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Congressional Panel Is Investigating FDA Oversight Of Generic Cancer Drugs

A Congressional panel is conducting an investigation of FDA's oversight of the production of several generic cancer drugs, **The Cancer Letter** has learned.

The Oversight and Investigations Subcommittee of the House Committee on Commerce is preparing an investigation that is expected to include two cancer-related issues:

• The adequacy of FDA procedures for ensuring the quality of cancer drugs manufactured outside the US. Specifically, the subcommittee is

(Continued to page 2)

In Brief

FDA Seeks Applicants For Oncology Div. Head; Croce Wins Pasarow Award; CRI Honors Five

FDA CENTER FOR Drug Evaluation and Research is recruiting for a director for the Div. of Oncology Drug Products. The director is responsible for managing a multi-disciplinary scientific and administrative staff of 50 engaged in the pre-market evaluation and post-market surveillance of drugs developed for the treatment or prevention of cancer. Salary range: physician may be eligible for compensation up to $148,000 based on experience, qualifications and medical specialty. Application must be made by Aug. 30. Submit curriculum vitae to: FDA, 5600 Fishers Ln. Rm 6B-17, HFD-505, Rockville, MD 20857, Attn: Russell Campbell (SRC 296). . . . **CARLO CROCE**, director, Jefferson Cancer Center, received the 1995 Robert J. and Claire Pasarow Foundation Medical Research Award for his work in leukemias and lymphomas. . . . **CANCER RESEARCH INSTITUTE**, New York City, awarded its Oliver R. Grace Award for Distinguished Service in Advancing Cancer Research to **John Smith Jr.**, president and CEO of General Motors Corp., and **Gordon Binder**, chairman and CEO of Amgen Inc. **Malcolm Moore**, of Memorial Sloan-Kettering, and **Timothy Springer**, of Harvard Medical School, received the William B. Coley Award for Distinguished Research in Basic Immunology. **Ferdy Lejeune**, director of the Centre Pluridisciplinaire D'Oncologie, Lausanne, Switzerland, received the Coley Award for Clinical Immunology. . . . **PAUL KENNELLY** was named chief operating officer, Management Services Organization, City of Hope Oncology Network. He was CEO of Associated Physicians of Parkview, Riverside, CA. . . . **JANET ROWLEY,** Univ. of Chicago, was awarded the 1995 Kantor Family Prize for Cancer Research Excellence by the Hipple Cancer Research Center.

Panel To Investigate FDA Rules For Ensuring Generics' Quality

(Continued from page 1)

interested in problems revealed during an FDA inspection of a China-based manufacturing plant that produces the bulk materials for several generic cancer drugs, including doxorubicin and mitomycin C.

- The adequacy of FDA procedures for ensuring that generic drugs meet the bioequivalence standards with branded name drugs. Documents indicate that the subcommittee intends to focus on the cancer drug megestrol acetate, the generic version of the branded drug Megace.

The investigation is part of the subcommittee's hearings on FDA's drug approval process and enforcement policies.

The scope of the subcommittee's interest in generic cancer drugs was outlined in letters from Rep. Joe Barton (R-TX) to FDA Commissioner David Kessler, copies of which were obtained by **The Cancer Letter**.

Foreign Inspections

The correspondence indicates that the subcommittee is asking questions about a Chinese drug manufacturing facility called HaiMen Pharmaceutical Factory.

"FDA inspections of foreign pharmaceutical plants may be significantly less thorough than those conducted at US plants, with the result that the FDA cannot fully assure that all foreign plants produce finished or bulk products to the same standards as is demanded of the US industry," Barton wrote in a letter dated May 4.

"All the best research and well designed clinical trials will not assure the effectiveness of the ultimate product if the manufacturing process does not meet reasonable current good manufacturing standards," Barton wrote. "The subcommittee intends to conduct a full and careful review of this matter."

Following up on June 30, Barton asked specifically for reports of FDA inspections of the HaiMen Pharmaceutical Factory located in the Zhejiang Province of China.

