Policy and Research supports and conducts research, demonstration projects, and evaluations of health care services and systems delivering such services. This program announcement emphasizes a need for short term research (producing results within one to three years) to assess ways in which primary care services can contribute to health care reform.

A major AHCPR responsibility is support for research that focusses on problems of immediate concern to policy makers at the Federal and State levels. Consistent with this charge, AHCPR encourages research addressing questions raised in formulating policy changes to deal with significant problems in the health care sector, and specifically through this PA, in the primary care field.

To generate the required analytical effort on primary care in health care reform, the AHCPR encourages investigators to

use strategies that avoid primary data collection efforts, and focus instead on designs and methods that produce results quickly, such as the use of existing data, microsimulations, and rigorous syntheses.

Applications may be submitted by domestic and foreign non-profit organizations, public and private. This PA will use the research project grant (R01). It is anticipated that projects will be accomplished in one to three years.

Applicants are encouraged to apply by the earliest possible submission date. The first due date is June 1, 1993. Thereafter, the due dates for application are October 1, 1993, February 1, 1994, and June 1, 1994.

In response to continued growth in the cost of health care and the increasing numbers of persons without access to basic health care services, public attention is now focussed on major health care reform efforts.

States and a number of regional coalitions have already initiated reform programs. These programs provide natural laboratories for assessing the effects of specific organizational, financial, and regulatory mechanisms on utilization, costs, and access to primary care services.

Reform initiatives related to primary care that are in place or under development include: expanded Medicaid benefits for women and children, approaches that encourage or require Medicaid beneficiaries to enroll in managed care programs, the use of school based clinics to provide services to children and adolescents, and the establishment of primary care clinics in underserved areas.

Analysis and evaluation of the relationship between the delivery of primary care services, and the overall effects of such programs on costs, quality, and access, are critical for informing further decisions regarding national health care reform.

Primary care includes: first contact care, care that is longitudinal, care that is person centered rather than disease or problem specific, and care that is comprehensive. It addresses the most common problems in the population by providing preventive, curative, or rehabilitative services to maximize health and well being.

The U.S. does not have a clearly defined system of primary care delivery. Primary care services are provided by physicians in multiple specialties as well as nonphysician providers, predominately nurse practitioners, certified nurse midwives, and physician assistants, in a variety of settings.

While the majority of persons identify one provider as their usual source of care, a substantial number obtain primary care services from multiple providers. Some individuals obtain specialized services when referred by a primary care provider, while others seek specialists' care directly.

Studies have shown that access to primary care services is associated with improved health outcomes. Primary care providers also use fewer resources in the care of patients with chronic diseases than specialists, after adjusting for severity of illness.

However, existing studies are limited, and additional studies that isolate the effects of distinct organizational and provider characteristics on overall costs and patient outcomes are essential to inform health care reform. A broad array of research questions are relevant to primary care and health care reform.

Three research areas emerge as AHCPR priorities because of their relevance to the development of effective health care reform programs: (1) the effectiveness of primary care and overall costs; (2) the cost and quality implications of different modes of access to primary care; and (3) the organization of primary care providers.

In a health care system with a clearly defined primary care infrastructure, the decisions of primary care practitioners have important implications for the total expenditures for health care. Recent studies demonstrate that a lack of access to outpatient care can result in potentially avoidable hospital admissions. These studies suggest that improving the effectiveness of patient care may lead to substantial cost savings while improving the health status of the American people.

Of particular interest are studies of referral to specialty services. Further research is needed to develop and test mechanisms by which consultation and referral can be accomplished without disrupting continuity or coordination of care.

Research questions include:

--Can the provision of primary care services decrease the incidence of avoidable hospitalizations? Which primary care services, providers, and organizational models are most effective in reducing avoidable hospitalizations? How is provider training related to the
effectiveness of primary care services delivered to specific groups of patients, such as children, the elderly, and those residing in underserved areas?

--What proportion of variations in costs and use of expensive technologies is attributable to variations in referral by primary care providers? Are observed variations attributable to provider training, availability of specialists, patient characteristics, or other factors? Can improved referral practices result in more appropriate use of expensive technologies?

--How do nonphysician providers in a variety of settings refer patients to specialists, and what arrangement of physician backup is most effective?

Four general patterns of primary care include: episodic care from a hospital emergency room or urgent care center; longitudinal care from a "usual care" provider who may be a primary care provider or specialist; specialist provided primary care through direct (self) referral; and primary care from multiple providers. Most research confounds patient and practitioner characteristics, features of the organization, and reimbursement mechanisms.

Studies that examine the quality and cost implications of receiving ongoing primary care from a specialist compared to a primary care provider are important. Of particular relevance to women's health care are the cost and quality implications of using one or two primary care providers.

Studies are also needed that examine the cost and quality implications of restriction of self referral to specialty care. Isolating the confounding effects of cost sharing, provider training, and patient characteristics is essential.