The factory produces bulk agent for the generic versions of mitomycin C, doxorubicin, and its precursor daunorubicin. Also, the Chinese firm has recently begun to produce etoposide, said Peter Werth, of Chemwerth Inc. of Woodbridge, CT, HaiMen's US representative.

Werth confirmed that in the past HaiMen received warnings from FDA, but said the company's performance has improved.

"We have no idea of what these guys are up to and what they are looking at," Werth, said of the subcommittee inquiries. "FDA has recently completed another detailed inspection of our facility, and we understand the facility did very well."

According to Werth, HaiMen produces bulk drugs, which are later processed in accordance with Good Manufacturing Practices standards and sold in the US. Werth declined to reveal the name of the company that distributes the drugs in the US.

The Cancer Letter has obtained a copy of a report of an August 1993 inspection of the HaiMen facility by the FDA.

At that time, FDA found the following problems:

- Growth promotion tests were not equivalent to the ones in US Pharmacopoeia and were not checked regularly.
- Pyrogen test rabbits were given urban drinking water that was unsafe to drink.
- Purified water was tested for chloride, magnesium, pH and E. Coli. The USP requires the purified water be tested for ammonia, calcium , heavy metals, oxidable substances and total solids.
- Stability and retain samples were kept at temperatures that dipped below freezing, though US standards require that such samples be kept at room temperature.
- pH buffer solutions were not properly identified by date or expiration date, and no standardized buffer solutions were available to calibrate the pH meter.

In the report, FDA official Jorge Guadalupe noted that document searches are a problem in China. "It

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Editors: **Kirsten Boyd Goldberg**
Paul Goldberg
Founder & Contributing Editor: **Jerry D. Boyd**
P.O. Box 15189, Washington, D.C. 20003
Tel. (202) 543-7665 Fax: (202) 543-6879
E-Mail: 73322.2044@compuserve.com
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takes too long sometimes to get the documents requested, and since they are in Chinese, it also takes too long for the proper translation," Guadalupe wrote.

"Investigators are working against the clock, where a missed plane could mean a one-week delay before the next scheduled flight, and travel by bus or train between investigation sites could take days," he wrote.

According to the document, during his inspection Guadalupe was followed by 15 people, with all questions being answered through one official.

"If you look at any report from anywhere, you'll see that everybody gets 483's," Werth said in an interview, referring to FDA warnings. "These are correctable minor points."

Werth said the HaiMen factory, which he characterized as China's largest manufacturer of bulk oncology drugs, has been inspected by FDA every two years. "We have been inspected as much as any bulk drug manufacturer in the US," Werth said.

"Generally, the standards we shoot for are to be as good as, or better than, the innovator," Werth said. "We think [HaiMen does] a very good job at it. It's a learning process for them. Each year they get better and better."

How Equivalent Is Equivalent?

According to estimates accepted by the industry and FDA, up to 70 percent of bulk pharmaceutical chemicals used by US plants are imported.

Industry analysts predict an increasing role of foreign suppliers as US manufacturers continue to contract with foreign firms or move their plants outside the US.

The trend affects both the branded and generic drug manufacturers.

FDA internal documents obtained by **The Cancer Letter** indicate that the agency is aware of the challenge posed by an increasing importance of off-shore manufacturing and that assuring quality production methods will require tremendous adaptability from the agency.

"Recently, we have seen too many examples of contaminated and adulterated drugs (even counterfeit drugs) being imported into the US," a panel of FDA officials reported in a 1993 memorandum titled "Recommendations to Strengthen Surveillance and Enforcement Operations Associated With the Importation of Human Drugs."

The memorandum was prepared by group of five FDA officials headed by Richard Davis, who has since retired from his post as head of the agency's Philadelphia regional office.

"As we have learned through FDA history, the lack of agency surveillance and enforcement leads to illegal activities, in addition to adulterated drugs and drugs of low quality," the memorandum continued.

"Although the agency has taken steps in early fiscal 1993 to increase the number of foreign inspections and the number of employees assigned to this very important work, more is needed to bring the foreign inspection and import program to the level of regulatory rigor that is given to domestically produced products," the 19-page memo stated.

According to the memorandum, FDA lacked a list of foreign manufacturing plants that would be a required first step to starting regular scheduled inspections. Typically, all manufacturing plants in the US are inspected every two years.

FDA maintains a list of plants that have been inspected in the past. "But there are no means to locate the plants that have never been inspected," the memorandum, stated. "The absence of a data base makes it virtually impossible to manage and coordinate consistent and uniform surveillance and enforcement activities."

To make things worse, as of last year FDA officials had no easy way to look up the inspection history of foreign plants. "For example, in a local follow-up to contaminated sterile antibiotics made in Germany, we found that other foreign sterile antibiotics plants of this company had not been inspected in at least five years," the memorandum stated.

FDA officials were able to obtain this information by interviewing the company's US representative. The information the agent provided could be verified only by cross-checking several databases and conducting interviews with individuals familiar with the business.

"Nevertheless, it is highly unlikely that a sterile antibiotic plant would remain uninspected in the US for such a long period of time," the memo said.

The Cancer Letter Schedules Two-Week Publication Break

The Cancer Letter will take its annual summer publication break for the next two weeks.

The next issue of **The Cancer Letter**, Vol. 21, No. 34, will be dated Sept. 8, 1995.

According to the document, the FDA officials are poorly prepared for conduct of inspections and so heavily scheduled that that they are unable to conduct meaningful investigations.

"A well planned inspection trip will require the application of new philosophies and procedures," the memo stated. "The current procedure of collecting inspection requests from several sources, and then calling the investigator to [FDA] headquarters for a day or two prior to the trip is insufficient preparation for the inspection and results in insufficient use of agency resources and may reduce overall effectiveness."

Once on site, the inspectors are virtually unable to follow their hunches.

"Our policy of scheduling an inspection of two days duration with specific schedules to meet in various foreign countries makes it almost impossible for our investigators to deviate from the planned schedule.

"Most investigators will not request a rescheduling of the inspection trip, and will do the best that they can under the circumstances," the memo said.

Equivalence of Generic Drugs

The Oversight and Investigations Subcommittee appears to be particularly interested in the issue of bioequivalence of generic megestrol acetate tablets and the branded drug manufactured by Bristol-Myers Squibb.

"The subcommittee seeks information about FDA's handling of a serious matter involving the bioequivalence of generic megestrol acetate tablets manufactured by Par Pharmaceutical as compared to the pioneer drug, Megace," Barton wrote in a June 30 letter to Kessler.

Documents obtained by **The Cancer Letter** indicate that for over five years, Bristol has been urging FDA to take action against two manufacturers of the generic version of the drug, who, according to Bristol-sponsored studies have been making products of greater bioavailability than the branded drug.

One of the manufacturers, Pharmaceutical Basics Inc. of Chicago (**Cancer Economics**, March 1990) stopped producing megestrol acetate after encountering FDA sanctions.

It is unclear whether Bristol's letters to FDA played a role in bringing about those sanction, sources said.

Another manufacturer, Par Pharmaceutical Inc. of Spring Valley, NY, continues to make the drug which, according to Bristol-sponsored studies, is superbioavailable and not bioequivalent to Megace.

"The subcommittee is aware of letters to the FDA's Office of the Commissioner, Office of the General Counsel and Office of Generic Drugs concerning data documenting that Par's drug was substantially different from the pioneer drug in that it was superpotent or `superbioavailable,'" Barton wrote.

"Leading oncologists have indicated that unknowingly switching to the superpotent product could result in a patient receiving more drug than necessary and a higher incidence of side effects," Barton wrote. "Conversely, subsequent substitution of Megace might result in a patient relapse due to underdosing."

The PBI Drug

Bristol first attempted to get FDA to apply sanctions PBI five years ago. At that time, Bristol hired two laboratories, Hazleton Laboratories and Harris Laboratories, to compare the generic and the branded drugs.

Following a comparison that included a test in healthy male volunteers and a separate laboratory analysis, Bristol concluded that the bioavailability of the generic was approximately 162 percent above that of the branded drug.