Research that uses existing data to develop or refine case mix measures for application to ambulatory problems is also needed.

Research questions include:

--What are the effects on cost and quality of care of receiving primary care from a primary care provider compared with multiple providers or specialists?

--What are the effects on cost and quality of limiting direct

access to specialists for continuity care? Are there differential effects on patient outcomes for patients with special needs, such as persons with disabilities and persons with chronic diseases?

--Will recent changes in Medicare reimbursement that increase payment for some primary care services enhance the delivery of primary care services to all persons?

Managed care organizations, particularly health maintenance organizations (HMOs), have a clearly defined system for delivering primary care services.

Research on staff model HMOs, in which the ratio of primary care providers to specialists is higher than for the health care system as a whole, suggests that this type of organization provides more cost effective care than traditional fee for service practice. Studies that isolate the specific components of these arrangements that are most effective (e.g., type of primary care providers, staffing ratios, mechanisms for utilization review) could provide important guidance to policy makers.

Recent State initiatives to enroll Medicaid recipients in managed care programs may offer the potential for studies using existing data to evaluate the effects of these programs on health outcomes, health costs, and utilization of services. In particular, information that links the effects of State regulations on the scope of practice of advanced practice nurses and physician assistants to the effective delivery of primary care services is urgently needed.

Research is also needed on organizational characteristics that enhance the outcomes of primary care. Additional research that examines the relationship of continuity, accessibility, and comprehensiveness of primary care on cost, quality, and access in health care is critical for planning and organizing more effective and efficient services.

Inquiries may be directed to Dr. Carolyn Clancy, Center for General Health Services Extramural Research, Agency for Health Care Policy and Research, Executive Office Center, Suite 502, 2101 East Jefferson Street, Rockville, MD 20852-4908; Tel. 301/227-8357.

NCI Contract Awards

Title: Laboratory support for processing and storage of biological specimens from persons at high risk from cancer
Contractor: Biotech Research Laboratories Inc., Rockville, MD; $898,011.

Title: Support services for occupational studies
Contractor: Survey Research Associates Inc., Baltimore, MD; $6,688,382.

Title: Biochemical genetic monitoring of rodents
Contractor: Texas A&M Research Foundation, College Station, TX; $333,215.

Title: International epidemiology survey of human retroviruses
Contractor: Research Triangle Institute, $3,895,255.

Title: Provide animal facilities and performance of routine experiments and tests
Contractor: Advanced BioScience Laboratories Inc., Kensington, MD; $4,226,579.

In Brief

PHS Recommends Routine HIV Tests In Hospitals; ONS Research Award

(Continued from page 1)

. . . **PUBLIC HEALTH SERVICE** "strongly recommends" that hospitals in areas with signficant numbers of AIDS cases offer routine counseling and HIV testing to all patients, whether treated in emergency rooms or admitted to the hospital. In the recommendations, published by the Centers for Disease Control and Prevention, hospitals should anonymously test to see if 1% or more of their patients are infected. If so, they should offer routine counseling and testing to all patients. PHS has a new phone consultation service for doctors treating HIV infections and AIDS: 800/933-3413, operating from 10:30 a.m.-8 p.m. EST, M-F. . . . **NIH REAUTHORIZATION** bill, having cleared the House last week, has gone to a House-Senate conference. The bill authorizes NCI funding at the bypass budget level of $3.2 billion. However, the measure has acquired a new earmark, inserted by Rep. Henry Waxman (D-CA), to study the incidence of breast cancer in two counties on Long Island and two other counties in the Northeast. No spending level is authorized. . . . **ONCOLOGY NURSING** Society, with the support of Cetus Oncology, has established the ONS/Cetus Oncology Research Fellowship Award to support short term training for ONS members who lack access to either a graduate level curriculum in oncology nursing or to a senior oncology nurse researcher. The award is a maximum of $10,000 for expenses and up to $1,700 to attend the ONS Congress. Deadline is June 1. For application information, contact ONS Research Dept., 501 Holiday Dr., Pittsburgh, PA, 15220, phone 412/921-7373. . . **GRANTS & GIFTS:** Theodora B. Betz Foundation in Philadelphia has made two grant awards to Fox Chase Cancer Center: A $300,000 grant to **Margie Clapper** in chemoprevention. Clapper is testing the ability of substances including cruciferous vegetables, dried broccoli tablets, and the synthetic Oltipraz to increase an individual's level of protective enzymes. A grant of $370,000 will support the research of **Gary Kruh** in identification of genes responsible for anticancer drug resistance. The W.W. Smith Charitable Trust has awarded three grants to Fox Chase for basic research: **Susan Astrin** will receive more than $166,000 for two years for study of AIDS related B-cell lymphoma. **Jonathan Chernoff** will get $230,000 over three years for research in the cancer-causing gene v-src. **James Sherley** received $71,000 for p53 gene research.