"We urge FDA to institute appropriate regulatory action as soon as possible in the interest of protecting the cancer patient," Bruce Ross, then president of the Bristol-Myers US Pharmaceutical Group, wrote in a Dec. 14, 1989, letter to FDA.

FDA's response promised that the agency would consider the data provided by Ross and requested evidence that the drug poses a health hazard.

Bristol was unable to demonstrate a public health hazard. "No clinical trials exist which specifically document this effect, nor are such trials likely to exist," Ross wrote in a response to FDA.

"We have consulted with Dr. Robert Young, president of Fox Chase Cancer Center in Philadelphia, concerning the possible consequences of the superpotent PBI product," Ross continued in his letter dated Jan. 26, 1990.

"According to Dr. Young, unknowingly switching to a superpotent product could result in a patient receiving more drug than necessary and potentially resulting in a higher incidence of the side effects noted

in the labeling," Ross wrote. "Subsequent substitution of Megace might result in a patient relapsing due to `underdosing.'"

The Par Drug

Par, currently the only manufacturer of generic megestrol acetate, has had prior dealings with the Oversight & Investigations Subcommittee.

In 1989, the subcommittee held hearings that focused on the company's manufacturing and business practices. At those hearings, FDA officials said Par had engaged in unapproved deviations in the manufacture and formulations of generic drugs.

Subsequently, the company's founder pled guilty to giving illegal gratuities to an FDA supervisory chemist, and, in another action, the company pled guilty to 10 federal charges including distribution of adulterated generic drugs. The company also agreed to pay a $2.5 million fine.

Par survived the controversy dubbed "The Generics Scandal" in the subcommittee lore.

"From our perspective this is ancient history," Stuart Rose, Par's execitive vice president, operations, said to **The Cancer Letter**. Rose said the company has not been contacted by either FDA or the subcommittee in the most recent investigation. "It's our opinion that the inquiry is related to the subcommittee examining the FDA decision-making process, and Par's product is not the focal point of the investigation."

Bristol did not give up on its monitoring of the bioequivalence of megestrol acetate and the branded drug.

Documents obtained by **The Cancer Letter** indicate that in 1992 and in 1993, Bristol provided FDA with its comparisons of the two drugs.

According to information Bristol provided to FDA, the pharmaceutical company sponsored a study that tested the two products in a two-way crossover study in 24 healthy male volunteers. The study was conducted by Harris Laboratories.

"The Par product was found to be superbioavailable and not bioequivalent," Bristol's Washington attorney Alan Bennett wrote to FDA in a letter dated Aug. 11, 1992.

"On average, the maximum observed plasma concentration (CMAX) for the Par product was approximately 25 percent more than the CMAX of Megace," Bennett wrote. "[Relative] bioavailability of the Par product [was] approximately 127 percent that of Megace. All the pharmacokinetic parameters fell outside the equivalence interval (80-120 percent) determined by the one-sided procedure.

"Based on these data, Harris Laboratories concluded that the 40mg megestrol acetate tablets manufactured by Par are not bioequivalent to the innovator product, 40 mg Megace tablets," wrote Bennett, an attorney with the Washington firm of Fox, Bennett & Turner.

It took FDA nearly a year to review the materials Bennett submitted. On June 15, 1993, the agency wrote back to request the raw data and other materials on which the Harris study was based. The agency also requested that a different statistical model be used in the analysis of the results.

On Dec. 10, Bristol provided the materials and the reanalysis requested by FDA, and at this writing the company is still awaiting response, sources said.

In a pointed reference to FDA's silence on megestrol acetate, subcommittee chairman Barton wrote:

"Nearly three years have elapsed since the FDA was made aware of possibly serious problems with this generic cancer drug," Barton wrote in his June 30 letter to Kessler. "The subcommittee is interested in why there has been a lack of FDA action without any explanation."

Par official Rose said the conclusion of the Bristol-sponsored study was incorrect. "We are fully confident about the bioequivalence of our product," he said in an interview. "We disagree with Bristol's conclusions, and we believe FDA also disagrees with Bristol's conclusions, which is why they haven't done anything."

Bruce Ross, the former Bristol official who made the company's initial report to FDA, said the agency has ignored repeated warnings on megestrol acetate.

"Any Congressional committee with an interest either in the well-being of cancer patients or in the responsibilities of the FDA should thoroughly look into this," Ross said to **The Cancer Letter**.

"The FDA has never addressed the fact that the product was superpotent, and, according to several prominent oncologists, posed a significant health hazard.

"FDA is refusing to take action. I think it's unconscionable. They've failed to act twice," said Ross, now the CEO of the National Cancer Center Network, a coalition of academic cancer centers.

The current investigation by the subcommittee

picks up on a similar inquiry initiated last August by the subcommittee's former chairman, Rep. John Dingell (D-MI).

LeMaistre To Retire Next Year As President Of M.D. Anderson

Charles A. LeMaistre will retire next year as president of the University of Texas M.D. Anderson Cancer Center.

LeMaistre will step down on Aug. 31, 1996, at age 72, following an 18-year tenure as president of the Houston-based comprehensive cancer center.

LeMaistre's plans were announced by Bernard Rapoport, chairman of the UT System Board of Regents, during a regents' meeting Aug. 10 in San Antonio.

"M.D. Anderson and the UT System have been greatly blessed by Dr. LeMaistre's extraordinary leadership," Rapoport said. "His dedication and wisdom have helped make M.D. Anderson one of the world's premier centers for cancer treatment, research, education and prevention.We cannot adequately express our gratitude for the contributions that Dr. LeMaistre has made to a healthier and more eniightened state, nation and worid."

An advisory committee is expected to be appointed to recommend candidates for LeMaistre's successor to the Board of Regents.

"It is with great reluctance that we accept [LeMaistre's] resignation," Tom Loeffler, chairman of the regents' Health Affairs Committee, said. "He is an incisive administrator, but a man of compassion and kindness, as well. That blend seems so important for anyone asked to run an institution whose calling is the fight against cancer.... Dr. LeMaistre will be a tough act to follow."

LeMaistre spent much of his career in academic medicine, serving on the faculties of Cornell Univ., Emory Univ. and UT Southwestern in Dallas, where he was an associate dean. He was chairman of preventive medicine at Emory.

He moved to Dallas in 1959 to begin a 36-year career with the UT System. After six years at Southwestern, he joined the UT System staff in Austin to lead the development of UT's health-related programs in the mid-1960s. Expansion during that era included new medical schools in San Antonio and Houston and a host of other new allied health and research programs.

The Board of Regents appointed him chancellor of the UT System in 1971, and he is the only physician in the university's history to hold that post. He was chancellor for seven years until he returned to medicine in 1978, becoming only the second full-time president of M.D. Anderson.

By most measures—number of patients, research grants, and students—M.D. Anderson is nearly twice the size it was when LeMaistre arrived in 1978.

"Cancer is a tough foe, but the people here are the finest, and the chance to make a lasting contribution is unmatched," LeMaistre said. "I know M. D. Anderson deserves its reputation for pioneering advances against cancer. I have been blessed with many opportunities in my career—but none has equaled the privilege of serving the patients who place their trust in M. D. Anderson."

In the early years of Dr. LeMaistre's presidency, his priorities included building a strong research program, creating new support services for patients coping with cancer, recruiting new faculty, and raising funds for program endowments and badly needed new buildings.

He also was a strong supporter of the faculty as they moved patient care increasingly from the hospital bed to the outpatient setting, pioneered new forms of treatment and unraveled the mysteries of how cancer develops and spreads. Perhaps more than any other individual at M. D. Anderson, he argued that many cancers should be preventable and became the motivating force behind the development of Anderson's first cancer prevention programs.

More recently, he has focused on M.D. Anderson's continued success in the rapidly changing environment of US health care. This has included cutting costs and redesigning patient care programs to be more competitive in managed care. To ensure that patients continue to have access to M.D. Anderson, he has led efforts to build a network of quality centers linked to Houston. This now includes both M.D. Anderson Cancer Center-Orlando and M.D. Anderson-Moncrief Cancer Center at Fort Worth.

LeMaistre has led the institution's efforts to become financially self-sufficient, as state support dropped from more than 40 percent of the operating budget to 15 percent and was replaced by funds earned by the faculty through patient care services, research grants and philanthropic support.

LeMaistre is completing a $151 million capital

campaign, the largest in the institution's history. The campaign will help to finance the addition of three patient care and research facilities to the Houston campus

LeMaistre served as national president of the American Cancer Society in 1986. He has received the President's Award of the American Lung Association and the Distinguished Service Award of the American Medical Association. He holds five honorary degrees and the distinguished alumni award of both his alma maters, the Univ. of Alabama and Cornell.

LeMaistre's early career interests in pulmonary diseases led to his appointment in 1963 by President John Kennedy as the youngest member of the first US Surgeon General's advisory committee on smoking and health.

During the coming academic year, LeMaistre will concentrate on enhancing revenues, cutting costs and other strategic changes "to assure the long-range stability and success of M.D. Anderson," he said.

Beyond that, he said, his future plans are uncertain. LeMaistre and his wife Joyce have four children and six grandchildren.

LeMaistre has had only two predecessors at M.D. Anderson since the institution was created by the Texas Legislature in 1941. Ernst Bertner, a Houston gynecologist, served part-time as acting director from 1942-1946, and R. Lee Clark served as director and then president from 1946-1978.

Clinton Gives FDA Authority To Regulate Tobacco Sales; Goal To Prevent Teen Smoking

President Clinton last week announced a package of regulatory restrictions intended to make cigarettes less available to young people and restrict the glamorous images the industry uses to penetrate the youth market.

"Teenagers just don't `happen' to smoke," he said in a weekly radio address. "They're victims of billions of dollars of marketing and promotional campaigns designed by top psychologists and advertising experts."

Clinton said the aim of such campaigns is to addict teenagers to nicotine and create lifetime smokers. "So let's end the hypocrisy of pretending that while sales to teens are illegal, marketing to teens is legal," he said. "Let's stop pretending that a cartoon camel in a funny costume is trying to sell to adults, not children."

Clinton's plan would give FDA limited authority over tobacco products, ban cigarette vending machines, and forbid makers from sponsoring sports events and advertising their brands on sportswear. It also calls for cigarette ads in magazines with a large teen readership to be deglamorized.

US Tobacco filed suit against the FDA, claiming that its commissioner lacks jurisdiction to regulate smokeless tobacco products.

The company, a unit of UST Inc., filed suit Aug. 11 in the US District Court for the Middle District of Tennessee.

Among UST's products are the Copenhagen and Skoal smokeless tobacco brands. The company makes almost 90 percent of the moist snuff sold in the US.

Other plaintiffs involved in the suit are Conwood Co. LP and the Eastern Dark Fired Tobacco Growers Association.

In a statement, US Tobacco said it believes "the White House, by ignoring the long history of Congressional oversight of tobacco products and now seeking to give the FDA that authority, has clearly overstepped its bounds."

The company said it believes President Clinton has begun to move toward an outright prohibition of tobacco products. It said it "strongly believes that those who enjoy its products should be adults" and said it had devoted resources to try to prevent the sale of its products to minors.

LaMar McGinnis, president of the American Cancer Society, praised Clinton's action. "The President has made one of the most significant public health decisions in history," McGinnis said in a statement. "Despite enormous political and corporate pressures against him, President Clinton has moved to protect children from tobacco more than any President, or any Congress, ever has. Literally thousands of lives will be saved because of his decision."

FDA assumption of regulatory control over tobacco "is the best approach for the health of the nation, since tobacco is an addictive substance that is also lethal, taking more than 400,000 lives a year," McGinnis said. "The focus of our efforts should be to work with the FDA to see that these new standards and regulations are fairly enforced, so that smoking will no longer be common among the children of our country."

RFP Available

RFP NCI-CM-67244-30

Title: **Plant Collection And Taxonomy**

The NCI Div. of Cancer Treatment, Development Therapeutics Program, anticipates the award of three cost-reimbursement contracts, for a base period of three years, with two one-year option years, beginning on or about Sept. 1, 1996. The objective of this project is to establish contracts for the collection and taxonomy of plants from the following regions designated as follows: Task A: tropical Africa, with emphasis on Madagascar; Task B: Southeast Asia, with emphasis on Papua New Guinea; and Task C: the continental United States of America. The collections will be evaluated as sources of potential antineoplastic and anti-AIDS agents, with the ultimate goal being the discovery of novel structural types that can be developed for the selective treatment of cancer and AIDS in man.

Successful offerors will be expected to provide qualified personnel, materials, and equipment for the collection, identification, storage, and shipping of plant samples (500 per year each from Africa and Southeast Asia and 1000 from the United States) to an NCI-designated extraction facility. Collections will comprise approximately 0.3-1.0kg (dry weight) of each sample and each plant will be identified as far as possible at the time of collection. Properly prepared voucher specimens for each plant will be collected for the purposes of unambiguous identification, and for permanent deposition of, at a minimum, two herbaria designated by NCI. The contractor will be expected to provide detailed documentation, including complete identification of each plant collected. The collection team should include a qualified plant taxonomist and personnel experienced in plant collection and identification, and having familiarity with the customs of the local populations. The Principal Investigator should be trained in botany or a related field and should have at least five years of experience in plant collection and identification. It is anticipated that re-collections of up to 10 plants per year in quantities of 10-50 kg will be required starting in the second year of the contract. The number of initial small scale collections will be reduced in proportion to the number and size of the large scale re-collections undertaken. Collections will include species from as wide a variety of families genera as possible. A list of genera with number of species collected in each genus since 1986 will be provided. In the case of trees and large shrubs, samples of plant parts may be collected and stored separately for individual evaluation, with each part being considered equivalent to plant sample. In addition, a list of countries in which collections have been performed and the number of samples collected in each country will be provided. The contractor will be responsible for obtaining all necessary permits including shipping and expert permits from foreign governments and agencies, for delivery of samples and voucher specimens to facilities in the US. The government anticipates the award of one contract for each of the regions designated in Task A, B, and C. This is a recompetition of a group of contractors performing similar collections.

Contract Officer: Elsa Carlton, RCB, Executive Plaza South Rm 603, 6120 Executive Blvd. MSC 7220, Bethesda, MD 20892-7220.

RFA Available

RFA AI-95-014

Title: **National Cooperative Drug Discovery Groups For The Treatment Of Opportunistic Infections In AIDS**

Letter of Intent Receipt Date: Nov. 1

Application Receipt Date: Dec. 21

The Opportunistic Infection Research Branch of the Treatment Research Program in the Div. of AIDS, National Institute of Allergy and Infectious Diseases, invites cooperative agreement applications on the discovery and rational design of new therapies with potential to treat and/or prevent infection caused by opportunistic infections (OIs) in individuals infected with HIV. The opportunistic pathogens emphasized in this RFA are Mycobacterium tuberculosis, Cryptosporidium parvum, and the Microsporidia (e.g., Enterocytozoon bieneusi, Septata intestinalis). Responsive applications will be directed toward discovery of selective drugs or molecular strategies that are lethal for these pathogens with minimal toxicity for the host. Investigators pursuing similar drug discovery for other AIDS-associated opportunistic infections are strongly encouraged to contact program staff listed below to discuss opportunities for support through other research support mechanisms.

Applications that include collaborations, research projects, or core components from the private sector (e.g., pharmaceutical, chemical, or biotechnological companies) are strongly encouraged. It is anticipated that multidisciplinary approaches by scientists from a combination of academic, non-profit research, and commercial organizations, with the assistance of NIAID, will be necessary to effectively accelerate discovery of new therapeutics. The focus of this RFA is on targeted drug discovery research; random or large scale screening as well as clinical trials will not be supported under this RFA.

It is anticipated that approximately $2.4 million will be available in FY 1996 to fund three to six new and/or recompeting applications.

Inquiries: Barbara Laughon, Div. of AIDS, NIAID, Solar Bldg, Rm 2C26, 6003 Executive Blvd., Bethesda, MD 20892-7620, tel: 301/402-2304, fax: 301/402-3171, Email: Barbara_Laughon@nih.gov